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Research article

Limb circumference measurements contributing to the diagnosis of snake venom-induced compartment syndrome

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A R T I C L E I N F O

Keywords:
Snakebite
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Limb circumference

A B S T R A C T

Background: The present study aimed to investigate the relationship between swollen limb circumference and compartment pressure after a snakebite and to evaluate the diagnostic value of the circumference difference between the healthy and affected sides and the circumference growth rate for snake venom-induced compartment syndrome (CS).
Method: The study was based on a prospective cohort study of snakebite patients at the emergency department of West China Hospital from May 2021 to October 2022. The snakebite patients were divided into the CS and non-compartment syndrome (NCS) groups. The diagnostic value of the circumference of the swollen limb for the CS after snakebite was evaluated using a receiver-operating characteristic curve analysis, and the cut-off value of the circumference of the swollen limb for CS after snakebite was calculated with sensitivity and specificity.
Result: The present study enrolled 115 patients with severely swollen limbs after snakebite. The mean age was 59.1 ± 13.6 years, with 58 (50.4 %) female cases and 57 (49.6 %) male cases. There were 33 (28.7 %) cases where the upper limbs were injured and 82 (71.3 %) cases where the lower limbs were injured. These patients were divided into CS (n = 19) and NCS (n = 96) groups. The area under the curve (AUC) for the 15 cm circumference difference and circumferential growth rate of the upper edge of the patella was 0.683 (95 % CI 0.508 to 0.858, P = 0.037), and 0.685 (95 % CI 0.512 to 0.858, P = 0.035). The optimal cut-off values for the 15 cm circumference difference and circumferential growth rate of the upper edge of the patella to distinguish CS and NCS were 2.8 cm (sensitivity = 76.9 %, specificity = 66.7 %) and 7 % (sensitivity = 76.9 %, specificity = 66.7 %), respectively.
Conclusion: Limb circumference measurement is a non-invasive, convenient, effective, and repeatable bedside test that can assist clinicians in the early detection of suspected snake venom-induced CS in patients exhibiting limb swelling after snake bites.

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1. Introduction

Compartment syndrome is a clinical syndrome caused by increased pressure in a closed anatomical space, leading to insufficient local tissue perfusion and ischemic necrosis of muscles and nerves. It most commonly occurs in the lower leg and forearm [1,2].Snake venom-induced compartment syndrome (CS) is an unusual and serious complication of snakebite. Severe pain, pallor, pulselessness, abnormal sensation, and limitation of limb movement are the main clinical symptoms. The incidence of CS after snakebite has been reported to be about 0.2–3% in various regions [3–5,1]. Swollen limbs are prevalent clinical manifestation of snakebite. If not recognized promptly, snake venom-induced CS can lead to permanent muscle and nerve tissue necrosis, resulting in disability and deformity, seriously affecting the patient's quality of life [6]. Early identification of CS after snakebite and fasciotomy will prevent muscle and nerve tissue necrosis and avoid irreversible and devastating outcomes. However, unnecessary fasciotomy will increase complications in these patients, such as delayed limb healing, skin grafting, infection, bleeding, and scar formation [7].Although relevant studies have confirmed that most limb swelling after snakebite is caused by subcutaneous tissue and muscle injury rather than fascial compartment syndrome [8,9].As limb swelling continues to worsen, pressure within the compartment may rise, causing further impairment of tissue perfusion and ischemic hypoxia. This leads to a vicious cycle of limb swelling and CS. Therefore, one of the significant challenges in clinical management is the early identification of snake venom-induced CS in many patients with swollen limbs after a snakebite. Currently, snake venom induced CS is diagnosed based on clinical manifestations or pressure measurements. The clinical manifestation-based diagnosis has several drawbacks, including ambiguous diagnostic criteria, a lack of objective detection values, and difficulty reproducing subjective clinical symptom evaluations. Furthermore, Measurement of intra-compartmental pressure is not always feasible in many medical centers. Compartment pressure measurement is not only considered to be the most objective and authoritative adjunct to the diagnosis of compartment syndrome, but is also helpful in diagnosing patients with suspected compartment syndrome, especially when the diagnosis is ambiguous [2].However, measuring compartment pressure is an invasive procedure that can cause bleeding and infection and increase the risk of tissue damage. The use of single-compartment pressure to diagnose CS is debatable. The serial measurement of the compartment pressure has a higher diagnostic value for the dynamic monitoring of changes in the compartment pressure [10].

In contrast, constant monitoring of compartment pressure changes requires multiple punctures, increasing patient acceptance and the risk of the operation. Few studies on snake venom-induced CS and circumference have been conducted, with case reports predominating. In our clinical practice, we have observed that limb circumference may be related to compartment pressure. The present study aimed to determine whether changes in limb circumference after snake bites were associated with compartment pressures and compartment syndrome.

2. Material and methods

2.1. Study design

Snakebite patients were enrolled in this prospective cohort study in the emergency department of West China Hospital of Sichuan University from May 2021 to October 2022. The main venomous snakes in the Sichuan region are *Protobothrops mucrosquamatus, Ovophis monticola, Gloydius brevicaudus,* and *Glordius strauchi, as shown in* Fig. 1. *Protobothrops mucrosquamatus* and *Ovophis monticola*

Fig. 1. A. *Protobothrops mucrosquamatus*; B. *Ovophis monticola*; C. *Gloydius brevicaudus*; and D. *Glordius strauchi.*

are venomous snakes that affect blood circulation and are members of the family Viperidae and subfamily Crotalinae. *Gloydius brevicaudus* also belongs to the family Viperidae and subfamily Crotalinae. It has a mixed venom that contains both haemotoxic and mild neurotoxic components. The *Glordius strauchi* is found in the western mountainous or plateau regions of Sichuan, China, at altitudes ranging from 3500 to 4000 m.

2.2. Patient recruitment and management

The study followed the Declaration of Helsinki, and the Human Ethical Committee of West China Hospital of Sichuan University approved the study protocol.

2.3. Inclusion and exclusion criteria

The inclusion criteria for the study were.

1) A confirmed history of snakebites was presented, accompanied by one or more systemic or localised symptoms of poisoning
2) Limb swelling, moderate and severe
3) Age ≥18year
4) Signed an informed consent form
5) Snakebite patients who have completed simultaneous compartment pressure measurement of the affected limbs and circumference size measurements of the affected and healthy limbs.

The exclusion criteria for the study were.

1) Venous thrombosis of the extremities
2) Peripheral arterial occlusive disease
3) Patients who sign informed consent and then refuse to take part in the study

2.4. Data collection

Data were collected after obtaining consent through interviews with patients and their families using a predesigned and structured questionnaire. The survey questionnaire included the following questions: demographic characteristics (age, sex); snakebite characteristics (bite site, type of snake, time from bite to admission); and limb swelling classification. Limb swelling was categorized as mild, moderate, or severe. Mild swelling extends to the wrist or ankle joint. Moderate swelling reaches the wrist or ankle but not the elbow or knee joints. Severe swelling extends to the elbow and knee joints. Laboratory tests included: Alkaline phosphatase (ALP), Alanine aminotransferase (ALT), Aspartate aminotransferase (AST), Lactate dehydrogenase (LDH), Hydroxybutyrate dehydrogenase (HBDH), Fibrinogen, Gamma-glutamyl transferase (GGT), White blood cell (WBC), Myoglobin (MB), Creatine Kinase (CK), and Creatine Kinase-MB (CK-MB). The groups were formed based on measured compartment pressure, following the 2016 World Health Organization guideline [11],with values ≥ 40 mmHg representing the snake venom-induced CS group and values < 40 mmHg representing the NCS group. Subgroup analysis was performed according to bite site injury as upper and lower extremities.

2.5. Pressure measurements

The physicians involved in this study are either junior or senior medical professionals who underwent specialized training in emergency medicine and toxicology, focusing particularly on the management of venomous bites. A modified Whiteside manometry was used for intra-compartment pressure measurement(ICP).The procedure of measuring intra-compartment: 1) Patients with severe pain, swelling, and unusual numbness in the arm or leg after a snakebite were asked to provide informed consent and sign an informed consent form. 2) Patients should lie or sit semi-recumbently and relax the limb. 3) After disinfection the proposed pressure measurement area, a 1.2 gauge needle is prepared to connect to the pressure sensor and infusion line, and the air is evacuated by slowly infusing saline. The needle was inserted about 2.5–3.0 cm into the most swollen part of the affected limb. The puncture needle was connected to the Myriad (Benevision N17) monitor, and the cystometric module was used to measure intra-compartmental pressure. For bites on the lower limb, pressure was measured in the deep posterior compartment or the lateral compartment. For bites on the upper limb, pressure was measured in the volar compartment or the mobile wad compartment. After the continuous measurement data of the monitor was stabilized, the value of the monitor was recorded, and the average value of the three measurements was taken thrice. Some of them had their compartment pressure measured multiple times. Fig. 3 illustrates the measurement sites and methodology used to measure compartment pressures during bites on the lower and upper limbs, respectively. A threshold of 40 mmHg was established for the diagnosis of CS.

2.6. Limb circumference measurement procedure

Before measuring the compartment pressure of the limb, the circumference was measured first, then the compartment pressure measurement. Limb circumference measurements are performed utilizing a plastic tape measure with a precision of 1 mm and standardized methodologies, resulting in a measurement accuracy of up to 1 mm. The circumference was measured around the palm, wrist, and 10 cm below the olecranon and 10 cm above the transverse elbow when the bite site was the upper limb. In contrast, the circumference was measured around the sole, ankle, and 15 cm below and 15 cm above the patella when the bite site was the lower limb. Simultaneously, the circumference of the healthy limb was also measured. The circumference growth rate = (affected limb circumference - healthy limb circumference)/healthy limb circumference × 100 %. The diagram of treatment was shown in Fig. 4.

2.7. Statistical analysis

Depending on the distribution types, continuous variables were displayed as the median and interquartile range (IQR) or means ± standard deviations, and categorical variables as frequencies and percentages. For continuous variables, Mann–Whitney U and independent-sample t-tests were used to compare the two groups of CS versus NCS. We used the chi-square or Fisher's exact test to present categorical variables as frequencies (proportions). The circumference difference and circumferential growth rate of the limb were evaluated using receiver operating characteristic (ROC) curves for the diagnosis of snake venom-induced CS. A two-sided P-value <0.05 was considered statistically significant for all tests. All analyses were performed using SPSS statistical software version 26.0 (IBM Corporation, Armonk, NY).

3. Results

3.1. Characteristics of eligible patients

Between May 2021 and October 2022, A total of 130 patients underwent pressure and limb circumference measurements. Exclusions included 12 patients with no limb circumference records, 1 patient with venous thrombosis of the extremities, and 2 patients lost to follow-up. As a result, 19 patients were included in the CS group and 96 in the NCS group, totaling 115 patients (Fig. 2). The mean age of the enrolled patients was 59.1 ± 13.6 years, with 58 (50.4 %) females and 57 (49.6 %) males. All patients suffered 33 upper limb injuries and 82 lower limb injuries. There were no differences in age, sex, and bite area between the CS and NCS groups. The distribution of ALP, ALT, AST, fibrinogen, GGT, and WBC was not significantly different between the two groups ($P > 0.05$). However, the distribution of HBDH, LDH, MB, CK between the two groups differs significantly ($P < 0.05$), as presented in Table 1.

3.2. Distribution of limb circumference in the CS group versus the NCS group

There were six (31.6 %) cases of upper limb bite injuries and 13 (68.4 %) cases of lower limb bite injuries in the CS group. While the NCS group had 27 (28.1 %) cases of upper limb bite injuries and 69 (71.9 %) cases of lower limb bite injuries in the NCS group. There was no difference in the site of bite injuries between the two groups. When the upper extremity was bitten, there was no significant difference between the two groups in the circumference of 10 cm circumference diameter above the transverse pattern of the affected elbow, 10 cm circumference diameter below the olecranon of the affected limb, wrist and palm. Additionally, there was no significant

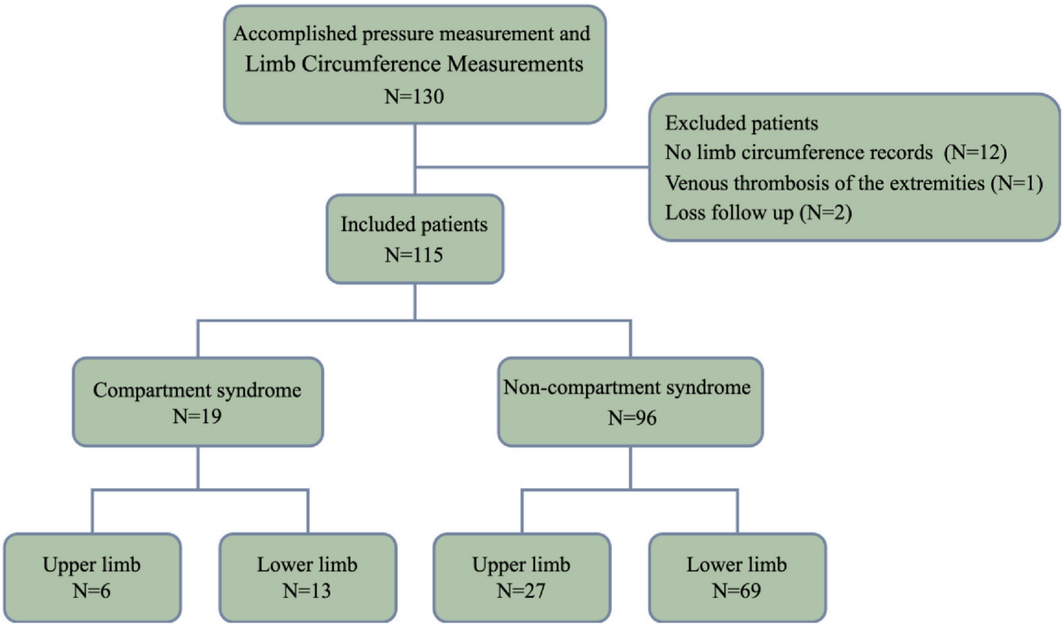

Fig. 2. Flow diagram of included patients.

Fig. 3. (A) A 45-year-old male, 3 h after being bitten by a snake on the right foot, had a compartment pressure of 39 mmHg measured in the right lower limb; (B) A 58-year-old male, 5 h after being bitten by a snake on the right finger, had a compartment pressure of 11 mmHg measured in the right upper limb.

difference in the rim of each part and the rate of change in the circumference of each part. The distribution of upper limb circumference between the two groups is shown in Table 2.

When the lower limb was bitten, there were significant differences in the circumference difference and circumferential growth rate of 15 cm of the upper edge of the patella, with a median difference of 4.00 cm (1.90 cm, 7.35 cm), P = 0.037, and a median circumferential growth rate of 10 % (5 %, 19 %) of the circumference of 15 cm of the upper edge of the patella, P = 0.035. The circumference of other parts did not differ significantly between the two groups. The distribution of lower limb circumference between the two groups is shown in Table 3.

3.3. Evaluation of the ability of a 15 cm circumference difference of the upper edge of the patella to diagnose CS following a snakebite

Patients were divided into two groups based on the ICP: CS (n = 19) and NCS (n = 96). The AUC of the 15 cm circumference difference between the upper edge of the patella was 0.683 (95 % CI 0.508 to 0.858, P = 0.037). The optimal cut-off value for distinguishing CS and NCS for the 15 cm circumference difference of the upper edge of the patella was 2.8 cm (sensitivity = 76.9 %, and specificity = 66.7 %). The AUC of the 15 cm circumferential growth rate of the upper edge of the patella was 0.685 (95 % CI 0.512 to 0.858, P = 0.035).Fig. 5 depicts the optimal cut-off value for distinguishing CS and NCS at the 15 cm circumferential growth rate of the upper edge of the patella to 7 % (sensitivity = 76.9 %, specificity = 66.7 %).

3.4. Surgical intervention situation and remeasurement of pressure and limb circumference

Fasciotomy was performed on two of the 115 snakebite patients. In two cases, the compartment pressures were 65 mmHg and 60.67 mmHg, and the time from bite to incision was 13 and 33 h, respectively. Limb swelling in two cases resolved completely 30 and 180 days after injury. Five patients had their compartment pressures and limb circumferences re-measured on the second day after the initial measurements. All of them, both measurements were lower than before. In one case, the initial intro-compartmental pressure was 90 mmHg which was reduced to 68 mmHg after additional antivenom treatment. He did not undergo fasciotomy and the limb swelling resolved 30 days after the bite. The clinical characteristics of these five patients are presented in Table 4, with the numbers arranged by date of consultation.

4. Discussion

Compartment syndrome (CS) caused by snake venom manifests as limb pain, swelling, sensory and motor abnormalities, and loss of

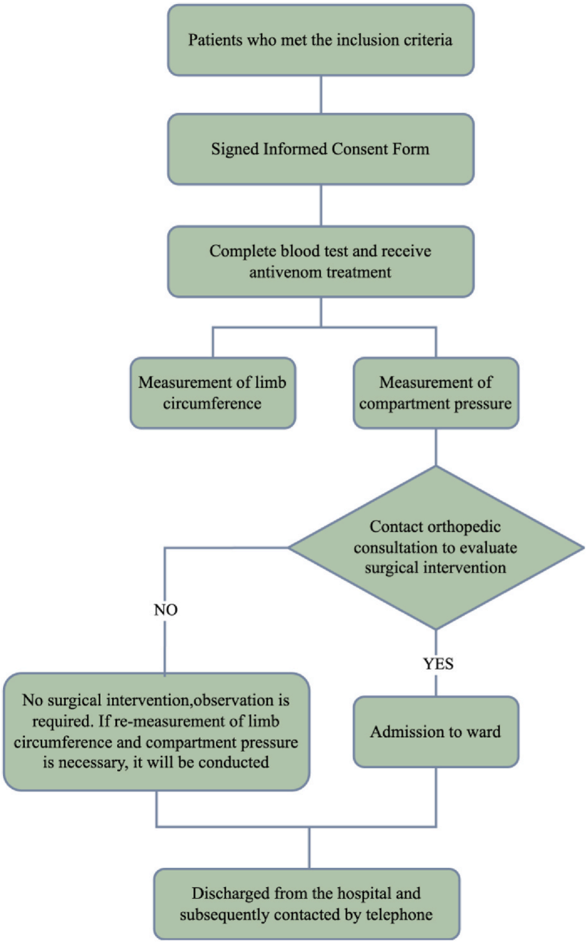

Fig. 4. The diagram of snakebite treatment protocols.

arterial pulsation. Snake venom induced CS is common worldwide, particularly in tropical and subtropical regions. Its incidence varies significantly across regions and snake species, with some areas reporting incidence rates as low as < 0.5 % [12,13] and others reporting rates as high as 10.18 % [14]. Morbidity and disability rates depend on snake venom toxicity, poisoning amount, and treatment measures.

CS diagnosis often is based on clinical presentation and signs, leading many patients to undergo unnecessary fasciotomy [15]. In addition, diagnosing of snake venom-induced CS relies on clinical signs and symptoms, and there are no objective diagnostic indicators, and a high degree of human interference. Although compartment manometry can assist in diagnosing compartment syndrome in patients with suspected compartment syndrome or impaired consciousness, its value is limited in some areas due to a lack of manometry equipment. Normal compartment pressure is approximately 8 mmHg in adults and 10–15 mmHg in children [1]. The diagnostic threshold for CS is still controversial, with many recent studies suggesting that a difference of ≤30 mmHg between diastolic pressure and ICP is more accurate than the absolute value of intra-compartment pressure [1,16]. However, these studies were all focused on post-fracture compartment syndrome, and it is worth exploring the applicability of snake venom-induced compartment syndrome. In Taiwan, in a study of 183 patients with Chinese cobra bites, 46 (26.6 %) patients required fasciotomy when CS was diagnosed by intra-compartment pressure >30 mmHg [17]. Yong Hun Kim et al. studied 158 snakebite patients. They performed fasciotomy in 33 patients with suspected snake venom-induced CS using compartment pressure measurement when the compartment pressure value was >40 mmHg. The pressure did not decrease after 4 h of antivenom treatment. Finally, 17 patients met the objective criteria for CS diagnosis and underwent fasciotomy. The mean intra-compartmental pressure was 49.6 mmHg(37–88 mmHg), resulting in a fasciotomy decompression rate of 10.8 % [18]. In our study, 19 patients had ICP values > 40 mmHg, and only 2 (2/115, 1.7 %) underwent fasciotomy. We later identified other patients without fasciotomies who did not have a severe physical disability or neurological impairment through telephone follow-up. Although we diagnosed compartment syndrome through ICP, we remained cautious in deciding whether to perform fasciotomy. Therefore, our findings are consistent with clinical guidelines recommending greater caution in diagnosing snake venom-induced CS with fasciotomy [6,17]. The threshold for diagnosing snake venom-induced acute compartment pressure based on compartment pressure values warrants further investigation. Our study found that the ROC value for limb circumference difference in diagnosing compartment syndrome is 0.685. It indicates that although the difference in limb

Table 1
Demographic and disease characteristics of the patient.

Variables	Overall (n = 115)	CS group (n = 19)	NCS group (n = 96)	P-value
Sex, No, (%)				
Male	57 (49.6)	13 (68.4)	44 (45.8)	0.072
Female	58 (50.4)	6 (31.6)	52 (54.2)	
Year, y (median ± SD)	59.2 ± 13.9	58.0 ± 12.1	59.4 ± 13.8	0.690
Time from bite to admission, h (median, IQR)	4.1 (3.1, 9.9)	3.70 (3.1, 5.5)	4.50 (3.0, 15.9)	0.340
Bite area, n (%)				
Upper limb	33 (28.7 %)	6 (31.6 %)	27 (28.1 %)	0.761
Lower limb	82 (71.3 %)	13 (68.4 %)	69 (71.9 %)	
Wound infection, n(%)				
Yes	16(13.9 %)	4(21.6 %)	12(13.4 %)	0.300
No	99(86.1 %)	15(78.9 %)	84(82.6 %)	
Laboratory data				
ALP, U/L	80.5 (68.0, 95.7)	84.0(59.0, 101.0)	80.0 (69.0, 95.0)	0.965
ALT, U/L	19.0 (15.0, 25.7)	25.0 (20.0, 41.0)	18.00 (14.0, 23.5)	0.001
AST, U/L	26.0 (20.0, 33.0)	31.0 (22.0, 83.0)	25.0 (19.0, 32.0)	0.019
Fibrinogen, g/L	2.70 (2.34, 3.2)	2.6 (2.3, 3.4)	2.7(2.3, 3.1)	0.389
GGT, U/L	19.0 (13.0, 27.0)	20.0 (12.0, 39.0)	19.0 (14.0, 27.0)	0.996
HBDH, U/L	165.0 (142.0, 193.0)	193.0(161.0298.0)	161.0 (139.0, 182.0)	0.007
LDH, U/L	206.0 (181.0, 253.0)	250.0(235.0,353.0)	203.0 (180.3, 236.8)	0.002
WBC, 10ˆ9/L	10.6 (8.2, 13.8)	12.4 (10.0, 13.9)	10.2 (7.8, 13.6)	0.129
MB, ng/ml	75.9 (34.6, 204.0)	316.5 (59.7, 740.9)	71.7 (34.3, 164.1)	0.059
CK, U/L	199.0 (105.0, 495.0)	327.0(199.0,1949.0)	158.5 (101.0, 486.8)	0.015
CK-MB,ng/mL	3.5 (2.0, 7.9)	10.7, (3.5, 35.5)	3.2 (1.9, 6.4)	0.020
Fasciotomy No, (%)				
Yes	2 (1.7 %)	2 (10.5 %)	0	0.026
No	113 (98.3 %)	17 (89.5 %)	96 (100 %)	
Time from bite to swelling elimination, (d)	16.0 (10.0, 30.0)	18.0 (9.3, 30.0)	16.0 (10.0, 31.3)	0.896

ALP= Alkaline phosphatase; ALT = Alanine aminotransferase; AST = Aspartate aminotransferase; LDH= Lactate dehydrogenase; HBDH = Hydroxybutyrate dehydrogenase; GGT = Gamma-glutamyl Transferase; WBC= White blood cell, MB = Myoglobin; CK= Creatine Kinase; CK-MB= Creatine Kinase- Myoglobin.

Table 2
Distribution of limb circumference of upper limb in the CS group versus the NCS group.

Variable	CS group (n = 6)	NCS group (n = 27)	P-value
The 10 cm circumference difference above the transverse elbow line (cm)	5.60(1.93,7.50)	1.50(0.70,7.00)	0.624
The 10 cm circumference difference below the olecranon (cm)	3.25(1.60,4.63)	2.80(1.30,4.00)	0.107
The circumference difference of the wrist (cm)	2.00(1.53,2.35)	1.80(1.00,2.70)	0.761
The circumference difference of palm (cm)	5.00(2.60,6.00)	3.60(3.00,5.50)	0.482
The 10 cm circumferential growth rate above the transverse elbow line (%)	0.20(0.06,0.27)	0.05(0.03,0.25)	0.112
The 10 cm circumferential growth rate below the olecranon (%)	0.13(0.06,0.22)	0.12(0.06,0.17)	0.744
Circumferential growth rate of the wrist (%)	0.12(0.09,0.15)	0.11(0.06,0.15)	0.834
Circumferential growth rate of palm (%)	0.22(0.10,0.27)	0.17(0.14,0.25)	0.744

Table 3
Distribution of limb circumference of the lower limb in the CS group versus the NCS group.

Variable	CS group(n = 13)	NCS group(n = 69)	P-value
The 15 cm circumference difference of the upper edge of the patella	4.00(1.90,7.35)	1.90(0.50,3.85)	0.037
The 15 cm circumference difference of the below edge of the patella	4.20(2.00,5.60)	4.00(2.20,5.00)	0.76
The circumference difference of ankle	1.80(1.20,2.60)	1.50(0.75,2.40)	0.576
The circumference difference of foot	2.50(1.85,2.65)	2.00(1.40,3.00)	0.492
The 15 cm circumferential growth rate of the upper edge of the patella (%)	0.10(0.05,0.19)	0.05(0.01,0.10)	0.035
The 15 cm circumferential growth rate of the below edge of the patella (%)	0.11(0.06,0.17)	0.11(0.07,0.16)	0.829
The Circumferential growth rate of ankle (%)	0.08(0.06,0.14)	0.08(0.04,0.12)	0.526
Circumferential growth rate of sole (%)	0.10(0.08,0.12)	0.09(0.06,0.14)	0.505

circumference has some diagnostic value, it is not ideal. In certain scenarios, this metric can aid in the diagnosis, but needs to be used in conjunction with other diagnostic tools for a comprehensive evaluation. There is very little research literature on using limb circumference measurements to diagnose compartment syndrome. One case report indicated a correlation between compartment pressure and limb circumference difference after a snakebite. Maryann et al. reported that a 17-month-old girl was bitten by a copperhead and treated with additional antivenom, which reduced the compartment pressure from 85 mmHg to 55 mmHg. The

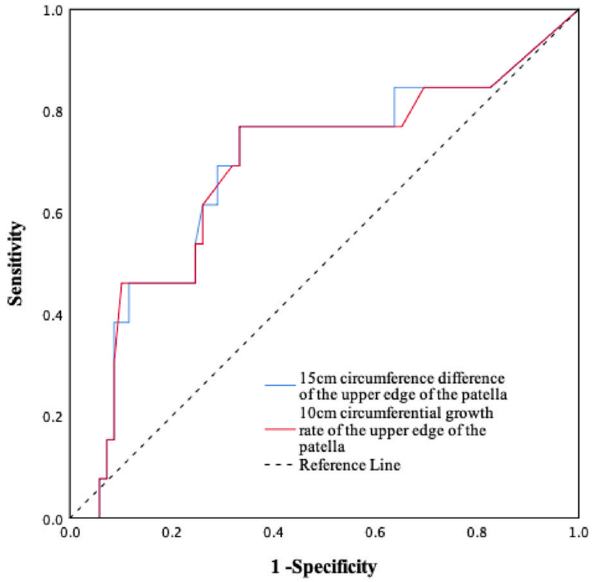

Fig. 5. ROC curve analysis for evaluating the diagnostic performance of the limb circumference measurement test.

Table 4
The case report of remeasured compartment pressure and limb circumference.

Number	Sex	Age	Bite area	Ordinal number	Pressure	ΔCd of upper	ΔCd of below	ΔCd of ankle/wrist	ΔCd of palm /foot	Time from bite to swelling elimination(d)
1	Male	52	Lower limb	First	60.67	8.60	4.20	1.80	2.50	180
				Second	54.67	8.40	4.00	1.80	2.40	
2	Female	69	Lower limb	First	60.00	8.70	4.50	4.30	3.30	120
				Second	40.00	7.20	3.80	2.70	3.00	
3	Male	51	Lower limb	First	63.67	5.00	4.70	4.80	2.50	30
				Second	35.67	2.00	3.70	2.00	1.00	
4	Male	66	Upper limb	First	40.30	1.70	1.00	0.70	1.10	N
				Second	26.30	1.00	0.50	0.70	0.60	
5	Male	46	Lower limb	First	90.00	7.40	3.40	1.40	2.50	30
				Second	68.00	6.80	2.60	1.20	1.70	

Footnote: ΔCd of upper = The 10 cm circumference difference above the transverse elbow line/The 15 cm circumference difference of the upper edge of the patella; ΔCd of below = The 10 cm circumference difference below the olecranon (cm)/The 15 cm circumference difference of the below edge of the patella; ΔCd of ankle/wrist = circumference difference of ankle/wrist; ΔCd of palm/foot = The circumference difference of palm/foot.

average limb circumference decreased 48 h after the bite was 2.2 cm, and no fasciotomy was performed. The limb circumference remained consistent two weeks after discharge from the hospital, and limb movement returned to normal [19]. The relatively small sample size in our study may have an impact on the statistical significance of the results. Furthermore, it is possible that some measurement errors may have occurred in the assessment of limb circumference, despite the implementation of standardised methods to minimise such errors. It is noteworthy that no significant differences were observed in the circumference difference and circumferential growth rate between the affected and healthy limbs in the CS group when the injury site was the upper limb. The findings indicate that the diagnostic value may be contingent upon the location of the injury. The AUC for the circumference difference at the 15 cm upper edge of the patella was significant, although further validation is required to confirm its diagnostic utility in broader populations. It is recommended that future studies employ more robust measurement techniques, utilise larger sample sizes, and validate the findings in different populations. Further research should also investigate the potential applications of this measurement index, which is not constrained by temporal, spatial, demographic, or instrumental factors, making it a potentially valuable tool in various clinical settings. Although the ROC value for limb circumference difference is not high, it can still be employed as an auxiliary diagnostic tool in clinical practice. It is recommended that limb circumference difference be used as an initial screening tool, with further confirmation of suspected cases conducted through the use of additional diagnostic methods. Several non-invasive methods for diagnosing CS are being developed. These included magnetic resonance imaging (MRI) [20], point-of-care ultrasound bedside ultrasound techniques to assess arterial blood flow in the limb [21], near-infrared spectroscopy (NIRS), ultrasound measurement of muscle elasticity [22] and continuous tissue stiffness measurements [23].

The findings of our study indicate that straightforward, non-invasive measurements can be effectively incorporated into the diagnostic process for snake venom-induced CS, particularly in resource-limited settings. In contrast, upper limb bites were less frequent, and the relatively small sample size for these cases could have impacted the representativeness and statistical robustness of our findings. Consequently, the results were more significant in the lower limbs.

The present study revealed that the CS group exhibited elevated levels of MB, CK, and WBC ($P < 0.05$). Wang et al. also identified CK-MB as a consistent risk factor for muscle necrosis after CS [24]. Chih-Po Hsu et al. identified increased WBC counts and elevated AST levels as risk factors for snake-venom induced CS [4]. Our study, Although the p-values for ALT and AST do indicate statistical significance, our analysis deems these changes to be clinically insignificant. This is due to the fact that both ALT and AST levels remain within the normal reference ranges for both groups. This discrepancy might be attributed to the different patient populations, types of snake venom, or study methodologies. Further research is needed to clarify the role of ALT in diagnosing and predicting compartment syndrome following snakebites.

5. Conclusion

Limb circumference measurement is a non-invasive, convenient, effective, and repeatable bedside test that can assist clinicians in the early detection of suspected snake venom-induced compartment syndrome in patients exhibiting limb swelling after snake bites.

Limitation

The present study has several limitations. First, it was a single-center study with a small sample size, limiting the generalizability of its findings. Secondly, identifying certain snake species during the study was challenging, which may have influenced the results. Thirdly, measurements of limb circumference and ICP were taken after antivenom administration, which could affect the findings applicability. Further investigation is warranted to address these limitations and confirm the results in broader populations.

Disclosure statement

No potential conflict of interest was reported by the authors.

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Data availability statement

The data supporting the findings of this study have not yet been uploaded to a public repository. It is available from the corresponding author upon request.

CRediT authorship contribution statement

Xiaoyan Xian: Writing – review & editing, Writing – original draft, Formal analysis, Data curation, Conceptualization. **Zhen Jiang:** Writing – review & editing, Writing – original draft, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Yan Ren:** Investigation, Formal analysis, Data curation. **Shiyuan Tang:** Resources, Methodology. **Yajun Liu:** Data curation. **Ting Bai:** Data curation. **Fang Chen:** Data curation. **Li Ding:** Resources, Investigation. **Shuyun Xu:** Writing – review & editing, Supervision, Resources, Project administration, Methodology, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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