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Capsular Management During Hip Arthroscopy

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Abstract

Purpose of Review Hip arthroscopy is widely used for the management of intra-articular pathology and there has been growing interest in strategies for management of the hip capsule during surgery. The hip capsule is an essential structure that provides stability to the joint and it is necessarily violated during procedures that address intra-articular pathology. This article reviews different approaches to capsular management during hip arthroscopy including anatomical considerations for capsulotomy, techniques, clinical outcomes, and the role of routine capsular repair. This article also reviews the concept of hip microinstability and its potential impact on capsular management options as well as iatrogenic complications that can occur as a result of poor capsular management.

Recent Findings Current research highlights the key functional role of the hip capsule and the importance of preserving its anatomy during surgery. Capsulotomies that involve less tissue violation (periportal and puncture-type approaches) do not appear to require routine capsular repair to achieve good outcomes. Many studies have investigated the role of capsular repair following more extensive capsulotomy types (interportal and T-type), with most authors reporting superior outcomes with routine capsular repair.

Summary Strategies for capsular management during hip arthroscopy range from conservative capsulotomy techniques aimed to minimize capsular violation to more extensive capsulotomies with routine capsule closure, all of which have good short- to mid-term outcomes. There is a growing trend towards decreasing iatrogenic capsular tissue injury when possible and fully repairing the capsule when larger capsulotomies are utilized. Future research may reveal that patients with microinstability may require a more specific approach to capsular management.

Keywords Hip arthroscopy · Femoroacetabular impingement · Hip capsule · Capsular management · Capsulotomy · Capsular repair

Introduction

Hip arthroscopy is now widely used for the management of intra-articular hip pathology, including femoroacetabular impingement syndrome (FAIS) and labral tears [1, 2]. Surgical treatment for intra-articular pathology, including hip arthroscopy procedures, necessarily violates hip capsular tissue in order to gain access to the joint. The hip capsule is an important anatomical structure that provides stability and optimizes functional mobility to the joint [3, 4, 5•, 6]. There has been growing interest in the literature in understanding how to best manage the hip capsule during arthroscopic procedures.

Options for capsular management range from those that involve minimal capsular violation, such as periportal [7•, 8] or puncture capsulotomies [9••], to more extensive capsular violation, such as with interportal and T-capsulotomies [10]. Failure to appreciate and appropriately manage the capsule can result in iatrogenic capsular insufficiency and resultant joint instability (gross instability or micro-instability), postoperative seroma formation, and inferior patient outcomes [11, 12••, 13]. Recent investigations have identified the particular importance of preserving and managing the capsule in patients with borderline hip dysplasia (BHD) or tissue hypermobility/connective tissue disorders [14, 15, 16•]. The

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primary objective of this paper is to review current literature regarding hip capsular management. Understanding the various forms of capsulotomy available, identifying specific patient factors that may indicate risk for microinstability, and appreciating the risk for iatrogenic capsular insufficiency if the capsule is not adequately managed will help clinicians make informed decisions regarding capsular management.

Capsular Anatomy and Biomechanics

The hip joint has inherent stability owing to the bony congruence between the femoral head and acetabulum, with additional stability provided by the suction seal between the labrum and femoral head, the surrounding dynamic stabilizers, and the capsuloligamentous complex. The capsule is a strong fibrous lining that surrounds the joint and contributes significantly to overall stability [3]. It is composed of four structural components: the iliofemoral ligament (Y ligament of Bigelow), ischiofemoral ligament, pubofemoral ligament, and the zona orbicularis. The ischiofemoral ligament resists hip extension/internal rotation, the pubofemoral ligament resists abduction/external rotation, and the zona orbicularis resists hip distraction. The iliofemoral ligament is the strongest of the ligaments and resists external rotation and extension [4]. It is also the ligament most disrupted by capsulotomies during hip arthroscopy, and cadaveric studies have demonstrated that insufficiency of the iliofemoral ligament can result in significant loss of resistance to external rotation stresses [3–6, 17]. A recent biomechanical study evaluated the important functional role of the iliofemoral ligament during walking [18]. The authors evaluated work required by the surrounding hip musculature with an intact iliofemoral ligament compared to a model simulating an incompetent ligament and found that the effort required by the hip flexors (iliopsoas) and sartorius reduced by 54% and 41%, respectively, with an intact ligament. This finding further highlights the need for thoughtful management of the hip capsule during hip arthroscopy.

Capsulotomy Techniques and Outcomes

Periportal Capsulotomy

A periportal capsulotomy approach to capsular management involves completing the procedure through two standard arthroscopic portals, without disrupting the tissue between the two portals. The technique is performed by establishing standard anterolateral and midanterior portals and minimally dilating the capsular tissue immediately adjacent to the portals with radiofrequency ablation to improve maneuverability of instruments within the joint [8]. An air arthrogram can be used at the beginning of the procedure, prior to pulling traction on the leg, to break the suction seal of the joint and improve the ease of achieving adequate joint distraction [19]. The periportal capsulotomy technique has been found to provide safe and sufficient access to the intra-articular space, without the need to further violate the capsular tissue.

Given the limited capsular tissue violation and ability to maintain the integrity of the iliofemoral ligament, it may not be necessary to routinely repair periportal capsulotomy sites. A retrospective cohort analysis of functional outcomes following unrepaired periportal capsulotomies in patients undergoing hip arthroscopy for FAIS found that at 2-year follow-up patients had sustained improvement in clinical outcomes with no evidence of postoperative instability [7•]. There may be instances however in which a repair or even plication of these capsulotomy sites should be considered, such as in the case of patients with generalized ligamentous laxity or joint hypermobility [20, 21••]. In these situations, closure/plication of the midanterior portal, which lies within the substance of the iliofemoral ligament, can be performed, but it may not be necessary to close the anterolateral portal as it lies within the "capsular interval" between the midanterior and anterolateral portal. A notable additional advantage of this conservative approach to capsule management is that it is not necessary for patients to use a brace or restrict their range of motion (ROM) in the immediate postoperative period.

Puncture Capsulotomy

A puncture capsulotomy approach has also been described as an option for addressing intra-articular pathology, which involves minimal violation of the capsular tissue [22]. Similar to the periportal approach, this option involves completing the procedure through various portal sites instead of cutting the capsule between portals, and similarly does not routinely require capsular repair. This technique uses four portals sites (anterolateral, anterior, midanterior, and Dienst portals), with the option again to use radiofrequency ablation to minimally debride capsular tissue immediately adjacent to the portal sites to improve instrument maneuverability. A recent retrospective review of functional outcomes following the use of puncture capsulotomy during the treatment of FAIS demonstrated significantly improved functional outcomes at minimum 2-year follow-up with a minimal complication rate [9•].

Interportal and T-Capsulotomy

An interportal capsulotomy involves incising the capsule transversely and connecting the two portals established at the beginning of the procedure, typically the anterolateral and midanterior (or direct anterior) portals. This technique

is performed by first establishing the anterolateral and midanterior portals in the usual fashion and then connecting them with a bladed instrument [10]. Importantly, an adequate amount (~1cm) of capsular tissue should remain on the acetabular side of the capsulotomy so a repair or plication can be performed at the conclusion of the procedure. Particular attention should be paid to the acetabular capsular remnant throughout the remainder of the procedure as a high rate of damage to the iliofemoral ligament during subspine decompression in the setting of a transverse interportal capsulotomy has been identified [23]. Cadaveric evaluation after interportal capsulotomy has also revealed that there is a short distance from the edges of the capsulotomy to the rectus femoris direct and reflected heads laterally (avg 6.8 and 6.3 mm, respectively) and the iliocapsularis medially (avg 11.5 mm) [23]. Surgeons should be aware of these anatomical considerations when performing this procedure to avoid potential iatrogenic injuries to the pericapsular structures. There is a growing understanding of the importance of these structures, particularly the iliocapsularis. A recent review of the iliocapsularis in hip pathology revealed that it may play an important role as a dynamic stabilizer of the hip by tightening the anterior capsule [24]. This may be particularly important for patients with bony instability due to insufficient acetabular containment, such as those with BHD.

An interportal capsulotomy can be converted to a T-shaped capsulotomy if desired, or if additional visualization is needed distally or posterolaterally [25]. This can be accomplished by introducing a bladed instrument through a distal anterolateral accessory portal and creating a vertical incision in the capsule, perpendicular to the interportal capsulotomy. Notably, if it is anticipated at the beginning of the procedure that a T-capsulotomy might be needed for visualization, the surgeon should shorten the length of the interportal capsulotomy as the vertical limb will improve visualization enough that an extended interportal incision may not be necessary, which can avoid unnecessary iatrogenic damage [25].

Interportal and T-capsulotomies are not benign procedures; they have profound impacts on joint stability. A cadaveric study evaluating hip mechanics following various capsulotomy types found that baseline hip ROM increased by 7% for a 4-cm interportal capsulotomy and 13% for a 6-cm interportal capsulotomy [26]. Similar results were found by Abrams et al. in a cadaveric study evaluating hip external rotation following various capsular states (intact, interportal capsulotomy, T-capsulotomy, repaired capsulotomies, and capsulectomy) [3]. The authors found that a T-capsulotomy increased hip external rotation even more than an interportal capsulotomy. A recent study by O'Neill et al. used an in vivo intraoperative model to evaluate distraction distances under various axial traction loads, based on various capsular states [27]. The authors found that an interportal capsulotomy significantly increased the distraction distance compared to a native capsule, but that a capsular repair restored the distraction distance to that similar to a native capsule, under all traction forces ranging from 25 to 100 pounds. Notably, these studies evaluated the ability to restore time zero capsular stability but do not evaluate capsular healing, the durability of the repairs, or clinical outcomes following repair.

Comparing Capsulotomy Types

Selecting the type of capsulotomy to use for each patient is based on several factors, ranging from surgeon preference to patient-specific factors and intra-articular pathology to be addressed. Periportal and puncture-type capsulotomies provide more limited visualization compared to interportal and T-capsulotomies. Cvetanovich et al. demonstrated in a cadaver model that the cross-sectional area of intra-articular visualization increases with increasing sizes of interportal and T-shaped capsulotomies [25]. It should be noted however that while these more extensive capsulotomies do improve visualization, it does not mean that the more capsular preserving approaches prevent the ability to adequately perform the necessary intra-articular work. Zhang and colleagues demonstrated that femoroplasty for large cam deformities can be safely and adequately performed with the use of a periportal approach to the capsulotomy [7•].

Several studies have directly compared some of the various capsulotomy types. The Multicenter Arthroscopic Study Group (MASH) performed a retrospective cohort study evaluating 2-year outcomes between patients that received either an interportal or T-capsulotomy during the treatment of FAIS [28••]. The authors analyzed 658 patients (329 interportal capsulotomies, 329 T-shaped capsulotomies) and found that capsulotomy type was not a predictor of 2-year outcomes or the percentage of patients achieving a minimal clinically important difference (MCID), patient acceptable symptomatic state (PASS), or substantial clinical benefit (SCB). Christoforetti and colleagues compared outcomes following either a periportal capsulotomy without closure or interportal capsulotomy with closure for the treatment of FAIS [29], and found that all patients had significant improvement in clinical outcomes at minimum 2-year follow-up and there was no difference in outcomes based on the capsulotomy type.

Evidence Supporting Capsular Closure

The decision whether or not to repair the capsule has been heavily investigated in recent years. This discussion pertains primarily to whether or not to repair interportal and T-capsulotomies, as a repair is typically not required or considered for periportal and puncture capsulotomies,

unless the patient has ligamentous laxity or joint hypermobility. Numerous recent studies, including a randomized control trial [30••], several prospective comparative studies [31–34], and various systematic reviews with meta-analyses, have investigated the role of capsule closure and largely found improved outcomes with capsular repair [30••, 31–34, 35••, 36••, 37–41].

A randomized controlled trial performed by Economopoulos et al. evaluated 2-year outcomes after assigning 150 patients to one of three groups: T-capsulotomy without closure, interportal capsulotomy without closure, and interportal capsulotomy with closure [30]. The authors found higher modified Harris Hip Score (mHHS), Hip Outcome Score-Activities of Daily Living (HOS-ADL), and Hip Outcome Score-Sports-Specific Subscale (HOS-SSS) with capsule closure compared to patients who did not undergo capsule closure.

Several short-term follow-up studies found evidence supporting capsule closure [31, 34]. Frank et al. performed a prospective cohort study comparing clinical outcomes after T-capsulotomy closure with either a partial (closing only the vertical limb, interportal left open) versus complete closure of both the vertical limb and interportal incision [31]. Sixty-four patients with minimum 2-year follow-up demonstrated superior outcomes (HOS-SSS and patient satisfaction) with complete closure compared to partial repair, though there was no difference in HOS-ADL or mHHS. Notably, the overall revision rate was 6.25% (4 patients) with all of these patients being in the partial repair group, equating to a 13% revision rate for the partial repair group (4 of 32 patients). Domb and colleagues recently evaluated minimum 2-year clinical outcomes and return to sport in competitive athletes who were treated with hip arthroscopy for FAIS and underwent an interportal capsulotomy that was either closed (84 hips) or left unrepaired (53 hips) [34]. The repaired group demonstrated significantly greater improvements in the Nonarthritic Hip Score (NAHS), HOS-SSS, and VAS score, and were significantly more likely to achieve MCID for HOS-SSS. The repaired group also trended toward a higher rate of return to sport at 80.6% versus 65.9% in the unrepaired group ($p = 0.129$), but the study was not adequately powered to evaluate this outcome measure.

Several midterm comparative studies have reported superior outcomes with capsule closure [32, 33]. Philippon and colleagues compared 42 patients without repair to 84 patients with repair, at mean 7.3- and 6.4-year follow-up, respectively, and found that patients in the repaired group achieved significantly higher scores for mHHS and HOS-ADL [32]. The repair group was also more likely to achieve a MCID for HOS-ADL and HOS-Sport compared to the unrepaired group. Notably, patients in the unrepaired group were also 6.8 times more likely to have undergone total hip arthroplasty (THA) during the follow-up period. Domb et al. similarly reported improved outcomes with closure in their minimum 5-year follow-up study of 130 patients who underwent hip arthroscopy and received either a capsular repair (n=65) or had their capsule unrepaired (n=65) [33]. The repair group demonstrated significant improvement in all outcomes measures (mHHS, NAHS, HOS-SSS, and VAS for pain) at both 2- and 5-year follow-up while the unrepaired group had a significant decrease in mHHS and patient satisfaction from 2- to 5-year follow-up. The unrepaired group also had a higher rate of conversion to THA compared to the repaired group (18.5% vs 6.4%).

Additional support for the benefit of routine capsular closure draws from studies investigating patients who underwent revision hip arthroscopy for capsular incompetency and hip instability [11, 12••]. Aoki and colleagues retrospectively reviewed 31 patients who underwent an isolated capsular repair during revision hip arthroscopy [12••]. Preoperatively, 87% of patients reported hip pain with activities of daily living, all patients had pain with sports or exercise, and all patients had evidence of capsular changes on pre-revision MRAs. Following revision surgery to repair the capsule, patients' mHHS improved by 20.3 points, HOS-SSS improved by 25.1 points, 87% reported improved physical ability, and 78% reported improved pain. Similarly, Nho and colleagues evaluated 90 patients undergoing revision hip arthroscopy and found 54.4% of these patients had MRI and intraoperative evidence of capsular incompetency [11]. Following capsular repair, these patients had significant improvements in HOS-ADL, HOS-SSS, mHHS, and VAS for pain, though only 66.7% achieved MCID at minimum 2-year follow-up. Collectively, these studies support routine capsular closure as they demonstrate that iatrogenic capsular insufficiency can result in poor outcomes, which subsequently improve once a revision surgery is performed to repair the capsule.

Evidence Against Capsular Closure

Several studies have reported contrasting results regarding the role of capsular repair and suggest that routine closure may not be necessary [42•, 43–45]. Bech et al. recently performed a patient-blinded randomized control trial evaluating clinical outcomes at 3 months and 1 year after hip arthroscopy performed with an interportal capsulotomy that was either closed or left unrepaired [42•]. A total of 116 patients were randomized and 109 were available for follow-up (53 unrepaired, 56 repaired). The Copenhagen Hip and Groin Outcomes Score (HAGOS) was collected at both 3 months and 1 year postoperatively and the authors found no difference in outcomes at either time point. The repaired group did trend towards higher achievement of minimally important changes (MIC) at 12 months compared to the unrepaired group (82%

vs 68%, $p = 0.09$). The authors did not report on the rate of revision surgery or conversion to THA.

Mei-Dan and colleagues performed several imaging-based studies using MRI to evaluate capsular healing at 6 and 24 weeks after surgery [43, 45]. The first study randomized 15 patients undergoing bilateral hip arthroscopy to receive a small- to medium-sized (<3cm) interportal capsulotomy that was closed on one side and left unrepaired on the contralateral side, with the patient blinded to the treatment received for each hip [45]. MRI was performed at 6 and 24 weeks after surgery and the imaging was blindly evaluated by two musculoskeletal radiologists. At 6 weeks postoperatively, the capsule appeared continuous in 53% of patients (n=8) who underwent repair and 20% (n=3) who did not undergo repair, but all capsules appeared continuous at 24-week follow-up and there was no difference in capsular thickness between groups. A second study was performed by the authors with similar methodology, with the exception of including patients undergoing both unilateral and bilateral hip arthroscopy [43]. Patients were again randomized to receive either closure or no closure following an interportal capsulotomy, bilateral patients were randomized for the first hip and the contralateral hip received the opposite treatment, and the musculoskeletal radiologists interpreting the studies at 6 and 24 weeks postoperatively were blinded to treatment allocation. Similar trends in capsular appearance were again identified after surgery. At 6 weeks postoperatively the capsule was in continuity in 43.4% of the capsular repair group and 15.4% of the unrepaired group but was in continuity in most patients by 24 weeks (83.3%, 25/30 hips) and there was no difference between treatment groups. Notably, these studies did not include any evaluation of clinical or functional outcomes after surgery.

It is important to highlight the short-term follow-up completed in these studies suggesting routine capsular repair may not be necessary. No mid-term follow-up studies are available to support the role of routinely leaving the capsule unrepaired. Longer-term follow-up studies are required, particularly given the evidence by Domb et al. that patients with repaired and unrepaired capsules had similar clinical outcomes at 2-year follow-up but patients with unrepaired capsules had deterioration in clinical outcomes at 5-year follow-up, which was not seen in patients with repaired capsules [33]. Finally, there is the concern for gross hip instability and dislocations if the capsule is left unrepaired following a large capsulotomy. A systematic review of hip dislocations or subluxations following hip arthroscopy investigated the risk factors for this complication among 11 patients reported in 10 articles [46]. The majority of patients received an interportal capsulotomy (n=10), one patient received a T-capsulotomy, and capsular closure was only performed in 2 of the cases (both interportal). Statistical analyses were not performed in this study but with 82% (9 of 11 patients) of patients having an unrepaired capsule, and it does suggest this to be a risk factor for postoperative hip instability.

Special Consideration—Microinstability

Microinstability, or subtle extraphysiologic movement of the femoral head within the acetabulum that results in subjective instability and hip pain, is a concept that has been gaining acceptance in recent years [15] and surgeons should be aware of factors that can contribute to this diagnosis as it can alter the approach to capsular management. An international panel of experts on hip microinstability recently published a consensus study using Delphi methodology to identify patient variables that suggest a patient might have microinstability [47••]. A series of questionnaires were completed by 27 members and variables were broken down into 14 major factors and 20 minor factors. All variables were subcategorized into patient history, physical examination, and imaging findings. The panel determined that both a minimum of six major factors and a minimum of four major or minor factors for each subcategory were required for diagnosis. To briefly review some of the major contributing factors: patient history included hip pain, sensations of instability or giving away, connective tissue disorders, or lack of a clear diagnosis to explain a patient's symptoms; physical examination included internal or external rotation >60°, positive anterior apprehension with hyperextension external rotation, or generalized hypermobility (as defined by Beighton score > 5 out of 9); and imaging factors included preoperative x-ray findings suggestive of dysplasia or femoral head subluxation or intra-operative findings such as ease of joint distraction with longitudinal traction prior to beginning the procedure or the ability to achieve 8–10mm of joint distraction with <40mm of fine screw traction. The authors state that the relative complexity of this diagnostic tool also illustrates the difficulty of diagnosing microinstability.

Ease of distraction was one of the major factors contributing to the diagnosis of microinstability [47••], and several recent studies have investigated ways to either preoperatively or intra-operatively predict patients that will be easier to distract [48–50]. A systematic review demonstrated that hip capsule thickness can be consistently measured using MRI and that a thinner anterior capsule may be associated with clinical laxity [48]. Aoki and colleagues evaluated joint distraction distances at 0 lb and 100 lb of axial traction force in an in vivo model and found that female sex and decreased thickness of the superior hip capsule were predictors of increased joint distraction [49]. Similarly, Spiker and colleagues found that female patients and those with a Beighton score > 4 were more likely to have thinner superior hip capsules on MRI [50].

Given the relatively new concept of hip microinstability and the inconsistency in its definition and diagnosis, there is an absence of studies investigating clinical outcomes as they relate to capsular management during the treatment of FAIS for patients with microinstability. There are several studies that investigate specific patient populations which would be categorized as having microinstability, such as those with BHD. Yang et al. recently evaluated clinical outcomes and changes in hip capsular thickness before and after surgery in 59 patients with BHD [16•]. All patients underwent an interportal capsulotomy with capsular closure and at minimum 2-year follow-up the majority of the capsules remained closed (93.2%); however, patients with thinner anterior capsules had significantly worse clinical outcomes compared to patients with capsules that re-constituted to near preoperative thickness. Notably, there were 25 patients that formed the study group that had thinner capsules, meaning 42.4% (25 of 59) of patients only partially healed their capsules. Therefore, for patients where there may be concern for microinstability, it may be beneficial to consider a periportal or puncture-type approach capsulotomy or to consider a capsular plication if an interportal or T-shaped capsulotomy is performed [51, 52].

Capsular Complications

Post arthroscopy iatrogenic capsular insufficiency is one cause for poor outcomes following primary hip arthroscopy and should be evaluated for in patients without residual cam morphology or a new labral tear on postoperative imaging. The residual capsular insufficiency can lead to microinstability, hip subluxation, and even hip dislocation. For these patients, an MRI arthrogram (MRA) can evaluate the integrity of the anterior hip capsule. O'Neill et al. reported that in 31 patients undergoing revision hip arthroscopy for isolated capsular repair, 100% of them had capsular changes on MRA [12••]. For patients with post arthroscopy capsular insufficiency, many of them improve with revision isolated arthroscopic capsular repair. In the same study by O'Neill et al., at a minimum of 3.3 years after surgery, average postoperative Harris Hip scores improved by 20.3 points, and 87% of patients reported improved physical ability and 78% of patients reported improved pain [12••].

In certain cases of aggressive capsular violation, there is insufficient tissue for repair. Capsular reconstruction can be performed as a salvage operation to improve hip stability. A systematic review of biomechanical studies on capsular reconstruction by Ankem et al. reported that capsular reconstruction resulted in improved resistance to maximum distraction force and rotational stability compared to capsulectomy, but did not restore the biomechanics to the native capsule state [53]. A variety of capsular reconstruction techniques have been reported including iliotibial band autograft (ITB), dermal allograft, and Achilles tendon allograft [54–56]. Fagotti et al. reported 2-year outcomes from 18 patients who underwent ITB capsular reconstruction and 18 patients who underwent dermal allograft reconstruction. There was an identical failure rate of 22% in both groups. However, the ITB group had improved clinical outcomes compared to the dermal allograft group. A recent biomechanical study by Pasic et al. found that both ITB and Achilles tendon allograft capsular reconstructions improved rotational hip stability and coronal plane hip stability compared to capsulectomy [56]. In cases of large postoperative capsular deficiency, capsular reconstruction can provide improved hip stability to patients.

Conclusion

The hip capsule plays an integral role in providing stability to the joint and optimizing its functional mobility; therefore, surgeons should take a thoughtful approach to its management during hip arthroscopy. A periportal or puncture capsulotomy, while minimizing tissue violation, provides less visualization of the joint than the more extensive interportal or T-capsulotomy. Periportal and puncture capsulotomies do not routinely require repair, but numerous studies in recent years suggest that it may be beneficial to routinely close more extensive capsulotomies such as interportal and T-capsulotomies. Patient-specific variables, particularly those that might suggest a patient is at risk for microinstability, should also be considered when determining the best approach to capsular management. Finally, surgeons should understand the anatomical and clinical significance of performing hip capsulotomies and that if not managed thoughtfully, they can result in significant iatrogenic damage and poor patient outcomes.

Compliance with Ethical Standards

Conflict of Interest Matthew Hartwell and Samuel Moulton declare that they have no conflict of interest. Alan Zhang is a consultant for Stryker and Depuy-Mitek.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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- • Of importance
- •• Of major importance

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