Comparison of Minimally Invasive Direct Anterior Versus Posterior Total Hip Arthroplasty Based on Inflammation and Muscle Damage Markers

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Background: A number of surgical approaches are utilized in total hip arthroplasty. It has been hypothesized that the anterior approach results in less muscle damage than the posterior approach. We prospectively analyzed biochemical markers of muscle damage and inflammation in patients treated with minimally invasive total hip arthroplasty with an anterior or posterior approach to provide objective evidence of the local soft-tissue injury at the time of arthroplasty.

Methods: Twenty-nine patients treated with minimally invasive total hip arthroplasty through a direct anterior approach and twenty-eight patients treated with the same procedure through a posterior approach were prospectively analyzed. Perioperative and radiographic data were collected to ensure cohorts with similar characteristics. Serum creatine kinase (CK), C-reactive protein (CRP), interleukin-6 (IL-6), interleukin-1 beta (IL-1β), and tumor necrosis factor-alpha (TNF-α) levels were measured preoperatively, in the post-anesthesia-care unit (except for the CRP level), and on postoperative days 1 and 2. The Student t test and Fisher exact test were used to make comparisons between the two groups. Independent predictors of elevation in levels of markers of inflammation and muscle damage were determined with use of multivariate logistic regression analysis.

Results: The levels of the markers of inflammation were slightly decreased in the direct-anterior-approach group as compared with those in the posterior-approach group. The rise in the CK level in the posterior-approach group was 5.5 times higher than that in the anterior-approach group in the post-anesthesia-care unit (mean difference, 150.3 units/L [95% CI, 70.4 to 230.2]; $p < 0.05$) and nearly twice as high cumulatively (mean difference, 305.0 units/L [95% CI, −46.7 to 656.8]; $p < 0.05$).

Conclusions: We believe that the anterior total hip arthroplasty approach used in this study caused significantly less muscle damage than did the posterior surgical approach, as indicated by serum CK levels. The clinical importance of the rise in the CK level needs to be delineated by additional clinical studies. The overall physiologic burden, as demonstrated by measurement of inflammation marker levels, appears to be similar between the anterior and posterior approaches. Objective measurement of muscle damage and inflammation markers provides an unbiased way of determining the immediate effects of surgical intervention in patients treated with total hip arthroplasty.

Level of Evidence: Therapeutic Level II. See Instructions to Authors for a complete description of levels of evidence.

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A commentary by Paul Manner, MD, is linked to the online version of this article at jbjs.org.

Two commonly used total hip arthroplasty approaches—the anterior, or Smith-Petersen, approach and the posterolateral approach—have been used with similar long-term success rates[1,2]. Continuing refinements of prostheses, instrumentation, and techniques have led to minimally invasive arthroplasty. Both anterior and posterior approaches have been adopted for minimally invasive surgery[3,4], and a retrospective study showed improved early clinical outcomes with the direct anterior approach[5] despite the steep learning curve that has been reported for this procedure[6].

Some of the challenges that investigators face when assessing the efficacy and results of minimally invasive arthroplasty are the biases inherent in surgeons' and patients' expectations. The measurement of serum markers of muscle damage and inflammation offers an objective method with which to determine the relative invasiveness of procedures. This technique helped form the rationale for laparoscopic cholecystectomy[7], herniorrhaphy[8], and hysterectomy[9]. This technique has been used to compare minimally invasive surgery and standard posterior approaches for total hip arthroplasty, with minimal differences reported[10-12]. Recently, similar methods were used to analyze total knee arthroplasties, and few differences in the increases in cytokine levels were found with various approaches[13]. The authors of that study stressed the importance of having a clear measureable outcome to define surgery as minimally invasive.

Although prior investigations have shown minimal effects related to incision length, we are not aware of any study comparing objective markers of muscle damage between anterior and posterior total hip arthroplasty. Conceptually, the anterior approach should cause less damage than the posterior approach, as it is performed through an internervous, intermuscular plane without muscle transection. We sought to determine whether levels of biochemical markers of muscle damage and inflammation differ between minimally invasive total hip arthroplasties done through anterior and posterior approaches. We hypothesized that patients treated with an anterior approach would have a significantly lower postoperative rise in the levels of these markers.

Materials and Methods

After receiving approval from their institutional review board, three total joint arthroplasty surgeons (A.S.U., J.H.G., and A.S.H.) in an urban academic medical center prospectively enrolled their patients for this study. Two of the surgeons (J.H.G. and A.S.H.) utilize the posterior approach, whereas the third utilizes the direct anterior approach. This formed the basis for two cohorts: those treated with a minimally invasive posterior approach and those treated with a minimally invasive direct anterior approach. Objective measurements of serum levels of inflammatory cytokines and a marker of muscle damage were compared between these two cohorts. Any patient with osteoarthritis of the hip who had had unsuccessful nonoperative management and for whom total hip arthroplasty was indicated, who had not had prior hip surgery, and who could tolerate general anesthesia was considered to be a candidate for inclusion. Exclusion criteria included inflammatory arthropathies, prior hip surgery, prior infection, an inability to tolerate general anesthesia, an arthroplasty to treat a fracture, or an unwillingness to participate in the study. Patients were sequentially enrolled if they met the above inclusion criteria.

Muscle damage was the primary outcome indicator, and a power analysis was conducted with use of 80% power and an alpha value of 0.05. A rise in the serum creatine kinase (CK) level after trauma, exercise, or surgery has been shown to directly correlate with muscle damage[14-17]. An analysis using the limited data available on the rise and variability in CK levels after total hip arthroplasty revealed the need for a sample size of fifty-eight patients to detect a difference between the two groups[12,13,18]. Because of the limited data set, we confirmed the results of the power analysis using C-reactive protein (CRP) levels after total hip arthroplasty, which have been better characterized over the last twenty years[13,19,20]. This showed that a study size of fifty-six patients was needed to detect a 25% difference between the two groups.

Although the study was not a randomized trial, the patient demographics were analyzed to ensure similar cohorts (Table I). The age at the time of surgery,

TABLE I Preoperative Characteristics of the Patients*

	Anterior Group† (29 Patients)	Posterior Group† (28 Patients)	Difference in Means (95% CI)	P Value
Age *(yr)*	68.8 ± 9.1	65.1 ± 11.3	3.6 (−2.1-9.4)	0.20
Sex (% male)	34	50	15.4 (−11.1-41.9)	0.40
BMI (kg/m²)	26.3 ± 5.0	27.8 ± 5.0	1.5 (−1.4-4.3)	0.34
ASA grade	2.0 ± 0.6	1.9 ± 0.5	0.1 (−0.2-0.3)	0.80
Harris hip score *(points)*	42.4 ± 6.0	43.0 ± 11.0	0.6 (−5.8-7.1)	0.84
WOMAC score *(points)*				
Pain subscore	12.4 ± 2.0	11.2 ± 4.3	1.2 (−1.3-3.7)	0.32
Stiffness subscore	5.5 ± 1.1	4.5 ± 1.9	1.0 (−0.1-2.2)	0.07
Physical function subscore	42.3 ± 5.8	39.8 ± 13.5	4.8 (−3.7-13.3)	0.51
Total	60.1 ± 7.4	55.4 ± 18.2	4.7 (−5.5-15.0)	0.35
Preoperative thigh circumference *(cm)*				
Trochanteric ridge	56.1 ± 5.6	60.0 ± 10.1	3.6 (−2.1-9.4)	0.17
Midthigh	49.0 ± 6.1	49.5 ± 8.2	0.4 (−4.5-5.2)	0.84

*Demographic and functional data in the two cohorts were analyzed to ensure comparable groups. There were no significant differences between the two cohorts. †The values are given as the mean and standard deviation (except for sex).

TABLE II Perioperative Patient Data*

	Anterior Group† (29 Patients)	Posterior Group† (28 Patients)	Difference in Means (95% CI)	P Value
Incision length *(cm)*	12.1 ± 4.1	15.4 ± 2.9	3.4 (1.3-5.6)	0.00
Operative time *(min)*	78 ± 17.9	118 ± 19.4	37 (27.4-46.9)	0.00
Estimated blood loss *(mL)*	360 ± 191	312 ± 138	55.6 (–38.0-149.2)	0.30
Transfusion requirements *(units)*	0.96 ± 0.8	0.59 ± 0.9	0.4 (–0.1-0.9)	0.11
Hematocrit drop *(%)*	9.7 ± 4.6	8.5 ± 2.8	1.2 (–1.2-3.6)	0.33
Duration of hospitalization *(days)*	3.9 ± 1.1	3.3 ± 1.4	0.6 (–0.2-1.3)	0.10
Disposition to home at discharge *(% of patients)*	66	81	15.4 (–8.4-39.1)	0.35
Postoperative thigh circumference *(cm)*				
Trochanteric ridge	64.1 ± 6.2	66.2 ± 9.8	2.1 (–4.2-7.3)	0.48
Midthigh	53.0 ± 4.7	54.1 ± 8.6	1.1 (–4.3-5.5)	0.66
Change in thigh circumference *(cm)*				
Trochanteric ridge	7.9 ± 4.4	6.0 ± 2.1	1.9 (–0.2-1.0)	0.18
Midthigh	3.9 ± 3.7	4.2 ± 2.1	0.3 (–1.5-2.2)	0.51

*Perioperative data were compared between the two cohorts. There were no significant differences in blood loss, swelling, or postoperative disposition. There were significant differences, however, in operative time and incision length. †The values are given as the mean and standard deviation (except for disposition to home at discharge).

body-mass index (BMI), American Society of Anesthesiologists (ASA) grade, and preoperative Harris hip and Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scores were calculated[18,21]. The preoperative thigh circumferences at the trochanteric region and at the midpart of the thigh were measured to ensure similar patient body habitus[11]. These characteristics are shown in Table I.

Twenty-nine patients treated with a direct anterior approach and twenty-eight patients treated with a posterior approach for minimally invasive total hip arthroplasty were prospectively analyzed. All patients underwent general anesthesia. The procedures are described in the Appendix. The operative time, estimated blood loss, duration of hospitalization, transfusion requirements, and disposition at the time of discharge were recorded to determine if there were any differences between the early outcomes of the two different approaches. The overall drop in the hematocrit was calculated as the difference between the hematocrits on postoperative days 1 and 2 and the preoperative level. To assess muscle damage, serum CK levels were measured immediately preoperatively, immediately postoperatively, and on postoperative days 1 and 2. CRP, interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and interleukin-1 beta (IL-1β) levels and the maximum body temperature were recorded as global measures of inflammation and surgical insult[22]. The CRP level was measured preoperatively and on postoperative days 1 and 2 (and not immediately postoperatively like the cytokine levels) as it rises more slowly postoperatively compared with the levels of the locally produced markers. The cumulative rise in the cytokine and CK levels were recorded as the “area under the curve” to detect subtle differences[23]. Maximum body temperature was measured on the day of the surgery and postoperative days 1 and 2. Descriptions of the laboratory processes used to determine the cytokine levels are provided in the Appendix.

Anteroposterior pelvic radiographs made at four weeks after surgery were reviewed to examine the positions of the arthroplasty components. These anteroposterior pelvic views were used to calculate the theta angle and colinearity of the femoral stem with the femoral shaft. The theta angle was measured on all radiographs by drawing a line between the ischial tuberosities and another line along the face of the acetabular component. To measure the varus and valgus orientations of the stem, the mechanical axis of the stem was drawn relative to the lateral border of the femoral cortex and the subtended angle was recorded. Outliers were defined as a stem position in $>2°$ of varus[19] and a cup abduction angle of $<55°$[20,24,25].

Statistical comparison of the anterior and posterior groups was carried out with use of the Student t test for continuous variables and the Fisher exact test for binomial data. Multivariate analysis was also conducted for each biochemical marker at each time point to determine independent predictors of marker-level elevation. Specifically, bivariate analysis was conducted with use of age, sex, BMI, surgical approach, ASA class, incision length, operative time, transfusion requirements, change in thigh circumference at the trochanteric ridge and midpart of the thigh, and duration of hospitalization as independent variables. Any associations seen during bivariate analysis were modeled with use of logistic regression analysis to find independent predictors of an elevation in biochemical marker levels.

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Results

Postoperative patient data were compared between the anterior and posterior-approach groups. As seen in Table II, the average incision length for the posterior approach was 3 cm longer than that for the direct anterior approach, and this difference was significant. The average operative time was also significantly longer for the surgery done with the posterior approach (118 versus seventy-eight minutes). Otherwise, the patients had similar surgical parameters apart from the approach that was used. There were no significant differences in the cumulative hematocrit decrease (9.7% versus 8.5%),

TABLE III Radiographic Analysis*

	Anterior Group (29 Patients)	Posterior Group (28 Patients)	Difference in Means (95% CI)	P Value
Femoral component position† *(deg)*	0.60 ± 1.6	0.70 ± 1.2	0.1 (–0.7-1.0)	0.81
Femoral component position in >2° of varus *(% of patients)*	15	19	3.8 (–16.7-24.4)	1.00
Acetabular abduction angle† *(deg)*	48.5 ± 3.3	46.9 ± 5.6	1.6 (–0.3-4.6)	0.20
Acetabular abduction angle <55° *(% of patients)*	97	93	3.9 (–10.5-10.8)	0.99

*Postoperative anteroposterior pelvic radiographs obtained at the four-week follow-up visit were reviewed to determine the femoral and acetabular component positions. There were no significant differences between the two groups. †The values are given as the mean and standard deviation).

estimated blood loss (360 versus 312 mL), or transfusion requirements (0.96 versus 0.59 unit). The percentages of patients discharged home (66% versus 81%) and the average durations of hospitalization (3.9 versus 3.3 days) were comparable between the groups. A comparison of postoperative changes in the thigh circumference at the midpart of the thigh and the trochanteric ridge was advocated as a measure of surgical trauma and postoperative swelling in a randomized trial comparing minimally invasive and standard total hip arthroplasty[11]. There were no significant differences in the absolute values or in the changes from the preoperative values between the groups in our study.

The findings of the radiographic analysis of the femoral stem and cup placement are presented in Table III. There were no significant differences between groups with regard to the placement of the implants. The average stem position was 0.6° of varus in the anterior group compared with 0.7° in the posterior group. Fifteen percent of the femoral stems were in >2° of varus in the anterior group, and 19% were in >2° of varus in the posterior group. The acetabular abduction angle (theta angle) averaged 46.9° in the posterior group compared with 48.5° in the anterior cohort. One patient in the anterior group and two patients in the posterior group had an abduction angle of >55°.

The primary outcome measure was the extent of the increase in the serum levels of cytokines and CK after surgery. There was a significant difference between the two groups with respect to the increases in the CK level immediately postoperatively and on postoperative day 1 and with regard to the cumulative rise in the CK level. In the post-anesthesia-care unit, the average increase in the posterior group was 5.5 times higher than that in the anterior group, with a mean difference of 150.3 units/L (95% confidence interval [CI], 70.4 to 230.2). The difference in the cumulative rise also reached significance; the cumulative rise was nearly twice as high in the posterior group (mean difference, 305.0 units/L [95% CI, −46.7 to 656.8]). The adjusted mean differences were calculated as part of the

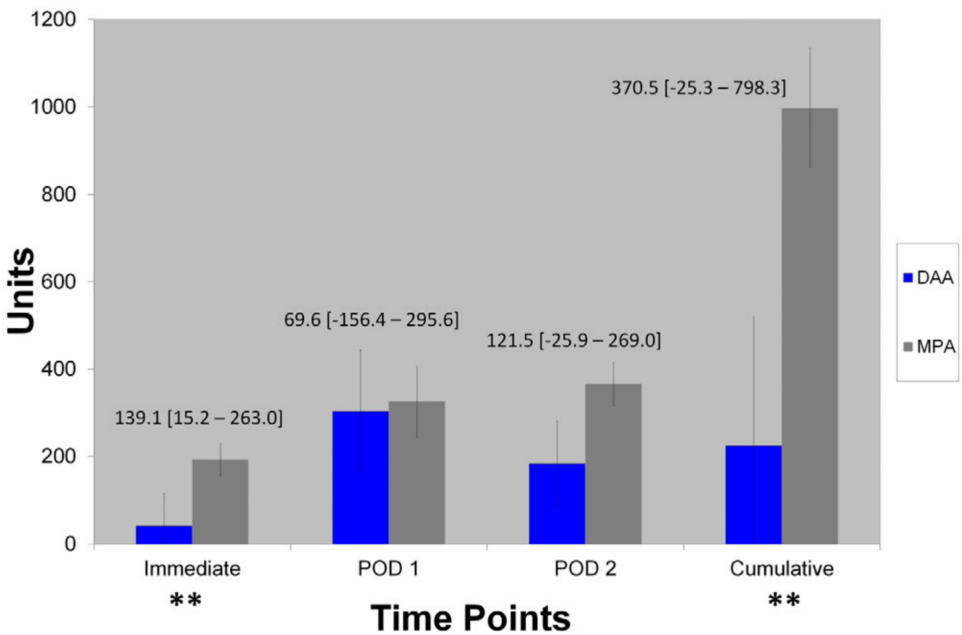

Fig. 1
Measurement of muscle damage. Serum CK levels (in units/L) were measured in the post-anesthesia-care unit (immediate) and on postoperative days 1 and 2 (POD 1 and POD 2) and were compared with the preoperative values. Significant differences between the anterior and posterior groups were seen in the post-anesthesia-care unit and in the cumulative rise (sum of the rises among all time points). Adjusted mean differences with 95% confidence intervals are displayed above the bar graphs. DAA = direct anterior approach and MPA = mini-posterior approach. ** = a significant difference between groups.

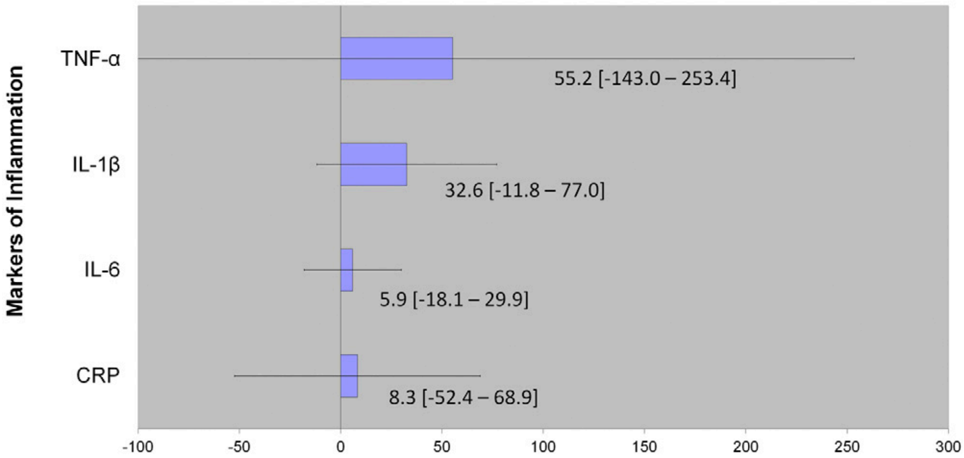

Fig. 2

Adjusted mean differences in the changes in the levels of inflammatory markers between the anterior and posterior groups. TNF-α, IL-1β, and IL-6 levels were measured in the post-anesthesia-care unit and on postoperative days 1 and 2 and were compared with the preoperative values. CRP levels were measured on postoperative days 1 and 2 and were compared with the preoperative values. The cumulative rise was calculated as the sum of the rises among all time points. The adjusted mean differences in the cumulative rises between the anterior and posterior groups are shown by the blue bars with 95% confidence intervals as error bars. The posterior group had a larger rise in the level of every marker, and the cumulative TNF-α levels differed significantly between the approaches. However, all of the confidence intervals crossed zero. The values on the x axis represent the levels of the markers in pg/mL for all markers except CRP, which is given in mg/dL.

multivariate analysis to account for differences in the two groups. These results are presented in Figure 1 and show significant differences in CK elevation in the post-anesthesia-care unit and in the cumulative rise despite two slightly different cohorts.

There were few substantial differences in the postoperative body temperatures at any point between the two cohorts. The average increase in the CRP level after the total hip arthroplasty in the posterior group was slightly higher than that in the anterior group, although no difference, at any of the time points or in the cumulative values, approached significance. The cumulative change was 240.8 mg/dL in the posterior group compared with 211.0 mg/dL in the anterior cohort. There was a twofold increase in the cumulative rise in the IL-6 level in the posterior group, as compared with that in the anterior group, but neither the difference in the cumulative values nor those in the individual values reached significance. IL-1β levels decreased at all time points compared with the preoperative levels, with a significant difference between the two groups at postoperative day 1 (the level decreased by 40.7 pg/mL in the anterior group compared with 3.4 pg/mL in the posterior group). The TNF-α levels showed the same downward trend in the anterior group but had an overall increase in the posterior group. When the cumulative values were analyzed, a 117.5-pg/mL drop was found in the anterior group compared with a 31.1-pg/mL rise in the posterior group; this difference was significant (Fig. 2).

Multivariate analysis was carried out to assess for potential confounding factors. A rise in the CK level was found to be independently associated with the surgical approach, estimated blood loss, and transfusion requirements. There was no association with operative time or incision length. Few associations were seen between the levels of markers of inflammation and surgical characteristics. IL-6 correlated with estimated blood loss, and IL-1β was associated with ASA grade, incision length, and transfusion requirements.

Early postoperative complications, including thromboembolic disease, dislocations, infections, and operative hematomas, were monitored. There was only one early postoperative complication in the anterior group. A patient developed persistent drainage on postoperative day 10 and was returned to the operating room for evacuation of the hematoma. Cultures were negative, and the patient had no further sequelae. There were no postoperative complications in the posterior group.

Discussion

This study was designed to provide an objective measure of muscle damage and inflammation following total hip arthroplasty done through two common surgical approaches. Whether or not this is a true measure of a procedure's "invasiveness" is a matter of current debate. Different surgeons define minimally invasive procedures according to different criteria, including incision length, speed of recovery, and the specific surgical dissection. While there have been comparisons between standard and minimally invasive surgery incisions, opponents of minimally invasive approaches argue that outcome measurements are biased by patient selection, perioperative care, and surgeon and patient expectations. This has led to relatively few randomized, blinded studies that have not shown significant differences between minimally invasive surgery and standard posterior approaches for total hip arthroplasty[11,26] and cadaveric studies that have semi-quantitatively demarcated the muscle damage inflicted from different surgical approaches[27,28]. Although a few investigators have performed isolated measurements of inflammatory cytokine levels, to our knowledge there are no studies in the literature in which serum markers of muscle damage and inflammation have been systematically analyzed in prospective cohorts.

In our study, there was a clear distinction between the anterior and posterior approaches in terms of the increase in serum CK levels at multiple time points postoperatively, despite similar preoperative functional and deformity scores. The 5.5-fold difference in the level of CK, a marker for muscle damage, was mitigated by the relatively modest differences in the levels of the more general inflammatory cytokines. The reason for this finding may be that the inflammatory cascade associated with total hip arthroplasty is not greatly influenced by the surgical approach and is defined more by bone removal and implant placement. The inflammatory cascade may also be partially suppressed by COX-2 (cyclooxygenase-2) antagonists, as both IL-1β and TNF-α levels showed decreases from preoperative values. There was an overall trend toward lower levels of markers of inflammation in the anterior group, as compared with those in the posterior group, and the difference reached significance for TNF-α. Further study of larger cohorts is necessary to determine if there are subtle differences in levels of inflammatory markers between surgical approaches. While our results may not support the contention that the anterior approach is less invasive, they do offer evidence of the anterior approach being a more muscle-sparing approach.

Multivariate analysis was undertaken to identify any associations with preoperative or perioperative factors that could also contribute to an elevation in the CK or inflammatory marker levels. This analysis confirmed the link between the surgical approach and rise in the CK level as well as an association between blood loss and muscle damage. Blood loss and transfusion requirements can be seen as signs of tissue trauma that correlate well with our hypothesis. There were few correlations with the markers of inflammation, although blood loss was associated with increases in both IL-6 and IL-1β levels. Changes in IL-1β levels were also associated with the ASA grade and incision length, which may indicate a higher inflammatory profile in larger, more chronically ill patients.

The strengths of this prospective study include having statistically similar cohorts in terms of the patients' age, weight, body habitus, and Harris hip and WOMAC scores. Objective laboratory data were obtained in a blinded fashion to provide an outcome measure that was independent of patients' or surgeons' expectations. Importantly, there were few other perioperative differences and no difference in implant position between the groups. The largest differences between the cohorts—namely, the differences in incision length and operative time—were controlled for with multivariate analysis that identified only surgical approach and blood loss as independent predictors of muscle damage.

The importance of any minimally invasive or muscle-sparing approach lies in how it relates to functional outcomes. There have been reports that, compared with the mini-posterior exposure, the direct anterior approach leads to better early results in terms of pain and function[5]. However, we did not assess postoperative functional outcomes in our study. With different surgeons performing the different procedures, our study had the same inherent biases due to patients' and surgeons' expectations as have been found with other protocols for evaluating minimally invasive procedures. The use of different surgeons for the different approaches is a limitation of this study. While a randomized trial with one surgeon would have provided a higher level of evidence, the surgeons chose their approach on the basis of their training and experience as opposed to any specific patient characteristics. Another limitation of our study is the lack of other objective outcome measurements. Specifically, gait analysis or electromyographic data would have been helpful to correlate the increase in the CK level with functional deficits in a more meaningful way. This study is not meant to show superiority of one approach over another. While levels of biochemical markers of muscle damage were lower with the anterior approach, the functional relevance of this finding is not yet known. We report a method with which to objectively measure some differences in modern "minimally invasive" approaches, and correlation with short and long-term functional outcome measures is needed. Also, the direct anterior approach has been shown to have a steep learning curve, and this approach and these results may not be immediately applicable without proper training and experience[6,29].

In summary, the direct anterior approach used in this study resulted in significantly less muscle damage than did the posterior exposure. The similar inflammatory profiles suggest that, although this finding may be clinically important, it is difficult to claim that the anterior approach is less "invasive." Measurement of serum inflammatory cytokine levels and use of CK as a marker of muscle damage is a specific and objective method with which to evaluate the invasiveness of surgical procedures and technical refinements. While there needs to be further clinical correlation with the results of our study, including an examination of the capacity for regeneration of the damaged muscle tissue, we believe that this methodology is an important step in defining the impact of surgical approaches in arthroplasty.

Appendix

eA Descriptions of the surgical procedures and the biochemical analysis of inflammatory markers are available with the online version of this article at jbjs.org. ■

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