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ORIGINAL RESEARCH

Incidence of Traumatic Sciatic Nerve Injury in Association with Acetabular Fracture: A Retrospective Observational Single-Center Study

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Purpose: Traumatic sciatic nerve injury is one of the most serious consequences of acetabular fracture. However, reports on this type of injury are rare. In this study, we investigated the demographics of acetabular fracture with traumatic sciatic nerve injury, the clinical characteristics of patients with these injuries, and potential risk factors.

Patients and Methods: We retrospectively reviewed patients diagnosed to have acetabular fracture at our trauma center between January 2014 and June 2021. Data on patient demographics, characteristics of the acetabular fracture, whether or not sciatic nerve injury occurred, types of sciatic nerve injury, and risk factors were analyzed.

Results: A total of 195 patients met the diagnostic criteria for acetabular fractures. The average Injury Severity Score was 25.9 and the average Abbreviated Injury Scale score was 12.4. Road traffic accidents and falls from height were the main causes. Chest injuries and lower extremity fractures were the most common associated injuries. Posterior wall fractures were the most common fracture type. After exclusion of spinal cord and iatrogenic sciatic nerve injuries, 18 patients with acetabular fractures had traumatic sciatic nerve injury. Four of the 19 sides with traumatic sciatic nerve injury involved the common peroneal nerve division and 15 involved both the common peroneal and tibial nerve divisions. Logistic regression analysis identified a higher AIS score, posterior column fracture, and posterior hip dislocation to be predictors of traumatic sciatic nerve injury.

Conclusion: Acetabular fractures were mostly high-energy injuries. Posterior wall fractures were the most common acetabular fracture types. Most patients sustained injury to the sciatic nerve as well as injury to the common peroneal and tibial nerve divisions. A higher AIS score, posterior column fracture, and posterior hip dislocation were predictors of acetabular fracture combined with traumatic sciatic nerve injury.

Keywords: acetabular fractures, traumatic sciatic nerve injury, posterior hip dislocation

Introduction

Acetabular fracture is a severe intra-articular injury and is more common in men.[1] These fractures are mostly high-energy in nature, such as those sustained in road traffic accidents (RTAs) and falls from height.[2,3] Most acetabular fractures are associated with polytrauma involving the brain, thorax, abdomen, extremities, or other regions. Traumatic sciatic nerve injury is one of the most serious injuries associated with acetabular fracture.[4,5]

The sciatic nerve is the largest and longest nerve in the body. It is the motor nerve supplying the hamstrings, calf, and foot muscles and is also an important sensory nerve supplying the calf and foot. The sensory and motor functions of almost all areas below the knee are innervated by the sciatic nerve.[6,7] The common trunk of the sciatic nerve runs deep into the gluteus maximus, is

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adjacent to the acetabulum, and is separated from the hip joint by only a small amount of soft tissue. Therefore, the sciatic nerve is highly susceptible to injury as a result of a displaced acetabular fracture or dislocated femoral head.[8,9] Incorrect diagnosis and treatment may have a severe impact on the functional status of the affected lower extremity.

Acetabular fracture combined with traumatic sciatic nerve damage is a serious injury with a reported incidence of about 3.3–33% in all cases of acetabular fractures.[4,10,11] Letournel and Judet[12] found that the highest incidence of sciatic nerve injury occurred in association with a posterior fracture or dislocation of the hip joint. Issack and Helfet[13] noted that all patients with a post-traumatic sciatic nerve injury showed a fracture pattern that included the posterior wall or posterior column. However, there are relatively few reports on acetabular fracture combined with traumatic sciatic nerve injury.[4] Furthermore, most studies have pooled traumatic and iatrogenic injuries for analysis or included sciatic nerve injury with other nerve injuries at the hip. Few studies have focused specifically on traumatic sciatic nerve injury.[4,14]

In this study, we reviewed the demographics of patients with acetabular fracture combined with traumatic sciatic nerve injury, documented the clinical characteristics of these patients, and sought to identify risk factors for traumatic sciatic nerve injury in association with acetabular fracture.

Materials and Methods

We retrospectively identified all patients diagnosed with acetabular fracture at our trauma center between January 2014 and June 2021. All patients were under the care of the Shandong Provincial Hospital Affiliated to Shandong First Medical University. The study was approved by the Medical Ethical Committee of the authors' institution. The present study conforms to the Declaration of Helsinki. All patients involved gave informed consent (the patients under 18 years of age signed the informed consent by the parent or legal guardian of patients) and all data were anonymized before the analysis to safeguard patient privacy.

Information was collected on age, sex, mechanism of injury, Injury Severity Score (ISS) and Abbreviated Injury Scale (AIS) score, associated injuries, type of fracture based on the Letournel-Judet classification system,[15] whether or not hip dislocation was present and sciatic nerve injury occurred, and types of sciatic nerve injury.

According to the Letournel-Judet classification, acetabular fractures were classified by two attending traumatology orthopaedic physicians. If there is a disagreement, a senior physician will check to ensure the accuracy of the classification. For the data with subjective aspects such as ISS and AIS score, two researchers strictly follow the scoring standards to ensure the accuracy of the scoring.

Statistical Analysis

The measurement data (age, ISS, AIS score, etc.) are presented as the mean ± standard deviation and count data (sex, mechanism of injury, associated injuries, etc.). Normally distributed data and variables that affected the likelihood of traumatic sciatic nerve injury were analyzed using Fisher's exact test and the chi-square test. The presence of sciatic nerve injury was used as the dependent variable, and variables found to be a *P*-value of <0.05 in univariate analysis were entered into a multivariate logistic regression model. All statistical analyses were performed using SPSS software version 24.0 (IBM Corp., Armonk, NY, USA). A *P*-value of <0.05 was considered statistically significant.

Results

General Information

A total of 195 patients (144 male, 51 female) with complete clinical and radiographic data were eligible for inclusion in the study. The mean age was 43.5 years (range 15–85). MVC (motor vehicle collision) was the most common cause of injury (in 39.5% of cases), followed by a fall from height (in 35.4%) (Table 1).

The average ISS was 25.9 (range 5–66) and the average AIS score was 12.4 (range 3–56). An associated injury was sustained in 72.3% of cases. The most common associated injury involved the chest, followed by lower extremity fractures, spinal injuries. Seven of the 44 spinal injuries involved the spinal cord (including 1 case with bilateral acetabular fractures) (Table 1).

Table 1 Demographic Information, Trauma Scoring, Mechanism of Injury and Additional Injuries

Characteristics	Mean (±SD)/No. of Patients (n=195)	Range/Percentage
Age (y)	43.5±14.0	15~85
ISS	25.9±10.9	5~66
AIS	12.4±8.0	3~56
No. sex (%)	144 (73.8%) **male**, 51 (26.2%) **female**	
Mechanism of injury		
Motor vehicle collision	77	39.5%
Fall from height	69	35.4%
Struck by falling objects	14	7.2%
Fall from bicycle	13	6.7%
Motorcycle collision	5	2.6%
Mechanical crush injury	3	1.5%
Pedestrian	6	3.1%
Truck crush	3	1.5%
Other	5	2.6%
Additional injuries		
Head	26	13.3%
Chest	65	33.3%
Spine	44	22.6%
Abdomen	27	13.8%
Pelvic cavity	13	6.7%
Upper extremity	43	22.1%
Ipsilateral lower extremity	48	24.6%
Contralateral lower extremity	4	2.1%
Bilateral lower extremity	10	5.1%

Abbreviations: ISS, Injury Severity Score; AIS, Abbreviated Injury Scale.

Classification of Acetabular Fractures

Nine of the 195 patients sustained acetabular injuries, giving a total of 204 acetabular fractures. Posterior wall fractures were the most common type, followed by associated both column fractures, T-shaped fractures, transverse fractures, transverse and posterior wall fractures, anterior column fractures. posterior column fractures, posterior column and posterior wall fractures, anterior column posterior hemi-transverse fractures, and anterior wall fractures were relatively rare (Table 2).

Seventy-one sides were combined with hip dislocation: 52 cases had posterior dislocation, 19 had central dislocation, and none had anterior dislocation (Table 2).

Twelve patients sustained a femoral head fracture. These fractures involved the posterior wall in 4 cases and were T-shaped fractures in 2 cases, transverse fractures in 2 cases, and transverse and posterior wall fractures in 2 cases (Table 2).

Incidence and Types of Sciatic Nerve Injury

Excluding the patients with spinal cord injury (7 cases, 8 sides) and iatrogenic sciatic nerve injury (2 cases, 2 sides), 18 (9.7%) of the remaining 186 patients with acetabular fractures sustained traumatic sciatic nerve injury, which was bilateral in one case. Four (21.1%) of the 19 sides with traumatic sciatic nerve injury involved the common peroneal nerve division and 15 (78.9%) involved both the common peroneal and tibial nerve divisions. There were no cases of isolated tibial nerve division injury.

Comparison of Patients According to Traumatic Sciatic Nerve Injury Status

Baseline

There were significant between-group differences in the ISS and AIS score, the frequency of acetabular fractures combined with upper abdominal trauma or bilateral lower extremity fractures, and the frequency of hemorrhagic shock. There was no significant difference in age, sex, cause of injury, or other combined injuries between the two groups (Table 3).

Table 2 Fracture Classification and Related Injuries of Acetabular Fractures

	No. of Acetabular Fractures (n=204)	Percentage
Classification		
Posterior wall	42	20.6%
Posterior column	5	2.5%
Anterior wall	2	1.0%
Anterior column	18	8.8%
Transverse	28	13.7%
T-type	38	18.6%
Posterior column and posterior wall	4	2.0%
Transverse and posterior wall	25	12.3%
Anterior column posterior hemitransverse	3	1.5%
Associated both column	39	19.1%
Related injuries		
Posterior dislocation	52	73.2%
Central dislocation	19	26.8%
Femoral head fracture	12	5.9%

Table 3 Demographics and Injury Features for Patients with and without Nerve Injury

	All Patients (n=186)	Nerve Injury (n=18, 9.7%)	No Nerve Injury (n=168, 90.3%)	*P*
Mean age (year)	43.6±13.8	43.1±16.6	43.7±13.7	0.861
Male	136 (73.1%)	11 (61.1%)	125 (74.4%)	0.353
Mean ISS	25.4±10.6	32.5±13.0	24.6±10.0	0.022*
Mean AIS	12.0±7.2	20.4±8.5	11.1±6.8	0.000***
Mechanism of injury				
Motor vehicle collision	74 (39.8%)	11 (61.1%)	63 (37.5%)	0.052
Fall from height	65 (34.9%)	3 (16.7%)	62 (36.9%)	0.087
Struck by falling objects	13 (7.0%)	2 (11.1%)	11 (6.5%)	0.814
Fall from bicycle	13 (7.0%)	1 (5.6%)	12 (7.1%)	1.000
Motorcycle collision	5 (2.7%)	0 (0)	5 (3.0%)	1.000
Mechanical crush	3 (1.6%)	0 (0)	3 (1.8%)	1.000
Pedestrian	6 (3.2%)	0 (0)	6 (3.6%)	1.000
Truck crush	2 (1.1%)	1 (5.6%)	1 (0.6%)	0.185
Other	5 (2.7%)	0 (0)	5 (3.0%)	1.000
Hemorrhagic shock	45 (24.2%)	10 (55.6%)	35 (20.8%)	0.003**
Additional injuries				
Head	24 (12.9%)	3 (16.7%)	21 (12.5%)	0.896
Chest	60 (32.3%)	8 (42.1%)	52 (31.0%)	0.245
Spine (without spinal cord injury)	36 (19.4%)	3 (16.7%)	33 (19.6%)	1.000
Abdomen	25 (13.4%)	7 (38.9%)	18 (10.7%)	0.003**
Pelvic cavity	13 (6.7%)	3 (16.7%)	10 (4.8%)	0.227
Upper extremity	40 (21.5%)	6 (33.3%)	34 (20.2%)	0.325
Ipsilateral lower extremity	47 (25.3%)	4 (22.2%)	43 (25.6%)	0.978
Contralateral lower extremity	4 (2.2%)	0 (0)	4 (2.4%)	1.000
Bilateral lower extremity	7 (4.3%)	4 (22.2%)	3 (2.4%)	0.002**

Notes: *$P<0.05$, **$P<0.01$, ***$P<0.001$.
Abbreviations: ISS, Injury Severity Score; AIS, Abbreviated Injury Scale.

Comparison of Fracture Type and Frequency of Hip Dislocation and Femoral Head Fracture Between the Two Groups

In the group without sciatic nerve injury, posterior wall fracture was the most common type of acetabular fracture (20.6%, 36/175), followed by T-type fracture (19.4%) and fracture of both columns (18.3%). In the group with sciatic nerve injury, the most common type of fracture involved both columns (26.3%, 5/19), followed by T-type fractures and transverse and posterior wall fractures (15.8%, 3/19). There was no significant between-group difference in the probability of a particular type of fracture ($P>0.05$), except for fracture of the posterior column of the acetabulum ($P<0.05$) (Table 4).

Posterior hip dislocation was sustained on 9 sides (47.4%) in the group with sciatic nerve injury and in 38 (21.7%) in the group without sciatic nerve injury; the between-group difference was significant ($P<0.05$). There was no significant difference in the incidence of central hip dislocation between the groups with and without sciatic nerve injury (2 sides [10.5%] vs 16 sides [9.1%]; $P>0.05$) or in the respective incidence of femoral head fractures (2 [10.5%] vs 10 [5.7%]) (Table 4).

Risk Factors for Traumatic Sciatic Nerve Injury

In order to control the influence of confounding factors on each potential variable, factors that were statistically significant in univariate analysis, including the ISS, AIS score, bilateral lower extremity fracture, posterior column fracture, and posterior dislocation of the hip, were examined in a multivariate logistic regression model. A higher AIS score, posterior column fracture, and posterior dislocation of the hip joint were identified to be predictors of acetabular fracture combined with traumatic sciatic nerve injury (Table 5).

Discussion

Acetabular fracture is a severe trauma and is mostly caused by high-energy injury, particularly RTAs and falls from height.[16,17] With developments in the transport and construction industries, there have been some changes in the incidence and characteristics of acetabular fractures. Kelly et al[18] repeated a meta-analysis (using data for 2005–2018) originally published by Giannoudis et al[19] in 2005 (using data for 1980–2003) to update knowledge concerning patients with acetabular fracture, mechanisms of injury, management, complications, and functional outcomes. Their findings

Table 4 Fracture Pattern and Related Injuries for Patients with and without Nerve Injury

	All Sides (n=194)		Nerve Injury (n=19, 9.8%)		No Nerve Injury (n=175, 90.2%)		P
Classification							
Posterior wall	38	19.6%	2	10.5%	36	20.6%	0.457
Posterior column	3	1.5%	2	10.5%	1	0.6%	0.026*
Anterior wall	2	1.0%	0	0.0%	2	1.1%	1.000
Anterior column	16	8.2%	0	0.0%	16	9.1%	0.349
Transverse	28	14.4%	2	10.5%	26	14.9%	0.868
T-type	38	19.6%	3	15.8%	35	20.0%	0.893
Posterior column and posterior wall	4	2.1%	1	5.3%	3	1.7%	0.340
Transverse and posterior wall	24	12.4%	3	15.8%	21	12.0%	0.913
Anterior column posterior hemitransverse	3	1.5%	1	5.3%	2	1.1%	0.267
Associated both column	38	19.6%	5	26.3%	33	18.9%	0.636
Posterior wall injury group	63	32.5%	6	31.6%	57	32.6%	0.930
Related injuries							
Posterior dislocation	47	24.2%	9	47.4%	38	21.7%	0.028*
Central dislocation	19	9.8%	2	10.5%	17	9.7%	1.000
Femoral head fracture	12	6.2%	2	10.5%	10	5.7%	0.745

Notes: *$P<0.05$. Posterior wall injury group was the sum of posterior wall fractures, posterior column and posterior wall fractures and transverse and posterior wall fractures.

Table 5 Multivariate Logistic Regression Analysis of Risk Factors for Traumatic Sciatic Nerve Injury

	Partial Regression Coefficient	Standard Error	Wald	*P*	OR	95% Confidence Interval for the OR Value	
						Lower Limit	Upper Limit
Mean ISS	−0.012	0.038	0.093	0.761	0.989	0.918	1.065
Mean AIS	0.141	0.053	7.019	0.008**	1.152	1.038	1.279
Bilateral lower extremity fracture	1.795	1.129	2.528	0.112	6.017	0.659	54.968
Posterior column	4.145	1.375	9.082	0.003**	63.097	4.259	934.727
Posterior hip dislocation	1.531	0.629	5.933	0.015*	4.623	1.349	15.851
Constant	−4.915	0.941	27.257	0.000	0.007		

Notes: *$P<0.05$, **$P<0.01$.
Abbreviations: ISS, Injury Severity Score; AIS, Abbreviated Injury Scale.

included an increase in the mean age of patients from 38.6 years to 45.2 years, a decrease in the proportion of injuries resulting from RTAs from over 80% to 66.5%, and an increase in the proportion of injuries caused by falls from just over 10% to 25%. Studies around the world have similarly reached the conclusion that RTAs and falls from height are the main causes of acetabular fracture and that the majority of these injuries are sustained by men.[14] In the present study, the mean patient age was 43.5 years, 73.8% were men, and the injuries were sustained in a MVC in 39.5% and as a result of a fall from the height in 35.4%, which is consistent with recent reports in the literature.

Acetabular fractures are often associated with multiple trauma in other areas of the body, including the brain, chest, abdomen, extremities, and other regions. Additional fractures and chest, head, and abdominal injuries are the most common.[18] However, the ISS values reported in the literature have been variable, ranging from 21.4 ± 11.9 in a study by Simske et al to 15.9 ± 12.5 in a study by Kelly et al[4,18] Moreover, the mean ISS score in another retrospective study of 2236 patients in 29 hospitals was 13 ± 8; only 3% of the patients in that study had polytrauma and had a mean ISS of 21 ± 11.[9] In our study, most patients sustained multiple injuries, with chest injuries (32.8%) and lower extremity fractures (31.8%) being the most common. The mean ISS and AIS scores were 25.9 ± 10.4 and 12.4 ± 8.0, respectively, indicating severe injuries. These high scores may reflect the fact that our study was performed at a single level III trauma center (equivalent to a level I trauma center in Western countries such as the United States and Germany), where the majority of patients have multiple and severe injuries; some are transferred to our center for management of complex injuries after stabilization at local hospitals.

According to the Letournel-Judet classification system, the most common types of fracture involved the posterior wall or associated with both column or T-type fractures. Depending on the cause of injury, the most common type of acetabular fracture associated with an MVC was a posterior wall fracture (27.3%, 21/77) followed by fracture of both columns (18.2%). Falls from heights were the most common cause of T-type fractures (27.6%), followed by associated fractures of both columns (26.1%) and posterior wall fractures (15.9%). Most (64.6%) of the acetabular fractures involving the posterior wall (posterior wall fracture, posterior column and posterior wall fracture, transverse and posterior wall fracture) were associated with posterior hip dislocation. Acetabular fractures combined with femoral head fractures are relatively uncommon, occurring in 6.2% of the patients in our study. These data are consistent with previous reports.[4,9,20–22]

Concomitant sciatic nerve injury is one of the most serious complications of acetabular fracture. Incorrect diagnosis and treatment may seriously affect lower extremity function.[11,13] In our study, the incidence of acetabular fractures combined with traumatic sciatic nerve injury was 9.8% (19/194), of which 4 (21.1%) involved the common peroneal nerve division and 15 (78.9%) involved both the common peroneal and tibial nerve divisions. There were no cases of isolated tibial nerve division injury in our series. In the study by Simske et al[4] the common peroneal nerve branch was injured in 68.0% of cases (17/25) and the entire sciatic nerve was damaged in 32.0% (8/25). There were also no cases of isolated tibial nerve branch injury. However, the results of most of the other studies of acetabular fracture combined with sciatic nerve injury are consistent with our findings. The common peroneal nerve division is more likely to be injured than the tibial nerve division, the main reasons for that are as follows: (1) lower excursion of the peroneal division due to tethering of the nerve at the neck of the fibula and the greater sciatic notch; (2) the peroneal division has fewer nerve bundles, which are smaller in diameter and separated by less connective tissue than is the case for the tibial division; and (3) the peroneal division runs on the lateral side of the sciatic nerve, the fracture or femoral head is displaced inward, backward, and upward, and the peroneal branch is pierced or compressed first.[11,13,14,23]

In the present study, we found that age, sex, and cause of injury had no significant effect on the incidence of acetabular fracture combined with sciatic nerve injury, which is in line with the findings of other studies.[4,14] The incidence of traumatic sciatic nerve injury was significantly affected by the presence of upper abdominal organ injury, acetabular fracture combined with bilateral lower extremity fracture, the trauma severity score, fracture of the posterior column of the acetabulum, and combined posterior dislocation of the hip joint. We used a multivariate logistic regression model to identify statistically significant predictors of sciatic nerve injury. In univariate analysis, sciatic nerve injury was more likely to occur in patients with upper abdominal organ injury, but no correlation was found in multivariate logistic regression analysis.

Most acetabular fractures are the result of high-energy force that is transmitted to the acetabulum through a lower extremity, and acetabular fractures combined with lower extremity fractures are common. We found that the probability of sciatic nerve injury was significantly higher when an acetabular fracture was combined with bilateral lower extremity fractures, which may reflect the fact that patients with bilateral lower extremity fractures are likely to sustain higher-energy trauma to the acetabulum, causing damage to the sciatic nerve. Interestingly, logistic regression analysis did not reveal any correlation between sciatic nerve injury and bilateral lower extremity fractures, which may be attributable to the small sample size and the results being somewhat contingency.

The trauma severity score can reflect the patient's status and prognosis to a certain extent, and the ISS value and AIS score are commonly used to assess the severity of injury.[24–27] Sciatic nerve injury is reportedly associated with trauma severity scores in patients with acetabular fractures.[4,18] The more trauma the patient sustains, the higher the probability of traumatic sciatic nerve injury. Simske et al[4] found that the average ISS value was significantly higher in their patients with nerve injury than in those without nerve injury. In our study, the ISS value and AIS score were also significantly higher in the group with traumatic sciatic nerve injury, and logistic regression analysis showed that the AIS score was correlated with this injury.

Traumatic sciatic nerve injury is common in patients with fractures involving the posterior wall or posterior column of the acetabulum and posterior dislocation of the hip joint and is related to the mechanism of this type of injury.[4,28,29] Unlike the previous studies, we found that none of the fracture types involving the posterior column had a significant effect on the incidence of sciatic nerve injury, even those involving the posterior wall. In logistic regression analysis, there was a significant difference in the incidence of posterior column fractures between the groups with and without sciatic nerve injury. However, the small size of the group with simple posterior column fractures may have some effect on our results. It has been reported that posterior dislocation of the hip joint is the main cause of sciatic nerve injury in patients with acetabular fractures.[4,30] In our study, the incidence of posterior dislocation of the hip joint was significantly higher in the group with sciatic nerve injury. A possible explanation for this finding is that the injured hip joint made the distance between the sciatic nerve and acetabulum or the femoral head, which may increase the likelihood of nerve damage. In this study, posterior hip dislocation was the main risk factor for sciatic nerve injury in both univariate and multivariate logistic regression analysis, which suggests that sciatic nerve injury is more likely to occur in association with posterior dislocation of the hip joint. Central hip dislocations and femoral head fractures had no significant impact on the sciatic nerve.

This study has some limitations, in particular a retrospective design and a small sample size. However, such cases are relatively rare, and larger multicenter studies are required in the future.

Conclusions

Acetabular fractures were mostly high-energy injuries and mostly combined with associated injuries. Posterior wall, double-column, and T-type fractures were the most common fracture types. Acetabular fractures with severe trauma are more likely to be associated with sciatic nerve injury. There appears to be no relationship between sciatic nerve injury and sex, age, cause of injury, fracture type, central hip dislocation, or femoral head fracture. In this study, an isolated posterior wall fracture of the acetabulum did not significantly affect the incidence of sciatic nerve injury. Acetabular fracture combined with posterior dislocation of the hip joint was the main predictor of sciatic nerve injury.

Abbreviations

ISS, Injury Severity Score; AIS, Abbreviated Injury Scale; MVC, Motor vehicle collision; RTA, Road traffic accident.

Data Sharing Statement

All data generated or analyzed during this study are included in this article. Further enquiries can be directed to the corresponding author.

Ethics Approval and Informed Consent

The experimental protocol was established according to the ethical guidelines of the Helsinki Declaration and approved by the Human Ethics Committee of Shandong Provincial Hospital Affiliated to Shandong First Medical University. Written informed consent was obtained from all study participants.

Consent for Publication

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

All authors report no conflict of interest in connection with this article.

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