Feasibility of a Randomized Clinical Trial for Treatment of Femoroacetabular Impingement of the Hip

Gloria N. Boye,* BA, Kerri Murray,* MPH, John C. Clohisy,† MD, and Young-Jo Kim,*‡ MD, PhD

Investigation performed at Boston Children's Hospital, Boston, Massachusetts, USA, and Washington University School of Medicine, St Louis, Missouri, USA

Background: Symptomatic femoroacetabular impingement (FAI) is currently corrected by surgery. However, it is possible that nonsurgical treatment could resolve symptomatic FAI in some patients; thus, uncertainty about the necessity of surgical treatment exists. The current equipoise concerning FAI treatment presents an opportunity to conduct a randomized controlled trial (RCT) of surgical and nonsurgical treatment options. Given the unique challenge of adequate patient enrollment in RCTs, it is important that a preliminary study is done to appraise the feasibility of conducting an RCT.

Purpose: To estimate enrollment rates of a planned future RCT to compare surgical and nonsurgical treatments for symptomatic FAI and to identify factors associated with patients' willingness to participate in the randomized trial.

Study Design: Cross-sectional study; Level of evidence, 4.

Methods: Patients diagnosed with FAI at 2 orthopaedic centers were presented with a hypothetical randomized trial comparing 2 treatment options for FAI. All patients completed forms providing information regarding their willingness to participate and treatment preferences.

Results: A total of 75 patients participated in the study: 53 and 22 from 2 centers, respectively. Twenty-eight percent indicated absolute willingness to participate in the trial, 40% were probably willing or unsure, and 32% were definitely not willing; 18.7% had a strong preference for surgery while 2.7% strongly preferred nonsurgical treatment. The majority (78.6%) had no strong preference for either treatment arm. There were correlations between treatment preferences and willingness to participate. Patients with a strong treatment preference and/or a preference for surgery were less likely to be willing to participate.

Conclusion: The study findings suggest that sufficient patient accrual for a randomized trial of FAI treatment is currently feasible while equipoise still exists among patients and surgeons.

Keywords: femoroacetabular impingement (FAI); randomized clinical trial; feasibility study; surgical treatment; nonsurgical treatment

Femoroacetabular impingement (FAI) is a pathologic mechanical condition of increasing interest because of its high prevalence and role in the development of osteoarthritis (OA) of the hip.[2] It is characterized by a femoral head-neck deformity (cam) that leads to eccentric loading within the joint or an acetabular overcoverage deformity (pincer) that leads to restriction of hip motion, or a combination of the 2 (mixed) deformities. A cross-sectional study done by Reichenbach et al[10] indicated that approximately 25% of young male adults have the FAI deformity. Several epidemiologic studies also point to the importance of this deformity in the development of hip OA.[1,5,9] It is therefore apparent that investment in advancing treatment options for FAI will not only relieve symptoms but also potentially decrease the progression of hip OA.[2]

Femoroacetabular impingement represents a varied spectrum of disease patterns among a diverse patient population requiring a range of evolving treatment strategies.[3] Because of the complexity of the FAI deformity, there exists much variability in treatment options. Increasing evidence suggests the efficacy of surgical procedures in correcting the deformity and relieving symptoms. Nonetheless, lower

‡Address correspondence to Young-Jo Kim, MD, PhD, Department of Orthopedic Surgery, Boston Children's Hospital, Harvard Medical School, 300 Longwood Avenue, Boston, MA 02115, USA (email: young-jo.kim@childrens.harvard.edu).

*Department of Orthopedic Surgery, Boston Children's Hospital, Harvard Medical School, Boston, Massachusetts, USA.

†Department of Orthopedic Surgery, Washington University School of Medicine, St Louis, Missouri, USA.

The authors declared that they have no conflicts of interest in the authorship and publication of this contribution.

The Orthopaedic Journal of Sports Medicine, 3(7), 2325967115592844
DOI: 10.1177/2325967115592844

level evidence studies form the main source of this evidence. Cohort studies have also suggested that nonsurgical treatment can relieve symptomatic FAI.[4,8] At this time, surgeon equipoise persists, and payers remain doubtful of the effectiveness of surgery,[2] providing us the opportunity and the need to perform randomized controlled trials.

The hierarchy of clinical research is established,[7] and randomized controlled trials (RCTs) are considered the highest level of evidence. However, RCTs comparing surgical and nonsurgical treatments can present particular obstacles relative to the study design and feasibility. One major disadvantage is the potential for low patient enrollment, which should be thoroughly considered while planning an RCT.

An RCT feasibility analysis was conducted by Creel et al[3] prior to their undertaking of the Meniscal Tear in Osteoarthritis Research (MeTeOR) trial. They utilized a method proposed by Halpern[6] called *prospective preference assessment*, which helps mimic recruitment and predict enrollment rates. We also undertook this assessment by presenting a hypothetical randomized trial of arthroscopic and nonsurgical therapy for managing FAI. The primary purpose of our feasibility study was to estimate the proportion of FAI patients who would be willing to enroll in the trial. Other aims were to determine the appropriate set of enrollment criteria defining the type of FAI deformity to be represented in the cohort for the forthcoming RCT and identify factors associated with willingness to participate. This analysis will enable us to effect needed modifications in trial design and recruitment strategy.

METHODS

On receiving institutional review board approval, patients were recruited from 2 large academic referral centers: one primarily an adult (center A) and the other a primarily pediatric care center (center B). Each center took a different approach in creating a cohort of subjects for the feasibility study. Center A enrolled all patients who had been diagnosed with FAI deformity. Center B had additional eligibility criteria for recruitment to participate in the study: a minimum modified Dunn lateral view alpha angle of 60° as evidence of cam-type impingement, ≤15° of hip internal rotation in 90° of flexion, a pain score of at least 5 of 20 on the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) 5-item pain scale, and at least 3 months of symptoms secondary to FAI. All subjects recruited from both centers were 18 years or older. Those with a history of hip surgery, inflammatory arthritis, skeletal dysplasia, or neuromuscular disorders were not included in the study.

A research coordinator approached eligible patients at clinic visits either before or after consultation with the surgeon to introduce the concept of the feasibility study and administer the study survey. We used a standardized script that explained the design of a hypothetical randomized trial comparing 2 treatment options for FAI: surgical (arthroscopy) and nonsurgical (management with physical therapy and anti-inflammatories). The script also mentioned that while FAI is usually treated by surgery, nonoperative treatment was also a possibility that lacked significant investigation. A flowchart helped the patient follow the randomization process.

TABLE 1
Possible Influential Factors Presented to Patients in Survey

Factors Influencing Willingness to Participate	Factors Influencing Treatment Preference
1. I don't want to participate in research	1. How my physician thinks my hip-related problem should be treated
2. I don't want to be randomized	2. How my family thinks my hip-related problem should be treated
3. I already know that I want surgery	3. The advice and experience of my friends
4. I am not willing to wait 6 months to have surgery	4. My ability to go to work or go about my daily activities
5. I don't believe that physical therapy and anti-inflammatories will make me better	5. Not wanting to be a burden on my family
6. I already know that I don't want surgery	6. Worries about money
7. I don't believe surgery will make me better	7. Concerns about the potential surgical risks
8. I want to contribute to research	8. Worries about side effects or risks of addiction to pain medication
9. Getting paid	9. Nonoperative treatment has not been effective for me

After establishing patients' understandings of both the feasibility and hypothetical studies, we invited them to complete the survey form. This form queried patients' willingness to participate in a randomized trial, treatment preferences, and factors influencing their choices. We used a 5-point scale to categorize willingness to participate: definitely, probably, unsure, probably not, and definitely not. Patients were then asked to indicate as many factors out of 9 options that influenced their decision about participating (Table 1). Treatment preference was categorized into the following: definitely nonsurgical, probably nonsurgical, unsure/no preference, probably surgery, and definitely surgery. Again, we gave opportunity to select reasons for their preference (Table 1). Demographic data were collected, and WOMAC pain scores were documented from questionnaires they completed as part of standard procedure for their clinical care.

For analysis, patients' willingness to participate in the described trial was grouped into 3 categories: definitely willing, probably willing or unsure, and probably or definitely not willing. We evaluated the association of age, sex, education, race, employment, and pain with willingness to participate. The continuous factors, age and WOMAC pain score, were compared across the categorical variables using 1-way analysis of variance and independent *t* tests as appropriate. We employed the chi-square and Fisher exact tests in assessing relations between categorical factors and the variables. We also used these tests to see how willingness to participate in a randomized trial correlated

TABLE 2
Distribution of Subjects From Center A by Willingness to Participate in a Randomized Control Trial[a]

Factor	Definitely Willing (n = 18)	Probably Willing or Unsure (n = 24)	Not Willing (n = 11)	Total (n = 53)	*P* Value
Age, y, mean ± SD	37.61 ± 10.44	32.13 ± 9.6	29.27 ± 8.92	33.40 ± 10.11	.067
Sex					
Male	8 (44.4)	10 (41.7)	8 (72.7)	26 (49.1)	
Female	10 (55.6)	14 (58.3)	3 (27.3)	27 (50.9)	.2
Race					
Nonwhite	3 (16.7)	1 (4.3)	0 (0)	4 (7.7)	
White	15 (83.3)	22 (95.7)	11 (100)	48 (92.3)	.19
Education					
High school or lower	2 (11.1)	5 (20.8)	2 (18.2)	9 (17)	
Some college or technical college	6 (33.3)	3 (12.5)	4 (36.4)	13 (24.5)	
College graduate	10 (55.6)	16 (66.7)	5 (45.5)	31 (58.5)	.43
Employment status					
Full-/part-time work	14 (77.8)	19 (79.2)	5 (45.5)	38 (71.7)	
Not working	4 (22.2)	5 (20.8)	6 (54.5)	15 (28.3)	.094
WOMAC pain score, mean ± SD	8.41 ± 3.392	6.04 ± 4.28	5.82 ± 3.37	6.78 ± 3.92	.109

[a]Results are reported as n (%) unless otherwise indicated. WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

TABLE 3
Distribution Within Categories of Treatment Preference[a]

Treatment Preference	Definitely Willing (n = 18)	Probably Willing or Unsure (n = 24)	Not Willing (n = 11)	Total (n = 53)	*P* Value, χ^2 for Trend
Definite preference	3 (16.7)	1 (4.2)	6 (54.5)	10 (18.9)	
No definite preference	15 (83.3)	21 (87.5)	5 (45.5)	41 (77.4)	.039
Surgical preference	5 (27.8)	11 (45.8)	8 (72.7)	24 (45.3)	
No surgical preference	13 (72.2)	13 (54.2)	3 (27.3)	29 (54.7)	.02

[a]Results are reported as n (%).

with treatment preference. Significance was defined as $P < .05$. Both center and combined specific analyses were done. We determined the frequency of influential factors of willingness and treatment preferences within the cohort of patients from both centers who met the stricter inclusion criteria. Statistical analysis was performed using SPSS version 19.0 (IBM Corp) and Microsoft Excel.

RESULTS

Center A

At center A, 53 patients were identified to be eligible, and all agreed to participate in the feasibility study. Of the 53 who participated, 51% were female and 90.6% were white. The mean age was 33.4 ± 10.1 years, and the mean WOMAC pain score (range, 0-20) was 6.8 ± 3.9. Concerning willingness to participate in the hypothetical randomized trial, 34% (n = 18) were definitely interested in participating, 34% (n = 18) were probably willing, 11.3% (n = 6) were unsure, 13.2% (n = 7) were probably not willing, and 7.5% (n = 4) were definitely not going to participate in the randomized trial. None of the demographic identifiers assessed nor WOMAC pain score were found to significantly correlate with willingness to participate, as shown in Table 2.

For treatment preferences, 15.1% (n = 8) absolutely wanted surgery while 3.8% (n = 2) had strong preference for nonsurgical options; 28.3% (n = 15) said they probably would like to have surgery, 15.1% (n = 8) probably wanted nonsurgical treatment, and 37.7% (n = 20) were unsure. There were strong associations between treatment preference and willingness to participate (Table 3). Six of 10 (60%) subjects with a strong preference of treatment were unwilling to participate compared with 5 of 43 (11.6%) of those with no strong preference who were also not willing to participate in the hypothetical trial (chi-square for trend, $P = .04$). Five of 24 (20.8%) subjects who were leaning toward surgical treatment were definitely willing to participate, while 13 of 29 (44.8%) with no preference for surgery expressed certainty about participating in the study (chi-square for trend, $P = .02$).

If the more specific inclusion criteria used at center B were applied to the center A cohort, 30.2% (16/53) of the subjects from center A were eligible. Of the 16, 25% (n = 4) were sure they would participate in the randomized trial, 50% (n = 8) said they probably would participate, and 25% (n = 4) were unwilling to be part of the trial.

TABLE 4
Distribution of Subjects From Center B by Willingness to Participate in a Randomized Control Trial[a]

Factor	Definitely Willing (n = 3)	Probably Willing or Unsure (n = 6)	Not Willing (n = 13)	Total (n = 22)	*P* Value
Age, y, mean ± SD	32.00 ± 12.77	35.50 ± 9.65	28.31 ± 8.7	30.77 ± 9.6	.32
Sex					
Male	2 (66.7)	5 (83.3)	9 (69.2)	16 (72.7)	
Female	1 (33.3)	1 (16.7)	4 (30.8)	6 (27.3)	.79
Race					
Nonwhite	2 (66.7)	6 (100)	10 (76.9)	18 (81.8)	
White	1 (33.3)	0 (0)	3 (23.1)	4 (18.2)	.37
Education					
High school or lower	1 (33.3)	0 (0)	2 (15.4)	3 (13.6)	
Some college or technical college	1 (33.3)	2 (33.3)	7 (53.8)	10 (45.5)	
College graduate	1 (33.3)	4 (66.7)	4 (30.8)	9 (40.9)	.47
Employment status					
Full-/part-time work	3 (100)	5 (83.3)	6 (46.2)	14 (63.6)	
Not working	0 (0)	1 (16.7)	7 (53.8)	8 (36.4)	.11
WOMAC pain score, mean ± SD	8.00 ± 5.20	7.50 ± 2.81	9.85 ± 4.26	8.95 ± 4.01	.47

[a]Results are reported as n (%) unless otherwise indicated. WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

TABLE 5
Distribution Within Categories of Treatment Preference[a]

Treatment Preference	Definitely Willing (n = 3)	Probably Willing or Unsure (n = 6)	Not Willing (n = 13)	Total (n = 22)	*P* Value, χ^2 for Trend
Definite preference	2 (66.7)	0 (0)	4 (30.8)	6 (27.3)	
No definite preference	1 (33.3)	6 (100)	9 (69.2)	16 (72.7)	.6
Surgical preference	2 (66.7)	0 (0)	8 (61.5)	10 (45.5)	
No surgical preference	1 (33.3)	6 (100)	5 (38.5)	12 (54.5)	.4

[a]Results are reported as n (%).

Center B

At center B, 121 patients were screened for eligibility, with 18% (22/121) meeting inclusion criteria for enrollment. Age (24% were younger than 18 years), cut-off alpha angle (22%), and WOMAC pain score (11%) were major factors that accounted for exclusion. All 22 eligible patients agreed to complete the feasibility study. In this group, 72.7% were male and 92.3% white. The mean age was 32 ± 12.8 years, and the mean pain score was 8 ± 5.2. The percentage of this cohort definitely willing to be part of the randomized study was 13.6% (3/22). Five (22.7%) of them expressed possible interest in participating, and 1 subject was not sure. On the other end of the spectrum, 36.4% (n = 8) indicated they probably would not participate, and 22.7% (n = 5) were sure they would not participate. Neither pain nor the demographic factors examined related with willingness to participate in this group as well (Table 4). There was no subject in this group who surely wanted nonsurgical treatment. Three (13.6%) subjects indicated they would possibly opt for nonsurgical treatment, while 4 (18.2%) showed likely preference for surgery, 6 (27.3%) specified absolute preference for surgery, and 9 (40.9%) were unsure. The relationship between treatment preference and willingness to participate was not found to be statistically significant for this group (Table 5).

Combined

The center A and B cohorts meeting the stricter inclusion criteria were combined to provide a total of 38 subjects: 16 from center A and 22 from center B. A basic epidemiological description of this cohort showed 63% male, 87% white, and mean age of 31.8 ± 9.3 years. Within this group, 18% expressed strong interest in participating in the hypothetical randomized trial, 34% indicated they were likely to participate, 3% were unsure, 26% said probably not, and 18% stated absolute unwillingness to be part of the trial (Figure 1).

A descriptive analysis of the most important factors influencing willingness to participate in the combined cohorts meeting the stricter inclusion criteria were (1) I don't want to be randomized (36%), (2) I know I want surgery (34%), (3) I want to contribute to research (24%), (4) I don't believe physical therapy and anti-inflammatories will help (21%), and (5) I am not willing to wait 6 months to have surgery (21%).

Regarding treatment preference, 26% definitely wanted surgery, 16% probably wanted surgery, 13% probably wanted nonoperative treatment, 5% stated definite preference for nonsurgical treatment, and 40% were ambivalent. The physician's recommendation was the most popular

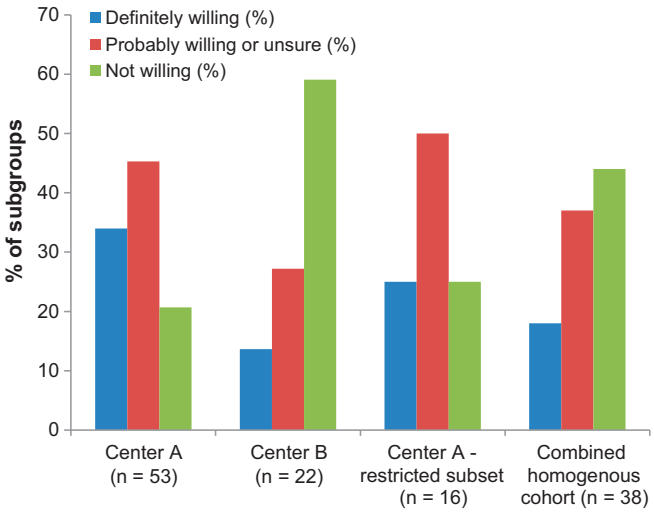

Figure 1. Willingness to participate in different groups.

influential factor for treatment preference, with 71% choosing this option. Other notable factors were functional ability (45%) and ineffectiveness of prior nonsurgical management (24%).

DISCUSSION

Our 2-center study was designed to allow us to estimate enrollment rates for a future randomized controlled trial of arthroscopic treatment versus nonsurgical management of FAI and also identify the group of FAI patients with whom the trial would be feasible. One center recruited patients to create a cohort representative of the heterogeneity of FAI deformities while the other took a more selective method forming a group in which one form of FAI morphology was predominant. The main advantage of the former approach is a higher proportion of eligible patients, as evidenced in our results whereas the latter allows for a more focused research study. These 2 factors must be weighed carefully when designing an RCT with regard to the feasibility of enrolling a sufficient number of subjects versus a more defined cohort perhaps producing a more consistent result. Our study provides the range of subjects that must be screened for both approaches to designing the inclusion criteria.

Our different enrollment criteria introduced some limitations to our feasibility study. The pediatric center's recruiting strategy resulted in the exclusion of 24% of eligible patients because they were younger than 18 years. However, since FAI is increasingly diagnosed in adolescents, extending the age range to include skeletally mature patients younger than 18 years may increase enrollment numbers. The stricter eligibility criteria used at the pediatric center also excluded many patients from participating in the study on the basis of the type of FAI deformity, thereby making it difficult to ascertain the enrollment potential from that center if the criteria were altered to expand the pool of eligible patients.

Another limitation of our feasibility study design was that it precluded the analysis of the effect of each center's research history and environment on willingness to participate. It is possible that varying levels of patient experience with clinical research or staff experience in recruitment at different centers is associated with patients' willingness to participate in the RCT. Our results showed a higher proportion of patients from the pediatric center (center B) not willing to participate in the future trial. This may be attributed to differences in how each center presented the research plan to patients, or it may just be due to regional variations in patient populations we did not account for (Figure 1). All the same, a multicenter study design will ensure that one center's shortage of willing study participants is offset by a significant number of participating patients from other centers.

Our findings suggest that enrollment for our planned randomized trial may benefit if more relaxed inclusion criteria were used. We conducted a subanalysis to evaluate the potential effect of relaxing the eligibility criterion of minimum alpha angle from 60° to 55°. This included 21 more participants from the adult care center, and there was a slight increase from 18% to 25.4% in the proportion of subjects definitely willing to participate. A previous prospective assessment study on willingness to participate in a comparable randomized trial for the treatment of meniscal tears found a similar proportion of 22% of potential subjects who were definitely willing to participate in the trial.[3] The prospective assessment predicted quite accurately the 26% of eligible patients who participated in the actual randomized trial.[7]

Analysis of the association of stated willingness to participate and treatment preferences in the adult care center group revealed a significant relationship consistent with findings from other studies.[3] A majority of the patients with stronger treatment preferences, as well as those with preference for surgery, were less willing to participate in the randomized trial (Table 3). As expected, patients who favor one treatment arm highly over another will likely find the randomization process disturbing because they could be given the less-wanted treatment. Nevertheless, our data suggest that patients with definite treatment preferences are in the minority (Tables 3 and 5). With respect to surgical treatment, it is not surprising that more of those with preference for this were less willing to be in a randomized study. We found that most of the patients had already tried conservative treatment methods and felt they were ineffective. In another feasibility study of an RCT for FAI treatment done in the United Kingdom, it was found that although more patients were troubled about their risk of developing OA than their current symptoms, patients were not willing to continue with nonsurgical management for more than 6 months if their symptoms had not improved.[9] This demonstrates how crucial patients' equipoise is in enrolling for a trial comparing 2 treatment arms. A balanced perception of the risks and benefits of both treatment methods may not only enhance enrollment rates but also minimize the incidence of cross-overs and dropouts.

It is also possible that greater understanding of treatment specifics could lead to less willingness to participate

in the randomized trial. Given the recent growing interest in the etiology, treatment, and treatment outcomes of FAI deformities, there is an expanding base of knowledge available to patients and surgeons alike. A person may learn of the advantages or pitfalls of one treatment approach as compared with others, leading to consolidation of a treatment preference. This trend will have an effect on the implementation of high–evidence level studies on FAI treatment outcomes. It is therefore important that an RCT is undertaken now while it is feasible.

The findings of this study show that participant accrual for a randomized trial comparing treatments for FAI is currently achievable. Waiting on this may be detrimental to the successful implementation of the trial, as treatment preferences seem to influence willingness to participate in the trial. Our findings, with respect to inclusion criteria and regional variations in patient populations, will influence the design of a planned randomized trial to maximize enrollment.

REFERENCES

1. Clohisy JC, Dobson MA, Robison JF, et al. Radiographic structural abnormalities associated with premature, natural hip-joint failure. *J Bone Joint Surg Am*. 2011;93(suppl 2):3-9.
2. Clohisy JC, Kim YJ. Femoroacetabular impingement research symposium. *J Am Acad Orthop Surg*. 2013;21(suppl 1):vi-viii.
3. Creel AH, Losina E, Mandl LA, et al. An assessment of willingness to participate in a randomized trial of arthroscopic knee surgery in patients with osteoarthritis. *Contemp Clin Trials*. 2005;26:169-178.
4. Emara K, Samir W, Motasem el H, Ghafar KA. Conservative treatment for mild femoroacetabular impingement. *J Orthop Surg (Hong Kong)*. 2011;19:41-45.
5. Gregory JS, Waarsing JH, Day J, et al. Early identification of radiographic osteoarthritis of the hip using an active shape model to quantify changes in bone morphometric features: can hip shape tell us anything about the progression of osteoarthritis? *Arthritis Rheum*. 2007;56:3634-3643.
6. Halpern SD. Prospective preference assessment: a method to enhance the ethics and efficiency of randomized controlled trials. *Control Clin Trials*. 2002;23:274-288.
7. Hoppe DJ, Schemitsch EH, Morshed S, Tornetta P 3rd, Bhandari M. Hierarchy of evidence: where observational studies fit in and why we need them. *J Bone Joint Surg Am*. 2009;91(suppl 3):2-9.
8. Hunt D, Prather H, Harris Hayes M, Clohisy JC. Clinical outcomes analysis of conservative and surgical treatment of patients with clinical indications of prearthritic, intra-articular hip disorders. *PM R*. 2012;4:479-487.
9. Nicholls AS, Kiran A, Pollard TC, et al. The association between hip morphology parameters and nineteen-year risk of end-stage osteoarthritis of the hip: a nested case-control study. *Arthritis Rheum*. 2011;63:3392-3400.
10. Reichenbach S, Jüni P, Werlen S, et al. Prevalence of cam-type deformity on hip magnetic resonance imaging in young males: a cross-sectional study. *Arthritis Care Res (Hoboken)*. 2010;62:1319-1327.