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EDITOR'S NOTE

Perspectives on Wilderness

I am humbled to have been named the editor-in-chief of the *Wilderness & Environmental Medicine* journal. It is almost incomprehensible for me to imagine working in the same capacity as emeritus editors Paul Auerbach, Oswald Oelz, William Robinson, Robert Norris, Scott McIntosh, and our most recent editor-in-chief, Neal Pollock. Their expertise and insights have guided this journal from its inception, and I can only hope to come close to their level of excellence.

Since joining the journal, I have contemplated how we comprehend wilderness and environmental medicine in our increasingly urban society. The concept of wilderness has undergone numerous iterations. In biblical times, wilderness was a morally abandoned and feral region, where humanity could lose its soul. As William Cronon noted, wilderness was where "Christ struggled with the devil and endured his temptations … When Adam and Eve were driven from that garden, the world they entered was a wilderness only their labor and pain could redeem."[1] Wilderness was a savage and desolate region to be avoided.

But in the last two centuries wilderness developed another meaning—the wilderness was a place where one could meet God and his creation. This sublime and romantic view of wilderness, promulgated during the 19th century, acted as a counterpoint to industrialization, and in the United States led to the creation of the national park system. Concurrently, another construct of wilderness was born. Primitivism, seen as an antidote to 18th and 19th century industrialism, helped foster the myth of the frontier. In this theory, immigrants and settlers could shed civilization's trappings and display the rugged individualism that defined the American spirit, and led to a westward expansion and manifest destiny. The offspring of this myth, which essentially looked backwards at simpler times, combined with the sublime romanticist view of wilderness, led to the environmental movement of the 20th century.

Cronon, in his seminal essay, "The Trouble with Wilderness; or Getting Back to the Wrong Nature," offers yet a different perspective. Wilderness is our own creation.

> It is not a pristine sanctuary where the last remnant of an untouched, endangered, but still transcendent nature can for at least a little while longer be encountered without the contaminating taint of civilization. Instead, it's a product of that civilization, and could hardly be contaminated by the very stuff of which it is made. Wilderness hides its unnaturalness behind a mask that is all the more beguiling because it seems so natural. As we gaze into the mirror it holds up for us, we too easily imagine that what we behold is Nature when in fact we see the reflection of our own unexamined longings and desires.[1]

WMS founders Drs Paul Auerbach, Ed Geehr, and Ken Kizer presciently anticipated Cronon's paradigm-shifting essay. Auerbach, Geehr, and Kizer recognized that since antiquity, humans have explored unforgiving habitats and pushed their limits, perhaps to better understand their environment and certainly to better understand themselves. Wilderness medicine, spawned by anecdote and dogma, was codified in an evidence-based fashion. The founders recognized that in the modern era, optimal, sophisticated medicine could not consistently be delivered in austere, rural, or wilderness settings.[2] In conceiving the Wilderness Medical Society, they created a forum to discuss the impact of austere environments on human physiology as well as to examine the demands of delivering health care, one of humanity's greatest creations, in geographically challenging regions. By creating the WMS, they uncovered the sweet spot where wilderness and civilization met in the form of medicine.

Almost 40 years later, we continue to investigate the ramifications of human endeavor, but we are now also confronted with the challenges of delivering care in regions impacted by a changing climate. Wilderness and environmental medicine's relevance is seen daily. The shrinking of the barriers between the human/animal world has led to an increase in spillover diseases. The recent flooding in Pakistan, the result of record monsoons and melting glaciers has led to one-third of the nation being submerged, and offers new challenges to the delivery of health care in a transiently (for the time being) altered environment. Meanwhile, continued drought in numerous regions across the globe anticipates new migration patterns. The WMS's founders have provided a blueprint demonstrating that medical care must adapt and improvise and they have offered an opening for WEM to expand its horizons.

As we move forward with the next few years of WEM, we welcome contributions from every continent

examining both wilderness *and* environmental medicine. Numerous fellowships in wilderness medicine, disaster medicine, and climate change and health are springing up, and are creating the next generation of researchers who will carry on the work inaugurated by the WMS founders. I know I speak for all of the WEM journal's editors when I offer the publication as a medium for continued work in our growing field.

William D. Binder, MD
Editor-in-Chief

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CLINICAL TOXINOLOGY SPECIAL SECTION

COMMENTARY

Navigating the Partly Charted Seas of Clinical Toxinology

Frequently credited as the founder of toxicology, Paracelsus (1493-1541) famously observed,

"Alle Ding' sind Gift, und nichts ohn' Gift; allein die Dosis macht, daß ein Ding kein Giftist" ("All things are poison and nothing is without poison, only the dose permits something not to be poisonous"). With keen insight, this early Renaissance medical practitioner/astrologer thereby identified the commonly thin line that can define tolerance, toxicity, or medical benefit of a given substance. The central concept of "dose makes the poison" assumes direct relevance in clinical toxinology which is concerned with the human and veterinary medical effects of injected or inoculated animal venoms or ingested/absorbed poisons/toxins from animals, plants, fungi, and microorganisms. The quantity of venom injected into a person by a spider or snake, as well as the amount of toxic compound present in the seeds, stems, fruit, or leaves of an ingested plant or bioconcentrated toxic mollusc have central importance in the clinical evolution and medical management of the presenting envenomed or poisoned patient. These characteristics of venomous and poisonous lifeforms have compelled scientific debate and pertinent investigation; do venomous snakes meter the quantity of venom delivered in a given strike? Do blue-ringed octopuses (*Hapalochlaena* spp, Octopodidae) and the rough-skinned newt (*Taricha granulosa*, Salamandridae) synthesize tetrodotoxin, the powerful antagonist of several subtypes of Na_v channels, or is it produced from endosymbiosis by an assortment of facultative bacterial taxa? To some observers, the first impression of such questions may suggest that the answers would primarily constitute "knowledge for knowledge's sake." However, these phenomena are more often applicable for our sake than commonly acknowledged.

Unfortunately, diagnosis and management of patients affected by these "natural toxins," constituting the practice of "clinical toxinology," is sometimes viewed as "different." This is commonly because of the need to comprehend the biology of the etiological agents, the living complex organisms, that contribute to the presenting patient's disease. However, the general basis for this needed understanding does not substantially differ from medical parasitology or most infectious diseases, although it may be more complex when considering the organisms, their venoms or poisons, and their myriad effects on human beings from diverse backgrounds and cultures.

While certainly substantial, the global significance of envenoming and poisoning remains imprecise. Annually, toxin-induced disease undoubtedly affects millions of people, and the most important form of envenoming, snakebite envenoming, predominantly impacts rural and semi-rural populations in economically-challenged nations. Thus, it constitutes a serious public health hazard among these communities that often lack the resources necessary to provide evidence-based management sufficient to achieve favorable outcomes in many seriously envenomed patients. Therefore, the global impact of snakebite envenoming also tragically highlights one of a number of prominent inequities posed by the burden of mortality and morbidity borne by economically disadvantaged populations.

In common with other scientific disciplines, the advent of "omics," single cell technologies, and other innovations have advanced toxinology research. However, in comparison with many other avenues of biomedical investigation, support is minimal and scarce. This is also clinically relevant; eg, RNA polymerase II transcription inhibition is a well-acknowledged mechanism of α-amanitin toxicity in poisoning by some of the medically important "death angel" mushrooms (*Amanita* spp, Amanitaceae). However, other pathophysiological mechanisms may contribute to the fulminant hepatotoxicity that follows serious poisoning by these species, and investigation of these is highly desirable.

Not surprisingly, clinical diagnosis and some interventions for the envenomed or poisoned patient can lack a high-powered evidence-base and/or may be controversial. For example, vinegar, as well as hot- or cold-water immersion, have all been recommended as effective first aid for stings from cnidarians such as cubozoans and hydrozoans (the former seeking to inactivate non-discharged nematocysts adherent to the

victim's skin, the latter primarily as analgesia); however, these have been mainly tested with limited, low-powered observational trials. Likewise, the efficacy of some antivenoms such as those used for severe envenoming by widow spiders (*Latrodectus* spp, Theridiidae) and some medically important scorpions, has been questioned by some investigators, while others firmly support their effectiveness. Several of these sometimes hotly debated issues in clinical toxinology can serve as a reminder that in reality evidence-based medicine is often an *unequal* ratio of composite observed beneficial interventions and outcomes, considered recommendations from formal trials (when available), and patient expectations.

In this issue, several groups of investigators provide contributions that address some important concerns in clinical toxinology. For example: Rongzhi Liu and colleagues report on the outcome of using hybrid blood purification for life-threatening mass wasp stings in Sichuan Province, China; R.M.M.K. Namal Rathnayaka and colleagues describe using therapeutic plasma exchange, a notably controversial intervention, for management of severe complications (eg, acute kidney injury and thrombotic microangiopathy) following hump-nosed viper (*Hypnale* spp Viperidae, Crotalinae) envenoming in Sri Lanka (there is no antivenom available for treating bites by these pit vipers); and a random controlled trial conducted by Kasım Turgut and associates compares the clinical efficacy of several analgesics for pediatric patients with painful scorpion envenoming in southeastern Turkey.

Hopefully, further documentation of investigations and considered approaches to clinical management will provide improved outcomes for patients affected by venomous and poisonous animals, plants, and fungi, whether in an austere or urban locale. These contributions are reminders that seeking the best benefit and outcome for the envenomed or poisoned patient does not differ at all from the approach to any other distressed human being presenting for medical care: "The good physician treats the disease; the great physician treats the patient who has the disease" (William Osler, 1849-1919).

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CLINICAL TOXINOLOGY SPECIAL SECTION

ORIGINAL RESEARCH

Diagnostic Tests for Hypofibrinogenemia Resulting from Green Pit Viper (*Trimeresurus albolabris*) Envenomation: A Simulated In Vitro Study

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Introduction—The green pit viper (GPV) *Trimeresurus albolabris* is found in Southeast Asia. Its venom has a thrombin-like activity that can cause hypofibrinogenemia. Fibrinogen measurement is not always available. We aimed to establish a more available diagnostic tool indicating hypofibrinogenemia caused by GPV envenomation.

Methods—This was an in vitro study, in which healthy subjects aged 20 to 45 y were enrolled. There were 2 experiments. In Experiment 1, blood samples from 1 subject had varying amounts of *T albolabris* venom added to determine its effect on the fibrinogen level (FL). In Experiment 2, 3 sets of blood samples were obtained from another 25 subjects. The 2 venom doses established in Experiment 1 were used on 2 sets of the samples to simulate severe (FL <1.0 $g{\cdot}L^{-1}$) and mild hypofibrinogenemia (FL 1.0–1.7 $g{\cdot}L^{-1}$). The third set of samples was venom-free. All samples were used for platelet counts, prothrombin time (PT)/international normalized ratio (INR)/activated partial thromboplastin time (aPTT), and 2 bedside clotting tests. Diagnostic parameters were calculated against the target FL of <1.0 $g{\cdot}L^{-1}$ and <1.7 $g{\cdot}L^{-1}$.

Results—Twenty-five subjects were enrolled in Experiment 2. On referencing normal cutoff values (platelet count >150,000 cells/mm^3, venous clotting time <15 min, normal 20-min whole blood clotting time, INR <1.2, aPTT <30), we found abnormalities of 5, 0, 0, 3, and 22%, respectively. The highest correlation with hypofibrinogenemia was provided by PT/INR. For an FL of <1.0 $g{\cdot}L^{-1}$, PT and INR revealed the highest areas under the receiver operating characteristic curve, 0.76 (95% CI, 0.55–0.97) and 0.76 (95% CI, 0.57–0.97), respectively. The highest accuracy and the highest sensitivity were provided by PT/INR.

Conclusions—PT/INR could be used as a diagnostic test for severe hypofibrinogenemia in GPV envenomation because of its high accuracy and area under the receiver operating characteristic curve.

Keywords: Trimeresurus macrops, *Trimeresurus* spp, snakebite, venous clotting time, prothrombin time, whole blood clotting time

Introduction

A green pit viper (GPV) (*Trimeresurus* spp) bite is the most common snakebite in Thailand.[1] The 2 most common GPV species, especially in the Bangkok area, are *Trimeresurus albolabris* (the white-lipped pit viper) and *Trimeresurus macrops* (the big-eyed pit viper).[2] The venom components of the 2 species are similar; however, the venom from *T albolabris* is more potent.[3] A study on the proteomes of *T albolabris* venom revealed that the venom mainly contains metalloproteinases (37%), phospholipases A2 (19%), disintegrin (14%), serine protease (13%), and C-type lectin (9%).[4] In clinical practice, the main systemic effects from a bite of these species are due to hypofibrinogenemia and

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thrombocytopenia.[5] Hypofibrinogenemia is caused by the synergism of several venom components, of which the thrombin-like enzyme (TLE), GPV-TL1/albolabrase,[6–8] is likely the most essential.[4] The TLE cleaves only fibrinopeptide A from fibrinogen, but not fibrinopeptide B, before fibrin polymerization to form a clot. The clot formed from stimulation of the venom is friable and dissolved quickly by the fibrinolytic system.[9] The entire process leads to the depletion of fibrinogen. Another mechanism for systemic bleeding is thrombocytopenia caused by C-type lectins, alboaggregin B and D, which promote platelet aggregation.[4] In addition, disintegrin potentiates platelet dysfunction.[4] Through these mechanisms, GPV envenomation can cause systemic bleeding; however, in clinical practice, this occurs uncommonly. Most commonly, GPV envenomation causes local effects and mild or moderate coagulopathy.[2]

Available guidelines for GPV bites recommend using platelet count and either venous clotting time (VCT) or 20-min whole blood clotting time (20WBCT) as diagnostic laboratory tests to indicate systemic envenomation and for antivenom therapy.[10–12] A study published in 2012 revealed that prothrombin time (PT) and international normalized ratio (INR) provided the highest areas under the receiver operating characteristic curve (AUROCC) when a fibrinogen level of <1.0 $g{\cdot}L^{-1}$ was used to indicate severe coagulopathy from GPV envenomation because of the risk of systemic bleeding.[13] The study also demonstrated that an INR of ≥1.2 s had the highest sensitivity in predicting severe hypofibrinogenemia.

On one hand, fibrinogen measurement is not widely available in Thailand. On the other hand, PT and INR tests are much more available; they can be done any time; and because they are standardized and highly reproducible, we thought that they might have great potential to replace bedside diagnostic tests (VCT and 20WBCT). However, to the best of our knowledge, there is only 1 published study demonstrating great diagnostic accuracy of PT/INR for evaluating hypofibrinogenemia from systemic envenomation by GPV.[13] More studies on PT/INR are needed to determine its utility in confirming GPV envenomation.

The objective of this study was to evaluate a widely available diagnostic test that may be useful to detect hypofibrinogenemia from GPV envenomation.

Methods

This was a simulated in vitro study. With the in vitro design, we had many more blood samples with fibrinogen levels of <1.0 $g{\cdot}L^{-1}$ than would be expected in severe coagulopathy from a GPV bite.

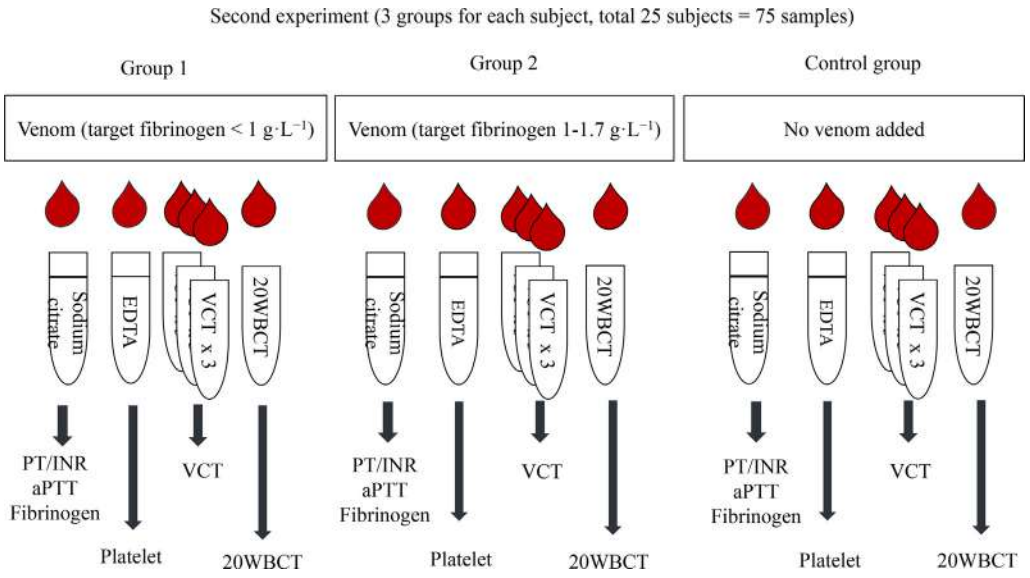
Our study period was between January 1 and June 30, 2016. The inclusion criteria were healthy volunteers aged between 20 and 45 y, with no history of regular medication or use of any medication within the previous 2 wk, and literate in the Thai language. Volunteers who were pregnant or had any abnormal baseline blood test results were excluded. Only 2 venipunctures were permitted per protocol to obtain blood samples. Written informed consent was obtained from participants prior to enrollment. The study protocol was approved by the ethics committee of the Faculty of Medicine, Vajira Hospital (COA 74/2558).

This study consisted of 2 experiments. In Experiment 1, the blood samples of 1 subject had varying amounts of GPV venom added to determine its effect on the fibrinogen level in the sample. The optimal dose of venom to reduce the fibrinogen level in 3 mL of blood to <1.0 $g{\cdot}L^{-1}$ (to simulate severe hypofibrinogenemia) and to a range of 1.0 to 1.7 $g{\cdot}L^{-1}$ (to simulate mild hypofibrinogenemia) was determined. A fibrinogen level of <1.0 $g{\cdot}L^{-1}$ was derived from a previous study,[13] which was thought to be associated with clinical systemic bleeding, whereas the level of 1.7 $g{\cdot}L^{-1}$ was the lower limit of the normal reference range of the fibrinogen level.

The venom used in this study was a horse-derived lyophilized form produced from the pooled venom of *T albolabris*. The venom was produced by the Queen Saovabha Memorial Institute, Thai Red Cross Society, a World Health Organization collaborating center for venomous snake toxicology and research. The institute produces products such as snake venom/antivenom and rabies vaccine/immunoglobulin according to Good Manufacturing Practice and World Health Organization regulations. The laboratory was accredited with an ISO/IEC 17025 certificate in 2005 (https://www.saovabha.org/about_saovabha/QSMI-Vision).

There were 2 steps in Experiment 1. Because the doses of GPV venom that could cause hypofibrinogenemia in 3-mL blood were unknown, we prepared 10 tubes of 3-mL blood for venom titration to yield the 2 ranges of required fibrinogen levels. All blood samples in this experiment were from 1 healthy volunteer. The first 4 sodium citrate tubes were initially used to roughly estimate the doses by titrating from 1.0, 0.1, 0.01, to 0.001 mg of venom. The fibrinogen level in each of the first 4 tubes was measured. The remaining 6 sodium citrate tubes were used to finely adjust for more precise doses. The acquired 2 final doses of venom were used to simulate severe and mild hypofibrinogenemia in Experiment 2.

In Experiment 2, we collected blood samples from another 25 healthy volunteers (the only subject in Experiment 1 was not included in this experiment), 60



Figures 1. Figure 1. Second experiment: process and equipment preparation for each group. 20WBCT, 20-min whole blood clotting time; aPTT, activated partial thromboplastin time; EDTA, ethylenediaminetetraacetic acid; INR, international normalized ratio; PT, prothrombin time; VCT, venous clotting time.

mL per person. Blood from each of them was allocated into 3 groups, group 1 (to simulate severe hypofibrinogenemia), group 2 (to simulate mild hypofibrinogenemia), and group 3 (control). Six tubes were needed per group, 1 blue-top (sodium citrate—for PT/INR, activated partial thromboplastin time [aPTT], and fibrinogen level), 1 purple-top (ethylenediaminetetraacetic acid [EDTA]—for complete blood count with platelet count), and 4 clean glass tubes (3 for VCT, 1 for 20WBCT) as seen in Figure 1.

In group 1, the venom dose expected to lower the fibrinogen level to <1.0 $g{\cdot}L^{-1}$ yielded from Experiment 1 was added to the first 25 blood samples to simulate severe hypofibrinogenemia. In group 2, the venom dose derived from Experiment 1 that was expected to lower the fibrinogen level to between 1.0 and 1.7 $g{\cdot}L^{-1}$ was added to another 25 blood samples to simulate mild hypofibrinogenemia. In group 3, no venom was added to the last 25 blood samples, and this served as a control and simulated a "dry bite."

All tubes in group 1 and group 2 were prefilled with the venom (dose obtained from Experiment 1). The venom was prepared in the morning just before enrolling subjects on the designated days. Once blood was drawn from each individual subject, 3 mL of blood was immediately placed in each tube in all the 3 groups and then mixed well. For the VCT and 20WBCT, we started the clock immediately after the blood touched the tube. For the sodium citrate and EDTA tubes, they were transported to the laboratory next door, and all the processes were started within 3 to 5 min. The sodium citrate tube was centrifuged at 3000 revolutions per min for 15 min; then, it was placed in a Sysmex CS2100i machine, a fully automated blood hemostasis analyzer, for analysis of fibrinogen, PT/INR, and aPTT. The EDTA tube was placed in a Sysmex XT-4000i machine for platelet count. Because the lower limit of detection of fibrinogen level from the Sysmex CS2100i is 0.3 $g{\cdot}L^{-1}$, we substituted the undetectable value of the fibrinogen level with 0 $g{\cdot}L^{-1}$ for data analysis.

VCT is a bedside test. In this study, 9 mL of blood was drawn from a vein, and 3 mL was placed in 3 glass tubes each in sequence. The first tube was marked with the number 3, the next with number 2, and the last one with number 1. A clock was started when blood touched the tube number 3. They were undisturbed for 5 min. After 5 min had passed, tube number 1 was first tilted approximately 45° every 30 to 60 s until a clot was seen, then tube number 2 was tilted until a clot was seen, and then the same process was repeated with tube number 3. The time from starting the clock to observing clot formation in tube number 3 was the VCT.[2] For 20WBCT, the process was similar to that for VCT; however, only 1 tube of 3-mL blood was required, and it was left undisturbed for 20 min to allow a clot to form. The tube was tilted only once, at the end of 20 min, to check, and if the blood was still liquid, this was taken to mean that it was unclotted.[11]

SPSS (version 21.0; SPSS Inc, Chicago, IL) was used for statistical analysis. Quantitative data, that is, the results of VCT, 20WBCT, platelet count, PT/INR, aPTT, and fibrinogen level, are presented as mean±SD. Our statistical analysis consisted of the diagnostic parameters, including sensitivity, specificity, accuracy, correlation

Table 1. Fibrinogen levels according to the amount of venom titration

Titration	*Venom (mg)*	*Fibrinogen level (g·L^{-1})*
Coarse titration	1.000	No coagulation[a]
	0.100	No coagulation[a]
	0.010	No coagulation[a]
	0.001	1.757
Fine titration	0.002	1.700
	0.004	0.645
	0.006	0.440
	0.008	No coagulation[a]
	Control	2.230

[a]No coagulation represents a fibrinogen level of <0.3 g·L^{-1}.

coefficient, and AUROCC, in which a fibrinogen level of <1.0 g·L^{-1} was used as an indicator for severe coagulopathy. Statistical significance was defined as a *P* value of *<0.05*.

Results

Twenty-six healthy volunteers were recruited; 1 for Experiment 1 and 25 for Experiment 2. The subject of Experiment 1 was a 26-y-old man; the subjects of Experiment 2 were 17 (68%) women and 8 men, with a group age of 33±6 y.

In Experiment 1, 1.0, 0.1, 0.01, and 0.001 mg of lyophilized GPV venom were added to each of the first 4 tubes. Fibrinogen levels according to the amount of venom titration are shown in Table 1. Doses of 1 to 0.01 mg resulted in an undetectable fibrinogen level (<0.3 g·L^{-1}), whereas a dose of 0.001 mg lowered the fibrinogen level to 1.757 g·L^{-1}. After fine titration, we selected a dose of 0.008 mg and 0.004 mg to be used in Experiment 2. The normal range of fibrinogen level is 2 to 4 g·L^{-1}. The control fibrinogen level obtained from the 1 subject in Experiment 1 was 2.23 g·L^{-1}, which was on the lower side of the normal range. We were concerned that the remaining 25 healthy volunteers may have had higher fibrinogen levels, for example, between 3 and 4 g·L^{-1}, and as a result, selecting a venom dose lower than 0.004 mg may have not decreased fibrinogen levels to between 1.0 and 1.7 g·L^{-1}. As such, we selected 0.004 mg of venom for group 2 in Experiment 2 (to bring down the fibrinogen level to 1.0–1.7 g·L^{-1}) and 0.008 mg of venom for group 1 in Experiment 2 to reduce the fibrinogen level below 1.0 g·L^{-1}.

In Experiment 2, of the 75 samples (25·3 groups), only 59 (79%) were adequate for final analysis. Sixteen samples were excluded from the analysis because of unexpected rapid gelatinization of the serum after adding venom to those sodium citrate blood samples. In addition, some of the samples for complete blood count and platelet count exhibited clotting, which precluded further testing for coagulogram or platelet count because the machine could not work with samples in solid form. Table 2 presents the results of blood samples with venom and those without venom. Platelet count and fibrinogen level were lower in the group with venom than in the control samples. In Experiment 2, of the 59 samples, 6 (10%) had severe hypofibrinogenemia, 8 (14%) had mild hypofibrinogenemia, and 45 (76%) had normal fibrinogen levels. Even though 10% of the samples had severe hypofibrinogenemia, none of the 20WBCT test samples were unclotted.

Table 3 shows that platelets and VCT had no significant correlation with fibrinogen level in this simulated in vitro GPV bite study. In contrast, PT/INR and aPTT showed a significant negative correlation with fibrinogen level. When the fibrinogen level was reduced, PT/INR and aPTT became prolonged. We found that PT and INR had a stronger correlation coefficient (−0.34 and −0.33, respectively) than that of aPTT (−0.29).

Using a fibrinogen level of <1.0 g·L^{-1} as an indicator for severe hypofibrinogenemia and risk of systemic bleeding, PT and INR showed the highest AUROCC,

Table 2. Comparison of mean and standard deviation of each test between the blood samples with and without venom

Test	*Control group (no venom)*		*Samples with venom*	
	n=25		*n=34*	
	Mean	*SD*	*Mean*	*SD*
Platelet (cells/mm^3)	266,520.00	65,466.00	248,853.00	60,755.00
VCT (min)	9.50	2.50	10.40	2.30
PT (s)	11.80	0.60	12.60	0.90
INR	1.01	0.62	1.07	0.07
aPTT (s)	25.70	1.80	29.20	2.40
Fibrinogen (g·L^{-1})	2.76	0.58	1.77	1.05

VCT, venous clotting time; PT, prothrombin time; INR, international normalized ratio; aPTT, activated partial thromboplastin time.

Table 3. Correlation coefficient between fibrinogen level and other laboratory testing parameters and the AUROCC for severe hypofibrinogenemia

Test	*Correlation coefficient with fibrinogen levels and P-value*		*AUROCC for a fibrinogen level of <1 g·L^{-1}*	*95% CI*
Platelet	0.26	*P*=0.051	0.59	0.34–0.84
VCT	−0.22	*P*=0.097	0.58	0.56–0.86
PT	−0.34	*P*=0.010	0.76	0.55–0.97
INR	−0.33	*P*=0.010	0.76	0.57–0.97
aPTT	−0.29	*P*=0.024	0.63	0.57–0.97

VCT, venous clotting time; PT, prothrombin time; INR, international normalized ratio; aPTT, activated partial thromboplastin time; AUROCC, area under the receiver operating characteristic curve.

0.76 (0.55–0.97) and 0.76 (0.57–0.97), respectively (Table 3, Figure 2).

For samples with severe hypofibrinogenemia, a VCT of >15 min, abnormal 20 WBCT, an INR of >1.2, and a PT of >13.4 s had the same high accuracy at 90%, unlike an aPTT of >30 s, which had much lower accuracy (68%) (Table 4). On changing the fibrinogen level to <1.7 g·L^{-1} to indicate coagulopathy, all the diagnostic laboratory test parameters had low accuracy (<80%), except aPTT, which had a higher accuracy but was still <80%.

Discussion

The major mechanism of coagulopathy from a GPV bite is likely from the TLEs of the venom that cause hypofibrinogenemia. We used 1.0 g·L^{-1} as the cutoff for fibrinogen to indicate severe hypofibrinogenemia because it was used in a previous study on a similar matter.[13] In another study, a fibrinogen level of <1.0 g·L^{-1} was a strong risk factor for death in acutely injured patients requiring a massive transfusion[14] and because clotting problems occurred when fibrinogen was below this level.[15]

Ideally, obtaining a fibrinogen level measurement in a timely manner would be the best way to guide physicians to make a decision as to whether antivenom (considered the definitive treatment, but with limited availability) should be prescribed. Only a limited number of large or university hospitals in Thailand are capable of measuring the fibrinogen level. In this study, we attempted to find other widely available diagnostic tests that could be used to accurately detect hypofibrinogenemia, especially in severe cases. Through our experiments, we demonstrated that PT/INR and aPTT had a significant negative correlation coefficient with fibrinogen levels; however, the correlation of PT/INR was higher than that of aPTT. In addition, the AUROCC of PT/INR was larger than that of aPTT (Table 3, Figure 2). These findings support those in a previous

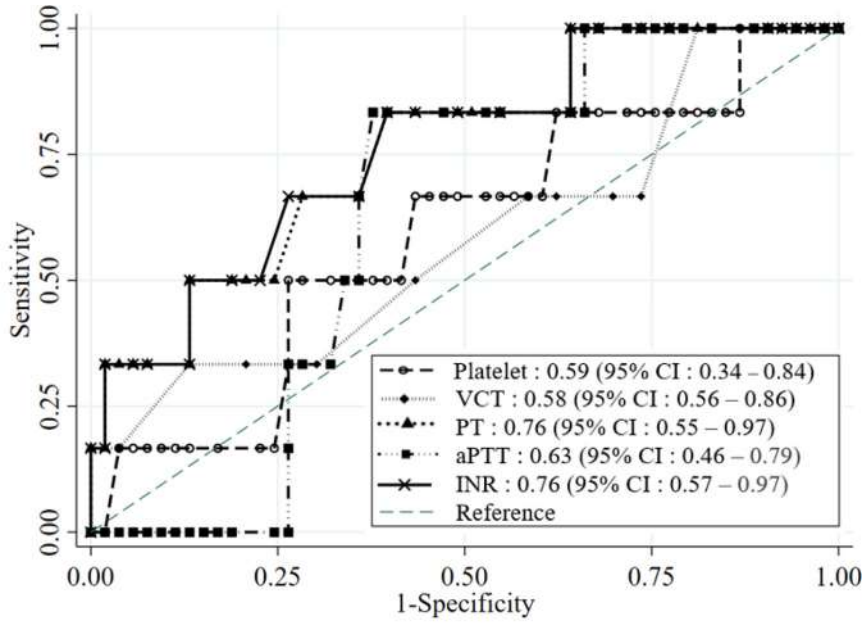


Figure 2

Figure 2. Area under the receiver operating characteristic curve of each diagnostic laboratory test against fibrinogen level <1 g·L^{-1} in this in vitro simulated green pit viper envenomation. aPTT, activated partial thromboplastin time; INR, international normalized ratio; PT, prothrombin time; VCT, venous clotting time

Table 4. Cutoff values, sensitivity, specificity, and accuracy by each test in simulated severe and mild hypofibrinogenemia (a fibrinogen level of <1 and <1.7 g·L^{-1})

Cutoff point	*Abnormality (%)*	*Fibrinogen level <1 g·L^{-1}*			*Fibrinogen level <1.7 g·L^{-1}*		
		Sensitivity (%)	*Specificity (%)*	*Accuracy (%)*	*Sensitivity (%)*	*Specificity (%)*	*Accuracy (%)*
Platelet <150,000	5	16.7 (0.4–64.1)	96.2 (87.0–99.5)	88.1	7.1 (0.2–33.9)	95.6 (84.9–99.5)	74.6
VCT>15 min	0	0.0 (0.0–45.9)	100.0 (93.7–100.0)	89.8	0.0 (0.0–23.2)	100.0 (92.1–100.0)	76.3
20WBCT (unclotted)	0	0.0 (0.0–45.9)	100.0 (93.3–100.0)	89.8	0.0 (0.0–23.2)	100.0 (92.1–100.0)	76.3
INR>1.2	3	16.7 (0.4–64.1)	98.1 (89.9–100.0)	89.8	14.3 (1.6–42.8)	100.0 (92.1–100.0)	79.7
PT>13.4s	7	33.3 (4.3–77.7)	96.2 (87.0–99.5)	89.8	21.4 (4.7–50.8)	97.8 (88.2–99.9)	71.2
aPTT>30s	22.0	0.0 (0.0–45.9)	75.5 (61.6–86.2)	67.8	35.7 (12.8–64.9)	82.2 (67.9–92.0)	79.6

VCT, venous clotting time; 20WBCT, 20-min whole blood clotting time; INR, international normalized ratio; PT, prothrombin time; aPTT, activated partial thromboplastin time.

study.[13] We conclude that PT/INR could be an effective test to indicate severe hypofibrinogenemia.

Platelet count, however, did not have a significant correlation with the fibrinogen level. As briefly discussed in the introduction, thrombocytopenia is caused by C-type lectins, alboaggregin B and D, which promote platelet aggregation; however, hypofibrinogenemia results from TLEs.[4] These results mirrored our findings in clinical practice that in some GPV bite cases, the only laboratory abnormality was thrombocytopenia, and other laboratory test findings, such as VCT, PT/INR, or even fibrinogen levels, were normal.[16] Because the AUROCC of platelet counts against the fibrinogen level of <1.0 g·L^{-1} was poor (0.59), when paired with the nonsignificant correlation with the fibrinogen levels, platelet count should not be used as a diagnostic test for hypofibrinogenemia. Instead, we suggest that platelet counts be ordered and interpreted separately from the coagulogram.

The platelet count cutoff value of <150,000 that showed high accuracy for the fibrinogen level of <1.0 g·L^{-1} (Table 4) should be interpreted cautiously because thrombocytopenia and hypofibrinogenemia develop through 2 different mechanisms as pointed out earlier. Both hypofibrinogenemia (using VCT as a surrogate for clotting abnormality) and thrombocytopenia could occur together, especially in severe cases. Having both abnormalities was a predictor for systemic bleeding in a multivariate analysis; however, isolated hypofibrinogenemia and isolated thrombocytopenia can also occur.[5,16]

For the cutoff values of other tests (Table 4), a VCT of >15, unclotted 20WBCT, an INR of >1.2, and a PT of >13.4 had high and comparable accuracy of nearly 90%, unlike aPTT that had a much lower accuracy for severe hypofibrinogenemia. These laboratory test parameters had lower accuracy when we changed the reference point of the fibrinogen level from <1.0 g·L^{-1} to the higher one (<1.7 g·L^{-1}), except aPTT, which had a higher accuracy. All laboratory test parameters had an accuracy of <80%, which was similar to that in the previous study.[13]

A high accuracy with a high specificity was reported for VCT and 20WBCT; however, they had a sensitivity of 0%. In this study, 10% (6 of 59) of samples had a fibrinogen level of <1.0 g·L^{-1}; however, VCT and 20WBCT were not sensitive enough to show an abnormality although the specificity was 100% for both. They could be used as confirmation tests, instead of screening tests. However, these are bedside tests that have been criticized regarding their reliability when performed by different operators.[17]

In another study conducted in Thailand, PT/INR provided the highest AUROCC for a fibrinogen level of <1.0 g·L^{-1}; however, this study demonstrated, at the cutoff of an INR of >1.2, both high sensitivity at 86% and very high specificity at 96%.[13] However, other studies did not demonstrate such high sensitivity; they found only 26% (INR >1.2), 33% (PT >13.5 s),[18] 50% (INR >1.2),[19] and 50% (PT >13 s),[20] to predict a fibrinogen level of <1.0 g·L^{-1}, even though they all had very high specificity at 96, 96, 94, and 100%, respectively. The results of these 3 studies[18–20] are more similar to the results of this study in that the sensitivity of an INR of >1.2 or a PT of >13.4 is poor; however, the specificity and accuracy are excellent.

We found new cutoff values using Youden's index, and if we adjusted the INR cutoff value from >1.2 to >1.15, the sensitivity, specificity, and accuracy increased to 33, 98, and 92%, respectively. In another study performed on Malayan pit viper bites (the venom of which also has TLEs, causing hypofibrinogenemia), the authors selected an INR of >1.155 to be their best cutoff value to indicate severe hypofibrinogenemia, with a sensitivity and specificity of 79% and 90%, respectively.[21] As a result, we propose using a new INR cutoff value of >1.15, instead of >1.2, to provide better sensitivity, specificity, and accuracy.

From this study, the aPTT should not be used because it had the worst accuracy, with poor specificity and 0% sensitivity, compared with that of other diagnostic test parameters, which were similar to those reported in a previous study,[20] in which sensitivity was also shown to be 0%.

LIMITATIONS

This study has limitations. The first limitation is the small sample size, which was further compromised by 21% unreadable samples (16 of 75) in Experiment 2. Second, the study had no individual baseline measure of fibrinogen in Experiment 2 because the normal range of fibrinogen was wide, from 2 to 4 $g{\cdot}L^{-1}$ (200–400 $mg{\cdot}dL^{-1}$), and the fibrinogen level of the only subject in Experiment 1 was only 2.23 $g{\cdot}L^{-1}$ (lower end of the normal range). As a result, the 2 venom doses obtained in Experiment 1 were probably too small to simulate hypofibrinogenemia in Experiment 2, especially for severe cases (6 [10%] of 59 samples). This may affect the sensitivity and specificity of our study. Last, because there are a number of species of GPV and the venom used in this study was only from the pooled venom of *T albolabris*, sensitivity and specificity of those laboratory test parameters may be different with venoms of other species.

Conclusions

This simulated in vitro study suggests that PT/INR could be used as a diagnostic test for hypofibrinogenemia in *T albolabris* envenomation because of its high accuracy and AUROCC. We also found that using an INR cutoff value of >1.15, instead of >1.2, improved sensitivity, specificity, and accuracy. Platelet count should be ordered in addition to PT/INR because thrombocytopenia develops through a different mechanism and has no correlation with the fibrinogen level.

Author Contributions: Study concept and design (RO); conducting the experiment (GT, SL); data acquisition (GT); data analysis (RO, GT); drafting of the manuscript (GT, RO); critical revision of the manuscript (RO); approval of the final manuscript (RO, GT, SL).

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Disclosures: None.

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CLINICAL TOXINOLOGY SPECIAL SECTION

ORIGINAL RESEARCH

Comparison of Intravenous Paracetamol, Dexketoprofen Trometamol, or Topical Lidocaine Use for Pain Relief in Scorpion Stings: A Placebo-Controlled, Randomized Study

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Introduction—After a scorpion sting, patients commonly present to hospitals with pain. Our study sought to compare the analgesic efficacy of IV paracetamol, IV dexketoprofen trometamol, topical lidocaine, and placebo in patients reporting pain after presenting with a history of scorpion sting.

Methods—This double-blind, randomized, placebo-controlled study was conducted in the emergency department of a tertiary hospital. Adult patients who presented with the complaint of pain after a scorpion sting and did not have systemic findings were randomly assigned to 1 of the following 4 groups: IV paracetamol, IV dexketoprofen trometamol, topical lidocaine, and placebo. The visual analog scale scores were measured at the time of presentation to the emergency department and at 30 and 60 min to determine the pain intensity.

Results—The study included 106 patients, of whom 30 were in the paracetamol group, 26 in the dexketoprofen trometamol group, 25 in the topical lidocaine group, and 25 in the placebo group. We did not find a different analgesic effect among the groups in the first 30 min (P=0.185). IV paracetamol, dexketoprofen trometamol, and topical lidocaine did not show different analgesic effects in the first 60 min (P>0.05). IV paracetamol and dexketoprofen trometamol were found to provide a more effective analgesia than the placebo at 60 min (P<0.05). The analgesic effects of topical lidocaine and placebo did not differ (P=0.330).

Conclusions—IV paracetamol and IV dexketoprofen trometamol provided analgesia in the first 60 min, similar to topical lidocaine but superior to placebo.

Keywords: analgesia, visual analog scale, emergency

Introduction

Scorpion stings occur globally, especially in Africa, the southwestern United States, Latin America, South Asia, and the Middle East, and they cause significant health problems. Among the approximately 2700 known species, 30 species reportedly are dangerous to humans.[1-3] Our study was conducted in southeastern Turkey where a higher number of scorpion stings are seen compared to other parts of the country, and the most common species are *Androctonus crassicauda*, *Leiurus quinquestriatus*, *Mesobuthus gibbosus*, and *Mesobuthus eupeus* species that belong to the Buthidae family.[4] Although scorpion stings are rarely fatal in developed countries, they are still a significant contributor to mortality from envenomation in developing countries.[1] This situation can be explained by the fact that health authorities in developed countries properly organize the management of scorpion stings.[3] According to recent

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studies, 7 regions in the world where scorpion stings are at high risk have been identified. These are north Saharan Africa, Sahelian Africa, South Africa, South India, Near and Middle East, and Latin America, east of the Andes. Globally, the estimated annual number of scorpion stings exceeds 1.2 million and the number of deaths exceeds 3250 (0.27%).[3] Deaths from scorpion stings are usually due to pulmonary edema and cardiogenic shock, whereas post-sting anaphylactic shock can also cause mortality.[1,5] The type, age, and size of the scorpion, nutritional status, number of stings, venom injection depth, the sting being located closer to the head and neck, and age and health status of the patient may affect the clinical course.[6]

Scorpion venoms are mixtures of many biologically active components, some of which are hemolysins and neurotoxins; the latter often act on ion channels.[7] When bound to these channels, inactivation is inhibited, leading to neuroexcitation and thus prolonged depolarization.[1] Because of these properties, scorpion venom can cause neurological, cardiovascular, hematological, and renal effects and local findings, such as pain, redness, burning, and swelling.[8] Scorpion stings more frequently cause local effects rather than systemic envenomation. Pain is usually sudden, intense, and persistent; recurrence/relapse after recovery may occur.[9] The main pathogenesis of pain is the sensitization of nociceptors via substance P and serotonin release at the site of the sting or the increase in smooth muscle contractions through the inhibition of potassium channels by the toxin.[10] In most cases, the pain lasts for 2 h after the scorpion sting and can last for an average of 15 h and sometimes 24 h. Also, this pain can refer throughout the regional dermatomes.[3,11]

The main elements in the management of scorpion stings are fluid replacement, tetanus vaccine, antivenom administration, use of analgesics, and use of antibiotics if necessary. Although it is the most effective method, the use of antivenom has been further challenged because it may lead to allergic complications.[12] Pain relief is the major concern in the first response to scorpion sting in the emergency department (ED). Paracetamol, ice application, and lidocaine have been recommended as analgesics in scorpion stings. However, there are insufficient studies in the literature to clarify which method is more effective.[9]

In this study, the analgesic efficacy of IV paracetamol, IV dexketoprofen trometamol, topical lidocaine, and placebo was compared in scorpion stings, which account for a large number of presentations to the ED in our region.

Methods

This randomized, double-blind, placebo-controlled study was conducted between September 1, 2020, and August 31, 2021, in the ED of a tertiary hospital with 350,000 annual patient admissions. The hospital is located in southeastern Turkey, and the patients included in the study were also from that region. The study was designed as a superiority trial to determine which drug would provide better analgesia in scorpion stings. Written consent was obtained from all patients before inclusion in the study. Ethical approval was received from the central ethics committee (number: 2019-5-1, date: March 28, 2020), the Turkish Medicines and Medical Devices Agency (ID: 20-AKD-100), and the study was registered at ClinicalTrials.gov (NCT05125796). The study was reported in accordance with the Consolidated Standards of Reporting Trials guidelines.[13]

All patients aged 18 y and older, who presented to our ED with the main complaint of pain after scorpion stings, which were determined as grade I, were included in the study in a consecutive manner. Patients who refused to participate in the study, those with grades II to IV scorpion stings, those with known allergies to the drugs to be used in the study, pregnant women, patients with renal disease, and patients who had taken analgesics within 6 h before presenting to the ED were excluded. The cases who were admitted to the ED more than 6 h after the sting were also excluded. Patients were screened for eligibility in the study for 24 h a day and 7 d a week. A senior emergency medicine resident or emergency medicine specialist determined patients' eligibility for enrollment. Unfortunately, the presenting patients did not provide scorpion specimens for identification and described features were insufficient for the assignment of the possible species responsible for the sting(s). Although some of these stings may be considered "presumed," the patients presented with history and signs/symptoms fully consistent with scorpion sting/local envenoming.

In the evaluation of eligibility for inclusion in the study, the grading of scorpion stings was performed as follows: grade I if there were only localized reactions such as pain and/or paresthesia at the site of the scorpion sting; grade II if fever, chills, profuse sweating, nausea, vomiting, diarrhea, hypertension, and priapism were present; grade III or IV if there were systemic symptoms such as cranial nerve abnormalities, somatic skeletal neuromuscular dysfunction, nausea, vomiting, and pulmonary edema.[14]

As the 4 inventions being compared included IV and topical delivery methods, all participants received 2 interventions: 1 IV and 1 topical. A topical drug, not exceeding 5 g in total, was applied to and around the site of the scorpion sting. The placebo group received both 100 mL of normal saline IV and an ointment with the same color, hardness, and odor as lidocaine. The lidocaine group received both 100 mL of normal saline IV and 5 g of 5% topical lidocaine (Anestol ointment;

Sandoz). The test IV groups either received 1 g of IV paracetamol (Perfalgan; Bristol Myers Squibb) or 50 mg of IV dexketoprofen trometamol in 100 mL of normal saline (Arveles; UFSA) and the placebo topical application. The package of the serum and cream used was covered so that the label was not seen. All the IV administered drugs had the same color and package shape. In patients with insufficient pain relief after 60 min, 1 $mg \cdot kg^{-1}$ tramadol in normal saline was applied as an IV infusion (Madol ampule 100 mg; Koçak Farma) as a rescue medication. All the treatments were performed following local wound care practices, and tetanus prophylaxis was performed in cases where required.

Randomization blocks were created on the computer by a person blinded to the study. The group to which each patient was assigned was determined by letters written in an opaque envelope. A senior emergency medicine resident or emergency medicine specialist identified the patient to be included in the study, and one of them obtained written informed consent from the patient. Afterward, the preprepared envelope was opened by the nurse who prepared the medicines. In this envelope, statements such as group A-treatment X and group B-treatment Y were written. Another nurse who was blinded to the identity of the medication was responsible for treating the patient. At the same time, the doctor recorded the first visual analog scale (VAS) measurement before starting the treatment. The doctor who followed the treatment made VAS measurements again at 30 and 60 min and recorded them in the patient's file. The data obtained with these code names were given to the statistician. The statistician also was blinded to group and medication. The physician, nurse, patient, and statistician remained blinded to the drug groups of the patients until after the last patient completed the study and the statistical analysis was completed. At this stage, the groups were identified for the team writing the article and evaluating the results.

The 100-mm VAS (0, no pain to 100 mm, excruciating pain) was used to measure the pain intensity. It is based on the fact that the patient indicates the pain that they feel by marking on a line, and it is frequently used in healthcare for measuring pain intensity and pain follow-up.[15] Previous VAS scores were not made available to the patient. Then, a different physician measured this

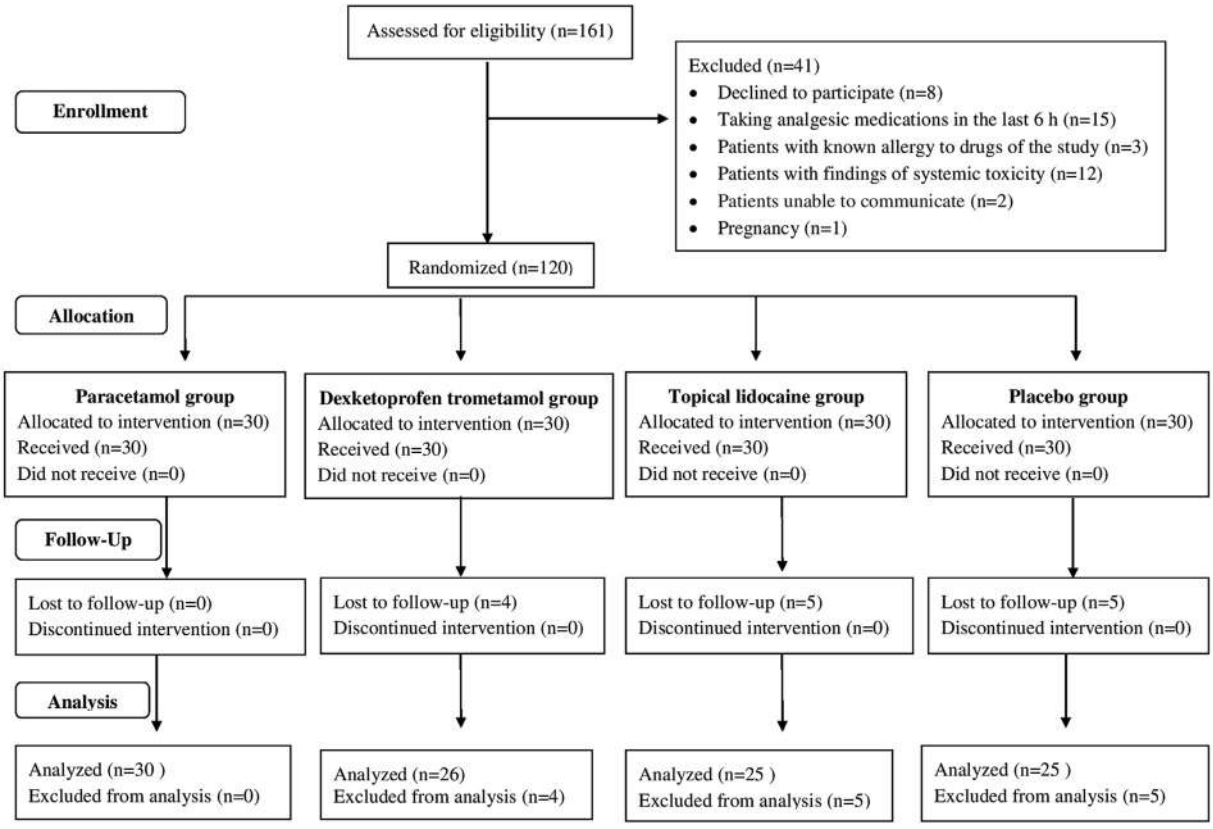

Figure 1. Participant flow diagram.

Table 1. Characteristics of patients

Variable	*Total (n=106)*	*Paracetamol (n=30)*	*Dexketoprofen trometamol (n=26)*	*Topical lidocaine (n=25)*	*Placebo (n=25)*	*P value*
Age, y	43±17	41±16	39±15	49±17	46±18	0.127
Female sex, n (%)	60 (57)	17 (57)	13 (50)	14 (56)	16 (64)	0.796
Pulse, beats·min^{-1}	91±15	90±15	93±16	86±14	94±15	0.279
MAP, mm Hg	91±14	88±10	91±15	93±14	92±16	0.517
WBC count, 10^3·μL^{-1}	8±2	8±2	8±2	8±2	8±2	0.785
VAS0, mm	59±25	58±19	65±22	63±29	52±28	0.212
Arrival time, min	60 (30–60)	53 (30–68)	60 (30–60)	60 (30–120)	60 (45–75)	0.217

MAP, mean arterial pressure; VAS, visual analog scale; VAS0, visual analog scale score at presentation; WBC, white blood cell. Arrival time is presented as median (interquartile range); age, pulse, MAP, WBC, and VAS0 are presented as mean±SD.

marking place with a ruler from point 0 (cm scale ± 0.5 mm). Pain measurements were performed at the time of presentation and at 30 and 60 min. Drug side effects were investigated by the physician who followed up the patient by observing and asking them. If there was no regression or improvement in their pain after 60 min, rescue medication was administered.

The primary outcome measure was the change in the VAS pain score at 30 and 60 min. We had planned to measure at 15, 30, and 60 min in the study. However, after the study started and several patients were recruited, we observed that the analgesics did not show any effect within 15 min. For this reason, we changed the VAS measurement times to 30 and 60 min and adjusted the outcome measurements accordingly. The secondary outcome measures were the need for rescue medication and drug side effects.

The sample size was estimated using G-Power for Mac OS X (version 3.1.9.2; Universitat Düsseldorf). To detect 15-mm differences in VAS scores,[8] assuming a 2-tailed alpha value of 0.05 and a standard deviation of 19 mm according to a study on analgesic use in back pain,[16] we calculated that there should be a minimum of 27 patients in each group to reach 80% power.

In the study, the conformance of numerical data to the normal distribution was determined with the Shapiro-Wilk test, and Levene's statistics were used for the homogeneity test of variances. At baseline, groups were compared as appropriate using either the 1-way analysis of variance or the Kruskal-Wallis H test. A repeated-measures mixed-model analysis of variance was used for simultaneous statistical analysis of pain scores at 30 and 60 min to compare the treatment groups. Group differences were identified pairwise using the Tukey honestly significant difference test or Bonferroni's multiple comparisons. As appropriate, categorical variables were compared using the χ^2 test or Fisher exact χ^2 test. Results were reported as counts and percentages. A *P* value of

Table 2. Comparison of theVAS score changes between the treatment groups

	VAS change at 30 min	*VAS change at 60 min*	*P** value
Paracetamol (n=30)	16±13	33[a]±21	0.0013
Dexketoprofen trometamol (n=26)	18±16	41[a]±22	<0.0001
Topical lidocaine (n=25)	15±13	27[a,b]±19	0.0858
Placebo (n=25)	10±14	17[b]±24	0.5904
P*† *value	0.185	<0.001	

†A one way repeated measures Anova test showing the *P* value of the treatments effect, [a,b]The groups sharing the same superscript letter are not significantly different (P<0.05, Tukey's test), *The Bonferroni adjustment was used for pairwise comparisons.

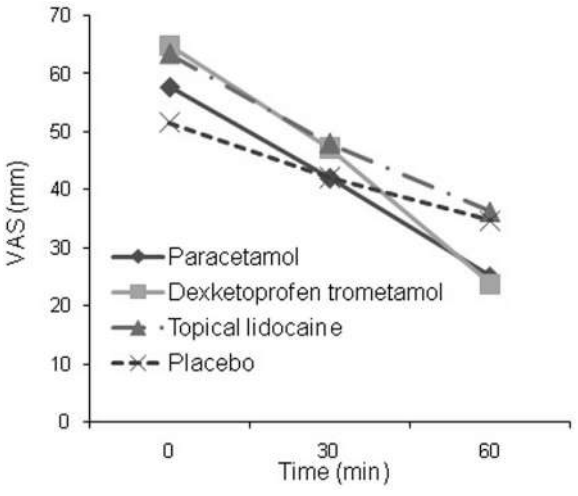

Figure 2. Mean VAS scores of the patients in intervention group.

<0.05 was considered statistically significant. Results were reported as mean±SD or median (interquartile range). All the data were analyzed using SPSS version 22.0 and Graphpad version 8.0.2.

Results

A total of 161 patients were identified to have presented to the ED with scorpion stings during the study period. Of these, 8 refused to participate in the study, 15 had taken analgesics before presenting to the ED, 3 were allergic to analgesics, 12 had systemic envenomation findings, 2 were not able to cooperate (intellectual disability), and 1 was pregnant; therefore, these patients were excluded from the study. The remaining 120 patients were randomized into 4 groups (30 individuals in each group). After inclusion in the study, 4 subjects in the dexketoprofen trometamol group, 5 subjects in the topical lidocaine group, and 5 subjects in the placebo group were excluded from analysis because of deviations in following the protocol (request for withdrawal of data use). The excluded cases did not receive allocated interventions. Ultimately, the study was conducted with 106 patients. A participant flow diagram is shown in Figure 1.

Among the patients included in the analysis, 1000-mg IV paracetamol was given to 30 subjects, 50-mg IV dexketoprofen trometamol to 26 subjects, and topical lidocaine ointment not exceeding 5 g to 25 subjects. Twenty-five people were included in the placebo group. The age of the whole sample was 43±17 y, and no significant difference was found between the groups (P=0.127). The female ratio was 57%, and there was no significant numerical difference between the groups in terms of sex (P=0.796). The heart rate of the patients was 91±15 beats·min^{-1} and the mean arterial pressure was 91±14 mm Hg, and neither significantly differed between the groups (P>0.05) (Table 1).

The scorpion stings were mostly located in the right upper extremity (35%), followed by the right lower extremity (23%), upper left extremity (19%), lower left extremity (15%), multiple areas (5%), and trunk (4%). Sixty-seven percent of the scorpion sting presentations occurred in June, July, and August.

There was no statistically significant difference between the groups regarding the VAS scores obtained at the time of presentation (P=0.212, Table 1). Between the time of presentation and 30 min, there was no significant difference in the VAS change scores among the 4 groups (P=0.185). There was a significant difference among the 4 groups in the VAS change scores at 60 min (P<0.001). The post hoc test indicated no significant difference among the 3 drug groups, but the patients in the placebo group had significantly less pain reduction than those in the paracetamol and dexketoprofen trometamol groups. The VAS score changes were not significantly different between the topical lidocaine and placebo groups for 0 to 60 min (P=0.330). Changes in VAS score within 30 and 60 min were statistically significant in the paracetamol (P=0.0013) and dexketoprofen trometamol groups (P<0.0001) but not in topical lidocaine (P=0.0858) and placebo groups (P=0.5904) (Table 2).

Figure 2 presents the graph of the changes in the VAS scores at 0, 30, and 60 min and reveals the differences among the study groups. Rescue medication was required in 39% (n=41) of the whole sample, and no adverse drug effect occurred in any patient. There was no significant difference among the groups in the percentage requiring rescue medication (P=0.2566); 27% in the dexketoprofen trometamol group, 33% in the paracetamol group, 44% in the topical lidocaine group, and 52% in the placebo group.

Discussion

The most common symptom after a scorpion sting is pain at the site of the sting.[6,7,12,17,18] In cases of scorpion stings without systemic findings, providing analgesia is one of the most important steps of emergency intervention. However, as stated in a meta-analysis, there are insufficient studies that determine the analgesic(s) that are most effective for scorpion stings.[1]

The only study in the literature comparing analgesics for scorpion stings was undertaken in Turkey.[9] The authors compared the analgesic efficacy of paracetamol, topical lidocaine, and ice application methods but did not use a placebo. Among these methods, topical lidocaine was reported to provide more effective analgesia. They obtained a median 40-mm VAS score decrease with topical lidocaine in the first 60 min, whereas our study showed a mean decrease of 27 mm with topical lidocaine, 33 mm with paracetamol, and 41 mm with dexketoprofen in the same time.[9] We did not find that IV paracetamol, IV dexketoprofen trometamol, topical lidocaine, and placebo had different analgesic effects in the first 30 min. IV paracetamol and dexketoprofen trometamol showed analgesia equal to that of topical lidocaine and superior to that of placebo in the first 60 min. No differential analgesic effects of topical lidocaine and placebo were found in the first 60 min.

The topical form of lidocaine, a local anesthetic agent, can be used in the management of acute and chronic pain

due to its few systemic side effects and effective analgesic properties.[19] In the literature, effective analgesia was achieved with the preprocedural application of topical lidocaine[20] for arterial gas sampling[21] for thoracentesis and abdominocentesis. Topical lidocaine has also been suggested to be more effective than paracetamol and ice application for pain relief of scorpion stings.[9] We determined that topical lidocaine provided analgesic efficacy similar to paracetamol and dexketoprofen trometamol. We did not find any study comparing topical lidocaine and IV dexketoprofen trometamol in the literature. In studies comparing IV lidocaine and IV dexketoprofen trometamol in patients with migraine, the former was shown to provide a more effective analgesia than the latter.[22,23]

Different treatments have been tested in the literature for the management of pain caused by scorpion stings. It was reported that the use of alcohol in scorpion stings did not provide sufficient analgesia.[24] In addition, effective analgesia was provided in 1 case where chloroquine was used[25]; however, apart from this single case report, there is no other study on chloroquine in the literature. Other studies suggest that the use of nonsteroidal anti-inflammatory drugs such as aspirin may provide symptomatic benefits, but caution is warranted as it may cause Reye's syndrome in children; IV non-steroidal anti-inflammatory drugs may also be contraindicated in patients with increased risk of renal insufficiency. Despite being very effective, morphine and its derivatives or analogs (codeine and tramadol) should be avoided because opioid receptor agonists inhibit noradrenaline reuptake, which may potentiate their effects. They may also worsen the patients' respiratory function by causing respiratory depression.[26]

Limitations

There were some limitations to our study. First, the number of patients in the groups was not equal. We planned to study an equal number of patients in each group; however, some of our patients were excluded from the study during follow-up, and those who dropped out caused the number of patients in the groups to be unequal. Additionally, the 4 groups had significantly different dropout rates, and this implies that the blinding may not have been effective or that the equivalence at baseline may not have been maintained. The pattern observed in ineffective blinding and dropout is consistent with a negative preference for topicals and a strong positive preference for IV groups. Second, we measured patients' pain with the VAS, which is a subjective scale, and the pain threshold of individuals was different for each person. Third, we did not know the species of scorpions that caused the envenomation, which is an important limitation. Fourth, the follow-up time (1 h) was limited because of the overcrowded nature of our ED. Finally, the fact that we did not register the patients who came 6 h after the sting and consequently we did not have patients' data was an important limitation.

Conclusions

We found that paracetamol and dexketoprofen trometamol provided superior analgesia compared to placebo in the first 60 min after local envenoming from a scorpion sting that did not cause systemic symptoms. In secondary analyses, we did not observe a difference in analgesic efficacy between paracetamol and dexketoprofen trometamol or between paracetamol and topical lidocaine. The analgesic effects of topical lidocaine and placebo were comparable.

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CLINICAL TOXINOLOGY SPECIAL SECTION

ORIGINAL RESEARCH

Therapeutic Plasma Exchange for Venom-Induced Thrombotic Microangiopathy Following Hump-Nosed Pit Viper (Genus: *Hypnale*) Bites: A Prospective Observational Study

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Introduction—Thrombotic microangiopathy (TMA), which is the triad of acute kidney injury (AKI), microangiopathic hemolytic anemia (MAHA), and thrombocytopenia, is a rare complication of snakebites, and in Sri Lanka, it is commonly seen with hump-nosed pit viper (HNPV) bites.

Methods—We conducted a prospective observational study of patients with AKI caused by HNPV bites in Teaching Hospital, Ratnapura, Sri Lanka for 6 y, commencing in June 2015. Some patients with TMA underwent therapeutic plasma exchange (TPE) and some did not. These 2 groups were compared. Statistical analysis was carried out using Minitab 18.1. Data were presented as median (IQR).

Results—There were 52 (8%) patients with TMA, of whom 21 (45%) were in the TPE group and 26 (55%) were in the non-TPE group. TPE improved time to platelet correction (4 d [IQR, 4–5 d] vs 7 d [IQR, 5–9 d]; P=0.009), time to MAHA correction (5 d [IQR, 3–4 d] vs 7 d [IQR, 6–9 d]; P=0.004), time to prothrombin time (PT)/international normalized ratio (INR) correction (1 d [IQR, 1–2 d] vs 3 d [IQR, 3–4 d]; P=0.003), and time to 20 min whole blood clotting test (WBCT20) correction (2 d [IQR, 1–2 d] vs 3 d [1QR 2–3 d]; P=0.020). Renal recovery was predicted by TPE (P=0.048) and highest creatinine level (P=0.001). There was no association between TPE and dialysis dependency at discharge (P=0.597), length of hospital stay (P=0.220), and the number of dialysis cycles prior to discharge (P=0.540). TPE did not improve the number of blood transfusions (5 packs [IQR, 3–8.5 packs] vs 4 packs [IQR, 0–9 packs]; P=0.290).

Conclusions—TPE is effective for TMA in the early correction of platelet counts, MAHA, PT/INR, and WBCT20 in HNPV bites.

Keywords: snakebites, acute kidney injury, coagulopathy, plasmapheresis, Sri Lanka

Introduction

There are 7 highest medically important land snakes in Sri Lanka: Russell's viper (*Daboia russelii*), saw-scaled viper (*Echis carinatus*), cobra (*Naja naja*), Ceylon krait (*Bungarus ceylonicus*), common krait (*Bungarus caeruleus*), hump-nosed pit viper (HNPV) (Genus: *Hypnale*), and Sri Lankan Green pit viper (*Craspedocephalus trigonocephalus*). Out of these, HNPV causes the

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commonest venomous snakebites in Sri Lanka[1] and is widely distributed all over the country except in Jaffna peninsula in northern Sri Lanka. The genus comprises 3 species, namely, *H hypnale*, *H zara,* and *H nepa*. Thrombotic microangiopathy (TMA) is a clinicopathological condition that includes the triad of microangiopathic hemolytic anemia (MAHA), thrombocytopenia, and microvascular thrombi that cause end-organ damage like in acute kidney injury (AKI), pituitary infarction, and digital gangrene. The recognized syndromes associated with TMA are hemolytic uremic syndrome (HUS) and thrombotic thrombocytopenic purpura (TTP), which have almost similar clinical and laboratory features and are, therefore, known as TTP/HUS clinical syndrome. Thrombotic microangiopathy has been previously reported following bites by *H hypnale*[2–4] and *H zara.*[5] As no antivenom is currently available for HNPV envenoming in Sri Lanka or India, these patients endlessly suffer from severe morbidities, particularly AKI, which progresses to chronic kidney disease (CKD) that needs regular renal replacement therapy. On the other hand, acute deaths may occur due to complications of venom-induced consumption coagulopathy (VICC) such as pulmonary hemorrhage,[6] intracerebral hemorrhage,[7] and cardiac effects.[8] Therefore, alternative treatment modalities instead of antivenom have to be followed for HNPV bites.

According to the American Society for Apheresis guidelines, the indication of TPE in snakebites is classified under category III Grade 2C recommendation.[9] Even though this is a weak recommendation, TPE has been successfully used in many parts of the world for snakebite-associated TMA.[2,3,10–14] However, some evidence shows that TPE is not beneficial for snakebite-associated TMA, and its role is yet to be defined.[15–20]

The HNPVs are medically important because of 2 reasons: no antivenom is currently available for their bites in Sri Lanka or India and the occurrence of unpredictable complications after their bites such as VICC and AKI, which progress to CKD.[3,4,7,21] Even deaths have also been reported following HNPV bites.[6,8] Because of the severity of complications, the World Health Organization categorized *H hypnale* under the category I snake (highly venomous), which requires the development of antivenom.[22] Considering the unique nature of epidemiology and clinical manifestations of HNPV bites with the unavailability of antivenom, the objectives of this study were to describe the outcomes of patients with TMA treated with TPE and to compare them with those in the non-TMA group of HNPV bites.

Methods

This prospective observational clinical study was conducted from June 2015 to May 2021 in the Teaching Hospital, Ratnapura, the only tertiary care center in Sabaragamuwa Province in Sri Lanka, approximately 100 km away from the capital Colombo. The hospital receives

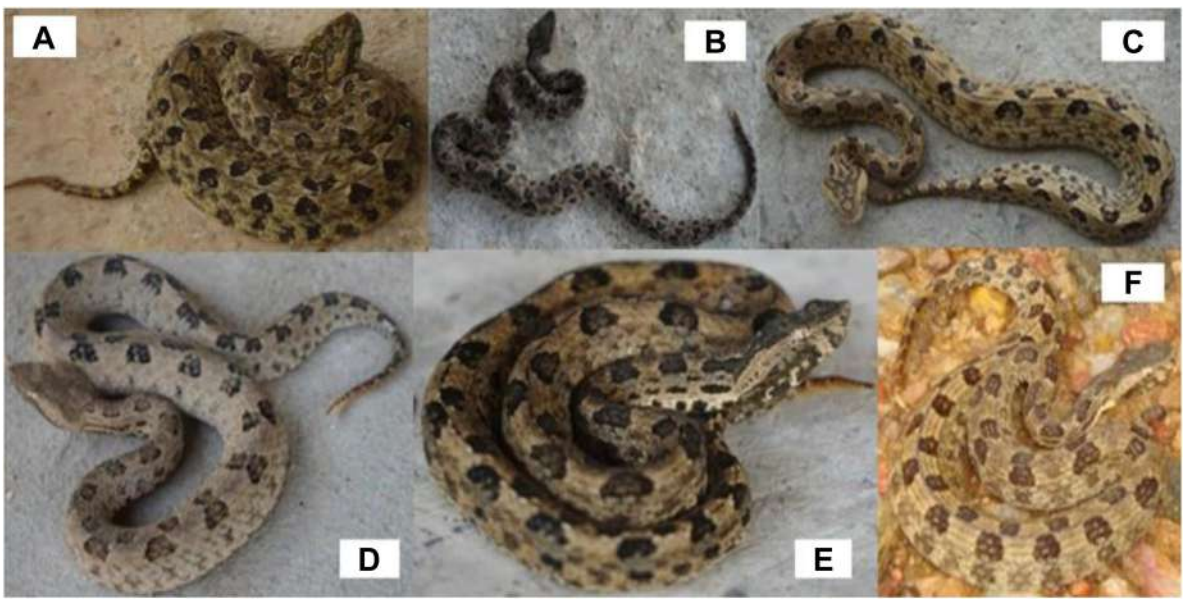

Figure 1. Ground color variations of adult *Hypnale hypnale* in different locations of Ratnapura District (06°40' N, 80°24' elevation 130 m [430 ft]) in Sri Lanka: A, Gilimale. B, Ratnapura. C, Ehaliyagoda. D, Kuruvita. E, Hangamuwa. F, Balangoda.

transfers from other local hospitals situated all over the Ratnapura District with a population of 3 million and approximately 138,000 patients present at the hospital per year, of which 280 to 350 are admitted because of snakebites. Ethical approval for the study was obtained from the Faculty of Medicine, University of Peradeniya (2015/EC/20).

All adult patients with AKI following HNPV bites were included in the study. On admission, they were assessed by the corresponding author and reassessed daily until hospital discharge (primary data). Epidemiological information, clinical manifestations, laboratory findings, treatment, and outcomes were recorded in a formatted data sheet. In order to assess the renal function, urine output, blood urea, serum creatinine, and serum potassium levels were measured. Coagulopathy was assessed by looking for bleeding manifestations, 20-min whole blood clotting test (WBCT20), and clotting profile (prothrombin time [PT]/international normalized ratio [INR], activated partial thromboplastin time [aPTT]). The reference ranges of INR and hemoglobin (Hb) were 1 to 1.4 and 11 to 16 $g{\cdot}dL^{-1}$, respectively. AKI and CKD were defined according to the Kidney Disease: Improving Global Outcomes criteria.[23] Microangiopathic hemolytic anemia was defined as anemia with the presence of fragmented red blood cells in the peripheral blood film. A platelet count of less than $150 \times 10^3\ \mu L^{-1}$ was considered to be thrombocytopenia. The diagnosis of TMA was made when a patient had the triad of AKI, thrombocytopenia, and microangiopathic hemolysis. In TMA, if renal impairment was predominant without neurological involvement, it was considered HUS, whereas the presence of neurological manifestations with renal impairment was diagnosed as TTP.[24] According to the treating physician's clinical judgment regarding the severity of the patient, some patients with TMA underwent TPE, whereas others did not. Mainly, this decision was based on platelet counts, creatinine levels, PT/INR, urine output (oliguria/anuria), and the duration (d) after the snakebite. However, clear cut-off values were not used for these parameters. Thus, we had 2 groups of patients with TMA—a group with TPE and a group without TPE (non-TPE group). These 2 groups were compared in order to assess the effectiveness of TPE for TMA using the following outcomes: 1) days taken to normalize the platelet counts ($>150 \times 10^3\ \mu L^{-1}$); 2) number of blood transfusions needed to correct anemia; 3) days needed to reduce the percentage of fragmented red blood cells in a high power field of peripheral blood film (days of starting the correction of microangiopathic hemolysis); 4) days needed for the clotting profile (PT/INR and WBCT20) to normalize; 5) number of in-patient hemodialysis cycles; 6) length of hospital stay; 7) dialysis dependency at discharge; and 8) renal recovery at discharge or after following up 2 to 6 mo of discharge with serum creatinine levels and renal ultrasound scan.

Hemodialysis and TPE were performed via a femoral venous catheter. Fresh frozen plasma (FFP) was used as the replacement fluid in TPE. All live or dead specimens of the offending snakes were identified by the corresponding author using a standard key.[25]

The ground color of HNPVs vastly differs according to the geographical area that they inhabit (Figure 1). The morphological characteristics of all snakes, such as sex, head length, tail length, snout-to-vent length, total length, and scale counts, were recorded, and dead specimens were preserved in 10% formalin and labeled with the patient's serial number and the date of admission. They were deposited at the Teaching Hospital, Ratnapura, for proof, and the live snakes were released into their natural habitat. All statistical analyses were carried out using Minitab 18.1. Normally distributed data are presented as mean±SD (range). Nonnormally distributed data are presented as median and interquartile range (IQR). Differences between the medians were compared using the Mann-Whitney U test. Differences between categorical variables were analyzed using the Pearson χ^2 and Fisher exact tests. Kaplan-Meier method was used in calculating the survival estimates and creating the survival plot. Log-rank test was used to compare survival data. A 2-tailed P value of <0.05 was considered statistically significant.

Results

Out of 77 patients in the cohort of AKI, 32 (42%) brought the specimens of HNPV, of which 29 (90%) were killed specimens and 3 (9%) were live snakes. Photographs of live snakes were available for 3 (4%) patients. Out of 35 specimens, 33 (94%) were *H hypnale,* and 2 (6%) were *H zara*. Female snakes were 23 (72%), and male snakes were 9 (28%). The total length was 407±74 mm, snout-to-vent length was 349±68 mm, head length was 23±5 mm, and tail length was 57±10 mm. The number of scale counts were 147 (143−152), 41 (38−45), and 15 (15−17) for ventral, subcaudal, and mid-dorsal scales, respectively. Forty-two (54%) patients did not bring the offending snake to the hospital.

There were 683 HNPV bites during the study period, and 77 (11%) patients who were bitten had AKI. TMA was found in 52 (8%) patients. Epidemiological features are shown in Table 1. In the cohort of AKI, the male patients (n=61; 79%) outnumbered the female patients (n=16; 21%), and the age was 58±14 (25−93) y. Most patients (n=49; 64%) were bitten at day time

Table 1. Epidemiological features of the cohort of acute kidney injury following hump-nosed pit viper bites

Epidemiological feature	*Number (%)*
Age (y), median (range)	60 (25–93)
Sex	
Male	61 (79)
Female	16 (21)
Time of bite	
Day 0600-1759	50 (65)
Night 1800-0559	27 (35)
Site of bites	
Lower limb	50 (65)
Toes	11 (14)
Feet	36 (47)
Ankles	3 (4)
Upper limb	27 (35)
Fingers	20 (26)
Hands	5 (6)
Forearm	2 (3)
Places of bites	
Home gardens	28 (36)
Tea estates	17 (22)
Footpaths	14 (18)
Others	18 (24)
Time of bite to admission	
0–24 h	42 (55)
24–48 h	13 (17)
48–72 h	5 (6)
3–6 d	8 (10)
6–9 d	2 (3)
>9 d (late admissions)	7 (9)
Length of hospital stay	
1–10 d	31 (47)
11–20 d	21 (32)
21–30 d	8 (12)
>30 d	6 (9)
First aid measures	
Washing the bite sites	51 (66)
Ligation	35 (45)
Provoked bites	11 (14)
Native treatments	41 (53)
Education	
No	8 (10)
Less than Grade 5	22 (29)
Grade 5–11	37 (48)
Up to ordinary level examination	8 (10)
Up to advanced level examination	2 (3)
Occupation	
None	25 (32)
Farmers	15 (20)
Manual laborers	11 (14)
Gem miners	9 (12)
Others	17 (22)
Past medical history	
Hypertension	15 (20)
Diabetes mellitus	7 (9)
Ischemic heart disease	2 (3)
Not significant	54 (70)
Transferred from local hospital	45 (58)
Left against medical advice	2 (2)
Transfer to National Hospital, Sri Lanka	4 (5)

(0600–1759) on the lower limbs (n=50; 65%) in their home gardens (n=28; 36%). The length of hospital stay ranged from 2 to 47 d (median, 12 d; IQR, 6–18 d). In the non-TMA group, it was 2 to 39 d (median, 5 d; IQR, 3–9 d), whereas in the TMA group, it was 5 to 47 d (median, 15 d; IQR, 10–22 d). The duration from the day of bite to the first cycle of TPE was 4 d (IQR, 4–6 d).

Local pain was observed as mild (n=21; 27%), moderate (n=22; 29%), and severe (n=28; 36%). Local swelling was also graded as mild (n=17; 22%), moderate (n=37; 48%), and severe (n=17; 22%). Other local manifestations were necrosis at the site of bite (n=25; 33%), hemorrhagic blistering (n=20; 26%), bruising (n=16; 21%), lymphadenopathy (n=15; 20%), and local bleeding (n=8; 10%). Myalgia (n=27; 35%), thrombocytopenia (n=56; 73%), and microangiopathic hemolysis (n=57; 74%) were also found. In the whole group of AKI, VICC developed in 19 (25%) patients, and in the TMA group (n=52), VICC was observed in 18 (35%) patients. CKD was diagnosed in 19 (25%) patients in this AKI cohort from which, 16 (21%) were in TMA group [4 (5%) in TPE group and 12 (16%) in non-TPE group] and 3 (4%) were in non-TMA group.

Out of 77 patients, 52 (68%) fulfilled the criteria for the inclusion of TMA (TMA group). Of the patients who did not fulfill the criteria for TMA (non-TMA group), 4 had only thrombocytopenia and 5 had only MAHA. Four patients from the TMA group and 2 from the non-TMA group were lost to follow-up. Thus, 48 patients from the TMA group and 23 patients from the non-TMA group were available for the comparison of the outcome analysis. Two patients from the TMA group died on Days 4 and 35. The patient who died on Day 4 was excluded from the final outcome analysis because of inadequate data. Thus, 21 (45%) patients who underwent TPE and 26 (55%) who did not undergo TPE were available for the final analysis (Figure 2). The clinico-epidemiological features of the TPE and non-TPE groups are shown in Tables 2 and 3, respectively.

Comparison between the TMA and non-TMA groups (all patients with AKI) is shown in Table 4 and Figure 3. Patients who underwent TPE had significantly higher

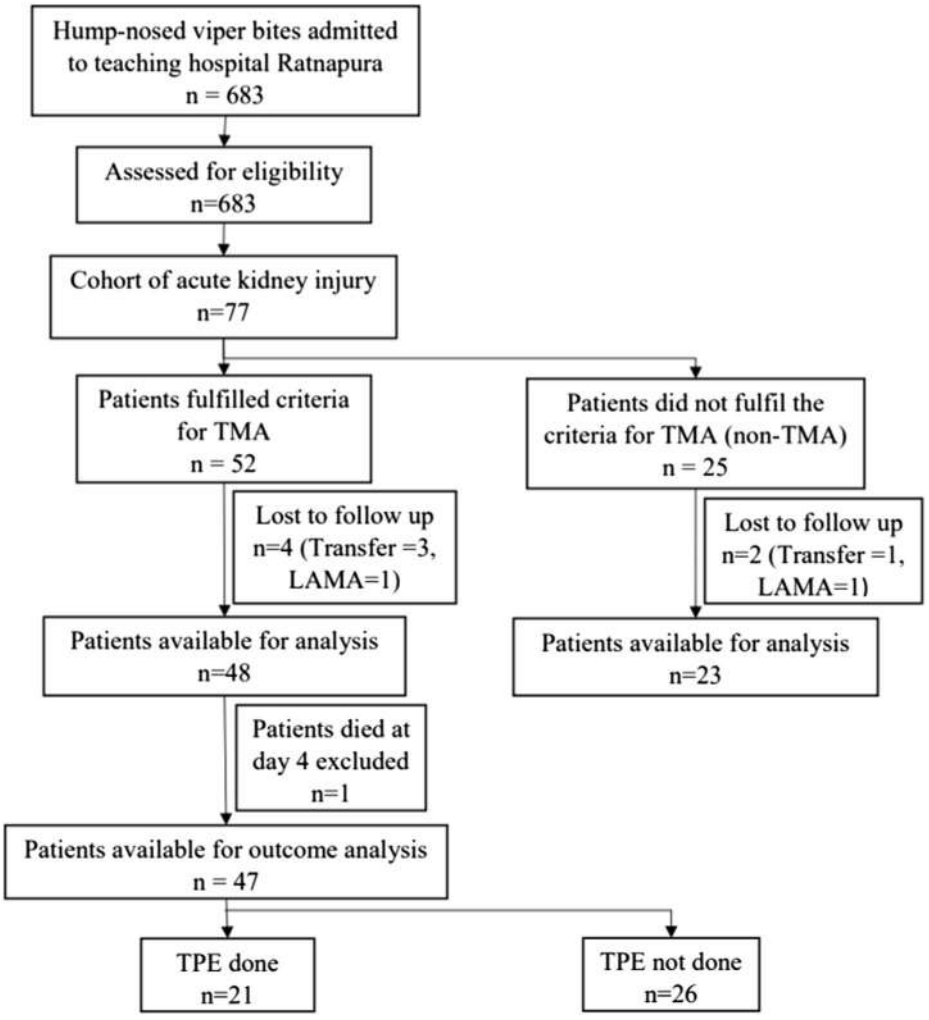

Figure 2. Flow chart of the study (52 patients with TMA vs 25 patients without TMA leading to acute kidney injury following hump-nosed pit viper bites). LAMA, left against medical advice; TMA, thrombotic microangiopathy; TPE, therapeutic plasma exchange.

blood transfusions than patients who did not undergo TPE. There were no significant associations between TPE and dialysis dependency at discharge, length of hospital stay, and number of dialysis cycles prior to discharge. Renal recovery depends on TPE (P=0.048) and the highest creatinine level (P=0.001). Multiple linear regression models were fitted to determine the exposure variables for number of blood transfusions and the number of dialysis cycles prior to discharge. A significant regression equation was found for the number of blood transfusions (P<0.000; R^2=0.56). The lowest Hb (P<0.001) and highest creatinine (P=0.026) levels significantly predicted the number of blood transfusions of the patients. However, TPE did not improve the number of blood transfusions of the patient (P=0.290) (Figure 4). The best model that predicted number of dialysis cycles prior to discharge was significant (P<0.000; R^2=0.56). Highest creatinine level, urine output, and hypertension significantly predicted the number of dialysis cycles prior to discharge. However, TPE was not associated with number of dialysis cycles prior to discharge.

Linear logistic models were fitted to determine the exposure variables for renal recovery and selected exposure variables. The best model predicting the renal recovery is summarized in Table 5. The goodness-of-fit test deviance (P=0.423), Pearson χ^2 test (P=0.444), and Hosmer-Lemeshow test (P=0.607) indicated that the model was adequate. According to the model, renal recovery could be significantly predicted by TPE (P=0.048) and the highest creatinine level (P=0.001) (Figures 5A and B). The best linear logistic model that predicted dialysis dependency at discharge is summarized in Table 6. The goodness-of-fit test deviance (P=0.774),

Table 2. Clinico-epidemiological features of thrombotic microangiopathy in the TPE group

Serial No.	*Species*	*Sex*	*Age (y)*	*Current illnesses*	*Site of bite*	*VICC*	*Type of TMA*	*TPE cycles*	*HD cycles prior to discharge*	*Dialysis dependency at discharge*	*Renal recovery*
11	*H hypnale*	Male	57	No	Finger	No	HUS	1	2	No	Yes
12	n/a	Male	38	No	Foot	Yes	HUS	4	9	No	Yes
14	*H hypnale*	Female	55	Diabetes, dyslipidemia	Foot	yes	TTP	1	5	No	No - CKD
15	n/a	Male	70	No	Thumb	No	HUS	3	7	No	Yes
16	*H hypnale*	Female	40	No	Foot	No	HUS	1	3	No	Yes
17	n/a	Male	66	Hypertension, dyslipidemia	Foot	No	HUS	6	11	Yes	No - CKD
18	n/a	Male	50	No	Finger	No	HUS	1	5	No	Yes
19	n/a	Male	50	No	Foot	No	HUS	3	6	No	Yes
24	n/a	Male	29	No	Foot	Yes	HUS	2	4	No	Yes
26	n/a	Female	59	No	Foot	Yes	HUS	1	8	No	Yes
27	n/a	Male	56	No	Toe	Yes	HUS	1	2	No	Yes
33	*H hypnale*	Male	68	No	Foot	No	HUS	2	7	No	Yes
34	n/a	Male	56	No	Foot	No	HUS	1	1	No	Yes
35	n/a	Male	68	No	Finger	Yes	HUS	1	1	No	Yes
36	n/a	Female	56	No	Finger	No	HUS	2	5	No	Yes
37	*H hypnale*	Male	56	No	Toe	No	HUS	1	15	Yes	Died on Day 35
40	n/a	Female	54	No	Foot	Yes	HUS	2	8	No	Yes
41	n/a	Male	64	No	Finger	No	HUS	3	19	Yes	No - CKD
42	n/a	Male	68	Asthma	Foot	Yes	HUS	3	9	Yes	No - CKD
44	n/a	Male	65	Hypertension, diabetes	Finger	No	HUS	2	3	No	Yes
47	*H hypnale*	Female	65	No	Foot	No	HUS	4	5	No	Yes

TMA, thrombotic microangiopathy; TPE, therapeutic plasma exchange; VICC, venom-induced consumption coagulopathy; HD, hemodialysis; n/a, not available; HUS, hemolytic uremic syndrome; TTP, thrombotic thrombocytopenic purpura; CKD, chronic kidney disease.

Pearson χ^2 test (P=0.676), and Hosmer-Lemeshow test (P=0.384) indicated that the model was adequate. The highest creatinine level significantly predicted the dialysis dependency at discharge (P=0.012) (Figures 5C and D), and there was no sufficient evidence to show an association between TPE and dialysis dependency at discharge (P=0.597). Further, TPE significantly improved the time to platelet correction, time to the initiation of microangiopathic hemolysis correction, time to PT/INR correction, and time to WBCT20 correction (Table 7 and Figure 6). We did not observe any adverse reaction related to TPE, including FFP transfusion in any patient of this cohort.

Discussion

In the current study, the prevalence of AKI and TMA were 11% and 8% of all HNPV bites, respectively. These manifestations are caused by both *H hypnale* and *H zara* in different frequencies. TMA following snakebites is a rare complication; in Sri Lanka and India, it is caused by Viperidae snakes, including HNPV[2–5,10,11,26,27] and Russell's viper.[15,28–31] Envenoming by some non–Sri Lankan species may also cause TMA; these include Australian elapids such as several species of Australian brown snakes (*Pseudonaja spp*),[32] a common tiger snake (*Notechis scutatus*),[16] and coastal taipan (*Oxyuranus scutellatus*).[17] Snakebite is an important cause of morbidity and mortality in tropical and subtropical countries, where there are many deadly venomous snakes.[1] It is also an occupational hazard, mostly affecting the agricultural regions. The ideal therapy for snakebite envenoming is antivenom specific to the species that inflicted the bite. However, these antivenoms are not available in every country for even some of the most medically important species. Another important consideration is the high risk of adverse side effects, including anaphylaxis, that are associated with some antivenoms.[33] Therefore, alternatives to

Table 3. Clinico-epidemiological features of thrombotic microangiopathy in the non-TPE group

Serial No.	*Species*	*Sex*	*Age (y)*	*Past medical history/Current illnesses*	*Site of bite*	*VICC*	*Type of TMA*	*HD cycles prior to discharge*	*Dialysis dependency at discharge*	*Renal recovery*
1	*H hypnale*	Male	69	Hypertension	Toe	No	TMA	No	No	Yes
2	*H hypnale*	Male	25	No	Foot	No	TMA	No	No	Yes
3	*H hypnale*	Male	48	No	Foot	No	TMA	No	No	Yes
4	n/a	Male	52	Gastritis	Foot	No	HUS	3	No	Yes
5	n/a	Male	58	No	Finger	No	HUS	5	No	Yes
6	*H hypnale*	Female	57	Asthma	Toe	No	HUS	7	No	No - CKD
7	*H hypnale*	Male	74	No	Forearm	No	HUS	7	No	No - CKD
8	n/a	Female	65	Hypertension	Toe	No	HUS	3	No	No - CKD
9	*H hypnale*	Male	74	hypertension	Foot	No	HUS	15	Yes	No - CKD
10	n/a	Male	63	Diabetes	Foot	No	HUS	2	Yes	No - CKD
13	*H hypnale*	Male	59	No	Foot	Yes	HUS	No	No	Yes
20	*H hypnale*	Female	39	No	Foot	No	HUS	2	No	Yes
21	*H hypnale*	Male	72	Hypertension, dyslipidemia, ischemic heart disease	Finger	No	HUS	10	No	No - CKD
22	n/a	Male	69	No	Foot	Yes	HUS	7	No	Yes
23	n/a	Male	44	No	Finger	No	HUS	10	Yes	No - CKD
25	*H zara*	Male	65	No	Foot	Yes	HUS	9	Yes	No - CKD
28	*H hypnale*	Male	56	No	Finger	Yes	TMA	No	No	Yes
29	*H hypnale*	Male	66	No	Foot	Yes	TTP	2	n/a	Died on Day 4
30	n/a	Male	49	No	Foot	No	HUS	9	No	No - CKD
31	n/a	Male	32	No	Finger	No	HUS	9	No	No - CKD
32	*H hypnale*	Male	70	No	Hand	Yes	TMA	No	No	Yes
38	n/a	Male	43	No	Ankle	No	HUS	2	No	Yes
39	n/a	Male	50	No	Big toe	No	TMA	No	No	Yes
43	*H hypnale*	Male	62	Diabetes	Big toe	Yes	TMA	No	No	Yes
45	n/a	Male	62	No	Toe	Yes	TMA	No	No	Yes
46	n/a	Male	65	Hypertension, diabetes, asthma	Toe	Yes	HUS	16	Yes	No - CKD
48	n/a	Male	75	No	Hand	No	HUS	6	No	No - CKD

TPE, therapeutic plasma exchange; VICC, venom-induced consumption coagulopathy; TMA, thrombotic microangiopathy; HD, hemodialysis; HUS, hemolytic uremic syndrome; n/a, not available; CKD, chronic kidney disease; TTP, thrombotic thrombocytopenic purpura.

antivenom, when unavailable, can comprise an essential approach to managing seriously envenomed patients. One such option is TPE; however, because of the mixed evidence concerning this intervention, TPE should be considered on a case-by-case basis for life-threatening envenoming when antivenom is not available.

In the current study, the length of hospital stay, number of blood transfusions, number of dialysis sessions prior to discharge, VICC, and laboratory findings such as highest creatinine, lowest Hb, lowest platelet count, highest total bilirubin and highest serum glutamic-oxaloacetic transaminase/serum glutamic-pyruvic transaminase levels were higher in patients in the TMA group than in those in the non-TMA group. Patients in the TMA group needed more blood transfusions, more dialysis cycles, and lengthier hospital stay. Also, more patients in the TMA group had VICC, myalgia, anuria, and oliguria. Patients in the non-TMA group had less severe laboratory findings related to platelet counts, Hb, creatinine, total bilirubin, and liver enzymes. These findings are compatible with Indian studies regarding snakebite-associated TMA.[20,34] Renal recovery and dialysis dependency at discharge were not different in both the TMA and non-TMA groups (Table 4). This is because, in the current study, all patients in the non-TMA group had AKI, and some of these patients (4%) progressed to

Table 4. Comparison of the TMA group (n=48) and the non-TMA group (n=23)

Epidemiological, clinical, and laboratory parameters	*TMA group*	*Non-TMA group*	P *value*
Age (y), median (IQR)	59 (50–66)	64 (50–69)	0.168
Sex			
Male, n (%)	39 (81)	17 (74)	0.541
Female, n (%)	9 (19)	6 (26)	0.541
Time of bites			
Day 0600–1759, n (%)	33 (69)	12 (52)	0.175
Night 1800–0559, n (%)	15 (31)	11 (48)	0.175
Site of bites			
Lower limb, n (%)	33 (69)	12 (52)	0.175
Upper limb, n (%)	15 (31)	11 (48)	0.175
Late admissions, n (%)	2 (4)	4 (17)	0.082
First aid measures			
Washing the bite sites n (%)	34 (71)	12 (52)	0.123
Ligation, n (%)	25 (52)	7 (30)	0.086
Previous snakebites, n (%)	11 (23)	4 (17)	0.759
Current medical illnesses			
Diabetes, n (%)	5 (10)	2 (9)	1
Hypertension, n (%)	6 (12)	7 (30)	0.100
Native treatments, n (%)	28 (58)	9 (39)	0.130
Length of hospital stay, median (IQR)	15 (10–22.5)	5 (3–8.75)	0.000
No. of dialyses prior to discharge, median (IQR)	5 (2–8.75)	0 (0–2.25)	0.000
No. of blood transfusions, median (IQR)	1 (0–2.75)	0 (0–1)	0.001
Dialysis dependency at discharge, n (%)	9 (19)	2 (10)	0.483
Renal recovery, n (%)	31 (65)	18 (82)	0.144
Clinical features			
Local pain, n (%)			
No pain	2 (4)	3 (13)	0.221
Mild	12 (25)	6 (26)	0.221
Moderate	13 (27)	7 (30)	0.221
Severe	21 (44)	7 (30)	0.221
Local swelling n (%)			
No swelling	2 (4)	3 (13)	0.185
Mild	11 (23)	4 (17)	0.185
Moderate	22 (46)	14 (61)	0.185
Severe	13 (27)	2 (9)	0.185
Blistering, n (%)	13 (27)	5 (22)	0.628
Necrosis, n (%)	17 (35)	6 (26)	0.432
Local bleeding, n (%)	5 (10)	3 (13)	0.708
Lymphadenopathy, n (%)	9 (19)	4 (17)	1.0
Bruising, n (%)	8 (17)	7 (30)	0.184
Myalgia, n (%)	20 (42)	4 (17)	0.043
Urine output n (%)			
Anuria	15 (31)	1 (4)	0.024
Oliguria	25 (52)	14 (61)	0.024
Normal urine output	8 (17)	8 (35)	0.024
Venom-induced consumption coagulopathy, n (%)	17 (35)	1 (4)	0.005
Laboratory finding			
Lowest platelet count, (10^9 L^{-1}), median (IQR)	63 (38–92)	233 (163–285)	0.000
Lowest hemoglobin ($g \cdot dL^{-1}$), median (IQR)	7.5 (6.4–8.6)	10.3 (7.1–11.8)	0.000
Highest creatinine ($\mu mol \cdot L^{-1}$), median (IQR)	646 (482–902)	324 (123–835)	0.026
Highest potassium ($mmol \cdot L^{-1}$), median (IQR)	5 (4.4–5.5)	4.6 (4.2–5.2)	0.238
Highest blood urea ($mg \cdot dL^{-1}$), median (IQR)	20 (15–28)	17 (8–25)	0.115
Highest SGOT/AST ($IU \cdot L^{-1}$), median (IQR)	74 (39–152)	31 (22–54)	0.001

(continued on next page)

Table 4 *(continued)*

Epidemiological, clinical, and laboratory parameters	*TMA group*	*Non-TMA group*	P *value*
Highest SGPT/ALT ($IU \cdot L^{-1}$), median (IQR)	49 (28–79)	24 (14–40)	0.002
Highest total bilirubin ($mg \cdot dL^{-1}$), median (IQR)	21 (12–50)	7 (4–11)	0.000
Highest sodium ($mmol \cdot L^{-1}$), median (IQR)	141 (138–148)	142 (138–144)	0.820

TMA, thrombotic microangiopathy; IQR, interquartile range; SGOT, serum glutamic-oxaloacetic transaminase; AST, aspartate aminotransferase; SGPT, serum glutamic-pyruvic transaminase; ALT, alanine transaminase.

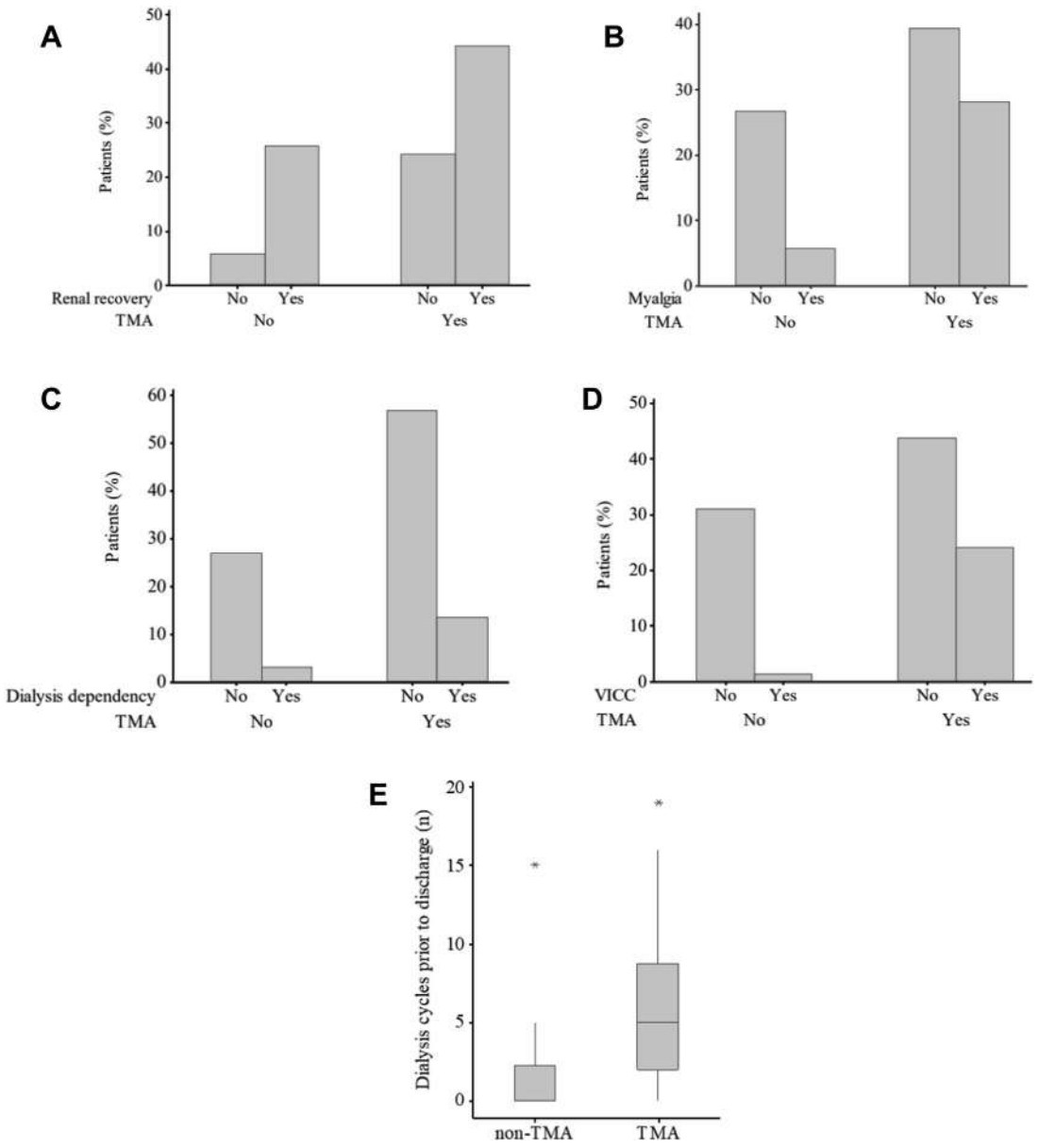

Figure 3. Comparison of TMA and non-TMA groups: A, Renal recovery; B, Myalgia; C, Dialysis-dependent at discharge; D, VICC; E, Number of dialysis cycles prior to discharge. TMA, thrombotic microangiopathy; VICC, venom-induced consumption coagulopathy.

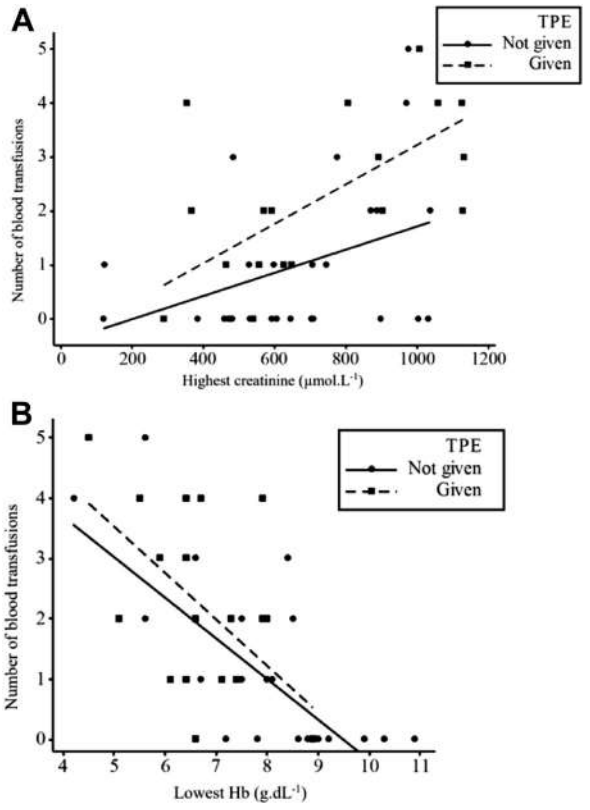

Figure 4. Effects of the highest creatinine and lowest Hb levels on the number of blood transfusions in the TPE and non-TPE groups. Hb, hemoglobin; TPE, therapeutic plasma exchange.

CKD. These findings are compatible with those of a study conducted in Sri Lanka.[15] It was evidenced that both patients with TMA and AKI following HNPV bites may progress to CKD.[3,21]

Days to platelet correction, days to starting the correction of microangiopathic hemolysis, and days to PT/INR and WBCT20 correction were significantly lower in the TPE group than in the non-TPE group (Table 7), which conveys the effectiveness of TPE in the early correction of TMA. However, a previous systematic review concluded that TPE is not effective for TMA.[15,18] The time lapse from snakebite to the first cycle of TPE is a very crucial factor when assessing the effectiveness of TPE. This should be as short as possible because when the time goes on, kidney damage is possible because the envenoming-induced kidney damage is progressive and the resulting damage cannot be reversed by any procedure. In the current study, this median time lapse was 4 d, and our outcomes such as dialysis dependency at discharge, length of hospital stay, and the number of dialysis cycles prior to discharge might be improved if the first TPE cycle could have been performed within 2 to 3 d of snakebite. Therefore, from our perspective, in order to optimize the efficacy of TPE, it should be performed within the shortest possible time following the snakebite. Unfortunately, some patients are initially directed to native treatment and get late admission to the hospital. Out of the 2 groups in the current study, the non-TPE group included more individuals with chronic potentially vasculopathic diseases (hypertension and diabetes) and older age, which could have skewed the results in favor of the TPE group. Even though theoretically there is a potential risk of using TPE because of its adverse effects such as hypotension and allergic reactions, we did not observe any of them in this study. The disadvantages of TPE are that it is costly and needs experienced hands to perform. In the current study, the improvement of PT/INR and a rising trend of platelet counts were the treatment endpoint of TPE.

Limitations

There were some limitations of the current study; the sample size (n=47) was small, the study recruitment was non-randomized, and TPE was offered to patients with more severe disease who were nonresponsive to the standard treatments. This adds a bias to the study. Also, it is important to reinforce that when the use of TPE is considered, risk vs

Table 5. Statistics of renal recovery

Source	*Coefficient*	*Deviance*	P *value*	*Odds ratio*	*95% Confidence interval*
Regression		16.128	0.001		
Constant	7.64				
Highest creatinine	−0.00546	12.106	0.001	0.99	(0.99−1.0)
Age (y)	−0.0597	3.170	0.075	0.94	(0.88−1.0)
TPE	1.560	3.908	0.048	4.76	(0.90−25)
Error		44.156			
Total		60.284			

TPE, therapeutic plasma exchange.

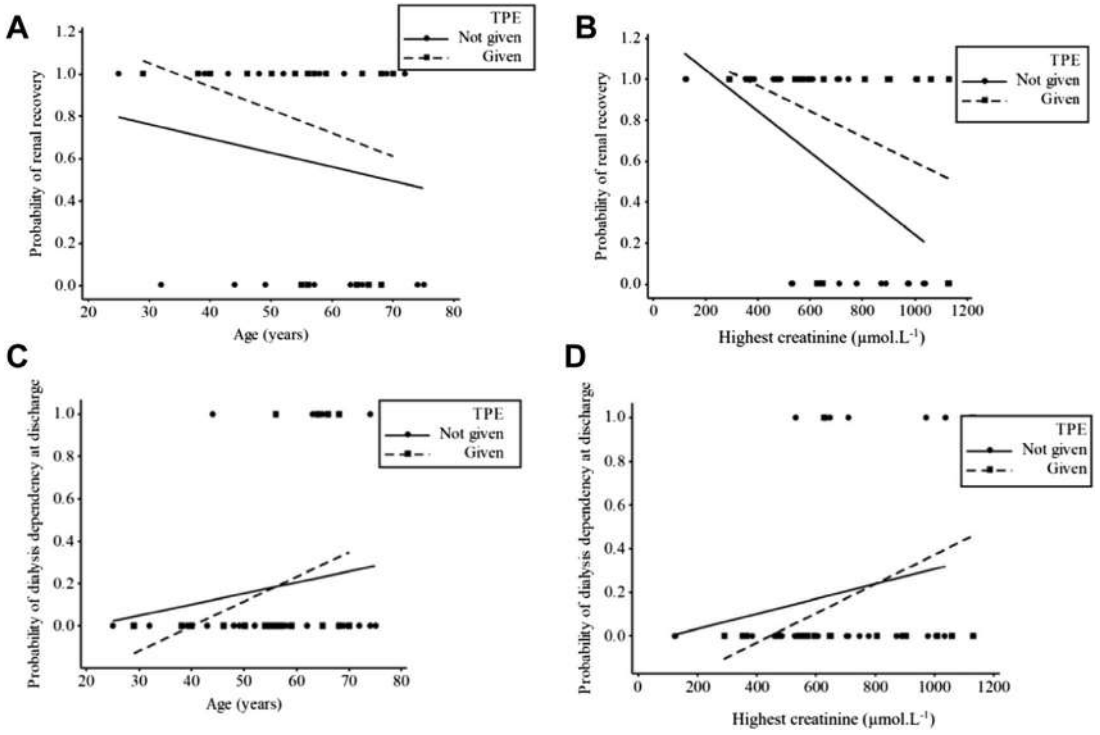

Figure 5. Effects of age and highest creatinine level on renal recovery and the probability of dialysis dependency at discharge in the TPE and non-TPE groups. TPE, therapeutic plasma exchange.

Table 6. Statistics of dialysis dependency at discharge

Source	*Coefficient*	*Deviance*	P *value*	*Odds ratio*	*95% Confidence interval*
Regression		9.205	0.010		
Constant	−9.18				
Highest creatinine	0.00439	6.350	0.012	1.0	(1.0−1.01)
Age	0.0728	3.457	0.063	1.08	(0.99−1.17)
Error		36.702			
Total		45.907			

Table 7. Summary of survival analysis

Variable (d)	*TPE group, median (IQR)*	*Non-TPE group, median (IQR)*	P *value (log-rank test)*
Time to platelet correction	4 (4−5)	7 (5−9)	0.009
Time to initiation of correction of microangiopathic hemolysis	5 (4−3)	7 (6−9)	0.004
Time to PT/INR correction	1 (1−2)	3 (3−4)	0.003
Time to WBCT20 correction	2 (1−2)	3 (2−3)	0.020

TPE, therapeutic plasma exchange; IQR, interquartile range; PT, prothrombin time; INR, international normalized ratio; WBCT20, 20 min whole blood clotting test.

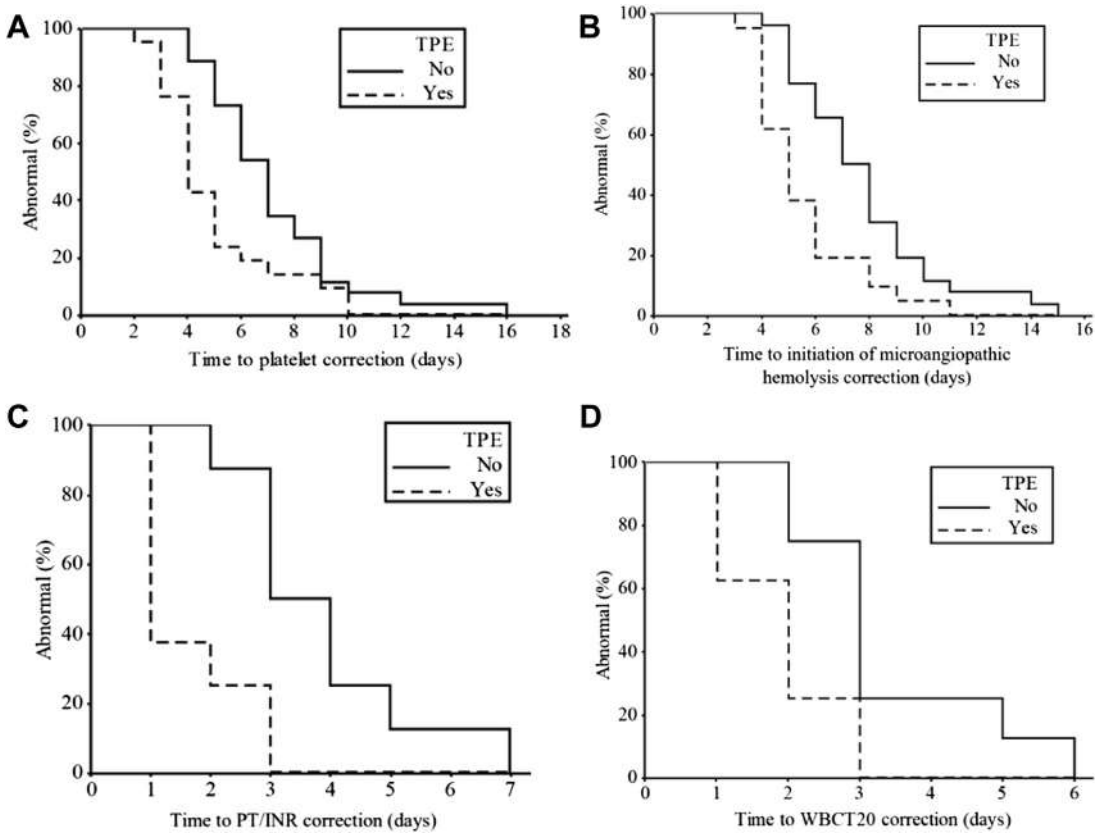

Figure 6. Survival plots for the TPE and non-TPE groups: A, time to platelet correction; B, time to initiation of microangiopathic hemolysis correction; C, time to PT/INR correction; D, time to WBCT20 correction. INR, international normalized ratio; PT, prothrombin time; TPE, therapeutic plasma exchange; WBCT20, 20 min whole blood clotting test.

benefit must be carefully assessed on a patient-by-patient basis. Further, randomized controlled trials may be needed in the field to generate more evidence.

Conclusions

Among our small sampling of patients, TPE was effective in the early correction of platelet counts, microangiopathic hemolysis, PT/INR, and WBCT20 for HNPV envenoming complicated with TMA. Renal recovery was associated with both TPE and creatinine level. However, dialysis dependency at discharge, length of inpatient management, and the number of dialysis cycles prior to discharge are not improved by TPE. Further, dialysis dependency at discharge depends on the highest creatinine level. While among this series of patients TPE was deemed beneficial, further evidence is required in order to support the use of this intervention in patients with similar clinical presentations.

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Author Contributions: patients' management and literature search (RMMKNR, PEANR); snake handling and obtaining their morphological features (RMMKNR); statistical analysis (KS, RMMKNR); drafted the first manuscript (RMMKN, SAMK, PEANR); reading of final manuscript (RMMKN, SAMK, PEANR, KS); approval of final manuscript (RMMKN, SAMK, PEANR, KS).

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CLINICAL TOXINOLOGY SPECIAL SECTION

CASE REPORT

Hump-Nosed Pit Viper Envenomation in Western Coastal India: A Case Series

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The hump-nosed pit viper (HNPV) has historically been considered less medically significant, causing local envenomation, renal injury, and coagulopathy; however, now, it is known to cause life-threatening complications. We describe the clinical presentation, treatment, and complications of 3 confirmed HNPV bites from the state of Karnataka (southwest coastal India). Patient 1, an 88-y-old woman, reported with the live specimen and developed venom-induced consumption coagulopathy (VICC) and thrombotic microangiopathy leading to acute kidney injury requiring blood product transfusions and dialysis. Patient 2, a 60-y-old woman, reported 3 d after envenomation followed by treatment at another hospital where 30 vials of polyvalent anti-snake venom (ASV) were given. She developed VICC and acute kidney injury requiring dialysis. On Day 9 of treatment, she developed a pontine hemorrhage. She died after a transfer to another treatment center closer to her residence. Patient 3, a 25-y-old man, was brought to our emergency department 6 h after being envenomed. He received topical ayurvedic treatment before arrival. He was unconscious and found to have severe VICC with a massive middle cerebral artery infarct. All 3 patients received Indian polyvalent ASV, which does not cover HNPV envenomation, clearly demonstrating the absence of paraspecificity and neutralization in a clinical setting. To our knowledge, *Hypnale hypnale* envenomation has not previously been reported from Karnataka state. The diagnosis of HNPV envenomation in a country without snake venom detection kits, under-reporting despite serious complications, financial burdens on rural populations afflicted, and poor outcomes due to the lack of a specific antivenom are discussed.

Keywords: snakebite, *Hypnale hypnale*, anti-snake venom, venom-induced coagulopathy, acute kidney injury, stroke

Introduction

The hump-nosed pit viper (HNPV) is a venomous snake inhabiting Sri Lanka and the Western Ghats of India. Three species are known, *Hypnale hypnale*, *Hypnale zara*, and *Hypnale nepa*, of which only *H hypnale* is found in India.[1] Earlier believed to cause only local envenomation, it is now known to cause severe systemic toxicity and mortality.[2-4] HNPV envenomation is under-reported in India. Identification of the culprit species often does not occur, and physicians are commonly uninformed about the biodiversity of regional herpetofauna, thereby adding to the paucity of data. Limited awareness about the specificity and clinical effectiveness of locally available antivenoms may subject the envenomed patient to ineffective treatment and unnecessary risk. We report the cases of 3 patients with *H hypnale* envenoming who presented to our emergency department and the associated concerns about treating patients affected by envenoming by this species in India.

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Case Report

All 3 cases were managed in the emergency department and emergency intensive care unit by the authors and therefore identified for this report; evidence for

identification was either the dead or live specimen or a photograph of the snake being produced by the family members. The specimens were identified on the basis of their morphology by an emergency physician (one of the authors, FMS) with expertise on venomous snakes in the region. The medical record file numbers were identified through the emergency department registers. An application for permissions to study the files and the electronic medical records of the patients was submitted to the institutional ethics committee. After approval, the files and electronic medical records were reviewed and data collected on a case proforma. Radiographic images and laboratory data were extracted. Informed consent was obtained from each patient/family to collect images at the time of presentation and further for the use of the images. Polyvalent anti-snake venom (ASV) used in these patients was produced by Bharat Serums Pvt Ltd. When reconstituted, each vial contains 10 mL; the manufacturer provides the following venom neutralization: 0.6 mg of *Naja naja* venom/mL of ASV, 0.45 mg of *Bungarus caeruleus* venom/mL of ASV, 0.6 mg of *Daboia russelli* venom/mL of ASV, and 0.45 mg of *Echis carinatus* venom/mL of ASV. This polyvalent ASV is not manufactured to neutralize the venom of *H hypnale* and is completely ineffective against it.

CASE 1

An 88-y-old woman with no known comorbidities was bitten on her right hand while she was working in the garden. A glycerin magnesium sulfate dressing was applied to the bitten limb (Figure 1A). The snake was captured and brought to the hospital and was identified as an HNPV (Figure 1B). She was administered 38 vials of ASV in 4 separate infusions over the course of her treatment despite knowing that no ASV manufactured anywhere in the world specifically neutralizes HNPV venom. She developed hypotension during the first infusion, which was treated with antihistamines and adrenaline for anaphylactic shock. The second and third doses administered on Day 1 were given at 125 $mL{\cdot}h^{-1}$, whereas the last dose of 8 vials was given at 40 $mL{\cdot}h^{-1}$. She was found to have thrombocytopenia and anemia. A peripheral smear showed schistocytes, while coagulation and renal parameters, which were normal on Day 1, showed a progressive decline from the second day. She remained anuric until discharge. She underwent 3 cycles of saline hemodialysis: 1.5 h on Day 1, 3 h on Day 3, and 4 h on Day 4. Owing to the persistent coagulopathy, she received 1 packed red blood cell and 10 fresh frozen plasma transfusions (Table 1, Case 1). She was discharged against medical advice, with persistent acute

Figure 1. A, Bitten index finger of the right hand. B, Live culprit snake. Specimen location: Karkala (13.2151°N, 74.9962°E). Approximate distance from the hospital: 33.8 km.

Table 1. Coagulation parameters, renal function, and treatment administered based on the findings of cases 1, 2, and 3

Time	*PT, s (reference range, 9.6–12.5 s)*	*INR (reference range, 0.8–1.1)*	*aPTT, s (reference range, 26.8–33.2 s)*	*Serum creatinine, mg·dL^{-1} (reference range, 0.7–1.2 mg·dL^{-1})*	*Treatment*
			Case 1		
4 h	11.8	1.1	31.3	1.1	10 vials ASV
15 h	24	2.3	30.2	n/a	10 vials ASV
23 h	38.2	3.8	28.2	2	10 vials ASV, 2 FFP, HD
Day 3	40.5	4.0	28.3	2.9	8 vials ASV, 4 FFP
Day 3	18.8	1.8	27.9	n/a	n/a
Day 4	31	3.0	28.3	4.1	4 FFP, 1 PRBC, HD
Day 5	27.2	2.6	26.5	3.7	HD
			Case 2		
Day 3	19.3	1.8	26	5.5	30 vials ASV
Day 4	n/a	n/a	n/a	7.0	4 FFP
Day 5	n/a	n/a	22.1	4.8	4 FFP, 2 HD, 4 vials ASV
Day 6	11.9	1.1	22.1	2.6	5 FFP, HD
Day 7	n/a	n/a	n/a	2.4	HD
Day 8	n/a	n/a	n/a	5.1	5 FFP
Day 9	n/a	n/a	n/a	3.5	HD
Day 10	18	1.7	28.2	3.4	HD
Day 11	n/a	n/a	n/a	5.0	n/a
Day 12	n/a	n/a	n/a	5.2	n/a
			Case 3		
9 h	>120	n/a	>120	1.4	20 vials ASV
14 h	>120	n/a	>120	n/a	7 CRYO, 4 FFP, 10 vials ASV
18 h	>120	n/a	29.8	1.2	2 FFP
22 h	18.3	1.8	25.7	n/a	n/a
28 h	22.9	2.2	25.4	n/a	n/a

PT, prothrombin time; INR, international normalized ratio; aPTT, activated partial thromboplastin time; n/a, not available/not done; ASV, anti-snake venom; FFP, fresh frozen plasma; HD, saline hemodialysis; PRBC, packed red blood cell; CRYO, cryoprecipitate.

kidney injury and coagulopathy. On telephonic follow-up, no clinical symptoms of renal dysfunction or bleeding diathesis were reported.

CASE 2

A 60-y-old woman, a known hypertensive on 5-mg amlodipine once daily with no other comorbidities, was bitten by an HNPV (Figure 2A) while working in her garden, after which she developed signs of envenomation. She was taken to a local hospital on Day 2, where she was administered 30 vials of ASV. She developed anuria and vomiting because of which she was referred to our center on Day 3; she was found to have mild coagulopathy, thrombocytopenia, and deranged renal parameters for which hemodialysis was initiated with fresh frozen plasma transfusions (Table 1, Case 2). She was administered an additional 4 vials of ASV. On Day 9, she developed sudden-onset altered mental status after undergoing dialysis; a plain computed tomography scan of her brain showed a large pontine bleed (Figure 2B). The patient was discharged against medical advice on mechanical ventilation and was hemodynamically unstable. The family's decision was due to an evidently poor outcome and increasing costs of care. On follow-up, she had passed away at a local hospital with minimal critical care.

CASE 3

A 25-y-old man with no known comorbidities or atopy was brought to the emergency department with an alleged history of snakebite 6 h before admission; after the bite, he had an episode of loss of consciousness and altered mental status. The patient received ayurvedic treatment (Figure 3A) and later was evaluated at a local hospital before being referred to our hospital for further treatment. In the emergency department, he was intubated owing to a low Glasgow Coma Scale score (E1V1M5) and was found to have severe coagulopathy with a prothrombin time of >120 s. Treatment with polyvalent ASV was immediately started; however, anaphylaxis developed in

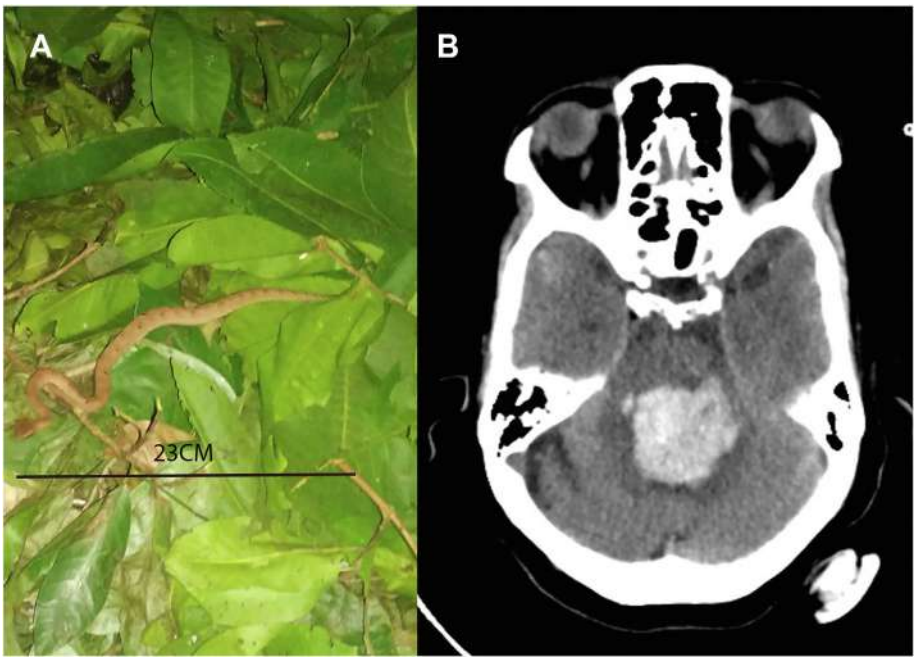

Figure 2. A, Photographic evidence of the culprit snake. Specimen location: Kundapura (13.6235°N, 74.6917°E). Approximate distance from the hospital: 61.2 km. B, Computed tomography scan of the brain showing pontine bleed.

him, for which antihistamines and adrenaline were administered. Treatment with ASV was restarted once he stabilized. On further evaluation, he was found to have right-sided hemiparesis. A plain computed tomography scan of the brain was obtained, which revealed a massive left middle cerebral artery territory infarct with cerebral edema (Figure 3B). A neurosurgical opinion was taken to consider decompressive craniotomy. In spite of 30 vials of ASV transfused, there was no improvement. Initially suspected to be a Russell viper bite on the basis of the syndrome, it was later identified as an HNPV envenomation on the basis of the lack of response to ASV and the identification of the specimen, which was later found and produced (Figure 3C). The family members were requested to locate and bring the killed specimen, which had been discarded at the location where the bite occurred. Therefore, further doses of ASV were withheld. Measures to control the brain edema (mannitol, blood pressure control, and head end elevation) were initiated, and antiplatelet therapy was withheld because of the coagulopathy. A decompressive craniotomy was considered, in view of the raised intracranial pressure and significant midline shift; however, it would be considered only after correction of the coagulopathy. Owing to the unresolved venom-induced consumption coagulopathy (VICC), which showed no response to 30 vials of ASV, cryoprecipitate and fresh frozen plasma were administered, after which the international normalized ratio improved to 2.24 (Table 1, Case 3). However, the family members were not willing to consent to a craniotomy in view of a poor prognosis and high risk of death and requested that the patient be discharged against medical advice. The family members took the patient home. No further in-hospital care was provided.

Discussion

In the Western Ghats, there is no antivenom available for several species of medically important venomous snakes, including the HNPV (*H hypnale*), Malabar pit viper (*Craspedocephalus malabaricus*), bamboo pit viper (*Craspedocephalus gramineus*), large-scaled pit viper (*Craspedocephalus macrolepis*), and king cobra (*Ophiophagus hannah*).[5,6] In a proteomic study, the investigators reported that monovalent *Calloselasma rhodostoma* (Malayan pit viper) ASV from Thai Red cross partially neutralized HNPV venom in vitro. They also reported that HNPV venom is geographically variable, emphasizing the need for venom analysis of *H hypnale* occurring in southwest coastal India.[7,8]

Syndromic similarities of juvenile Russell viper, saw-scaled viper, and HNPV envenomation pose a challenge.[9] The absence of a regionally specific molecular diagnostic kit to differentiate envenomations from a region is a burden of great significance.[10] Delayed onset of

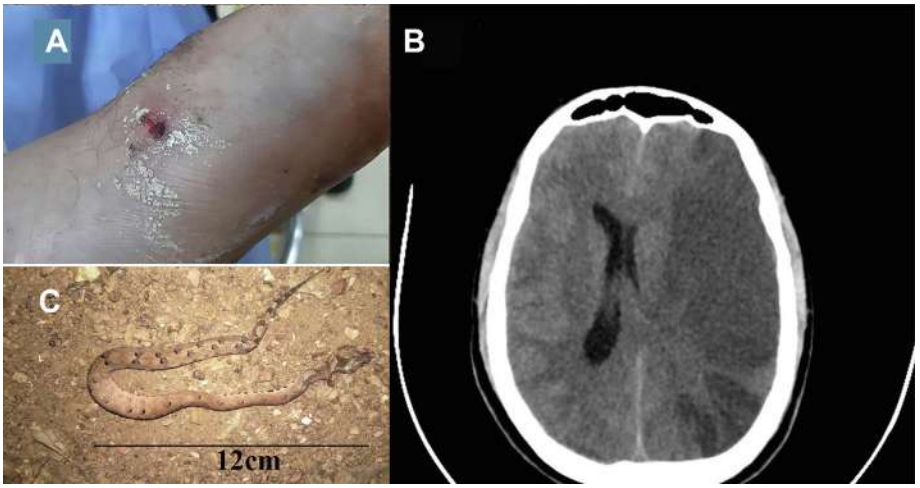

Figure 3. A, Bite site showing fang marks with oozing blood. B, Computed tomography scan of the brain showing large middle cerebral artery territory infarct with midline shift. C, Photographic evidence: snake killed and photographed. Specimen location: Bhatkal (13.9993°N, 74.5408°E). Approximate distance from the hospital: 93 km

coagulopathy, as seen in Patients 1 and 2, is common and may not be detected by a 20-min whole blood clotting test.[11] Public awareness about capturing photographic evidence to aid physicians in the treatment of snakebites is variable. In some communities, an offending snake is burned and buried. In Case 1, the live snake was produced at the hospital—apart from identification, the snake had to be held captive and later released. The family members of the patient in Case 2 produced a low-quality image of the culprit snake but with just enough detail for a morphological identification. In Case 3, the culprit snake was killed but no photographs were taken and the snake was not brought to the hospital; the family members had to travel 93 km one way to retrieve the decaying and damaged specimen for identification, by which time standard therapeutic measures were complete.

HNPV envenomation shows some clinical features that are common to *D russelli*, *E carinatus*, *and C malabaricus*.[9] Common to all 4 are VICC and cellulitis or edema of the bitten part. Acute kidney injury is common in Russell viper and HNPV envenomation and rare in saw-scaled viper bites. The time of onset and progression of coagulopathy and acute kidney injury is variable, which can be hours, as seen in Case 3, and days, as in Case 1.[11] Thrombotic microangiopathy, seen in Patients 1 and 2, is a known complication of HNPV envenomation.[12] Patient 1 developed severe renal dysfunction but eventually improved and was free of symptoms after discharge. Patient 2 developed renal injury requiring hemodialysis and, on Day 9, developed a pontine hemorrhage. VICC may increase the incidence of hemorrhagic stroke in patients, especially those with risk factors, such as hypertension, which was present in this case. Patient 3, a young man with no comorbidities, developed a massive ischemic stroke within hours of being bitten. As the evidence of the culprit snake was initially unavailable, 30 vials of ASV were administered but clearly did not lead to improvement in coagulopathy, demonstrating ineffective neutralization of the circulating venom. The venom of HNPV contains phospholipases, C-type lectins, and L-amino acid oxidases, which are anticoagulants; however, it also contains thrombin-like enzymes that can cause thrombotic effects such as ischemic stroke.[13,14]

Local, vascular, hematological, cardiac, direct neurotoxicity, ischemic stroke, pulmonary, and renal manifestations have been described with regard to HNPV bites.[3,12,14-18] However, the frequency of systemic manifestations from India is more than that from Sri Lanka.[19] Coagulopathy was common with *H hypnale* compared with *H zara* and *H nepa*.[17] Only *H hypnale* is found in India, which may explain the higher incidence of systemic toxicity. Other known complications associated with *H hypnale* bites include ischemic and hemorrhagic stroke, acute coronary syndrome and toxic myocarditis, atrial fibrillation, and seizures.[14,20-22]

None of the 3 patients responded to Indian polyvalent ASV. ASV is often administered because of a delay in the identification of the species (as in Case 3). It is clear in all

the 3 cases that administration of Indian polyvalent ASV may actually do more harm than good in HNPV envenomation.[23] Coagulopathy may be corrected with blood products in the presence of life-threatening bleeding manifestations, although the addition of clotting factors may result in an increase of systemic clot burden without prior neutralization of the venom.[24] Severe life-threatening VICC detected early may be treated with therapeutic plasma exchange and replacement of coagulation factors because of the absence of any antivenom. It is associated with a high risk of complications along with limited clinical benefit.[25,26]

In general, *Hypnale* envenomation is not widely known, resulting in under-reporting and delayed hospitalization. There is a preference for alternative medicine, as seen in Case 3. The economic burden on rural populations is high, which is highlighted in these cases, in which premature discharge was taken in Cases 1 and 3. Patients 2 and 3 required prolonged critical care with poor outcomes. Healthcare schemes for farmers and populations at risk can be customized to include therapeutics such as hemodialysis, therapeutic plasma exchange, and surgical interventions in some complex cases of snakebite so that discharges against medical advice and resultant tragic outcomes are avoided.

Conclusions

There is a need for *H hypnale* antivenom. In the interim, treatment including transfusion of blood products and plasmapheresis may be considered in severe cases only. The delayed onset of systemic manifestations warrants observation and frequent evaluation over 48 to 72 h. Involvement of the primary care system in the monitoring of such patients with 20-min whole blood clotting test or prothrombin time with international normalized ratio tests and renal function tests should be considered, particularly in rural and remote regions to identify cases with delayed systemic envenomation. Identification of the culprit snake must not be missed wherever possible. HNPV envenomation may result in complications such as VICCs, strokes, and thrombotic microangiopathy with acute kidney injury.

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Author Contributions: original draft of manuscript, imaging of snakes and bite site, identification of snakes, institutional ethics committee approval (FMS); draft of manuscript, review, and editing (VL); critical review of manuscript (JMB); approval of final manuscript (FMS, VL, JMB).

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CLINICAL TOXINOLOGY SPECIAL SECTION

CASE REPORT

Hybrid Blood Purification in the Treatment of Multiple Organ Dysfunction Syndrome Following a Wasp Attack

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Severe wasp sting symptoms can progress rapidly, often causing multiple organ dysfunction syndrome (MODS) and, in some cases, even death. Early and comprehensive treatment is needed to avoid these outcomes. Here, we report the case of a patient with MODS due to severe wasp stings. The patient received conventional treatment combined with glucocorticoids, plasma exchange, hemoperfusion, and continuous renal replacement therapy and had a successful recovery. MODS is a serious potential complication of wasp stings. Early local wound treatment, antiallergy interventions, antishock therapy, fluid replacement, glucocorticoid administration, and blood purification treatments are required to treat MODS secondary to wasp stings. Our results suggest that a hybrid blood purification method involving plasma exchange combined with hemoperfusion and continuous renal replacement therapy is more clinically effective than the single blood purification method. Early use of high-dose glucocorticoids combined with a hybrid blood purification treatment method had a positive effect in managing our patient and may improve the prognosis of other patients with MODS.

Keywords: continuous renal replacement therapy, glucocorticoids, hemoperfusion, plasma exchange, acute kidney injury

Introduction

Wasp stings are hazardous for farmers and others engaged in outdoor work or leisure in rural tropical regions.[1] Frequent incidents of severe wasp stings have recently been reported in China, causing considerable mortality and serious public health problems.[2] Multiple wasp stings can cause multiple organ dysfunction syndrome (MODS); however, MODS is a rare phenomenon. Physicians may be the first contact point for patients with wasp stings. Physicians must be aware of the most appropriate approaches to treatment to prevent death or permanent organ damage. Here, we report a case of MODS that involved rhabdomyolysis, acute renal failure, intravascular hemolysis, liver injury, myocardial injury, coagulopathy, respiratory failure, and nervous system damage due to multiple wasp stings. This case report may help inform clinicians managing patients with complications resulting from mass wasp stings.

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Case Report

Informed consent for publication was obtained from the patient and the hospital's ethics committee.

A 77-y-old male farmer was admitted to our hospital's nephrology department following a wasp attack while working in a field. Overall, 106 stings were identified on the head, back, and arms. His presenting symptoms included headache, palpitations, nausea, vomiting, and slightly blurred vision. He had initially been taken to a local community health hospital where he received intravenous fluids (approximately 2000 mL) and antihistamine medication. However, his symptoms worsened, and on the day after hospital admission, his urine was dark brown; thus, he was referred to our hospital. The patient had no prior medical history and was conscious on admission. On examination, the patient was tachycardic (heart rate, 130 beats·min^{-1}),

Figure 1. Wasp sting marks on the head, neck, and upper limbs.

with a blood pressure of 166/98 mm Hg, a finger pulse oximetry of 90%, yellowish discoloration of the sclera, and swollen head, face, and limbs. The sting lesions were black with central necrosis (Figure 1). His urine was dark brown to black (Figure 2). Urinalysis results showed 2+ proteinuria and hematuria, and his daily urine output was <400 mL. Laboratory test results indicated severe acute hepatitis, acute myocardial damage, acute renal failure, thrombocytopenia, coagulopathy, and rhabdomyolysis (Table 1).

On admission, oxygen was administered based on the finger pulse oximetry of 90%, and he underwent an electrocardiogram. Electrocardiogram results showed sinus rhythm and ST-T changes (Figure 3). However, the patient had no previous history of heart disease or hypertension and usually did not have specific symptoms such as chest tightness, chest pain, and syncope, among others. A cardiologist was consulted, and it was considered that the wasp stings caused acute myocardial injury. The patient received no special cardiac drug treatment, and as his condition improved, his troponin level fell to the normal range on the 11th day of admission. His head was shaved, all the venom sacs were carefully removed, and each lesion was washed with normal saline. He was administered oral Chinese medicine, which was also applied to each wound. Because of patent protection, the precise ingredients of this Chinese medicine are unknown. It it known by the name "Jidesheng snake tablet." In China, it is often used in patients stung by wasps and bitten by snakes to reduce wound edema. We did not observe any adverse reactions or evidenced benefit from this traditional Chinese medicine, and it did not complicate the management of our patient.

After rehydration (1000 mL of 0.9% sodium chloride solution within 30 min), we administered the following medications: furosemide (20 mg) via an intravenous bolus, 5% sodium bicarbonate for urine alkalization, methylprednisolone for an anti-inflammatory response (120 mg once a day, then 80 mg after 3 d, 40 mg after 6 d, 20 mg after 10 d, and stopped completely after 15 d), red blood cell suspension and platelet infusion for blood product replacement and support, and polyene phosphatidylcholine to reduce liver transaminases. Following consent provided by the patient's relatives, a tube was inserted into

Figure 2. Gross hematuria was observed following the wasp attack.

Table 1. Laboratory test results

Variable	*Normal range*	*Day 1*	*Day 2*	*Day 8*	*Day 11*	*Day 25*
Hemoglobin ($g \cdot L^{-1}$)	130–175	124	44	70	87	101
Platelet count test ($\times 10^9 \cdot L^{-1}$)	125–350	275	68	42	90	277
Alanine aminotransferase ($U \cdot L^{-1}$)	9–50	108	136	67	34	-
Aspartate aminotransferase ($U \cdot L^{-1}$)	15–40	532	582	70	28	-
Creatinine ($\mu mol \cdot L^{-1}$)	59–104	87	195	292	312	98
Creatinine kinase ($U \cdot L^{-1}$)	38–174	574	5708	2502	310	-
Creatine kinase myocardial band ($ng \cdot mL^{-1}$)	0–5.2	-	51.1	10.4	2.8	-
High-sensitivity cardiac troponin ($pg \cdot mL^{-1}$)	0–34.2	45.3	1008.9	62.1	15.8	-
Activated partial thromboplastin time (s)	25.0–45.0	112.3	>180.0	35.0	45.8	-

the right femoral vein, and continuous renal replacement therapy (CRRT) was started as continuous venovenous hemofiltration combined with hemoperfusion (HP) and plasma exchange (PE), with a replacement volume of 2000 mL each round. CRRT was performed for 112 h, and 4 rounds of HP and 6 rounds of PE were performed. On Day 2, the patient became increasingly agitated, removed the right femoral vein catheter, and became unconscious. Pressure was immediately applied to the catheter puncture site to regain hemostasis, CRRT was temporarily suspended, diazepam was administered for sedation, and the left femoral vein was catheterized. Following vein catheterization, CRRT was restarted.Over the next few days, the patient remained unconscious. His blood pressure dropped to 75/51 mm Hg, his finger pulse oximetry dropped to 75%, and his pupils showed anisocoria. He underwent a head computed tomography scan and blood gas analysis, and no abnormalities were observed. Fluids were administered with dopamine to maintain his blood pressure. At this stage, he was dyspneic, and obvious moist rales could be heard in both lungs. Despite increasing the oxygen inhalation concentration, the patient's fingertip oxygen saturation remained low, and the dyspnea remained unresolved. Therefore, mechanical ventilation in the high acuity intensive care unit was recommended; however, his family did not consent. Oxygen administration via mask and 3 combined blood purification treatments (CRRT + HP + PE) were continued. During this treatment, the patient developed black stools, which were positive for occult blood, and his hemoglobin decreased significantly to 44 $g \cdot L^{-1}$. This prompted the administration of proton pump inhibitors, fresh plasma, and 2 units of packed red blood cells. Approximately 1 wk later, the patient was less agitated, responded to personal questions, and his blood pressure returned to normal. The CRRT was stopped, and he underwent 3 sessions of intermittent hemodialysis. On Day 10, his urine output increased to 1500 mL per day. On Day 17, his blood creatinine level decreased remarkably and his urine output reached 4000 mL daily; he was conscious and responsive to personal questions. He appeared less restless and irritable than on previous days. After 27 hospital days, the patient had fully recovered, with no complaints of discomfort and with normal urine color and laboratory test results, including myoglobin, troponin, and electrocardiogram.

Discussion

Wasp venom can result in multiple detrimental effects such as hemolysis, thrombocytopenia, neurotoxicity, anaphylactic shock and, in severe cases, MODS. Wasp venom is complex and consists predominantly of enzymes, peptides, and biogenic amines.[3-5] Melittin is a major venom component; it alters the integrity of the cell membrane and is strongly hemolytic. Hyaluronidase hydrolyzes the hyaluronic acid between cells, probably facilitating a smooth entry of toxins into body tissues, possibly exacerbating local inflammation.[6] In this study, the patient had normal platelets on admission, which decreased to $42 \times 10^9 \cdot L^{-1}$ on Day 8 of admission. A report in India demonstrated that thrombocytopenia was found in patients stung by wasps, and the authors suggested that thrombocytopenia is a direct result of wasp venom's effect on platelets.[7] The severity of a person's condition after wasp stings depends mainly on the strength of the venom and severity of the stings. Mild cases show allergic reactions with local redness and pain, and most of these do not require medical attention.

Nervous system toxicity after wasp sting injury is rare, but several cases have been reported worldwide. These typically involve cranial neuropathy, stroke, and encephalitis.[8,9] During the disease, patients have differing degrees of altered mental state and decreased pulse oximetry, suggestive of diminished peripheral perfusion. Patients with neurological damage due to wasp stings often have a poor prognosis, and the severity is related to a patient's age, sting site, the number of wasp stings, health condition, and degree of inflammatory response.[10] Early hybrid blood purification treatment should be

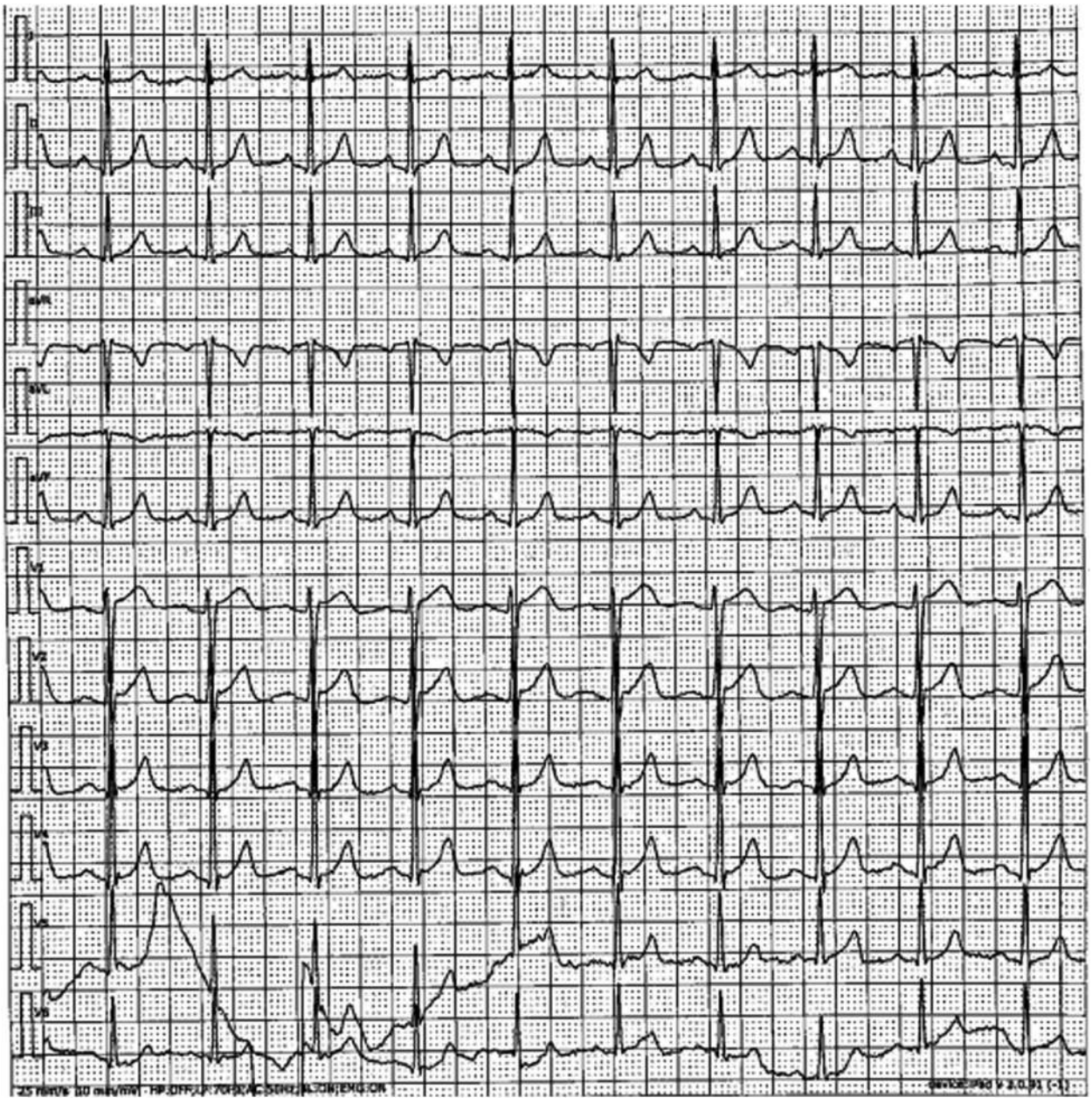

Figure 3. Electrocardiogram results show sinus rhythm and ST-T changes.

considered for patients with altered sensorium/consciousness after multiple wasp stings.

Acute laryngeal edema, anaphylactic shock, and respiratory muscle paralysis are all early causes of death in patients with severe reactions to multiple wasp stings, followed by MODS and infections.[11] Allergic reaction is the earliest and most common clinical manifestation of a wasp sting. The symptoms of an allergic reaction can be divided into 4 grades[12]; allergic reactions above grade II require an immediate injection of epinephrine.[13] The human physiological response to wasp stings includes a potent immune response, including the release of many inflammatory mediators, which are amplified step by step through the cascading effects of the inflammatory process. Endothelial cell damage, inflammatory mediators, and the resulting abnormal blood coagulation are key factors affecting organ function, causing abnormal blood vessel tension and inhibiting myocardial pump function, ultimately leading to organ damage.[14]

The first 24 h to 2 wk after a person is stung by a swarm of wasps is a critical period to prevent and treat MODS. Urine output and color changes must be recorded every hour for the first 48 h. The observation of a patient's appetite, abdominal pain, bloating, nausea, vomiting, stool color, and skin and mucous membrane color is necessary. Routine blood tests, kidney and liver function tests, and muscle enzyme spectrum tests are needed each day, in addition to administering fluid replacement, antihistamines, and urine alkalization. Blood purification treatment may be required.[13]

Multiple organ damage and inflammatory reactions caused by wasp venom provide a theoretical basis for glucocorticoid use to control inflammatory mediators. Reportedly, patients with MODS respond well to intravenous steroid administrations[15]; however, a standard uniform dosage of glucocorticoids treating wasp stings has not been reported. According to a 2018 consensus of Chinese experts on the standardized diagnosis and treatment of wasp stings, patients with mild stings can be prescribed intravenous methylprednisolone (40−80 mg) or hydrocortisone (200−400 mg) once daily, and those with moderate or severe stings can be administered intravenous methylprednisolone (120−240 mg) once daily.[12] When the systemic allergic reaction had subsided, hemolysis and rhabdomyolysis were reduced; this high dose of methylprednisolone was reduced by 50% every 3 d to 40 mg, maintained for 2 to 3 d, and gradually stopped within 3 wk.

In our region, the peak period for wasp stings is from August to October. In general, blood purification can be considered when a presenting patient has sustained >20 stings or when the patient presents with early hemolysis, rhabdomyolysis, kidney damage, or a decreased finger pulse oximetry. When blood purification is deemed necessary, hybrid blood should be encouraged. We recommend that patients in serious conditions should be first stabilized with CRRT before performing PE or HP. Combining blood purification and glucocorticoid therapy is key to treating severe wasp stings and preventing MODS.[16,17] A single mode of blood purification is insufficient to meet all the therapeutic needs of the affected patient. Glucocorticoids, rehydration, and early CRRT are essential to rapidly clear the body of wasp venom and prevent multisystem damage. The patient had abnormal coagulation function and required PE to supplement plasma proteins and coagulation factors. Although blood perfusion removes whatever venom remains in circulation through adsorption, combined blood purification can better remove toxins and inflammatory mediators, stabilize hemostasis, and thus, support and protect organ function. In renal failure, hemodialysis can be used clinically to clear small molecules, such as creatinine, create a synergistic effect in treating severe wasp stings, and achieve an optimal outcome.

Conclusions

This case report involved a patient who experienced a severe reaction to multiple wasp stings, resulting in MODS. He received fluids, antishock and antiallergic medications, blood transfusion, glucocorticoids, CRRT, PE, and HP treatment and recovered completely. For patients who develop MODS due to multiple wasp stings, a standard single blood purification mode may be insufficient to meet treatment needs. Hybrid blood purification may be more effective in removing wasp toxins and inflammatory mediators and stabilizing hemostasis while supporting and protecting organ function. Our case emphasizes that early detection of rare complications, such as MODS, prompts referral and early intervention, and, if indicated, aggressive blood purification therapy can help achieve satisfactory recovery and prevent death.

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CLINICAL TOXINOLOGY SPECIAL SECTION

CASE REPORT

Two Cases of Severe *Amanita Muscaria* Poisoning Including a Fatality

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Ingestion of *Amanita muscaria* mushrooms results in transient central nervous system excitation and depression mediated by its components, ibotenic acid and muscimol. The mushroom is distributed worldwide and ingestions occur with some frequency. Although these ingestions have traditionally been considered benign, serious complications can occur. We present 2 cases of serious toxicity, including a fatality. The first case was a 44-y-old man who presented to the emergency department (ED) after cardiopulmonary arrest approximately 10 h after ingesting 4 to 5 dried *A muscaria* mushroom caps, which he used for their mind-altering effects. Despite successful resuscitation, he remained unresponsive and hypotensive and died 9 days later. The second case was a 75-y-old man who presented to the ED after accidentally consuming one large *A muscaria* mushroom cap he foraged in Eastern Turkey. The patient initially presented to the ED with hallucinations followed by lethargy, and he was intubated for airway protection. The patient's condition gradually improved, and he made a full recovery. *A muscaria* ingestion should not be considered benign as serious outcomes do occur. An understanding of how the main neuroactive chemicals, ibotenic acid and muscimol, affect the brain can help anticipate outcomes. Several high-risk features that portend a more serious course are identified.

Keywords: mushrooms, toxicity, mycotoxins, ibotenic acid, muscimol

Introduction

Amanita muscaria (Figure 1), also called "fly agaric" in reference to its use as an insecticide, is a mushroom found throughout both the northern and southern hemispheres in temperate and boreal climates.[1] Historically, *A muscaria* has been used by shamans in religious ceremonies to enter a trance state after ingestion.[2]

The genus *Amanita* consists of an estimated 900 to 1000 species of which approximately 500 have been described.[3] Due to the toxicity associated with various *Amanita* species, specifically those containing amatoxin, it is the best studied genus of all mushrooms. Despite the name, however, most species within the *Amanita* genus, including *A muscaria*, do not contain amatoxin.[4]

A muscaria ingestion causes euphoria and psychotropic effects that are owing to 2 neurotoxins, ibotenic acid and muscimol. As a result, *A muscaria* is often consumed purposefully and ranks second after the psilocybin-containing mushrooms for mushrooms ingested intentionally.[5–12]

In contrast to other psychoactive mushrooms, *A muscaria* is often not regulated and is readily available for purchase over the internet. The mushroom is legal in many countries including the United States where it is legal in all states except for Louisiana, which banned it in 2005.[13]

A muscaria can produce central nervous system (CNS) excitation and depression that is usually brief. Although usually mild, there are rare reports of more severe

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Figure 1. *Amanita muscaria*, Nelson Lakes National Park, New Zealand (photo by E. Meisel). *A muscaria* have a distinctive red to orange cap that can fade over time. These mushrooms are covered in white scales and have striate margins with white gills. They can grow up to 20 cm (8 in) tall and often have rings below the annulus that extend up the stipe from the bulbous volva.

outcomes. From 2011 to 2018, the American Association of Poison Control Centers reported 312 exposures to ibotenic acid-containing mushrooms. Of these, only 15 had a major outcome with 1 death.[5–12] A review of 6 case series accounted for 98 patients of which 7 were intubated without any deaths reported.[14–18]

We present 2 cases of *A muscaria* toxicity with a severe outcome. We follow this with a discussion of the toxicity associated with the ingestion of these mushrooms based on the current literature.

Case Reports

CASE 1

A 44-y-old man with no past medical history presented to an emergency department (ED) in the United States following a cardiac arrest after ingesting 6 to 10 dried mushrooms identified as *A muscaria* earlier in the day (Figure 2). The mushrooms were given to him by a friend who had purchased them online from a website called IamShaman.com, which sold them as *A muscaria* mushrooms. The 2 men shared similar views on holistic medicine and ingested the mushrooms for their alleged health benefit.

Approximately 30 min after ingestion, the patient was described having fallen asleep. Over the course of the next several hours, the patient developed generalized extremity jerking, shivering, and an episode of emesis. The friend took measures to warm him up by laying him in the sun and then moved him to a warm bath.

Approximately 9 to 11 h after the ingestion, the patient was found in asystole. Cardiopulmonary resuscitation was initiated by prehospital providers with a return of spontaneous circulation after endotracheal intubation and administration of 3 rounds of epinephrine and atropine.

In the ED, vital signs revealed a pulse of 135 beats·min^{-1}, blood pressure of 78/37 mm Hg, and oxygen saturation of 100% on 100% oxygen. Despite the absence of sedation, the patient was unresponsive to noxious stimuli with flaccid limbs. Both corneal and gag reflexes were absent and there were no spontaneous respirations. The pupils were pinpoint and fixed. An electrocardiogram (ECG) showed a narrow complex tachycardia with ST depressions in the inferior leads. Laboratory analysis revealed an elevated white blood cell count of 17.0x10^{3}μL^{-1}, a hemoglobin of 13.7 g·dL^{-1}, a hematocrit of 41%, and a platelet count of 173x10^{3}μL^{-1}. Additional laboratory values included a serum glucose of 170 mg·dL^{-1}, a blood urea nitrogen of 17 mg·dL^{-1}, creatinine of 2.4 mg·dL^{-1}, a sodium of 155 mmol·L^{-1}, a CO2 of 16 mmol·L^{-1}, a potassium of 2.8 mmol·L^{-1}, and a calcium of 7.6 mg·dL^{-1}. Serum ethanol, acetaminophen, and salicylates were undetectable, as were drugs of abuse as shown through an immunoassay for the presence of cocaine, opioids, THC, and amphetamines. A serum tricyclic antidepressant screen was also undetectable.

The patient ultimately died on day 9 after life support was discontinued because of lack of any improvement in his neurological status.

Results of the autopsy revealed no alternative explanation for the patient's demise and concluded that the probable cause of death was *A muscaria* poisoning and the manner of death was accidental.

CASE 2

A 75-y-old man with diabetes mellitus and chronic obstructive pulmonary disease presented to an ED in

Figure 2. Photo of ingested mushroom retrieved from law enforcement in case 1.

northeastern Turkey with nausea and vomiting 30 min after consuming a wild mushroom cap collected from his backyard for a family dinner. On presentation, he had stable vital signs and a normal exam except for visual and auditory hallucinations. Five hours later he became confused, his Glasgow Coma Score (GCS) score decreased to 8, his blood pressure decreased to 70/50 mm Hg, and his heart rate decreased to 45 beats·min^{-1}. He was intubated for airway protection, received 2 mg of atropine for bradycardia, and was started on a norepinephrine infusion. On repeat exam, his GCS was 3 without sedation and his pupils were 1 mm bilaterally. Laboratory analysis was unremarkable except for elevated blood urea nitrogen of 45 mg·dL^{-1} and serum creatinine of 1.45 mg·dL^{-1}. An ECG revealed a right bundle block. Imaging studies, including brain computed tomography and magnetic resonance imaging, were normal and an infiltrate was noted on his chest x-ray. Twenty-four hours after arrival, the patient's GCS improved to 14; however, he had a prolonged hospital stay because he developed aspiration pneumonia that later resolved. Muscimol and ibotenic acid were detected in the collected mushroom samples as well as the patient's blood samples using liquid chromatography with tandem mass spectrometry. A mycologist identified the mushroom to be *A muscaria*.

Discussion

Between 1999 and 2018 there were >145,000 mushroom exposures reported to US poison centers. Fortunately, most cases were not severe with only 0.04% resulting in death.[5,6,16] Over the last 8 y, of the 23 reported deaths related to mushroom ingestion, only 1 was related to mushrooms containing ibotenic acid.[5–12]

A muscaria, *Amanita pantherina*, and *Amanita gemmata*, along with several other species, belong to a group of mushrooms that can produce a poisoning syndrome known as pantherina-muscaria syndrome.[17] Due to its distinctive appearance, poisoning with *A muscaria* is unlikely to be accidental when compared to *A pantherina* and *A gemmata*, although sometimes it can be mistaken for *Amanita Caesarea*, a highly sought-after flavorful mushroom.[1,5–12,17–19] Usually ingestion is intentional because of the mushroom's psychoactive properties. *A pantherina*, with its brown coloring and white warts, has a less distinctive appearance and ingestion is typically related to misidentification.[17] Reviewing US poison center data over the last 8 y, which categorizes both *A muscaria* and *A pantherina* together with all other ibotenic acid and muscimol containing mushrooms, found that 46% of reported ingestions were intentional.[5–12]

The toxic effect of these mushrooms is attributed to the psychoactive isoxazoles, ibotenic acid and muscimol, which act on the glutamic acid receptors and gamma-aminobutyric acid receptors respectively.[20,21] Furthermore, ibotenic acid undergoes decarboxylation to muscimol thereby increasing the concentration of the latter.[22,23] Other components have been isolated in smaller concentrations from these mushrooms including muscazone, choline, acetylcholine, betaine, muscarine, hyoscyamine, atropine, scopolamine, and bufotenine and may contribute to the overall toxidrome as well as the occasionally observed cholinergic and anticholinergic manifestations.[24] These other components may also account for the bradycardia and hypotension experienced by our patient in the second case.

After ingestion, symptom onset is rapid, occurring within 30 min to 2 h.[14,16,17] The toxidrome is primarily neurological, with the excitatory effects of ibotenic acid seen first, including hallucinations, confusion, and agitation. Convulsions, although not common, have been reported.[14,15] The CNS depressive effects of muscimol follow this excitatory stage with progression to lethargy and coma. Multisystem dysfunction is not observed, and symptoms resolve within 24 h.[16,18]

Gastrointestinal symptoms, consisting of mostly nausea and vomiting, are reported in approximately 50% of poisonings and appear more frequent with *A pantherina*.[14,17,18] Toxicity with *A pantherina* has less of an excitatory stage with decreased level of consciousness being more common and often the initial presenting symptom.[17] This is likely due to higher concentrations of muscimol relative to ibotenic acid.[20]

Cholinergic and anticholinergic manifestations, attributed to muscarine and other neuroactive compounds present in smaller amounts, have also been inconsistently described with both *A muscaria* and *A pantherina*. These characterizations are more prevalent in earlier literature and mostly anecdotal. Review of more recent cases, including the 2 largest case series to date, reveal cholinergic and anticholinergic symptoms to be rare.[17,18]

Seizures, which may be more common in children, pose a unique challenge.[14] Benzodiazepines are the treatment of choice, but given that CNS toxicity typically progresses from an excitation to depression state, patients are already at high risk for profound CNS depression. Not surprisingly, there is an association between benzodiazepine administration and the need for intubation. In the case series by Moss et al, 5 of 34 patients required intubation, of which 4 received benzodiazepines beforehand. There was also one intubation reported in a 9-patient pediatric case series as well as a separate publication reporting a single case requiring intubation.[14,15] Despite the lack of a control group in these studies, CNS depression with resultant need

for intubation should be anticipated, especially in patients presenting with seizure and in patients receiving benzodiazepines.

Although toxicity from *A muscaria* and *A pantherina* share similarities, there can be a spectrum of clinical effects leading some experts to suggest that they be classified as 2 separate toxidromes. The different ratios of ibotenic acid and muscimol between the 2 species is certainly a contributing factor to the differing onset and progression of toxicity between the 2 species. Whether the ingestion was intentional or not may also affect the dose and resultant toxicity. The active toxins, although not heat labile, are water soluble, so boiling or soaking in water prior to consumption may alter the toxic effects.[20] Toxicity from fresh mushrooms, which are higher in ibotenic acid, will be different from than that of dried mushrooms which will contain higher concentrations of muscimol related to increased conversion of ibotenic acid to muscimol during the drying process.[23] It has also been suggested that, along with geographical variation, the season can affect the concentrations of the various neurotoxins.[14]

In the first case, we were able to obtain the mushroom samples, and ingestion of *A muscaria* was confirmed by a mycologist and coroner examination. Unfortunately, confirmation by qualitative testing of preserved specimens in this case was not performed, which does pose limitations. In the second case, we were able to confirm the presence of ibotenic acid and muscimol in both the serum and mushroom samples with liquid chromatography with tandem mass spectrometry.

Conclusion

Toxicity from *Amanita* mushrooms that contain ibotenic acid and muscimol is generally considered low-risk; however, our cases and a review of the literature demonstrated that severe outcomes do occur. Central nervous system excitation followed by CNS depression with complete resolution of symptoms within 24 h is typical, but the possibility of more deleterious effects, including seizure and respiratory depression, should be anticipated and patients should be monitored closely until symptoms have completely resolved. An understanding of the main neuroactive chemicals is necessary to understanding the resultant toxidrome and anticipating symptoms. The number of mushrooms consumed, how the mushrooms were prepared, and when and where the mushrooms were picked, can potentially affect the resultant toxicity.

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CLINICAL TOXINOLOGY SPECIAL SECTION

CASE REPORT

Angina and Arrhythmia Symptoms Following Multiple Bee Stings: Kounis Syndrome

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Kounis syndrome (KS) is an acute coronary syndrome including coronary spasm, acute myocardial infarction, and stent thrombosis preceded by an anaphylactic, anaphylactoid, allergic, or hypersensitivity injury. In this case presentation, we discussed Type I and Type II KS. Case 1 was a 72-y-old man who presented to the emergency department with allergic symptoms and chest pain that developed after multiple bee stings. Electrocardiography showed ST depression in the lateral leads. Case 2 was a 42-y-old woman who presented to the emergency department with complaints of chest pain, dizziness, and presyncope that developed after multiple bee stings. Mobitz Type II Block with right bundle branch block was observed in 42 beats·min^{-1} in the electrocardiography. Both patients were first treated for allergic reaction. Although early percutaneous coronary intervention was performed for graft thrombosis in Case 1, a permanent pacemaker was inserted in Case 2. The patients were discharged without any complications. Increasing physician awareness towards the existence of KS can prevent fatal outcomes with early diagnosis and treatment.

Keywords: allergy, bee venom, bradycardia, chest pain, coronary angiography, pacemaker

Introduction

Defined as the emergence of acute coronary syndrome in an allergic hypersensitivity or anaphylactic state, Kounis syndrome (KS) is a life-threatening medical emergency. It is thought that platelet activation, which leads to the degranulation of mast cells and releasing of multiple inflammatory mediators, makes arterial circulation susceptible to acute cardiac events. Vasospastic allergic angina (Type I), allergic myocardial infarction (Type II), and stent thrombosis forming an obstructive thrombus caused by eosinophils and/or mast cells (Type III) are the 3 variants of this syndrome that have been reported so far.[1] Various causes have been found to trigger KS, and their number is increasing rapidly. Various types of food, drugs, environmental exposures, and insect bites are the most frequently reported causes.[1] Bee venom is also one of the triggers. Although cardiovascular events after bee sting are mostly described as related to anaphylactic shock, some reports highlight that bee venom causes myocardial infarction with a direct effect on the heart and coronary circulation.[2-4] In this study, we present patients with Type I and Type II KS with electrocardiography (ECG) changes and heart block after multiple bee stings.

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Case Presentation

CASE 1

A 72-y-old man was admitted to the emergency service of another hospital with allergic symptoms after multiple bee stings. He had a history of coronary artery bypass grafting in 2016 and surveillance angiography in 2019, which found the circumflex artery was 95% occluded. A bare metal stent was applied to the circumflex artery in the same session.

Since the stent insertion in 2019, the patient had been using daily ramipril (5 mg), acetylsalicylic acid (100 mg), metoprolol (50 mg), clopidogrel (75 mg), and atorvastatin (40 mg), and his coronary artery disease had been stable for the last 2 y. The patient had no known allergic disease.

After the patient's admission following the multiple bee stings, intravenous prednisolone, diphenhydramine, and ranitidine were administered to the patient in the emergency service for widespread urticarial rash and itching that developed from multiple bee stings.

After the allergic treatment, rashes and itching improved. Chest pain radiating to the left arm started approximately 1 h after the bee sting. Thereupon, the patient was transferred by ambulance to our emergency department for further examination and treatment. Vital signs at the time of arrival to our emergency department were as follows: temperature 36.2°C, blood pressure 145/80 mm Hg, heart rate 85 beats·min^{-1}, respiratory rate 21 breaths·min^{-1}, and SaO_2 98% (in room air). In physical examination, there was diffuse hyperemia in the body. There was no urticarial rash or uvular edema, and lung sounds were normal. An ECG showed ST segment depression in the lateral leads. The burning sensation in his chest persisted. The high sensitivity troponin I value taken approximately 2 h after the bee sting was 1544 ng·L^{-1} (normal range 0–16 ng·L^{-1}) and CKMB value was 27.5 μg·L^{-1} (normal range 0.6–6.3 μg·L^{-1}). Other laboratory parameters (metabolic panel and blood counts) were normal.

The patient was hospitalized in the coronary intensive care unit and coronary angiography was performed. Coronary angiography revealed thrombosis in the bypass graft (aorta–saphenous vein graft–obtrusive marginal arteries). Percutaneous coronary intervention was successfully performed in the same session as coronary angiography. The patient was diagnosed with Type II KS. The patient was followed in the hospital for 4 d and was discharged without any complications.

CASE 2

A 42-y-old woman with no known disease other than asthma and hypertension was brought to our emergency department by ambulance with complaints of chest pain in her left arm, dizziness, and presyncope that developed within 1 h after multiple bee stings. The patient had no known allergic disease. The patient had no symptoms until the bee sting and was performing normal activities. Her vital signs at the time of admission to the emergency service were as follows: temperature 36.4°C, blood pressure 120/80 mm Hg, heart rate 42 beats·min^{-1}, respiratory rate 21 breaths·min^{-1}, and SaO_2 98% (in room air). In physical examination, there was widespread hyperemia in the body. Urticarial plaques and uvula edema were absent, and lung sounds were normal. Intravenous prednisolone and diphenhydramine were administered to the patient in the emergency service for the allergic reaction. Mobitz Type II Block with right bundle branch block was observed in 42 beats·min^{-1} in the ECG. The high sensitivity troponin I value taken approximately 90 min after the bee sting was 941 ng·L^{-1} (normal range 0–16 ng·L^{-1}) and CKMB value was 6.9 μg·L^{-1} (normal range 0.6–6.3 μg·L^{-1}). Other laboratory parameters (metabolic panel and blood counts) were normal. The patient was evaluated as non-ST elevation myocardial infarction. The patient, to whom a transcutaneous pacemaker was implanted in the first intervention in the emergency service for symptomatic bradycardia, was transferred to the coronary intensive care unit. During the coronary intensive care follow-ups, the patient continued to have symptomatic bradycardia. A permanent pacemaker was implanted approximately 24 h later, and coronary angiography was performed in the same session. The patient, whose angiography was reported as normal coronary and in whom Type I KS was considered, was discharged without any complications after 5 d of follow-up and treatment.

Discussion

KS is the concurrence of hypersensitivity disease with acute coronary syndrome after exposure to drugs, foods, environmental factors, and other triggers.[5] The prevalence of KS, which was defined as "allergic angina syndrome" in 1991,[6] is estimated to be 1% among patients hospitalized for allergic reactions in the United States.[7]

It is thought that the release of vasoactive inflammatory mediators such as histamine, serotonin, proteases, and various cytokines following an allergic reaction, along with vasospasm, and platelet activation play a role in the pathogenesis of KS-related anginal symptoms.[6,8] During the degranulation of mast cells, the release of histamine and arachidonic acid products such as leukotrienes, thromboxane, prostaglandins, tryptase, and chymase might lead to vasoconstriction of coronary arteries, plaque eruption, and platelet aggregation.[9] With these mechanisms, 3 types of KS occur in patients.

Type I KS is defined as coronary artery vasospasm that develops with acute release of inflammatory mediators because of the underlying anaphylactic reaction in patients with no obstructive coronary artery disease or predisposing factors for coronary artery disease. Coronary artery vasospasm may develop with or without progression to acute myocardial infarction and cardiac enzyme elevation.[1] Vasospasm causes temporary and excessive lumen narrowing of the epicardial coronary arteries and ultimately leads to the limitation—or even complete cessation—of coronary blood flow, leading to

ischemia.[10] Various complications can occur with coronary vasospasm including myocardial necrosis, syncope, arrhythmias (eg, ventricular tachycardia and complete AV block) and cardiac arrest.[11] Because the right coronary artery supplies the AV nodal artery, its occlusion and/or vasospasm may lead to abnormalities of the AV conduction system.[12] Therefore, the most likely explanation for bradycardia in Type I KS may be vasospasm stemming from allergic causes in the right coronary artery due to the degranulation of mast cells. Coronary vasospasm or stenosis may be demonstrated by cardiac catheterization. However, spontaneous spasm during coronary arteriography is observed only incidentally in patients with findings suggestive of vasospastic angina. Therefore, provocative tests (intravenous or intracoronary ergonovine, intracoronary acetylcholine, etc.) can be applied to show the presence and type of coronary spasm.[13] Nevertheless, these tests are known to have a potential risk of arrhythmic complications, including ventricular tachycardia, ventricular fibrillation, and brady-arrhythmias.[14–16] Considering the associated risks, provocative testing is not performed on every patient. In Type I KS, the reversal of the inflammatory response is often sufficient to control coronary vasospasm. The patient in Case 2, who had no cardiac history, required permanent pacing for symptomatic bradycardia after bee sting. Possible Type I KS was considered in the patient whose coronary angiography was normal. Considering the associated arrhythmic risks during angiography, a provocative test was not applied to the patient to diagnose vasospasm. It is likely no signs of vasospasm were observed because the patient received treatment for an allergic reaction in the emergency service and coronary angiography was performed 24 h after the symptoms were relieved.

Type 2 KS is the type in which mediators released after an allergic reaction induce coronary artery spasm and plaque erosion or rupture manifesting themselves as acute myocardial infarction in patients with underlying asymptomatic coronary artery disease. Echocardiography changes and elevated cardiac enzymes can be seen in patients with KS. The reported ECG changes include ST elevations[2] or depressions, heart block,[17] and various cardiac arrhythmias.[9] In Case 1, the patient—who had a history of coronary artery disease—developed ischemic chest pain, high cardiac troponin level, and ischemic ECG changes after multiple bee stings. Percutaneous coronary intervention was applied successfully to the patient who had thrombosis in the bypass graft in his coronary angiography. Acute myocardial infarction due to allergic reaction, which is Type II KS, was considered in the case.

Type 3 KS is a subtype that includes patients with coronary artery stent thrombosis caused by an allergic reaction.[1] Stent components include the metal strut made from stainless steel containing nickel, chromium, manganese, titanium, and molybdenum, the polymer coating and the eluted drugs.[18] At the same time, post-stent patients must also use known allergens clopidogrel and aspirin.[18] Together, with these drugs, stent components (6 elements) act as antigens after environmental exposure, such as any drug or insect sting, and cause hypersensitivity inflammation. The stents attract inflammatory cells like a magnet and lead to KS and stent thrombosis inducing possible intracoronary mast cell degranulation.[18]

The most common triggers of KS are antibiotics and insect bites, with 80% of cases occurring within the first hour after exposure to the trigger.[5] Bee venom is one of the most important triggers. Bee venom can generally cause local reactions (erythema, edema, itching, pain), local and systemic allergic reactions triggered by immunoglobulin E (urticaria, angioedema, bronchoconstriction, and anaphylactic shock), and severe systemic toxic reactions.[19] A single bee sting usually releases the pheromone isoamyl acetate, which attracts other bees and causes multiple stings.[20,21] Each sting releases approximately 140 μg of venom into the circulation.[21] The severity of serious systemic toxic reactions will generally depend on the amount of venom injected, which is correlated with the number of stings. Reported systemic toxic reactions from multiple bee stings are acute kidney injury,[22] acute myocardial infarction (KS),[23] cerebrovascular disease,[24] and death.

In the pathogenesis of KS, apart from the allergic reaction, bee venom also plays an active role in cardiac side effects. Apitoxin (from Latin apis [bee] and Greek toxikon [poison]) can be dangerous because of its neurotoxic, allergic, cardiovascular, and renal effects.[25] Apitoxin (bee venom) consists of vasoconstrictors like adrenaline and noradrenaline, and vasodilators such as histamine. Histamine modulates inflammatory cells, activates platelets, and can lead to coronary vasoconstriction.[8] In a study, intravenous injection of bee venom to mice caused cardiac noradrenaline elevation and acute myocardial infarction.[26] After the injection, transient reductions in heart rate and mean arterial pressure, and ECG changes similar to Bezold-Jarisch reflex, have been reported. Melittin, which consists of a complex mixture of proteins, 26 amino acids, phospholipids, sugars, and biogenic amines, etc.,[27] is the main active and most toxic component that makes up 50 to 60%[25] of bee venom (apitoxin). Melittin is the main pain-producing agent of bee venom, and its use has been associated with cardiac

toxicity and cardiac hypersensitivity.[28] It is responsible for the release of catecholamines. Metalloproteinases mediate hypersensitivity reactions and are responsible for serious cardiac effects, including coronary vasospasm and plaque destabilization.[29] Apamin is a polypeptide bee venom also responsible for cardiac side effects and has been associated with the blockade of calcium-dependent potassium channels. Binding tightly to slow calcium channels, it blocks the slow action potential of the heart muscle.[30] In a study showing the effects of bee venom on the heart muscle of frogs, the poison has been shown to cause severe bradycardia and an increase in the P-R interval and R-wave amplitude.[31] In a study conducted on 152 honeybee bite patients, bradycardia was reported in <0.7% of patients.[16] Bee stings usually cause temporary electrocardiographic changes, considering the local vasoactive, cardiotoxic, or anaphylactic effects found in their venom.[2] A permanent pacemaker has been required in some patients after a bee sting.[32] Our Case 2 patient was exposed to high doses of apitoxin (bee venom) because of multiple bee stings. The bradycardia and heart block observed in the case may have developed as a result of coronary vasospam effect of bee venom melittin and the blocking effect of apamin on myocardial Ca^{+2} mediated potassium channels.

The first step in KS management is to remove the victim from the trigger. Management in emergency service requires a multidisciplinary approach. The patient's allergic symptoms may progress from local to severe systemic reactions. Although patients are being treated with intravenous fluids, steroids, and antihistamines, severe systemic reactions may require adrenaline or even cardiac resuscitation. In this case, the diagnosis of KS becomes difficult because of the treatment management focusing on the severity of acute allergic reactions. However, it should not be forgotten that the treatment differs. Although early percutaneous coronary intervention was performed for graft thrombosis in Case 1, a permanent pacemaker was inserted in Case 2 in the cardiac laboratory.

Conclusion

Bee venoms can be potentially fatal for humans due to allergic reactions and the cardiotoxic effects. Regardless of the severity of allergic reactions, additional complaints such as chest pain, syncope, and dizziness should be investigated by physicians. While treating the allergic reactions, it should not be forgotten that in KS, early cardiac intervention may be required.

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Supplemental Material(s)

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ORIGINAL RESEARCH

Electromagnetic Interference from Heated Gloves May Compromise Avalanche Transceiver Function

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Introduction—Rapid location of avalanche victims by companions using avalanche transceivers is of utmost importance to prevent asphyxiation. The objective was to determine whether electromagnetic interference from heating elements in gloves worn by rescuers or victims can impair the receiving or transmitting function of avalanche beacons.

Methods—Commercially available heated gloves from 3 different manufacturers were examined during a simulated search with 3 common brands of avalanche transceivers. Distance to target beacon at first signal detection and accuracy of direction to target, as indicated by the arrow from the direction indicator, were evaluated.

Results—Preliminary tests showed that transmitting and receiving signals are degraded by electromagnetic interference caused by rectangular pulses emitted by activated heating elements. Field tests revealed significantly reduced distances of first signal detection when heated gloves were turned on near receiving avalanche transceivers ($P<0.001$; Wilcoxon signed-rank test). Decreased distance to target beacon ranged between 1.9 m (5%) and 41.5 m (94%) at first detection, depending on the avalanche transceiver used.

Conclusions—Avalanche transceivers are susceptible to electromagnetic interference from gloves with electric heating elements. We do not recommend using heated gloves when performing a transceiver search for avalanche victims because it can lead to a delay in rescue.

Keywords: avalanche beacon, emergency equipment, mountain rescue, skiing, snow sports, wilderness

Introduction

Rapid location and extrication of completely buried avalanche victims by companion and organized rescue is of utmost importance to prevent asphyxiation. The use of avalanche transceivers (ATs) has been shown to significantly reduce burial time.[1] Extrication of avalanche victims within 15 min is associated with increased chance of survival and favorable outcomes.[1-3] During signal search with the rescuer AT (receiving AT), multiple-antenna digital beacons can transmit and detect electromagnetic waves and display the estimated distance from the source.[4,5] Once a signal is received, the AT displays an arrow to guide the rescuer to the target AT (transmitting AT). Coarse search is performed to rapidly detect signals from buried victims, whereas fine search specifies the accurate location. During the initial coarse search, the displayed distance should rapidly decrease as the rescuer approaches the buried avalanche victim. Within 3 m of the victim, fine search is assisted by increased frequency of beeping as the rescuer approaches the victim. Metallic objects and magnetic or electric devices close to the rescuer AT can significantly delay rescue.[6] Even worse, such objects can cause rescuer ATs to give false readings of distance and direction to the source and impair signal processing if there are multiple buried victims with ATs.[7] Electromagnetic interference (EMI) of ATs from

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simultaneous use of mobile phones or digital cameras already has been reported.[8,9] It has been recommended that electronic devices should be kept further than 40 cm from the rescuer AT.[8] Pacemakers, continuous glucose monitors, and insulin pumps have been shown to compromise rescuer AT readings during searching when the device is close to the receiving beacon.[10,11] Use of gloves, socks, and shoes with electric heating elements (HEs) in cold environments is becoming more common. So far, no scientific information is available on EMI from HEs on AT function.[12]

We investigated whether EMI from HEs of heated gloves affect receiving and transmitting function of avalanche rescue beacons during field application.

Methods

The influence of electric HE on the function of ATs was investigated in the laboratory and under true environmental field conditions. According to the ethics committee of the Medical University of Innsbruck, the study was exempted of approval because no research on human beings was conducted. Five voluntary investigators from Mountain Rescue Tyrol performed the test runs. Written consent of investigators for publication of results and permission for their likeness to be reproduced in the article was obtained. The study followed the checklist for evaluations based on observational methodology and the checklist for experimental design.[13,14]

We examined 3 pairs of commercially available heated gloves from 3 different manufacturers, namely, Hestra Power Heater 5 Finger (Martin Magnusson & Co AB, Hestra, Sweden), Sunwill (Sea&Mew Consulting, Paris, France), and Zanier Heat.stx Finger (Zanier-Sport Gesellschaft m.b.H., Innsbruck, Austria). Measurements were made with 3 different brands of ATs (Mammut Barryvox S [Mammut Sports Group AG, Seon, Suisse], Pieps Pro BT [PIEPS GmbH, Lebring, Austria], and Ortovox 3+ [ORTOVOX Sportartikel GmbH, Taufkirchen, Germany]).

According to the principles of translational research, preliminary tests were conducted in a shielded radio frequency chamber in a laboratory to verify EMI from HEs of the gloves. Oscillographic recording displayed the characteristic rectangular pulse (positive-going edge followed by a negative-going one) from the current drawn by the heating gloves. Electric HEs of gloves were turned on at a distance of 10 cm of a target AT. Oscillography (TDS 2024, Tektornix GmbH, Köln, Germany), recorded by an Ortovox F1 AT (ORTOVOX Sportartikel GmbH, Taufkirchen, Germany) via earphone jack connection in receiving mode, was obtained and visually analyzed. Intense EMI from HEs of the gloves is illustrated in Figure 1. The distance between the target AT and rescuer AT was 2 m. Our oscillographic investigation of the current drawn from the batteries of the HE revealed a pulse width modulation frequency (frequency of variation between high-amplitude signal and low-amplitude signal) between 10 Hz and 49 Hz and a duty cycle (ratio between time on and time off) ranging from 25% to 96%, depending on brand and energy levels.

Five volunteers of the Austrian Mountain Rescue used 3 brands of common ATs in receive mode to search for a buried AT in transmit mode. The target AT (Mammut Barryvox S) was buried horizontally below 1 m of snow with the display facing up toward the snow surface and with the x-antenna in a direct line to search the run starting point.[15,16] Fifty meters from the target AT, investigators started to walk at a constant speed (range: 1–2 $m \cdot s^{-1}$) directly to the transmitter, following a measuring tape on the ground (Figure 2). The investigators were holding the rescuer AT horizontally in the right hand, aligned in walking direction, with the right arm in front of the body and the left arm hanging by the side. The power setting of the heated gloves was at maximum output during the investigations. All electronic devices other than those that used ATs (eg, cellphone) were removed from the test area before the investigations. We performed 3 measurements at the point of first signal detection: 1) distance to target AT when the first signal was detected (from the measuring tape on the ground); 2) deviation in displayed distance to target AT compared with the actual distance (calculated difference between distance to target AT by measuring tape and distance to target AT on rescuer AT display); and 3) accuracy of direction to target AT as indicated by the arrow from the direction indicator on the rescuer AT display (Figure 3). The transition to fine search was triggered by the displayed distance on the rescuer AT within approximately 3 m from the target AT.[3] We did not measure time to completion but watched for the occurrence of EMI throughout the complete search run from the starting point until the rescuer AT was positioned directly above the target AT. Reduction was defined as the difference between mean of the reference (measurements without heating gloves) and the mean of the used brand of ATs in on-state per investigated HE.

In the first scenario, we observed EMI from HE on the rescuer AT. Gloves with on-state HEs were worn by the rescuer during the search. In the second scenario, we observed EMI from the HE on the target AT (Figure 3). The HE was placed directly above the buried transmitter. For each scenario we performed 5 runs with each brand of HEs in on-state (maximum power setting, 3.7 W, new set of fully charged batteries) and 5 runs with HEs in off-state. For

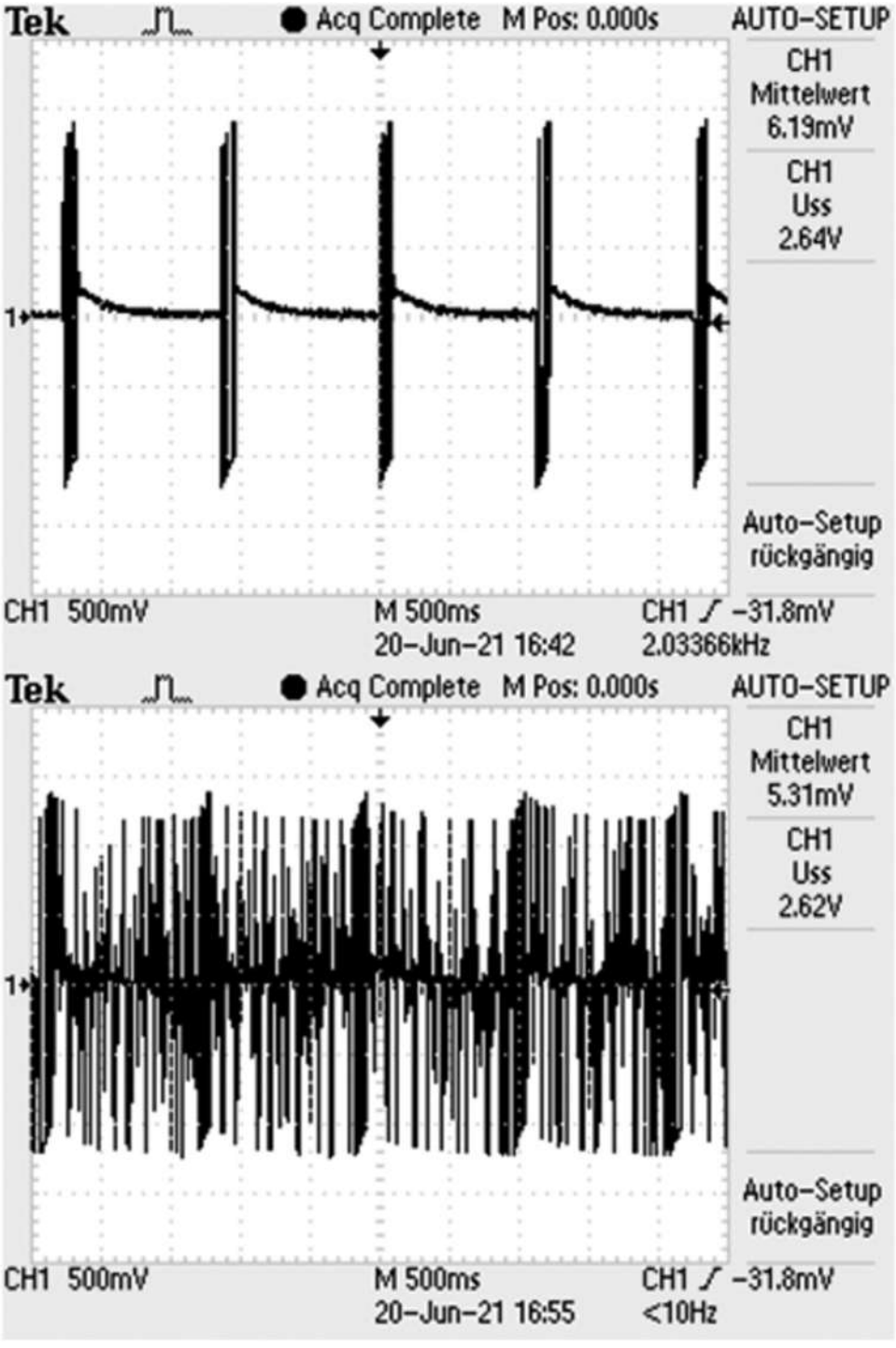

Figure 1. Oscillograms for operating mode of Ortovox F1 while receiving signal from transmitting avalanche transceiver (AT). Upper display shows regular signals of the transmitting AT; lower display shows noise from external interference of on-state heating element (Hestra Power Heater 5 Finger) at high amplitude between the regular signals of the transmitting AT.

reference measurements the participants performed 5 runs with each of the 3 brands of ATs but without heated gloves. Overall, 150 runs were performed (Figure 3).

The alternate hypothesis was that EMI from HEs impairs the function of commonly used ATs. It was not our intention to analyze variety of user applications,

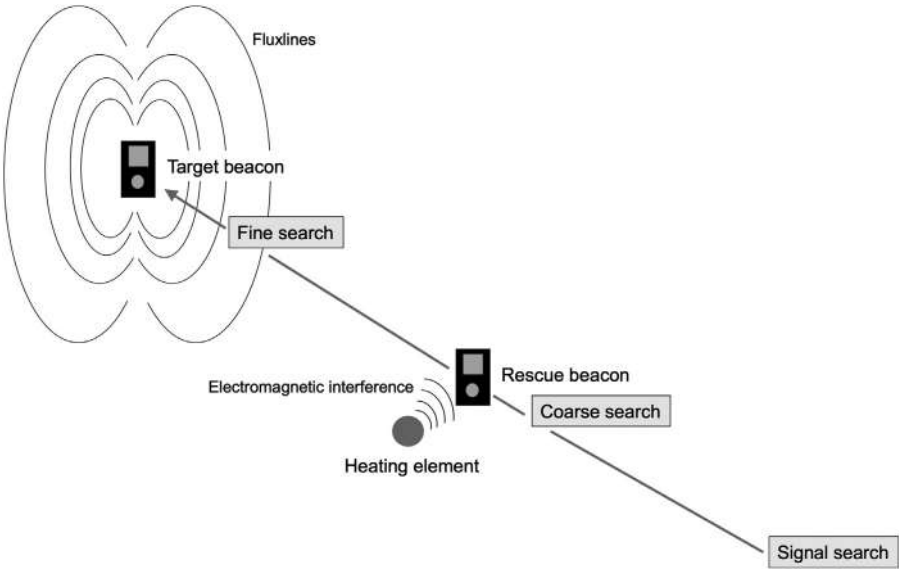

Figure 2. Potential electromagnetic interference from heating elements during signal search, coarse search, and fine search of avalanche victims.

differences between brands of AT, or differences between manufactured products with HEs. Assuming a correlation of 0.99 under null hypothesis using Fisher z-transformation, the estimated sample size was minimum 5 investigations per scenario to achieve a power of 80% and a level of significance of 5% (2-sided). The primary end point was distance to target when the first signal was received. The secondary end point was deviation of distance to target AT on display compared with distance to target AT by measuring tape. The tertiary end point was accuracy of the direction indicator on rescuer AT display. The null hypothesis was that the 2 groups were equal. Data analysis was performed using SPSS (version 25; SPSS INC, IBM, Armonk, NY). Distribution of normality was assessed by Kolmogorov-Smirnov test. Mean values and standard deviation as a measure of statistical dispersion were reported for between device nonparametric statistics using the Wilcoxon signed-rank test. *P* values of <0.05 were deemed significant.

Results

Reference measurements without HE revealed first signal detection at distances between 36.4 m and 44.3 m for 3 different brands of ATs (Table 1). When operating rescuer ATs with heated gloves, reduced distances of first signal detection were observed. On-state heated gloves revealed distances between 2.8 m (6% of baseline measurement) and 25.3 m (57%) at first signal detection. Off-state heated gloves were associated with less reduction in distances of first signal detection (Table 1). Average reduction of distance at first signal detection from all beacons tested was significantly decreased with on-state heated gloves ($P<0.001$) compared with references. The maximum reduction in distance of first signal detection was 41.5 m (94%). When heated gloves were in close vicinity of the target, signal interferences were observed only in a few cases. Incorrect direction indications at the rescuer AT display were observed on 2 occasions, whereas signal loss and an additional ghost signal occurred once. Moreover, EMI was not identified by product-specific software of one of the ATs during the investigations.

Effects of HEs on target ATs were less pronounced than effects on rescuer ATs. Distance of first signal detection differed significantly among the 3 brands of HEs ($P<0.003$). Off-state heated gloves had little observed effect on distance to AT signal detection. Display indications of distance to target did not differ significantly between rescuer ATs and target ATs during fine search and differed less than 10 cm. Overall, display indications of direction frequently revealed little deviations from the accurate direction. Marked deviations of more than 90° were observed twice with one brand of AT.

Discussion

We observed that gloves with HEs markedly affect AT function. Especially in rescuer ATs, the gloves from the 3 tested brands significantly decreased reception of the first signal.

Table 1. Comparison of pooled reductions in distance of first signal detection with 3 brands of heating gloves using 3 different brands of avalanche rescue beacons

	Mammut Barryvox S	*Pieps Pro BT*	*Ortovox 3+*	P *value*
	Mean±SD	Mean±SD	Mean±SD	
Reference [a] **(m)**	44.3±2.1	37.6±3.4	36.4±3.4	
Hestra				
On-mode (m)	2.8±4.9	23.6±1.9	31.9±2.5	0.001
Off-mode (m)	43.4±1.1	26.9±6.4	33.2±3.3	0.232
Reduction (%)	41.5 (94)	14.0 (38)	4.5 (12)	<0.001
Sunwill				
On-mode (m)	25.3±5.5	25.7±3.0	34.5±1.5	0.001
Off-mode (m)	40.3±4.6	35.1±2.7	33.1±1.9	0.021
Reduction (%)	19.0 (43)	11.9 (32)	1.9 (5)	<0.001
Zanier				
On-mode (m)	24.9±3.9	31.9±3.5	33.9±1.7	0.002
Off-mode (m)	41.7±2.6	39.1±0.9	33.3±3.6	0.300
Reduction (%)	19.4 (44)	5.7 (15)	2.5 (7)	<0.001

Brands of tested on-state heating gloves (Hestra, Sunwill, Zanier).
Brands of used avalanche beacons (Mammut Barryvox S, Pieps Pro BT, Ortovox 3+).
[a]Reference values: without gloves.

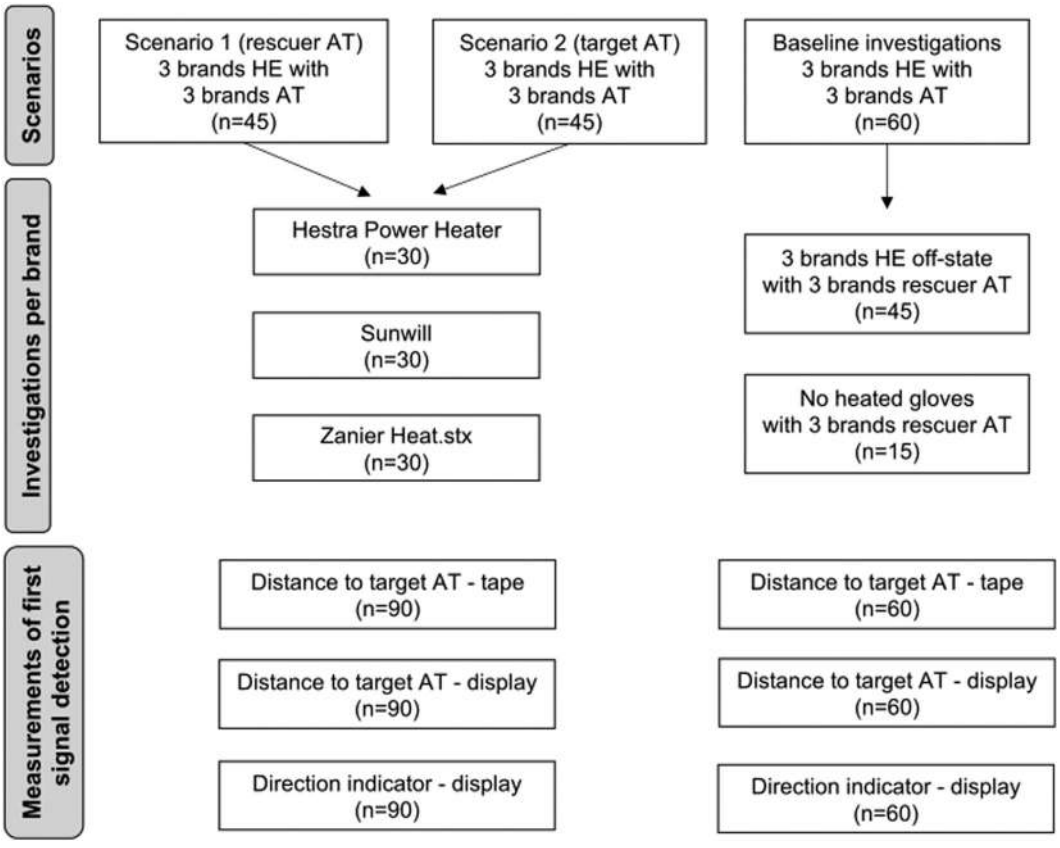

Figure 3. Trial setup and numbers of investigations and measurements. AT, avalanche transceiver; HE, heating element.

The oscillographic investigation of the current drawn from the batteries of the HE revealed different magnetic fields depending on whether HEs were on-state or off-state. Accordingly, the magnetic fields of the HEs interfered with the transmitted signal of the AT. When testing heated gloves at maximum power, EMI occurred with a frequency of 49 Hz. Impairment of first signal detection and false direction indication as observed in our study can lead to delayed location and extrication of the victim in avalanche accidents. Delayed extrication of avalanche victims is associated with reduced survival and worsened clinical outcome.[4,17,18] Rescue algorithms for avalanche accidents should consider the potential of prolonged search and rescue missions from EMI caused by electric devices.[5,19]

Furthermore, EMI caused by HE was more pronounced in rescuer ATs. Interference by on-state HEs was most frequently observed during the initial signal detection and coarse search but not during fine search. The fact that electronic devices compromise AT function is more pronounced in receiving mode than in transmitting mode is known and has been previously reported.[20] Our study revealed that even off-state heated gloves can interfere with AT function depending on the brand. This should be investigated more in detail in further studies.

There was only minor impairment of target AT function when HEs were in close vicinity buried under the snow. There was little signal impairment from the target AT during fine search and incorrect direction indications at the AT display were observed only twice. Presumably, the stronger signal in close range to the target AT is more robust to EMI. According to manufacturer's information, the Pulse Barryvox S can alert the user with a 457 send failure message in case of identified EMI. When the beacon shows "457 SEND failure!" on the display, any electronic device within 40 cm distance has to be moved away. We cannot determine why EMI was not identified by the product-specific software of the AT during the investigations.

LIMITATIONS

Tests were not performed in real avalanche accident scenarios. Potential confounders such as extreme environmental and weather conditions were not accounted for. We did not record intervals between starting search and locating the victim. In addition, we did not evaluate individual performance of AT users in difficult terrain. Brands of the used AT, the location of the target AT, and direction of search were known to participants and investigators. Furthermore, the target AT was placed on a straight surface in a burial depth of 1 m superficially enough to allow EMI. Our study only evaluated 3 types of gloves with HEs and 3 brands of AT; it is unknown whether other products have similar performance.

Conclusions

Impairment of AT function by electric devices has been reported. With our study, we add another device to this list of potential confounders. Backcountry recreationists and mountain rescuers should be aware that EMI from HEs of gloves can compromise detection of signals by avalanche rescue beacons. We recommend avoiding the use of heated gloves in companion or during search of avalanche victims in order to avoid delay of rescue.

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Author Contributions: study concept (MI, WL); study design (WT, MI, WL); acquisition of the data (WT, MI, TL); analysis of the data (WT, FJW, WL); drafting and critical revision of the manuscript (WT, MI, TL, FJW, WL). All authors approved the final manuscript.

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ORIGINAL RESEARCH

Perceptions Among Backcountry Skiers During the COVID-19 Pandemic: Avalanche Safety and Backcountry Habits of New and Established Skiers

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Introduction—The coronavirus disease 2019 (COVID-19) pandemic impacted the ski industry worldwide by closing or limiting access to ski resorts. Subsequently, anecdotal reports of increased backcountry use emerged in the press, with concerns of inexperienced skiers causing or having problems in the backcountry. This study attempted to quantify this and identify motivations for new backcountry skiers.

Methods—Self-identified backcountry skiers and snowboarders (aged ≥18 y) in the United States and Canada completed an anonymous 29-question online survey distributed by regional avalanche centers, education providers, and skiing organizations (n=4792). Respondents were stratified by backcountry experience, defining "newcomers" who began backcountry skiing from 2019 to 2021, coincident with the COVID-19 pandemic. Percentages of ski days spent in the backcountry were compared before and during the COVID-19 pandemic using paired *t*-tests and across cohorts using repeated-measures analysis of variance. Avalanche education was compared using unpaired χ^2 tests.

Results—Of established skiers, 81% noticed more people in the backcountry and 27% reported increasing their own use. Participants reported spending 17% (95% CI, 15.8–17.9) more of their days in the backcountry during the COVID-19 pandemic, with newcomers increasing their time spent by 36% and established skiers increasing their time spent by 13% ($P<0.0001$). Of newcomers, 27% cited the COVID-19 pandemic as motivation to enter the backcountry and 24% lacked formal avalanche education, which is significantly higher than the 14% of established skiers ($P<0.0001$).

Conclusions—Influenced by factors related to COVID-19, reported backcountry use increased during the pandemic. Newcomers had a lower level of avalanche education and less confidence in evaluating terrain. Because 80% of participants were recruited from avalanche safety or education websites, this likely underestimates skiers lacking avalanche awareness or education and is further limited by the nature of online surveys.

Keywords: snow sports, mountaineering, risk assessment, risk-taking, motivation, education

Introduction

The coronavirus disease 2019 (COVID-19) pandemic affected the operation of many ski resorts in the latter half of the 2019 to 2020 ski season. As reported by the National Ski Area Association in 2020, the American ski industry suffered a $2 billion estimated loss when 93% of US ski resorts closed operations in March, months before many had planned. The effects of the pandemic on the US ski industry continued into the 2020 to 2021 season, with restricted ticket and pass sales and limited daily capacity, often requiring reservations in advance. In Europe, the effect of the pandemic during the 2020 to 2021 season was even greater, with many ski resorts remaining closed despite good snow conditions. As a result of these changes, many skiers and snowboarders were left with limited or no access to ski resorts. Others

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were forced to weigh their desire to ski at their favorite resorts against the risk of COVID-19 itself and uncertainty in ski resort operations, access, and lift lines.

In 2021, the International Report on Snow and Mountain Tourism reported 400 million annual skier visits worldwide (https://www.vanat.ch/RM-world-report-2021.pdf). Although 95% of participants ride at ski resorts, backcountry skiing has been the most rapidly growing aspect of the sport, increasing 8-fold from 1995 to 2017.[1] Instead of riding a powered ski lift, backcountry skiers typically hike uphill using touring equipment, although many use snowmobiles, or access backcountry terrain from ski lifts by exiting the ski resort boundary into "sidecountry" terrain. In the backcountry, avalanche hazards are neither assessed nor mitigated by ski patrols, and there is no expedient ski patrol rescue in case of injuries or avalanche. This greatly increases personal risks for backcountry skiers and necessitates higher levels of preparedness. The American Avalanche Association defines education standards for avalanche safety and rescue courses and recommends obtaining at least Level 1 certification and purchasing relevant safety equipment, such as an avalanche beacon, probe, and shovel, before entering avalanche terrain.[2] These factors make the choice to pursue backcountry skiing a significant investment in time, money, and avalanche education.

With the pandemic and its associated impacts on ski resorts, there have been many anecdotal and media reports of a surge in backcountry use and concerns of a commensurate increase in backcountry avalanche incidents and fatalities (Mander B. Ski in the Wild. *Wall Street Journal*. November 28, 2020; Branch J. Virus rules may factor into avalanche deaths. *New York Times*. February 10, 2021. B:8). This study was undertaken to help quantify that perception and assess how those first entering the backcountry during the pandemic differ from experienced backcountry skiers.

Methods

The data collection instrument was an anonymous cross-sectional online questionnaire with 29 items, incorporating multiple choice questions, numeric items, Likert-type items, visual-analog scales, numeric sliders, and free text entry responses (see online Appendix). The University of Nevada and Montana State University Institutional Review Boards approved the study as an "Exempt Protocol" (1690716-1 and JJ020521-EX, respectively). The survey was hosted on a common major commercial platform, and participants were recruited via online postings by regional avalanche centers, avalanche education providers, winter sports news sites and storefronts, and personal social media, including Facebook and Instagram. Recruitment material was directly targeted toward backcountry recreationalists through calls to action worded, "Are you a backcountry skier or snowboarder?"

Interested participants were directed to a landing page that explained the inclusion criteria (self-identified backcountry skiers or snowboarders aged of >18 y). If they chose to proceed, they were consented, shown a standardized legal disclaimer as required by one of our hosting institutions, and allowed to proceed. The instrument assessed several target areas of our study, including the participant's self-reported skiing/riding ability level, level of avalanche education, comfort with risk, and confidence in assessing avalanche terrain and the impact of the COVID-19 pandemic. These questions, where applicable, were modeled after items in prior studies that demonstrated a high degree of content validity.[3,4] For brevity, the term "skier" is used throughout the article to refer to both backcountry skiers and snowboarders.

Participants were classified into 2 cohorts on the basis of their reported seasons of backcountry experience; respondents who answered that 2020 to 2021 was either their first or their second season comprised the novice category—which, for simplicity, we called the "newcomer cohort," because their first season in the backcountry coincided with the COVID-19 pandemic. Likewise, respondents with >2 y of experience were identified as the "established cohort." Similarly, participants were categorized into those who received no formal avalanche education and those who reported taking a Level 1 course or higher. Simple demographics, including gender, age, and zip code, were optionally reported. Statistical analysis was performed using R version 4.0.4,[5] and figures were produced using the package ggplot2.[6] Initial data cleaning was done to exclude participants who dropped out before completing at least the first 2 survey questions (which asked about experience level). Because no items were mandatory, all other statistical analyses were made to exclude nonresponders to relevant items, and participants were not included in paired analyses unless all items were answered.

Several items were analyzed as ordinal data using nonparametric Mann-Whitney *U* test (MW*U*) (for unpaired), Wilcoxon signed-rank test (WSR) (for paired), or Kruskal-Wallis *H* test (for paired/unpaired samples of ≥3 levels). For these tests, a delta of 1.00, which equates to a difference of 1 ordinal level, was chosen to define significance. *P* values were 2-tailed and considered significant at <0.05, and all CIs are reported at 95%. Data are presented as mean±SD for normal distributions and median (interquartile rate) for nonnormal distributions. Except as noted in the article, all analyses of variance (ANOVAs) are 1-way and between-subjects, with effect size reported as η^2. Because a large sample size, by

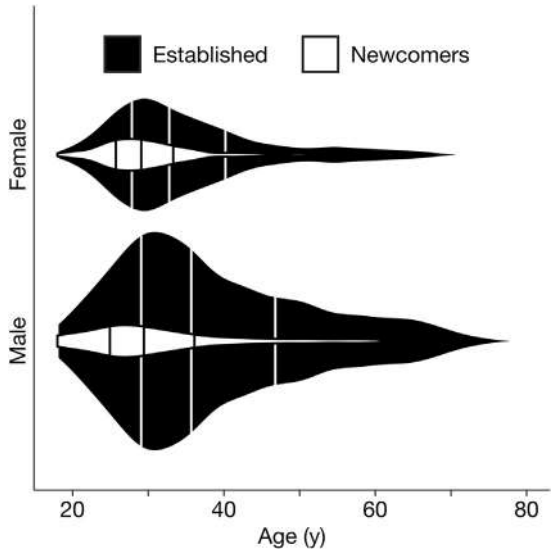

Figure 1. Age of respondents by sex. The age distribution of survey respondents by male or female sex and study cohort. The vertical lines within each category denote quartiles with respect to age (n=4558). Respondents reporting as neither male nor female (n=30) or those aged >80 y (n=4 males) are insufficiently numerous to be meaningfully visualized and are omitted for clarity.

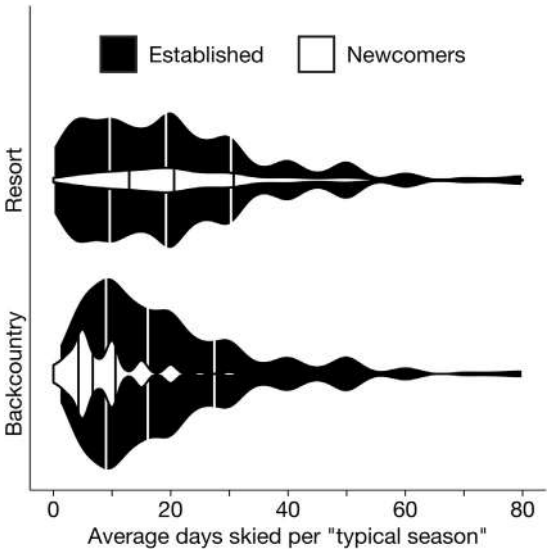

Figure 2. Average days skied in resorts and backcountry per season. The distribution of days skied in the backcountry and at ski resorts for established and newcomer respondents in a "typical season" as defined by the respondent. The vertical lines within each category denote quartiles with respect to days (resort, n=4646; backcountry, n=4650).

nature, reduces variability and lowers the threshold of difference needed to meet statistical significance, we additionally report effect size next to *P* values, where appropriate, to assist the reader in estimating the importance of the finding or magnitude of difference.

Responses to questions using paired interactive numeric sliders, namely those about time split between the backcountry and resorts before and during the COVID-19 pandemic, were recoded using a simple linear transformation from the original (−100 to 100) scale to approximate a percentage scale. These sliders, unlike other item types, recorded a default, "placeholder" value even without any participant interaction. Because the paired sliders defaulted to the same random position, nonresponders were easily identified and removed from analysis on these questions.

Results

The survey produced a total of 5674 raw responses over the survey period of March 1, 2021 to March 31, 2021, with 4792 responses after eliminating 882 early drop-out participants. By recruitment source, the largest group of responses (49%, n=2338) was from organizations in backcountry and avalanche education, followed by US avalanche centers (31%, n=1494), and media or social media websites (16%, n=746). Most responses were from the United States, with only 21 (0.4%) participants reporting Canadian postal codes. Respondents were predominantly young males, as visualized in Figure 1, and mostly established backcountry skiers (84%) with >10 y of resort experience and 4 to 6 y of backcountry experience, as shown in Figure 2. They reported spending an average of 15 d in the backcountry and 20 d at resorts in a "typical season."

Since the onset of the COVID-19 pandemic, survey participants reported spending a significantly higher proportion of their time in the backcountry instead of at resorts (Figure 3). Overall, since the COVID-19 pandemic began, participants reported spending 17% (95% CI, 15.8−17.9) more of their ski days in the backcountry; Welch's paired t (3026)=32, n=3027, $P<0.0001$, $d=0.57$. Participants in the newcomer cohort reported a greater shift, spending 36% [95% CI, 33.3−38.7] more of their ski days in the backcountry (n=475) during the COVID-19 pandemic, compared with 13% [95% CI, 12.2−14.3] among established backcountry skiers (n=2446), which was significant on a 2-way repeated-measures ANOVA; $F(1, 5836)=122$, $P<0.0001$, $\eta^2=0.02$.

In addition, during the COVID-19 pandemic 19% of all participants reported spending almost all (95% or more) of their time in the backcountry, substantially higher than the 8% who did so before the COVID-19 pandemic. These shifts were significant on McNemar's tests of paired proportions: X^2 (1)=359, $P<0.0001$, $g=0.45$; and X^2 (1)=101, $P<0.0001$, $g=0.25$,

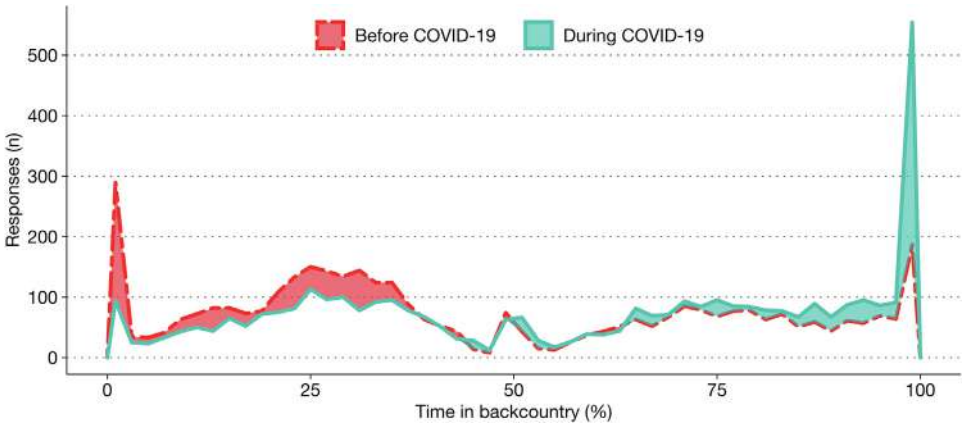

Figure 3. Increase in backcountry versus resort days during the COVID-19 pandemic. Percentage of ski days spent in the backcountry versus in resorts before and during the COVID-19 pandemic. Participants reported spending a higher percentage of their ski days in the backcountry since the beginning of the pandemic. Additionally, during the pandemic, the number of participants who reported skiing almost exclusively at resorts decreased, whereas the number of participants who reported skiing almost exclusively in the backcountry increased (n=3,027). COVID-19, coronavirus disease 2019.

respectively; n=3027. When asked about their perceptions of overall backcountry use, 81% of established skiers reported noticing more people in the backcountry during the COVID-19 pandemic (n=3898).

Established skiers were also surveyed on changes in their own habits due to the COVID-19 pandemic. The majority (97%) reported entering the backcountry with the same number of partners, with none reporting fewer partners (n=2632). No respondents reported changing the distance they toured from the trailhead (n=3125). When surveyed on whether the COVID-19 pandemic had influenced the frequency of their backcountry use, 27% reported more frequent use, 56% reported no change, and 17% reported less frequent use (n=4026). As a validation measure, these responses were tested in participants against reported changes to the percentage of days in the backcountry (as reported above). A 2-way repeated-measures ANOVA demonstrated significance to the expected (commensurate) relationship, suggesting consistency within respondents' answers; F (2, 6456)=204, P<0.0001, η^2=0.06.

The newcomer cohort respondents (n=572) were surveyed about whether certain consequences of the COVID-19 pandemic were important in their decision to first enter the backcountry. The consequences that participants agreed or strongly agreed were important included resort closures (27%), uncertainty about resort operations (26%), and limited resort access (35%).

All participants were also surveyed on their perceptions of the relative risks of sustaining injury and getting COVID-19 in the backcountry compared with at a resort. The majority (91%) of respondents believed that they had at least a somewhat higher chance of getting COVID-19 at a resort (n=4224). Conversely, 72% of the newcomer cohort believed that they were more likely to get injured in the backcountry, a significantly higher proportion than the 56% of established skiers who shared this belief; unpaired t (739)=8.4, P<0.0001, n=3679, d=0.36.

Participants reported a median self-perceived ability level of "Advanced/Expert" for resort skiing, which was 1 full level higher than that in the backcountry cohort, in which the median was "Strong" (95% CI, 1.00−1.00) (WSR, W=3896198, n=4719, P<0.0001, r=0.96). There was also an association between seasons of experience and self-perceived backcountry ability (Figure 4), with the newcomer cohort reporting lower ability (median "Intermediate" versus "Strong") by 1 level (95% CI, −1.00 to −1.00) (MWU=542,551, n=4761, P<0.0001, r=0.55).

Although most respondents reported having formal avalanche training (Level 1 or higher), 24% of the newcomer cohort lacked any formal avalanche training. This proportion was significantly higher than the established cohort's 14%; unpaired χ^2 (1)=42, P<0.0001, V=0.10 (Figure 5). The effect of survey referral source on reported avalanche education is demonstrated in Figure 6: participants who reported having formal training (n=4023) were more likely to have been referred to the survey via avalanche education organizations (55%) than those without formal avalanche education (n=728), who were predominantly referred through local avalanche forecast centers (50%) or online media and social media outlets (30%); unpaired χ^2 (3)=408, P<0.0001, V=0.30. Almost all participants reported carrying appropriate avalanche safety equipment (avalanche beacon, probe,

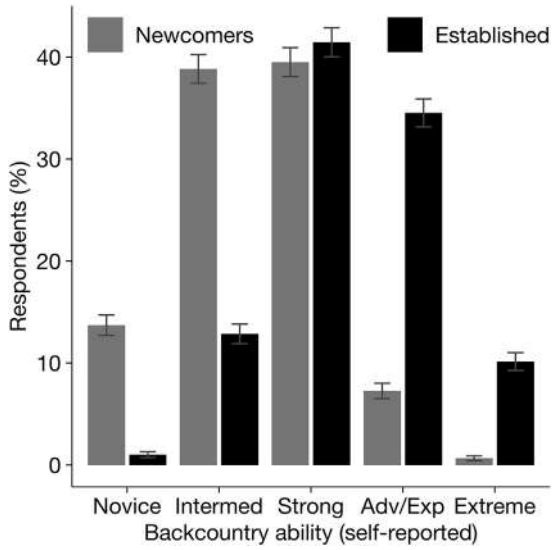

Figure 4. Backcountry skiing/riding ability by cohort. Collectively, the established cohort reported having a significantly higher backcountry skiing ability compared with the newcomer cohort (n=4761). CIs are shown at 95%. Adv/Exp, advanced/expert; Intermed, intermediate.

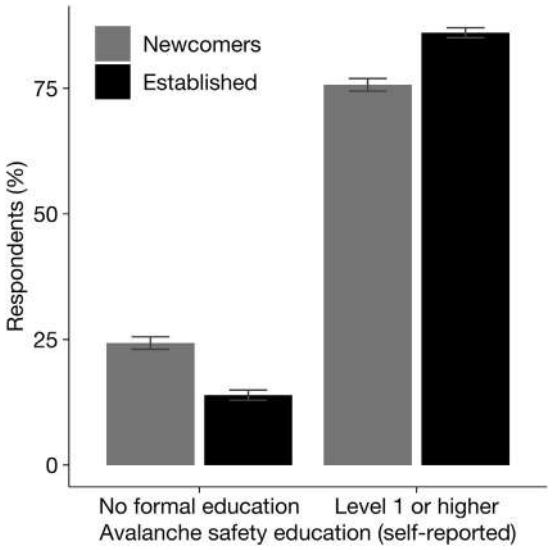

Figure 5. Formal avalanche education by cohort. The participants in the newcomer cohort reported lower overall levels of avalanche education, and a significantly higher proportion of respondents in this cohort lacked any formal education in avalanche safety. CIs are shown at 95%.

and shovel) while in the backcountry, with 97% carrying all 3 and only 2% of people carrying none (total n=4621).

When surveyed on their willingness to accept risk in the backcountry on a scale of 1 to 10 (from completely unwilling to very willing to take risks), the newcomer cohort reported a willingness of 2.8±1.7 to take risks compared with the established cohort at 3.4±1.9, with a difference in means of −0.61 (95% CI, −0.76 to −0.46); unpaired t (754)=−7.9, $P<0.0001$, n=4364, $d=0.33$. As shown in Figure 7, the newcomer cohort also reported feeling less comfortable assessing avalanche risk in various conditions and terrain than the established cohort. Newcomers reported a median confidence in assessing "simple" conditions and terrain, which was 1 full degree lower (95% CI, 1.00−1.00) than that in the established cohort at "moderately complex"; MW$U=629336$, $P<0.0001$, $r=0.47$.

Discussion

The COVID-19 pandemic had a complex effect on skiing and riding, both in resorts and the backcountry, with many skiers shifting their choice of where to ski and how to access the terrain. This study attempted to identify new backcountry skiers and ascertain attitudes and perceptions of both new and established backcountry skiers regarding several downstream effects of the COVID-19 pandemic. Four main findings of this study merit further comment: 1) both new and experienced backcountry skiers reported spending more of their time in the backcountry since the pandemic started; 2) for many, changes in ski area operations were a significant factor for this increase; 3) this cohort of inexperienced backcountry skiers expressed less confidence in their ability to assess avalanche risk than the experienced cohort; and 4) almost one-quarter of new backcountry skiers lacked any formal avalanche education.

Our finding that people reported spending more time in the backcountry supports what has been reported in the media and experienced anecdotally by many (including 81% of our respondents). This qualitative study did not aim to quantify overall how many new backcountry skiers were created during the COVID-19 pandemic; however, it does demonstrate that both new and established backcountry skiers reported spending significantly more of their time (17%) in the backcountry since the start of the COVID-19 pandemic. It is also notable that the proportion of our respondents who spent nearly all their time at resorts before the pandemic was cut in half, whereas those who spent nearly all their time in the backcountry had doubled.

Although most new backcountry users did not report that COVID-19 was a major factor in their decision to start backcountry skiing or riding, it is notable that more than one-quarter did consider resort closures due to COVID-19 and uncertainty of resort operations as important factors in their decision and that 35% believed

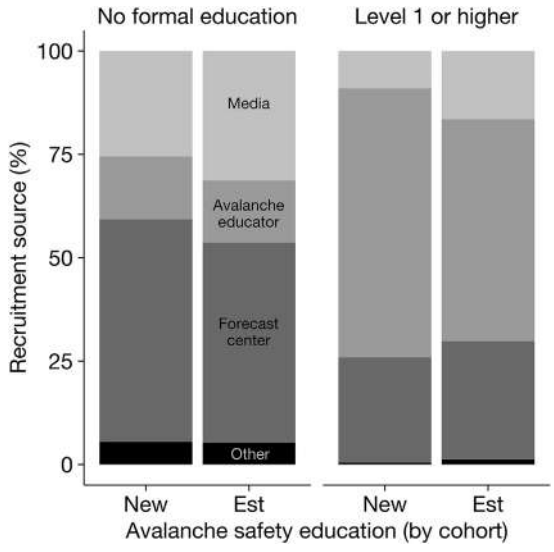

Figure 6. Formal avalanche education by survey referral source. The participants who reported having formal (Level 1 or higher) avalanche education (n=4023) were more likely to have been referred to the study through the websites of avalanche education providers, such as the American Institute for Avalanche Research or the American Avalanche Institute. Those reporting no formal education (n=738) were more likely to have been referred through online media and social media outlets or from local avalanche forecast centers. New, newcomer cohort; Est, established cohort.

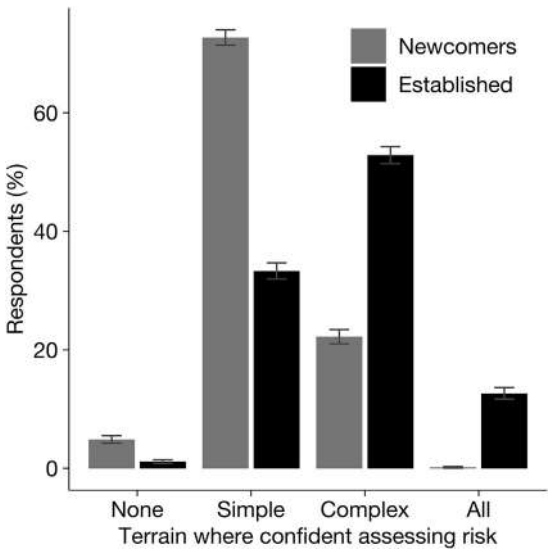

Figure 7. Confidence in assessing avalanche risk in various conditions and terrain. The participants in the newcomer cohort reported a median confidence in assessing avalanche risk in "simple" conditions and terrain, which was significantly lower than that of the participants in the established cohort, who felt comfortable assessing risk in "moderately complex" conditions and terrain (n=4566). CIs are shown at 95%. None, not confident at all; Complex, moderately complex.

that limited resort access was an important motivator. Even before the COVID-19 pandemic, backcountry skiing had already seen its greatest year-over-year growth; hence, any further increase in popularity represents a profound impact on the sport, as evidenced by the reports of ski shops selling out of backcountry touring equipment and avalanche education providers being overwhelmed by skiers' demand (Mander B. Ski in the Wild. *Wall Street Journal*. November 28, 2020).

Not surprisingly, the risk perceptions of the newer skiers differed from those of the more experienced skiers. On average, they perceived a higher injury risk in the backcountry and had less confidence in their ability to assess avalanche terrain. They also reported a lower overall self-perceived skiing ability, both in the backcountry and at resorts. Although a detailed analysis of the downstream incidence of avalanche and search and rescue use between these cohorts was beyond the scope of this study, these traits seem to be grossly reflected in the avalanche fatalities through these years. The winter of 2020 to 2021 was unique not only because of the COVID-19 pandemic but also because of the persistent and widespread unstable snowpack across the wider United States mountain west. This, unfortunately, was reflected by a historic number of avalanche fatalities.[7] Contrary to popular belief, the US Forest Service notes that most of these recent avalanche fatalities (among all types of backcountry users, including snowmobilers) were experienced recreationalists.[7,8] This may be a reflection of the self-described differences in ability and risk perception reported by the more experienced established cohort.

Lastly, almost one-quarter of the newcomer cohort lacked any formal avalanche training, a figure which is likely underrepresented given that 80% of our respondents were recruited from avalanche education providers or avalanche centers. Given the serious danger of avalanches and the importance of both mitigating risk through careful decision making and training for immediate companion rescue in case of a burial, the lack of formal education among the newcomer cohort is a substantial concern to public health. As this cohort continues to ski without this training, their risk-taking behaviors are likely to increase with more comfort in the backcountry environment and positive reinforcement from each run completed without consequences despite having made potentially dangerous choices.[9]

LIMITATIONS

We report several limitations to this study, including those common to all web-based surveys, such as but not

limited to biases, such as sampling, selection, nonresponse, social desirability, acquiescence, anchoring, and recall. Asking respondents about their backcountry use "before COVID-19" begets a substantial inherent risk of recall bias. Similarly, although our instrument employed such phrasing to frame relevant questions as comparing before or during the COVID-19 pandemic to facilitate statistics, participants reported their seasons of experience in terms of whole seasons. Because the COVID-19 pandemic onset part way through the 2019 to 2020 season, it is expected that some participants reporting this as their first backcountry season (n=263) may have entered the sport before its onset, which limits our ability to absolutely associate all newcomers with the pandemic. Further, responses were only collected for a single month during ski season because unexpectedly high participation rates achieved our participation target fairly early. It is expected that a longitudinal survey over many months may capture some skiers who are only active for part of the season or in areas with variable snow conditions and avalanche risk throughout the year.

Additionally, although we attempted to reach inexperienced backcountry skiers by requesting that ski areas and retailers recruit skiers to our survey on their websites, this was met with limited engagement, and most of our recruitment was ultimately through avalanche educators (49%) and avalanche forecast centers (31%). This likely biases responses toward persons already engaged with avalanche safety, with the expectation that this likely causes our estimates and conclusions to substantially underestimate skiers with little to no avalanche education, and those who are not aware of avalanche danger. Similarly, we recognize that our conclusions may have suffered from nonresponse bias from those with limited education or experience and who may have, therefore, decided not to complete our survey. Additionally, respondents were predominantly from the western United States, further limiting generalizability, especially to American Northeast skiers.

When evaluating changes to the percentage of ski days spent in the backcountry, we attempted to exclude nonresponders by eliminating what we identified as placeholder values recorded by our survey platform, as detailed in the methods section. Although all efforts were taken to accurately identify such cases, we were unable to identify any participants who agreed with and so purposefully left the placeholder or whose purposeful responses inadvertently mimic a placeholder. Because of this, some true respondents were likely eliminated, the mathematical result being some degree of overestimation of the magnitude of change reported. For process integrity, we ran these statistics without eliminations, and significance was retained on all tests at a similar high degree. Lastly, our study was only intended to assess subjective changes in backcountry use and perceptions, and was not designed nor able to assess the quantitative growth, or exactly how many new backcountry skiers the conditions around the COVID-19 pandemic have created compared with baseline.

Conclusions

Our participants' responses support the media reports that backcountry use increased substantially during the COVID-19 pandemic, and that the pandemic was influential in many people's decision to first enter the backcountry. The fact that nearly one-quarter of our respondents who started backcountry skiing since the beginning of the pandemic reported having no formal avalanche training is concerning—a figure that is likely underestimated by this study. Avalanches offer no warning and occur in a wide variety of terrain; without training, most avalanche risks are incredibly difficult to assess, if not entirely invisible. As such, the newcomer cohort represents an especially important demographic for outreach and education efforts in the coming seasons as backcountry skiing becomes increasingly more popular each year.

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Author Contributions: Study concept and design (EAV, APC, SJHT, JH, JDJ, DCF); data acquisition (EAV, APC, SJHT, DCF); data analysis (EAV); drafting of the manuscript (EAV, APC, SJHT, DCF); critical revision of the manuscript (EAV, JH, JDJ, DCF); and approval of final manuscript (EAV, APC, SJHT, JH, JDJ, DCF).

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Disclosures: DCF is a volunteer board member and medical advisor of the Sierra Avalanche Center. His involvement with this research is independent of that appointment, and the Sierra Avalanche Center has not endorsed or otherwise supported this study other than hosting our survey URL on their webpage.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.wem.2022.08.005.

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ORIGINAL RESEARCH

Rescue Activity of a Civilian Helicopter Emergency Medical Service in the Western Cape, South Africa: A 5-Year Retrospective Review

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Introduction—Helicopter search and rescue (SAR) in Africa is conducted primarily by military organizations. Since 2002, the Western Cape of South Africa has had a dedicated contracted civilian helicopter emergency medical service (HEMS) conducting air ambulance, terrestrial, and aquatic rescue. To our knowledge, this is the first description of the operations of an African helicopter rescue service.

Methods—A 5-y retrospective review of the terrestrial and aquatic helicopter rescue activity of a civilian-operated HEMS in the Western Cape, South Africa, from January 1, 2012 through December 31, 2016, was conducted. Data were extracted from the organization's operational database, aviation documents, rescue reports, and patient care records. Patient demographics and activity at the time of rescue, temporal and geographical distribution, crewing compositions, patient injury, triage, clinical interventions, and rescue techniques were analyzed.

Results—A total of 581 SAR missions were conducted, of which 451 were terrestrial and 130 were aquatic rescues. The highest volume of rescues was conducted within the urban Cape Peninsula. Hoisting using a rescue harness was the most common rescue technique used. A total of 644 patients were rescued, with no or minor injuries representing 79% of the sample. Trauma (33%, 196/644) was the most common medical reason for rescue, with lower limb trauma predominant (15%, 90/644). The most common clinical interventions performed were intravenous access (n=108, 24%), spinal immobilization (n=92, 21%), splinting (n=76, 17%), and analgesia administration (n=58, 13%).

Conclusions—The rescue techniques utilized are similar to those described in high-income settings. Uninjured patients comprised the majority of the patients rescued.

Keywords: helicopter rescue, hoist, longline, helicopter emergency medical service, rescue techniques, search and rescue

Introduction

The use of helicopters for search and rescue (SAR) reduces morbidity and mortality by decreasing time to access to emergency medical care and evacuation to an appropriate medical facility.[1,2] Helicopter rescue systems operate predominantly in high-resource settings and have contributed significantly to the capabilities of rescue services in dangerous or inaccessible terrain through rapid patient access, delivery of appropriately trained personnel, and timely transport to medical facilities for critically ill and injured patients.[2,3]

In Africa, helicopter emergency medical service (HEMS) SAR capabilities are limited and are generally conducted by the military. The Western Cape Province of South Africa is the exception, where a civilian-operated HEMS, subcontracted by the provincial government, has partnered with volunteer rescue organizations and

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provincial emergency medical services (EMS) to conduct terrestrial and aquatic rescues since 2002. The South African Red Cross Air Mercy Service (SARC AMS), a nonprofit organization, operates 2 helicopter bases in the Western Cape—one in Cape Town in the west of the province and one in Oudtshoorn in the east. Each base has 1 helicopter. The subcontracted model includes air ambulance operations, with a focus on rural aeromedical retrieval as well as rescue operations. Missions are dispatched centrally through a specialized provincial EMS dispatch center, with authorization for dispatch of the HEMS for all missions obtained from a core group of senior medical doctors from provincial EMS management.

The SARC AMS utilizes the single-engine Augusta Westland AW119 helicopter as a rescue platform, with hoisting and longline capabilities. All rescues are conducted under visual flight rules as a single pilot operation with assistance from an external load operator. Rescues are conducted using mission-dependent deployable multidisciplinary teams from various organizations and with varying medical training. The medical crew is primarily EMS personnel with qualifications ranging from basic to advanced life support. Doctors are utilised when specifically required, with limited availability.

The Western Cape is the southernmost of the 9 South African provinces, spanning 129,462 km^2, with approximately 6.2 million inhabitants, the majority of whom are located within the Cape Town metropolis. The province is a popular travel destination for local and international travelers with seasonal influxes of visitors over the hot and dry summer months from December to February. Of specific interest to this study, Table Mountain National Park (TMNP) is an open-access national park within the Cape Town metropolis, spanning 212 km^2 from Table Mountain to Cape Point, and receives an estimated 4 million visitors per annum, including 1 million summiting Table Mountain via cable car. The role of a helicopter-based rescue service in low-resource settings is not yet well described. A better understanding of this service within a resource-constrained public sector could provide insights to other low-middle income settings with an emphasis on the provision of services with equitable benefit. By bringing an external resource into a limited resource setting, such as in rural health systems, aeromedical services do not deplete limited local resources. This is particularly important when highly skilled resources are required or protracted transport times delay the return of potentially limited local resources to their service area.

In this mixed-service operation, the availability of HEMS must be closely managed to regulate costs and provide maximum benefit to patients and the EMS system. Through an improved understanding of the utilization of the service for SAR operations, multiple factors affecting the rescue operations such as budget allocation, equipment, training, and personnel requirements can be optimized. Of importance, in this setting, helicopters occupied in SAR operations are not available for air ambulance services, and as such, SAR dispatch criteria should be evidence based, as has been developed for HEMS.[4]

To our knowledge, there are no published data to understand the overall service demand and delivery of an African HEMS SAR service. The aim of this study was to describe the helicopter rescue activity of a civilian-operated HEMS in the Western Cape, South Africa.

Methodology

A retrospective descriptive analysis was conducted over the 5-y period from January 1, 2012 through December 31, 2016. For the purposes of this study, rescue was defined as a helicopter flight including the search for and/or extrication of persons with medical or situational difficulties in terrestrial (such as mountainous or remote terrain) or aquatic (including sea, river, and any expanse of water) terrain. All helicopter missions that were not rescue related were excluded from analysis.

Multiple primary data sources, including organizational aviation documents, operational rescue reports, and patient care records, were utilized for data collection. The data captured for analysis included geographical, temporal, patient, and operational rescue data. The patient and clinical data collected were limited to age, sex, activity prior/leading to rescue, medical interventions performed, patient acuity, provisional diagnosis, and disposition. Patient acuity was described using the South African Triage Score (SATS), a previously validated triage scale utilized by the Western Cape Emergency Medical Services.[5] Red code patients require immediate medical care; orange code patients require urgent care; yellow code patients and green code patients require less urgent medical attention. Critical patients were defined as patients with initial triage of red or orange code, including patients who died during the rescue. Patients triaged as blue were fatalities. The geographical data included rescue location and terrain. The operational rescue data included rescue crew composition, highest medical crew qualifications, and rescue techniques used to conduct the rescue.

The broad criteria for inclusion into the study included the following: helicopter rescue activity of the Cape Town and Oudsthoorn bases of the SARC AMS, including both aquatic and terrestrial helicopter rescues conducted during the defined study period. Cases were excluded if they were terrestrial or aquatic helicopter

Table 1. Aquatic and terrestrial rescue missions per annum

Rescue type	*2012*	*2013*	*2014*	*2015*	*2016*	*Total, n (%)*
Aquatic	47	30	18	22	13	130 (22)
Terrestrial	99	86	80	97	89	451 (78)
Total	146	116	98	119	102	581 (100)

rescues completed by other organizations, were conducted outside of the Western Cape Province of South Africa, or were service requests for rescue missions during which the helicopter did not take off or reach the rescue scene. When the minimum required patient data were missing or incomplete, the rescue information was included for analysis but not the patient data.

Univariate descriptive analysis was used to summarize and report on the geographical, temporal, patient, and operational rescue data. Means±standard deviation (range), medians (interquartile range [IQR]), and range were used to describe all summarized data. Data were captured using Microsoft Excel (version 16.22, Microsoft, Washington, DC) and analyzed using Microsoft Excel and Tableau Desktop Professional (version 2019.1.10). Ethical approval was granted by the University of Cape Town's human research ethics committee (296/2017).

Results

Between January 1, 2012 and December 31, 2016, a total of 4998 HEMS missions were conducted by SARC AMS in the Western Cape, of which 581 (12%) were rescue missions (Table 1). In general, helicopter rescue activity did not increase per annum over the 5-y sample; however, a reduction in aquatic rescue activity was apparent (Table 1, Figure 1). A seasonal surge was evident in the summer months, with 42% (245/581) of rescues conducted between December and February (Figure 2). Peak rescue times occurred between 1300 and 1800 (Figure 3) and on weekends (45%, 266/581; Figure 4).

In 71% (410/581) of the missions, a patient or party was located and extracted by helicopter. In an additional 8% (48/581) of the missions, the rescued patient or party was extricated by alternative means such as a boat or ground crew. No person was found by any party (ground or HEMS) at the conclusion of 19% (108/581) of the SAR missions (Figure 5). In 15 missions, the aircraft was stood down, unable to complete the mission because of safety concerns or because data were missing (Figure 5). The mission time from take-off to mission completion (ie, helicopter returned to base) was 2:15±2:53 (range, 0:18–9:29) for terrestrial rescue and 1:34±01:15 (range, 0:18–9:32) for aquatic rescue. The highest medical qualification of the personnel deployed to the patient during rescue was a doctor in 3% (15/581), an advanced life support paramedic in 71% (414/581), and an intermediate life support practitioner in 21% (120/581) of the missions. In 4% (22/581) of the missions, only a nonmedical technical rescuer or rescue swimmer was deployed.

Rescues around the Cape Town metropolis accounted for 66% (299/451) of terrestrial rescues, with 50% (226/451) of all terrestrial rescues occurring in the TMNP (Figures 5 and 6). Nearly half of all rescue activity within TMNP was conducted on the popular hiking trails

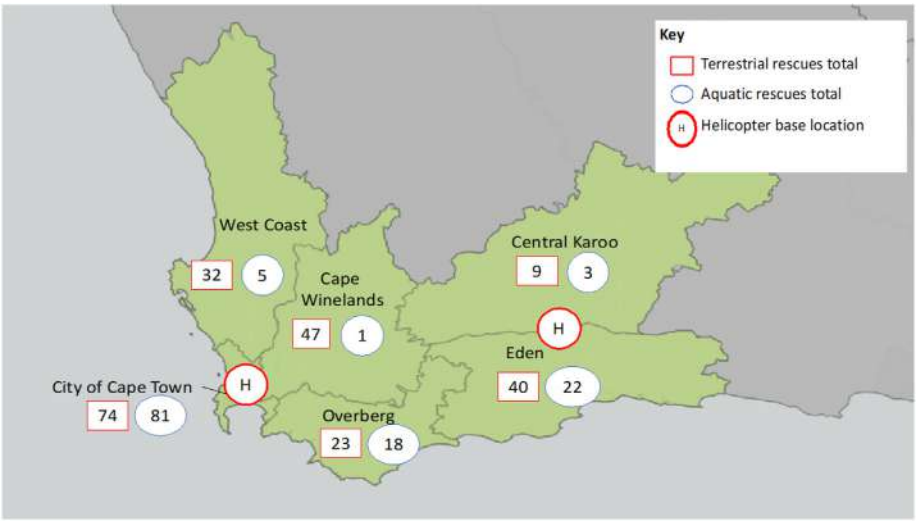

Figure 1. Map of rescue activity over 5 y by the municipal district in the Western Cape. Emergency medical service resources are distributed by municipal district. This figure represents the rescue activity per district, highlighting areas of frequent rescue activity.

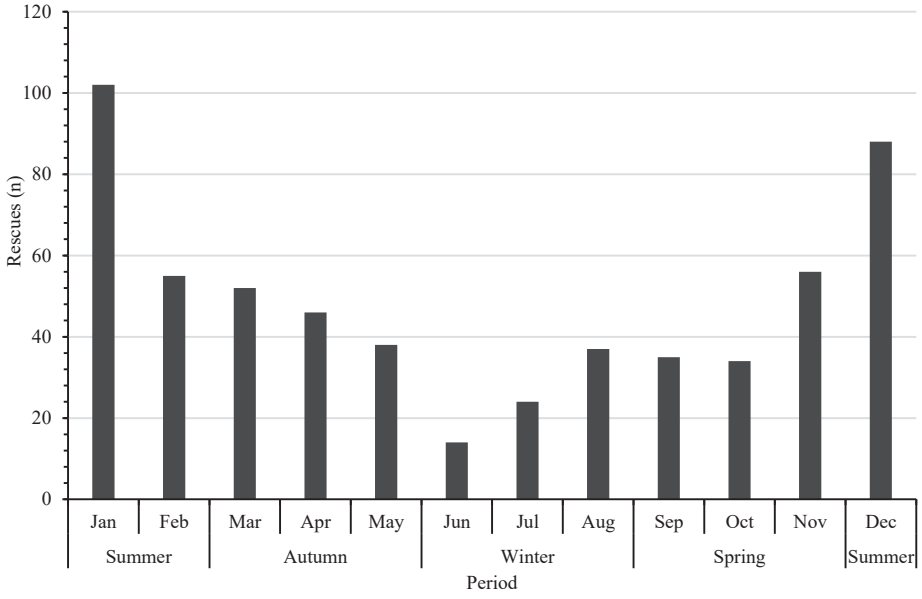

Figure 2. Temporal distribution of rescue activity.

Platteklip Gorge (n=74, 25%), Lions Head (n=47, 16%), and India Venster (n=14, 5%) on Table Mountain (Figure 6). Dehydration or heat-related illness was the primary reason for rescue in 14% of patients rescued from TMNP.

For aquatic activity, patients were rescued using a helicopter in 14% (18/130) of missions undertaken, with 54% (70/130) of the missions resulting in unsuccessful searches in which no patient was found (Figure 5). There was patient contact by the HEMS crew in 41 (32%) of total aquatic rescue cases, of which 50% (20/41) were fatalities.

Patient details were available for 93% (600/644) of persons rescued by helicopter. Adult patients (≥18 y) comprised 93% (551/600) of the sample. The patients were more commonly men (61%, 352/600), with a median age of 40 y (IQR, 19–85 y) for both sexes. The median age of adolescent patients (age, 13–18 y) was 16 y (13–18 y, age recorded for 27/32). Pediatric patients represented 2% (11/600) of the sample, with a median age of 7.5 y (3–11 y, age recorded for 8/11). Hiking and swimming were the most frequent activities, accounting for 71% (429/600) and 7% (40/600), respectively. Single patient rescues accounted for 60% (354/581) of all rescue missions, with multiple patients rescued in 14%. More than 3 persons were rescued in 6% of rescues undertaken, with all patients uninjured in rescues involving 6 to 20 patients.

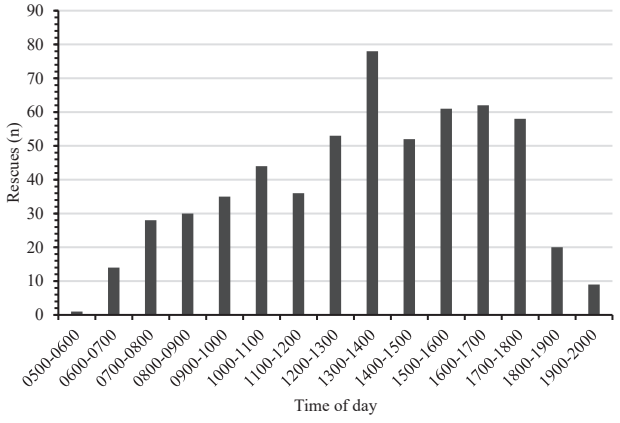

Figure 3. Time of departure for rescue.

Uninjured and less urgent patients (SATS triage coded green and yellow) comprised 79% of the sample (Table 2), received the fewest interventions, and were least likely to receive further care. Medical assistance was required for 343 (57%) patients, of whom 230 (60%) were transported to hospital for further care: 73 by helicopter and 157 by ground ambulance. Patient care records were available for 35% (119/343) of the patients treated. Patient care records were not available for 41% (19/45) of patients who were triaged as red code.

Lower limb trauma, dehydration, and spinal injury were the most common diagnosis (Table 2). Polytrauma patients comprised 7% (40/600) of all patients and accounted for 38% (22/58) of critical patients triaged orange or red code.

A total of 444 medical interventions were performed on 230 of the 343 patients requiring medical assistance (Table 3). The most common interventions were

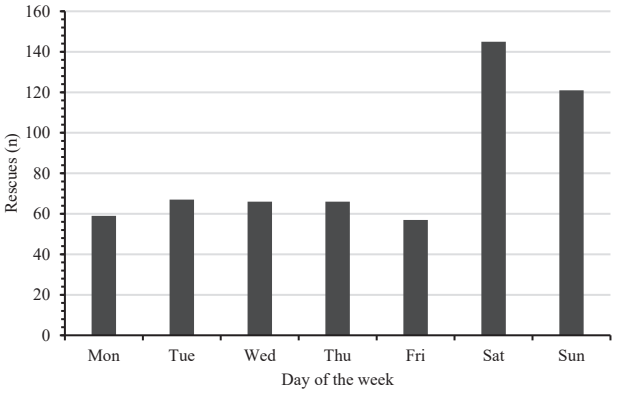

Figure 4. Number of rescues per day of the week.

intravenous access, spinal immobilization, and limb splinting (Table 3). Trauma patients required 77% (340/444) of all interventions. Critical patients (10%, 58/600), defined as patients who triaged orange or red, required 43% (189/444) of the interventions, including endotracheal intubation, assisted ventilation, sedation, drug administration, intraosseous access, and needle thoracentesis. The medications administered included analgesics, sedatives, cardiac drugs, dextrose, antiemetics, and inotropes. Return of spontaneous circulation was achieved in 3 of 7 attempted resuscitations, including 2 children who were successfully resuscitated after drowning. The number of interventions during cardiopulmonary resuscitation was 6 (range, 6–8).

There were 64 deceased patients recovered, with hiking (41%, 26/64), swimming (16%, 10/64), and fishing (6%, 4/64) accounting for the most activity in this subset. On arrival of rescue personnel, 94% (60/64) were deceased on first contact, and 4 patients died during the rescue.

Discussion

These data suggest that the SAR operations of a civilian-operated HEMS in the Western Cape of South Africa are not unlike rescue operations described in the international literature, most of which are in high-income settings, although the differing methodologies make comparison difficult. Temporal peaks, rescue techniques, and crewing configurations are similar to high-income countries across Europe, North America, and Australia.[6-10] In this mixed-use aeromedical model, the utilization of HEMS for rescue represented 12% of all missions undertaken, which is higher than other mixed-model operations with similar crewing configurations.[6]

The Western Cape is a popular tourist destination for local and international visitors during summer periods, which correlates with the increase in rescue activity. Popular travel destinations in Europe, North America, and Asia have reported similar temporal trends in HEMS rescues.[11-14] The increase in rescue demands over weekends and afternoons further demonstrates the largely recreational activities, such as hiking and running, requiring rescue efforts.

The usage of helicopters in SAR has demonstrated patient benefit, with rapid rescue preventing further harm and

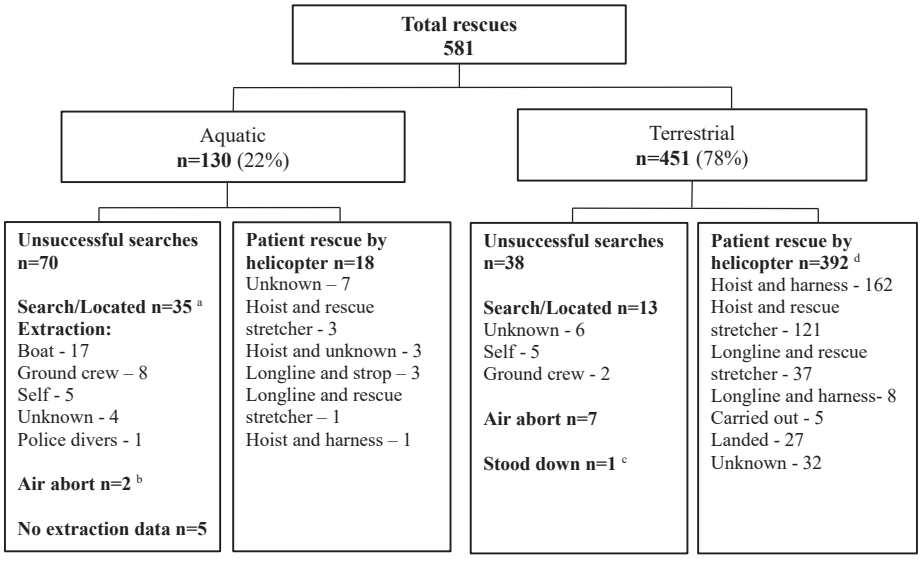

Figure 5. Rescue missions and patient extrication techniques utilized. [a]On 7 rescues, patients extricated by boat and ground crew required medical intervention from helicopter emergency medical service crew. [b]Helicopter mission stopped because of unsafe conditions such as weather or technical safety concerns. [c]Stand down during search as patient found safe elsewhere. [d]Some rescues involved multiple patients.

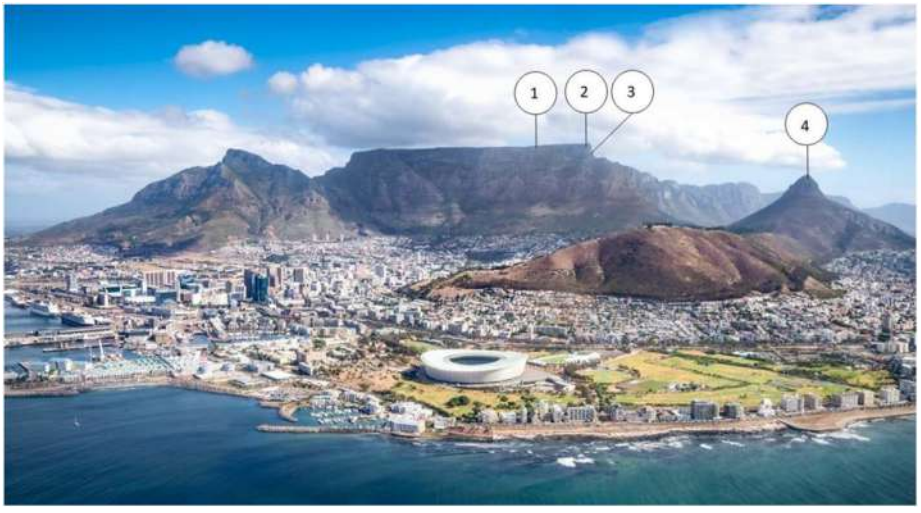

Figure 6. Common rescue sites in Table Mountain National Park. 1, Top of Platteklip Gorge hiking trail; 2, Table Mountain cable car station; 3, Top of India Venster hiking trail; 4, Top of Lions Head hiking trail.

limiting risk for both patients and rescuers and providing expeditious access to medical care.[2] The use of helicopters for SAR has been shown to reduce morbidity and mortality.[1,2] Helicopter SAR epidemiology globally demonstrates 2 predominant groups of persons requiring rescue: uninjured persons and those who have sustained trauma.[6,7,12,14-18] Over 40% of the persons rescued in this study were uninjured and required situational assistance because of inaccessibility, as reported in other HEMS SAR operations.[6,7,14,19] In Australia, persons with minor or no injuries have been reported to constitute 90% of HEMS SAR missions.[6] Male adult patients who had sustained trauma were found to be the most common group requiring rescue, which aligns with trends in international systems.[8,12,14,17,20] In Canada, Europe, Australia, Nepal, Taiwan, and the United States, male patients sustaining minor trauma comprise a large proportion of rescues.[6-8,12-14,17,21-23] The proportion has been reported as high as 78% of all persons rescued.[8]

The data highlighted several high-risk areas where frequent helicopter rescues occur, which can inform injury prevention strategies. Most terrestrial rescues occurred on popular hiking trails and tourist destinations in TMNP. Two hiking trails in TMNP, namely, Platteklip Gorge and Lions Head, accounted for one-quarter of all terrestrial rescues undertaken in the province, with the predominant reasons for rescue including dehydration and heat-related illness. One in 10 patients in the Western Cape required rescue for dehydration or heat-related illness, some of whom were critically ill and required advanced life support intervention. The substantial proportion of patients with potentially preventable causes for rescue, such as dehydration and heat-related illness on popular hiking trails and drowning near popular beaches, provide areas of focus for injury prevention strategies.[24] Interventions, such as increased signage and public awareness campaigns, would seem to be viable prevention strategies.[24]

Drowning is a significant cause of unintentional death in South Africa, especially among children under the age of 15, with no national drowning prevention strategy in place. In the Western Cape, 42% of fatal drownings occur during the peak summer period, consistent with the increased aquatic rescue activity.[25] The high incidence of drowning around the coastline of the Cape Town metropolis and increases in drowning over weekends align with findings in the provincial drowning prevention framework. Although helicopters have been shown to be effective in aquatic SAR and are used extensively in both military and civilian settings, patients were rescued by helicopter in only a small proportion of aquatic rescue missions in the Western Cape.[10,26] The factors affecting the aquatic rescue success may include the time between incident occurrence and request for assistance and response time to the scene. These factors require further investigation to optimize resource utilization and benefit. During aquatic rescue, the multiagency approach was evident in boat and ground crew patient extractions following helicopter location of the patient.

The rescue configuration and standard crewing of the SARC AMS meets international helicopter medical rescue recommendations.[2] Although many international systems use doctors for HEMS rescue, the availability of doctors in the prehospital setting in South Africa is

Table 2. Patient diagnosis and triage

Category n (%)	*Diagnosis*	*Red*	*Orange*	*Yellow*	*Green*	*Blue*[a]	*Total n (%)*
Uninjured 257 (43%)					257		257 (43)
Deceased 53 (9%)	Unknown cause					53	53 (9)
Medical	Dehydration	1		21	17		39 (7)
88 (15%)	Heat-related illness	5		10	6		21(4)
	Seizures	4		2			6 (1)
	Drowning	2		2		2	6 (1)
	Chest pain	2		3			5 (1)
	Envenomation			2	1		3 (0)
	Hypothermia			3			3 (0)
	Miscellaneous[b]	2		2	1		5 (1)
Trauma	Trauma - lower limb	3	4	77	6		90(15)
196 (33%)	Polytrauma	19	3	13		5	40 (7)
	Spinal injury	1	3	25			29 (5)
	Head injury	4		7	2		13 (2)
	Trauma - upper limb		2	8	1		11(2)
	Unspecified	2			1	4	7 (1)
	Soft tissue injury			2	2		4 (1)
	Trauma - chest	1		1			2 (0)
Total, n (%)		46 (8%)	12 (2%)	178 (30%)	294 (49%)	64 (11%)	594[c]

[a]Deceased persons.
[b]Includes abdominal pain, anaphylaxis, overdose (unknown substance), shortness of breath, and syncope.
[c]Six patients with no triage or diagnosis documented were excluded from the table.

Table 3. Most frequent clinical interventions performed[a]

Intervention	*n (%)*
Intravenous access	108 (24)
Spinal immobilization	92 (21)
Splint	76 (17)
Analgesia	58 (13)
Oxygen	37 (8)
Assisted ventilation	13 (3)
Medication administration	13 (3)
Sedation	10 (2)
Endotracheal intubation	10 (2)
Oral fluid	8 (2)
Cardiopulmonary resuscitation	7 (2)
Other[b]	12 (3)
Total	444

[a]Some patients required multiple interventions.
[b]Warming, cooling, dextrose administration, intraosseous access, and needle thoracentesis.

limited. The most common medical interventions performed in HEMS SAR include analgesia, intravenous fluid administration, and oxygen administration in international HEMS rescue,[2,6,21] with splinting and spinal immobilization also frequently performed in the Western Cape. Critical care interventions, such as endotracheal intubation, are uncommon in the HEMS rescue setting.[27] Advanced life support paramedics were most commonly utilized as the primary medical provider in this setting and would seem to be appropriate given that they are able to perform all common interventions as well as critical interventions such as rapid sequence intubation.

Patients with an initial SATS triage code of red, including 4 in-care deaths during rescue, comprised 10% of the sample and required more clinical interventions than the other triage groups. Nearly half of red triage patients sustained significant polytrauma requiring advanced life support interventions. Although critical advanced life support skills such as advanced airway management are infrequently performed in the rescue environment before extraction, these skills are important to prevent further morbidity and reduce mortality.[28] International guidelines on the determination of death in the wilderness environment detail the difficulties experienced in patient examination, access, poor patient history, and access to cardiac monitoring.[29]

Multipatient incidents accounted for 14% of rescues, and although not as frequent as single-patient rescues, multipatient rescues of >3 persons pose significant logistical and operational challenges for rescue personnel, including carrying limited equipment for extrication. It is of note that the large multipatient rescues undertaken in this sample involved largely uninjured patients, requiring primarily situational assistance. Helicopters are beneficial for multipatient incidents and can be used to both deploy extra assistance at the scene as well as in patient evacuation.[30]

The SARC AMS HEMS operation serves as a rescue platform and an aeromedical service, performing interfacility transfers and primary emergency scenes and servicing a vast low-resource rural population. The selection of cases for dispatch of this resource must be considered in the light of beneficence, and further research is required to describe the case-mix of the operation. Rescue missions may require several hours of dedicated time, limiting the availability of the resource for medical missions. Although some data describe no trauma mortality benefit for the use of HEMS in the South African setting,[31] further research on dispatch criteria and benefit in the rescue setting is needed.

Limitations

Only missions conducted utilizing the SARC AMS helicopters were described, with the exclusion of the South African Air Force and any ground rescue operations. The South African Air Force performed only 10 terrestrial helicopter rescues during the sample period, which were not included in this research. This research represents the activity of a single civilian-operated service providing both aeromedical and rescue services in a state service within a single province with unique and varied geography, which may limit applicability to other settings.

Data were limited by the consistency of the records kept and the availability of records, particularly patient care records. Clinical information was limited by the availability of the records, with missing records possibly because of patients being handed over to EMS staff for transport or further treatment. More than half of records for patients requiring medical treatment or who triaged red were not available, which limits the strength of data in this area.

As the research was retrospective, the data set was not designed for the purpose of this research. Records were captured as found, with incomplete data detailed in the results. The challenges in data capture included incompleteness of records and records being kept in different sites in the organization, prolonging the time period required for data capturing because of travel.

Conclusions

Rescue techniques and crewing configurations are similar to those described in high-income settings. Uninjured and less urgent patients comprised the majority

of the sample, with trauma the most common medical reason for rescue. Evidence-based prevention strategies should be considered to strategically decrease rescue demand. Improved understanding of the SAR operations of this service can inform beneficent and fair utilization of resources in a mixed-model aeromedical and rescue HEMS operation in a resource-constrained prehospital setting.

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Author Contributions: Study concept and design (JFPR, IH, PH); data acquisition (JFPR); data analysis (JFPR, IH, PH); drafting of the manuscript (JFPR, IH, PH); critical revision of the manuscript (JFPR, IH, PH); approval of final manuscript (JFPR, IH, PH).

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Disclosures: JPR and IH are former employees of the SA Red Cross Air Mercy Service and as such recognize the potential for organizational bias.

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BRIEF REPORT

Sri Lankan Sloth Bear (*Melursus ursinus inornatus*) Attacks on Humans

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The sloth bear (*Melursus ursinus*) is an omnivore that has been reported around most parts of South Asia. Although rare, sloth bear attacks can inflict potentially life-threatening injuries. This cross-sectional study analyzed 10 patients who had been mauled by sloth bears and who presented to rural hospitals in the Anuradhapura district of Sri Lanka between 2015 and 2019. All of the patients were male farmers. The human–bear encounters occurred in the jungle during the daytime. Ten victims sustained multiple soft tissue and bone injuries, mainly to the face and arms. The injuries ranged from minor abrasions to extensive deep lacerations and bone fractures. All of the patients were managed in the tertiary care hospital by multidisciplinary surgical teams. Sloth bear-inflicted wounds must be treated as major trauma. There is a need to formulate guidelines and train medical officers in managing animal-inflicted injuries in Sri Lanka.

Keywords: animal attacks, bear attacks, Sri Lanka, injuries, human–bear encounters

Introduction

The sloth bear (*Melursus ursinus*) is an omnivore that has been reported in Sri Lanka, India, Bangladesh, and Nepal.[1] The Sri Lankan subspecies (*Melursus ursinus inornatus*) (Figure 1A and B) is found primarily at low elevations (≤300 m) in open forests with lower human population densities.[2,3]

The Sri Lankan sloth bear has a large head and powerful forefeet but weaker hindquarters. The average height of adult male is about 90 cm at the shoulder and female is about 60 cm.[4] They weigh between 75 to 100 kg.[4] The fur of the body is rather long, shaggy, and sparse.[2] The claws are well developed (Figure 1C and D), enabling the bears to climb trees and dig for termites.[2] They have powerful jaws and strong teeth with prominent canines. The claws and teeth can inflict terrible injuries. They have a fearsome reputation among farmers as an animal that attacks without provocation.[5,6] The Sri Lankan sloth bear does not have a distinct breeding season.[2] They have unique adaptations for feeding on termites and are fond of honey and fruit.[2,5]

Attacks on humans have been reported in Sri Lanka since the 19th century,[7] but details of injuries and medical management have rarely been documented. Almost all bear attacks occur in dry zones, and a significant number are in the Anuradhapura district.[5] Bear attacks can cause physical disability, which profoundly affects the earning capacity of victims, and concomitant physical disfigurements affect their psychosocial wellbeing.

The objectives of this study were to describe the demographics, clinical manifestations of injuries, and management outcomes of bear attack cases admitted to the Teaching Hospital Anuradhapura (THA) over 5 y.

Methods

A cross-sectional retrospective analysis of medical records of bear attack victims presented to the university surgical unit and clinic at THA from January 2015

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Figure 1. A and B, Sri Lankan sloth bear (*Melursus ursinus inornatus*) front & side view. C and D, sharp claws. (Figure 1A, C & D taken by author BTBW and Figure 1B taken by Dr. PADM Senarachchi, in Wilpaththu National Park in Sri Lanka).

through December 2019 was carried out. The clinical data of patients were extracted from the medical records by a medical officer within few days or weeks after leaving the hospital. Later, after informed consent, the patients were contacted over the phone and interviewed. The patient demographics, circumstances of the incident, the number of bears involved in the attack, injury profile, defensive strategy, first aid used, management, and complications were recorded. Descriptive statistics were calculated using an online calculator (QuickCalcsl; GraphPad Software). Ethical clearance was obtained from the ethics review committee of the faculty of medicine and allied sciences, Rajarata University of Sri Lanka. Data are presented as mean±SD with range.

Figure 2. A, Case 1–Fibular fracture; B, Case 3–Abdominal laceration and, C, Case 4–Laceration near right knee.

Table 1. Summary of bear attack cases

Patient number	*Age (y) and sex*	*Incidents*		*Injuries*	*Name of the primary/ secondary care hospital. Initial vitals and medical/surgical management.*	*Initial vitals and management at tertiary care hospital.*		*Duration of hospital stay in days and outcome.*
		Month, year, time.	*Nature of encounter, number of bears.*			*Medical*	*Surgical*	
01	43 M	Aug 2015, 1345.	A wild bear attacked the victim while he was searching for cattle in the jungle.	Two abrasions in right scapula region. Superficial lacerations in right scalp and right thumb. Deep lacerations in lateral right leg, left wrist, right scapular region (5 by 7 cm) & left scapula region (1 x 1 cm). Compound fractures in right fibula (Figure 2A) & distal phalanx of the right thumb.	Base Hospital Padaviya. Conscious and rational, PR 88 beats·min^{-1}, BP 90/60 mm Hg, IV fluid, IV cefuroxime, IV metronidazole, IM pethidine, IM promethazine, IM tetanus toxoid.	Conscious and rational, PR 98 beats·min^{-1}, BP 100/60 mm Hg, IV fluid, IV cefuroxime, IV metronidazole, IV gentamycin, blood transfusion−1 unit of red cell concentrate, PO PPI, PO diclofenac sodium, PO tramadol, PO paracetamol, ARV, RIG.	Wound toilet, all laceration sutured after cleaning.	6; survived.
02	53 M	Jan 2016, 1200.	The victim entered the jungle with 2 friends. A female bear with cubs attacked him on the face and bit his scalp. The 2 friends ran away, and then returned and chased the bear away.	Lacerations on right frontoparietal (1 x 1 cm), left frontoparietal (1 x 1 cm), nasal (1 x 1 cm), left hand, left thumb (2 x 4 cm), left thigh (10 x 4.5 cm), penile laceration (1 x 1 cm)	Divisional Hospital Galenbindunuwewa. Vitals were not recorded; IV fluid, IV cefuroxime, IM tetanus toxoid.	Conscious and rational, PR 80 beats·min^{-1}, BP 120/70 mm Hg, IV metronidazole, IV gentamicin, PO cloxacillin, PO PPI, PO diclofenac sodium, PO tramadol, PO paracetamol, ARV, RIG.	Wound toilet lacerations sutured physiotherapy to the hand.	11; survived.
03	40 M	Nov 2016, 1800.	The victim went in search of cattle near a lake. A bear that was lying down attacked him.	Laceration in right arm (1 x 2 cm), right forearm (1 x 1 cm) right abdomen (1 x 1 cm, 2 x 2 cm, 6 cm) (Figure 2B)	Divisional Hospital Horowpathana. Conscious, rational, and in pain, vitals not recorded, IV fluid, IV cefuroxime, IM tetanus toxoid.	Conscious and rational, PR 88 beats·min^{-1}, BP 130/60 mm Hg, IV cefuroxime, IV metronidazole, PO PPI, PO diclofenac sodium, PO paracetamol, ARV, RIG.	Wound irrigation, 10% povidone iodine-soaked gauze packing.	2; survived.
04	53 M	Dec 2016, 1630−1700.	The victim went to pick dragon's eye (*Dimocarpuslongun*) fruit with 4 people. The bear rushed in, bellowing. The victim hit it, the bear fell and bit his left leg.	Laceration to right fibular region (5 x 10 cm) (Figure 2C) and peroneal nerve palsy.	Not recorded during the admission.	Conscious and rational, IV piperacillin, PO PPI, PO diclofenac sodium, PO tramadol, PO paracetamol, IM tetanus toxoid, ARV, RIG.	Wound toilet suturing of muscle and skin; neurology follow-up.	5; survived.
05	27 M	Jun 2017, 1330.	The victim went into the jungle searching for "Palu" fruit (ironwood, *Manilkarahexandra*). A female-bear with 2 cubs bit the left arm and thigh.	Frontal scalp laceration, multiple lacerations on right and left arm (length not recorded in datasheet), left ear laceration.	Divisional Hospital Thanthirimale. PR 76 beats·min^{-1}, BP 110/70 mm Hg, IV co-amoxiclav, IV metronidazole, PO diclofenac sodium, PO paracetamol.	Conscious, rational, and in pain, PR 88 beats·min^{-1}, BP 110/70 mm Hg, IV co-amoxiclav, IV metronidazole, PO PPI, PO diclofenac sodium, PO tramadol, PO paracetamol, IM tetanus toxoid, ARV, RIG.	Wound toilet and delayed primary suturing (suturing of left extensor muscles and left ear laceration).	5; survived.

(continued on next page)

Table 1 *(continued)*

Patient number	*Age (y) and sex*	*Incidents*		*Injuries*	*Name of the primary/ secondary care hospital. Initial vitals and medical/surgical management.*	*Initial vitals and management at tertiary care hospital.*		*Duration of hospital stay in days and outcome.*
		Month, year, time.	*Nature of encounter, number of bears.*			*Medical*	*Surgical*	
06	39 M	Jul 2018, 1230.	The bear attacked the victim on the right hand and left leg.	Laceration in right hand dorsum and palm; left leg lateral side, multiple; length not recorded.	Base Hospital Padaviya. Vitals were not recorded, IV co-amoxiclav, IV gentamycin, IV metronidazole, tetanus toxoid.	Conscious, rational, and in pain, IV co-amoxiclav, IV metronidazole, PO PPI, PO diclofenac sodium, PO tramadol, PO paracetamol, ARV, RIG.	Wound toilet and delayed primary suturing.	2; survived.
07	20 M	Oct 2018, 1500.	On his way home from a chena (a farm in the jungle), 2 bears came behind him and attacked him. He fell and pretended to be dead. The bears left him. He walked back to the chena.	Facial laceration extend to nasal cavity 2 cm (septal cartilage separated), right facial laceration, right pinna evulsion, laceration in posterior triangle, right temporalis muscle laceration (through and through laceration), buccal laceration.	Directly brought to THA.	Conscious and rational, PR- 90 beats·min^{-1}, BP 140/90 mm Hg, blood transfusion—1 unit of red cell concentrate, IV cefuroxime, IV metronidazole, PO PPI, PO diclofenac sodium, PO tramadol, PO paracetamol, IM tetanus toxoid, ARV, RIG.	Laceration and trapezius and temporalis muscles sutured. Devitalized tissues excised. Ear and nose lesions sutured. Septum placed between vestibule mastoid fixation.	11; survived.
08	50 M	Jan 2019, 0730.	On the border of a chena, 2 bears attacked, and 1 jumped at him.	Bilateral eyelid laceration, visual acuity normal, no globe injury, CSF rhinorrhea, forehead laceration (5 x 5 cm), occiput laceration (5 x 3 cm), right pinna laceration (1 x 2 cm), right forearm laceration (2 x 5 cm), right thigh posterior laceration (1 x 2 cm), right radioulnar fracture, right elbow dislocation, zygomatic fracture.	Divisional Hospital Ranorawa. Initial management not recorded by the medical officer.	IV piperacillin, IV metronidazole, fucidic acid eye ointment, chlorampenicol eye ointment, betadine cream to scalp, blood transfusion—1 unit of red cell concentrate, PO PPI, PO diclofenac sodium, PO tramadol, PO paracetamol, IM tetanus toxoid, ARV, RIG.	Facial and scalp reconstruction done; right wrist wound toilet with K wire; POP B/S elbow relocated; ORIF of Zygomatic fracture; bilateral orbital reconstruction done; forehead flap necrosis; wound debridement done.	17; survived.
09	39 M	May 2015, 1000.	The victim went to collect bee honey in the jungle and was attacked by a bear.	Lacerations in left posterior forearm below elbow (1 x 1 cm), (2 x 1 cm), (2 x 4 cm).	Base Hospital Kebithigollewa. Initial management not recorded by the medical officer.	Conscious and rational, PR 78 beats·min^{-1}, BP 120/80 mm Hg, IV cefuroxime, IV metronidazole, PO PPI, PO diclofenac sodium, PO paracetamol, IM tetanus toxoid, ARV, RIG.	Wound toilet and delayed primary suturing.	3; survived.
10	37 M	May 2019, 13.30.	The victim went to the jungle to collect wood with 2 friends. The bear attacked, the victim fell face down, and 2 friends chased the bear away.	Scalp laceration in right parietal region (12 cm). Occipital laceration 5cm, left arm 3 lacerations, (2 × 2 cm, 4 × 6 cm, 1 × 4 cm), right palm 3 lacerations (2 cm, 2 cm, and 4 cm)	Base Hospital Kebithigollewa. PR 78 beats·min^{-1}, BP 110/70 mm Hg, IV metoclopramide, PO cloxacillin, PO metronidazole, IV fluid.	PR 84 beats·min^{-1}, BP 110/70 mm Hg, PO cloxacillin, PO metronidazole, PO PPI, PO diclofenac sodium, PO paracetamol, tetanus toxoid, ARV, RIG.	Wound cleaning and suturing done.	4; survived.

M, man; PR, pulse rate; BP, blood pressure; IV, intravenous; IM, intramuscular; PO, per oral; PPI, proton pump inhibitor; ARV, anti-rabies vaccine; RIG, rabies immunoglobulin; THA, Teaching Hospital Anuradhapura; CSF, cerebrospinal fluid POP, plaster of Paris; ORIF, open reduction and internal fixation.

Results

All 10 patients were male, 40±11 (20−53) y of age. There were 2 attacks in the northeast-monsoon season (Dec−Feb), 1 attack in the first inter-monsoon season (Mar−Apr), 5 attacks in the southwest-monsoon season (May−Sep), and 2 attacks in the second inter-monsoon season (Oct−Nov). Human and bear encounters occurred between 0730 and 1800. Six attacks occurred between 1200 and 1500. Nine attacks occurred in the jungle (unprotected areas), and 1 in a chena (swidden farming practiced in Asian countries). Six occasions involved a solitary bear. In 3 of these encounters, the victims were mauled while searching for fruits of the ironwood tree (*Manilkara hexandra*), the dragon's eye tree (*Dimocarpus longan*), or for bee honey. These are all common sources of food for bears and humans.

Two attacks involved 2 bears. Two bears jumped on the victim from a close distance in the first attack, whereas 2 bears emerged from behind an anthill and attacked in the other instance. Two other incidents involved female bears accompanied by cubs.

In 8 incidents, bears made a frontal attack; the victims sustained soft tissue injuries to the scalp, face, nose, ears, muscles, and buttocks and fractures to the upper and lower limbs and the mastoid and zygomatic bones. When they fell, the bear bit various parts of the body, causing multiple injuries. On 2 occasions, the victims were initially bitten on the leg. In the first instance, the bear charged for about 15 to 20 min, bellowing. The victim hit it with a wooden pole, and the bear fell and bit the patient's left calf, which resulted in left common peroneal nerve injury followed by nerve palsy. On the other occasion, the victim nearly stepped on a bear lying on the ground and was bitten on the leg.

One patient developed cerebrospinal fluid rhinorrhea and pneumocephalus and was given empirical antibiotics to prevent meningitis. He did not developed meningitis during his hospital stay of 17 d. Nine patients were initially admitted to peripheral hospitals, and 1 to the THA. Upon admission to the peripheral hospital, the hemodynamic statuses of 6 patients were not recorded; 3 patients' hemodynamic statuses were recorded. Two patients (Table 1, patients 05 and 10) were hemodynamically stable. One patient (Table 1, patient 01) had a blood pressure (BP) of 90/60 mm Hg and a pulse rate of 88 beats·min^{-1}. Because both blood and blood products were not available in the peripheral hospitals, IV fluid resuscitation with crystalloid was started for this patient, whereas for the other 3 patients, IV access was established. Empirical IV antibiotics were administered to 5 patients, and another received oral antibiotics. Four out of 9 patients were given tetanus toxoid injections. Subsequently, all 9 patients were transferred to the THA within 40 to 100 min. At the time of admission to the THA, 9 out of 10 patients were hemodynamically stable. One patient (Table 1, patient 01) transferred from a peripheral hospital had a BP of 100/60 mm Hg and a pulse rate of 98 beats·min^{-1}.

All had x-rays of their limbs and chest, but 2 patients who had sustained extensive facial and scalp injuries had CT scans of the skull, brain, and face.

Intravenous fluids were continued for 4 patients and started for others to maintain IV access. The IV antibiotics were administered empirically to cover gram-positive, negative, and anaerobes. All were given nonsteroidal anti-inflammatory drugs and proton pump inhibitors in combination with paracetamol. An opioid was added for 6 patients. Tetanus toxoid was administered to the 5 patients who did not receive it at the peripheral hospital. Due to the risk of contracting rabies, all patients were immunized against rabies (immunoglobulin followed by a course of rabies vaccine).

After initial management, the wounds were explored; the devitalized tissues were excised, and the wounds were thoroughly irrigated with normal saline under general anesthesia and aseptic conditions in the operating theater. In 6 cases, primary suturing was done. In the remaining 4, wounds were dressed in 10% povidone-iodine-soaked gauze. Delayed primary suturing was performed for 3 patients (Table 1, patients 05, 06, and 07) within 24 to 48 h, but in 1 patient, the timing of suturing was not recorded. Two patients (Table 1, patients 07 and 08) with extensive soft tissue injuries and fractures were managed by teams of plastic, oromaxillofacial, orthopedic, and otolaryngology surgeons. One of them was managed in the intensive care unit for 1 d, in anticipation of breathing problems due to significant facial edema.

Patient 1 had tachycardia and a BP of 100/60 mm Hg on admission to the THA. Two others (Table 1, patients 07 and 08) lost blood in the perioperative period. These 3 patients had blood transfusions (1 unit of red cell concentrate each) to compensate for blood loss. The hospital stay was 7±5 (2−17) d. Two patients (Table 1, patients 07 and 08) who sustained multiple severe injuries were kept in the hospital for 11 and 17 d, respectively.

While in the hospital, 1 patient developed flap necrosis of the scalp and another developed common peroneal nerve palsy. None of the patients died from their injuries.

Discussion

Dwindling forest cover, increased population density, and encroachment on traditional bear habitats has led to a rise in human−bear encounters, causing increased mortality and morbidity of both humans and bears. A study carried

out in the dry zone of Sri Lanka showed that the number of bear attacks on humans doubled every 5 y for the past 20 y.[5] All of our patients were men, similar to other studies done in the region.[5,8–10] In South Asian countries, men are the primary income earners. They visit forests to gather livestock, hunt, and collect nontimber forest products. They tend to travel alone and walk deeper into the forest than women, thus increasing the probability of encountering bears.[9] There is a positive relationship between outdoor activities and bear attacks.[11,12] Mauling by bears can lead to significant disabilities, affecting the victim's ability to engage in previous occupations.

Our victims encountered bears during the daytime hours. The same time range was observed in 2 studies carried out in Sri Lanka and India.[5,9] All of the encounters took place in unprotected areas (not in national parks or wildlife sanctuaries), indicating that bears venture from the protected areas to forage for food. Most human activities leading to conflict with bears happen during the daytime in the jungle. A single bear attacked in the majority of our cases, and similar patterns were observed in other studies.[5,9,13–16] A single person and a solitary bear traveling in the jungle would not make much noise; therefore, the likelihood of encountering each other is high. In the encounters where cubs accompanied a female bear, she would have attacked without provocation to protect her offspring. The occasions on which two bears were involved were close encounters; therefore, the bears would have been startled, leading to an unprovoked attack.

In most of the incidents, the bear made a frontal attack; it was upright and made sweeping motions with its paws leading to facial and scalp injuries. This is typical of sloth bear attacks.[8,9,16] Bears are intelligent; they attack the face to weaken the victim, who then cannot retaliate.[17] Most of our patients sustained injuries to multiple sites, although in other studies this ranged from 25 to 52%.[9,14]

Nine encounters were sudden, where the bear and the victim surprised each other; hence, these attacks could have been defensive. Sloth bears share the same habitats used by other large carnivores[18] and have adopted highly aggressive behaviors, such as standing on their hind legs, bellowing loudly, and rushing to deter the potential predator.[5,9]

In 4 of our patients, IV access was established at primary care hospitals. All of these patients sustained extensive injuries. Their condition may have deteriorated while being transferred since it took considerable time to transfer patients to the tertiary care hospital. Therefore, it was vital to establish IV access/IV fluid resuscitation at first contact to prevent or mitigate hypovolemia. Ideally the first patient should have had blood transfusion in the primary care hospital, but these hospitals do not have facilities to store blood and blood products.

Bears carry multiple microbes in their mouths.[19] Bear bites are usually deep and highly susceptible to developing anaerobic infections, including tetanus.[5] Wounds would have been contaminated with soil and other elements because of the ferocity of the altercations. Indications for antibiotic therapy are contamination, infected bites, fresh, large penetrating wounds, or full-thickness skin punctures.[20] Bear bites fulfill these criteria. Anticipating infections by aerobes and anaerobes, the patients received empiric broad-spectrum antibiotics. A tetanus toxoid was given, either at the peripheral hospital or the THA. Bears can potentially transmit rabies.[21,22] Consequently, vaccines and immunoglobulin to protect against rabies were administered.

Irrigation of wounds with antibiotics solutions or saline, and wound debridement are key to successful wound management.[20,22] Some injuries required special investigations and multidisciplinary team involvement. Therefore, bear attack victims should ideally be managed in a tertiary care hospital.

None of our patients died from their injuries. In comparison, in an Indian study, the mortality rate was 2 to 11%.[13] This difference could be because of several reasons. In Sri Lanka, some victims might have died or gone missing in the jungle, or there may have been under-reporting because victims who engage in illegal activities (eg, poaching or growing cannabis) would not come to the hospital for treatment.

The patient with pneumocephalus and cerebrospinal fluid rhinorrhoea was given empheric antibiotics and did not developed meningitis. This is in contrast to a Nepali study, in which a patient with pneumocephalus came to the hospital 24 h after the incident and subsequently developed meningitis.[23] Medical officers should be trained to identify the patients who are more prone to developing meningitis after bear attacks and administer antibiotics without undue delay.

This study raises a few important points in managing patients sustaining bear attacks in Sri Lanka. There is a lack of uniformity in the management. The most probable reasons are the nonavailability of necessary equipment and medications, lack of knowledge, and the absence of clear protocols and guidelines at the peripheral hospitals. A practical problem is the unavailability of data due to deficiencies in record keeping; as data are essential in making guidelines, improvements in record keeping must be addressed. Guidelines for the management of animal bites, especially with regards to IV access, administration of tetanus toxoid, antibiotics, analgesics, control of hemorrhage, and expedited transfer to a tertiary care hospital should be developed and implemented.

Furthermore, ensuring the continuous availability of essential medications, dressings, and other equipment is a necessity. Medical officers and the supporting staff working in peripheral hospitals should be trained in the initial management of acute trauma patients. At the tertiary care centers, protocols should be made on subsequent management regarding investigations, timely referrals, multidisciplinary team approaches, timing, and the extent of wound management.

Conserving the Sri Lankan bear while reducing the mortality and morbidity to the humans is a daunting task. Minimizing human–bear encounters is the key strategy. Even though there is no consensus on the best protective action against sloth bear attacks, several measures could be adopted to mitigate human–bear conflicts. People can make noises while traveling in areas where encounters with bears are more likely, or when searching for common food sources, such as bee honey and fruits. In fact, the Veddas (indigenous people living in Sri Lanka) either shout or chant in loud voice when they travel in bear-infested terrain, giving bears ample warning to move away.[24] Bears are reluctant to attack humans who travel in groups.[5,25] When venturing into a forest, travel as a group and when moving apart, keep in touch with each other by verbal communication or visual sighting. If a bear is seen at a distance, avoid it by quietly moving out of the way.[5,25]

Finally, communities should be educated regarding the unique status and value of the Sri Lankan sloth bear and the vital role it plays in maintaining ecological balance.

Limitations

The limitations in our study were that, compared with other studies, our numbers were small, making the comparisons and conclusions challenging. Another limitation of this study was the retrospective nature of some of the events, which were subjected to recall bias. There were also a few inadequacies in the data because of gaps in record maintenance. A few patients did not come for follow up or respond despite repeated attempts to contact them.

Conclusion

In our study, the attacks occurred during daytime, across all seasons, in the forest or its vicinity. Most of these encounters were unexpected. The majority of the attacks were frontal, leading to extensive soft tissue injuries in the upper torso.

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CONCEPTS

Ten Years of the Nepal Ambulance Service: Successful and Sustainable Efforts

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We describe the evolution of the nonprofit Nepal Ambulance Service (NAS) in a narrative of its 10-y history, presenting geographical, social, cultural, and financial considerations that permeated the development of NAS. We gathered narrative information from the NAS leadership and partners to detail key organizational considerations regarding the implementation and maintenance of the prehospital system in Nepal. We describe the response of NAS to the 2015 earthquake and summarize transport data for 6 mo before and 6 mo after the event. The data collected included the date and time of calls received, time to ambulance dispatch, on-scene time, time to arrival at the hospital, time until the ambulance crew was back in service, patient age and sex, chief complaints, and work shift time of the ambulance crew. To characterize the time to response and transport after the 2015 earthquake, we present the means and standard deviations of the time intervals. There was an overall increase in calls and, specifically, trauma-related calls after the 2015 earthquake. The time from a call placed to dispatch was stable, approximately 2 min, throughout the period, whereas the time from dispatch to the scene and arrival at the scene varied widely. We discuss the response to coronavirus disease 2019 (COVID-19). The NAS provided care to 1230 patients with COVID-19. The descriptive data show how well NAS responded to a major national disaster and the recent pandemic.

Keywords: prehospital care, emergency medicine, global health, Nepal, sustainable development

Introduction

The 10th anniversary of the Nepal Ambulance Service (NAS) provides an opportunity to tell the story of a sustainable out-of-hospital operation and detail some of the organizational elements that may be useful in other countries. The NAS currently operates 10 ambulances in 4 locations in Nepal and is working with the Ministry of Health and Population, Nepal, to provide training to prehospital providers in each Nepali province. With >60,000 calls and 57 safe obstetric deliveries to its credit, NAS has proven that it has a role in responding to the emergency medical needs of Nepal. In the spirit of continuous quality improvement and offering context to other similar efforts, we reviewed the history and progress of NAS. Even with successful launch of a project, it is important to take stock, adjust, and improve if possible.[1] By detailing creative solutions to financial and cultural challenges, educational program designs, and response to crisis, we describe one example of successful development of a nonprofit health system that could be helpful for other groups that may face similar organizational challenges.

Nepal covers 147,000 km^2, similar in size to the US state of Georgia, and is home to 8 of the 14 highest mountains in the world. Since the first successful Mount Everest summit via the Nepali route (South Col) in 1953, a steady stream of mountaineers, photographers, and trekkers has led to an increasing number of visitors in Nepal. The need for medical care for locals and visitors

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led to the establishment of networks such as the Himalayan Rescue Association and NAS, which aim to provide emergency care and link trained health workforces in Nepal. However, Nepal's geography presents a profound barrier to emergency care. Much of the population lives outside of the Kathmandu Valley and has limited transportation options,[2,3] some in areas accessible only by foot, pack animals, or helicopters. In comparison, 9% of Nepal's population resides in the Kathmandu Valley, which covers 336 km^2 and includes 3 major cities: Kathmandu, Lalitpur, and Bhaktapur. There are more than a dozen hospitals in the Kathmandu Valley. Despite the relative availability of clinical sites and trained physicians in the Kathmandu Valley compared with those in rural Nepal, until recently, medical care was still greatly hindered by lack of prehospital emergency care.[4] In 2009, the majority of patients (53%) in Kathmandu arrived at hospitals by taxis, and only 14% of the category with the highest severity triage arrived by ambulances.[5] Only 10% of patients came by ambulances, which were ill equipped and had no trained health workers.[5] Public emergency telephone numbers and certified ambulances were nonexistent. At the launch of NAS in 2011, the initial goal was to cover densely populated areas near the Kathmandu Ring Road[6] and later expand.

Development of NAS

In April 2011, the nonprofit organization NAS was launched with the mission to provide rapid ambulance transport to hospitals along with lifesaving medical care by trained emergency medical technicians (EMTs) for sick and injured people regardless of their ability to pay. The key founding members included Nepali leaders in entrepreneurship and philanthropy, disaster preparedness experts, Patan Academy of Health Sciences faculty, and several volunteer international students and fellows. After 2 y of collaborative work among NAS, Nepal Telecom, and the Ministry of Information and Communications, a 3-digit toll-free emergency number (102) was established.[7]

The NAS began operations with 2 ambulances and by 2012, was operating 5 ambulances. Currently, NAS operates 10 ambulances: 6 in Kathmandu, 2 in Pokhara, 1 in Chitwan, and 1 in Butwal. Pokhara and Chitwan are major international travel destinations, and Butwal provides access to key transportation routes. Each vehicle is equipped with basic life support equipment. Today, NAS employs 27 EMTs, 20 ambulance drivers, 6 dispatchers, and 5 administrative support personnel. Each ambulance is staffed by an EMT and emergency first responder (EFR).

EFR training is more basic than EMT training but is crucial to both scene safety and patient transport. The ambulances and dispatch center are staffed 24 h/d, 7 d/wk. Crews work 48 h/wk in 12-h shifts from 0700 to 1900, with 2 dispatchers per 12-h shift. The NAS operates with assistance from Nepali police services, which allow ambulances and EMTs to stage on their properties. Radio communication was banned during the launch in 2011 because of government security concerns, forcing parties to communicate over unreliable mobile phone networks. In April 2020, this prohibition was finally lifted. The NAS installed a walkie-talkie repeater to use very-high-frequency communication.

Financial Aspects

The NAS provides care to patients regardless of their ability to pay. For those who can pay, NAS initially charged 20 rupees ($0.17 US dollar [USD]) per kilometer one way plus the cost of medication and disposable medical equipment. The charge has since increased to 25 rupees ($0.21 USD) per kilometer. The average total cost to patients is approximately 600 rupees ($5 USD) per encounter, with funding supplemented through several means. The NAS continues to operate at a deficit of approximately $500 USD/mo. Fundraising for the initial launch of NAS was achieved through private philanthropic and corporate donations. The initial 5 ambulances, each costing approximately $25,000 USD, were donated by local donors. Medical equipment, such as cervical spine collars, backboards, and splints, was produced locally. For most operations, the Nepali government did not contribute to costs. Beginning in 2019, financial support was provided by the Kathmandu metropolitan city council to cover ongoing operational deficits. Local Nepali businesses and donors from within Nepal and abroad contributed to the operational costs of overhead, equipment, and ambulances. Education and training materials continue to be provided through an academic partnership with the Stanford Department of Emergency Medicine and through several nonprofit organizations committed to the success of NAS. The ongoing operational support for NAS from academic and nonprofit organizations includes mentoring of Nepali EMTs and international students completing electives to create data-driven reports for NAS to use in grant writing. Additional international support was granted to NAS

Table 1. Nepal Ambulance Service training material for respiratory assessment

Respiratory assessment card
RIPPAS
R=RR
I=Inspect the patient's chest
P=Palpate for chest movement/injury
P=Percuss for resonance
A=Auscultate for lung sounds
S=SpO_2
SpO_2
Patients without COPD=94–98%
Patients with COPD=88–92%
Use oxygen therapy as required

RR, respiratory rate; SpO_2, saturation reading; COPD, chronic obstructive pulmonary disease.

after the 2015 earthquake, increasing the number of ambulances and expanding the system. Unfortunately, because income continues to lag, it is unlikely for NAS to become financially independent in 2022.

Education

The Essential Out of Hospital Care course was developed in partnership with faculty from Stanford medical school and Patan Academy of Health Sciences. The course was used to train the first class of EMTs in 2010, with students selected from medicine-adjunct fields that included health assistant, assistant nurse midwife, and community medical assistant. The learning tools included classroom lectures, skills workshops, and written assignments. As an example of the training tools, we presented the training material for respiratory assessment in Table 1. To date, 3 courses have been organized, training approximately 140 EMTs. The third course was conducted entirely by Nepali trainers. A Nepali medical director and Nepali physicians also lead quality improvement and continuing education while promoting awareness of and gathering support from the local community. Education for the local community by NAS takes place in schools (teaching young people how and when to call for help in an emergency) and community venues (to highlight the importance of recognizing the urgency of common issues, such as chest pain or stroke, in older populations). By including the community in education and awareness efforts, NAS hopes to improve the quality of care provided in a timely manner.

During the initial training course for each class of EMTs, key EMT and external defibrillator first-responder skills are organized into the following categories: IV placement and fluid resuscitation, basic life support, emergency childbirth and obstetric skills, trauma management, triage and disaster response, leadership, medical management, ambulance operations and transport, and communication. The level of care is above what is normally provided by a basic US EMT but below that provided by a US paramedic. Following this course, EMTs receive training twice a year to refresh basic concepts such as airway management, shock, cardiovascular emergencies, cardiopulmonary resuscitation, automated external defibrillator use, cardiac monitoring, respiratory emergencies, neonatal resuscitation, trauma resuscitation, pharmacology, and obstetrical emergencies. The refresher training sessions are from 3 to 5 d and run in partnership with foreign volunteer instructors and nonprofit financial support for training equipment. In addition, senior international paramedics provide mentorship with established NAS crews on dispatched calls to ensure smooth transition from in-classroom skills to active duty.

Recently, Nepal's Ministry of Health and Population established a new collaboration between the national dispatch center and NAS. The directive also gave NAS responsibility for training EMTs and EMDs in each of the 7 provinces, which required the development of 1 dispatch center in each province. The NAS will manage the national dispatch center and provide technical support to each provincial dispatch center. The emergency number 102 will be designated as a national toll-free number. The ultimate goal of NAS is to operate a nonprofit national ambulance service with funding and operational support from the Nepali government.

Overcoming Cultural Barriers

The organization Friends of NAS has used local advocacy and social media promotion to raise awareness of ambulance availability. Currently, after a decade of operation, dispatch remains underutilized, with approximately 15 to 20 calls/d, meaning that many sick patients choose to arrive at hospitals by taxis or other means. An increase in calls during a crisis in Nepal can make adequate staffing difficult, a challenge seen in other countries as well because of limited numbers of trained providers. When Kathmandu nears complete shutdown because of political rallies, the calls increase to 70 to 100/d, indicating that people are aware of the dispatch system but tend to take alternative transportation. The causes of this phenomenon are likely to be multifactorial, including a fear of billing and poor cultural understanding of out-of-hospital care. Unlike countries that have long-standing

ambulance services, readily available cardiopulmonary resuscitation courses, and Stop the Bleed campaigns, Nepali citizens are not routinely trained to recognize critical illness. Since 2017, Friends of NAS has worked with EMTs to arrange first aid classes in local schools and public places to highlight the importance of out-of-hospital care.

NAS INVOLVEMENT IN RESCUE AFTER THE 2015 EARTHQUAKE

The 2015 earthquake had catastrophic consequences for Nepal. On April 25 at 1156 Nepal Standard Time, an earthquake centered in the Gorkha region struck Nepal and its neighboring countries. The initial quake had a magnitude of 7.8. Aftershocks began immediately, with over 400 aftershocks recorded by the beginning of 2016. Two aftershocks occurred, one with M_w=6.7 on April 26 and one with M_w=7.3 on May 12.[8] Avalanches and landslides started within minutes of the initial earthquake.[8-10] In Nepal alone, the toll from the earthquake was >8000 deaths caused by the initial earthquake and approximately 700 additional deaths caused by aftershocks and landslides. More than 22,000 people were injured. Nearly 500,000 buildings were destroyed, and >250,000 were partially damaged, leaving 3.5 million people homeless. An ice avalanche on Pumori, a mountain 8 km away from the Everest Base Camp, killed 24 people and injured >60. The Everest Base Camp avalanche resulted in the deadliest single day on the mountain.[9]

There were severe impacts on hospitals and the prehospital medical system in Kathmandu. Damage to major thoroughfares and disruption of sewage structures hindered transportation and care. Tribhuvan International Airport was initially closed but reopened late in the day exclusively for relief flights. A postdisaster needs assessment conducted by the Nepali government and published by the World Bank found that >1000 public and private health facilities were completely destroyed or damaged. The earthquake affected over one third of health facilities in Nepal and caused 6.33 billion rupees ($53 million USD) in damage to healthcare structures.[10]

By noon, just 4 min after the initial earthquake, the NAS headquarters sustained enough damage to be nonoperational. The phone number 102 and most telephone lines were out of order. Although no calls were recorded by dispatch on April 25, the ambulance crews drove with army and police personnel into areas of fallen buildings and transferred victims to local hospitals. By April 26, NAS was able to create a Facebook post announcing that ambulances were still available despite damage to the headquarters and call lines. That day, an ambulance was called to a home for the blind in Bhaktapur, 13 km east of Kathmandu. The NAS EMTs extricated and resuscitated victims found in the rubble. In the following days, NAS arranged to use the police emergency number 100 and stationed ambulances at the main police station in Ratna Park, Kathmandu. By April 27, NAS began working with the Federation of Nepali Chamber of Commerce & Industries on a relief operation utilizing ambulances for disaster rescue. For 10 d, ambulances continued to be dispatched in collaboration with the army and police. For weeks thereafter, NAS transported people rescued locally in the Kathmandu Valley and patients flown from rural areas of Nepal who arrived at Tribhuvan International Airport. Because the number of victims soon outpaced capacity, only critically injured patients were transported by ambulances. Unfortunately, because of damage to the call center, we lack official records of ambulance runs from handwritten records. Seven hundred sixteen victims were transferred by NAS during the aftermath of the earthquake.

Transport Data

The NAS provided the transport log with deidentified data collected by ambulance dispatchers and recorded on monthly spreadsheets from October 2014 to October 2015. The data were collected for quality improvement as part of standard operations. No training was provided on data collection. After the 2015 earthquake, NAS was able to provide operational ambulance services (except for April 25, 2015), although the damage to the headquarters and communications systems impaired data collection. No calls were recorded from April 25, 2015, to May 1, 2015.

The data collected included the date and time of calls received, time to ambulance dispatch, on-scene time, time to arrival at hospital, time until the ambulance was back in service, patient age and sex, chief complaints, and interventions. Patients were stratified as adult and pediatric (age <18 y), and the mean ages were calculated. All data used for the analysis were deidentified, ie, the data did not contain protected health information. The study was exempted from human subjects' research by the Stanford medical school institutional review board, protocol number 63658. NAS leadership provided data and permission to analyze and report transport data. The data are presented as mean±standard deviation (range).

From October 2014 to October 2015, a total of 2585 patients were transported: 2407 adults and 178 children. The monthly proportion of calls related to male patients (52%) was similar to that of calls related to female patients (48%).

The data on the time of calls were collected only from April 2015 to October 2015. During this period, a greater number of calls were placed during the day (0700−1859) than at night (1900−0659), with the overall calls during the day accounting for 58% of calls.

The chief complaints that initiated the dispatched calls were grouped into categories based on the frequency of recorded calls. The complaints were categorized as breathing problems, chest pain, altitude-related illness, gastrointestinal, genitourinary, fever/infection, neurological, obstetrics/gynecological, endocrine, toxicology, psychiatric, trauma, hypertension, and unconsciousness. Overall, 21% of patients were trauma victims. There was an increase in trauma cases following the earthquake, from 16% before the earthquake to 27% in May and 28% in June. Among the transported patients, 19% presented with breathing problems. For these patients, oxygen administration was the most frequently used intervention by emergency medical service (EMS) providers.

The time from the initial call to placing an ambulance back in service was divided into intervals and summarized by month. The time in minutes from a call placed to dispatch appeared to be stable throughout the period observed: 2.0±0.1 (1.9−2.2) min. The time from dispatch to arrival at the scene varied widely, with the greatest values observed in April and May 2015: 17.5±5.1 (12−25) min. The time at the scene also showed wide variability: 11.2±3.0 (6−15) min. Compared with the time needed to arrive at the scene, the time from dispatch from the scene to arrival at the hospital varied less: 21.4±2.9 (16−22) min. Mean total time in April and May was 73 ±9.4 (46−77) min.

Limitations

Because the 2015 earthquake significantly damaged Kathmandu's infrastructure, few data are available for the week following the earthquake. We had to make assumptions based on our observations. Communication for the NAS system was routinely maintained through cellular phones; however, their function was compromised because of network outages immediately after the earthquake. Although the cellular network was re-established within hours after the first earthquake, there continued to be sporadic disruptions. The software system was built uniquely for the system described above, without a backup system. We also have much less data on staffing immediately after the event, adequacy, and applicability of training in disaster response and skills for assessing scene safety.

Our ability to assess whether the NAS EMS system was built adequately to respond to a disaster was impaired by lack of data collection from April 25, 2015, to May 1, 2015. However, as opposed to solely using observations by individuals, objective data provide some context.

NAS IN COVID-19 PANDEMIC RESPONSE

In 2020, when the SARS CoV-2 pandemic began, NAS was tasked with transferring patients COVID-19 in the Kathmandu Valley to the COVID-19 crisis management center, a government body. Nepal was the first country in South Asia to report a confirmed case of the virus on January 23, and cases rose slowly until May.[11] The increase was slow, in part because the government initiated a strict lockdown on March 24 that included closing land borders to neighboring India and China, canceling all arriving international flights, and closing schools. However, with easing of travel restrictions on June 1, 2020, thousands of workers arrived home from India and China, resulting in a 10-fold rise in cases. Phased reopening began on June 15, with the lockdown ending on July 21, 2020. As of November 2021, the Ministry of Health and Population had confirmed 821,000 cases and over 11,500 deaths.

Before the 2020 lockdown, there were approximately 23 ambulance runs daily. From late March until July, the calls increased to approximately 130/d. The NAS responded by doubling on-duty dispatchers, serving approximately 11,700 patients during the lockdown, 1230 with suspected or confirmed COVID-19. Decontamination of ambulances and acquisition of personal protective equipment proved to be challenges. Also, there were limited treatment options. International academic and nonprofit partners helped with the provision of materials as well as training sessions to teach evolving COVID-19 best practices and the use of inexpensive locally available materials such as dilute bleach and homemade alcohol-based sanitizing fluids. Several initiatives resulted in funding and in-kind donations for face masks, thermometers, and gowns. NAS ground ambulances continue to be staged at the Kathmandu airport to receive helicopter evacuations from regions unreachable by ground ambulances but requiring medical transport (major trauma, COVID-19, or severe illness).

Discussion

The success of this nonprofit organization was based on several factors. The first was the collaboration with medical institutions in Nepal and higher-income countries,[4] especially with Stanford medical school, which helped to ensure quality standards for the developing EMS system. This collaboration was essential for training of EMS personnel and establishing a system of education for continued operation. The train-the-trainer model enabled the third EMT course to be conducted without the help of the outside educators, demonstrating the ability of NAS to create a sustainable workforce and staffing model. The second cornerstone of success was the ability of NAS to address financial and cultural barriers. Public awareness campaigns increased the ability of NAS to respond to the community's concerns and build trust. Although currently, NAS still operates under a financial deficit, the deficit is only 2%. Funding has been sustained by cooperative efforts among institutions, local government, and the local business community. There is continued involvement from foreign communities, which facilitates sustained integration of global technical expertise and fundraising.

The analysis of the NAS response to the natural disaster of the 2015 earthquake and the COVID-19 pandemic showed that NAS can continue providing services during mass casualty incidents. Since the launch of NAS in 2011, the Nepali government has increased its commitment to NAS by increasing financial support and granting NAS oversight of the national dispatch center and EMT education. Nepalis increase their calls to NAS during crises, suggesting growing confidence in the dependability of NAS and recognition of NAS by Nepali communities. NAS also demonstrated its ability to rise to unforeseen challenges of the COVID-19 crisis by organizing training with new techniques for care of patients, protection of providers, and partnering to fundraise for these purposes.

Future Development

In the future, NAS plans to improve operations by building redundancy into the tracking system. If another natural disaster were to damage infrastructure, data collection and ambulance function would not be hindered to as great a degree as during the 2015 earthquake. In addition, NAS aims to expand operations by training EMTs from all 7 provinces. The NAS is well prepared for its ongoing responsibilities bestowed by the government and looks forward to continuing its pivotal role in the continuing development of a national EMS system in Nepal.

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CASE REPORT

Surviving a 400 m Fall on Mount Everest

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Mountaineering is a dangerous recreational activity with falls causing severe injuries and deaths. Survival from falls longer than 100 m is uncommon. We present a case of a high-altitude porter on Mount Everest who fell 400 m and survived. He slipped from a ridge at 7000 m (22,900 ft). A rescue party found him above Camp 2 (6600 m, 21,600 ft) and arranged a helicopter rescue. The Everest ER medical team at Everest Base Camp (5400 m, 17,700 ft) received the climber. They identified a head injury without signs of other serious trauma. A doctor provided manual inline stabilization of the cervical spine, airway support, and ventilation for the patient during the helicopter and ground transport to a tertiary hospital in Kathmandu. The time from the fall to definitive hospital care was 2.5 h. The hospital emergency team diagnosed an epidural hematoma and subarachnoid hemorrhage without midline shift and right parietal, orbital, and maxillary fractures. The neurosurgical team evacuated the intracranial bleed. The patient spent 6 d in the hospital. He had a positive neurological outcome. He had mild cognitive impairment and vision loss in his left eye but could perform activities of daily living. He returned to physical work, but not to climbing. This case report provides evidence that survival is possible after falls from extreme heights and sheds light on the challenges of an evacuation from austere environments.

Keywords: mountain recreation, accidents, risk, mortality, death risk

Introduction

Mountaineering is one of the most dangerous recreational activities, with a high number of injuries and deaths from trauma.[1] Falls cause most nonfatal injuries in mountain climbers.[2,3] Worldwide, falling is the most common cause of death in mountain climbing accidents, outnumbering avalanches, exposure, high altitude illness, and other causes.[4] Mountain climbers often traverse steep and icy terrain in remote areas. This puts them at risk of slipping and falling in regions far from definitive medical care.[4]

Falls are a leading cause of climbing deaths in the Himalayas. Based on the Himalayan database, a computerized registry of climbing expeditions in the Nepali Himalayas, in the period from 2010 to 2019, 42 of 222 attributable deaths (19%) were caused by falls.[5] On Mount Everest, falls are the most common cause of death among climbers.[5,6] There were 32 fatal falls from 2010 to 2019.[5] The site of the accident usually determined whether the event was fatal. If an accident occurred on steep terrain, it was more likely to have serious consequences.[5,7,8] Victims who have uncontrolled hemorrhaging or multiple critical injuries after falling can have poor outcomes.[9,10]

Backpack weight distribution affects a climber's balance and can contribute to a fall.[11] Heavy loads in the upper part of the backpack and unsecured equipment hanging outside the backpack increase the risk of a fall.

We present a case of a climber who survived a 400 m fall on Mount Everest. We discuss the challenges of evacuating patients from Mount Everest and the role of a rapid medical response.

The Himalayan Rescue Association (HRA) can provide rapid medical responses on Mount Everest. The HRA is a voluntary nonprofit organization established in 1973 with the objective of decreasing morbidity and mortality in the Nepali Himalayas. The HRA runs Everest ER, the only medical clinic on the Nepali side of Mount Everest not associated with a commercial climbing company.[12] Everest ER delivers primary care and emergency services to a population of >1600 climbers, guides, porters, and support staff stationed at the Everest Base Camp during spring climbing season.

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Case Report

One day in early May at about 1430 (0 min), Everest ER received a radio call that a climber had fallen on Mount Everest. The details were limited, but the initial report indicated that the victim was a Nepali high altitude porter who was descending after carrying oxygen to Camp 4 (8000 m, 26,200 ft) for a commercial expedition.

Subsequent reports indicated that the victim was a 36-y-old climber who seemed confused prior to the accident and had unclipped from the fixed rope. He wandered off despite multiple attempts from the rest of his party to call him back to the fixed line. The party lost sight of him. Observers from other points on the mountain witnessed the victim fall from a ridge on Lhotse face below Camp 3 (7300 m, 24,000 ft). Observers had clear lines of sight. The climber fell a vertical distance of approximately 400 m (1300 ft), from 7000 m (22,900 ft) to 6600 m (21,600 ft). A rescue team of climbers from various commercial expeditions found him alive near the bottom of Lhotse Face between Camps 2 and 3.

The rescuers placed outwear over the victim and secured him in a sled. They pulled the sled about 200 m to an improvised helicopter landing zone near Camp 2 (6600 m, 21,600 ft). At +15 min, the rescuers requested a helicopter rescue. The victim was picked up and flown to the Everest ER helipad (5400 m, 17,700 ft) for assessment before their transfer to definitive care at a tertiary hospital in Kathmandu. The helicopter arrived at the Everest ER helipad at +45 min. The victim was unloaded from the helicopter to the helipad with spinal precautions. The patient was assessed by 2 doctors from the Everest ER team with assistance from an emergency medical technician. The medical team performed a rapid trauma assessment. The primary survey revealed no significant external hemorrhage. The airway was patent. The patient had blood-stained teeth, but no blood pooling in his mouth. He was breathing at 18 breaths·min^{-1}. His heart rate was 90 beats·min^{-1} with strong carotid and femoral pulses. He had a capillary refill time of 1 to 2 s at the index fingers. The Glasgow Coma Scale (GCS) score was 5 (E1 V1 M3). The pupils were equal, round, and reactive to light (3−2 mm). The team did not have a thermometer, but the patient's skin felt warm. There was no evidence of spinal injury. There was ecchymosis of the right frontoparietal and maxillary areas. Clear fluid, possibly cerebrospinal fluid, was running from the nose. There were contusions of the anterior chest. There was no obvious injury of the pelvis or long bones.

One of the doctors cleared the airway with a manual suction device and inserted an oropharyngeal airway. The team was preparing for endotracheal intubation when the patient started making purposeful movements. The GCS score was 9 (E2 V2 M5). The team decided to keep the airway open using a chin-lift and jaw thrust rather than by intubation. Before evacuation, the team administered dexamethasone 8 mg intramuscularly to treat possible high altitude cerebral edema (HACE). They applied a pelvic binder. They also covered the patient with warm blankets. The team transferred the patient into the helicopter using a spine board. They removed the board once they had loaded the patient. An Everest ER doctor accompanied the patient in the helicopter.

During the flight, the doctor stabilized the cervical spine with both knees and used a jaw-thrust to help maintain an open airway. The patient required assisted ventilation intermittently during the flight. The doctor ventilated the patient with a bag-valve mask at a rate of 10 to 12 breaths·min^{-1} targeting a lung-protective tidal volume of 500 mL.

After the helicopter landed at Lukla Airport (+75 min), the doctor and 3 airport ground crew transferred the patient using spinal precautions into a fully fueled helicopter. The transfer took approximately 5 mins. The doctor re-evaluated the patient finding his condition unchanged and continued manual inline stabilization of the c-spine, airway support, and ventilation until the patient arrived at the hospital.

The patient arrived at Tribhuvan international airport in Kathmandu at +120 min. The doctor and the ambulance crew transferred the patient into the ground ambulance using spinal precautions. The emergency department received the patient at +150 min.

The trauma team met the patient in the emergency department. The vital signs were: respiratory rate 18 breaths·min^{-1}, heart rate 97 beats·min^{-1}, blood pressure 133/62 mm Hg, temperature 36.4°C, and oxygen saturation on room air 97%. The GCS score was 5 (E1 V3 M1). The team performed a rapid sequence intubation and administered intravenous ceftriaxone and normal saline (1 L).

Computed tomographic (CT) images of the head showed an epidural hematoma and subarachnoid hemorrhage without midline shift, a linear skull fracture from the right supraorbital region to the right parietal region overlying the hematoma, and a lateral wall fracture of the right maxillary sinus (Figures 1 and 2). The CT images of the spine, chest, abdomen, and pelvis did not reveal traumatic injuries.

The trauma team took the patient to the operating room for craniotomy, evacuation of the epidural hematoma, wound excision, scalp repair, and repair of the facial lacerations.

Postoperatively, the patient was admitted to the intensive care unit. He was extubated on Day 3 and transferred to the ward. He was discharged from the

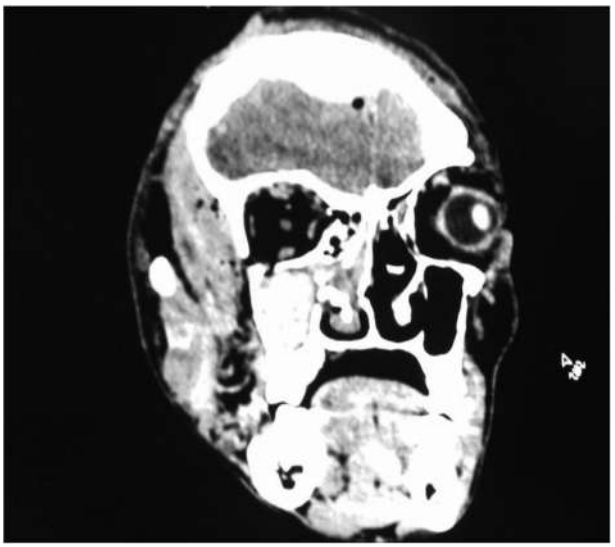

Figure 1. CT scan showing skull fracture in the right frontoparietal region, with lateral wall fracture of the right maxillary sinus with hemosinus involving right maxillary, sphenoid, and bilateral ethmoidal sinus.

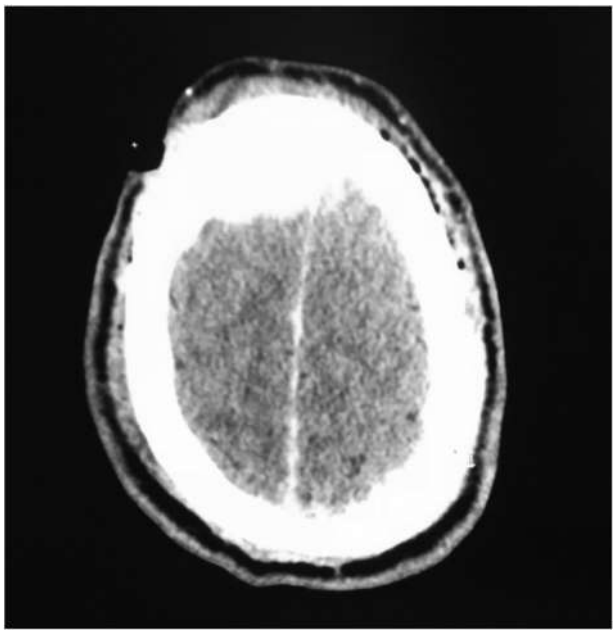

Figure 2. CT scan showing skull fracture in the right frontoparietal area, with subarachnoid hemorrhage and epidural hematoma formation.

hospital on Day 6. The patient had minimal, persistent cognitive impairment, but could perform activities of daily living. He had complete loss of vision in his left eye. He returned to physical work, but not to climbing.

Discussion

Survival from mountaineering falls >100 m is uncommon. We were not aware of other cases in the published literature. This case highlighted the challenges associated with rescuing victims from remote regions, such as the Khumbu region.

Despite the high-impact mechanism of injury, only the head injuries were severe enough to require surgical treatment. Airway management was the most immediate priority. Airway management was complicated by suspected traumatic brain injury and facial fractures. The team chose to defer intubation prior to transfer because of the high risk of a failed intubation with a technically difficult airway in an uncontrolled setting without signs of imminent airway collapse. The team also did not use a supraglottic airway, because the placement of a supraglottic airway might have triggered the gag reflex, causing vomiting and aspiration.[13–15]

The team managed the patient on the helipad because carrying him 100 m over rough terrain to the medical tent would have been time consuming and technically difficult.

The reported ataxia and confusion preceding the fall suggested a diagnosis of HACE. The suspected traumatic brain injury made it impossible to determine if the patient had HACE, so the team treated him for HACE with intramuscular dexamethasone. There was no evidence that poor distribution of backpack weight contributed to the fall.

The Aerospatiale B3 (Écureuil) helicopters and the ground ambulance were not equipped to provide critical care. This might have contributed to a worse outcome if the patient had more critical injuries.

Despite the challenges, the outcome was positive. The patient survived with a good neurological outcome. Luckily, he did not have an immediately life-threatening condition such as uncontrolled major hemorrhage. Prompt airway support likely contributed to a favorable outcome. The time from the accident to the arrival at the hospital was 2.5 h. This is faster than the average transport times for rescues and acute rural transfers in many developed countries.[16–18]

Conclusion

This report documented the survival of an individual after a long fall on Mount Everest. The patient survived because he did not sustain trauma requiring immediate intervention. Rapid rescue, prompt initial resuscitation, and timely evacuation to definitive care may also have contributed to the favorable outcome.

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CASE REPORT

Nonfatal, Nonpredatory Jaguar Attacks in Brazil: A Case Series

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The jaguar, *Panthera onca* (Linnaeus, 1758), is the biggest felid in the Americas. Its range extends from the southwestern United States to northern Argentina. Herein, we present 5 nonfatal jaguar attacks that occurred in Brazil between March 2010 and November 2021. Most of the cases occurred when the victim encountered a jaguar guarding its food or cubs or devouring prey; none appeared to be the result of predatory behavior.

Keywords: animal attacks on humans, animal bite and scratch injuries, large felid attacks on humans

Introduction

The jaguar, *Panthera onca* (Linnaeus, 1758) is the biggest felid in the Americas, having a body weight of 60 to 115 kg (132–253 lb) and length up to 190 cm (75 in). Its range extends from the southwestern United States to northern Argentina around the Iguaçu Falls border region between Brazil and Paraguay (Figure 1). It is an endangered animal, and there are imprecise data about the size of its remaining populations.[1–3]

Jaguar attacks on humans seem to have increased in recent years in the Pantanal region of Brazil.[1–3] We present 5 cases of nonfatal jaguar attacks occurring in Brazil between March 2010 and November 2021. All cases happened when the victim surprised a jaguar that was eating or with cubs; none of the attacks seems to have resulted from predatory behavior. The attacks occurred in rural areas in the states of Mato Grosso,[3] Mato Grosso do Sul,[1] and Amazonas.[1]

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Case presentations

CASE 1

Upon investigating a disturbance on his rural farm, a 28-y-old man found a jaguar attacking his dogs. When he attempted to rescue the dogs, the jaguar pounced upon him. Fellow workers rescued him and took him to the nearest hospital where he was found to have multiple lacerations (defensive wounds), primarily on his arms (Figure 2). His wounds were irrigated and debrided and closed primarily. He was prescribed antibiotics (not specified). No secondary infection is known to have occurred.

CASE 2

A 33-y-old man was attacked in the downtown area of a small village by a jaguar that had previously been observed to be accompanied by 2 cubs. He sustained numerous lacerations and contusions of his face and arms, including full-thickness 35 cm and 20 cm long wounds of the left and right arms, respectively (Figure 3). Radiographs revealed no fractures. He was prescribed oral ciprofloxacin, 500 mg BID and clindamycin, 300 mg every 6 h, for 1 wk, and was administered a rabies vaccination. No follow-up information was available.

CASE 3

When looking for a missing horse, a 46-y-old man was attacked by a jaguar that was devouring the carcass of an alligator. He sustained deep lacerations and open

Figure 1. Jaguar (*Panthera onca*). Upper right: Jaguar skull showing teeth used for predation. Photos: Kleber José Barbosa and Vidal Haddad Junior.

Figure 3. Wounds caused by the jaguar's claws on the victim's arms and face after initial care. Photos: Dr. Renato Mazzaro Ferrari, Sorriso town, Mato Grosso State, Brazil.

fractures of his left forearm (Figure 4). His wounds were surgically treated at a regional hospital with irrigation, debridement, primary closure with drains, and other measures. The fractures were reduced and internally fixed with rods. Antibiotic treatment included cephalothin, 1.0 g IV every 6 h, and gentamicin, 60 mg IV every 8 h. An anti-tetanus serum, 5000 units, was administered intramuscularly, and he was vaccinated against rabies and given rabies immunoglobulin (20 international units per kg). He was discharged with a prescription for oral antibiotics (unspecified) for 7 d, along with wound care and follow-up instructions.

CASE 4

When going into the bush with his 5 dogs to investigate a "bad smell," a 58-y-old male farmer was attacked by a jaguar, suffering bite and claw scratch wounds to his back (Figure 5). The jaguar was feeding on a dead animal. His dogs chased the jaguar away. The local fire department transported the man to the nearest hospital, but no treatment details were provided.

Figure 2. Incised and lacerated wounds on the victim's arm caused by the jaguar's claws. Photo: Public domain.

CASE 5

A 36-y-old man was attacked by a jaguar while tending to his cattle. The jaguar rushed out of a den, where it was with 2 cubs. It knocked the man off his horse and inflicted deep bite and claw scratch wounds to his head, face, and right arm. On examination at a metropolitan hospital, he was found to have multiple deep contused lacerations of the head extending through to the bone. The largest of these measured 20 cm and extended from the medial canthus of left upper eyelid to the middle third of the left eyebrow (Figure 6). One of the bites punctured his skull. A deep linear laceration was present on his upper right arm. He was prescribed oral cephalexin (2.0 $g \cdot d^{-1}$) and the wounds and lacerations were loosely closed after cleaning to control bleedings. The perforation of the skull was evaluated and treated by a neurosurgeon, details of which were not available.

Discussion

These 5 attacks illustrate the types of injuries that may result from jaguars defending their prey or cubs.[1,2] Four of the cases occurred in or near the Pantanal ecoregion where farms and cattle fields are close to forest and swamps within ecologically protected areas. An increase in ecotourism in these protected areas may have led to the normally very secretive and reclusive jaguars becoming

Figure 4. Patient who suffered an attack on the left arm from a jaguar bite. Top: Admission of the patient to the hospital and detail of the arm with the bite. Bottom: Clean trauma area and radiography showing a double radius and ulna fracture. Photos: Manoel de Campos Neto, Cáceres town, Mato Grosso State, Brazil.

Figure 5. Injuries caused by the jaguar's claws on the dorsum of the patient after the jaguar was surprised when feeding. Photos: Dr Diego Ruiz, Porto Murtinho town, Mato Grosso do Sul State, Brazil.

Figure 6. Extensive cuts and scratches on the head of the victim caused by the claws and bites. Photos: Dr Fabrício Rodrigues do Amaral, Várzea Grande town, Mato Grosso State, Brazil.

familiarized with humans.[1,2] Ecotourism has been well-developed in Pantanal, and jaguars are intentionally attracted to certain spots by food baits to increase the chances of tourist sightings. This behavior may also increase the likelihood of human-jaguar interactions among agricultural workers or local sportsmen.[3] These reasons seem to have been the major causes of cases 1, 3, and 4. Cases 2 and 5 seem to have been a mother jaguar protecting her cubs.

Big cats of all kinds (eg, lions, tigers, leopards, cougars, and jaguars) usually kill their prey through bites to the skull and cervical spine (neck).[4] Such attacks are compatible with predatory attacks. The injuries observed in this case series mostly appeared to be defensive wounds, indicative of nonpredatory behavior of the animals.[4]

Nonpredatory jaguar attacks, such as described here, are usually not fatal but may involve extensive injury from claw scratch lacerations and deep puncture wounds. Bite injuries may also occur but are less common than in predatory attacks. Most nonpredatory attack injuries occur on the arms (defensive attitude of the victims) but may involve other body parts, including the face. Internal injuries are rare in these attacks.[1,2] Victims of nonpredatory attacks are at risk of major hemorrhage, as well as infections and other complications.

Medical management of these injuries primarily includes control of hemorrhage, wound irrigation and debridement, primary closure (depending on the wound), and antibiotic prophylaxis. These wounds have a high rate of bacterial infections can be a problem, mainly by *streptococci*, *staphylococci*, and *Pasteurella multocida*.[5] Wounds that are sutured must be thoroughly cleaned, (possibly including irrigatione with water under pressure). The risk of infection is greater in wounds located in areas of poor vascularization, in deep wounds, or in wounds with crushed tissues, as well in elderly or immunocompromised persons.[1,2,5] Four of the 5 cases presented here were treated with prophylactic antibiotics, although variable amounts of information was available about the antibiotics used and whether secondary infection occurred. Appropriate antibiotics include penicillin, amoxicillin, a first- or second-generation cephalosporin or clindamycin, and a

fluoroquinolone.[1,2,5] Tetanus prophylaxis is necessary and rabies postexposure prophylaxis should be considered.[5]

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CASE REPORT

Survival After Being Wedged in a Crevasse for 16 Hours in Alaska

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We present a case of an un-roped mountaineer who fell into a crevasse during descent from the summit of Denali (Mount McKinley). He was wedged about 20 m deep in the crevasse for a total of 16 h; this included 4.5 h waiting for a rescue team to arrive, and an 11.5 h extrication process. His condition deteriorated and he eventually lost consciousness. Even though the rescue team collectively felt there was little or no chance of survival, they continued until the victim was extricated from the crevasse. He was almost immediately placed in a hypothermia wrap with active warming, loaded on a rescue helicopter, and transported for 1 h 40 min to a hospital in Fairbanks, Alaska. During the flight, he was placed on supplemental oxygen. He was cold to the touch; respiration was detectable, but a pulse was not, and he was responsive to verbal stimuli. Initial bladder temperature in hospital was 26.1°C. He was released from hospital after 14 d and made a full recovery. This case highlights an important mix of preventative and resuscitative lessons regarding crevasse rescue in an isolated location. The lessons include the dangers of travelling un-roped on a crevassed glacier, the challenges of extrication from a confined space, the fact that respirations are often more easily detected than pulses, an extended transport time to medical facilities, and the necessity of trying unorthodox extrication methods. This case emphasized the need to continue extrication and treatment efforts for a cold patient even when survival with hypothermia seems impossible.

Keywords: cold exposure, crevasse rescue, insulation, circum-rescue collapse, post-rescue collapse, rescue collapse

Introduction

The main threats to survival for someone who has fallen un-roped into a crevasse are trauma, asphyxiation from inability to expand the chest, and cold exposure.[1] The longest documented survival in a crevasse was 6 d for a victim who fell into a crevasse and sat on the snow at the bottom.[2] In contrast, one victim died from hypothermia after being wedged in a crevasse for only 4 h.[3]

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We present a case of a mountaineer who fell into a crevasse during an un-roped descent from Denali (Mount McKinley) in Alaska. It took about 4.5 h for a rescue team to arrive. His condition gradually deteriorated, and he became unconscious after about 12 h, at which point he was assumed to have died. However, he was extricated 4 h later and fully recovered. This case highlighted the difficulties of crevasse rescue and the importance of continuing extrication efforts even when survival from hypothermia seems impossible.

Case Report

On June 4, 2017, 7 climbers were descending from a successful summit bid on Denali, Alaska. After arriving at Camp 1 on the Kahiltna Glacier (2400 m), a 38-y old

Figure 1. Top: Site of incident on crevassed Kahiltna Glacier (site circled in red). Bottom: Rescue site. Crevasse runs in direction from overturned sled to wands which marked the danger area.

male climber continued to descend un-roped on snowshoes with his partner at about 2330 h (Figure 1, top). About 200 to 300 m from the camp, he stopped near what was marked as a danger spot. He took one step on a snow bridge and broke through into a crevasse (Figure 1, bottom).[4] He fell about 20 m and became wedged between smooth narrowing ice walls which were 18 to 23 cm apart. He was in an upright vertical position with his backpack bunched up at shoulder level. Although he could still breathe, no further movements were possible. Surface air temperature ranged between −7 and −2°C. The top of the crevasse was about 90 cm wide.

The climbing partner returned to Camp 1 to get help. Within 20 to 30 min a mountain guide was lowered to free the victim. With limited specialized equipment, extrication was not possible. A radio call was made to Talkeetna, Alaska for help from the Denali National Park and Preserve mountaineering rangers. Bad weather delayed departure of a helicopter until 0300 h on June 5.

After arriving at about 0400 h, the lead ranger was lowered into the crevasse but could not descend further than about 3 m above the victim. At this point the crevasse was about 25 cm wide. The victim was repeatedly calling out "help, snowshoe," for about 12 h until he became unconscious at about 1130 h. The ranger tried to widen a passage below himself using the adze of his ice axe. Eventually he clipped a rope onto the victim's pack. Rescuers on the surface pulled on the rope until the pack straps broke. After this, the victim could breathe more easily.

At one point, the ranger was having difficulty breathing and yelled to the surface team to pull him up. For a brief period however, the surface team was not directly observing him and did not hear the request. After yelling, the ranger slipped deeper into the crevasse. Because his chest was further constricted, his next attempt to yell for assistance was muted. At this point the surface team noticed the situation and pulled him up so he could breathe.

Meanwhile, rangers in Talkeetna collected several potentially useful tools from a hardware store and had

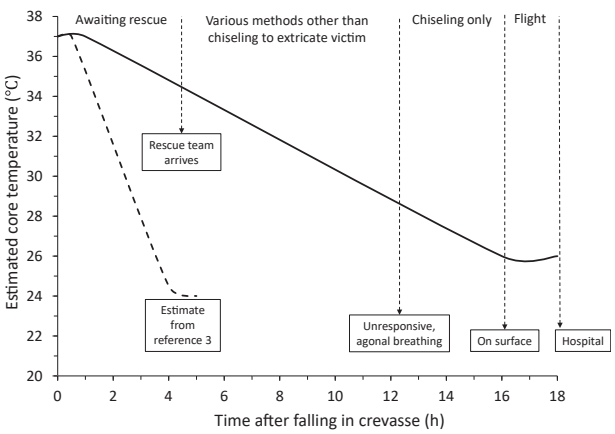

Figure 2. Estimated core temperature (based on symptoms and initial hospital core temperature) for victim during crevasse rescue and flight to the hospital (solid line). The dotted line illustrates a much faster rate of core cooling for a victim who died 4 h after falling into a crevasse in Antarctica.[3]

them flown to the accident site. After 2 h of minimal progress, the rescuers stopped to discuss other options. An attempt to use a chain saw was unsuccessful because there was limited room to maneuver. A blow torch, antifreeze, and even boiling water were used to try to melt the ice with varying levels of success. At this point everyone in the rescue team felt there was no chance that the victim could survive long enough to be rescued successfully. However, they continued their efforts with 1-h shifts of chopping ice with their adzes. They finally reached the victim at about 1200 h. He was unresponsive and had what was described as agonal breathing (Figure 2). Once a rescuer got low enough, he clipped a rope to the harness and the entire surface team pulled on the rope as hard as they could, without moving the victim at all.

At about 1200 h the helicopter delivered a pneumatic hammer-chisel borrowed from the Talkeetna Fire Department and the rescuers started chiseling. At about 1400 h, the victim had been unresponsive for about 2 h and was assumed to be dead. He then briefly gained consciousness, looked around, and lost consciousness again.

After almost 3 h of chiseling, a rescuer was able to reach the snowshoe straps. The limiting factor seemed to be that the snowshoes were wedged in the crevasse. It took about 40 min to cut the straps. For the first time, at 1520 h, the victim moved upward when the rescuers pulled on the rope. They then pulled him to the surface and over the edge of the crevasse at 1535 h. He responded to verbal stimuli, respiration was detectable, but pulse was not. Rescuers immediately brought him into a tent shelter and placed him in a hypothermia wrap. They cut off his wet clothes and sandwiched him between 2 dry chemical heating blankets (Ready Heat II "38x48"; TechTrade, Hoboken, NJ) within a −30°C down sleeping bag. Three 1-L Nalgene water bottles (Rochester, NY) were filled with warm water and placed inside the sleeping bag. He was packaged into a MedTech vacuum spine board (MedTech Sweden Inc, Geneseo, IL) and loaded onto a waiting helicopter that departed at 1541 h.

Because of bad weather in Talkeetna, the helicopter had to make a longer trip (1 h, 40 min vs 30 min to Talkeetna) to the hospital in Fairbanks, Alaska. Although the attending paramedic could not feel a pulse, breathing was detectable, and the victim remained responsive to verbal stimuli. Shivering was never observed. The only in-flight care was supplemental oxygen administered via nasal prongs at a rate of 8-10 $L \cdot min^{-1}$. Because of the extended flight, the flow rate was lowered to 3 to 4 $L \cdot min^{-1}$; however, both oxygen bottles ran out as the helicopter arrived at Fairbanks at 1723 h.

At 1800 h, his initial bladder temperature was 26.1°C (79°F). Surface warming was achieved via forced-air warming. The patient was admitted to the intensive care unit where he required renal dialysis. After 14 d, he was released and has since resumed climbing.

Discussion

This case provided valuable insights into victim physiology during extended cold exposure and the challenges for responders rescuing and providing medical care in extremely confined spaces.

The victim survived a longer period of exposure than might have been expected when wedged tightly between 2 ice walls.[3] Because he did not sustain any significant traumatic injury, his condition worsened solely from hypothermia. He was initially conscious and coherent. His voice became progressively weaker until he stopped talking after about 12 h. Loss of consciousness probably did not occur at a core temperature >30°C and he likely would not have remained conscious at a core temperature <27 to 28°C (Figure 2). He survived another 4 h in the crevasse and was breathing and responsive to verbal stimuli during almost 2 h of helicopter transport.

The victim was severely hypothermic and at risk of cardiac arrest while being hauled up to the snow surface and during the transfer from the crevasse to the helicopter. At low cardiac temperatures, cardiac arrest can be triggered by rough handling.[5] The fact that a tent and the hypothermia wrap had been set up beforehand increased the likelihood of an efficient, smooth transition.[6] We could not explain the brief period of regaining consciousness and movement at about 1400 h, after 2 h of unconsciousness. This episode should serve as a reminder that the physiological condition of a cold victim may be better than signs and symptoms seem to indicate.

Core temperature at the time of extrication from the crevasse was approximately 26°C (assuming a generally linear cooling rate in the crevasse and an after-drop that was probably reversed during the 1 h 40 min transport) (Figure 2). The core cooling rate was therefore $<1.0°C \cdot h^{-1}$. This is much slower than in the case of a helicopter pilot who died soon after extrication after being wedged in a crevasse for only 4 h. His core cooling rate was $>3°C \cdot h^{-1}$.[3] In comparison to the mountaineer in the present case, the pilot was older (62 vs 32-y-old), was not wearing cold weather clothing, was probably not as fit, and was in colder air (−14 vs −4°C). Other than these factors, it is not clear why the pilot cooled so much faster.

If a victim can continually speak, it is unlikely that the chest is the main wedge point. If the chest were wedged, each expiration would allow the victim to slide

downward to a tighter space until chest expansion would be negligible. This was the experience of the rescuer who needed to be pulled up so he could breathe. If a victim can speak, the wedge point is likely to be an object such as snowshoes, a helmet, or even a backpack. This would help explain why the victim could breathe more easily once the pack was removed. This knowledge may inform strategies for freeing a wedged victim.

The rescue team performed a very difficult rescue in a severely confined space for a protracted period of about 11.5 h. Although they thought the time required for extrication would be far longer than the victim could survive, they kept working even though progress was slow. This emphasizes the necessity to not give up on a cold victim if there are no obvious fatal injuries or signs of death.

Recommendations

This case provided potential lessons regarding rescue/medical operations during extended crevasse rescue. Climbers should always rope up for glacier travel in areas with known or possible crevasses. Surface rescue teams must have at least one person continuously observing any rescuers in the crevasse, preferably with radio contact, in case they need immediate assistance, and an organization that deploys responders to a crevasse rescue should prepare a specific "crevasse rescue and cold kit" that can be immediately loaded onto a helicopter. The Denali National Park and Preserve mountaineering rangers have now created a kit that includes a pneumatic hammer-chisel to aid in extrication, a tripod and winch, and a hypothermia wrap, including a sleeping bag and chemical heat blankets.[6] They have also included an adapter that allows connection of a patient's mask or nasal prongs to the helicopter onboard oxygen supply. Other valuable items could include a mechanical chest compression device, automated external defibrillator, and IV saline with a fluid warmer.

Warm water was placed in rigid bottles for patient warming. Rescuers should confirm that the water will not burn the patient's skin[7] by placing their hand in the water for 10 to 15 s before filling the warming container. Water bags or bladders are recommended over rigid bottles because a greater surface area (almost 50%) can contact the skin.

All search and rescue personnel should be aware of the causes, symptoms, and prevention of rescue collapse (also called circum-rescue collapse).[8] They should be trained with the principle that "the colder the victim is, the more care is required to perform horizontal extrication as gently as possible." Adding a few minutes for gentle handling and to reposition will not significantly increase cold exposure, but will greatly minimize the chance of rescue collapse.[5]

Crevasse rescue training should include techniques for transitioning a victim gently from vertical to a horizontal supine or, for narrower passages, to a lateral decubitus position. Training should also emphasize that, even if a victim must be hauled up in a vertical position, a simple technique using a sling or rope under the knees allows a simple, gentle, and horizontal extrication from the crevasse to the surface.[3]

Conclusion

This case emphasizes the need for rescue teams to pre-plan equipment and procedures specific to crevasse rescue of potentially cold patients. It is critical to continue extrication and treatment efforts for a cold patient even when survival with hypothermia seems impossible. Rescuers should take enough time to ensure the patient is always handled gently and placed in a horizontal position as much, and as soon, as possible to minimize hypotension.

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CASE REPORT

Lichtenberg Figures: How a Cutaneous Sign Can Solve Suspicious Death Cases

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Lightning is a natural weather phenomenon that occurs most commonly during the summer months in the afternoon or early evening. Lightning strikes can cause accidental deaths. In developed countries, lightning fatalities occur almost exclusively outdoors. Deaths from lightning may be in remote places with no witnesses. Forensic pathologists may not be able to reach the scene of death because it is too hazardous or inaccessible. Bodies may have neither evidence of skin burns nor torn areas on their clothes. The presumption of accidental death may be difficult to prove. We present 3 cases in which neither the examination of the death scene nor the examination of the bodies by those who attested to the death were performed. The bodies were transported to the morgue for a forensic autopsy because the deaths were considered suspicious. Physicians who attest to death in open spaces during weather that could produce lightning should actively search for Lichtenberg figures, which are considered irrefutable proof of fatal lightning in such settings. They should also photograph them and submit them as evidence. Nevertheless, physicians should keep in mind that Lichtenberg figures are not considered pathognomonic of lightning because some skin manifestations may mimic them.

Keywords: autopsy, forensic pathology, lightning injury, natural disaster, skin manifestation

Introduction

Lightning is one of the leading causes of weather-related deaths, occurring mainly during the summer, in the afternoon or early evening of stormy rainy days.[1] It is a transfer of an electrical charge of very high intensity (10,000–200,000 A) and extremely high voltage (20 million–1 billion V). The duration of a lightning discharge is approximately between 10 to 100 ms, exposing the body to intense heat (as high as 30,000°C) and an overpressure (almost 100 atm) which may cause injuries with a mortality rate of 10 to 30%.[2,3]

Lightning may leave bodies with neither evidence of skin burns nor barotraumatic injuries. It also may not leave clothes with burn marks or torn areas. There may be no witnesses or evidence (eg, tree damage or dead animals). In such situations, identifying the Lichtenberg figures (LFs) may be the key to death by lightning diagnosis.

The LFs are named for the German physicist Georg Christoph Lichtenberg who observed similar patterns on an electrified insulating plate covered with dust in 1777.[4,5] The LFs are superficial red, painless skin signs. They are linear and irregular with fernlike patterns mainly appearing on the torso and the limbs. They appear especially when the skin is clammy from sweating or wet from the rain. They are considered to be a pathognomonic sign of lightning injury.[6,7]

Herein, we reported 3 cases of a suspicious death in which LFs played a key role in attesting to the cause of death.

CASE 1

The body of a 16-y-old boy was found abandoned in a field on the afternoon of a stormy rainy summer day. The heavy rain prevented investigators from examining the scene of death. The body was removed quickly from the area following a flash flood warning. Because there was

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Figure 1. Lichtenberg figures on the anterior chest (Case 1). A superficial erythematous arborization with a fern-like pattern (arrow).

Figure 2. Lichtenberg figures on the left hip extending superiorly (Case 2). A superficial reddish arborization (arrow).

no obvious cause of death, a judicial inquiry was opened. External examination of the body revealed the presence of LFs on the anterior chest (Figure 1).

CASE 2

A 28-y-old shepherdess was found lying unconscious in front of her barn by a neighbor on an early summer evening. Because the stormy weather had made the local roads impassable, the medical rescue team was delayed in reaching the patient. Death occurred less than an hour after the patient arrived at the hospital despite cardiopulmonary resuscitation. The doctor, who examined the body without completely undressing it, observed traumatic lesions, including an abrasion on the right side of the face and a bruise posterior to the right ear. He contacted the police because he thought the patient might have been assaulted. A forensic autopsy was performed. External examination revealed abrasions of the face that were not the cause of death. LFs were seen over the left hip, buttocks, and lower back (Figure 2).

CASE 3

Three friends were found unconscious by a forest ranger on a spring afternoon in a mountainous region. The weather conditions that day were not conducive to outdoor activity because of torrential rains. When the rescue team arrived, 1 of the 3 victims had died while the other 2 were comatose. The ranger suggested the possibility of poisoning by the ingestion of toxic mushrooms. Because it was impossible to question the survivors, a forensic autopsy was requested to establish the cause of death of the third victim. External examination of the body revealed LFs on the anterior thighs (Figure 3).

Discussion

In the 3 cases we describe, internal examination revealed neither traumatic injuries nor pathological findings. The toxicological analyses of the body fluids (blood and urine) were negative for all tested substances (ethanol, opiates, benzodiazepines, barbiturates, and cannabinoids). Based on the presence of LFs on the body of each victim, lightning injury was the cause of death in each case.

A person struck by lightning may have injuries that are apparent, or they may be struck and killed without visible

Figure 3. Lichtenberg figures on the anterior thighs (Case 3). A superficial erythematous arborization with a fern-like pattern (arrow).

injury. The most common causes of death by lightning are dysrhythmias, such as ventricular tachycardia or ventricular fibrillation,[2,8,9] myocardial infarction,[10–12] and respiratory arrest caused by central nervous system effects.[2] Barotrauma may cause pneumomediastinum, rupture of the tympanic membrane, and injuries to the gastrointestinal tract.[13,14] Lightning may also cause blunt force trauma, blast injuries,[14] and gunshot-like injuries.[15]

The cutaneous signs of lightning depend on the mechanism of injury. Injuries caused by heat may include linear burns. Histologic skin findings include hemorrhage with coagulation necrosis in the deep and superficial dermis and flattening and congealing of the epidermis with the appearance of spikes on the surface.[15] The burn site may appear scorched with a singed smell. Body hair may also be charred.[14] Electrical injuries may cause spark-like lesions. The LFs are a premortem tissue reaction. The pathogenesis of LFs is a matter of debate.[14] There is a scarcity of histologic evidence.[16,17]

The LFs generally appear in 1 h then gradually fade and disappear without a trace within 48 h. The LFs may be green, if putrified,[18] or maybe hyperpigmented.[15,19] They can sometimes remain visible for several days postmortem.[18–20] Because LFs are transient, the rescuers and physicians arriving at the scene should look for them and should take photographs for legal purposes.

The LFs can be observed after lightning injury or in high-voltage burns. In open areas without a source of high voltage, LFs are pathognomonic for lightning.[21] There is a reported case of arborescent pressure-induced vasodilation that was said to mimic LFs. The lesion, in this case, was easily distinguishable from LFs because it lacked ferning.[22]

The primary concern of a forensic expert is to determine whether a death was accidental or caused by a third party. In the cases we present, the occurrence of death in the afternoon of stormy, rainy summer days and the presence of LFs with no internal traumatic injuries demonstrated that lightning was the cause of death. If the LFs had vanished before the autopsies were performed, it would have been difficult to determine that lightning was the cause of death. The first rescuers to examine the bodies should look for and photograph LFs. A full autopsy should still be performed to not miss the involvement of a third party, such as a person who was poisoned or was a victim of homicidal smothering and then struck by lightning.

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CASE REPORT

Successful Nonextracorporeal Life Support Resuscitation and Rewarming of a Patient with Hypothermia in Cardiac Arrest

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We report full recovery of a patient with hypothermia in cardiac arrest following continuous and prolonged cardiopulmonary resuscitation (CPR) and conventional, nonextracorporeal life support (non-ECLS) methods. A 57-y-old man presented with unwitnessed cardiac arrest and a core temperature of 23°C (73°F). The presenting cardiac rhythm was ventricular fibrillation. The team administered epinephrine and performed defibrillation and CPR. Because ECLS was unavailable at the facility, the medical team externally and internally rewarmed the patient using heated blankets, forced warmed air, thoracic lavage, and warmed IV fluids. The patient achieved return of spontaneous circulation after 4 h 56 min of continuous CPR and rewarming. The medical team admitted the patient to the intensive care unit. He achieved full neurologic recovery the following day. When ECLS is not available and transfer is not appropriate because of patient instability or hospital location, conventional rewarming methods and continuous, prolonged CPR can lead to successful outcomes in patients with hypothermia in cardiac arrest. This case demonstrates that CPR in patients with hypothermia-associated cardiac arrest can lead to full recovery.

Keywords: cardiopulmonary resuscitation, extracorporeal membrane oxygenation, resource availability

Introduction

Cardiac arrest is a potential consequence of severe hypothermia. Extracorporeal life support (ECLS) is considered the optimal method of resuscitation for patients with hypothermia in cardiac arrest. Extracorporeal life support has been shown to increase the odds of survival and return to normal neurologic function.[1-5] However, this treatment is not offered by all hospitals. If ECLS is not available, an alternative approach is the use of conventional rewarming techniques with continuous cardiopulmonary resuscitation (CPR).[5]

We report the case of a patient with hypothermia in cardiac arrest, in which rewarming techniques and CPR were successfully used because ECLS was not available.

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Case Presentation

At 2048 (elapsed time, 0) on a midwinter Wisconsin night, emergency medical services (EMS) brought a 57-y-old man with ventricular fibrillation and cardiac arrest to the emergency department. The EMS had found the patient outside in freezing conditions with an unwitnessed arrest. En route to the hospital, the EMS performed continuous CPR, attempted defibrillation, and administered 3 doses of epinephrine. There was no note of core temperature during EMS handoff to the emergency medicine team. After arrival, the medical team administered 4 additional rounds of epinephrine along with continued attempts of manual CPR and defibrillation. They used classic pad positioning for the majority of defibrillation attempts. However, they attempted anterior/posterior positioning for the last 2 rounds. Additionally, they administered IV amiodarone (300+150 mg), 2 doses

of calcium chloride (1 g × 2), and sodium bicarbonate ampules (50 mEq × 2) while the patient was briefly in pulseless electrical activity. At 30 min, the physician performed point-of-care ultrasound (POCUS) echocardiography, which showed no cardiac activity. The physician performing POCUS noticed that the patient felt cool to the touch. The team then measured the patient's rectal temperature. This was 22.8°C, indicating that the patient was severely hypothermic. Because CPR should not be terminated until asystole persists with a core temperature of >32°C, the physician immediately started rewarming the patient using conventional methods.[2] These included placing a forced air blanket, placing heated blankets on the patient's upper torso, and administering warmed Ringer lactate solution through 2 antecubital 16-gauge IV lines. The team continued manual CPR because ECLS was not available. The team attempted to transfer the patient to an ECLS-capable hospital 30 min away. This hospital refused the transfer because they had no protocol to receive patients with hypothermia in cardiac arrest.

The core temperature, monitored using an indwelling urinary catheter, rose slowly. At 1 h 45 min, the physician successfully inserted 2 chest tubes into the patient's right hemithorax. The right side of the chest was continuously irrigated with warmed normal saline using the 2-tube technique. The team did not irrigate the left hemithorax to avoid the risk of cardiac irritation.[6] They continuously irrigated the patient's bladder with warmed saline through the indwelling urinary catheter.

The complete blood count, basic metabolic panel, serum lactate level, and venous blood gases levels were normal. The potassium level was 4.0 $mmol{\cdot}L^{-1}$. The termination of CPR based on potassium level should not be considered unless the serum potassium level is >12.0 $mmol{\cdot}L^{-1}$.[7]

At 2 h 12 min, the emergency medicine physician intubated the patient to protect his airway. Because the patient was in cardiac arrest, no sedative or paralytic was necessary. Because there was possible active movement of the larynx during intubation, the team repeated POCUS echocardiography and again observed no cardiac activity. At this point, the physician placed the patient on a mechanical chest compression device, which was set at 100 $beats{\cdot}min^{-1}$. The team continued active internal and external rewarming while the patient underwent mechanical chest compressions and ventilation. At 4 h 56 min, the monitor showed ventricular tachycardia. The team then successfully defibrillated the patient (at 200 J), converting the heart rhythm into normal sinus rhythm. The patient began to open his eyes and attempted to extubate himself. The physician started a propofol infusion for sedation and admitted the patient to the intensive care unit. The intensive care unit team extubated the patient the following day, with complete neurologic recovery. The patient discharged himself against medical advice roughly 24 h after admission to the intensive care unit.

Discussion

Cardiac arrest can be a consequence of severe hypothermia. While ECLS is the optimal method for resuscitation, it may not always be an option.[2,7,8] Clinicians should be aware of other methods for treating patients with severe hypothermia.

This case demonstrates that the use of conventional rewarming methods and non-ECLS techniques can lead to a successful outcome. Non-ECLS techniques may be the only option at hospitals without ECLS capabilities.

This is an example of prolonged CPR being used to successfully achieve return of spontaneous circulation in a patient with severe hypothermia in cardiac arrest. There are other reported cases of patients with hypothermia with cardiac arrest, with successful recovery after prolonged CPR.[9-12] A patient with hypothermia in cardiac arrest with a reasonable chance of recovery being treated at a hospital without ECLS capability should be transferred to an ECLS-capable center if the transfer can be accomplished within 6 h of the start of resuscitation. The chance of recovery if placed on ECLS can be assessed using guidelines such as the hypothermia outcome prediction after extracorporeal life support (HOPE) score.[2] In the case we described, the HOPE score would have indicated a survival probability of 80% after 30 min of CPR.[13,14]

For some patients with severe hypothermia in cardiac arrest at hospitals without ECLS capabilities, when transfer to an ECLS center is not possible, the use of CPR and conventional rewarming may lead to successful outcomes, with full neurologic recovery.

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REVIEW ARTICLE

Head Injuries in Rock Climbing: A Scoping Review

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Rock climbing was recognized as a sport at the 2020 Tokyo Olympics. Despite its increasing participation, there is no knowledge synthesis of head injuries (HIs), defined as any injury to the head, associated with climbing, making it challenging for clinicians to provide evidence-based care. Our aim was to synthesize HI literature within rock climbing and identify knowledge gaps. Six databases (Medline, Embase, Sports Medicine & Education Index, SPORTDiscus, CINAHL, and Cochrane) were searched. Two reviewers screened 345 studies and 31 studies were selected for data abstraction. We found the quality of individual studies mainly "fair" to "good." Both HI and traumatic brain injury (TBI) had inconsistent definitions and categorization. The HIs represented between 0 to 36% of reported climbing injuries. Between 11 to 100% of HIs were TBIs, defined as an HI with permanent or temporary neurological sequelae. The most common causes of HIs were outdoor falls and falling objects. Climbing-specific factors associated with the causes were infrequently examined in the literature. Data sources of safety practices were incomplete. Overall, there was a lack of literature examining HIs, mechanisms of injury, and safety practices associated with climbing. To improve the tracking of HIs in climbing, we suggest the use of consistent reporting standards and the creation of a climbing injury surveillance system.

Keywords: traumatic brain injury, craniocerebral trauma, concussion, sport climbing, bouldering, lead climbing

Introduction

Rock climbing has been steadily growing as a sport and debuted at the 2020 Tokyo Olympics.[1,2] With the increasing participation, climbing injuries are on the rise. In the United States, climbing injuries grew approximately 10% per year between 2008 and 2016.[2,3] These injuries occurred in all climbing disciplines, posing unique management challenges.[4,5]

There are several different forms of rock climbing disciplines.[5] In *traditional* and *sport* climbing, climbers wear a harness with an attached rope to provide safety during falls.[5] The lead climber ascends while the belayer controls the rope and maintains adequate tension in case the lead climber falls.[6] *Traditional* lead climbing has the lead climber placing temporary safety gear during ascent, such as cams, in natural rock as fall protection.[6] In contrast, lead climbers use anchors bolted into natural or artificial walls to clip in safety gear when sport climbing.[7] Other disciplines are *bouldering* and *speed* climbing. *Bouldering*, which occurs on natural rock or artificial surfaces, involves ropeless climbing on routes limited to a few meters in height with crash pads and spotters for safety.[7] *Speed* climbing occurs when a climber races up a predetermined artificial route alongside a competitor in a short sprint-like fashion.[8] Speed climbers are protected with an automatic belay device. Rock climbing can occur on different settings, including natural rock (outdoor) or artificial surfaces (indoor).[7]

A variety of injuries occur within rock climbing.[4,5,9] However, head injuries (HIs), defined as any injury occurring to the head, have not been studied to the extent of extremity injuries.[4,5,9–13] Within the HI spectrum is

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traumatic brain injury (TBI), defined as an HI with transient or permanent neurological sequelae.[14] As TBIs are associated with morbidity when an athlete undergoes premature return to activity,[15,16] national sport organizations (NSO) require concussion protocols. In fact, certain jurisdictions such as Ontario, Canada, have laws that mandate concussion protocols within NSOs.[17,18] When Climbing Escalade Canada, a new NSO, was required to develop a concussion protocol, it sought clinician input.[17]

Because of the limited HI literature in climbing, clinicians are challenged when developing concussion protocols, or caring for climbers with HIs. It would be useful to understand the relative distribution of HI and TBI among injured climbers, injury mechanisms, and risk factors. Our objective was to examine what is known about HI in all disciplines and settings of rock climbing to identify the knowledge gaps.

Methods

We chose the scoping review because it allowed us to examine the evidence broadly and distill it into themes.[19] We used the preferred reporting items for systematic reviews and meta-analysis extension for scoping reviews guidelines.[20]

We included published outdoor or indoor rock climbing injury literature with HI data. The literature without HI data was excluded. We excluded climbing literature not involving rock climbing such as alpinism, ice climbing, or mountaineering, as well as review articles, non-English language publications, and grey literature.

Injury definitions were adapted from the International Mountaineering and Climbing Federation (UIAA). The UIAA classifies mountaineering and climbing injuries as those resulting from a mechanical external or internal force while climbing.[21] An HI was defined as injuries of the head or face.[21] Traumatic brain injury was a head injury associated with transient or permanent neurological symptoms.[14] Mild traumatic brain injury (mTBI) or concussion were TBI with a Glasgow Coma Scale (GCS) score of ≥13.[14]

Six databases were searched from 1946 to July 2020: Medline, Embase, Sports Medicine & Education Index, SPORTDiscus, CINAHL, and Cochrane (Table 1). The duplicates were removed and the final search was exported into a review software Rayyan.ai (Rayyan Systems, Cambridge, MA, USA).

Two independent reviewers screened the studies. Eligibility was reviewed from the titles and abstracts and then all selected papers subsequently underwent full text review. The review process was unblinded after each step. To critically appraise included studies, we used the National Heart, Lung, and Blood Institute quality assessment tool.[22] A third independent reviewer resolved any disagreement after unblinding, or after critical appraisal.

Two reviewers developed a standardized data abstraction form, which was calibrated with a random sample of 5 studies through joint extraction. Afterward, the reviewers independently extracted data and discrepancies were resolved through consensus. If consensus was not reached, a third reviewer independently examined the data to provide resolution. Data charting was prospective and progressive. If the data could not be categorized in the standardized form, they were charted on a modified data abstraction form after team input.

Abstracted data included study characteristics such as sample size, demographics, data collection methods

Table 1. Search strategy

	Search terms
Climbing terms	1. (Rock* OR sport* OR lead OR speed OR Olympic*) Adj Climb*
	2. (Boulder* AND climb*) OR rock-climbing OR rock climbing
	3. Top rope
	4. Boulderer* OR bouldering
Injury MeSH headings	5. Craniocerebral trauma (exp)
	6. Spinal Injuries (exp)
	7. Head injures (exp)
	8. Brain Injures (exp)
Keywords	9. (head injur* or concussion*)
	10. (head or cranio* or forehead or skull* or occipital* or frontal or parietal or temporal or spine or spinal or brain) adj (trauma* or injur* or impact or confusion or wound*)
	11. (Sport* injur* or athletic injur* or rock climbing injur* or rock-climbing injur*)
	12. UIAA or "international climbing and mountaineering federation"
Search strategy	Climbing terms: 1 to 4 combined with OR Injury terms: 5 to 12 combined with OR Climbing terms AND injury terms

MeSH, medical subject headings; UIAA, Union Internationale des Associations d'Alpinisme

*indicates a wildcard search made.

(database review, surveys), and study design. We documented HI proportions (relative to cases), HI classifications, TBI presentations, mechanism of injury (falls, falling objects), climbing discipline, and setting (inside and outside). We also collected information on safety practices such as helmet use.

We used Microsoft Excel (Microsoft, Redmond, WA, USA) for data collection and analysis. The HI proportion was presented as standard ratios. When the total case numbers were unavailable, the total number of climbers were used as a proxy measure to calculate proportions. TBI proportion was defined as the number of identifiable TBIs divided by the total number of HIs. Cohen's Kappa was calculated to assess inter-rater agreement between the reviewers for full text selection.

Results

During study selection, a third reviewer resolved 24 screening and 9 full-text discrepancies. Given relevant findings, 3 abstracts without full text were included in our review (Figure 1).[23–25] The inter-rater reliability of final synthesis was Cohen's k=0.81. We critically appraised 31 papers and determined 9 were good, 15 were fair, 4 were poor, and 3 were indeterminate quality. The study descriptions are outlined in Table 2. Two studies only reviewed HI in rock climbing.[23,26] Twenty-nine studies reviewed HI in addition to other injuries, such as musculoskeletal injuries.

The reporting of HIs was heterogeneous and incomplete. The HIs were reported in combination with injuries from different anatomical regions of the head, neck, and face (Table 2). The injuries included the following: combined head, neck, and face, combined head and neck, combined head and face, and head only. When multisystem trauma was reported, minimal description was provided, making it difficult to identify presence of HI.

Similarly, TBI data were heterogeneous and inconsistent. We found that many studies reported an mTBI without defining it.[5,7,26,32,33,35,37] Although using the same registry, different studies reported different HI and TBI rates.[2,26,37] There were also studies that did not differentiate HIs from TBI or minor injuries, such as a facial laceration.[2,3,10,24,25,27,30,32,38,39,41,44] However, if studies reported HI with major trauma,[27,30,38,39,44] high injury severity,[32,41] or loss of consciousness,[29,32,38] we categorized these injuries as TBIs because they fulfilled our definitions.

Among injury cases, HIs ranged between 0 (0 HI of 836 cases) and 36% (18 HI of 50 cases). Climbing TBI was between 11 and 100% of HI (Table 2).[4,5,7,23,26,29,32,33,37,38,45] The mTBI was between 11 and 50% of HI.[26,32,37] We found that self-reported mTBI rates were higher in survey studies.[5,7]

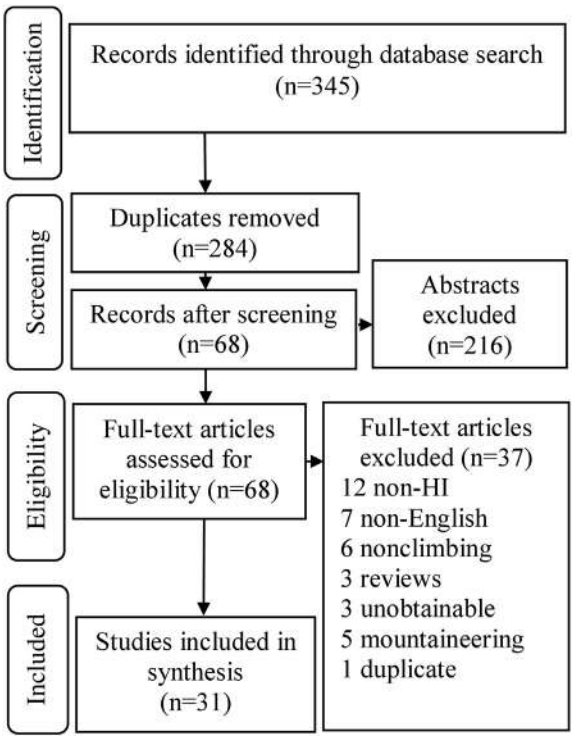

Figure 1. Preferred reporting items for systemic review flow diagram of study selection. HI, head injuries.

For mechanisms of injury, outdoor falls were the leading cause of HI.[26] Though >6 m (>20 ft) falls were associated with all-cause fractures and hospitalizations,[2,25,37,45] the association of fall distance with HI-related morbidity is unclear. A few studies found >6 m (>20 ft) fall-related HI was associated with morbidity[26] and hospital admissions;[25,26] however, others did not find any association.[27,32,37,41–45] Three studies suggested there were climbing-specific protective factors during falls, such as rope elasticity, reducing overall injury.[41,42,45] Studies have proposed that climbing HI was infrequent because harnesses rotate the body to a foot-first falling position.[27,37,41] Consequently, studies have suggested there would be a higher risk of spine or lower limb injury in falls.[27,32,37,43,44]

The second mechanism for climbing HI was falling objects.[23,26,37] For the setting, outdoor traditional and outdoor sport climbing had more HIs than indoor climbing.[4,5] Examining the discipline, there were no discernable differences in HI rates between outdoor sport and traditional climbing.[4,5,42] Although outdoor HIs were more common, occasional indoor HIs occurred,[5,33,34,39] from human error at gyms[33] or competitions.[34] However, other competitions reported no HIs.[28,40] There were

no studies determining which indoor discipline had the most HIs.

For helmets, 8 studies reported 5% to 36% use.[5,7,10,23,26,27,30,45] Helmets were regarded as beneficial;[27,45] however, many studies had incomplete data.[5,10,23,26,27] One study found helmets did not influence overall HI severity, but the paper concluded this was from selection bias.[27]

Discussion

This review examined climbing HIs, mechanisms, discipline, settings, and safety practices. We found gaps in the literature on climbing HIs, as well as factors influencing mechanisms, such as fall distance. In a sport with increasing participation,[2,3] there is a rare but serious risk of HI, which can lead to hospitalization.[25,26] A better understanding of climbing HI may help development of clinical guidelines, protocols, and safety parameters.

The TBIs are important to identify since under-recognition can lead to morbidity. In the sports literature, there is evidence that TBIs have significant consequences. In boxing, severe TBI with loss of consciousness is associated with subdural hemorrhage and death.[46,47] Acceleration and deceleration forces during impact can cause diffuse axonal injury leading to transient neurological symptoms.[46] There are potential links between an mTBI and neurodegenerative disease, such as chronic traumatic encephalopathy.[48] Climbing TBIs could potentially have the same morbidity and mortality as other sports.

There is evidence to suggest that climbing HI is under-recognized and under-reported, and the true incidence is unknown. Because of inconsistent data collection and categorization, climbing literature poorly differentiates between TBI or minor injuries. Although not ideal, we needed to deduce if a study was reporting a TBI with injury scores such as the HI abbreviated injury scale >2 ("moderate" severity including transient loss of consciousness >15 min).[49] The limitations of TBI data are not unique to rock climbing. Some injury registries are only able to capture sport TBIs when it is the primary diagnosis.[50] Furthermore, the diagnostic codes for sport TBIs are limited and underused.[50] Despite this, an improvement in recognition and surveillance led to the increased reporting of sport mTBI.[50]

If severe or mild TBIs are not registered, TBIs would be under-reported. It is estimated that 94 to 97% of climbing deaths occur prior to emergency department arrival.[3] Severe HIs causing death would not enter the hospital or be registered. We also found that self-reported mTBI rates were higher than injury registries. This suggests that climbers with an mTBI do not seek hospital care. Sports literature has recognized the limited ability to capture the true prevalence of mTBI because the injured are less likely to seek care in a healthcare settings.[50,51] Similarly, because climbers infrequently seek medical care for injuries,[5,10,36] mTBI would likely be under-reported.

For mechanisms related to climbing HI, there were knowledge gaps. Studies found that falls >6 m (>20 ft) were associated with HI morbidity.[23,25,26] It is unclear why longer falls were associated with morbidity as there are multiple factors that can contribute to or prevent injury, such as climber experience, human error, environment, protection placement, fall factor, or rope drag.[41,42,45] We found studies stating that rockfall was a cause of HI, but no further data was provided.[23,26,37] Another study described rockfall risks, such as loose holds, freeze thaw cycles, or belayer positioning.[52] The specific mechanisms of climbing falls or falling objects are out of this review's scope, and the authors recommended that climbers consult local experts, mountaineering organizations, and climbing guides. There is an opportunity for further study by examining these factors more readily in the medical literature.

For discipline, most HIs were associated with outdoor traditional and sport climbing. However, HI risk might be related to the outdoor setting rather than the discipline. We also hypothesized that we found less HIs indoors since route-setters specifically design climbing routes to be safe. Given the lack of indoor climbing HI data, we could not make any conclusions on discipline risk.

Helmet use is standard of practice in outdoor climbing given its safety benefits. However, there is a lack of data on helmet use in climbing compared to other sports, such as skateboarding.[53] Although a few studies reported low rates of helmet use,[5,27] the barriers to wearing helmets while climbing are unknown.

Overall, there is evidence of HIs and TBIs in climbing. Given the knowledge gaps, there is an opportunity improve our knowledge on HIs and climbing through further research. This would help develop guidelines for the management of climbers who have sustained HIs.

Limitations

There was a limited amount of literature on climbing HIs. To acquire as much literature as possible, we included non-peer–reviewed abstracts. These sources had greater potential for bias. For feasibility, we excluded papers in non-English, limiting data sources.

We also included studies where the primary objective was not examining HIs. Consequently, the study methods were heterogeneous, resulting in wide variation of HIs and TBIs. In addition, HI data were inconsistent or

Table 2. Table of results summarizing findings of studies examined in the review

Authors	*Study sample*	*Data collection method, study design*	*Quality*[f]	*HI/Cases (%)*[g]	*Key findings*
Chou (2020)[26]	National estimate 5067 cases	ED database search, cross sectional	Fair	n/a[a]	HIs included concussion (44%), skull fracture (3%), facial fracture (3%) intracranial hemorrhage (3%) indicating a burden of TBI. HI were from falls (75%) and being struck by an object (8%). Falls increased odds for facial fracture (OR 8), ICH (OR 952) and skull fracture (OR 81). 2% of climbers wore helmets.
Bernard (2020)[27]	1176 patients, 301 climbers	Cases presenting to hospital, cross sectional	Fair	98/301 (33%)[a]	TBI numbers were not reported but all HI were from traumatic falls. Non-climbers had higher incidence of severe HI compared to climbers despite similar fall distances. 19% of climbers wore helmets. This did not lead to differences in head injury severity, overall injury severity or mortality.
Steffen (2020)[28]	42 climbers	Competition setting, case series	Good	0/42 (0%)[a]	No HI were reported despite injury reporting system allowing for HI detection.
McDonough (2020)[29]	1 patient	Case report, mountain rescue	Good	n/a[a]	A case report of severe HI, with multiple craniofacial fractures, subarachnoid hemorrhage, and trace pneumocephalus.
Bernard (2019)[30]	40 climbers, 111 non-climbers, 151 cases	Cases presenting to hospital, cross sectional	Fair	14/40 (35%)[b]	TBI numbers were not reported but all HI were from traumatic falls. Non-climbers had higher incidence of severe HIs compared with climbers, despite similar fall distances. 5% of climbers wore helmets.
Buzzacott (2019)[2]	National estimate 34,785 cases	ED database search, cross sectional	Fair	4234/ 34785 (12%)[e]	TBI numbers were not reported. Most HIs were from falls, suggesting TBI. Falls increased odds of all-cause hospitalization (OR 12) and fracture (OR 7).
Lutter (2019)[31]	198 climbers	Cases presenting to clinic, cross sectional	Fair	0/198 (0%)[b]	No HIs were reported despite injury reporting system allowing for HI detection.
Weber (2018)[32]	35 climbers, 278 non-climbers	International trauma database, retrospective cohort	Good	10/35 (29%)[a]	HIs consisted of lacerations 7 (70%), facial lacerations 5 (50%), and mTBI/LOC 5 (50%). Some patients had both lacerations and mTBI. All HIs had AIS >2 indicating TBI. Also, average climber GCS of 13 in trauma indicated some TBI despite injuries not documented as HIs.
Petrin (2018)[24]	1146 cases	ED database search, abstract	n/a	102/1146 (9%)[d]	TBI numbers were not reported. Younger age was associated with increased odds for HI (OR 51).
Forrester (2018)[3]	3275 cases	ED database search, cross sectional	Fair	156/3275 (5%)[c]	TBI numbers were not reported. 60% of non-HI patients had multisystem trauma, where TBI may be under reported.
McDonald (2017)[5]	708 climbers, 975 cases	Internet survey, cross sectional	Fair	20/975 (2%)[b]	14 (70%) of the HIs were TBI. mTBI were more frequent with outdoor sport/traditional climbing compared to indoor climbing or outdoor bouldering. 12% of climbers wore helmets.

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Table 2 *(continued)*

Authors	*Study sample*	*Data collection method, study design*	*Quality*[f]	*HI/Cases (%)*[g]	*Key findings*
Pierpoint (2017)[25]	National estimate 39285 cases	ED database search, abstract	n/a	n/a[d]	TBI numbers were not reported. HIs led to 20% of all hospitalizations likely indicating high burden of TBI. Falls increased odd ratio for hospitalization (OR 8).
Williams (2015)[23]	28 rock climbers, 2 ice climbers	ED database search, abstract	n/a	n/a[a]	8 (27%) of the HIs were TBI. Injures were to the face (56%), side of head (33%), occiput (23%), crown (20%), and caused by falls (93%), falling objects (3%). 23% wore helmets, 17% did not wear helmets, 60% were unknown.
Schöffl (2015)[9]	836 climbers, 911 injuries	Cases presenting to clinic and ED; Case series	Good	0/836 (0%)[b]	No HIs were reported despite injury reporting system allowing for HI detection.
Woollings (2015)[7]	73 climbers	Surveys at climbing venues, cross sectional	Fair	3/73 (4%)[d]	All HIs were TBI. Helmet use was associated with increased odds of overall injury (OR 1.3).
Schöffl (2013)[33]	30 cases, 515,337 climbing visits	Prospective injury reporting, case series	Good	2/30 (7%)[a]	Two cases of HIs were reported. One from belay failure and fall leading to concussion, and the other from a rope caught in the jaw.
Hosaini (2013)[34]	15 cases	Cases in competition, case series	Good	2/15 (13%)[a]	Two HI, unlikely TBI. One rope contact during fall and another bouldering fall.
Hasler (2012)[35]	113 climbers, 50 cases	Survey of cases in hospital, case control	Fair	18/50 (36%)[b]	TBI numbers were not reported. All HIs were mild. GCS≤14 cases were excluded.
Neuhof (2011)[12]	560 cases, 836 injuries	Internet survey, cross sectional	Poor	30/560 (5%)[d]	TBI numbers were not reported. No further details on the reported HIs were provided.
Jones (2008)[36]	201 climbers	Surveys at climbing venues, cross sectional	Fair	0 (0%)[d]	No HIs were reported despite injury reporting system allowing for HI detection.
Backe (2009)[4]	106 cases, 335 climbers	Postal survey, cross sectional	Fair	1/106 (1%)[e]	1 TBI in outdoor climbing. No HIs in indoor settings.
Nelson (2009)[37]	National estimate 40,282 cases	ED database search, cross sectional	Fair	4910/ 40282 (12%)[e]	1% of all-cause injury were concussions but excluded from the reported HI numbers. This represents approximately 11% of overall HIs being mTBI. Being struck or hit by an object increased odds ratio of HI (OR 3).
Hohlrieder (2007)[38]	113 climbers	ED database search, cross sectional	Fair	15/113 (13%)[b]	Only traumatic fall injuries were included. Six (40%) HI had LOC. 12% of all cases involved multisystem trauma which likely included TBI.
Josephsen (2007)[39]	53 climbers, 60 injuries	Surveys at climbing venues and internet surveys, cross sectional	Fair	1/53 (2%)[d]	TBI numbers were not reported. The 1 (2%) HI represents an incident case. When lifetime HIs were surveyed among participants, mechanisms of injury included 3 falls, 3 spotting related injury, and 3 climbing injuries.
Gerdes (2006)[10]	1547 cases, 2472 injuries	Internet survey, cross sectional	Poor	84/1547 (5%)[b]	TBI numbers were not reported. 37% of climbers wore helmets, 19% did not wear helmets.

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Table 2 *(continued)*

Authors	*Study sample*	*Data collection method, study design*	*Quality*[f]	*HI/Cases (%)*[g]	*Key findings*
Schöffl (2006)[40]	443 climbers, 18 injuries	Cases in competition, case series	Good	0/443 (0%)[a]	No HI were reported despite injury reporting system allowing for HI detection.
Locker (2004)[41]	27 climbers, 132 non-climbers	Cases presenting to hospital, retrospective cohort	Good	1/27 (5%)[a]	1 HI had >2 AIS likely being TBI. Being a rock climber had lower odds ratio of severe injury and HI (OR 0.2). Authors suggested fall distance alone cannot predict injury severity.
Paige (1998)[42]	251 cases, 94 injuries	Internet and mailed survey, cross sectional	Poor	4/251 (2%)[b]	TBI numbers were not reported. HI were from outdoor climbing, including 2 traditional climbing and 2 sport climbing. None occurred indoors. Authors suggested fall distance alone cannot predict injury severity.
Wyatt (1996)[43]	19 climbers	Cases presenting to hospital, case series	Fair	0/19 (0%)[d]	No HI were reported despite injury reporting system allowing for HI detection. Study authors suspected this may be because of casualty prior to hospital transport.
Maitland (1992)[44]	148 climbers, 124 injuries	Climbing venues, in person survey, cross sectional	Poor	3/148 (2%)[b]	TBI numbers were not reported. All included HI were from traumatic injury.
Bowie (1988)[45]	220 cases, 451 injuries	Cases presenting to clinic or hospital, case series	Good	25/220 (11%)[a]	All HI cases were TBI. TBI deaths occurred prior to hospital transport. Deaths included 4 lead falls, 1 rappelling off rope, 1 rock fall, and 2 belay anchor failure. None wore helmets. Authors suggested fall distance alone cannot predict injury severity.

ED, emergency department; HI, head injury; TBI, traumatic brain injury; OR, odds ratio; ICH, intracerebral hemorrhage; mTBI, mild traumatic brain injury; LOC, loss of consciousness; AIS, abbreviated injury scale; GCS, Glascow Coma Scale; n/a, not applicable.

[a]Head injury only.

[b]Head and facial injury.

[c]Head and neck injuries.

[d]Not specified.

[e]Combined head neck and facial injuries.

[a–e]Indicate the anatomical areas reported as a single injury number with head injury.

[f]Study quality determined by the NHLBI rating tool.[22]

[g]Proportion of head injury relative to all injuries documented in the study.

lacking detail, especially when combined with other injuries. This limited our ability to make firm conclusions.

The quality of study designs was low, with individual study execution being "good" to "fair." Most of the studies were hypothesis-generating and used observational designs, which may predispose the risk of selection or information bias. The studies using online surveys could have recall bias. Most of studies had small sample sizes and none of the studies were powered to detect association between risk factors and HI.

Because of the knowledge gaps and limitations in the literature, there is an opportunity to improve climbing-related HI research with consistent and high-quality data, which includes climbing-specific injury mechanisms. First, the inconsistent definitions and categories could be organized though the Orchard Sports Injury and Illness Classification System (OSIICS) endorsed by the UIAA.[21,54,55] The OSIICS provides consistent categorization of injury by anatomical sites, and facilitates reporting injury types, which reduces ambiguity. Applying this approach would allow for improved injury comparison in climbing literature. Secondly, to collect injury mechanism data, we suggest a rock climbing injury surveillance system, independent of alpine or trauma registries. Alpine and trauma registry diagnostic codes are not specific to sport injuries.[55] Additionally, mountaineering injuries differ from rock climbing.[56,57] This surveillance system should be developed by climbing experts and researchers to capture relevant data related to climbing HI. Collected data through injury reporting forms could address current knowledge gaps examining rock climbing specific injury mechanisms, helmet use, climbing discipline, and setting. This is not a new concept. Sports such as cricket have used surveillance systems to guide injury prevention.[55,58,59] Development of rock-climbing surveillance systems could guide future research efforts to improve safety standards.[58–60]

Conclusion

There are HIs in rock climbing with TBIs possibly representing a significant proportion of such injuries. The HIs from climbing were mainly outdoors and mechanisms included falls or falling objects. We found a knowledge gap on HIs from climbing and its relationship to injury mechanisms, discipline, setting, and safety practices. There is a need for continued higher quality studies. We suggest the creation of a climbing-injury surveillance system, aligned with OSIICS, to promote consistent data collection to improve climbing research.

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Letters to the Editor

Wilderness-Telemedicine, a New Training Paradigm

To the Editor:

One aspect of advanced training in wilderness medicine is that experience in managing wilderness medical conditions can be difficult to acquire in training. Wilderness is defined by its lack of people, infrastructure, and resources. Those needing medical care in the wilderness are usually difficult to access. Additionally, patients with serious conditions in wilderness environments often first require search and rescue expertise,[1] a set of team-based skills and disciplines primarily devoted to patient location and transport. An informed evaluation and treatment of medical problems that arise in the wilderness clearly has the potential to save lives[2] and can be tremendously valuable for many reasons. However, in cases where an individual was not already part of the group, the chances that a wilderness medicine specialist and a patient requiring medical care in the wilderness will be in the same place at the same time are small.

Fellowship training[3] in wilderness medicine in the United States is currently offered in 18 programs, all but one of them within academic emergency medicine departments,[4] at various hospitals and universities across the country. Although wilderness medicine fellowship training may focus on many areas (eg, pre-trip evaluation, race support, wilderness emergency medical services/search and rescue support, and wilderness medicine education), at present, one of the most specific applications of wilderness fellowship training is to accompany expeditions to wilderness settings. However, the groups intentionally seeking out remote wilderness, or extreme environmental conditions, such as in deserts, polar regions, or at high altitude, tend to be limited in number; in this circumstance, a healthcare provider with expertise in wilderness medicine could be seen almost as a form of insurance rather than a resource that will definitely be required. We believe that going forward, the most efficient and effective means for providing medical care to those in wilderness or austere settings will be virtually.

The world is evermore connected; it has been noted that soon there will be very few places on the face of the planet that will be inaccessible to inexpensive, satellite-based broadband communication.[5] The implication of this for the growing number of people who seek out the wilderness is that, in the not too distant future, it will be possible to access real-time expertise from wilderness medicine specialists[6] virtually from anywhere. The COVID-19 pandemic has dramatically increased use and acceptance of telemedicine as a safe, efficient, effective way for patients to access medical care; its adoption in wilderness medicine seems all but preordained, since in this way those with expertise in wilderness medicine will be available, in principle, to anyone needing their care.

Telemedicine use has evolved rapidly. Some have speculated it may lead to the proliferation of virtual ERs (ie, emergency care outside of brick-and mortar facilities); at least one existing program is trying this approach.[7] Training in telemedicine is quickly becoming recognized as a critical skill for trainees and experienced practitioners. The American Association of Medical Colleges recently released expert consensus on telehealth competencies.[8] Telehealth skills and competencies will soon be integrated into medical student and residency curricula. Telemedicine is also being increasingly adapted to wilderness settings[6] and austere environments.[9] Associated with telemedicine is the growing adoption of tele-ultrasound,[10] which has the capacity to extend remote evaluations by wilderness specialists of patients in austere environments.

We recently created a hybrid fellowship in wilderness/telemedicine at the George Washington University School of Medicine. Fellows spend 18 m to 2 y exploring a wide-ranging curriculum including course work in specific wilderness medicine topics,[3] such as high altitude, dive, survival, search, and rescue. They also master in-depth applications of telehealth including use cases, training, optimization, implementation, and quality assurance. The department's long-standing maritime medical access program provides fellows the opportunity to apply skills via phone, video, and asynchronous communication to mariners located in remote and austere environments for prolonged periods of time. The fellowship includes a requirement that a scholarly project merging aspects of wilderness and telemedicine be completed. These might include pilot projects involving various kinds of remote telemetry, the innovative use of mobile phone communication for medical purposes in remote environments, or examining instances where telemedicine is already being used in remote areas.

We believe that the future of wilderness medicine is in remote evaluation because this will ultimately provide the greatest benefit to patients in austere environments. We also believe that the practice of this specialty will come into its own with the growth of communication

technologies, remote diagnostic capabilities, and the adoption of telemedicine techniques and practices

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To the Editor:

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The authors referenced a study that found there were more Instagram than Twitter posts across multiple national parks in South Africa and Finland, and additionally found Instagram to be a more reliable predictor of park visitation than other social media platforms.[2] The data from Instagram use in the parks could be very helpful in their research, particularly the geotagged usage data that could point to specific areas inside the park. Did the authors attempt to use Instagram or other social media platform data, and, if so, why where the authors not able to use it?

Additionally, we wondered if Twitter might offer an additional layer of useful data. Because the data used in the paper were all aggregate, it seems that it was difficult to find more specific and meaningful correlations between visitation, Twitter activity, and search and rescue (SAR) activity. The authors mention in the paper that the Cloudberry application also collects geographic data on Twitter posts. Is there the possibility of using these data rather than keywords to locate where users are posting? We also wondered if there is any way to gather data from individuals on personal social media use and SAR activations? It would be very interesting to know if social media activity increases an individual's risk of being the subject of a SAR mission.

This paper shared insights that may inspire further research on social media and wilderness safety. An awareness of any methodological limitations the authors encountered might inform future investigations.

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Social media is a continually evolving and valuable way in which people communicate. As national parks continue to gain popularity, attracting hundreds of millions of visitors every year, it is imperative to both develop ways of employing social media as a unique storytelling forum and encourage safe practices and environmental stewardship.

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The sensitivity of some to even the mention of this work seems to surface every generation or so of researchers. Our colleague, the late John Hayward, studied hypothermia during the 1970s and 80s and often referred to the Dachau studies with the usual "unethical" caveat.[5] This created some controversy, and some articles have addressed the topic.[6,7] The first author of this letter started his career the year after Dr Hayward retired, and he met with similar, though less intense, debate when he referenced the Dachau experiments in several papers solely to provide a full historical context.[8,9] In fact, after submitting one

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manuscript for publication, one referee suggested the reference be left out, whereas the other referee insisted the reference be left in; it was indeed left in. Now the concern has risen again for a new generation of medical researchers and practitioners.

At the core of the issue are two opposing views: 1) we should not give validity to these atrocious studies by even referring to them in any way; and 2) if the data can be used for any positive use, it should be, so that the tragic victims would not have died in vain.

One important question is, "What does it mean to 'use' the data?" It certainly does not mean using it to inform clinical guidelines, although it has informed some mathematical modeling of core cooling (see below). We feel there is some value in providing an important historical record of cold research, specifically, and all World War II atrocities in general.

Hayward and his colleagues carefully considered how some results of the Dachau studies related to their own work. In one example, they noted that once a prisoner's core temperature started to drop, it followed a linear pattern to low core temperatures that could never again be studied (Martin Collis, personal communication, June 2022). Therefore, Hayward's group created prediction equations that extrapolated linear cooling rates below their ethically obtained lowest observed core temperatures.[5] This principle of linear cooling rates is now commonly accepted.

As we review our own research careers, we have noted that in addressing a natural progression of questions, we have addressed many of the questions posed in the Alexander report, with the caveat that our studies were all ethically approved and safely conducted on willing healthy volunteers. Notably, many of our conclusions were qualitatively similar. Now we have a new generation of medical practitioners and researchers, some of whom will focus on the human in the cold. We suspect that very few are familiar with the Dachau experiments and even fewer have knowledge of the Alexander report.

Thinking about this issue in more detail, we have come to a startling conclusion. Instead of burying these atrocities in the historical dustbin, we might do well to provide a detailed historical summary of what went on in that horrendous prison camp during that dark period of history. In almost all other areas we ardently revisit atrocities (eg, all concentration camp experiences) and tragedies (eg, slavery) with two goals in mind: "never forget" and "never again." One publication on this topic asked a relevant question about these cold research atrocities with a section heading titled "A Futuristic Scenario: Can It Happen Again?"[4] We think it would benefit many, especially our new generation of researchers and practitioners, to provide such a historical review at some future medical meeting. We would be willing to provide such a review to support these two important goals: "never forget" and "never again."

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WILDERNESS & ENVIRONMENTAL MEDICINE 2022; 33(4): 492–3

WILDERNESS IMAGE

Scorpions (*Tityus dinizi*) in a Historical Site of the State of Amazonas, Brazil

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[2]*Pós-Graduação em Biotecnologia e Recursos Naturais da Amazônia, Universidade do Estado do Amazonas, Manaus, AM, Brazil*

Figure 1. Historic site of Paricatuba in the state of Amazonas, Brazil (top); *Tityus dinizi* on an inner wall of the building (bottom).

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The natural beauty of the Amazon attracts tourists and natural historians from all over the world.[1,2] In the region of Manaus, capital of the state of Amazonas, the tourist attractions include places such as museums, jungle hotels, zoos, walks through the forest, rivers, and beaches.[2] A popular site is the ruins of Village of Paricatuba (3°04'58.1"S 60°14'04.6"W), located on the banks of the Rio Negro, Municipality of Iranduba, state of Amazonas,

Brazil.[1] These buildings opened in the 19th century and served as an agricultural school, hospital, and public prison.[1] During our scientific expedition (November 2020) to this site (Figure 1, top), we identified 15 adult specimens of *Tityus dinizi* Lourenço, 1997, inside these ruins. An adult male found inside the buildings was approximately 1 m above the ground (Figure 1, bottom). In Brazil, there are a total of 170 species of scorpions known,[3,4] and approximately 28% of this fauna occurs in the state of Amazonas.[4]

The type locality of the scorpion *Tityus dinizi* (Buthidae) is the Anavilhanas archipelago, Rio Negro region, state of Amazonas, Brazil.[5,6] *Tityus dinizi* belongs to the subgenus *Atreus* Gervais, 1843, that contains some potentially medically significant species.[6] Although this scorpion originates from primary forest,[3] the ruins where it was found are surrounded by a riverside community established on the banks of the Rio Negro.[1] Those who visit the Village of Paricatuba can have free access to the beaches and the dependencies of the historic buildings.[1] Venomous animals like scorpions can hide very easily where they live, and the color pattern of some of these arachnids has an enigmatic function that helps them not be easily detected.[3,5] In general, tourists do not use safety equipment and are not aware of the presence of venomous animals in the historic site of Paricatuba.[1] Although the possible medical significance of *Tityus dinizi* is so far unknown, it is recommended that visitors to sites like this wear closed shoes, remain aware of their surroundings, and avoid contact with the walls and other structures in the ruins.

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