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Original article

Obesity may be a risk factor for recurrent heterotopic ossification in post-traumatic stiff elbow among children and teenagers

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ABSTRACT

Background: Post-traumatic elbow stiffness and heterotopic ossification (HO) affects long-term life quality, as commonly in children and teenagers as in grownups. Childhood obesity considerably influences public health because it causes stroke, hypertension and diabetes mellitus. Previous research discussed its clinical complications in orthopedic diseases. However, no clinical research reveals the interaction between childhood obesity and HO after elbow injuries.
Hypothesis: Obesity might be a risk factor of recurrent HO after elbow arthrolysis in children and teenagers, correlated with the severity of postoperative HO.
Methods: Fifty seven post-traumatic children and teenagers undergoing elbow arthrolysis were retrospectively reviewed and divided into underweight/normal-weight group ($n = 28$) and overweight/obese group ($n = 29$) according to the gender-specific body mass index (BMI)-for-age growth chart. The Hastings and Graham classification was used to evaluate HO recurrence. We also assessed Mayo elbow performance scores and range of motion.
Results: The mean age, gender, pathogenesis, side of injury, time of injury, follow-up duration were analyzed. Overweight/obese children and teenagers were more likely to develop recurrent HO ($p = 0.005$) than underweight/normal-weight children and teenagers. A significant difference in the severity of recurrent HO between two groups was confirmed ($p = 0.028$). The range of motion was improved greatly in underweight/normal-weight group compared with that in overweight/obese group ($p = 0.001$).
Conclusions: The HO recurrence difference between two groups confirmed the hypothesis. Although underlying mechanisms are unclear, weight control might promote postoperative and long-term rehabilitation of the elbow joint for children and teenagers.
Level of evidence: III, retrospective cohort study, treatment study.

1. Introduction

Childhood obesity receives wide attention worldwide. A 20% increase of obesity was found in the US from 2003 to 2012 among teenagers between age 12 and 18 [1]. Among a sample of 1499 children under age 13 in some European cities, obese population rose dramatically from 1.24% to 10.6% in four decades [2]. In China, obesity increased from 0.4% in 1985 to 7.5% in 2010 [3]. Childhood overweight and obesity is a risk factor for stroke, hypertension, diabetes and mortality [4].

Heterotopic ossification (HO) is a pathological modality formed in soft tissues. It appears after trauma, brain injuries and surgeries [5]. Higher HO occurrence is discovered in ankylosing spondylitis [6], hip arthroplasty [7], Paget's disease [8], and diffuse idiopathic skeletal hyperostosis (DISH) [9].

Obese patients may have dissatisfactory outcomes after orthopedic surgeries. Griffin et al. found obese patients who received total elbow arthroplasty (TEA) ran some risk assessments for complications preoperatively because they were at a higher risk for secondary disorders after TEA [10]. Salazar et al. discovered obese patients were more prone to elbow motion restriction and HO after surgery [11].

However, the relationship between HO and obesity in post-traumatic elbow stiffness among children and teenagers who have faster bone development is unclear and receives inadequate attention. The objective of this study was to evaluate whether

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Table 1
Chinese children and teenagers BMI limit values chart.

Age	Boy		Girl	
	Overweight	Obese	Overweight	Obese
3	16.8~18.0	≥ 18.1	16.9~18.2	≥ 18.3
4	16.5~17.7	≥ 17.8	16.7~18.0	≥ 18.1
5	16.5~17.8	≥ 17.9	16.6~18.1	≥ 18.2
6	16.8~18.3	≥ 18.4	16.7~18.3	≥ 18.4
7	17.2~19.1	≥ 19.2	16.9~18.7	≥ 18.8
8	17.8~20.0	≥ 20.1	17.3~19.4	≥ 19.5
9	18.5~21.0	≥ 21.1	17.9~20.3	≥ 20.4
10	19.3~22.1	≥ 22.2	18.7~21.4	≥ 21.5
11	20.1~23.1	≥ 23.2	19.6~22.6	≥ 22.7
12	20.8~24.1	≥ 24.2	20.5~23.8	≥ 23.9
13	21.5~25.0	≥ 25.1	21.4~24.9	≥ 25.0
14	22.1~25.7	≥ 25.8	22.2~25.8	≥ 25.9
15	22.7~26.4	≥ 26.5	22.8~26.6	≥ 26.7
16	23.2~26.9	≥ 27.0	23.3~27.1	≥ 27.2
17	23.6~27.4	≥ 27.5	23.7~27.5	≥ 27.6
18	24.0~27.9	≥ 28.0	24.0~27.9	≥ 28.0

BMI: body mass index.

Table 2
Patient demographic and clinical characteristics.

Characteristics	Underweight/normal-weight	Overweight/obese	*p*-value
Gender, male/female, n	17/11	22/7	0.219
Age, mean(range), y	15.21 –18)	14.86 (4–18)	0.691
Side of injury, Left/Right	16/12	12/17	0.234
Pathogenesis			0.990
Intercondylar fracture	10	9	
Supracondylar fracture	7	8	
Elbow dislocation	6	6	
Olecranon fracture	6	5	
Radial head fracture	5	6	
Time of Injury, mean(range), mon	25.8 2(1–120)	28.24 (2–120)	0.742
Postoperative CRP, mean(range), mg/L	29.26 (3.69–67.90)	45.02 (8.91–78.20)	0.002
Postoperative ESR, mean(range), mm/h	8.32 (3–15)	8.52 (4–15)	0.821
Postoperative ulnar compression	3	3	/
Postoperative elbow instability	1	0	/
Follow-up time, mean(range), mon	9.89 (3–18)	9.83 (3–18)	0.950

n: number; y: year; mon: month; CRP: C-reactive protein; mg/L: milligram per liter; ESR: erythrocyte sedimentation rate; mm/h: millimeter per hour.

overweight/obesity influenced recurrent HO in post-traumatic elbow stiffness among children and teenagers. We hypothesized obesity might be a risk factor of recurrent HO after elbow arthrolysis in children and teenagers, correlated with HO severity.

2. Patients and Methods

All patients were retrospectively reviewed in our hospital from January 2013 to January 2016. The inclusion criteria was (1) children and teenagers of age under 18, (2) range of motion (ROM) < 90°, (3) patients experiencing HO-related post-traumatic elbow stiffness, (4) radiologic union at minimum follow-ups, (5) noticeable HO on preoperative X-rays and in the surgery. The followings were excluded (1) patients who formerly accepted operation(s) to remove elbow HO, (2) non-traumatic causes of HO, like burn, hereditary disorders or brain damage, (3) changes of body mass index (BMI) category at final follow-ups, (4) failure in postoperative rehabilitation. The operations were performed by the same doctor. Open approaches were used in combination with medial and lateral incisions. In the surgery, heterotopic bones were removed followed by capsule release as well as triceps muscle and collateral ligament reconstruction. All patients gained functional ROM postoperatively. Hinged external fixation was used for postoperative practice and long-term rehabilitation for 6 weeks. X-rays were required for further assessment of HO localization and severity preoperatively, at postoperative day 1 and at follow-ups.

BMI is commonly used to evaluate the amount of body fat. According to the gender-associated BMI chart for age under 18 by the National Health and Family Planning Commission of China [12], patients were categorized into two groups by their age-related BMI: underweight/normal-weight and overweight/obese (Table 1).

Fifty seven patients were diagnosed and treated in this study. No significant differences were discovered in gender, age, side of injury, pathogenesis, time of injury, follow-up duration and preoperative CRP and ESR values between groups (Table 2). There were no significant changes in weight of all patients from initial injury to being admitted in hospital. All patients received one former surgery before elbow arthrolysis.

2.1. Preoperative and postoperative assessment

We evaluated preoperative and postoperative ROM and Mayo Elbow Performance Scores (MEPS) between groups. HO was assessed by three radiologists according to Hastings and Graham classification [13] (Table 3, Fig. 1).

2.2. Surgical techniques

We used a medial and lateral approach. We transposed the ulnar nerve subcutaneously and exposed olecranon fossa. Abnormal callus, ectopic bones and posterior capsule were removed. We split triceps muscle to improve elbow flexion. For lateral side, we carefully separated soft tissues, and removed anterior capsule as well

Table 3
Hastings and Graham Classification.

Grade	Definition
Grade I	HO existence with no functional restrictions radiographically
Grade IIA	Restricted flexion/extension-related HO
Grade IIB	Restricted pronation/supination-related HO
Grade IIC	Restricted flexion/extension and pronation/supination-related HO
Grade IIIA	Complete stiffness of the flexion-extension plane resulting in HO
Grade IIIB	Complete stiffness of the pronation-supination plane resulting in HO
Grade IIIC	Complete stiffness of both planes resulting in HO

HO: heterotopic ossification.

as HO completely in the joint. We located the isometric point and drilled a bone channel by 2.0-mm Kirschner wire. Finally, we placed a suture anchor (Smith & Nephew, Andover, MA, USA) for repairing medial and lateral collateral ligaments.

2.3. Postoperative treatment

On postoperative day 1, patients began active and passive elbow exercises under our surveillance. They should achieve ideal elbow ROM respectively according to intraoperative results and complete elbow exercise for 30 times a day, which gradually increased to 300 times per day.

2.4. Statistical analysis

Descriptive analysis was performed by 2-tailed Fisher exact test, Mann–Whitney U–test and Pearson Chi^2 test. Numerical analysis was performed by independent-samples t test. A p-value of 0.05 was statistically significant (SPSS Statistics, version 19; IBM, Armonk, NY, USA).

3. Results

Inflammatory parameters like CRP and ESR were shown (Table 2).

Preoperative and postoperative ROM and MEPS were displayed (Table 4).

We confirmed complete HO removal by X-rays at postoperative day 1 in all patients. The incidence and severity of HO recurrence for different grades were listed (Table 5, Table 6), which measured recurrences of postoperative HO compared with preoperative HO by upgraded, unchanged, and degraded levels.

There were no notable differences regarding HO severity between two groups preoperatively ($p = 0.492$). Twenty-one out of 29 patients (72.41%) experienced recurrence in the overweight/obese compared with 10 out of 28 (35.71%) in the underweight/normal-weight group ($p = 0.005$). Though grade I was characteristic of obvious ectopic bone in X-rays, these patients experienced no restriction in elbow function. Therefore, we only identified grades II and III as recurrence, occupying 32.14% and 65.52% in each group ($p = 0.012$). Recurrence was identified by X-rays at final follow-ups. Five boys and 5 girls in the underweight/normal-weight compared with 14 boys and 7 girls in the overweight/obese group appeared in the recurrence group. Furthermore, we analyzed the severity of recurrent HO among different grades of patients (Table 6). There were 4 degraded cases, 4 unchanged cases and 2 upgraded cases in underweight/normal-weight group. However, in overweight/obese group, there were 3 degraded cases, 5 unchanged cases and 13 upgraded cases. Representative cases of HO recurrence were displayed (Fig. 2). There was a significant difference between underweight/normal-weight group and overweight/obese group ($p = 0.028$).

3.1. Postoperative complications

In spite of a remarkable difference in CRP on postoperative day 1 between two groups, it returned to normal value on day 3, indicating patients restored health from surgeries. All patients received cefaclor intravenously for infection prevention for 24 hours. There was no remarkable difference in ulnar nerve compression and elbow instability at follow-ups (Table 2). No complaints of pain were noticed.

4. Discussion

In this study, we found obesity might be a risk factor of recurrent HO after elbow arthrolysis in children and teenagers, correlated with HO severity. Overweight/obese patients experienced high recurrence rate of HO and more severe HO formation. Meanwhile, they displayed dissatisfactory elbow functions. Massive HO around the elbow caused ROM decrease and function restriction (classic intraoperative presentation of excessive HO displayed in Fig. 3).

The research on the interaction between obesity and HO is rare, especially in children and teenagers. Fat influences bone initiation and reabsorption through adipokines [14]. Previous research indicated obesity positively affected bone formation and diseases [15]. As a major cytokine produced by fat, leptin plays a key role in bone diseases, like osteoporosis [16], osteoarthritis [17], and fractures [18]. Takeda et al. reported leptin regulated bone metabolism by binding to its receptors in the hypothalamus, where

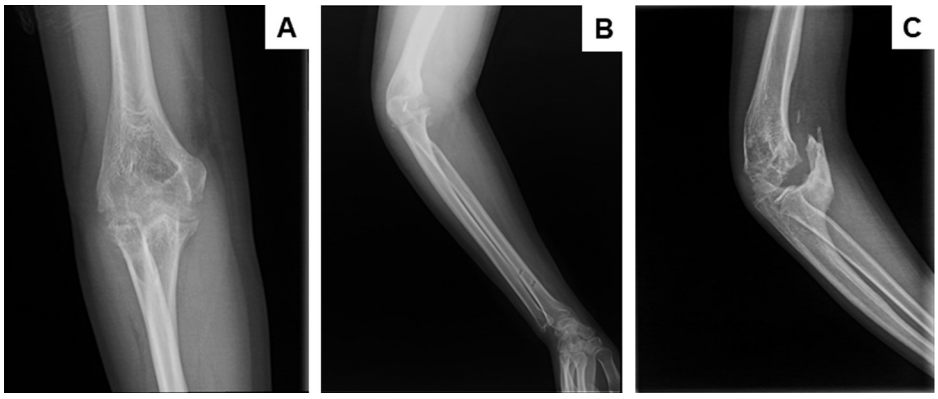

Fig. 1. Radiological presentation of Hastings and Graham Classification. Grade I (A); Grade II (B); Grade III (C).

Table 4
Preoperative and postoperative ROM and MEPS.

Measures	Underweight/normal–weight	Overweight/obese	*p*-value
Preoperative ROM, mean(range)	41.96 (0–100)	41.55 (0–130)	0.959
Extension	43.61 (0–80)	39.31 (0–95)	0.475
Flexion	85.57 (30–130)	80.86 (40–130)	0.475
Pronation	46.96 (−15–90)	40.00 (0–80)	0.349
Supination	66.07 (0–90)	57.24 (0–90)	0.307
Postoperative ROM, mean(range)	102.29 (55–155)	75.10 (20–145)	0.001
Extension	19.14 (−5–40)	27.90 (0–60)	0.021
Flexion	121.43 (80–150)	103.00 (40–145)	0.001
Pronation	44.64 (−10–85)	41.03 (10–60)	0.524
Supination	76.07 (45–90)	64.83 (30–90)	0.014
MEPS, mean(range)			
Preoperative	73.04 (55–95)	70.52 (50–100)	0.471
Postoperative	84.82 (55–00)	76.03 (50–100)	0.005

MEPS: Mayo Elbow Performance Scores; ROM: range of motion.

Table 5
Incidence of HO by Hastings and Graham Classification.

	Preoperative occurrence			Postoperative recurrence		
	Underweight/normal-weight	Overweight/obese	*p*-value	Underweight/normal-weight	Overweight/obese	*p*-value
0	–	–	–	18 (64.29%)	8 (27.59%)	0.005
I	2 (7.14%)	1 (3.45%)	0.492	1 (3.57%)	2 (6.90%)	0.012
II	24 (85.71%)	25 (86.21%)		9, (32.14%)	19 (65.51%)	
III	2 (7.14%)	3 (10.34%)				

HO: heterotopic ossification.

it acted upon the sympathetic nervous system [19]. Martin et al. found leptin maintained a balance between energy intake and the IGF-I pathway for bone metabolism regulation [20]. Rőszer et al. mentioned leptin was promising for treating diseases of bone formation, such as impaired fracture healing [21]. Ebinger et al. found overweight people displayed higher trabecular bone density contrasted to normal-weight people [22]. Morbidly obese patients (BMI $\geq$ 40 kg/m^2) undergoing hip replacement had longer hospitalization time and rates of comorbidities compared with normal-weight patients [23]. Macrophages were activated from fat in overweight patients (BMI > 25) after injury and were vital to adipokines release and HO occurrence [24]. Leptin might be related to HO formation in pediatric elbow stiffness.

This study evaluated the role of obesity in children and teenagers, and other aspects including demographic, clinical and radiologic factors in HO development.

There are quite a few known factors that can potentially induce HO onset. They are composed of demographic, injury-oriented and treatment-associated factors, including gender, age, injury type, surgical procedures, surgical approaches, time of injury, number of former operations and certain bone diseases, like ankylosing spondylitis, Paget's disease and DISH [5]. In this study, among patient-related demographic factors, no obvious difference was noticed in gender and age between two groups (Table 2). We ruled out potential influence from demographic factors on recurrent HO, although no previous studies we are aware have identified any demographic predictors [25]. We also excluded the impact from injury-oriented factors, like type of injury or side of injury since Wiggers et al. saw complete ulnohumeral dislocation as a predictor of HO restricting motion [26]. Injury-oriented factors did not show remarkable differences between two groups either. Vigorita et al. reported patients had an increased risk for HO development following a THA or trochanteric osteotomy. Surgical procedure and approaches increase the risk for HO. THA with lateral approach more likely led to HO development [5].

In this study, all patients received the same surgical procedures. We adopted a medial and lateral approach for all patients to achieve appropriate exposure to diseased tissues and the best surgical outcomes. No radiotherapy was used in any patient. Nonsteroidal anti-inflammatory drugs (NSAIDS) can reduce HO recurrence postoperatively. Nevertheless, we applied no NSAIDS due to their potential toxicity to children and teenagers.

Furthermore, younger patients have better osteogenesis and are more prone to HO onset. Gagliardi et al. reported displaced radial neck fractures in five children treated with flexible titanium intramedullary nails had postoperative HO without restrictions of elbow functions [27]. However, this research showed very limited implications due to its relatively small quantity. Bell discovered open treatment of extra-articular distal humerus fractures in adolescents caused less predictable clinical and radiographic outcomes as well as later motion recovery and more comorbidities, like HO and postoperative infections compared with closed reduction [28]. In this study, all patients were under age 18 and exhibited elbow stiffness due to traumatic HO. Preoperative HO did not display any notable differences between underweight/normal-weight group and overweight/obese group. This might result from long time period from initial surgery to mobilization, which enabled all patients to develop similar HO severity and hid the real differences among people with various BMIs. Therefore, we suggested patients initiate active and passive elbow exercise from postoperative day 1. Nevertheless, a significant difference was shown in the postoperative ROM ($p = 0.001$) and MEPS ($p = 0.005$) between two groups. Moreover, postoperative HO recurrence displayed a remarkable difference ($p = 0.005$), indicating patients from overweight/obese group were more prone to developing HO again though they received standard elbow arthrolysis and persisted active and passive rehabilitation exercise. As shown in Table 6,

Table 6
The degree of HO recurrence by Hastings and Graham Classification.

	Underweight/normal-weight	Overweight/obese	*p*-value
Degraded	4	3	0.028
Unchanged	4	5	
Upgraded	2	13	

HO: heterotopic ossification.

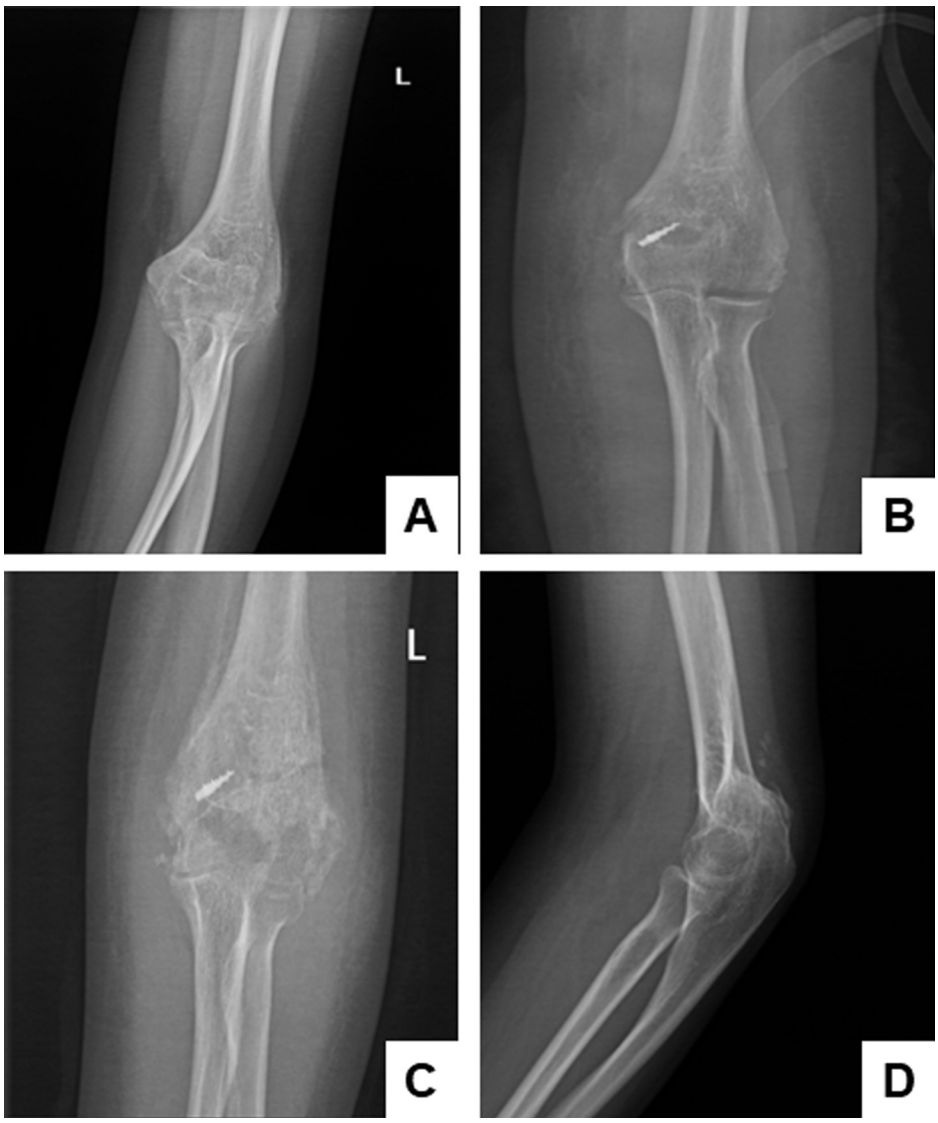

Fig. 2. Preoperative anteroposterior and lateral radiograph (A,B) 1-week postoperatively, anterosuperior radiograph (C), and 1-year postoperative anteroposterior radiograph (D) for an overweight patient (year 18, female, BMI:29.2).

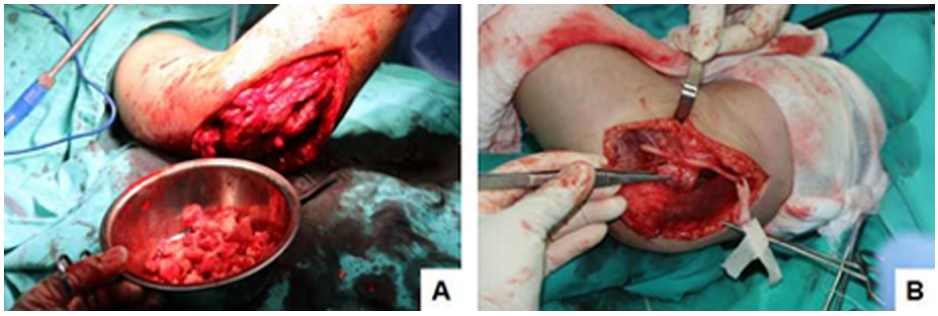

Fig. 3. Classic intraoperative presentation of massive HO.

the severity of recurrent HO differed from overweight/obese group to underweight/normal-weight group ($p = 0.028$), which indicated that in addition to a higher postoperative recurrent rate of HO, the degree of postoperative HO was generally upgraded other than degraded or unchanged compared with that of preoperative HO in overweight/obese group. This proved the important role of obesity as a risk factor in HO pathogenesis and relapsing elbow stiffness in children and teenagers.

There were several limitations in this study. First, it was a retrospective study. Some patients without data like weight and height were excluded. Secondly, the sample was relatively small. The study lacked sufficient power to detect meaningful differences between two groups. Thirdly, all patients were stratified by BMI, which was not an accurate a measure of body fat, especially for tall and sportive boys who have a BMI over 25 without being overweight.

5. Conclusion

Obesity might be a risk factor of recurrent HO after open elbow arthrolysis in children and teenagers, correlated with HO severity. Weight control might improve postoperative and long-term elbow rehabilitation.

IRB

The Ethics Committee of Shanghai Sixth People's Hospital East Campus concluded that no approval was necessary for study based on its retrospective design. Data were analyzed anonymously; all patients approved the results of this study by oral consent. The oral consent approval was documented in the patients' files. This was approved by the Ethics Committee of Shanghai Sixth People's Hospital East Campus.

Disclosure of interests

The authors declare that they have no competing interests.

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None.

Authors' contribution

C. Fan and W. Wang conceived the initial idea and the conceptualization, participated in the data extraction. Y. Qian and W. Liu conceived and participated in its design, searched databases, extracted and assessed studies and drafted the manuscript. Y. Qian wrote and revised the manuscript. All authors read and approved the final manuscript.

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