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Understanding the pain experience of lionfish envenomation

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Abstract

Introduction: Stings from the lionfish (Pterois volitans) constitute one of the most painful wounds in the ocean. This species has invaded the Atlantic coast of the United States, Gulf of Mexico, Caribbean, and Mediterranean Sea. In addition to its ecological impact on local fish populations, stings from the lionfish pose a medical problem because of the debilitating nature of the pain they produce. However, there are no studies examining the human pain experience of lionfish stings.
Objective: To characterize the various aspects of the pain experience following a lionfish sting.
Methods: We developed a pain questionnaire that includes validated scales used with patients having acute or chronic pain to understand the pain variability, as well as the use of health care resources and treatments.
Results: We provide the first study of the pain experience from lionfish stings. Here, we show that the pain is intense from the start and peaks approximately 1 hour later, resolving itself in 7 days for most victims. Furthermore, pain intensity can be influenced by several factors, including (1) age of the victim, where older victims experience significantly higher pain intensities, (2) the number of spines involved, (3) and whether infection occurred at the injury site. However, pain intensity was not different between male and female participants.
Conclusion: These findings will inform the medical community on the pain experience and can be used by local authorities to better appreciate the impact of lionfish envenomations to develop programs aimed at curtailing the expansion of the lionfish.

Keywords: Lionfish, Pain, Envenomation, Sting, Questionnaire

1. Introduction

The lionfish (*Pterois volitans*) is a venomous fish endemic to the Indo-Pacific that has, over the past 30 years, invaded the Caribbean, Gulf of Mexico, Northwestern Atlantic, and Mediterranean Sea. The fish has spread at an alarming rate because of its rapid reproductive capacity and its lack of natural predators in the invaded regions.[23] Lionfish tend to predate any fish smaller than them, resulting in a steep reduction in reef biodiversity in affected areas.[6,13,17,22,23,26] These effects on the ecosystem have led local governments to setup spearfishing initiatives to control the spread of the lionfish. This resulted in a rapid increase in the number of individuals handling lionfish and ultimately in the number of stings.[20] Although initiatives aimed at curtailing this invasion focus on limiting ecological impact, the medical aspect of this invasion must also be appreciated. This includes the pain that is experienced by victims of lionfish stings, which can affect various aspects of daily life.

Lionfish stings occur when a victim's skin is punctured by one or more of their 18 venomous spines. These cartilaginous spines are coated with an integumentary sheath, underneath which is the venom gland tissue. Once skin is punctured by a spine, the sheath is torn, and venom diffuses into the victim.[15,20,27] Lionfish stings produce painful sensations and result in swelling, redness, and many other unpleasant symptoms.[1,12,14,19,20,24] However, there is no data regarding the venom's toxin composition, and little understanding of the venom's molecular mechanism of action. A prior preclinical study from our group characterized the pain

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following intraplantar injections of lionfish venom in mice, as well as a cellular characterization of the venom's activity on nociceptors.[16] Although that study helped understand pain following lionfish sting, the pain experienced by humans following lionfish stings remains poorly documented and understood. There exist numerous case studies of extreme envenomations,[1,12,14,19,20,24] but because the average lionfish sting does not usually result in hospitalization, there are no characterizations of the average human pain. In addition, case studies mostly place a focus on the swelling, redness, and nonpain symptoms of lionfish envenomations. Yet, pain is the cardinal symptom reported from lionfish stings.

There is an overall lack of pain-focused questionnaires for victims of stings from any species, and those that have been done did not take advantage of well-validated scales, thus lacking standardization and making results hard to compare.[28] We sought to solve this problem by assembling a pain questionnaire designed for victims of lionfish sting, including validated scales/questionnaires used with patients having acute or chronic pain from a variety of different underlying sources. The objectives of this study were (1) to characterize various aspects of the pain experience by victims of lionfish sting, including its severity, qualities, and impact on various aspects of daily life, (2) to investigate contributions of various factors in the variability of pain experience including factors surrounding the sting itself, and (3) document the use of health care resources and treatments used to control the pain associated with lionfish sting.

2. Methods

2.1. Study design and setting

We assembled a questionnaire to investigate the pain caused by lionfish envenomations and to quantify and analyze factors surrounding the envenomations that may or may not affect pain and discomfort. This questionnaire was composed of 44 questions and hosted at the URL www.lionfishpain.org. The questionnaire was created using the survey platform Typeform and integrated into the hosting URL. To prevent duplicate submissions, responders were asked whether they had completed the questionnaire before, and if they responded "Yes," their second submission was not considered in our analysis. Furthermore, duplicate email addresses, which were voluntarily submitted by most participants, were flagged, and second submissions from these individuals were not considered in our analysis.

The protocol was approved by the Faculty of Medicine and Health Sciences Institutional Review Board of the McGill University on February 3, 2021 (A02-M09-21B), and it was conducted in conformity with the published guidelines of the Tri-Council Policy Statement 2, in compliance with the *Plan d'action ministériel en éthique de la recherche et en intégrité scientifique* (MSSS, 1998), and the Food and Drugs Act (17 June 2001); it acts in accordance with the US Code of Federal Regulations that govern research on human subjects (FWA 00004545). Participants were automatically assigned a token ID number by Typeform, and once data were exported, nominal data and token ID numbers were separated from the main file and kept in a separate password-protected Excel file. From that point onward, only the token ID numbers were associated with participant data, and all nominal data were removed from the main analysis file.

2.2. Participant recruitment

The questionnaire was advertised by email and distributed through a variety of marine biologists who study the lionfish, as well as on social media accounts through lionfish hunters and within their communities. The questionnaire was also advertised at a variety of lionfish hunting events across Florida. Cards with the website URL and information on the questionnaire were distributed at a variety of lionfish hunting events and through lionfish hunting communities to people who were interested.

2.3. Procedures

Using targeted questions, adapted from the standardized NIH PROMIS questionnaire (for pain intensity),[8,11] the short-form DN4 questionnaire (for pain characteristics),[4,18] and some context-specific questions, we sought to gain insights into the characteristics of the sting sites, intensity of the victims' pain, and the qualities of their pain. Furthermore, we assessed the interference of the pain on daily activities using the Brief Pain Inventory. Overall, respondents were asked to quantify pain intensity over 5 different time points, qualities of their pain, how pain interfered in their normal lives, and a variety of different factors that we hypothesized may affect the pain caused by a lionfish sting. The questionnaire was made public online on February 23, 2021, and was available up to February 2022. We received 605 submissions within 1 year (analyses for this study were performed using data collected up until February 2022). Exclusion criteria for responses included long delays between the sting event and completing the questionnaire (more than 10 years), incomplete filling of the questionnaire (more than one-thirds of the questionnaire left unanswered), third-party reports of lionfish stings, and duplicate reports of lionfish stings from the same individual. Our host URL, lionfishpain.org received 901 unique visitors between February 23, 2021, and February 25, 2022, 652 of these individuals were located in the United States, 65 in Canada, 35 in the United Kingdom, 32 in Bonaire, and the rest were spread across the world (48 other countries).

Using the short-form DN4 questionnaire, we asked participants to report whether their pain matched any of the following qualities to gain insights into whether the pain caused by a lionfish sting had any neuropathic qualities. For each participant, a "yes" to each of these qualities was scored as a value of 1, and their DN4 score was tabulated based on counting how many of these qualities each patient reported, for which the maximum score was 7.

We asked participants to complete a series of pain interference questions using a modified version of the Brief Pain Inventory (BPI) Pain Interference Scales 10[9,11] and indicate a score from 0 to 10 for how much each of the named activities were affected due to the pain they experienced following a lionfish sting. Items that were considered for this score included general activity, mood, walking ability, normal work, sleep, enjoyment of life, and social activities. A global pain interference score was calculated for each patient by calculating the sum of their scores in each category, with a maximum possible score of 70.

To characterize the time course of the pain experienced by sting victims, we asked participants to score the intensity of their pain on the NIH PROMIS Short Form Pain Intensity Questionnaire on a scale of 0 to 10, where 0 indicated no pain, and 10 worst imaginable pain at 5 different time points: immediately after the sting, then 1, 2, 3, 24 hours, and 1 week after the sting.

2.4. Statistical analysis

Data were exported from Typeform and saved as a .csv file to reformat the data for analysis. All analyses were performed using Python. Descriptive statistics were used to depict the participants' demographics, the characteristics of their pain experience, and the types of pain management modalities they used. Mean, median, standard deviation, and interquartile range (IQR) values were computed for continuous variables, whereas percentages and frequencies were computed for categorical variables. The evolution of pain over time was analyzed using a mixed model for repeated measurements (MMRM), considering participants' sex and age, history of allergies, fish status (live or dead), number of spines involved in the sting, and whether the sting ultimately resulted in an infection. The type of variance–covariance matrix was compound symmetry. An analysis of covariance (ANCOVA) was performed to identify factors statistically associated with pain at each time of measurement. Mixed model for repeated measurements and ANCOVA analyses were performed using SAS software (version 9.4; SAS Institute Inc, Cary, NC).

3. Results

3.1. Characteristics of the responders

In the 1-year period during which we collected responses to our survey, we received 605 submissions, 50 of which we had to remove because of a variety of exclusion factors (see Methods). **Table 1** and **Figure 1** show the demographic characteristics of the responders (N = 555). Close to 80% were males with a mean age of 46.71 years (SD = 13.23) (**Table 1** and **Fig. 1A, B**). The median time elapsed between the sting and the completion of the questionnaire was 336 days (interquartile range, 580 days).

3.2. Circumstances surrounding the lionfish stings

As shown in **Table 2**, the most common activities performed by participants at the time of their lionfish sting were spearfishing (72.07% of participants, **Fig. 1C** blue bar and **Table 2**) and diving or snorkeling (14.95% of participants, **Fig. 1C** purple bar and **Table 2**). Furthermore, the most stung body part was the hand/arm (90.63% of participants, see **Table 2**), consistent with common lionfish sting injuries stemming from spearfishing and diving/snorkeling. Most of the questionnaire participants were in the United States at the time of their sting (67.03% of participants, see **Table 2**), with the majority of the others distributed across the Caribbean, consistent with the fact that lionfish are invasive in the Gulf of Mexico and Caribbean.

For the 85.95% of participants, the lionfish was alive at the time of their sting (**Table 2**), and for 86.67% of participants, the sting took place underwater (**Table 2**). Finally, we found that 22.16% of participants had a history of allergies, and only 3.24% of participants experienced an infection at the site of their sting in the days and weeks following the sting (**Table 2**).

Table 1

Demographic data describing lionfish pain questionnaire participants.

Age, y	
Under 20	7
20–29	52
30–39	127
40–49	116
50–59	157
60–69	71
70–79	24
Mean (SEM)	46.71 (0.5622)
Sex	
Male	441
Female	109
Race	
White	509
Hispanic or Latino	26
Black or African American	4
Asian/Pacific Islander	4
Other	11
Time since sting	
Mean (SEM)	1854.479 (298.47)
Median	336
Mode	730

Survey responses regarding responders' age, sex, and race as well as the delay in days between the sting and responding to the questionnaire. Data are expressed as counts (N) with percentage distributions indicated in brackets or means with standard deviations in brackets (SD), as indicated.

3.3. Sting characteristics and pain qualities

As shown in **Table 3**, all participants experienced pain after the sting. Three-quarters of the responders (76.22%) reported that their pain was continuous, whereas it was an intermittent type of pain in the other cases. Other sting characteristics included reported soreness (69.37% of the participants), redness (68.83% of the participants), swelling (85.59%), bruising (11.71%), blistering (11.53%), paleness (7.75%), and necrosis (4.68%).

Table 3 shows the results obtained on each item of the DN4 Questionnaire. The most common reported sensations were burning sensation (55.68%), tingling (46.49%), and numbness (45.95%) (**Table 3**). The mean DN4 score was 2.36 (±1.61) out of a maximum possible score of 7 (**Table 3**).

Less common symptoms experienced (and their abundances) were nausea (80 of 555 or 14.41% of participants), sweating (93 of 555 or 16.76%), trouble sleeping (54 of 555 or 9.73%), accelerated heart rate (74 of 555 or 13.33%), shock (18 of 555 or 3.24%), and fainting (10 of 555 or 1.80%) (**Table 3**).

3.4. Pain intensity

The mean (±SD) pain rating immediately after the sting was 4.97 (±2.40) and peaked to 7.25 (±2.69) at 1 hour after the sting (**Table 3**). This number dropped to 6.10 (±3.01) at 2 hours after the sting, and it was still present the following day at 2.87 (±2.49). It eventually dissipated a week later, reaching 1.05 (±8.99).

3.5. Pain interference on daily living

We sought to evaluate how the pain experience from a lionfish sting can affect an individual's normal activities. **Table 4** shows the extent to which lionfish sting pain affected various aspects of daily living. In the BPI Pain Interference scales, scores at or above 4 out of 10 indicate moderate to severe interference. In our study, most scores were lower than 4 out of 10, with the highest scores being general activity (3.63 ± 2.49) and normal work (3.52 ± 3.09). Other categories for which responders reported low interference included self-care (2.18 ± 2.93), recreational activities (2.97 ± 2.95), mood (2.60 ± 2.33), walking ability (0.96 ± 2.31), sleep (2.55 ± 2.96), enjoyment of life (2.25 ± 2.91), and social activities (1.89 ± 2.99) (**Table 4**). More than two-thirds of the participants (69.37%) reported having needed to take time off from work because of their lionfish sting, reporting on average 17.98 (±17.33) hours of work missed.

3.6. History of stings

As shown in **Table 5**, just less than half of the participants (41.98%) had prior experiences with lionfish stings. The

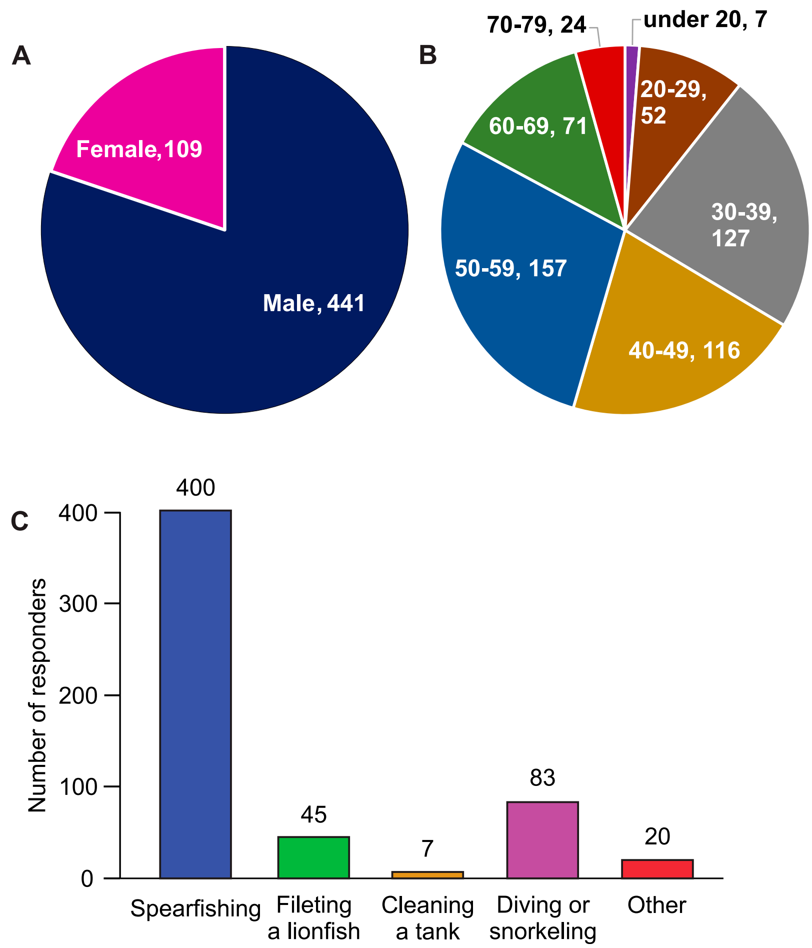

Figure 1. Description of sting survey participants' sex, age and activity they were doing at the time of their lionfish sting. (A) Pie chart depicting distribution of male vs female participants. Number following comma indicates the number of participants. (B) Pie chart depicting age distribution of participants. Number following comma indicates the number of participants. (C) Bar chart demonstrating different activities performed by participants at the time of their lionfish sting.

characteristics of the stings were similar to the one depicted for the most recent one. Almost half of the responders (47.64%) who had been stung before indicated that the pain was less intense than previous stings, whereas 39.48% (92 of 233 participants) reported that the pain was the same (**Table 5**). Only 13.3% indicated that their pain was more intense than that from past lionfish stings.

3.7. Factors associated with pain intensity

Figure 2 and **Table 6**, respectively, show the results of the MMRM analysis and the ANCOVAs using the general linear model procedure used to identify factors influencing variability in pain intensity following lionfish stings. We observed no significant sex differences in pain from lionfish stings (see **Fig. 2A**, **Table 6** and supplemental Table 1, available at http://links.lww.com/PR9/A202). The fact that the lionfish was alive or dead at the time of the sting did have a significant effect on pain at specific time points. Although we did not find that the fish being alive or dead had a global impact on reported pain in the MMRM analysis (although the result was close to statistical significance with $P = 0.0595$), the results of the ANCOVAs revealed that the variable had a significant influence on pain at specific time points. Immediately after the sting, there was no significant difference in pain between dead or alive fish groups, but there was a significant difference at 1 and 2 hours after the sting ($P = 0.0304$ and 0.0193, respectively, ANCOVA, **Fig. 2B**, **Table 6** and supplemental Table 1, available at http://links.lww.com/PR9/A202). Age was a variable that caused significant variation in pain experienced by sting victims, playing the largest role at 1 and 2 hours after the sting (1 hour later: $P = 0.0002$ and 2 hours later: $P = 0.0298$, repeated ANCOVAs with general linear model procedure, see **Table 6** and Supplemental Table 1, available at http://links.lww.com/PR9/A202). On average, older participants reported more intense pain than younger ones with the 50 to 59-year-old, 60 to 69-year-old and 70 to 79-year-old groups reporting more pain overall than the younger than 30 years group ($P = 0.0175$, 0.0019 and 0.0038, respectively, in the MMRM analysis, see Supplemental Table 1, available at http://links.lww.com/PR9/A202 and **Fig. 2C**). The sting victims' history of allergies had no effect on pain at any time point (see **Fig. 2D**, **Table 6** and Supplemental Table 1, available at http://links.lww.com/PR9/A202).

The number of spines from the lionfish that punctured the victim had a significant effect on the experience of pain. Overall, individuals stung by 3 or more spines experienced significantly more pain than those stung by 1 spine in our MMRM analysis ($P = 0.0009$, MMRM, see **Fig. 2E**). There was also a significant difference between the 1 spine and the 3+ spines groups at all time points except for immediately after the sting ($P = 0.005$, 0.002, <0.0001, and 0.003 at 1, 2, 24 hours and 1 week after the sting, respectively, ANCOVA analyses, see **Table 6** and Supplemental Table 1, available at http://links.lww.com/PR9/A202).

Table 2

General data describing context of reported lionfish stings.

Body part	
Hand/arm	503
Foot/leg	46
Torso	4
Face/head	2
No. of spines	
1 spine	340
2 spines	128
3+ spines	81
I don't remember	5
Activity at the time of the sting	
Spearfishing	400
Cleaning/fileting a lionfish	45
Cleaning my tank	7
Diving/snorkeling	83
Other	20
Country	
United States	372
Bonaire	32
Honduras	29
Belize	18
Bahamas	16
Aruba	11
Cayman Islands	7
Curacao	7
US Virgin Islands	6
Mexico	6
Nicaragua	5
Dominica	5
Other	41
Stung by a live fish	477
Stung underwater	481
History of allergies	123
Stung area got infected	18

Survey responses regarding context of lionfish stings, including the body part stung, the number of spines involved in the sting, the activity the individual was performing at the time of the sting, and the country the sting took place in. Bottom 4 rows represent further details providing context to the sting including whether the sting took place underwater and by a live lionfish, whether the victim has a history of allergies, and whether the stung area ultimately got infected during their recovery from the lionfish sting. Data are expressed as counts with percentage distributions indicated in brackets.

Table 3

Data describing details of sting appearance, pain intensity, and pain qualities.

Characteristics of stung area, N (%)	
Redness	382 (68.83%)
Paleness	43 (7.75%)
Swelling	475 (85.59%)
Bruising	65 (11.71%)
Blistering	64 (11.53%)
Necrosis	26 (4.68%)
Pain intensity (score/10), mean (SD)	
Immediately after the sting	4.973 (2.40)
1 h after the sting	7.252 (2.69)
2 h after the sting	6.10 (3.01)
1 d after the sting	2.87 (2.49)
1 wk after the sting	1.05 (8.99)
Pain qualities, N (%)	
Soreness	385 (69.27%)
Burning	309 (55.68%)
Cold	24 (4.32%)
Electric shocks	54 (9.37%)
Tingling	258 (46.49%)
Pins and needles	198 (35.68%)
Itchiness	211 (38.02%)
Numbness	255 (45.95%)
DN4 score (mean (SD))	2.359 (1.61)
Continuous or intermittent pain, N (%)	
Continuous	423 (76.22%)
Intermittent	132 (23.78%)
Other symptoms, N (%)	
Nausea	80 (14.41%)
Sweating	93 (16.76%)
Trouble sleeping	54 (9.73%)
Accelerated heart rate	74 (13.33%)
Shock	18 (3.24%)
Fainting	10 (1.80%)

Top: Participants self-reported visual features of their sting. Data are expressed as counts with percentage distributions indicated in brackets. *Second*: Participants self-reported pain intensity information in an adapted PROMIS questionnaire format. They were required to report pain from 1 to 10 at the different timepoints. Data are presented as mean (SEM). *Third*: Participants self-reported different qualities of their lionfish sting–induced pain based on the DN4 questionnaire, to tabulate a DN4 score. They also indicated whether their pain was continuous or intermittent. *Bottom*: Participants self-reported any other symptoms that have previously been reported with lionfish stings.

Infection was a variable that was found to be globally statistically significant in our MMRM model ($P = 0.0102$, MMRM, see **Fig. 2F**) and was also statistically significant at all time points except for immediately after the sting (P = 0.033, 0.007, 0.007, and 0.004 for 1, 2, 24 hours, and 1 week after the sting, ANCOVA, see **Table 6** and Supplemental Table 1, available at http://links.lww.com/PR9/A202).

Other factors that were statistically significant for certain time points in our ANCOVA model, but not in our MMRM model, included whether it was the first time that the individual had been stung and the delay between the sting and completion of the questionnaire. Prior experience with a lionfish sting proved to be a statistically significant variable at 2 hours, 1 day, and 1 week after the sting (P = 0.030; 0.036; and 0.035, respectively, ANCOVA model, see **Table 6** and Supplemental Table 1, available at http://links.lww.com/PR9/A202). For these time points, prior experience with a lionfish sting tended to cause a reduction in the reported pain by the victim, whereas first-time sting victims tended to report significantly more pain. Of all the participants, 26.14% sought medical care or advice from a physician, nurse, or pharmacist (data not shown). Interestingly, individuals who needed to take time off from work because of the pain did not report significantly more pain than those who did not need time off (**Table 6** and Supplemental Table 1, available at http://links.lww.com/PR9/A202).

4. Discussion

In this study, we provide the first large-scale study of the pain experience from lionfish stings. We assembled a questionnaire that may be used for other envenomations, including by other fish (eg, stonefish, scorpionfish), snakes, insects, and the like, to gain a wider understanding of the immediate pain and symptoms, as

Table 4

Self-reported life interference details (score on 10) caused by pain and discomfort caused by lionfish stings as well as participants' time lost from work (if needed) because of lionfish sting.

Altered activities (score/10) mean (SD)	
Self-care	2.184 (2.93)
Recreational activities	2.971 (2.95)
General activity	3.631 (2.49)
Mood	2.602 (2.33)
Walking ability	0.962 (2.31)
Normal work	3.515 (3.09)
Sleep	2.550 (2.96)
Enjoyment of life	2.245 (2.91)
Social activities	1.897 (2.99)
Pain interference score	17.402 (15.91)
Missed work (N (%))	385 (69.37%)

Data are reported as mean (±SD) of the reported score on 10.

Table 5

Details of past stings reported by participants who had been stung by lionfish before the sting reported in first part of questionnaire.

Stung in the past (N (%))	233 (41.98%)
Stung body part, N (%)	
Hand/arm	213 (91.42%)
Foot/leg	17 (7.30%)
Face/head	1 (0.43%)
Activity when sting occurred, N (%)	
Spearfishing	180 (77.28%)
Fileting a lionfish	18 (7.73%)
Diving/snorkeling	24 (10.30%)
Other	11 (4.72%)
No. of spines involved, N (%)	
1 spine	174 (74.67%)
2 spines	23 (9.87%)
3+ spines	25 (10.73%)
Pain compared with previous sting, N (%)	
The same	92 (39.48%)
Less intense	111 (47.64%)
More intense	31 (13.30%)

Data are reported as counts with percentage distributions indicated in brackets.

well as the impact of stings on the individual's life and work potential. We surveyed 555 individuals who have been stung by lionfish and obtained detailed information about the circumstances surrounding their sting, the conditions of their sting, the pain they experienced, and the interference the sting had on their personal lives.

By far, the most common activity that study participants were engaged in when they were stung by lionfish was spearfishing. This is not surprising considering that spearfishing requires a hunter to get close to the fish and to manipulate the fish with their hands to either remove them from their spear or empty their containment unit. Alarmingly, the invasion of the lionfish shows no sign of reversing soon,[10,17] resulting in an increase in the number of individuals stung by lionfish in the future. Therefore, it is important to gain a better understanding of the consequences of lionfish envenomations, both from a physiological point of view and from a life-interference point of view.

Because anecdotal evidence has pointed to the fact that stings from dead lionfish produce less pain than from live ones, we asked participants to indicate whether the lionfish was alive at the time of their sting. In our ANCOVA model (**Fig. 2B**), we show that indeed live lionfish produce stings that produce more long-lasting pain than those of dead fish. This would confirm our group's prior findings that the algogenic toxin in the venom may degrade quickly, suggesting that it is proteinaceous in nature because this algogenic factor seems to degrade rather quickly after the fish's death.[16]

The most reported side effects of lionfish stings are pain, swelling, and redness with some experiencing paleness, bruising, blistering, and necrosis, in extreme cases; we sought to evaluate the frequency of these symptoms among the responders of our questionnaire. Indeed, pain, soreness, redness, and swelling were experienced by the majority of our participants, with paleness, bruising, blistering, and necrosis being experienced by less than 15% of our participants. This finding confirms anecdotal evidence presented in the literature based on case studies of lionfish stings.[12,14,24,27]

The exact time course of the pain caused by lionfish stings varies greatly, with some experiencing pain for a matter of minutes and others experiencing pain for weeks. Using the NIH PROMIS Short Form Pain Intensity Questionnaire, we characterized the time course of the pain experienced by sting victims. Our results showed that lionfish stings produce a

Table 6

Statistical analysis of variables influencing pain experienced by the victim of sting at different time points.

Time point	Variable	F	*P*	Time point	Variable	F	*P*
Pain immediately	Age	1.76	0.119	Pain next day	Age	0.6	0.699
	Sex	0.01	0.911		Sex	0.01	0.933
	Allergies	0	0.962		Allergies	0.97	0.324
	Infection	0.44	0.508		Infection	7.34	0.007
	Delay since sting	3.23	0.022		Delay since sting	0.62	0.605
	Number of spines	0.22	0.805		Number of spines	10.74	<0.0001
	Fish alive	1.23	0.267		Fish alive	1.58	0.209
	1st time stung	2.63	0.106		1st time stung	4.41	0.036
	Time off work	0.26	0.613		Time off work	0.49	0.483
Pain 1 h later	Age	5.03	0.0002	Pain next week	Age	0.6	0.703
	Sex	0.01	0.923		Sex	1.54	0.215
	Allergies	0.26	0.609		Allergies	0.35	0.557
	Infection	4.54	0.034		Infection	8.36	0.004
	Delay since sting	12.39	<0.0001		Delay since sting	0.11	0.956
	Number of spines	5.36	0.005		Number of spines	5.8	0.003
	Fish alive	4.71	0.0304		Fish alive	0.52	0.471
	1st time stung	2.7	0.101		1st time stung	4.46	0.035
	Time off work	0.01	0.934		Time off work	2.01	0.157
Pain 2 h later	Age	2.5	0.023				
	Sex	1.53	0.216				
	Allergies	0.01	0.909				
	Infection	7.32	0.007				
	Delay since sting	4.84	0.003				
	Number of spines	6.17	0.002				
	Fish alive	5.51	0.019				
	1st time stung	4.72	0.030				
	Time off work	0	0.953				

Analysis was performed using repeated ANCOVAs using the general linear model procedure whereby the reported pain score for each time point were dependent variables, and the following variables were analyzed as independent variables: age, sex, history of allergies, sting site infection, delay since sing, number of spines, fish alive, first time stung, and need for time off from work. F and *P* values were reported.
ANCOVA, analysis of covariance.

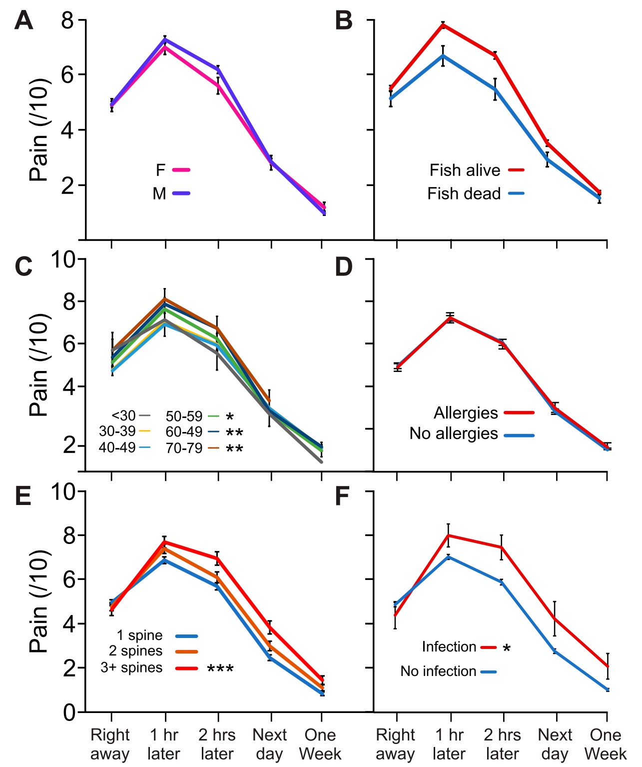

Figure 2. Self-reported lionfish pain over the course of 1 week after a sting. Mean (±SD) self-reported pain on 10 immediately after a lionfish sting, 1 hour later, 2 hours later, 1 day later, and 1 week later. (A) Male (441 individuals) vs female (109 individuals) participants. (B) Participants' pain divided based on whether the fish that stung them was alive (477 individuals) or dead (78 individuals). (C) Participants divided based on age range (younger than 30 years: 60 individuals, 30-39 years: 127 individuals, 40-49 years: 116 individuals, 50-59 years: 157 individuals, 60-69 years: 71 individuals, 70-79 years: 24 individuals). All statistical comparisons are relative to younger than 30 years age group, $*P < 0.05$, $**P < 0.01$. (D) Participants who have allergies (123 individuals) vs do not have allergies (432 individuals). (E) Participants' pain divided based on how many spines punctured the skin during the sting event (1 spine: 340 individuals, 2 spines: 128 individuals, 3+ spines: 81 individuals, unknown number of spines [not shown]: 5 individuals). $***P < 0.001$ (1 spine vs 3 spines). (F) Participants' pain divided based on whether their sting ultimately got infected (infected: 18 individuals, not infected: 537 individuals), $*P < 0.05$. Mixed model for repeated measures analysis for all panels.

moderate to significant amount of pain immediately after the sting, increasing until it reaches its peak at approximately 1 hour after the sting and reducing for the days following, healing completely within a week for most sting victims (**Fig. 2**). This pain varied based on the age of the victim, the number of spines they were stung by, whether the fish was alive or dead, and whether the site of the sting ultimately got infected. Importantly, however, the pain reported by victims did not vary based on sex (**Fig. 2** and **Table 6**).

Because a prior study by our group indicated that lionfish venom activates nonpeptidergic nociceptors to cause pain, we sought to characterize whether the pain matched symptoms associated with neuropathic pain.[16] To evaluate this, we used the self-reported portion of the DN4 questionnaire. Because the traditional cutoff for patients to be considered was 3,[4,18] we concluded that the pain caused by lionfish venom in this case did not match the qualities of traditional neuropathic pain. This was somewhat expected because venoms are cocktails of molecules that often contain components which, in addition to components that activate nociceptors directly, trigger inflammatory reactions to amplify pain and discomfort in sting victims.[2,5,7,25]

Because of the intensity of the pain caused by lionfish stings and the fact that they tend to occur on hands, we hypothesized that this would lead to a highly disruptive experience for sting victims. We sought to quantify the degree of this disruption using the BPI Interference item. The maximum possible score for this item is 70 and is quantified from 0 to 10 in 7 different categories: general activity, normal work, mood, walking ability, sleep, enjoyment of life, and social activities. The mean total interference score in our study was 17.40/70 (±15.91) (**Table 4**). For comparison, the mean interference core associated with osteoarthritis pain is approximately 67.[29] These results would suggest that although lionfish stings do not completely interfere or alter one's normal activities, a lionfish sting does pose a nuisance to its victims. In addition, more than two-thirds of the participants (69.37%) reported having needed to take time off from work because of their lionfish sting, reporting on average 17.98 (±17.33) hours of work missed. This would suggest that although lionfish stings pose a nuisance to everyday life, they also cause an average of approximately 2 missed workdays.

To determine whether pain from lionfish stings decreases as an individual gets stung more and more often, we asked participants to characterize whether the pain from the latest sting was less, the same, or more intense than the pain they experienced with past stings. In our ANCOVA model, we found that prior experience with a lionfish sting resulted in less pain for sting victims at the 2-hour time point and beyond. Thus, it seems that either prior experience with lionfish stings sets better expectations vis-à-vis the outcomes, producing less fear in victims of sting and ultimately resulting in less pain, or perhaps there exists some habituation mechanism that can be built by multiple exposures to lionfish venom.

Overall, pain-related questionnaires are very uncommon for victims of stings, and those that exist lack the line of questioning seen in comparable pain questionnaires, ultimately making it hard to compare results with existing pain data. The line of questioning followed in our study can be generalized to virtually any sting experience with some adaptation and would surely be beneficial for gaining insights into pain caused by stings and envenomations as well as the surrounding consequences of suffering from stings.

Government authorities are becoming increasingly aware of the damages caused by the invasion of the lionfish, especially on the local fish industries. Consequently, several initiatives have been set in place to help counter the impact of this invasion. Although it is known that individuals stung by the lionfish spines experience extreme pain, there remained several unknowns about the nature of the pain and how it affected the daily lives of the victims. In this study, we designed a clinical pain questionnaire that addressed these unknowns and have uncovered the important details on pain experience of individuals stung by lionfish, the risk factors that result in increased pain, and the extend of the interference of this pain on daily activities and work disability. These data not only will inform the general community to the risks associated with diving in lionfish-infested waters but also help in informing the medical community on the pain experience caused by a lionfish sting. Finally, these findings can also be used by local authorities to better appreciate the medical impact of the lionfish sting to further invest or develop new programs aimed at curtailing the expansion of the lionfish.

Recall bias remains a limitation of our study because participants may not have an exact memory of the pain they experienced at the time of their sting. Furthermore, the distribution of our questionnaire (throughout groups we knew had experience with lionfish stings) may have biased the demographics of our questionnaire to individuals in the southern states of the United States. Finally, the nature of the responses we received in this questionnaire were self-reported, thus potentially increasing overall variability between questionnaire participants or slightly overestimating reported pain.[3,21]

In conclusion, we have assembled the first large-scale study of the pain produced by lionfish stings. Data from our questionnaire have shown that victims of lionfish sting experience the peak of their pain approximately 1 hour after the sting and that most of the pain resolves itself around 7 days after sting. A variety of factors influence the intensity of the pain a victim will experience after being stung, including age, whether the fish was alive, the number of spines involved in the sting, infection, and prior experience with a lionfish sting. Taking all of these into account, we have provided novel insights into the nature of the pain, as well as which groups are likely to suffer more intensely from a lionfish sting and which factors correlate with elevated pain in victims of sting.

Disclosures

R.S.N. and S.M.C. have a startup company that developed a cream to treat the pain from the lionfish envenomation. M.C. declares no conflict of interest.

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Data availability statement: The authors are happy to make the data available upon request.

Appendix A. Supplemental digital content

Supplemental digital content associated with this article can be found online at http://links.lww.com/PR9/A202.

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