TRAUMA SURGERY



Focal osteonecrosis in the femoral head following stable anatomic fixation of displaced femoral neck fractures

Lionel E. Lazaro^{1,2,3} · Jonathan P. Dyke⁴ · Ryan R. Thacher^{1,2,3} · Joseph T. Nguyen⁵ · David L. Helfet^{1,2,3} · Hollis G. Potter⁶ · Dean G. Lorich^{1,2,3}

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Abstract

Introduction Femoral head (FH) osteonecrosis (ON) and subsequent segmental collapse is a major concern following displaced femoral neck fractures (FNF). We aimed to quantify residual perfusion to the FH following FNF and evaluate the viability of the FH overtime after surgical fixation.

Materials and methods Twenty-three patients with FNF underwent dynamic contrast-enhanced (DCE)-MRI to estimate bone perfusion in the FH, using the contralateral side as control. Following open anatomic reduction and a length/angle-stable fixation, a special MRI sequence evaluated the FH for ON changes over time at 3 and 12 months after surgery.

Results We found significant compromise of both arterial inflow [83.1%—initial area under the curve (IAUC) and 73.8%—peak) and venous outflow (243.2%—elimination rate (K_{el})] in the FH of the fractured side. The supero-medial quadrant suffered the greatest decrease in arterial inflow with a significant decrease of 71.6% (IAUC) and 68.5% (peak). Post-operative MRI revealed a high rate (87%—20/23) of

Lionel E. Lazaro lazarol@hss.edu

> Jonathan P. Dyke jpd2001@med.cornell.edu

Ryan R. Thacher rthacher@gmail.com

Joseph T. Nguyen nguyenj@hss.edu

David L. Helfet helfetd@hss.edu

Hollis G. Potter potterh@hss.edu

Dean G. Lorich lorichd@hss.edu

small ON segments within the FH, and all developed in the anterior aspect of the supero-medial quadrants. Fracture characteristics, including subcapital FNF, varus deformity, posterior roll-off $\geq 20^{\circ}$ and Pauwel's angle of $30^{\circ}-50^{\circ}$ demonstrated a greater decrease in perfusion compared to contralateral controls.

Conclusion FNF significantly impaired the vascular supply to the FH, resulting in high incidence of small ON segments in the supero-medial quadrant of the FH. However, maintained perfusion, probably through the inferior retinacular system, coupled with urgent open anatomic reduction and stable fixation resulted in excellent clinical and radiographic outcomes despite a high rate of small ON segments noted on MRI.

Level of evidence Level I: Prognostic Investigation.

Keywords Femoral head osteonecrosis · Dynamic contrast-enhanced MRI · Femoral neck fractures

- ¹ Hospital for Special Surgery and New York Presbyterian Hospital, 535 East 70th Street, New York, NY, USA
- ² Weill Medical College of Cornell University, New York, NY, USA
- ³ Orthopaedic Trauma Service, New York, USA
- ⁴ Citigroup Biomedical Imaging Center, Weill Medical College of Cornell University, New York, NY, USA
- ⁵ Departments of Epidemiology and Biostatistics Core, Hospital for Special Surgery, New York, NY, USA
- ⁶ Department of Radiology and Imaging, Hospital for Special Surgery and Weill Medical College of Cornell University, New York, NY, USA

Introduction

Osteonecrosis (ON) of the femoral head (FH) is a multifactorial disease process culminating in cellular demise within the FH secondary to compromised blood flow [1-3]. The initial stages are often asymptomatic, but the condition can continue to deteriorate and become debilitating [1, 3]. Development of ON and subsequent segmental collapse of the FH is major concern following displaced femoral neck fractures (FNF), and its occurrence seems to dictate functional prognosis [4]. Surgical decision-making for treatment of this fracture usually depends upon the overall risk of developing this devastating complication and potential for re-operations. Historically, the reported incidence of ON (25-45%) [5], late segmental collapse (25%) [6] and re-operations (20-64%) [7–12] is considerable, and often leads to arthroplasty [2, 20]. The presumed etiologic factor of this complication is decreased FH arterial inflow and venous outflow caused by either direct disruption of the terminal vessels and/or indirect tamponade secondary to development of an intraarticular fracture hematoma [13–20].

Functional vascular assessment of the FH using dynamic contrast-enhanced (DCE) MRI has previously demonstrated decreased blood flow in both the arterial and venous systems following FNF, suggestive of both an inflow and outflow problem [13]. We aimed to quantify residual perfusion to the FH following FNF, using DCE-MRI, and evaluate the viability of the FH overtime after surgical fixation, using a special MRI sequence. Our hypothesis was twofold: (1) the area of the FH that exhibits the most prominent decrease in perfusion is more likely to develop ON, and (2) subcapital FNF and angular deformity, including varus malposition and posterior roll-off, can further compromise FH perfusion.

Arterial supply to the femoral head

Three arterial systems provide the FH blood supply including the (1) retinacular arteries, (2) foveolar artery, and (3)intraosseous nutrient artery [21-27]. The retinacular systems (superior, inferior and anterior) are the primary arterial supply of the FH [21, 24, 26-31], with the superior retinacular arteries providing the greatest contribution [21, 23, 26–28, 30–36]. Both the superior and inferior retinacular systems are the intra-articular terminal branches of the medial femoral circumflex artery [22, 24, 27], and they course within the retinacula of Weitbrecht (fibrous extensions of the capsule wall) [21, 23, 27, 34, 37-39]. The superior retinacular system courses within the superior retinacula of Weitbrecht adjacent to the femoral neck, penetrating the posterior superior aspect of the femoral head-neck junction and arborizes to supply the superior/weight bearing portion of the FH [27, 28, 32]. The foveolar system flows through the ligamentum teres and branches to supply the peri-foveolar area [28, 32].

The inferior retinacular system runs through the inferior retinacula of Weitbrecht (elevated off the femoral neck), piercing the posterior-inferior aspect of the femoral head–neck junction and arborizes to supply the inferior FH [27, 28, 32]. There is a vast anastomosis between the retinacular and foveolar arterial systems [28, 32, 40].

Materials and methods

Our Institutional Review Board approved this prospective study. The senior author treated all patients enrolled in the study using the same surgical technique [41, 42]. Inclusion criteria consisted of: (1) an isolated injury; (2) age \geq 18 years; (3) complete set of advanced imaging (including pre- and post-operative MRI) and (4) radiographic follow-up duration of >12 months.

Pre-operative dynamic contrast-enhanced (DCE) MRI

Preoperatively, we obtained fat-suppressed DCE-MRIs, a technique that provides an estimate of bone perfusion in vivo over time for both the injured and uninjured proximal femur simultaneously [13]. Using a power injector, we injected 0.1 mM/kg of gadolinium-diethylenetriamine penta-acetic acid (Gd-DTPA) (Magnevist[®]; Bayer HealthCare Pharmaceuticals Inc., Wayne, NJ) at a rate of 2 cc/s. The DCE-MRI sequence used a coronal fat-suppressed 3D spoiled gradient echo pulse sequence (liver acquisition with volume acquisition, LAVA) with a temporal resolution of 7 s/image over 45 time points for a scan time of 6 min. We used the Brix 2-compartment model to analyze the DCE-MRI uptake curves in the normal and injured FH [13]. We created time intensity curves of the entire FH and defined quadrants with the average of all subjects' model parameters. Reflecting the arterial inflow are the following parameters: A (signal amplitude), k_{ep} (exchange rate between plasma and extravascular extracellular space), IAUC (initial area under the curve) and peak [13, 43]. We used the Brix model equation to calculate both the IAUC and peak value 90 s after injection. K_{el} (elimination rate) reflects venous outflow.

Surgical technique and post-operative care

The surgical technique consists of open anatomic reduction, intraoperative compression and a length- and angle-stable construct [41, 42] (Fig. 1). A strategically placed endosteal strut (fibular allograft), serving as a biologic dowel, was used to reconstruct the comminuted femoral neck and to augment the screw construct (consisting of two fully threaded cannulated screws). Transfixing through the fibular allograft creates a non-sliding fixed angle construct between the host bone and the allograft. This construct provides increased

Fig. 1 a Anteroposterior (AP) and lateral pre-operative radiographs of a 54-year-old male with a displaced femoral neck fracture including displacement in both the coronal and sagittal plane (with varus displacement and posterior roll-off). b The 12-month AP and lateral radiographs illustrate the fixation construct, and the maintenance of anatomic reduction, femoral neck length and hip joint space with neither radiographic signs of femoral head osteonecrosis nor segmental collapse



fixation stability enhancing osseous union and FH revascularization [41]. Several authors have recognized that anatomical reduction and stable fixation gives the best chances for success following open reduction and internal fixation (ORIF) of FNF [6, 41, 44–49].

Weight bearing status was limited to 20% of patient body weight for the first 3 months. Passive range of motion began immediately after surgery, but strengthening exercises were delayed for 6 weeks. At 3 months, patients advanced to full-weight bearing. Clinical and radiographic follow-up consisted of a visit at 2 and 6 weeks, then every 3 months up to a year, and finally at 2 years.

Post-operative multi-acquisition variable-resonance image combination (MAVRIC) MRI

Postoperatively, we obtained a MAVRIC-MRI 3 and 12 months after surgery. This sequence improves image

quality by reducing metallic artifacts caused by implants [50–52]. All MRI examinations were performed with a 1.5-T clinical scanner system (450 DVMR, system General Electric Health Care, Waukesha, WI) using an 8-channel phased-array cardiac coil (GE Healthcare, Waukesha, WI). MAVRIC images were obtained with the parameters: TR, 1000 ms; TE, 10–14 ms; RBW, \pm 125 kHz; slice thickness, 3.5 mm; slice spacing, 0 mm; acquisition matrix, 512 × 256; NEX, 0.5; ETL, 8; FOV, 38–44 cm. Scans were evaluated by an experienced musculoskeletal MRI radiologist (HGP) for signs of ON, characterized as the serpentine low signal-intensity focus within the high signal intensity of the fatty subchondral bone. We correlated the size and location of the ON segments with the injury DCE-MRI perfusion analysis and fracture characteristics.

Statistical analysis

We used the Shapiro-Wilk test to assess normality for all continuous variables. When the assumption of normality was not violated, independent sample t tests were used for pre-operative dynamic MRI parameters between fracture and non-fracture sides of the femoral head both at each quadrant and between the entire femoral head. Wherever normality was violated, we used Mann-Whitney U tests. We used similar analyses to assess differences between various fracture characteristics. In comparisons of three categories or more, we used one-way ANOVA to assess differences in dynamic MRI measures for normally distributed data, whereas Kruskal-Wallis tests were used for any non-parametric assessments. Two-factor ANOVA models were generated comparing mean differences in pre-operative dynamic MRI parameters between two independent factors in fracture characteristics and fracture group, as well as between postoperative MAVRIC-MRI characteristics and fracture group. All analyses were conducted using SPSS version 22.0 (IBM Corp., Armonk, NY).

Results

Thirty-seven patients with FNF presented at our institution during the study period (October 2009 to July 2013). Five patients were indicated for arthroplasty treatment and five (non-displaced fractures) underwent closed reduction and percutaneous pinning. Twenty-seven patients were indicated for open reduction and internal fixation, but one patient decline participation in the study, one patient suffered fracture non-union and underwent total hip arthroplasty and two patients suffered early catastrophic failure (one was noncomplaint with weight bearing restrictions and the other suffered a fall). Twenty-three patients (4 males, 19 females) with displaced/unstable fractures met inclusion criteria. At time of injury, average patient age was 60.1 years (range of 30–79). All patients achieved osseous union, and none demonstrated radiographic signs of ON or FH segmental collapse at latest follow-up on standardized anteroposterior (AP) and lateral radiographs. Average radiographic follow-up was 18.7 months (range of 12–45). As previously reported [41], all patients had excellent clinical and radiographic outcomes and maintained an anatomical reduction over time. All patients also recovered a painless normal gait. Table 1 lists distribution of fracture characteristics (fracture location, coronal/sagittal deformity and Pauwel's angle) at time of injury.

We obtained averaged time intensity curves, based on the DCE-MRI's fit parameters, of the entire FH and the four quadrants for both the fractured side and contralateral matched control (Fig. 2). Analysis revealed a significant (p < 0.05) compromise of both arterial inflow (83.1 and 73.8% decrease in IAUC and peak, respectively) and venous outflow (243.2% decrease of K_{el}) in the fractured side FH when compared to the contralateral control. A greater decrease was noted in arterial inflow within the injury side superior-medial quadrant with a significant decrease of 71.6% (IAUC) and 68.5% (peak) when compared to the uninjured side. Fracture characteristics, including subcapital FNF, varus deformity, posterior roll-off $>20^{\circ}$ and a 30–50° Pauwel's angle demonstrated a greater decrease in perfusion (IAUC and peak) when compared to contralateral controls, although these differences were not statistically significant. All cases maintained significant FH perfusion despite suffering a great decrease in blood flow following an FNF. None of the patients demonstrated ON changes in the preoperative MRI.

Post-operative MAVRIC-MRI revealed a high rate (87%; 20/23) of FH ON segments. All ON segments developed in the anterior aspect of the supero-medial quadrants (area

Table 1 Fracture characteristics (N = 23; male = 6, female = 17)

Characteristic	Number	Percent
Fracture location		
Subcapital	11	47.8
Midcervical	12	52.2
Coronal deformity		
None	2	8.7
Varus	4	17.4
Valgus	17	73.9
Posterior roll-off		
<20°	15	65.2
>20°	8	34.8
Pauwel's angle		
30°-50°	10	43.5
>50°	13	56.5









Fig. 2 Depicts the femoral head (FH) quadrant analysis that was performed and the averaged time-intensity curves, based on the preoperative dynamic contrast-enhanced-MRI's fit parameters, of the

of largest decrease in perfusion on pre-op DCE-MRI). FHs which developed ON showed a significantly higher decrease in perfusion, on pre-op DCE-MRI, to both the entire FH (70.5%; p = 0.001) and to the supero-medial quadrant (71.4%; p = 0.007) when compared to those that did not develop ON (Fig. 3). Comparing fracture side to the contralateral control, those that developed ON segments had greater decreases in perfusion to both the entire FH (79.5% p = 0.002 versus 25.4% p = 0.361) and the supero-medial

entire FH and the four FH quadrants; in comparison of the fracture side and the uninjured contralateral side

quadrant (66.6% p = 0.040 versus 47.1% p = 0.184) than those without ON. All fractures demonstrated decreased venous outflow (K_{el}) when compared to controls, but those that developed ON segments did not demonstrate a greater decrease in outflow than those that did not develop ON. This suggests a decrease in venous outflow (K_{el}) does not correlate with the ON development. The ON segments decreased in size over time (6.68 \rightarrow 5.84 cm³) and only involved a small percentage of the FH (13.9 \rightarrow 12.8%). Based on MRI





Fig. 3 Depicts a post-operative MAVRIC-MRI revealing the osteonecrosis segment in the superior quadrant of the femoral head. The graphs demonstrate the average time-intensity curves, based on the

data, 20% (4/20) of those patients with ON segments demonstrated minimal subchondral collapse (<2 mm), but none were symptomatic nor showed signs of collapse upon latest radiographic follow-up.

Discussion

Development of ON in the FH following FNF is a major concern, and usually dictates surgical treatment. Using DCE-MRI, we demonstrated maintenance of substantial perfusion to the entire FH, despite suffering a significantly compromised blood flow following a displaced FNF. A decreased FH perfusion of more than 67% resulted in subsequent ON development based on MAVRIC-MRI. All ON segments developed in the anterior superior-medial FH segment,

pre-operative dynamic contrast-enhanced-MRI's fit parameters, of the entire FH and the supero-medial quadrant comparing those patients who developed osteonecrosis segments and those who did not

which correlated with (1) area of greatest decrease in dynamic perfusion on pre-operative DCE-MRI; (2) the area mainly supplied by the superior retinacular artery and (3) the most distant region from the presumed residual sources of perfusion (inferior retinacular and foveolar arterial systems). Our cohort had a high ON incidence (87%) based on MRI, but ON segments were small (13% of the FH) and did not appear to lead to FH collapse on radiographs nor negatively affect the clinical outcomes at latest follow-up. Osteone-crosis segment and subchondral collapse on MRI were not noted on radiographs given the tomographic nature of MR acquisition and superior tissue contrast, yielding superior sensitivity to focal ON and subchondral collapse.

A small study group, hindering the study power for outcome prediction, limits our investigation. However, the primary purpose of the study was still achieved, which was to evaluate residual perfusion preoperatively and correlate it with the post-operative MRI findings of ON in the FH. We understand that a longer clinical and radiographic followup is required to assess the FH viability. However, at latest follow-up (18.7 months; range 12-45), patients were asymptomatic without radiographic evidence of segmental collapse in any patient. Additionally, based on MRI findings at 12 months postoperatively, no patient presented any of the prognostic factors for progression of the ON segment to FH collapse [3, 53-55]. Additionally, we rely on indirect measures, using advanced imaging, to evaluate biologic changes and FH viability. However, direct measures (histological) are not achievable in clinical practice outside an animal model. Nevertheless, MAVRIC-MRI provides an excellent non-invasive method for assessment of the FH around the metal implants.

Fracture of the femoral neck acts synergistically to affect the extra/intra-osseous arterial inflow, the sinusoidal flow and/or the extraosseous/intraosseous venous outflow of the FH leading to cellular death. Both the superior retinacular system and the intraosseous nutrient artery course in close proximity to or within the femoral neck and are prone to injury in the setting of femoral neck fracture [26, 27]. This leaves the inferior retinacular system (protected by the inferior retinacula of Weitbrecht and elevated off the femoral neck) [27, 56–58] and the foveolar systems as the remaining vascular supply to the FH [4]. The protective setting of the inferior retinacula of Weitbrecht was first detailed by Smith in 1953 [59]. More recently, Papadakis el al. [58] reported an intact inferior retinacula of Weitbrecht in 98% (108/110) of displaced FNF.

In our study, the injury DCE-MRIs demonstrated markedly decreased perfusion to the entire FH, but mainly to the superior head. This area is primarily supplied by the superior retinacular system [27, 28, 32], which presumably is disrupted. Notably, significant perfusion to the entire FH was maintained, particularly in the inferior head where the inferior retinacular system predominates [27, 28, 32], suggesting this vessel is preserved. Quadrant analysis revealed a prominent decrease in perfusion to the supero-medial quadrant, as well as significantly delayed washout in the injured side as compared to the uninjured side. This delayed washout may signify an outflow problem caused by either increased intraosseous/intraarticular pressure and/or disruption of the venous system. Accumulation of hemarthrosis increases intracapsular pressure creating a tamponade effect that jeopardizes both arterial inflow and venous outflow of the retinacular system [4, 13, 14, 16, 18-20]. Our cohort demonstrated a significant decrease in venous outflow in the fractured hips when compared to the control side, but we did not appreciate a significant difference when comparing between the developments of ON segments. All our patients underwent surgical fixation urgently (<24 h post-injury),

limiting ability to evaluate tamponade effect over time. The remaining arterial supply can be compromised by rotatory and coronal malalignment of the FH [56]. Our results revealed varus deformity and posterior roll-off $\geq 20^{\circ}$ led to a greater decrease in FH perfusion, perhaps due to compression of the inferior posterior retinacular arteries. An open anatomic reduction may help restore the FH perfusion by decompressing the tamponade effect created by the hemarthrosis and by unkinking the preserved retinacular vessels.

An interruption of blood flow following an FNF has been established as the primary etiologic factor in posttraumatic ON [2]. Several investigators have used different techniques to study the residual perfusion to the FH following FNF to identify the patients at risk for ON development and segmental FH collapse. Heuck et al. [60] implemented subtraction arteriography to show 97% of cases with established ON demonstrated changes in the arterial system supplying the FH. Intraosseous oxygen pressure measurements showed a correlation between elevated intraosseous pressure and decreased oxygen pressure noted in FH with ON [61, 62]. Sugamoto et al. [63.], using Doppler-laser flowmetry, documented severe vascular damage to the FH in displaced FNFs. Using bone scintigraphy, several authors reported great results with 85-90% accuracy in detecting pathologic scintigraphy changes that then developed ON [64–69]. Einert et al. [44] used 3-phase bone scintigraphy to evaluate residual perfusion and FH viability following ORIF of FNF, and reported that ON of the FH developed if there was persistent impairment of FH perfusion at 3 and 6 months postoperatively.

DCE-MRI demonstrated encouraging results for the early evaluation of FH osteonecrosis risk following FNFs using non-invasive means. Kamano et al. [70.] evaluated 29 FNF with DCE-MRI <24 h after injury and demonstrated excellent prognoses for those that had complete FH enhancement. Konishiike et al. [71.] performed a similar evaluation of 22 FNF and reported that in those with no enhancement, the DCE-MRI has high predictive value for subsequent ON risk with 89% accuracy. They detected ON of the FH when there was \geq 70% decrease in perfusion. In our study, subjects that developed ON had decreased perfusion ranging between 67 and 78%.

The reported prognostic factors for progression of ON to FH collapse include: (1) extent of the ON segment; (2) location of the lesion and (3) presence of bone marrow edema in the proximal femur [3]. Nam et al. [54] reported an FH collapse rate of 46–83% of medium- to large-size lesions (>30–50%) and 5% for small lesions (<30%). All except one of the ON segments in our cohort were small lesions (<30%; range 3.0–24.6%), with one patient with a medium lesion (31.8%). Nishii et al. [55] reported higher progression of collapse in lesions involving >2/3 of the weight bearing area. Ito et al. [53] reported significant association between

presence of bone marrow edema in the proximal femur and subsequent symptomatic collapse of the FH. None of the ON segments identified in our cohort occupied >2/3 of the weight bearing area nor were associated with bone marrow edema. In 1971, Garden [14] suggested hip joint incongruity, as result of severe malreduction following osseous union, leads to a remodeling process/late segmental collapse in the FH. In our cohort, all patients had an anatomic reduction and the fixation led to osseous union in anatomic position with hip joint congruity, potentially avoiding this remodeling process. Small ON segments, based on MRI, were detected in 87% of our cohort. Nevertheless, at latest follow-up no radiographic signs of FH collapse were noted.

Conclusion

An intracapsular femoral neck fracture compromises FH vascularity affecting both the inflow and outflow systems that lead to cellular death and segmental ON of the FH. Impaired vascularity and residual decrease perfusion of more than 67% will lead to ON segments. However, impairment of FH vascularity is not the sole etiologic factor for post-operative complications and FH collapse. In our cohort, an urgent open anatomic reduction coupled with an angle-and length-stable construct resulted in excellent clinical and radiographic outcomes despite high rate of small ON segments noted on MRI. We need a longer follow-up to evaluate the absolute fate of FH with ON changes.

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Compliance with ethical standards

Conflict of interest Each author certifies that he has no commercial associations (e.g., consultancies, stock ownership, equity interest, patent/licensing arrangements, etc.) that might pose a conflict of interest with the submitted article.

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Ethical approval Institutional ethical board approval has been received for this research study.

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