An Accuracy Comparison of Minimally Invasive Transclavicular-Transcortical Drilling with Free-Hand, C-Shape and Assembly-Type Guide Device: An In Vitro Study

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Objectives: Ensuring the accuracy of transclavicular-transcoracoid drilling in the anatomical reconstruction of the coracoclavicular ligament complex with minimally invasive incisions remains a major problem for inexperienced surgeons. The purpose of this study was to design an assembly guide device for transclavicular-transcoracoid drilling with minimally invasive incisions, to manufacture the finished product, and to compare its feasibility and accuracy with the existing C-shape guide devices and free-hand techniques.

Methods: An assembly-type guide device was designed and produced using computer-aided design and three-dimensional printing. The specimen data of 54 human shoulders from 27 gross specimen (14 males and 13 females) treated by free-hand drilling, C-shape device drilling, and assembly-type guide device drilling from October 2018 to January 2021 were analyzed in a controlled laboratory study. Fifty-four human shoulder specimens were randomly assigned into free-hand (n = 18), C-shape (n = 18), and assembly (n = 18) groups by drawing lots for transclavicular-transcoracoid drilling by three inexperienced surgeons. After the drilling procedure was completed and the devices were removed, the operation outcomes were assessed and evaluated. Distances from the tunnel edge to the coracoid’s medial (d_M) and lateral (d_L) edges, operation time, and tunnel location zones on the coracoid’s inferior surface of all specimens in the three groups were measured to evaluate the surgical accuracy and efficiency.

Results: All specimens in the three groups completed the drilling operation successfully and were correctly measured. The distance differences (d_d) between d_M and d_L in the free-hand, C-shape, and assembly groups were 3.2 ± 1.8 mm, 1.8 ± 1.0 mm, 1.0 ± 0.8 mm, respectively. The d_d of the free-hand group was higher than that of the other two groups (p < 0.001). The tunnel exit points on the inferior coracoid surface located in undesired zones were six (33%), one (6%), and zero in the free-hand group, C-shape group, and assembly-type group, respectively (p = 0.012). The...

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operation time in the free-hand, C-shape, and assembly groups were 198 ± 36 s, 256 ± 64 s, and 353 ± 88 s, respectively. The operation time of each group significantly differed from that of the others ($p < 0.001$).

**Conclusion:** The assembly-type devices may be the first choice for inexperienced surgeons while both the C shape devices and assembly-type guide devices achieved higher accuracy than free-hand techniques.

**Key words:** acromioclavicular joint; computer-aided design; coracoclavicular ligament; guide device; reconstruction; three-dimensional printing; transclavicular-transcoracoid drilling

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**Introduction**

Acromioclavicular (AC) joint dislocation is common among young and active sportsmen, accounting for nearly half of all athletic shoulder injuries. Surgical treatment is generally considered necessary in higher grades (IV-VI) of coracoclavicular (CC) ligament disruption, according to the Rockwood classification. Many surgical techniques have been described to restore the anatomic relationship of the lateral clavicle to the acromion. Anatomical reconstruction (AR) techniques of the CC ligament complex appear to yield good biomechanical results and functional outcomes. In many AR techniques, a transclavicular-transcoracoid tunnel is necessary, with subsequent insertion of either one or two synthetic rope systems for reduction maintenance and scaffold supply until the CC ligaments have healed. The tunnel’s orientation on the coracoid has an effect on the ultimate load-to-failure; the base-central position on the undersurface of the coracoid appeared to be the favorable position. Since the coracoid process is small in a complex spatial configuration with individual differences, improper tunnel placement easily occurs intraoperatively and inherently weakens the coracoid bone stability, leading to cortical breach, fracture of the coracoid, early loss of reduction, and implant failure.

In open surgery, transclavicular-transcoracoid drilling in a traditional AC joint reconstruction is relatively less difficult because a large incision from the lateral end of the clavicle to the coracoid process enables direct visualization of all necessary structures around the AC joint. However, this technique is associated with several problems such as a more obvious scar, slower soft tissue healing, and residual instability. Minimally invasive procedures have been recently introduced for AR to avoid large incisions and extensive soft tissue dissection. However, it is challenging to achieve an accurate transclavicular-transcoracoid drilling with minimally invasive incisions for inexperienced surgeons with inadequate exposure to the operative field. Ensuring the accuracy of transclavicular-transcoracoid drilling in the AR of the CC ligament complex with minimally invasive incisions is important to aid surgeons and ensure patient safety.

Several methods have been developed to improve the accuracy of transclavicular-transcoracoid drilling in AR of the CC ligament complex with minimally invasive incisions. The fluoroscopy C arm is employed to assist transclavicular-transcoracoid drilling; however, it extends the operation time and increases the radiation exposure. Arthroscopy-assisted transclavicular-transcoracoid drilling can achieve high accuracy; computer-aided navigation systems, mainly composed of optoelectronic or electromagnetic systems, have also been introduced to assist transclavicular-transcoracoid drilling. These navigations are expensive, time-consuming, and skill-intensive, which limits their wider application. Therefore, helping surgeons in drilling through the CC ligament complex quickly and accurately is the key to a successful AR.

A commercial C-ring drill guide has been reported to facilitate transclavicular-transcoracoid drilling. Compared with the aforementioned navigation methods, this guide device is relatively inexpensive and simple yet effective without radiation exposure. As limited by design, it might be impossible to locate the drilling tunnel of the inferior coracoid base accurately, which poses a potential risk in transclavicular-transcoracoid drilling, especially for inexperienced doctors; therefore, a modified guide device is required.

Compared with traditional manufacturing processes, three-dimensional (3D) printing is flexible for creating myriad structures in nearly any shape or size and has been widely used in various surgeries. Consequently, it enables doctors to design and create a new surgical instrument according to their needs as long as they master the primary ability of computer-aided design. Moreover, owing to its low-cost rapid printing, a new surgical instrument could be produced and used in a practical trial to identify and correct its insufficiency.

Because of its relatively simple and low-cost manufacturing method, the guide device made by 3D printing might be the most suitable assist for surgeons in remote and economically underdeveloped areas for transclavicular-transcoracoid drillings.

Therefore, the objectives of this study were: (i) to evaluate the efficacy and accuracy of transclavicular-transcoracoid drillings undertaken by inexperienced surgeons; (ii) to analyze the advantages and disadvantages of these methods and provide a new choice for transclavicular-transcoracoid drilling. We hypothesized that the coracoid tunnel placement accuracy would be improved with the use of two different types of guide devices compared to the free-hand drilling technique and the assembly guide device would show the best results.
**Materials and Methods**

**Inclusion Criteria**
Formalin-fixed, cadavers aged above 18 with intact scapulae, clavicle and their conjoined ligaments.

**Exclusion Criteria**
With (i) coracoid fracture or over narrow coracoid, (ii) open fracture or severe soft tissue contusion above clavicle, (iii) with mid-clavicle or distal clavicle fracture (iv) with joint dislocation or underwent surgical treatment.

**Specimens and Surgeons**
From October 2018 to January 2021, transclavicular-transcoracoid drilling in coracoclavicular ligament reconstruction were conducted in Southern Medical University. According to the inclusion and exclusion criteria, a total of 54 adult, formalin-fixed, cadaveric shoulder joints (27 cadavers, 14 males and 13 females; age from 26 to 82 years, mean age, 58 years) were enrolled in this study, 54 shoulder joints from 27 cadavers were averagely assigned to three inexperienced surgeons and placed in order by drawing lots to accomplish the operation with free-hand drilling (free-hand group), C-shape guide device-assisted drilling (C-shape group), and assembly-type guide device-assisted drilling (assembly group), respectively.

Surgeons randomly used three techniques to operate by drawing lots, while each technique involved six shoulders. The three surgeons had less than 3 years of clinical experience and had never performed a transclavicular-transcoracoid drilling without supervision. All procedures were performed without the assistance of fluoroscopy or arthroscopy.

**Materials**

**Development of an Assembly-Type Guide Device**
We had previously designed several guide devices, which had been verified as deficient in practice (Figure 1A, B), and finally determined the current design (Figure 1C). Considering the complexity of the model itself and that most of the device was outside the body when it was used, its main parameter settings are shown in Figure 2, and the hooks had four options to be applied to different sizes of coracoids. In addition to these parameters, it was required that every part of the device could be fixed when it was used. After practical application, we determined that the guiding device (the working diagram is shown in Figure 3A) basically met the needs of guiding transclavicular-transcoracoid drilling and applied it to the assembly group operation of this experiment. The center of the concentric arc coincided with the midpoint of the hook, which ensured that the preset tunnel path passed through the midpoint of the inferior coracoid base, regardless of the position of the guiding part on the arc. The angle-adjustable range was set from 50° to 140°, which met all the angle requirements in the study.

**Operation Procedure**

**Posture**
The cadavers were positioned at the beach chair position. A 1 cm transverse incision was made over the clavicle approximately 3.5 cm medial to its lateral edge, which was subsequently cleared of soft tissues (Figure 4). After the surgeon touched the coracoid, another 2 cm transverse incision was made on its skin projection, where the soft tissues were then split to expose the coracoid and cleared off all the way to its base. The medial and lateral edges of the coracoid at the base could be touched and identified through the incision, respectively.

**Operation of Transclavicular-Transcoracoid Drilling with Free-Hand Technique**
The position of the tunnel was defined by the landmarks on the superior clavicle and coracoid, which were approximately 3.5 cm medial to the AC joint, equidistant between the anterior and posterior edges of the clavicle, and the midpoint of the inferior coracoid base. In this group, the guide was the surgeon’s finger. The surgeon placed his forefinger on the bottom surface of the
FIGURE 2 The main parameter settings of assembly device: (A) Lateral view of outrigger, length 1 = 25 mm, length 2 = 110 mm, length 3 = 85 mm; (B) Front view of outrigger, length 4 = 10 mm; (C) Front view of guide tube, length 1 = 125 mm; (D) Bottom view of guide tube, diameter 1 = 5 mm, diameter 2 = 3 mm; (E) Lateral view of adapter, length 1 = 80 mm, length 2 = 115 mm, diameter 1 = 20 mm, angle 1 = 50°; (F) Front view of hook, length 1 = 12, 14, 16, 18 mm

FIGURE 3 (A) Transclavicular-transcoracoid drilling assisted by an assembly-type guide. A properly sized hook, based on the size of the coracoid base, was positioned to hook the media/lateral borders under the coracoid base. The guide tube was then positioned to the landmark of the upper clavicle. After locking, a 2 mm-diameter K-wire was drilled along with the guide tube to complete the transclavicular-transcoracoid drilling. (B) and (C) During the operation, after the insertion angle was determined, the guide tube was fixed, and the assembly guide was locked by the hook and K-wire by drilling a small pit into the cortical bone (lateral and upper views)
coracoid base. Then, a 2-mm-diameter K-wire (Hangzhou Yeshealth Medical Devices Co., China, Hangzhou) was drilled from the landmark of the clavicle toward his finger until it reached the base of the coracoid (Figure 5). Transclavicular-transcoracoid drilling was performed.

**Operation of Transclavicular-Transcoracoid Drilling with C-Shape Guide Device**

A C-shape guide was reverse engineered using a popular 3D design software, 3Ds MAX (Autodesk Corp., USA), and then produced by a stereolithographic 3D printer RS6000 (Shanghai Union 3D Technology Corp., Shanghai, China) with photosensitive resin, according to the commercial C-ring drill guide in previous literature. The C-shape guide had a guide tube and a tip positioned at the opposite ends of the C-shape. The tip was positioned on the extension line of the guide tube.

After the surgeon touched the medial and lateral sides of the coracoid base, the tip was placed at the middle of the bottom surface of the coracoid base by hand. The guide tube was then positioned at the upper clavicle, which was approximately 3.5 cm medial to the lateral edge of the clavicle. After the C-shape guide was locked, a 2-mm-diameter K-wire was drilled along with the guide tube to complete the transclavicular-transcoracoid drilling (Figure 6A–C).

**Operation of Transclavicular-Transcoracoid Drilling with Assembly-Type Guide Device**

A novel assembly-type guide was also designed using a popular 3D design software, 3Ds MAX (Autodesk Corp.), and produced by a stereolithographic 3D printer RS6000 (Shanghai Union 3D Technology Corp.) with photosensitive resin. The assembly-type guide had a guide tube and a size-selectable hook on the opposite ends of the C-ring. The hooks of optional size from 12 to 18 mm with 2 mm intervals had two short upward columns at the two ends. There were several slide and rotation structures, and their locking structures inside the assembly-type guide, which could adjust its position freely to fit the clavicle and coracoid process. Regardless of the position of the guide tube, it would always point toward the center of the hook.

To fix the hook end, a properly sized hook based on the size of the coracoid base was placed to hook the medial and lateral borders under the coracoid base. The guide tube was then positioned to the landmark of the upper clavicle, which was approximately 3.5 cm medial to the AC joint. After locking, a 2-mm-diameter K-wire was drilled along the guide tube to complete the transclavicular-transcoracoid drilling (Figure 3A–C). Because the distance from the upper end of the guide tube to the center of the hook was constant, the drilling depth of the K-wire was also predesigned. When the depth met the predesigned value, the drilling procedure was completed, and the guide tube and outrigger were easily removed and moved away without affecting the stability of the K-wire before further operation.

**Outcome Measures**

The main evaluation indicators were operation time, tunnel location zones on the coracoid’s inferior surface, and distances from the tunnel edge to the coracoid’s medial ($d_m$) and lateral ($d_l$) edges.
Clinical Evaluation
The operation time was compared among the three groups. Operation time refers to the time from positioning to the end of the drilling.

Drilling Position Accuracy Evaluation
The tunnel position and distance difference were used. All coracoid processes in the three groups were dissected and sectioned into five zones on their inferior surfaces, a base zone (BZ, proximal third of coracoid process) and a peripheral zone (PZ, distal two-thirds of coracoid process) and three sections from the medial to the lateral ridge (zones M, C, and L), according to Hoffmann’s literature19 (Figure 7). The tunnel position on the inferior surface of the coracoid process was recorded. Successful tunnel placement was defined as the tunnel exit point on the inferior surface of the coracoid located at the base-central position (zone C), without a cortical breach or fracture on either side. In our study, the target tunnel paths passed through the center of the inferior surface of the coracoid base, and the relative deviation of the drilling points on the coracoid process to the center of the inferior coracoid base surface could reflect the accuracy of the drilling methods. Therefore, the distance difference ($d_d$), defined as the absolute value of the difference between distance from the tunnel edge to the coracoid’s medial edge ($d_m$) and distance from the tunnel edge to the coracoid’s lateral edge ($d_l$), was calculated to represent the accuracies of transclavicular-transcoracoid drilling with minimally invasive incisions and guide devices/free-hand technique under direct visualization. The ideal $d_d$ is 0 mm.

$$d_d = |d_m - d_l|$$

Statistical Analysis
In this study, all the statistical analysis was performed using SPSS software (version 20.0; IBM Corporation, Armonk, NY, USA). The Shapiro–Wilk test was used to verify the distribution of the values of $d_d$ and operation time. K independent samples test was used to evaluate the differences in $d_d$ and operation time. The tunnel exit point locations were analyzed using Fisher’s exact test in crosstabs. The significant analysis was followed by the post-hoc test with the Bonferroni correction. $p < 0.05$ was considered statistically significant.
Results

General Results
No operation was failed in the study. The operation time in the free-hand, C-shape, and assembly groups were 198 ± 36 s, 256 ± 64 s, and 353 ± 88 s, respectively. The operation time of the free-hand and assembly groups were based on a Gaussian distribution, but those in the C-shape group were not ($p = 0.858, 0.338, \text{and } 0.004$, respectively). Statistical differences in operation time were found among the three groups ($p < 0.001$), and the mean ranks were 13.94, 26.94, and 41.61, respectively. The boxplot of the operation time among the three groups was shown in Figure 8. These outcomes were presented as the median (first quartile–third quartile). The operation time in the free-hand, C-shape, and assembly groups were 200 (170–227) s, 240 (210–287) s, and 332 (304–451) s. The operation time of the three surgeons were 284 ± 121 s, 258 ± 78 s, and 266 ± 71 s, respectively ($p = 0.358$). And the boxplot of the operation time among the three surgeons was shown in Figure 9.

Drilling Position Accuracy

Evaluation of Tunnel Exit Point Localization
Regarding the tunnel exit point localization on the inferior coracoid surface, all exit points were located at the base zone.

There were 12 tunnels (67%) located in Zone C and six tunnels (33%) located in Zone M or L in the free-hand group. There were 17 tunnels (94%) located in Zone C and one tunnel (6%) in Zone M in the C-shape group. Furthermore, all 18 tunnels (100%) of the assembly group were placed in Zone C (Table 1). The exits on the inferior coracoid surface differed significantly among the three groups ($p = 0.012$).

Comparison of Distance Difference ($d_d$)
The $d_d$ of the free-hand, C-shape, and assembly groups was $3.2 \pm 1.8$ mm, $1.8 \pm 1.0$ mm, and $1.0 \pm 0.8$ mm, respectively. The values of $d_d$ in the free-hand and assembly groups were in a Gaussian distribution ($p = 0.444$ and $p = 0.084$, respectively), while those in the C-shape group were not ($p = 0.003$). K independent samples test results showed a statistically significant difference in $d_d$ among the three groups ($p < 0.001$). The mean ranks of $d_d$ in the free-hand, C-shape, and assembly groups were 38.19, 28.08, and 16.22, respectively. The boxplot of the distance difference among the three groups was shown in Figure 10. The ranges of $d_d$ in the free-hand, C-shape, and assembly groups were 0.7 to 7.1 mm, 0.7 to 4.9 mm, and 0.0 to 2.9 mm. And their medians (interquartile range) were 3.4 (1.7–4.5) mm, 1.6 (1.2–2.1) mm, and 0.85 (0.3–1.5) mm. The $d_d$ of the three surgeons was $2.0 \pm 1.3$ mm, $1.8 \pm 1.8$ mm, and $2.2 \pm 1.6$ mm, respectively ($p = 0.691$).

FIGURE 8 The operation time among the free-hand, C-shape, and assembly groups. There were significant differences between the free-hand and C-shape groups, and between the free-hand and assembly groups (hash represents significant differences [$p < 0.001$]).
Discussion

In many surgical procedures of AR techniques for AC joint, in order to restore its stability of anatomical structures, and gain good biomechanical results and functional outcomes\(^8,9\), a transclavicular-transcoracoid tunnel is necessary, with subsequent insertion of either one or two synthetic rope systems for reduction maintenance and scaffold supply\(^7,8\). Since the morphological structure of coracoid process is with individual differences\(^11\), how to select and accurately locate the best location of the clavicle and coracoid tunnel in the drilling process to guide the reconstruction of CC ligament is one of the focuses of clinical research. Minimally invasive surgery can greatly reduce the injury of patients and accelerate the recovery\(^8,15,16\), ensuring the accuracy of transclavicular-transcoracoid drilling in the AR of the CC ligament complex, with minimally invasive incisions being important to aid surgeons and ensure patient safety. In our

![Figure 9](image1.png)

**Figure 9** The operation time among the three surgeons. No significant differences were observed.

![Figure 10](image2.png)

**Figure 10** The distance difference among the free-hand, C-shape, and assembly groups. There were significant differences between the free-hand and C-shape groups, and between the free-hand and assembly groups (hash represents significant differences \(p < 0.001\)).

| Region     | Free-hand group | C-shape group | Assembly group |
|------------|-----------------|---------------|---------------|
| Zone M     | 5 (27.8%)       | 1 (5.6%)      | 0             |
| Zone C     | 12 (66.6%)      | 17 (94.4%)    | 18 (100%)     |
| Zone L     | 1 (5.6%)        | 0             | 0             |

Abbreviations: Zone M, medial zone; Zone C, central zone; Zone L, lateral zone.
study, we developed the assembly guide device and found the distributions of $d_3$ were more concentrated in the groups using guiding devices. This result was similar to the study of Stübig et al.\textsuperscript{34}, which demonstrated that the assembly guide device could help to locate the tunnel.

**The Advantages of the Assembly Guide Device in Transclavicular-Transcoracoid Drilling**

Compared to c-arm fluoroscopy\textsuperscript{17,18} and arthroscopically assisted drilling\textsuperscript{8,15}, guide techniques have the advantages of being relatively inexpensive, simple, effective, and free of radiation exposure\textsuperscript{6,16,20}. But it is very difficult to locate the basement tunnel under the coracoid process without arthroscopic assistance. In this study, a practical low-cost assembly guide device for transclavicular-transcoracoid drilling was developed. After continuous improvement, the guiding device theoretically meets the needs of drilling through the clavicular coracoid process, the advantages of the assembly guiding device lie in the design of the adjustable hook part and the mobile concentric arc guiding part, which greatly improve the reliability and accuracy of the positioning of the drilling tunnels compared with the C-shape guide device. Its hook would ensure the location of the center point of the coracoid base by gripping two borders of the base of the coracoid to improve the success rate of transclavicular-transcoracoid drilling. The distance from the upper end of the guide tube to the center of the hook determines the drilling depth of the K-wire, which ensures accuracy and minimizes the risk of intraoperative injuries (brachial plexus, axillary artery and vein and others)\textsuperscript{24} and reduces the use of X-rays and arthroscopy. In addition, because the assembly-type guide combines slide and rotation structures, it can adjust its position freely to better meet personalized requirements.

**Accuracy and Convenience Evaluations of the Assembly Guide Device in Transclavicular-Transcoracoid Drilling**

The accuracies and operation times among the three methods of drilling performed by three surgeons were evaluated. The three surgeons showed similar operation times, which indicated that their operating skills were not very different. However, the assembly and C-shape groups showed higher accuracy than the free-hand group. The $d_3$ of the C-shape group and assembly group was significantly smaller compared with that of the free-hand group ($1.8 \pm 1.0$ mm and $1.0 \pm 0.8$ mm, respectively, vs $3.2 \pm 1.8$ mm) while more drilling points were located in the target area in the two guiding device groups, which indicated that the guiding devices in this experiment could ensure that more tunnel orientations could pass through the preset position, consistent with the previous research\textsuperscript{17}. It was proved that the guiding devices could effectively ensure that the tunnels were placed along the expected direction accurately and stably during transclavicular-transcoracoid drilling. From the results, the two guide devices were both of great significance in improving the accuracy of transclavicular-transcoracoid drilling, but a tunnel exit point occurred in an undesired location in the C-shape group. Although the assembly-type guide required a longer operation time than the C-shape guide (an average of about 97 s longer), it is not likely to represent appreciative differences in clinical practice. In several current-concepts reviews, an overall failure rate for AC-joint reconstruction with minimally invasive techniques were 18.3% to 20.5%\textsuperscript{25,26}. However, in this study, the success rate of the three techniques in the early place was 100% (assembly) > 94% (C-Shape) > 67% (free-hand), respectively. The assembly guide device outperformed the C-shape guide and free-hand techniques. It must be acknowledged, however, that there is no clear definition of success and failure rate\textsuperscript{25,26}. Moreover, during the operation, the deficiencies of the C-shape guide device were revealed. Even if transclavicular-transcoracoid drillings were successfully navigated, owing to its fixed structure and poor flexibility in application, the C-shape guide device may get stuck with the tissues around the minimally invasive field or hardly set a proper and stable angle for drilling, which affects the navigation accuracy and the convenience of surgical operation. During the operation, a raised tip is used to locate the middle of the bottom surface of the coracoid base by hand. Its placement is determined subjectively by the operator, which inevitably leads to further errors. Besides, during the operation, because of the shape of the tip, the fixing of the guide was not very secure, the surgeons found it more troublesome and laborious to use. Our practical experience has shown that the assembly guide provides an accurate, stable, and minimally invasive method for transclavicular-transcoracoid drilling positioning. Further study should be performed to testify its clinical effects.

**Limitations**

The present study had several limitations. First, it was limited to a cadaveric laboratory study. Follow-up studies need to be conducted in clinical settings to compare with arthroscopic reconstruction. Furthermore, as there were only inexperienced surgeons participating in our study, the participation and opinions of sophisticated physicians are expected in further studies.

**Conclusion**

In this cadaveric study, we evaluated the accuracy of two different guide devices in transclavicular-transcoracoid drilling compared with that of free-hand drilling. From the results, both the C-shape guide device and the assembly-type guide device achieved high accuracies. As the potential risk of unsuccessful drilling exists in the C-shape guide, the assembly-type guide device might be the first choice for inexperienced surgeons.

**Author Contributions**

Hongtao Zhang: Conception and design of study; Methodology; Project administration. Tiancheng Fan: Investigation; Improvement; Acquisition of data; Manuscript
preparation. Xiaowei Wu: Validation; Analysis; Manuscript preparation. Lutao Li: Acquisition of data; Analysis; Manuscript preparation. Wenrui Li: Analysis with constructive discussions. Lijun Lin: Project administration; Supervision; Reviewing and editing. Jianyi Li: Project administration; Supervision; Reviewing and editing. All authors: Approval of the final version of the paper for publication.

Ethics Statement
This study was approved by the Seventh Affiliated Hospital of Southern Medical University Ethics Committee.

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