The Journal of Arthroplasty xxx (2025) 1–8

Contents lists available at ScienceDirect

The Journal of Arthroplasty

journal homepage: www.arthroplastyjournal.org

The Femoral Head Edema Zone: A Novel Classification Scheme to Better Predict Osteonecrosis Progression

Deniz C. Ince, Vivek P. Shah, MD, Kenichi Kikuchi, MD, PhD, Kyle P. O'Connor, MD, Elizabeth L. Yanik, PhD, ScM, John C. Clohisy, MD, Cecilia Pascual-Garrido, MD, PhD *

Department of Orthopaedic Surgery, Washington University in St. Louis School of Medicine, Barnes-Jewish Hospital, St. Louis, Missouri

ARTICLE INFO

Article history:
Received 14 March 2025
Received in revised form
12 August 2025
Accepted 14 August 2025
Available online xxx

Keywords:
osteonecrosis
hip
core decompression
total hip arthroplasty
classification

ABSTRACT

Background: This study proposed a new classification, the Edema Zone classification, that uses magnetic resonance imaging images to grade the extent of edema in osteonecrosis of the femoral head. The purpose of the study was (1) to examine how the Edema Zone classification compared to the Japanese Investigation Committee (JIC) classification's prognostic ability for early conversion to total hip arthroplasty (THA), and (2) to determine how accurately and reliably the Edema Zone classification performed as a classification system.

Methods: This was a retrospective study of hips that converted to THA from a core decompression within 26 months compared to hips that received only core decompression. Preoperative magnetic resonance images were examined. Hips were graded by Edema Zone and JIC classifications. Edema Zone reliability was analyzed, and predictive accuracy of the classifications was compared.

Results: Inter-rater reliability for the edema zone classification was very high, with a κ of 0.87. Edema Zone grades were higher in hips that converted to THA (nine of 20 $\geq$ grade 3) compared to hips that did not (six of 74 $\geq$ grade 3, 8.1%, $P < 0.001$) and demonstrated a significant P-value for trend ($P < 0.001$). In contrast, JIC classification did not differ between patients who converted and those who did not ($P = 0.83$). Receiver operating characteristic curve analysis showed that the area under the curve for the Edema Zone classification was 0.71, substantially greater than the area under the curve for the JIC classification system at 0.52.

Conclusions: Edema Zone classification showed exceptional inter-rater reliability and was a more accurate predictor of THA conversion compared to the JIC classification. Furthermore, the severity of the Edema Zone grade demonstrated a statistically significant impact on the likelihood of conversion to THA, with higher grades associated with increased conversion rates. This new classification system can be a powerful tool in guiding appropriate surgical intervention for patients who have osteonecrosis of the femoral head.

Osteonecrosis of the femoral head (ONFH) is the death of cellular components of bone, usually due to disruption of blood supply to subchondral regions of the femoral head [1]. Progression of ONFH can lead to femoral head collapse, causing substantial pain, limited range of movement, and dysfunction. There are 20,000 to 30,000 patients diagnosed with ONFH annually in the United States, and it is estimated that 5 to 12% of patients who undergo total hip arthroplasty (THA) have a diagnosis of ONFH [2–4].

Core decompression is an established, hip-preserving surgery used for the treatment of early-stage ONFH. However, nearly 40%

This study was performed at Washington University School of Medicine, St. Louis, MO.

One or more of the authors of this paper have disclosed potential or pertinent conflicts of interest, which may include receipt of payment, either direct or indirect, institutional support, or association with an entity in the biomedical field which may be perceived to have potential conflict of interest with this work. For full disclosure statements refer to https://doi.org/10.1016/j.arth.2025.08.035.

* Address correspondence to: Cecilia Pascual-Garrido, MD, PhD, Washington University School of Medicine, Department of Orthopaedic Surgery, Adult Reconstruction - Adolescent and Young Adult Hip Service, 660 S. Euclid Avenue, MSC 8233-0004-5505, St. Louis, MO 63110.

https://doi.org/10.1016/j.arth.2025.08.035

of patients who undergo core decompression convert to THA within three years [5,6]. Converting from core decompression to THA indicates worsening osteonecrosis, joint damage, and pain. In addition, patients suffer a substantial cost burden, as conversion to THA within five years from core decompression represents poor cost-effectiveness, exceeding $50,000 cost per quality-adjusted life year gained [7]. It has been widely accepted that preservation should be attempted in patients who have necrosis and no collapse; however, many patients who present to the clinic with no femoral head collapse have major bone marrow edema. Based on our experience, this patient population does not perform well after core decompression. Thus, we aimed to investigate and develop a classification based on bone marrow edema that could predict the progression of the disease. Previous studies have shown that the presence of edema is associated with femoral head collapse [8,9].

Current classification systems for ONFH, including the Japanese Investigation Committee (JIC), modified Kerboul, and Steinberg, all describe the location and extent of osteonecrosis. The JIC classification is the most reliable and effective, especially among early-stage ONFH, where core decompression could be appropriately offered [10]. However, these classifications do not consider the strong prognostic factor of edema within the femoral head.

This study proposed a new classification, the Edema Zone classification, to grade the extent of edema in the femur, aiming to serve as a prognostic tool for femoral head collapse. The Edema Zone classification is simply assessed using a single imaging study, whereas classifications such as the Association Research Circulation Osseous Classification require, at minimum, x-ray and magnetic resonance imaging (MRI) findings in conjunction for full grading. This study's proposed classification was compared to the most reliable and effective classification that could be simply graded using a single imaging study, the JIC classification. The purpose of the study was to examine (1) how the Edema Zone classification compared to the JIC classification's prognostic ability for early conversion to THA and (2) how accurately and reliably the Edema Zone classification performed as a classification system.

Materials and Methods

Patient Selection

This was a retrospective study of all patients undergoing a core decompression who had a diagnosis of ONFH between June 13, 2018, and November 6, 2023. This was a single-institutional study, and all procedures were performed by one specialized hip surgeon (C.P.G.) who had extensive experience utilizing core decompression and THA for treatment of ONFH. The institutional review board evaluated and approved the study (#202210081).

Inclusion criteria included patients who failed conservative therapy (activity modifications, physical therapy, and nonsteroidal anti-inflammatory drugs), demonstrated clinical symptoms of ONFH, and had preoperative MRI images available for review in the electronic health record (EHR) with findings consistent with ONFH. The use of MRI is an established, highly accurate modality for early diagnosis of ONFH [3,11,12]. In cases of bilateral hip procedures, each hip was included as an individual data point, with each hip graded independently of the other hip. The current study used 26 months as the inclusion cutoff for early conversion to THA, based on literature indicating that the average time to THA conversion after core decompression was 26.3 months [6]. Exclusion criteria were patients who did not fit the inclusion criteria, had any surgery that was not THA on their core decompression hip, or lacked preoperative MRI images in the EHR (Figure 1).

Demographic and Risk Factors

Demographic data were collected and included age at surgery, time to THA conversion, laterality, and sex- the term sex refers to biologic classification (male or female) as documented in the

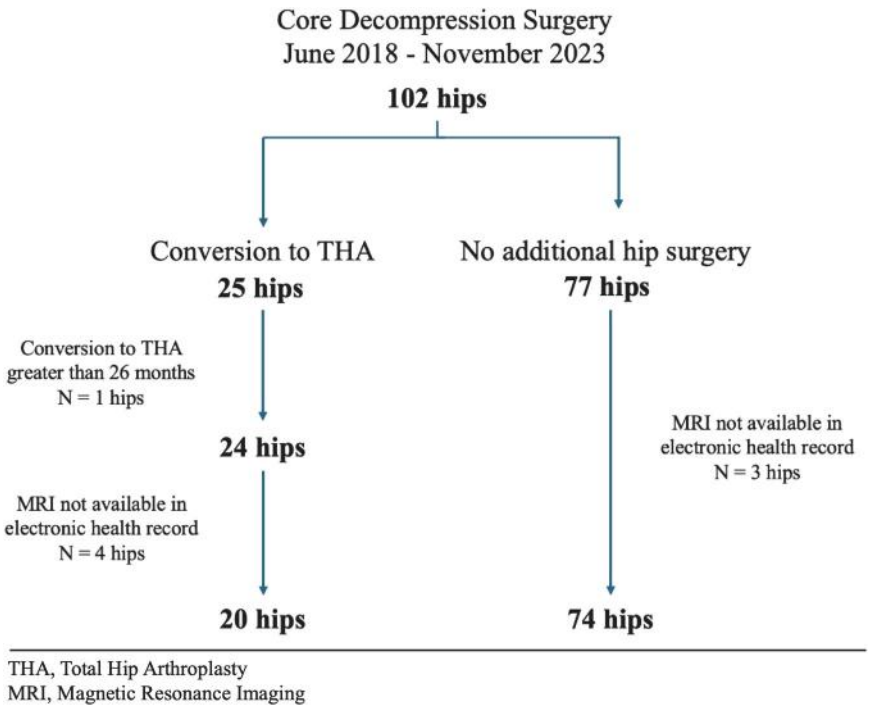


Figure 1. Flowchart of final study population. THA, total hip arthroplasty; MRI, magnetic resonance imaging.

medical record. Established risk factors for ONFH development and subsequent collapse were recorded and included corticosteroid use, body mass index (BMI), alcoholic drinks per week, trauma, human immunodeficiency virus, sickle cell disease, and sickle cell trait [3,8,13–16]. Positive corticosteroid use was defined as either a physician note citing chronic corticosteroid use, a prescription of greater than five mg oral prednisolone for greater than one month, or intravenous methylprednisolone at doses of greater than two grams for greater than three months [17,18]. The BMI groupings were based on National Health Service definitions of underweight (< 18.5), healthy weight (18.5 to 24.9), overweight (25 to 29.9), obese (30 to 39.9), and severe obesity (> 40.0) [19]. Alcoholic drinks per week were recorded as the highest amount reported in the EHR by a health care worker preoperatively, as patients generally report lower consumption habits in interviews compared to daily tracking [20]. Alcohol consumption groupings were based on definitions by the National Institute on Alcohol Abuse and Alcoholism, leading to groups including no alcohol on all notes, one drink or less per week, low to moderate alcohol consumption (≤ seven drinks a wk for women, ≤ 14 drinks a week for men), and heavy alcohol consumption (≥ eight drinks a week for women, ≥ 15 drinks a week for men, diagnosis of alcohol use disorder, or EHR note citing heavy alcohol consumption) [21]. Trauma was defined as a note citing a traumatic event leading to hip pain.

There were 20 hips (21.3%) that converted from core decompression to THA within 26 months. The average time to THA conversion was 13.5 ± 7.7 months. There were 74 hips (78.7%) that received a core decompression and did not convert. Of 64 patients, 30 (46.9%) had bilateral osteonecrosis. Of the hips that converted to THA, 12 (60%) had contralateral hip osteonecrosis treated with core decompression, and there were no bilateral conversions to THA. There was no significant difference in age at the time of core decompression in hips that converted (43 years ± 12.3) compared to unconverted hips (44 years ± 12.4, $P = 0.98$). There was no significant difference in the sex of patients whose hip converted (12 of 20, 60.0% women) compared to unconverted hips (32 of 74, 43.2% women, $P = 0.18$) (Table 1). Similarly, there was no statistically significant difference in established risk factors of BMI ($P = 0.072$), alcohol consumption ($P = 0.76$), corticosteroid use ($P = 0.77$), or inciting trauma ($P = 0.29$) (Table 2).

Table 2
Risk Factors.

Risk Factor	Core Decompression Converted to THA N = 20	Core Decompression Only N = 74	*P*-Value
BMI grouping			0.072
Underweight, < 18.5	0	0	
Healthy weight, 18.5 to 24.9	2 (10.0)	19 (25.7)	
Overweight, 25.0 to 29.9	7 (35.0)	26 (35.1)	
Obese, 30 to 30.9	8 (40.0)	26 (35.1)	
Severe obesity, > 40.0	3 (15.0)	3 (4.1)	
Alcohol consumption grouping[a]			0.76
No alcohol	5 (25.0)	10 (13.7)	
<1 week	4 (20.0)	22 (30.1)	
Low moderate	8 (40.0)	32 (43.8)	
Heavy	3 (15.0)	9 (12.3)	
Corticosteroid use			0.77
Yes	8 (40.0)	42 (56.8)	
No	12 (60.0)	32 (43.2)	
Inciting trauma			0.29
Yes	2 (10.0)	3 (4.1)	
No	18 (90.0)	71 (95.9)	

BMI, body mass index; THA, total hip arthroplasty.
[a] N = 73 for core decompression; only alcohol consumption grouping.

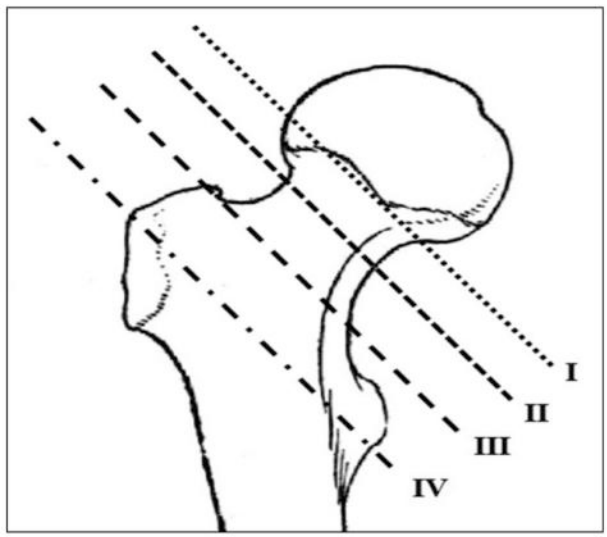
Edema Zone Classification

The Edema Zone classification was developed to define the extent of edema in the femur using a simple scheme. The scheme was created according to our experience with patient care of this population and inspired by the Delbet-Colonna classification, the most used classification for proximal femur fractures in children (Figure 2) [22,23]. We have observed a variable pattern of edema regardless of the size or location of the lesion. The Edema Zone classification uses the distal extent of edema rather than pure size, since classifications that focus on three-dimensional volumetric size, such as the Steinberg classification, are less effective than classifications based on two-dimensional imaging that consider components of both size and location [10]. Each zone corresponds to the greatest extent that edema can be visualized on MRI (Figure 3). Grade 0 was assigned to ONFH where edema was not appreciated on MRI or when edema was a thin border completely tangential to the osteonecrotic lesion. Grade 1 included edema that, at its greatest extent, did not extend distal to the midline of the femoral head. Grade 2 included edema that, at its greatest extent, was distal to the midline of the femoral head but proximal

Table 1
Patient Characteristics.

Characteristic	Core Decompression Converted to THA N = 20	Core Decompression Only N = 74	*P*-Value
Age at core decompression, years	43 ± 12.3	44 ± 12.4	0.98
Time to THA conversion, months	13.5 ± 7.7		
Sex			0.18
Men	8 (40.0)	42 (56.8)	
Women	12 (60.0)	32 (43.2)	
Laterality			0.31
Right	12 (60.0)	35 (47.3)	
Left	8 (40.0)	39 (52.7)	

THA, total hip arthroplasty.



Delbet-Colonna classification for pediatric femoral neck fractures; (I) Type I: Transphyseal, (II) Type II: Transcervical, (III) Type III: Basocervical and (IV) Type IV: Intertrochanteric fracture lines were shown.

Figure 2. Delbet-Colonna classification. *Reproduced with permission from Issin et al.* [22].

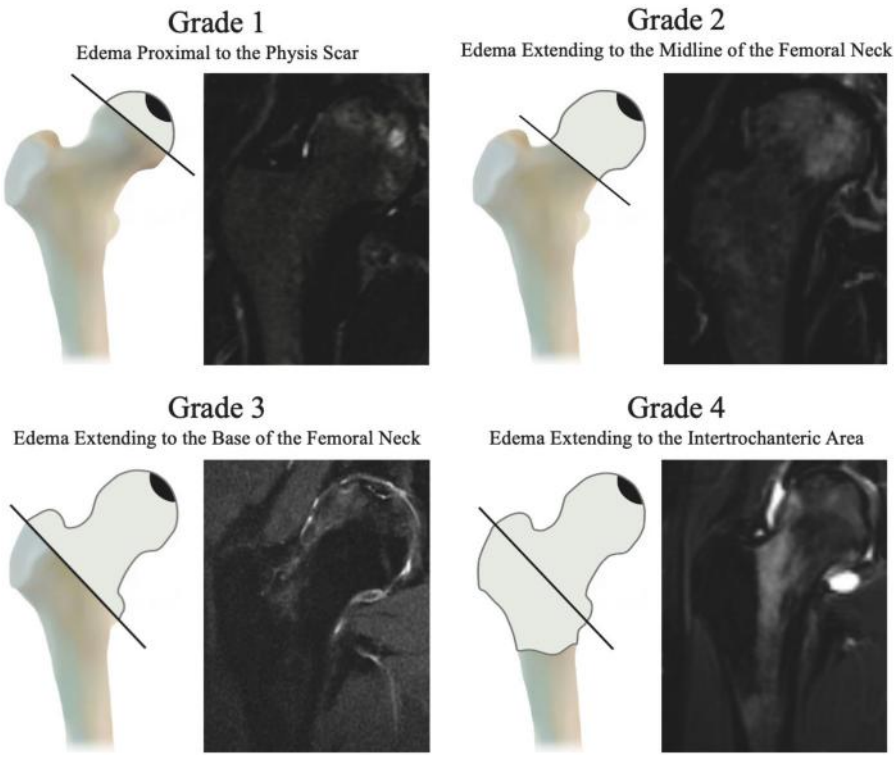


Figure 3. Edema Zone grades.

to the midline of the femoral neck. Grade 3 included edema that, at its greatest extent, was distal to the midline of the femoral neck but proximal to the line between the center of the greater and lesser trochanters. Lastly, grade 4 included edema that, at its greatest extent, was distal to the line between the center of the greater and lesser trochanters. Edema was visualized using the coronal images with T2 fat-suppressed, T1 short tau inversion recovery, or T1 turbo inversion recovery magnitude [24–29]. The coronal plane was chosen because we aimed to minimize variability and improve inter-rater reliability by standardizing our measurements to a single, reproducible plane. The coronal plane allowed for observation of the distal extent of edema while also easily tracking the anatomical landmarks of the greater trochanter, lesser trochanter, and femoral neck needed for this classification. Edema Zone and JIC grading were conducted independently by two authors (D.C.I, K.K), and any discrepancy was reviewed independently by a third author (K.P.O).

Data Analyses

Several statistical methods were used to compare classifications. Inter-rater reliability was calculated using Cohen's kappa (κ). Mann–Whitney *U*-tests were used to compare classification scores between patients who converted to THA and those who did not. Wilcoxon signed-rank tests were applied to assess differences between Edema Zone and JIC classification grades. Receiver operating characteristic curve analysis was performed to evaluate the predictive accuracy of both classification systems for THA conversion. A *P*-value for trend was calculated using the Cochran-Armitage test for trend to examine if the trend of increasing Edema Zone grade was statistically significant. Pearson *Chi*-square tests were utilized to examine the relationship between Edema Zone grades and THA conversion rates. Statistical significance was set at $P < 0.05$ for all analyses.

Results

Comparison of Classification Scores

Inter-rater reliability for the Edema Zone classification was substantial with a κ of 0.87 ($P < 0.001$). The Mann–Whitney *U* test revealed a significant difference in the Edema Zone grade between patients who converted to THA (median: 0.5, interquartile range (IQR): 0 to 4.0) compared to those who did not (median: 0, IQR: 0 to 0) (Table 3). There was no significant difference in JIC classification between patients who converted and those who did not, both with a median of 3.0 and IQR of 2.0 to 4.0 ($P = 0.83$).

The Wilcoxon signed-rank test demonstrated a statistically significant difference between the two classification scores (*Z* score: −5.8, $P < 0.001$), indicating that the Edema Zone classification may assess different aspects of osteonecrosis, including indication for THA.

Predictive Accuracy for Total Hip Arthroplasty (THA) Conversion

The receiver operating characteristic curve analysis assessed the predictive accuracy of both classification systems. The area

Table 3
Comparison of Classification Scores Based on Conversion to THA Status.

Classification	Core Decompression Only (Median [IQR])	Conversion to THA (Median [IQR])	*P*-Value
JIC classification	3.0 [2.0 to 4.0]	3.0 [2.0 to 4.0]	0.83
Edema Zone classification	0 [0 to 0]	0.5 [0 to 4.0]	**<0.001**

Bold values indicate statistical significance at $P < 0.05$.
THA, total hip arthroplasty; IQR, interquartile range; JIC, Japanese Investigation Committee.

Receiver Operating Characteristic Area Under the Curve

	AUC
JIC Classification	0.52
Edema Zone Classification	0.71
AUC Difference	0.19

JIC, Japanese Investigation Committee
ROC, Receiver Operating Characteristics
AUC, Area Under the Curve

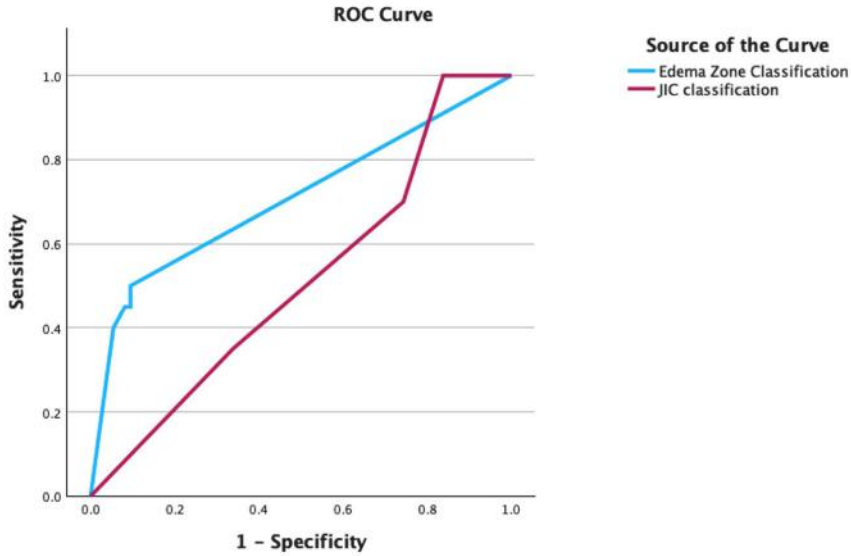


Figure 4. ROC curve. ROC, receiver operating characteristics; AUC, area under the curve; JIC, Japanese Investigation Committee.

under the curve (AUC) for the Edema Zone classification was 0.71, while the JIC classification AUC was 0.52 (Figure 4). This suggests superior predictive accuracy for THA conversion with the Edema Zone classification.

Impact of Edema Zone Classification on Total Hip Arthroplasty (THA) Conversion

The Pearson *Chi*-square test revealed a significant association between Edema Zone grades and conversion to THA ($P < 0.001$). There was a trend of increasing THA conversion rates with higher Edema Zone grades, indicating the extent of edema impacts the likelihood of progression to THA ($P < 0.001$) (Table 4). The JIC failed to show an association between higher grades and progression to THA ($P = 0.74$) (Table 5).

Table 4
Conversion to THA Status Based on Edema Zone Classification.

Edema Zone Grade	No Conversion	Conversion to THA	Conversion Rate (%)	Total
Zero grade	67	10	13.0	77
Grade 1	0	1	100.0	1
Grade 2	1	0	0.0	1
Grade 3	2	1	33.3	3
Grade 4	4	8	66.7	12
Total	74	20		94
P value for trend				**<0.001**

Bold values indicate statistical significance at $P < 0.05$.
THA, total hip arthroplasty.

Discussion

There is a need to establish an improved prognostic tool for core decompression failure, as nearly 40% of core decompression failures convert to THA within 26 months. This results in prolonged patient pain, increased complexity of THA, and greater overall costs and burden for both patients and the health care system. The Edema Zone classification outperformed the JIC classification as a prognostic tool for conversion to THA after core decompression for ONFH. This is further supported by our clinical experience, where hips with extensive edema convert to THA quickly, whereas hips with low-grade edema can have successful core decompression, with greater surgery at greater than five years follow-up (Figure 5). This novel classification system provides a simple scheme with high inter-rater reliability that offers critical insight into clinical decision-making for patients who have ONFH, potentially reducing the number of patients who receive a core decompression only to convert to THA shortly after.

Table 5
Conversion to THA Status Based on JIC Classification.

JIC Grade	No Conversion	Conversion to THA	Conversion Rate (%)	Total
Grade A	12	0	0	12
Grade B	7	6	46.2	13
Grade C1	30	7	18.9	37
Grade C2	25	7	21.9	32
Total	74	20		94
P value for trend				0.74

THA, total hip arthroplasty; JIC, Japanese Investigation Committee.

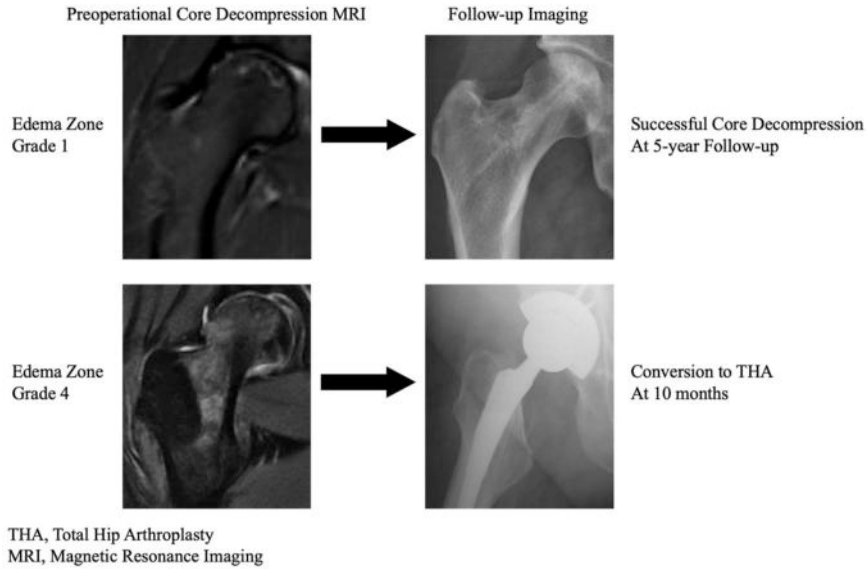


Figure 5. Clinical case examples.

The Edema Zone classification proved superior as a prognostic tool for conversion to THA compared to the JIC classification. The THA conversion group could be compared to the nonconversion group, as there were no significant differences in the established risk factors of age, sex, BMI, alcohol consumption, corticosteroid use, or inciting trauma among the patient groups. In total, 21.3% of hips treated with core decompression converted to THA within 26 months, which is in accordance with the current literature. Hips that converted to THA had greater Edema Zone grades, with nine of 20 (45.0%) converted hips ≥ grade 3 compared to unconverted hips with six of 74 (8.1%) ≥ grade 3 ($P < 0.001$). There was a statistically significant trend that higher rates of THA conversion were associated with higher Edema Zone grades ($P < 0.001$). There was no difference in JIC classification between hips that converted to THA and unconverted hips ($P = 0.83$). In AUC analysis, which compares the effectiveness of imaging classifications, Edema Zone classification, importantly, demonstrated superiority to JIC classification [30]. The JIC has been described as the most useful and reliable classification to identify femora with high and low risk for collapse, and the Edema Zone classification had a substantially greater AUC of 0.71 compared to the JIC classification AUC of 0.52 [10]. These AUC values show that JIC "fails" to predict collapse, while the Edema Zone was meaningfully better and considered in the acceptable range as a clinical predictor of THA conversion [31,32]. The large Z score of −5.8 ($P < 0.001$) demonstrated that the Edema Zone classification successfully assessed a different aspect of the osteonecrotic hips, edema, compared to the lesion size and location assessed in JIC. [33,34]. These results show that Edema Zone classification was both novel to JIC classification and a better prognostic tool for conversion to THA. Edema of the femoral head can occur transiently and may not always correlate exclusively with ONFH. Conditions such as *transient bone marrow edema syndrome* also cause edema of the femoral head; however, these patients' clinical symptoms usually respond well to conservative management with nonsteroidal anti-inflammatory drugs and have the edema regress or resolve within six to 12 months of symptom onset [35,36]. The transient nature of the edema seen in *transient osteoporosis of the hip,* combined with all participants in this study having failed conservative treatment, greatly reduces the chance that a patient who has transient edema was included in the cohort. In addition, all patients in this study had an identified necrotic lesion, confirming the edema was secondary to osteonecrosis and not true *transient bone marrow edema syndrome*. Clinically, it is important to consider the potential for a transient cause of edema before suggesting surgical management based on Edema Zone grading. We believe the Edema Zone classification can be implemented to define the best surgical treatment and patient counseling. In our practice, patients who have Edema Zone grades 3 and 4 who have failed conservative treatment are indicated to have a THA even when there is no collapse of the femoral head. We believe this approach results in a predictable outcome for the patient as well as substantially reduced cost and burden to the health care system.

The Edema Zone classification reliably conveyed the expected trend while also demonstrating consistent grading by different raters. A key component of the Edema Zone classification was that it followed a simple scheme. The effectiveness of this scheme was supported by the high inter-rater reliability with a κ of 0.87. This κ value demonstrated "almost perfect" agreement [37,38]. The Edema Zone inter-rater reliability κ was greater than the mean κ value reported for JIC (κ = 0.72), the modified Kerboul method (κ = 0.57), and the Steinberg classification (κ = 0.56) [10]. The positive association of Edema Zone grade with THA conversion, along with its excellent inter-rater reliability, established that Edema Zone classification achieved the intended goal and can be reliably implemented.

There were potential limitations to this study. The cohort size was small, with 20 hips that converted to THA and 74 hips that did not convert. This affected the ability to conduct a multivariate logistic regressions examining the impact that each risk factor had on conversion to THA, since successful logistic regressions would require five to 10 hips for each predictive factor [39]. The cohort size also prevented us from using multivariate logistic regression to compare Edema Zone classification to the established risk factors for femoral head collapse. In addition, our cohorts demonstrated no statistically significant difference in BMI between cohorts, but the difference neared a significant result. So, conducting this study in a larger cohort could elucidate the impact this risk factor may have on the Edema Zone classification. However, despite the cohort size, the study showed very strong statistical evidence that Edema Zone grade was a strong prognostic factor. In future studies, we hope to apply this classification to a larger cohort size to support the generalizability of this study's findings. Another limitation was that

the cohort consisted of patients treated by only one specialized hip surgeon, potentially decreasing the generalizability of the outcomes. Future studies will focus on increasing the cohort recruitment to conduct logistical regression and recording patient-reported outcomes to examine if the Edema Zone grade is associated with more than the risk for conversion to THA. Future larger studies will additionally help validate the concepts shared in this study. Future studies will also compare the Edema Zone classification to more complex grading systems such as the 2021 Association Research Circulation Osseous Classification system.

Conclusions

In conclusion, our findings suggest that the Edema Zone classification system was a more accurate predictor of THA conversion compared to the JIC classification and showed exceptional reliability across different raters. Furthermore, the severity of Edema Zone classification appears to have a substantial impact on the likelihood of conversion to THA, with higher grades associated with increased conversion rates. This classification system allows us to counsel patients and define the best surgical treatment for this patient population.

CRediT authorship contribution statement

Deniz C. Ince: Writing – review & editing, Writing – original draft, Visualization, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Vivek P. Shah:** Writing – review & editing, Writing – original draft, Visualization, Investigation, Formal analysis, Data curation. **Kenichi Kikuchi:** Validation, Investigation, Formal analysis, Data curation. **Kyle P. O'Connor:** Validation, Formal analysis, Data curation. **Elizabeth L. Yanik:** Writing – review & editing, Supervision, Methodology, Conceptualization. **John C. Clohisy:** Writing – review & editing, Supervision. **Cecilia Pascual-Garrido:** Writing – review & editing, Writing – original draft, Visualization, Supervision, Methodology, Conceptualization.

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