# Asymmetry of Posterior Condyles in Resection Plane and Axial Curvature for Total Knee Arthroplasty 

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#### Abstract

Objective: Understanding the morphology of the distal femur is essential for improving bone-implant match in total knee arthroplasty (TKA) and understanding the mechanisms behind knee kinematics. However, little is known about the asymmetry of the posterior condyles. Thus, this study aimed to thoroughly investigate asymmetries in sizes and shapes between the medial and lateral posterior condyles before and after femoral resections during TKA in osteoarthritic (OA) knees.


Methods: Three-dimensional femoral models of 74 OA knees were constructed using computed tomography images. The morphologic measurements of the posterior condyle pre- and post-simulated osteotomy for TKA included the radii of the posterior condyles fitted to a circle on the sagittal and axial planes of the femoral coordinate system, the inclination angle of the articular surface and resected surface, and the width and height of the resected surface. Differences in the data were assessed using Student's $t$-test, and correlations were evaluated using the Pearson product-moment correlation.

Results: The radii of the medial posterior condyles fitted to the circle were, on average, 6 mm larger than those of the lateral condyles on the axial plane ( $p<0.001$ ) and 0.7 mm smaller than those of the lateral condyles on the sagittal plane ( $p=0.046$ ). The inclination angles of the medial and lateral posterior condyles on the axial plane were significantly different with both pre-simulated and post-simulated osteotomy, respectively (both $p<0.001$ ). The resected plane of the lateral posterior condyles displaced opposite inclination directions between the distal and proximal portions. Neither heights or widths of the medial posterior condyles were significantly different from those of their lateral counterparts (both $p>0.107$ ).

Conclusions: This study found asymmetrical inclination of the resected surface and coronal radii between the medial and lateral posterior condyles, which may relate to the posterolateral overhang of the lateral condyle after TKA and the progression of the knee OA. These findings provides valuable morphological information and may help improve the implant designs for TKA.

Key words: morphometry; posterior condyle; three-dimensional; total knee arthroplasty

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## Introduction

Accurate sizing and bone-implant matching of prosthetic components are vital factors for the success and longterm survival of total knee arthroplasty (TKA) ${ }^{1-4}$, and designs of currently available prostheses have been developed based on the natural geometric and kinematic characteristics of the knee.

The size and surface of the femoral posterior condyles comprises the joint surface during the flexion phase of the knee joint motion ${ }^{4}$. Throughout flexion, the normal knee exhibits a medial pivot motion with external rotation of the femur relative to the tibia ${ }^{5,6}$. This asymmetrical knee motion is related to the morphometric asymmetries of the sagittal radius and the inclination angle of the articular surface between the medial and lateral posterior condyles ${ }^{5,6}$. It has been confirmed that using symmetrical design of posterior condyles changed the rotational pattern of the knee and may lead to altered knee function followingTKA ${ }^{5}$. Morphometric asymmetries are designed based on several temporary prostheses (e.g. Journey II; Smith \& Nephew) to improve knee motion after TKA ${ }^{4}$. However, few studies have described the asymmetries of the coronal radius of the posterior condyle.

In TKA, the prosthetic condyles should ideally fit with the contours of the resected bone, and the incidence of bone-implant mismatch that produces, such as overhang and uncovered areas, should be avoided ${ }^{7,8}$. Most prostheses available in the market are currently designed to be symmetrical on the bone-implant contact surface ${ }^{5}$. However, more recently, high incidences of posterolateral overhang were observed in Japanese and Indian populations ${ }^{9-11}$, and these mismatches may lead to femoropopliteal impingement after TKA ${ }^{12}$. Considering that the prosthetic posterior condyles are designed to be symmetrical, an overhang that occurs on the lateral condyle suggests that the resected surfaces are asymmetrical. However, morphometric studies on the resected plane of the posterior condyle have focused on the height or width ${ }^{13,14}$, which have been observed to be nearly symmetrical (approximately $1-2 \mathrm{~mm}$ difference) between the medial and lateral posterior condyles. Thus, new morphologic parameters aside from height and width are required to describe this asymmetry.

Given the insufficient knowledge on the asymmetry of the posterior condyles, the current study has two main goals: (i) to measure and compare the coronal radii between medial and lateral posterior condyles; (ii) to conduct a virtual TKA osteotomy of the posterior condyles and explore the inclination angles of the resected surface. These results could aid in developing TKA implant design, which may lower the incidence of the overhang and improve the knee joint function following TKA.

## Methods

## Participants

All patients included in this study visited our hospital in preparation for TKA between January 2019 and December 2019.

The inclusion criteria were as follows: (i) diagnosis of varus OA knee based on the medical history, symptoms, physical examination, and standing knee joint anteroposterior and lateral radiography; (ii) computed tomography (CT) scan of the entire length of the femur and the quality of the data sufficient to perform three-dimensional (3D) reconstruction; (iii) OA knees with Kellgren-Lawrence stage II-IV and intact posterior condyles without obvious deformation. The exclusion criteria were as follows: (i) previous lower extremity surgery, (ii) valgus or severe varus deformity of $\geq 15^{\circ}$, or (iii) severe osteoporosis. Ultimately, a total of 46 patients with 74 OA knees were enrolled. The mean age was $65.7 \pm 9.25$ (range: 51-82) years, and the mean body mass index was $32.4 \pm 18.7$ (range: $18.7-32.4$ ) $\mathrm{kg} / \mathrm{m}^{2}$.

Our institutional review board approved the study ([2019] 9), and written consent was obtained from all study participants.

## Imaging Procedure and Measuring Methods

All patients underwent CT (Siemens SOMATOM 16, Germany) with a $0.625-\mathrm{mm}$ slice thickness of the entire length of the femur. CT images were imported into Amira 6.7 (Thermo Fisher Scientific, Rockford, IL) to construct femoral models. Then, the 3D models of the femur were exported and then imported into Rhinoceros 5.0 software (RobertMcNeel \& Associates, Seattle, WA) to simulate femoral resection of the TKA. Measurements of the parameters of the posterior condyle are described below.

The anatomical coordinate systems of the femur were established by referencing several bony landmarks ${ }^{15}$ (Figure 1(A)). The middle point of the clinical transepicondylar axis (c-TEA), which connects the most prominent points of the medial and lateral epicondyles of the femur, was defined as the origin of the femoral coordinate system. The mechanical axis of the femur was set as the line from the center of the femoral head to the midpoint of the c-TEA. The c-TEA and the mechanical axis defined the coronal plane, and he plane passing through the femoral mechanical axis and perpendicular to the coronal plane was defined as the sagittal plane. The plane perpendicular to both the sagittal plane and coronal plane was defined as the axial plane.

The articular surface of the posterior condyle was selected and extracted from the 3D models and projected onto the coronal plane of the femoral coordinate system. Then, numerous lines parallel to the axial plane were drawn from the distal to the proximal portion of the posterior condyle plane in $1-\mathrm{mm}$ increments. The fit line of all the midpoints of all the parallel lines using the least-squares method was defined as the inclination of the articular surface (Figure 2(A)). An inclination tilting toward the proximal intercondylar fossa was defined as a positive value in both the medial and lateral condyles. In addition, we drew circles fitted to the medial and lateral posterior condyles projected on the sagittal and axial planes of the coordinate system


Fig. 1 (A) The establishment of coordinating system. (B) The virtual TKA distal and posterior resection of the femur are performed


Fig. 2 Measurements of the parameters. (A) Inclination angle of the posterior condyles presimulated osteotomy. (B) Radius of the posterior condyles presimulated osteotomy in the coronal plane. (C) Radius of the posterior condyles presimulated osteotomy in the sagittal plane. (D) Inclination angle of the posterior condyles postsimulated osteotomy. (E) Height and width of the posterior condyles presimulated osteotomy. (F) The inclination angle of the distal and proximal resected surface of lateral posterior condyle
(Figure 2(B,C)). The following parameters were evaluated before the simulated femoral cut of TKA: (1) the radii of the posterior condyles fitted to the circles in the sagittal and axial planes and (2) the inclination angle of the posterior condyles in the coronal plane (Figure 2(A-C)).

Moreover, we simulated the distal femoral osteotomy during TKA (Figure $1(\mathrm{~B})$ ). The distal cut plane for the resection was parallel to the axial plane of the femoral coordinate system and 7 mm proximal to the most distal point of the femoral condyle, and the posterior cut plane for the

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resection was parallel to the coronal plane of the femoral coordinate system and $7 \mathrm{~mm}^{5}$ anterior to the most posterior point of the posterior condyles. Lines were drawn on the cut surface from the distal to the proximal portion of the posterior condyle-resected surface in $1-\mathrm{mm}$ increments. For the medial posterior condyle cutting surface, the fit lines of all midpoints of the lines were defined as the inclinations of the medial resected surface (Figure 2(D)). For the lateral posterior condyle cutting surface, the inclination angles consisted of the laterally oriented proximal portion and the medially oriented distal portion were marked by the turning point. To evaluate the position of the turning point, the ratio was calculated by dividing the distance from the turning point to
the femoral distal bone cut plane (L1) by the proximodistal height of the resected lateral posterior condyle (Figure 2(E)) The following parameters were evaluated after the simulated femoral cut of TKA were evaluated: (1) the height and width of the resected posterior femoral condyle surface, (2) the inclination angle of the medial and lateral posterior condyles, (3) inclination angles of the proximal and distal parts of the lateral posterior condyle, and (4) the ratio of the turning point (Figure 2(D-F)).

## Statistical Analyses

Differences in the data were statistically analyzed using the Student's t-test, and correlations were evaluated using the

TABLE 1 Intraclass correlation coefficient of interobserver and intraobserver error of all parameters

| Parameters | Intraobserver |  | Interobserver |  |
| :---: | :---: | :---: | :---: | :---: |
|  | ICC | 95\% CI | ICC | 95\% CI |
| Presimulated osteotomy |  |  |  |  |
| Inclination angles of the medial posterior condyle ( ${ }^{\circ}$ ) | 0.875 | 0.809 to 0.919 | -0.81 | 0.712 to 0.877 |
| Inclination angles of the lateral posterior condyle | 0.848 | 0.769 to 0.902 | 0.833 | 0.738 to 0.894 |
| Axial radius of the medial posterior condyle | 0.838 | 0.736 to 0.899 | 0.905 | 0.853 to 0.939 |
| Axial radius of the lateral posterior condyle | 0.839 | 0.557 to 0.926 | 0.799 | 0.625 to 0.886 |
| Sagittal radius of the medial posterior condyle | 0.874 | 0.807 to 0.919 | 0.899 | 0.844 to 0.935 |
| Sagittal radius of the lateral posterior condyle | 0.852 | 0.775 to 0.904 | 0.885 | 0.800 to 0.932 |
| Postsimulated osteotomy |  |  |  |  |
| Inclination angles of the medial posterior condyle | 0.896 | 0.832 to 0.935 | 0.848 | 0.770 to 0.902 |
| Inclination angles of the lateral posterior condyle | 0.889 | 0.829 to 0.928 | 0.827 | 0.739 to 0.888 |
| Proximo-distal height of the medial posterior condyle | 0.962 | 0.923 to 0.980 | 0.958 | 0.843 to 0.982 |
| Proximo-distal height of the lateral posterior condyle | 0.95 | 0.907 to 0.971 | 0.89 | 0.759 to 0.943 |
| Medio-lateral width of the medial posterior condyle | 0.985 | 0.969 to 0.992 | 0.93 | 0.824 to 0.966 |
| Medio-lateral width of the lateral posterior condyle | 0.968 | 0.950 to 0.980 | 0.96 | 0.934 to 0.975 |
| Inclination angles of the distal part of lateral posterior condyle | 0.904 | 0.839 to 0.942 | 0.857 | 0.776 to 0.909 |
| Inclination angles of the proximal part of lateral posterior condyle | 0.853 | 0.731 to 0.915 | 0.828 | 0.741 to 0.888 |
| Ratio of the turning point | 0.972 | 0.92 to 0.987 | 0.93 | 0.891 to 0.955 |

[^0]TABLE 2 The parameters between medial and lateral posterior condyle

| Parameters | Medial posterior condyle |  |  | Lateral posterior condyle |  |  | $t$ | $p$-value* |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | Mean | SD | Range | Mean | SD | Range |  |  |
| Presimulated osteotomy |  |  |  |  |  |  |  |  |
| Inclination angles ( ${ }^{\circ}$ ) | 2.4 | 2.4 | -3.1 to 7.4 | 6.7 | 2.6 | 0.7 to 13.3 | -10.4 | <0.001* |
| Axial radius (mm) | 25.3 | 6.3 | 14.1 to 41.8 | 19.3 | 4.2 | 12.2 to 28.8 | 6.799 | <0.001* |
| Sagittal radius (mm) | 17.7 | 2.0 | 11.9 to 21.5 | 18.4 | 2.1 | 14.0 to 23.0 | -2.015 | <0.001* |
| Postsimulated osteotomy |  |  |  |  |  |  |  |  |
| Inclination angles ( ${ }^{\circ}$ ) | 4.0 | 3.8 | -4.3 to 11.6 | 7.29 | 2.9 | -1.3 to 13.7 | -6.025 | <0.001* |
| Proximo-distal height (mm) | 28.5 | 3.1 | 22.4 to 35.4 | 28.0 | 4.0 | 17.6 to 38.2 | 0.748 | 0.192 |
| Medio-lateral width (mm) | 27.7 | 2.9 | 21.3 to 34.5 | 27.0 | 3.6 | 20.4 to 35.9 | 1.348 | 0.108 |

[^1]Pearson product-moment correlation. To assess intra- and inter-observer measurement reliability, all measurements were re-measured $>3$ weeks apart by two independent observers (one senior orthopaedic resident and one fellowship-trained musculoskeletal radiologist). Differences were considered significant at $p<0.05$. All statistical analysis was performed using SPSS version 24 (SPSS Inc., Chicago, IL, US). A post hoc power analysis was performed using the
software G*Power (version 3.1.9, Kiel, Germany) to compare the medial and lateral posterior condyles by each parameter: power $=1.000$ in the inclination of the articular surface, power $=1.000$ in the radius of the condyles in the sagittal plane, power $=0.978$ in the radius of the condyles in the axial plane, power $=1.000$ in the inclination of the resected surface, power $=0.260$ in the height of the resected surface, and power $=0.360$ in the width of the resected surface.

## Radii on Transvers Plane



Fig. 3 Diagrams illustrating the correlation between the medial and lateral radius on axial plane


Fig. 4 Diagrams illustrating the correlation between the medial and lateral radius on sagittal plane

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## Results

A$1 l$ intraclass correlation coefficient values of the interobserver and interobserver reliabilities were high (Table 1).

## Pre-simulated Osteotomy of the Posterior Condyle

The inclination angles of the surface of the medial and lateral posterior condyles were $2.36^{\circ} \pm 2.41^{\circ}$ and $6.68^{\circ} \pm 2.64^{\circ}$, respectively. The lateral condyle tilted significantly more medially than the medial condyle ( $p<0.001$ ) (Table 2). The radiuses of the medial and lateral posterior condyles were $17.7 \pm 1.96 \mathrm{~mm}$ and $18.4 \pm 2.07 \mathrm{~mm}$, respectively, in the sagittal plane ( $p=0.350$ ). In the axial plane, the radius of the medial condyle was on average 6 mm larger than that of the lateral condyle $(p<0.001)$, and the radius of the medial posterior condyle correlated positively with that of its lateral counterpart on both the axial plane $(r=0.600, p<0.001)$ and sagittal plane ( $r=0.751, p<0.001$ ) (Figures 3 and 4).

## Post-simulated Osteotomy of the Posterior Condyle

After the posterior cut, the mean inclination angles of the lateral posterior condyle were more medial than those of the medial condyles $(p<0.001)$ (Table 2). For the lateral posterior condyle, the inclination angles of the distal and proximal parts were $14.4^{\circ} \pm 4.67^{\circ}$ (range: $-2.2^{\circ}$ to $25.3^{\circ}$ ) and $-13.8^{\circ} \pm 9.46^{\circ}$ (range: $-34.0^{\circ}$ to $8.7^{\circ}$ ), respectively. The mean ratio of the turning point was $0.74 \pm 0.08$. The boxplot in Figure 4 shows that more than three-quarters of the patients showed displacement in opposite inclination directions between the distal and proximal parts of the resection plane of the lateral posterior condyle. No significant differences were found in the height ( $p=0.192$ ) or width ( $p=0.108$ ) of the posterior resected plane between the medial and lateral condyles (Table 2).

## Discussion

TThe most important finding of current study was that the inclination pattern and angles were asymmetrical between the medial and lateral posterior condyles after the femoral resection, and that the radii of the lateral posterior condyles were proportionally larger than their medial counterparts in the axial plane.

## Advantages of Using CT-Based 3D Computer Models Technique

Advances in three-dimensional (3D) computer models based on radiographic images have resulted in the availability of preoperative measurement and virtual planning ${ }^{16}$, and the present study used CT-based 3D computer models to assessed the femoral posterior condyle. Compare to the traditional method of using calipers on bone specimen from patients or cadaver, the method of using 3D computer models obtains more accurate information and avoids the inherent measurement error or the possible error resulting from the soft tissue around the bone ${ }^{17,18}$. And the measurement reproducibility of the results in this study was proved to be excellent (intra- and interclass reliability coefficients $=0.80-0.99$ ). Furthermore, compared to 2D images or bone specimens, with the 3D computer model, the researcher is allowed to conduct additional analyses and difficult measurements, such as assessing the irregular shape of the posterior condyle, which was done in the current study (Figure 5).

## Asymmetry of the Posterior Condyles before TKA Ostectomy

Asymmetrical shape of the posterior condyles has been reported in previous studies. For example, Hokari et al. reported that the inclination angle of the medial posterior condyle was nearly vertical and that of the lateral condyle tilted medially ${ }^{5}$. Further, Howell et al. found that the radii of medial posterior condyles were smaller than those of the lateral condyle in the sagittal plane ${ }^{19}$. The results of the current

Inclination angel of the lateral posterior condyle after TKA bone cut

Fig. 5 Box plot for the inclination angle differences between proximal and distal resected surface of the posterior condyle


Proximal part

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study are in line with those previous reports, but we additionally found that the radii of the lateral posterior condyles were proportionally larger than their medial counterparts in the axial plane. This indicated that the asymmetry also existed in the axial plane, and few studies have reported this previously. The normal knee exhibits a medial pivot motion with external rotation of the femur relative to the tibia ${ }^{20,21}$. This knee asymmetrical motion is considered to relate to the asymmetrical shape of the posterior condyle ${ }^{5}$. Therefore, this new finding of the asymmetrical shape in axial plane may also have relation to the medial pivot motion.

A detailed understanding of disease progression in knee OA is critical to establish methods of prevention and treatment. Knee kinematics change along with the OA disease stage progress. Changes in knee kinematics increase tibiofemoral stress and further promote the progression of the OA knee ${ }^{22}$. Previous studies have reported that the


Fig. 6 The drawing shows that the articular surface of medial posterior condyle in axial plane is larger than lateral posterior condyle
rotational patterns of OA knees were different than normal $^{22,23}$. Since the asymmetrical knee rotational motion may relate to the shape asymmetry between the medial and lateral posterior condyles, it is plausible to infer that the differences in rotational patterns differences between normal and OA knees may relate to the change of the asymmetrical shape of the posterior condyle. Our study displayed that the asymmetry of posterior condyles' inclination angles in OA knees was $4^{\circ}$ in average, which was $5^{\circ}$ less than the normal knee shown in previous study ${ }^{5}$. These consistencies of the change in the medial pivot motion pattern and the change in the asymmetrical shape between OA and normal knees supported the above inference and may provide new insights into the mechanism of the kinematic changes in OA knees. Nevertheless, more knee biomechanics and kinematics are required to verify this.

## Asymmetry of the Posterior Condyles after TKA Ostectomy

Previous morphometric studies on the posterior condyle cut have mainly focused on its height and width ${ }^{13,14,24}$, which has been found to be symmetrical between the medial and lateral condyle. These results were the design bases for the current symmetrical design for the bone-implant contact surface of the femoral implant. However, using these symmetrical femoral components, high incidences of bone-implant mismatch of the posterior condyle were observed ${ }^{9,10,12}$. For example, Scott et al. reported that $2.7 \%$ of their study's patients presented with popliteal impingement with an overhanging metallic lateral posterior condyle ${ }^{10}$. Further, Hirakawa et al. ${ }^{9}$ and Shah et al. ${ }^{10}$ both used 3D anatomical analysis to evaluate 50 Indian and 40 Japanese OA patients, respectively. Both studies reported that the rate of the posterolateral overhang to be up to $62.5 \%$ following TKA, and redesigned of the posterior condyle portion of the femoral component were recommended. Since the overhangs merely occurred on the lateral posterior condyle using the


Fig. 7 The symmetrical design of the posterior condyle may lead to posterolateral overhang of the protheses

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Fig. 8 Posterolateral overhang of the protheses may lead to femoropopliteal impingement
symmetrical components under standard TKA bone cut, the asymmetry between medial and lateral resected surface of posterior condyle seemed to be the only explanation of the prothesis overhang. So exclusively evaluating the height and width of the resected plane provides insufficient information for this asymmetry (Figure 6).

Considering that the articular surface of the posterior condyle is tilted, it is reasonable to infer that its resected bone surface is also tilted. This study verified this inference and showed that the lateral resected bone surface tilted medially in the distal portion and laterally in the proximal portion, while the medial portion was nearly vertical with slightly medial tilt. When using the femoral component with asymmetrical vertical of the posterior condyle ${ }^{13}$, the overhang (Figure 7) and femoropopliteal impingement (Figure 8) at the posterolateral aspect of the lateral posterior condyle were expected following TKA ${ }^{9}$. This provides an explanation for the high incidences of posterolateral overhang after TKA. By improving the prosthetic posterior condyle to fit the irregular shape of the lateral posterior resected plane, less incidence of the prosthetic posterolateral overhang and less residual knee pain or stiffness after TKA may be achieved ${ }^{25}$.

## Limitation and Strengths

The current study uses the CT-based 3D computer model technique to assess the femoral posterior condyle for TKA, which has strengths in providing accurate morphological information with excellent reproducibility. In addition, the 3D computer model analyses allowed us to conduct measurements on the irregular shape of the posterior condyle and had some new finding for TKA implants' designing.

However, the results of this study should be interpreted in the context of the following limitations. First, this study evaluated arthritic knees, which may have been deformed by degeneration and pathological processes ${ }^{26,27}$. However, considering that most TKA procedures were performed on arthritic knees, measurement results of the OA knees are better for designing matched prostheses. Second, all measurements were performed using CT data without data on cartilage thickness. MRI analyses including cartilage are needed to evaluate the articular surface. However, CT data used in this study included the entire length of the femur, which was advantageous for constructing an accurate TKA-based coordinate system compared with MRI and is considered acceptable for articular measurements ${ }^{5}$. Furthermore, for TKA resected plane measurements, cartilage thickness had been taken into consideration for virtual TKA resection, and this method have been used in numerous previous investigations ${ }^{13-15}$. Third, the study population is relatively small for analyzing difference in heights and width between the medial and lateral resected surfaces of posterior condyles. Nevertheless, they were found to be symmetrical in previous studies ${ }^{13,14,24}$, and the differences were small (less than 1 mm ) in the current study. Thus, we would not expect these parameters to have significant differences in larger sample sizes. Fourth, the data were collected from the Chinese population exclusively. In the future, samples from other races should be included. If the femoral asymmetry is observed differently among races, these differences should also be considered in implant design.

## Conclusions

TThe radii of the medial posterior condyle in the axial plane were proportionally larger than those of the lateral condyle, which may account for the kinematic changes observed in the progression of the knee osteoarthritis. The inclination angle of the resected medial posterior condyle tilted medially and that of the lateral condyle was irregular in shape, with a medial inclination in the distal portion and lateral inclination in the proximal portion. A prosthetic overhang at the posterolateral aspect of the lateral posterior condyle may arise when a femoral prosthesis with a symmetrical vertical shape is used. These findings provide valuable morphological information and aid implant designs for TKA. Further studies are needed to investigate how these posterior condyle's asymmetry influence the knee's biomechanics and kinematics, and explore the implant's design and relative surgical implication according to these posterior condyle's asymmetry.

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## Conflict of Interest

N
o benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article.

## Ethics Statement

This study was approved by the institutional review board of General Hospital of Southern Theater Command (IRB No. [2019] 9).

## Author Contributions

CL, JC-conception, drafting, substantial revision; YY, YJ, CW, and TT-searched the literature and analyzed the data; PL-conception, searched the literature, revision.

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[^0]:    Abbreviations: CI, confidence interval; ICC, intra-class correlation coefficient.

[^1]:    Note: Data are presented as means, standard deviations and range.; * $p<0.05$.

