The purpose of this prospective study was to analyze the biochemical markers of muscle damage and inflammation in patients treated with the mini-midvastus approach or the medial parapatellar approach for total knee arthroplasty. Of 60 patients who underwent unilateral total knee arthroplasty, 30 were treated with the mini-midvastus approach (MMV group) and 30 were treated with the medial parapatellar approach (MPP group). Serum creatine kinase, myoglobin, lactate dehydrogenase, glutamic oxaloacetic transaminase, C-reactive protein, interleukin-6, and interleukin-1β levels were measured preoperatively, immediately postoperatively (except for C-reactive protein level), and on postoperative days 1, 2, and 3. Student’s t test, Pearson’s chi-square test, and Fisher’s exact test were used to compare the outcomes between the 2 groups. Compared with the MPP group, a significant increase in serum creatine kinase level existed in the MMV group on postoperative days 2 (\(P<.08\)) and 3 (\(P<.09\)) and cumulatively (\(P<.02\)). However, significantly elevated C-reactive protein and interleukin-6 levels existed in the MPP group.

According to the serum creatine kinase levels, the mini-midvastus approach has no superiority over the medial parapatellar approach in terms of sparing muscle and may cause more muscle damage. Further study is warranted to determine the correlation between biochemical markers and functional deficits.
The medial parapatellar approach is considered standard and is the most commonly used exposure in total knee arthroplasty (TKA). This approach is well tolerated, and the results are satisfactory in a high proportion of patients. However, some investigators argue that because of the ample visualization provided by this approach, it may cause damage to the quadriceps muscle. Studies show that TKA with the standard medial parapatellar approach can result in short- and long-term deficits in quadriceps muscle function. Furthermore, disruption of blood flow caused by patellar eversion in this approach can deteriorate quadriceps muscle function.

Due to these disadvantages, surgeons have developed minimally invasive surgical techniques for TKA. Compared with conventional approaches, minimally invasive approaches use a smaller incision and avoid patellar eversion and quadriceps muscle splitting. The mini-midvastus approach is the most commonly reported minimally invasive approach. Proponents of minimally invasive surgery have reported that minimally invasive approaches result in better outcomes intra- and postoperatively. However, the American Association of Hip and Knee Surgeons outlined a possible increased rate of complications associated with this new technique, including infection, blood loss, and implant malposition.

Many studies have compared standard and minimally invasive approaches, and the results are controversial. The outcome measurements used in these studies are always subjective or putatively objective. Subjective measures, such as patient satisfaction, cosmetic appearance, or pain, can be biased by patient or investigator expectations. Putatively objective measures, such as gait speed, knee range of motion (ROM), or length of hospital stay, can be influenced by preintervention expectations. Therefore, the current study compared the 2 procedures in a new way.

Commonly, serial assays of creatine kinase and myoglobin are used to diagnose myocardial injury. Many studies have reported that the serum level of these markers can change as a result of skeletal muscle injury. They have also confirmed that elevations in serum levels of creatine kinase and myoglobin can occur after orthopedic surgery in the absence of myocardial injury. Because these serum markers are objective measurements, they can not be affected by patient or investigator expectations or by preintervention expectations. Recently, some researchers have used muscle damage markers to compare different approaches in orthopedic surgery. The feasibility and effectiveness of this new approach have been proven.

The current study prospectively compared the medial parapatellar approach with the mini-midvastus approach in unilateral TKA according to muscle damage and inflammation markers and clinical and radiological results. The study quantitatively evaluated the degree of muscle damage by measuring postoperative serum levels of various inflammation and muscle damage markers, which, to the authors’ knowledge, few studies have done. The authors hypothesized that patients treated with the mini-midvastus approach would have a significantly lower postoperative increase in the levels of these markers.

**Materials and Methods**

This prospective, nonrandomized, comparative study was approved by the Institutional Review Board of West China Hospital of Sichuan University. All patients with symptomatic osteoarthritis of the knee not responding to conservative treatment were screened as potential participants for this trial. They were informed about the purpose of the study and gave written informed consent preoperatively. The patients were assessed as to whether they met the inclusion or exclusion criteria for enrollment in the study. Because the degree of muscle damage may be associated with the complexity of the operative procedure, bias caused by such complexity had to be excluded. Thus, inclusion criteria were patients (1) aged younger than 75 years, (2) with flexion deformity <30°, and (3) with varus or valgus deformity <30°. Exclusion criteria were patients (1) with a previous knee operation and (2) with serious internal diseases that could cause TKA failure. Each patient selected the procedure that he or she preferred after the surgeon explained the potential advantages and disadvantages of each procedure. Based on a power of 80% to detect a significant difference ($P<0.05$, 2-sided) of serum creatine kinase level, which is a primary outcome indicator of muscle damage, 29 patients were needed in each group. To ensure a more than sufficient number of patients for evaluation at final follow-up, 60 patients were enrolled in the study, 30 in the medial parapatellar (MPP) group and 30 in the mini-midvastus (MMV) group.

**Surgical Technique**

All surgeries were performed by 1 joint arthroplasty surgeon (B.S.) in the same laminar air flow operating room. The surgeon had performed more than 1000 TKAs using the standard medial parapatellar approach and more than 100 TKAs using the mini-midvastus approach prior to the start of the study.

All patients underwent general anesthesia. The standard medial parapatellar approach was performed as described by Klein and Hartzband and the mini-midvastus approach as described by Reid et al. The lateral retinacular release technique was used only when the no-thumb test or towel clip test was positive. A tourniquet (500 ELC; VBM Medizintechnik GmbH, Sulz, Germany) was used in all patients at 100 mm Hg above systolic blood pressure. The tourniquet cuff was 76 cm long and 8.0 cm wide. A single layer of cast padding was applied between the skin and cuff. Many studies have reported that tourniquet time
is associated with surgery injury.²⁰ In the MMV group, the tourniquet was released intraoperatively just after prosthesis placement, whereas in the MPP group, the tourniquet was released intraoperatively before wound closure. The only device used in this study was the Scorpion NRG Knee System (Stryker, Kalamazoo, Michigan).

Outcomes Assessment

Patients' age at surgery, body mass index, American Society of Anesthesiologists (ASA) grade, knee ROM, and preoperative Hospital for Special Surgery (HSS) knee score were calculated for both groups. Preoperative knee circumference at the upper and lower poles of the patella were measured to ensure similar patient body habitus between groups. Measurements were made with the patients’ knees in extension.

Operative time, tourniquet time, estimated blood loss, length of hospital stay, transfusion requirements, and the number of patients needing lateral retinacular release were compared between the 2 groups. Estimated blood loss was calculated by the Gross formula.²¹ The overall drop in hematocrit was calculated as the difference between hematocrit levels preoperatively and on postoperative days 1, 2, and 3. To qualify muscle damage, serum creatine kinase, myoglobin, lactate dehydrogenase, glutamic oxaloacetic transaminase, and creatinine were measured immediately preoperatively, immediately postoperatively, and on postoperative days 1, 2, and 3. C-reactive protein (CRP), interleukin-6 (IL-6), and interleukin-1β (IL-1β) are well-recognized measures of inflammation and surgical insult.²² According to White et al’s report that CRP rises more slowly postoperatively than the other indexes, CRP level was only measured immediately preoperatively and on postoperative days 1, 2, and 3. All collected serum samples were stored at −20°C after being labeled in a blinded fashion. All markers were measured by the Department of Laboratory Medicine of West China Hospital certified by the College of American Pathologists.

Standing anteroposterior hip-to-ankle radiographs and anteroposterior and lateral radiographs of the operated knees were taken on the day of discharge during inpatient clinical evaluation. The postoperative images were evaluated by an investigator (J.Y.) who was not a member of the operating team. Component alignment and tibial component posterior slope angle were calculated to determine whether the component’s position was good. Fluoroscopic guidance was used to control knee rotation when radiographs were taken.

To determine the functional outcomes between the 2 groups, HSS scores and knee ROM were recorded preoperatively and at discharge. The ROM of each knee was measured in the supine position with a standard 60-cm goniometer by 2 observers (Z.Y.H., J.M.) blinded to the type of approach used. To assess intraobserver reliability, the goniometer measurement was performed 3 times (with 4-hour intervals between each measurement). The chance-corrected kappa coefficient for intraobserver agreement ranged from 0.78 to 0.86. All clinical data were compiled and collected by a research associate.

Statistical Methods

All data management and statistical analyses were performed with SPSS version 18.0 software (SPSS, Inc, Chicago, Illinois). Student’s t test was used for continuous variables, and Pearson’s chi-square test and Fisher’s exact test were used for binomial data. To determine independent predictors of marker-level elevation, multivariate analysis was also conducted. Bivariate analysis was conducted with age, sex, body mass index, surgical approach, ASA grade, estimated blood loss, incision length, operative time, tourniquet time, transfusion requirements, change in knee circumference at the upper and lower poles of the patella, and length of hospital stay as independent variables. When associations were seen during bivariate analysis, logistic regression analysis was performed to find independent predictors of an elevation in biochemical marker levels.

RESULTS

Patient Demographics

Preoperative patient demographics showed no statistically significant differences between the 2 groups in age, sex, body mass index, preoperative ROM, ASA grade, HSS score, or knee circumference (Table 1). As shown in Table 2, mean incision length in the MMV group was 3.9 cm shorter than that in the MPP group, which was significant. Mean tourniquet time was 23 minutes shorter in the MMV group than in the MPP group. No statistically significant differences existed in operative time (P = .15), estimated blood loss (P = .45), transfusion requirements (P = .65), number of patients needing lateral retinacular release (P = 1), or hematocrit drop (P = .95). Mean length of hospital stay was also comparable between the 2 groups (P = .30). Knee circumference, which was considered a measure of surgical trauma and postoperative swelling, was also measured. Neither the absolute values nor the change from preoperative values was significant.

Outcomes of Inflammation and Muscle Damage Markers

The extent of the increased serum levels of inflammation and muscle damage markers at different time points was the primary outcome measure of the study. Among them, creatine kinase and CRP were the most important. A significant difference existed between the 2 groups with regard to the increase in creatine kinase level on postoperative days 2 (P = .08) and 3 (P = .09). The cumulative increase in creatine kinase level was also significantly different (P = .02). On postoperative day 2, mean increase in the MMV group was 201.8 ± 152.1 units/L (range, 38 to 728 units/L), whereas it was 104.9 ± 117.6
units/L (range, −17 to 539 units/L) in the MPP group. On postoperative day 3, the mean difference was 204.8±167.0 units/L (range, 13 to 642 units/L) in the MMV group and 88.0±163.9 units/L (range, −37 to 814 units/L) in the MPP group. The mean cumulative increase was 545.9±373.9 units/L (range, 81 to 1721 units/L) in the MMV group and 317.5±354.0 units/L (range, −214 to 1633 units/L) in the MPP group (Figure 1).

Increased myoglobin levels showed a significant difference only on postoperative day 1 (P<.02) (Figure 2). However, the serum levels of the other muscle damage markers, such as lactate dehydrogenase, glutamic oxaloacetic transaminase, and creatinine, showed no differences between the 2 groups.

Significantly elevated CRP and IL-6 levels were found in the MPP group. Mean increase in CRP levels after TKA was higher in the MPP group than in the MMV group, and the differences reached significance on postoperative days 2 (P=.03) and 3 (P=.03). On postoperative day 2, the mean increase was 70.3±48.4 mg/L (range, 11.9 to 188.1 mg/L) in the MMV group and 102.8±62.8 mg/L (range, 12.0 to 344.1 mg/L) in the MPP group. On postoperative day 3, the mean increase was 73.0±52.2 mg/L (range, 10.6 to 220.1 mg/L) in the MMV group and 107.1±63.3 mg/L (range, 13.7 to 359.1 mg/L) in the MPP group. A significant difference also existed in the cumulative change (P=.02): the mean increase was 168.6±111.8 mg/L (range, 37.0 to 474.7 mg/L) in the MMV group and 244.9±136.0 mg/L (range, 36.5 to 792.0 mg/L) in the MPP group. Interleukin-6 levels increased at all time points compared with preoperative levels, with significant differences at all time points (immediately postoperatively, P=.03; postoperative day 1, P<.01; postoperative day 2, P<.01; postoperative day 3, P=.04; cumulatively, P<.01). All results are illustrated in Figures 3 and 4. Interleukin-1β levels showed a more upward trend in the MPP

Table 1
Preoperative Patient Demographics

<table>
<thead>
<tr>
<th>Demographic</th>
<th>MMV Group (n=30)</th>
<th>MPP Group (n=30)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>66.1±5.8</td>
<td>66.0±7.7</td>
<td>.99</td>
</tr>
<tr>
<td>Men, %</td>
<td>20</td>
<td>20</td>
<td>1</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>26.3±3.8</td>
<td>27.1±3.3</td>
<td>.38</td>
</tr>
<tr>
<td>ASA grade</td>
<td>2.0±0.6</td>
<td>2.0±0.5</td>
<td>.80</td>
</tr>
<tr>
<td>Right side operated, %</td>
<td>50</td>
<td>47</td>
<td>.80</td>
</tr>
<tr>
<td>HSS score</td>
<td>57.7±6.5</td>
<td>56.4±6.9</td>
<td>.44</td>
</tr>
<tr>
<td>ROM, deg</td>
<td>98.8±14.4</td>
<td>95.3±11.2</td>
<td>.30</td>
</tr>
<tr>
<td>Preop knee circumference, cm</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper pole of patella</td>
<td>36.5±2.8</td>
<td>37.5±3.1</td>
<td>.24</td>
</tr>
<tr>
<td>Lower pole of patella</td>
<td>32.9±2.0</td>
<td>33.3±2.7</td>
<td>.52</td>
</tr>
</tbody>
</table>

Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index; deg, degrees; HSS, Hospital for Special Surgery; MMV, mini-midvastus; MPP, medial parapatellar; Preop, preoperative; ROM, range of motion.

Table 2
Intraoperative Data

<table>
<thead>
<tr>
<th>Variable</th>
<th>MMV Group (n=30)</th>
<th>MPP Group (n=30)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incision length, cm</td>
<td>10.1±0.8</td>
<td>14.0±1.3</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Operative time, min</td>
<td>89.1±18</td>
<td>98.1±27</td>
<td>.15</td>
</tr>
<tr>
<td>Tourniquet time, min</td>
<td>60.5±12.2</td>
<td>83.4±28.0</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>No. of patients needing LRR</td>
<td>2</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>EBL, mL</td>
<td>1364.2±560.3</td>
<td>1400.1±548.9</td>
<td>.81</td>
</tr>
<tr>
<td>Blood transfusion, units</td>
<td>0.4±1.0</td>
<td>0.3±0.9</td>
<td>.65</td>
</tr>
<tr>
<td>Hematocrit drop, %</td>
<td>41.5±0.1</td>
<td>41.7±0.1</td>
<td>.95</td>
</tr>
<tr>
<td>Hospital stay, d</td>
<td>11.7±2.3</td>
<td>12.3±2.5</td>
<td>.30</td>
</tr>
<tr>
<td>Postop knee circumference, cm</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper pole of patella</td>
<td>39.2±3.0</td>
<td>40.3±2.5</td>
<td>.13</td>
</tr>
<tr>
<td>Lower pole of patella</td>
<td>34.6±1.9</td>
<td>35.5±2.5</td>
<td>.14</td>
</tr>
<tr>
<td>Knee circumference change, cm</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper pole of patella</td>
<td>2.7±0.9</td>
<td>2.9±1.4</td>
<td>.56</td>
</tr>
<tr>
<td>Lower pole of patella</td>
<td>1.7±1.1</td>
<td>2.2±1.4</td>
<td>.15</td>
</tr>
</tbody>
</table>

Abbreviation: EBL, estimated blood loss; LRR, lateral retinacular release; MMV, mini-midvastus; MPP, medial parapatellar; Postop, postoperative.

Intraoperative data were compared between the 2 groups. No significant differences existed in operative time, number of patients needing LRR, estimated blood loss, blood transfusion, hematocrit drop, hospital stay, or knee circumference.

Data presented as mean±SD, except for No. of patients needing LRR.
Radiographic Findings

Radiographs revealed no implant malposition in any patient. All knees had a tibiofemoral angle ranging from 4° to 10° of valgus alignment on anteroposterior hip-to-ankle radiographs and a posterior slope angle of all tibial components ranging from 1° to 7° on lateral radiographs.

Functional Assessment

The HSS score assesses patient knee function. The baseline preoperative HSS scores between the 2 groups showed no difference (Table 1). Taking the approaches out of consideration, all patients showed substantial improvement in HSS scores at discharge (Table 3): mean HSS scores increased to 77.3±5.1 points in the MMV group and 75.3±5.2 points in the MPP group. The pre- and postoperative difference in scores was 0.6 points higher in the MMV group, although no difference approached significance.

Preoperatively, mean ROM was 105.6°±6.6° in the MMV group and 101.9°±8.2° in the MPP group. At final inpatient evaluation, no differences existed in ROM between the 2 groups, although the MMV group showed a larger upward trend than the MPP group.

Complications

Early postoperative complications were monitored during the inpatient period. One patient in the MMV group developed a superficial infection that was controlled with dressing changes and antibiotics. At discharge, the patient had a ROM of 95°. No early postoperative complications occurred in the MPP group.

Discussion

Although using blood enzymes is a common practice according to the surgical literature, its use to compare different surgical approaches began recently. The current study was designed to provide an objective measure to compare muscle damage and inflammation following TKA with 2 different approaches. Different surgeons choose different criteria to define minimally invasive surgical approaches, such as incision length,
operative time, and postoperative function; however, controversy exists over minimally invasive vs standard approaches. Some surgeons believe that subjective measures, such as patient satisfaction, cosmetic appearance, or pain, can be easily biased by patient or investigator expectations; even putatively objective measures, such as gait speed, ROM, or length of hospital stay, can be influenced by patient expectations. Although a few studies compare the serum levels of inflammation and muscle damage markers following total joint replacement with different approaches, to the authors’ knowledge, no studies have used serum levels of muscle damage and inflammation markers as primary outcomes to compare the mini-midvastus and medial parapatellar approaches.

In terms of the increase in serum creatine kinase levels, a clear difference existed between the MMV and MPP groups on postoperative days 2 and 3 and cumulatively, despite similar baselines in patient demographics. At each time point, mean increase in serum creatine kinase levels in the MMV group was almost double that in the MPP group. A significant difference also existed between the MMV and MPP groups in terms of increased serum myoglobin levels on postoperative day 1. These outcomes indicated that, compared with the standard medial parapatellar approach, the mini-midvastus approach was not muscle sparing and may cause more muscle damage. The incision into the rectus femoris tendon in the standard medial parapatellar approach is made along the line of fibers without invading the muscle fibers, whereas the incision in the mini-midvastus approach invades just into the muscle fibers of the vastus medialis. Also, surgeons must use more strength on the retractors to achieve proper visualization to place the prosthesis because of the limited visualization provided by the mini-midvastus approach. This may cause secondary muscle damage in these patients.

Significantly elevated CRP and IL-6 levels were found in the MPP group because, as reported by Larsson et al., an increased level of inflammation markers is more common in soft tissue, bone, and marrow injury than in skeletal muscle. The inflammation associated with TKA is not greatly affected by muscle damage but defined more by incision length, bone removal, and implant placement. In the current study, the MMP approach had a longer incision length, which could be more invasive to the other soft tissues than the MMV approach. Also, as reported by Hughes et al., elevated CRP and IL-6 levels are associated with tourniquet time. In the current study, mean tourniquet removal time in the MPP group was 23 minutes longer than that in the MMV group. This may have led to the significantly elevated CRP and IL-6 levels in the MPP approach.
group. These reasons may also explain why increased serum levels of muscle damage markers occurred in 1 group and increased serum levels of inflammation markers occurred in the other. In addition, studies have shown that inflammatory activity can decrease constitutive levels of serum creatine kinase, although the exact mechanism is still unknown.

Logistic regression analysis was performed to assess the potential confounding factors of increased serum creatine kinase, CRP, and IL-6 levels. The results confirmed the link between the surgical approach and the increase in serum creatine kinase, CRP, and IL-6 levels. The correlation between serum creatine kinase levels and estimated blood loss showed that estimated blood loss can also be considered a sign of muscle damage. Unlike previous studies, the current study revealed no correlation between the increase in serum creatine kinase level and tourniquet time. This finding agreed with studies about tourniquet-induced ischemia during elective orthopedic surgery, including TKA.

Changes in CRP and IL-6 levels were associated with tourniquet time, which was similar to the results of Hughes et al. This suggests that surgeons should minimize tourniquet time to reduce the activity of local inflammation. In a study by Niki et al., soft tissue balancing techniques elevated the levels of muscle-related enzymes. The current study showed no sign of this relationship because the patients in both groups were similar demographically and because all TKAs were performed by the same experienced surgeon with similar surgical techniques.

No significant differences existed in radiographic and functional assessments between the 2 groups in the current study. Functional assessment results confirmed that the MMV approach showed no superiority over the MPP approach in terms of muscle sparing. Further study of larger cohorts is warranted to confirm or refute these findings.

Regarding early postoperative complications, 1 patient in the MMV group had a superficial infection, whereas no early postoperative complications occurred in the MPP group. A longer operative time (120 minutes) may have contributed to the superficial infection. Because of the small study cohort, no correlation was found between biomarkers and postoperative complications. Future studies of larger cohorts are needed to find correlations.

The current study had the following strengths: it was a prospective study; the patient cohorts were similar terms of patient age, sex, body mass index, HSS score, and ROM; and the investigators and patients were blinded.

However, the study had several limitations. First, only the needed sample number was calculated according to serum creatine kinase level. To detect significant differences in other markers between the 2 groups, a larger sample size is needed. Second, inflammation and muscle damage markers were tested within 3 days postoperatively. According to another study, muscle damage markers such as lactate dehydrogenase and aspartate aminotransferase have a second peak on postoperative day 3. This may explain why no difference was detected in these biochemical markers between groups in the current study. Third, the inflammation activity’s influence on serum creatine kinase level was unable to be quantified. Finally, no other objective outcomes such as gait analysis, were used, which could have correlated biochemical markers with functional deficits more meaningfully.

<table>
<thead>
<tr>
<th>Table 3</th>
<th>Functional Assessment(^a)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variable</td>
<td>MMV Group (n=30)</td>
</tr>
<tr>
<td>ROM, deg</td>
<td></td>
</tr>
<tr>
<td>Preoperative</td>
<td>98.8±14.4</td>
</tr>
<tr>
<td>At discharge</td>
<td>105.6±6.6</td>
</tr>
<tr>
<td>Difference</td>
<td>6.8±12.7</td>
</tr>
<tr>
<td>P</td>
<td>.02</td>
</tr>
<tr>
<td>HSS score</td>
<td></td>
</tr>
<tr>
<td>Preoperative</td>
<td>57.7±6.5</td>
</tr>
<tr>
<td>At discharge</td>
<td>77.3±5.1</td>
</tr>
<tr>
<td>Difference</td>
<td>19.5±3.7</td>
</tr>
<tr>
<td>P</td>
<td>&lt;.01</td>
</tr>
</tbody>
</table>

Abbreviations: deg, degrees; HSS, Hospital for Special Surgery; MMV, mini-midvastus; MPP, medial parapatellar; ROM, range of motion.

\(^a\)Student’s t test used to determine differences between the 2 groups.
CONCLUSION

The mini-midvastus approach showed no superiority over the standard medial parapatellar approach in terms of muscle sparing and may cause more muscle damage. Differences in the serum levels of inflammation markers made it difficult to determine which approach was less invasive. Using inflammation and muscle damage markers to evaluate different approaches is an objective and scientific measure. Further studies should include the correlation between the biochemical markers and functional deficits. Well-designed studies are needed to determine which approach is less invasive.

REFERENCES