Is Restoration of Hip Center Mandatory for Total Hip Arthroplasty of Protrusio Acetabuli?

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Abstract

Background: While initial fixation by a press-fit of the acetabular cup is essential for the durability of the component, restoration of the hip center has been known as an attributable factor for implant survival and successful outcome. In protrusio acetabuli (PA), it might be difficult to obtain both restoration of the hip center and the press-fit of the acetabular cup simultaneously during total hip arthroplasty (THA). We tested a hypothesis that medialized cup, if press-fitted, does not compromise the implant stability and outcome after cementless THA of PA.

Methods: We reviewed 27 cementless THAs of 23 patients with PA. During THA, we prioritized press-fit of the cup than the hip center restoration. A press-fit was obtained in 24 hips. In the remaining 3 hips, a press-fit could not be obtained, and reinforcement acetabular components were used. The hip center was restored in 18 cups; 15 primary cups and 3 reinforcement components, while it was medialized in 9 cups. We compared implant stability and modified Harris hip score (mHHS) between the 2 groups at a mean of 5.2 (2-16) year follow-up.

Results: One restored reinforcement cup was loose. The remaining 26 cups; 17 restored cups and 9 medialized press-fitted cups, remained stable. The final mHHS was similar between the restored group and the medialized group (81.8 ± 10.8 vs 83.6 ± 12.1, \( p = 0.498 \)).

Conclusions: Press-fitted cups, irrespective of hip center restoration, rendered implant stability and favorable results. Initial fixation of the cup is more important than the restoration of hip center.

Background

Protrusio acetabuli (PA) is an intrapelvic displacement of acetabulum and femoral head [1, 2]. This deformity can develop due to various conditions that compromise the mechanical property of acetabulum [3, 4]. In patients with PA, total hip arthroplasty (THA) is technically demanding and has been known to be associated with a high rate of failure [5]. It is difficult to obtain a stable fixation of the acetabular cup due to deficient medial wall and thin peripheral edge of the acetabulum. The deficient bone stalk poses a risk of further migration and loosening of the acetabular cup [5].

Various techniques have been proposed for THA of PA [5–10]. While early studies used cemented acetabular components [11, 12], cementless acetabular components have been favored in recent studies [4]. Studies on cementless acetabular component emphasized that the restoration of hip center is essential for implant survival and successful outcome after THA [10]. However, initial fixation by a press-fit of acetabular component into the host bone is mandatory for the stability and durability of the component. To obtain a press-fit of acetabular component into the protruded acetabulum, some degree of medialization is inevitable. According to classic concept of THA by Charnley, cup medialization has biomechanical benefits, because the medialization increases the abductor moment arms [13]. In the presence of PA, it might be difficult to obtain the restoration of hip center as well as a press-fit of acetabular component simultaneously during THA. Thus, the restoration of cup center must be balanced against its tradeoff of unstable cup fixation. It is not certain which one of the two; medialized press-fit versus restoration of the hip center, is more beneficial for the implant survival and better functional outcome in THA of patients with PA.

The purpose of this study was to compare cup stability and functional outcome between medially press-fitted acetabular cups and anatomically restored cups in cementless THAs of PA patients.

Methods

From June 2003 to December 2017, 23 patients (27 hips) with PA, underwent primary THA at our institution. A diagnosis of PA was made when there was an intrapelvic displacement of the femoral head medial to the ilioischial line (Kohler’s line) on anteroposterior (AP) radiograph of hip (Fig. 1) [1, 6]. All of them were operated with cementless prostheses.
These patients were followed up for 2 to 16 years (average, 5.2 years) after the index THA. There were 5 men (7 hips) and 18 women (20 hips), their mean age at the time of THA was 60.5 years (range, 24.5 to 77 years), and their mean body mass index was 22.3 kg/m\(^2\) (range, 16.0 to 29.7 kg/m\(^2\)) (Table 1).

| Table 1 | Demographics of patients with protrusio acetabuli |
|---------|---------------------------------------------------|
|         | Overall (n = 27) | Medialized group (n = 9) | Restored group (n = 18) | p-value |
| Gender  |          |                              |                          |         |
| Male    | 7        | 2                             | 5                        | 0.756   |
| Female  | 20       | 7                             | 13                       |         |
| Age     | 60.5 ± 15.0 | 64.6 ± 12.7                   | 58.5 ± 15.9               | 0.348   |
| BMI     | 22.3 ± 3.4 | 23.3 ± 2.6                    | 21.8 ± 3.8                | 0.375   |
| Diagnosis |          |                              |                          | 0.905   |
| Rheumatoid arthritis | 14 | 5 | 9 |
| Post-traumatic arthritis | 7 | 4 | 3 |
| Ankylosing spondylitis | 4 | 0 | 4 |
| Post-radiation osteonecrosis | 1 | 0 | 1 |
| Previous infection | 1 | 0 | 1 |
| Grade   |          |                              |                          | 0.107   |
| Mild (<5mm) | 5 | 0 | 5 |
| Severe (>15mm) | 2 | 1 | 1 |
| Cup abduction (°) | 40.8 ± 6.9 | 37.4 ± 5.2 | 42.4 ± 7.1 | 0.023 |
| Cup anteversion (°) | 24.4 ± 9.2 | 23.7 ± 8.5 | 24.7 ± 9.7 | 0.820 |
| Postoperative LLD (cm) | 0.6 ± 1.0 | 0.2 ± 0.9 | 0.8 ± 1.0 | 0.131 |
| Follow-up duration (years) | 5.2 ± 3.3 | 5.3 ± 3.5 | 5.1 ± 3.1 | 0.875 |
| mHHS    | 82.4 ± 11.6 | 83.6 ± 12.1                  | 81.8 ± 10.8               | 0.498   |

*Abbreviations: BMI body mass index; LLD leg-length discrepancy, mHHS modified Harris hip score*

The causes of PA were rheumatoid arthritis in 14 hips, post-traumatic arthritis in 7 hips, ankylosing spondylitis in 4 hips, post-radiation osteonecrosis in 1 hip and previous infection in 1 hip.

We measured the amount of acetabular protrusion on hip AP view. Theoretically, the inner wall of the acetabulum, which appears as the pelvic tear-drop on the AP radiograph, would be the ideal reference structure to measure the amount of acetabular protrusion. However, the tear-drop was not visible or moved medially in 10 of our patients. Thus, we adopted the method of Sotelo-Garza and Chamley [14] for the measurement. We took the rim of the original pelvis, a projection of the upper margin of pubic ramus, as a reference line instead of the tear-drop and measured the distance between the original pelvic rim and the quadrilateral plate of protruded pelvis (Fig. 1).

The amount of acetabular protrusion ranged from 2.8 mm to 21.9 mm (mean, 9.4 mm). According to the Sotelo-Garza and Chamley system [14], the grade of protrusio acetabuli was mild (<5 mm) in 5 hips, moderate (6–15 mm) in 20 hips and
severe (> 15 mm) in 2 hips.

**Preoperative planning**

Preoperatively, AP and trans-lateral hip radiographs, scanography, and CT scans (Mx8000 IDT; Philips, Eindhoven, The Netherlands) of the pelvis and proximal femur were taken. We used on-screen templating with digital radiographs to decide the size of the implant [15]. On the preoperative CT scan, we measured abduction and anteversion of the acetabulum to guide the cup positioning [16].

**Surgical Techniques**

All operations were performed by 3 high-volume (> 200 hip surgeries/year) surgeons using Kocher-Langenbeck approach [17]. In all patients, the sciatic nerve was identified and protected during the operation.

When there was a risk of posterior wall fracture of the acetabulum during the dislocation maneuver, we did not dislocate the femoral head. Instead, 2 osteotomies; the first osteotomy below the femoral head and the second one at the base of the femoral neck, were made. Then, 1.5 to 2.5 cm thick block of the femoral neck was excised, and the femoral head was removed from the acetabulum [18].

We prioritized the press-fit fixation of acetabular cup than the restoration of hip center. Acetabular preparation was performed in 2 stages. We reamed the peripheral edge of the acetabulum first and gradually increased the diameter of the reamer until we obtained a surface reamed enough to obtain a press-fit of cementless acetabular cup. After then, cartilages and fibrous tissues of the medial floor inside the acetabulum were removed.

In 18 hips, there was a medial acetabular defect after reaming, and we filled the defect with autogenous bone graft from the excised femoral head. The bone graft was firmly impacted and was rounded using reverse reaming.

The acetabular cup was positioned using the CT measurements of acetabular abduction and anteversion as the alignment-guide [16]. The target abduction of the cup was 40°-45° [19]. The target anteversion of the cup was 15° until August 2009. After then, the cup was anteverted according to the concept of combined anteversion [16, 20]. We exclusively used cementless implants, because we were concerned of cement-related cardiopulmonary complications [21].

A press-fit of the acetabular cup was obtained in 24 hips. In the remaining 3 hips, a press-fit could not be obtained because the acetabular rim defect was > 50% or the acetabular rim was too thin. Thus, reinforcement acetabular components with a hook and three iliac flanges were used in these 3 hips.

PLASMACUP® SC (Aesculap, Tuttlingen, Germany) was used in 9 hips, Bencox cup (Corentec, Seoul, South Korea) in 7 hips, and Pinnacle cup (DePuy, Warsaw, IN) in 5 hips. G7 cup (Zimmer Biomet, Warsaw, IN) in 1 hip, ABT cup (Zimmer Biomet) in 1 hip and Delta TT cup (Lima Ito, Udine, Italy) in 1 hip. In 3 hips with defective rim of the acetabulum, we used SPH reinforcement cups (Lima Ito, Udine, Italy).

A nonunion was found at the transverse acetabular fracture site in 1 hip with posttraumatic osteoarthritis. The nonunion was fixed with a reconstruction plate.

BiCONTACT® stem (Aesculap) was used in 10 femurs, Bencox M stem (Corentec) in 8 femurs, Corail stem (DePuy) in 4 femurs, Taperloc Microplasty (Zimmer Biomet) in 2 femurs, KAR stem (DePuy) in 1 femur, Trilock stem (DePuy) in 1 femur, and Minima stem (Lima Ito) in 1 femur.

Delta ceramic-on-ceramic bearing (BIOLOX delta, CeramTec, Plochingen, Germany) was used in 16 hips, alumina ceramic-on-ceramic bearing (BIOLOX® forte, CeramTec) in 7 hips, alumina ceramic-on-polyethylene bearing in 3 hips, and a metal-
on-polyethylene bearing in 1 hip. The diameter of the femoral head was 28 mm in 9 hips, 32 mm in 11 hips, and 36 mm in 7 hips.

After the implantation and reduction of the hip prostheses, the posterior capsule and the short external rotators were tightly repaired to the crest of the greater trochanter [22].

**Postoperative care**

Patients were encouraged to walk with toe-touch weight bearing with the aid of 2 crutches for 4 weeks and then were allowed weight-bearing.

**Follow-up evaluations**

Follow-up evaluations were performed at 6 weeks, 3, 6, 9 and 12 months, and every year thereafter. At each follow-up, AP and trans-lateral hip radiographs were taken and modified Harris hips score (mHHS) were measured. Postoperative scanogram was taken at 6-week follow-up.

**Classification of medialized cup and restored cup**

The restoration or medialization of cup center was evaluated on postoperative 6-week AP radiograph. When any portion of the acetabular cup protruded medial to the Kohler’s line, the hip was classified as medialized group. When whole portion of the cup was located lateral to the Kohler’s line, the hip was classified as restored group.

Eighteen cups; 15 primary cups and 3 reinforcement components, were classified as restored group, and 9 cups as medialized group. In the medialized group, the amount of medialization ranged from 6.8 mm to 19.6 mm (mean, 11.8 mm) (Table 2).
Table 2
Hip center restoration, intraoperative press-fit and postoperative stability of cup in 27 total hip arthroplasties of 23 patients with protrusio acetabuli

| Patient | Sex | Age (year) | Side | Cause of protrusion       | Preoperative protrusion (mm) | Hip center restoration | Intraoperative press-fit of cup | Cup stability | Follow-up duration (years) |
|---------|-----|------------|------|---------------------------|------------------------------|------------------------|-------------------------------|--------------|---------------------------|
| #1      | F   | 77         | Rt.  | Post-radiation osteonecrosis | 11.3                         | Restored               | Not obtained                  | Loose        | 6.4                       |
| #2      | F   | 71         | Lt.  | Post-traumatic arthritis   | 11.7                         | Restored               | Obtained                      | Stable       | 7.2                       |
| #3      | M   | 36         | Rt.  | Ankylosing spondylitis     | 7.2                          | Restored               | Obtained                      | Stable       | 5.1                       |
|         |     |            |      |                           |                              |                        |                               |              |                           |
| #4      | M   | 68         | Rt.  | Rheumatoid arthritis       | 8.9                          | Restored               | Obtained                      | Stable       | 8.6                       |
| #5      | F   | 60         | Rt.  | Rheumatoid arthritis       | 15.9                         | Restored               | Obtained                      | Stable       | 5.4                       |
| #6      | F   | 69         | Lt.  | Post-traumatic arthritis   | 9.9                          | Restored               | Obtained                      | Stable       | 8.1                       |
| #7      | F   | 35         | Rt.  | Rheumatoid arthritis       | 3.1                          | Restored               | Obtained                      | Stable       | 2.0                       |
|         |     |            |      |                           |                              |                        |                               |              |                           |
| #8      | F   | 73         | Lt.  | Rheumatoid arthritis       | 4.7                          | Restored               | Obtained                      | Stable       | 3.9                       |
| #9      | M   | 67         | Rt.  | Ankylosing spondylitis     | 6.2                          | Restored               | Obtained                      | Stable       | 3.1                       |
| #10     | F   | 59         | Rt.  | Post-traumatic arthritis   | 5.3                          | Restored               | Obtained                      | Stable       | 8.3                       |
| #11     | F   | 49         | Rt.  | Ankylosing spondylitis     | 4.3                          | Restored               | Obtained                      | Stable       | 2.1                       |
| #12     | F   | 63         | Rt.  | Rheumatoid arthritis       | 8.3                          | Restored               | Obtained                      | Stable       | 2.2                       |
| #13     | M   | 62         | Lt.  | Previous infection         | 10.9                         | Restored               | Obtained                      | Stable       | 2.5                       |
| #14     | F   | 62         | Lt.  | Rheumatoid arthritis       | 4.8                          | Restored               | Obtained                      | Stable       | 3.7                       |
| #15     | F   | 74         | Rt.  | Rheumatoid arthritis       | 9.2                          | Restored               | Not obtained                  | Stable       | 4.1                       |

Patients #3, #7, #15 and #16 underwent bilateral total hip arthroplasties. Patients #1 and #2 were operated with reinforcement cups.
| Patient | Sex | Age (year) | Side | Cause of protrusion | Preoperative protrusion (mm) | Hip center restoration | Intraoperative press-fit of cup | Cup stability | Follow-up duration (years) |
|---------|-----|------------|------|---------------------|----------------------------|-----------------------|-------------------------------|---------------|--------------------------|
| 73      | Lt  | 70         | Lt   | Rheumatoid arthritis| 11.3                       | Medialized (9.0mm)     | Not obtained                  | Stable        | 4.5                      |
| #16     | M   | 70         | Lt   | Rheumatoid arthritis| 13.3                       | Restored               | Obtained                      | Stable        | 4.8                      |
| 69      | Rt  | 70         | Lt   | Rheumatoid arthritis| 14.3                       | Medialized (19.6mm)     | Obtained                      | Stable        | 5.3                      |
| #17     | F   | 66         | Rt   | Post-traumatic arthritis| 7.6                       | Medialized (8.6mm)      | Obtained                      | Stable        | 2.3                      |
| #18     | F   | 74         | Rt   | Rheumatoid arthritis| 9.0                        | Medialized (6.8mm)      | Obtained                      | Stable        | 2.8                      |
| #19     | M   | 74         | Rt   | Post-traumatic arthritis| 14.4                       | Medialized (15.8mm)     | Obtained                      | Stable        | 3.6                      |
| #20     | M   | 34         | Rt   | Post-traumatic arthritis| 12.5                       | Medialized (13.0mm)     | Obtained                      | Stable        | 8.4                      |
| #21     | F   | 55         | Rt   | Rheumatoid arthritis| 21.9                       | Medialized (11.5mm)     | Obtained                      | Stable        | 11.7                     |
| #22     | M   | 69         | Lt   | Rheumatoid arthritis| 10.4                       | Medialized (11.3mm)     | Obtained                      | Stable        | 2.3                      |
| #23     | F   | 66         | Lt   | Post-traumatic arthritis| 7.7                        | Medialized (10.1mm)     | Obtained                      | Stable        | 5.1                      |

Patients #3, #7, #15 and #16 underwent bilateral total hip arthroplasties. Patients #1 and #2 were operated with reinforcement cups.

**Cup position and radiological evaluations**

The cup position was measured on postoperative 6-week radiographs. The cup abduction was measured using the method described by Engh et al. [23], and the cup anteversion using the method of Woo and Morrey [24, 25].

We evaluated postoperative leg length discrepancy, migration of the acetabular cup, the stability of the acetabular and femoral components, wear of bearing surface and osteolysis.

The leg length discrepancy was measured on postoperative 6-week scanogram [26]. We measured the vertical length between the ankle mortise and upper body of the first sacral vertebra. When the first sacral vertebra was not visualized in the scanogram, we used both sciatic notches as the proximal reference.

The 6-week AP and cross-table lateral radiographs were used as the baseline studies for the assessment of cup migration, implant stability, bearing wear and osteolysis.

The stability of acetabular cup was evaluated using the method of Latimer and Lachiewicz [27], and that of the femoral stem using the method of Engh et al. [28]. The bearing was measured according to the method by Livermore et al. [29]. A diagnosis of osteolysis was made according the criteria of Engh et al. [30]. The osteolytic lesions were located according to the 3 zones of DeLee and Charnley [31] on the acetabular side, and the 7 zones of Gruen et al. [32] on the femoral side.
Radiological evaluations were done by two independent observers who did not participate in THAs.

**Clinical evaluation**

Clinical evaluations were done using modified Harris hip score [33].

**Comparison between the medialized group and restored group**

The postoperative migration of acetabular cup, implant stability, radiological change and modified Harris hip score at the final follow-up between the restored group and medialized group were compared.

The study design and protocol of this retrospective study were approved by the institutional review board in our hospital.

**Results**

The mean abduction and anteversion angles of the acetabular component were 37.4° (range, 29° to 44°) and 23.7° (range, 10° to 38°) in the medialized group and 42.4° (range, 20° to 52°) and 24.7° (range, 5° to 42°) in the restored group, respectively.

Postoperatively, the mean leg length discrepancy was 0.21 cm (range, -1.0 to 2.0 cm) in the medialized group and 0.75 cm (range, -0.5 to 3.2 cm) in the restored group.

One cup (patient 1) in the restored group was loose. The patient was a 76-year-old woman, who underwent THA on the right hip due to post radiation osteonecrosis of the femoral head and acetabulum. She had been treated radiation therapy due to uterine cervical carcinoma 15 years before the THA. She also had an internal fixation due to femoral neck fracture on the right side 7 years before the arthroplasty. During the THA, the acetabulum was weak and a press-fit could not be obtained with a primary cup trial. Thus, a reinforcement cup was used. After the THA, the cup showed a gradual rotational migration. Compared to the 6-week radiograph, the inferior hook of the cup moved 9 mm at 5.5-year follow-up. Even with the migration, hip pain was tolerable and patient could walk with crutches until the latest follow-up (Fig. 2).

The remaining 24 primary cups (8 medialized cups and 16 restored cups), and 2 reinforcement cups (1 medialized cup and 1 restored cup) had no migration and considered to have bone-ingrown stability. All of the 27 stems were well-fixed with bone-ingrowth (Figs. 3 and 4).

No hip dislocated in both groups during the follow-up. No measurable wear of bearing surface was detected on radiographs. Periprosthetic osteolysis was not seen in any hip.

One patient (patient 4) in the restored group sustained a Vancouver type B periprosthetic femoral fracture after a fall. The fracture was treated with internal fixation using 2 plates. Otherwise, no hip was revised during the follow-up.

The modified Harris hip scores were similar between two groups at the latest follow-up (mean, 81.8 points; range, 57–100 points in the restored group versus mean, 83.6 points; range, 65–100 points in the medialized group).

**Discussion**

Several techniques of cup implantation have been recommended for THA of PA. Nevertheless, the best recommendation remains unknown.

Our study showed that press-fitted cementless cups, irrespective of the restoration of hip center, were associated with durable implant stability and favorable functional outcome.
The restoration of hip center was emphasized in the literature. In 1980, Ranawat et al. reviewed 35 cemented THAs that were done in PA. In their study, the restoration of anatomical center of rotation appeared as a critical factor for stable fixation the acetabular component. Radiolucent line was present in 16 of 17 acetabular components, which was positioned 1 cm superiorly or medially beyond the anatomical position. In 13 acetabular components, which was positioned within 5 mm of the anatomical center, no radiolucent line was present [34]. After this study, other authors have advocated the restoration of hip center in THA of PA [35]. In 1987, Bayley et al. reviewed 93 cemented THAs in patients with PA. Fifty-three percent of the PA were treated with cement alone, 36% with mesh or anti-protrusio shell, and 11% with bone graft. Radiolucent lines were observed in a high percentage in all of the 3 groups. The highest rate of 50% occurred in the cement alone group, in which the center of rotation was not corrected to within 10 mm of the anatomic position. They concluded that the restoration of the anatomic cup position was vital irrespective of combined use mesh, anti-protrusio shell, or bone graft in cemented THA of PA [11]. Baghdadi et al. evaluated survivorship of 127 THAs for PA as a function of restoration of the hip center. In their 2 to 25-year follow-up study, the risk of cup loosening was increased by 24% for each 1 mm medialization of cup from the native hip center of rotation [10]. In 2015, the same authors conducted and extension study on 65 hips at longer than 10 years after the THA. At 15 years, the estimated survival rate from revision was 70% for the THA: 85.4% for the acetabular component, and 83% for the femoral component. Five unrevised acetabular components had evidence of non-progressive radiolucency [6].

To restore the native hip center, the medial defect should be filled with bone graft. To expect a satisfactory result of bone graft, enough contact between the acetabular component and the host bone is crucial [36]. Garbuz et al. compared results between cementless cups with host bone contact > 50% and those supported by < 50% of the host bone. The overall success rates were 90% and 76%, and the revision rates were 14% and 45%, respectively. They recommended the use of reinforcement ring, if the host bone support was less than 50% [37].

On the other hand, one study reported that an intraoperative secure fixation of the cup is mandatory to achieve durable stability of the cup in THA of PA [38]. Even though prior authors scrutinized medialization of the cup, the medialization with a respective increase in the femoral offset has been known to have a biomechanical benefit of increasing abductor moment arm [39].

In THA of hips with PA, it is difficult to restore the hip center and to obtain a press-fit of cup, simultaneously. In PA, the peripheral rim of acetabulum is often weak and thin, and it is difficult to obtain a press-fit of acetabular cup. In such situations, surgeons meet a dilemma which one to prioritize between the two; restoration of hip center with insecure fixation of the cup versus press-fit of the cup with medialization. In our study of PA patients, press-fitted cups, irrespective of the hip center restoration, had stable fixation and good clinical results after cementless THA.

There were limitations in this study. First, it was a retrospective review involving a small number of PA patients without control group. The operations were done by 3 surgeons and the enrollment period was quite long (15 years) and various implants were used in the limitation of the study. Second, our study was done in East Asia, and the mean body mass index of our patients was 22.3 kg/m². Our results might not be generalized to patients with large constitutions in Western countries.

We recommend secure initial fixation of cup with medialization than unstable cup with restoration of hip center in THA of PA patients.

Declarations

Ethics approval and consent to participate

This study was performed according to the guidelines of the Helsinki Declaration. The study was approved by the Seoul National University Bundang Hospital institutional review board (IRB No. B-2005/612-102). Patient consent to participate
was waived by the Seoul National University Bundang Hospital institutional review board as this is a retrospective study.

**Consent for publication**

Not applicable, as no identifying personal information is included in this manuscript.

**Data availability**

All data generated or analyzed during this study are included in this published article.

**Competing interests**

The authors declare that they have no competing interests.

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**Author's contribution**

YKL, YCH and KHK conceived and designed this research. BSL, HSK, JWP and OSK collected the data and performed the imaging analysis. BSL, HSK, JWP, and OSK interpreted and analyzed the data. YKL, YCH and KHK were involved in the critical review of this article. BSL and HSK wrote the manuscript and prepared figures. JWP and OSK provided administrative, technical, or material support. All authors read and approved the final manuscript.

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Beom Seok Lee and Hong Seok Kim equally contributed to this study and should be considered as co-first author.

**Conflict of interest**

Each author certifies that he or she has no commercial associations (e.g., consultancies, stock ownership, equity interest, patent/licensing arrangements, etc.) that might pose a conflict of interest in connection with the submitted article.

**Ethical review committee statement**

The present study was approved from Seoul National University Bundang Hospital institutional review board review.

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