



Relationship between hip joint medial space ratio and collapse of femoral head in non-traumatic osteonecrosis: a retrospective study

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ABSTRACT

To retrospectively analyze the medial space ratio (MSR) of the hip joint to evaluate its efficacy in predicting osteonecrosis of femoral head (ONFH)-induced collapse and its impacts on the mechanical environment of necrotic femoral head. In this retrospective analysis of traditional Chinese medicine, non-traumatic ONFH (NONFH) patients from January 2008 to December 2013 were selected. The patients were divided into collapse group and non-collapse group based on whether the femoral head collapsed. The anatomical parameters including center–edge (CE) angle, sharp angle, acetabular depth ratio and MSR were evaluated. Receiver operating characteristic curves were estimated to evaluate the sensitivity and specificity of MSR and CE angle in collapse prediction. The results showed that 135 patients (151 hips) were included in this study. The differences in CE angle and MSR between collapse group and non-collapse group were statistically significant. The mean survival time of the hips of patients with MSR <20.35 was greater ($P < 0.001$) than that of patients with MSR >20.35. The ONFH patients with MSR >20.35 were prone to stress concentration. We could conclude that the hip joint MSR and CE angle strongly correlated with the collapse of NONFH. The specificity of MSR is higher than that of CE angle. When MSR is >20.35, the collapse rate of ONFH will increase significantly.

BACKGROUND

Osteonecrosis of the femoral head (ONFH), a common hip disease as a result of trauma, steroid use, alcoholic abuse and other pathogenic factors, can bring about blood flow disorders and bone cell and bone marrow hematopoietic cell apoptosis in the femoral head. ONFH is an increasing global health problem [1–3]. The incidence of ONFH in women is higher than that in men, with the prevalence of bilateral ONFH found in up to 75% of the cases [4, 5]. Since the disability rate of young ONFH patients is very high, it is important to understand which patients are most likely to experience femoral head collapse [6]. Moreover, undiagnosed and untreated ONFH can eventually progress to collapse of the femoral head [7–9]—the most critical pathological feature in ONFH, which may attribute to both biological and biomechanical factors [10]. Andronic *et al.* [11] found that approximately 38% of patients underwent total hip replacement in an average of 26 months after core decompression. In addition to size and shape of the necrotic area, collapse is

also strongly associated with internal mechanical changes in the femoral head after necrosis. Therefore, an effective predictor of femoral head collapse is a prerequisite for the successful treatment of ONFH. Unfortunately, such indicators for the effective prediction of ONFH-induced collapse have not yet been found.

The hip joint medial space refers to the distance from the most medial margin of the femoral head to the pelvic teardrop. The hip joint medial space ratio (MSR) is defined as the ratio of the hip joint medial space to the distance from the pelvic teardrop to the outermost margin of the acetabulum. Two studies [12, 13] reported that the degree of hip dislocation evaluated by the medial hip space exhibited clinical implications of judging joint dysplasia or dislocation. Yoshida *et al.* [14] reported that in the development dysplasia of the hip, local stress concentration due to the reduction in the contact area of the hip joint resulted in asymmetric cartilage degeneration and the subsequent increases in joint contact pressure. Along with the size of the joint contact area that has the greatest influence on contact

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stress, from a biomechanical perspective, changes in the hip joint contact area in ONFH may have an impact on the stress environment inside the femoral head. On account of MSR that reflects the contact area between the acetabulum and the femoral head, we hypothesized that there could be a correlation between MSR and femoral head collapse in ONFH to predict the prognosis of ONFH. Therefore, the aim of this study was to explore the relationship between MRS and ONFH collapse and to improve the imaging evaluation system of ONFH for predicting the prognosis at an early stage. This study may shed new light on the early treatment of ONFH.

METHODS

Research object

This study retrospectively analyzed non-traumatic, non-surgical ONFH patients admitted to the First Affiliated Hospital of Guangzhou University of Chinese Medicine from January 2008 to December 2013. All patients with femoral head necrosis were diagnosed by clinical physical examination and imaging and met the diagnostic criteria of ONFH [15]. The inclusion criteria were defined as: (i) patients with complete imaging data and without collapse of the femoral head at the first visit, (ii) aged 19–60 years, (iii) who reported no hip trauma or a history of surgery. The exclusion criteria were as follows: the imaging data were incomplete during the follow-up or imaging data with poor quality (such as pelvic tilt) were available. Patients with cardiocerebral vascular diseases, nervous system diseases, severe illness or rheumatoid arthritis were also excluded. The demographic characteristics and clinical profiles including age, gender, side of hip, etiology, Japanese Investigation Committee (JIC) type [16], pain, body mass index (BMI) and follow-up duration were recorded. The JIC classification is usually based on MRI. The follow-up time was 8.6 ± 1.20 years, and were divided into collapse group and non-collapse group based on whether the femoral head collapsed (Fig. 1). This study had been approved

by the ethical review board of the First Affiliated Hospital of Guangzhou University of Chinese Medicine [No. Y(2019)118].

Conservative treatment

All patients accepted oral administrations with traditional Chinese medicine ‘Yuanshi Shengmai Chenggu’ tablet (six tablets each time, three times per day, institutional approval no. Z20070828) and ‘Fufang Shengmai Chenggu’ capsule (four capsules each time, three times per day, institutional approval no. Z20071224). The two drugs were prepared by the First Affiliated Hospital of Guangzhou University of Traditional Chinese Medicine (Guangzhou, China). The duration of the medication was 2 years. Along with the oral administration, muscle group exercises with emphasis on anterior flexor muscles, abductor muscles and adductor muscles and protective weight-bearing exercises were performed.

Angle measurement

All plain radiographs were taken by radiology technologists using standardized techniques. For the anteroposterior views, all projections were obtained in a supine position with the legs in 15° internal rotation and the crosshairs of the beam center midway between the symphysis pubis and the field included both iliac crests. The anatomical parameters including center–edge (CE) angle [17], sharp angle [18], acetabular depth ratio (ADR) [19] and MSR were evaluated. The MSR was defined as the ratio of the distance from the most medial margin of the femoral head to the pelvic teardrop (α) and the distance from the pelvic teardrop to the outermost margin of the acetabulum (β) multiplied by 100 (Fig. 2).

Statistical analysis

Statistical analysis was performed using SPSS version 24.0 software (IBM Corp., Armonk, NY, USA). All quantitative data are presented as mean \pm standard deviation. The independent samples *t*-test was used to compare the results of two independent groups. Categorical data were analyzed with chi-square test. To evaluate the cutoff point for MSR and CE angle, a receiver operating characteristic (ROC) curve was used. Youden’s index, computed as the sum of sensitivity and specificity minus 1, could range from 0 to 1 (no diagnostic efficacy to perfect diagnostic efficacy). It was used to assess the performance of these diagnostic thresholds. Kaplan–Meier survival analysis was performed using collapse of the femoral head as endpoint. A *P*-value <0.05 was considered statistically significant.

RESULTS

General information

A total of 135 patients (98 males and 37 females) and 151 hips were included in this study—16 of whom had bilateral ONFH. Of all hips, 67 cases (75 hips) of femoral head collapse were divided into collapse group, while the other 68 cases (76 hips) without femoral head collapse were divided into non-collapse group. There were no statistically significant differences in age, gender, side, BMI, etiology and follow-up duration between collapse and non-collapse groups ($P > 0.05$). The difference in JIC type between the two groups was statistically significant

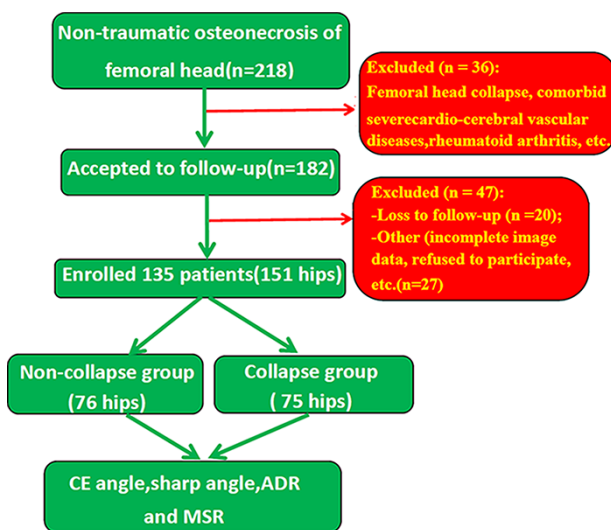


Fig. 1. The eligibility flowchart of subjects in the collapsed and non-collapsed groups. CE angle: center edge angle, ADR: acetabular depth ratio, MSR: medial space ratio.

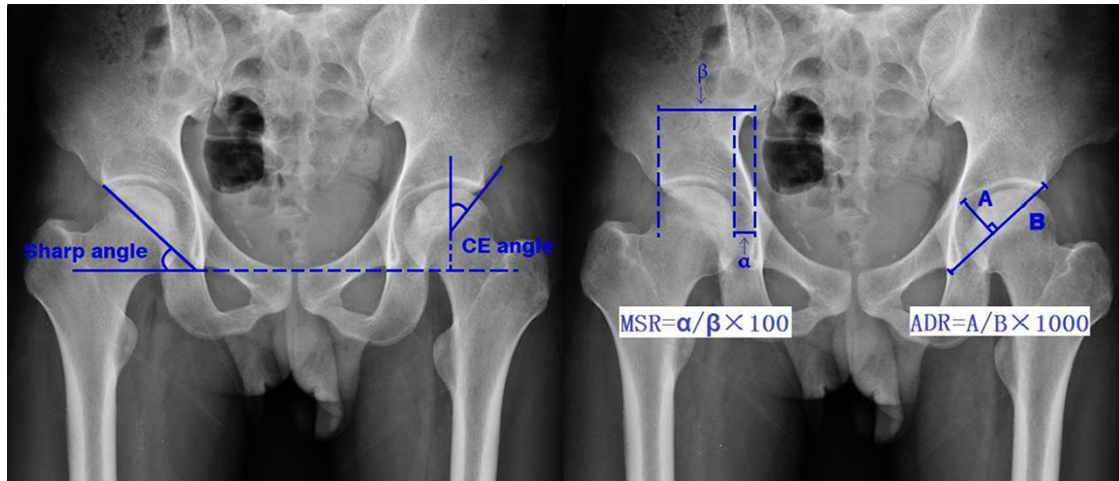


Fig. 2. Measurements of CE angle, sharp angle, ADR and MSR on AP pelvic radiograph.

Table I. Comparison of baseline characteristics between the non-collapse and collapse groups

Items	Groups		P-value
	Non-collapse [n = 68 (76 hips)]	Collapse [n = 67 (75 hips)]	
Age (years)	42.5 ± 7.21	42.5 ± 8.73	0.944
Gender, n (%)			
Male	50 (73.5)	48 (71.6)	0.806
Female	18 (26.5)	19 (28.4)	
Side, n (%)			
Left	32 (42.1)	33 (44)	0.814
Right	44 (57.9)	42 (56)	
BMI	23.5 ± 1.96	23.9 ± 2.34	0.214
Etiology, n (%)			
Steroid	38 (55.9)	35 (52.3)	0.705
Alcoholic	18 (26.5)	22 (32.8)	
Idiopathic	12 (17.6)	10 (14.9)	
JIC type, n (%)			
Type-A	32 (42.1)	0 (0)	<0.001
Type-B	25 (33.9)	7 (9.3)	
Type-C1	18 (23.7)	43 (57.3)	
Type-C2	1 (1.3)	25 (33.4)	
Pain, n (%)			
Yes	19 (25)	54 (72)	<0.001
No	57 (75)	21 (28)	
Follow-up duration (years)	8.4 ± 0.95	8.73 ± 1.41	0.201

($P < 0.001$). JIC-A type femoral head necrosis was most common in the non-collapse group, while JIC-C1 type was most common in the collapse group. The incidence of pain in the two groups was statistically significant ($P < 0.001$). The hip pain rate of patients in the collapse group was 72%, while the hip pain rate of the non-collapse group was 25%. The baseline clinical and demographic characteristics of these subjects are summarized in Table I.

Table II. Comparison of sharp angle, CE angle, MSR and ADR between the non-collapse and collapse groups

Items	Groups		P-value
	Non-collapse (n = 76 hips)	Collapse (n = 75 hips)	
Sharp angle (°)	35.4 ± 4.83	36.8 ± 4.93	0.071
CE angle (°)	31.5 ± 4.08	26.6 ± 3.98	<0.001
MSR	18.4 ± 2.60	23.0 ± 3.42	<0.001
ADR	301.3 ± 12.3	299.7 ± 9.52	0.367

Sharp angle, CE angle, MSR and ADR in the non-collapse versus collapse groups

The mean CE angle was significantly lower in the collapse group than in the non-collapse group (26.6 ± 3.98 versus 31.5 ± 4.08 , $P < 0.001$). However, the mean MSR was significantly higher in the collapse group than in the non-collapse group (23.0 ± 3.42 versus 18.4 ± 2.60 , $P < 0.001$). No remarkable difference in sharp angle and ADR was found between the two groups ($P > 0.05$) (Table II).

ROC curves are reported in Fig. 3. ROC analysis (Table III) revealed that the cutoff point of MSR was 20.35 (sensitivity = 80%, specificity = 86.8% and log-rank test: $P < 0.0001$). The cutoff point of CE angle was 29.5° (sensitivity = 80%, specificity = 71.1% and log-rank test: $P < 0.0001$) (Fig. 2). Based on the survivorship analysis (with femoral head collapse as the endpoint), the mean survival time of the hips of patients with MSR < 20.35 was greater ($P < 0.001$) than that of patients with MSR > 20.35 , with femoral head collapse occurring only in 18.5% of patients with MSR < 20.35 versus 85.8% of patients with MSR > 20.35 after a follow-up of 7 years (Fig. 4A). The survival analysis showed that the probability of occurrence of femoral head collapse within 7 years after conservative treatment was 35.3% for hips with CE angle $> 29.5^\circ$ and 67.5% for hips with CE angle $< 29.5^\circ$. The difference is statistically significant ($P < 0.05$) (Fig. 4B). Our clinical follow-up found that patients with femoral head necrosis with small MSR and large CE angle had good conservative treatment effects and fewer femoral head collapses

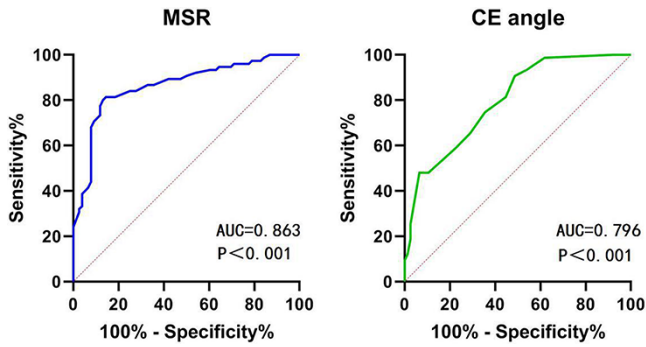


Fig. 3. Receiver operating characteristic (ROC) curve for MSR and CE angle predicting osteonecrosis of the femoral head collapse.

(Fig. 5). However, patients with femoral head necrosis with large MSR and small CE angle were prone to femoral head collapse (Fig. 6).

DISCUSSION

In this study, we included 135 patients (151 hips). The follow-up time was 8.6 ± 1.20 years, and were divided into collapse group and non-collapse group according to whether the femoral head collapsed. The anatomical parameters including CE angle, sharp angle, ADR and MSR were evaluated. ROC curves were estimated to evaluate the sensitivity and specificity of MSR and CE angle in collapse prediction. These results indicate that MSR, except for assessing the distance from the femoral head to the acetabulum, has the clinical implication of predicting the collapse of the femoral head in non-traumatic ONFH (NONFH) patients.

Clinical observations of ONFH patients show that the wider the medial hip joint space is, the more likely the collapse of

the femoral head is to occur. Anderson *et al.* [20] retrospectively studied changes in the medial space of the hip joint in patients diagnosed with Legg–Calve–Perthes disease in 1970. After analyzing imaging data from 50 patients with Legg–Calve–Perthes disease, they reported that >50% of the cases presented widened medial spaces, which was interpreted as a manifestation of joint instability. Moreover, Gershuni *et al.* [21] analyzed the medial hip joint space in patients with Legg–Calve–Perthes disease. Jaramillo *et al.* [22] conducted a prospective study of 12 cases of Legg–Calve–Perthes disease and measured changes in the medial hip joint spaces using MRI. They graded the joint instability as normal, mild, moderate and severe based on the medial spaces of the patients. Although the study results could not reach significant differences, they believed that there was an underlying association between the widened medial space and NONFH. The medial space width in normal individuals often remains stable under certain stress stimuli, and the changes in the joint space somewhat alter the variations in the hip joint [18]. In our present study, ROC analysis revealed that the cutoff point of MSR was 20.35 (sensitivity = 80% and specificity = 86.8%). Based on the survivorship analysis (with femoral head collapse as the endpoint), the collapse rate of ONFH will increase significantly when MSR is >20.35. The bigger the MSR was, the more likely the collapse of the femoral head was to occur and the lower the survival rate of the femoral head would be. This indicates that the MSR is an indicator for predicting femoral head collapse in ONFH.

Physiologically, the MSR reflects how well the acetabulum covers the femoral head. Accordingly, the relationship between the acetabulum and the femoral head can be speculated through variations in MSR. Taketa *et al.* [23] reported that acetabular dysplasia was an exacerbating factor of ONFH in 2003, but no further imaging measurements or analyses of acetabular morphology were performed. Besides, they reported that

Table III. Area under the ROC curve

Items	Area	Standard error	Progressive sig	Progressive 95% CI		Cutoff value	Youden's index
				Lower limit	Upper limit		
MSR	0.863	0.031	<0.001	0.803	0.923	20.35	0.668
CE angle	0.796	0.035	<0.001	0.727	0.865	29.5	0.551

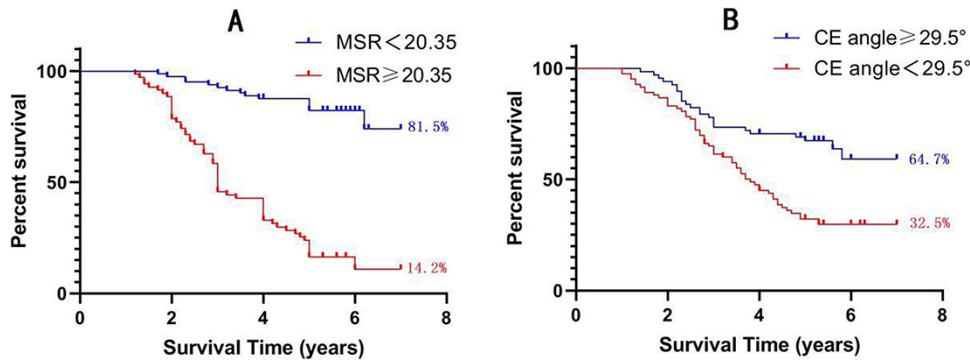


Fig. 4. (A) Kaplan–Meier survivorship analysis at 7 years with femoral head collapse as the end point showing the survival rate of hips from patients with MSR greater than 20.35 and MSR less than 20.35. (B) Kaplan–Meier survivorship analysis at 7 years with femoral head collapse as the end point showing the survival rates of hips from patients with greater than 29.5° and less than 29.5°.

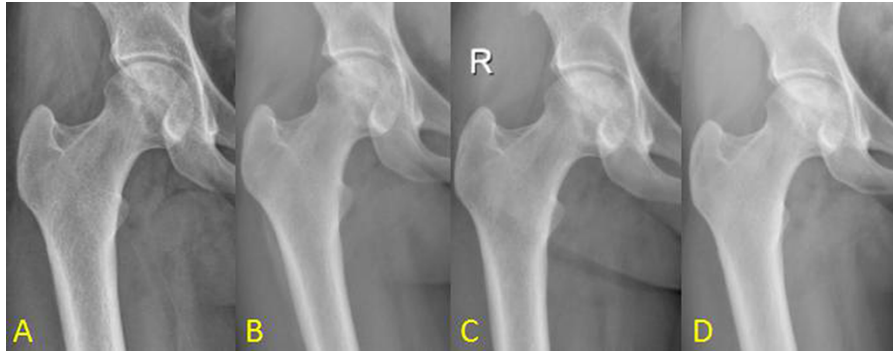


Fig. 5. A 25-year-old woman who had steroid-associated osteonecrosis in the left femoral head. (A) Her hip joint MSR was 12.8 and CE angle was 39.5° . (B) After conservative treatments with TCM for 1 year, no obvious collapse of the femoral head could be observed. (C) After 2-year TCM treatment, hip symptoms of the patient were improved, and the ONFH was being repaired. (D) After 5-year TCM treatment, her hip symptoms basically disappeared, and the necrotic area significantly decreased.

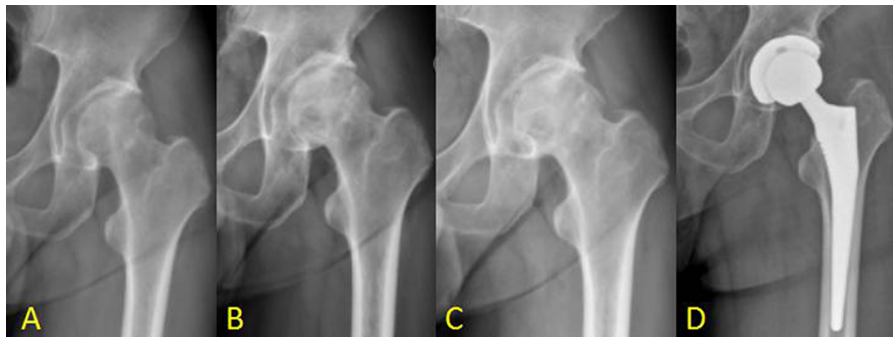


Fig. 6. Radiographs of a 43-year-old man who had alcoholic necrosis in the left femoral head. (A) His hip joint MSR was 22 and CE angle was 29.7° . (B) Mild collapse of the femoral head after 1-year TCM treatment. (C) After 2-year TCM treatment, collapse of the bearing surface became worse and the articular surface of the femoral head was rough. (D) The patient underwent a total hip replacement.

the incidence of ONFH was higher in patients with hip dysplasia. When the CE angle was small or the sharp angle was large, the incidence of ONFH rose. Russell *et al.* [24] compared the stress of the hip joint between normal controls and patients with hip dysplasia using a finite element analysis. They found that increases in the hip contact pressure of the patients were 1–2 times higher than the increases in normal controls. The bearing area was significantly reduced in the patients. A reduction in acetabular coverage to the femoral head causes the significant increase in hip contact pressure per unit area of the femoral head. Also, long-term weight-bearing squeeze can prolong the course of ONFH and accelerate the collapse of the femoral head. Researchers [25] reported that the pressure in the hip joint capsules with reduced acetabular coverage was significantly higher than that of normal hip joints. Our clinical observation found that patients with ONFH with a large MSR will increase the synovial membrane of the hip joint. There will also be an increase in synovial fluid exudation in the early stage. The widening of the medial space leads to a reduction in the coverage of the femoral head, directly increasing the stress intensity in the articular cavity of the hip joint. Also, the resulting insufficient blood supply to the femoral head and impaired venous return can, in turn, affect the repair of ONFH. Similarly, some studies demonstrated that less acetabular coverage could increase intracapsular pressure and excessive weight bearing in the hip joint can contribute

to the development of ONFH [26–29]. Zeng *et al.* [30] found that less acetabular coverage was associated with the development of ONFH in East Asian population, which was also a factor affecting the repair of ONFH. Thomas *et al.* [31] retrospectively investigated ONFH patients who accepted free vascularized fibular grafting and found that patients with less acetabular coverage (a CE angle $<30^\circ$) exhibited a higher prevalence of failure of repair than patients with a CE angle $>30^\circ$. In this study, the ROC analysis revealed that the cutoff point of CE angle was 29.5° (sensitivity = 80% and specificity = 71.1%). When CE angle is $<29.5^\circ$, the collapse rate of ONFH will increase significantly. This indicates that the CE angle is also an indicator for predicting femoral head collapse in ONFH. However, the specificity of MSR is higher than that of CE angle.

Due to distinct tissue properties between the necrotic area and the surrounding areas, the elastic modulus of the necrotic area decreased and the stress shielding effect of the surrounding normal tissues produced stress concentration particularly in the cortical bone. The formation of the material interface made it easier to generate stress concentration, which increased with the occurrence of lateral dislocation of the femoral head. Mismatched acetabulum and femoral head caused by widened medial space may have more severe effects on patients with NONFH, which is why the risk of collapse and the degree of collapse in necrotic patients with femoral head dislocation are higher than those

in non-necrotic ones in our clinical observation. Therefore, we believe that the hip joint instability induced by abnormal stress concentrations in the femoral head can be an important cause of collapse. The widening of the medial space and the mismatch between the acetabulum and femoral head exacerbate the instability of stress distribution in the femoral head. Ultimately, the risk of collapse rises, consistent with the results of previous clinical studies. Therefore, we preliminarily confirm that the MSR is a promising indicator for predicting the collapse of the femoral head.

In the present study, we innovatively explored the relationship between MSR of the hip joint and collapse of the femoral head, which provided a new indicator for predicting the prognosis of NONFH. There are some limitations in our study. First, the clinical research is a retrospective study, selection bias cannot be avoided, and most patients are diagnosed only after they have symptoms. In addition, this study is a single-center study. Whether our method can achieve good consistency in other centers remains to be further explored. Therefore, more randomized clinical and biomechanical trials are still needed to verify the value of MSR in predicting collapse of the femoral head.

CONCLUSION

The hip joint MSR and CE angle strongly correlated with the collapse of NONFH except for assessing the relationship between the femoral head and the acetabulum. The specificity of MSR is higher than that of CE angle. When MSR is >20.35 , the collapse rate of ONFH will increase significantly.

DATA AVAILABILITY

All data generated or analyzed during this study are included in this published article.

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ETHICAL APPROVAL

This study was conducted in agreement with the Declaration of Helsinki and its later amendments or comparable ethical standards and had been approved by the ethics board of the

First Affiliated Hospital of Guangzhou University of Chinese Medicine [No. Y(2019)118].

CONSENT FOR PUBLICATION

Not applicable.

CONFLICT OF INTEREST STATEMENT

None declared.

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