

Peer Review File

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Reviewer A

Comment 1: It is recommended to add the shortcomings of current THA in the abstract, so further improvements in surgical methods are needed.

Reply 1: We would like to thank the Reviewer A for this great comment.

Changes in the text: We rewrote the Abstract in the background section to read as “*However, prior studies have underlined the shortcomings of conventional approaches for THA, including higher dislocation, more blood loss, longer incisions, massive tissue damage, and delayed postoperative rehabilitation.*” (page 3, lines 39-41)

Comment 2: In the abstract, Harris hip score needs to be mentioned in the methods section.

Reply 2: We would like to thank the Reviewer A for this great comment.

Changes in the text: We rewrote the Abstract in the methods section to read as “*Perioperative status (operation time, incision length, intraoperative blood loss, soft tissue damage, and length of hospital stay), and postoperative function outcomes were evaluated using the following measures: range of motion (ROM), Pain visual analogue scale (VAS), and Harris Hip Score (HHS) in detail and compared between both groups at scheduled time points within 12 months postoperatively.*” (page 3, lines 47-51)

Comment 3: It is better to add the description of screening the patient's condition (such as joint range of motion, etc.) in the "Methods" section to obtain a more accurate contrast effect.

Reply 3: We would like to thank the Reviewer A for this valuable suggestion. In the present study, patient characteristics (age, gender, BMI, comorbidities, and ASA grade) were collected to determine whether the two cohorts were comparable at baseline. Analysis of variance (ANOVA) was used to compare age, body mass index (BMI). Chi-square test was used to compare gender, ASA grade, comorbidities, and transfusion rate.

Changes in the text: We rewrote the text in the Methods read as “*Patient characteristics (age, gender, BMI, comorbidities, and ASA grade) were collected to determine whether the two cohorts were comparable at baseline.*” (page 7, lines 115-116). Additional sentences in the

Statistical analysis have been added to read as “*Analysis of variance (ANOVA) was used to compare age, body mass index (BMI). Chi-square test was used to compare gender, ASA grade, comorbidities, and transfusion rate.*” (pages 11, lines 200-202).

Comment 4: In line 61, "SuperPath may be a minimally invasive technique...". Please change to "SuperPath may be a promising minimally invasive technique for the treatment of OA in the future."

Reply 4: Thank you very much for this comment.

Changes in the text: We rewrote the sentence to read as “*SuperPath may be a promising minimally invasive technique for the treatment of OA in the future.*” (page 4, lines 65-66)

Comment 5: Line 160, labels of all reference numbers should be in a uniform format.

Reply 5: We would like to thank the Reviewer A for this great suggestion.

Changes in the text: We have gone through the entire manuscript and corrected labels of all reference numbers as much as possible. We rewrote the sentence to read as “*The total blood loss was calculated applying the Gross formula (25) and the Nadler formula (26) as previously described (20).*” (page 9, lines 174-175)

Comment 6: Line 546, it is recommended to revise the annotation format of Figure 2.

Reply 6: Thank you very much for this comment. To better describe the figure, we have modified the annotation of the Figure 2 and expanded the figure legend with more information.

Changes in the text: We have revised the annotation format and its legend of Figure 2, reading as “*Perioperative changes of serum markers, including creatine kinase (CK), C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR), after unilateral total hip arthroplasty with either the SuperPath or through the mini-incision posterolateral approach (PLA) for hip osteoarthritis. Error bars represent the standard deviation of the data. *Significantly different ($p < 0.05$) between SuperPath group and PLA group.*” (page 34, lines 567-571)

Reviewer B

Comment 1: Line 82. Correct the orthography.

Reply 1: We thank the Reviewer B for this useful recommendation.

Changes in the text: We rewrote the sentence to read as “*Postoperative dislocation as one of the most common postoperative complications has been associated with traditional approaches of THA possibly due to the intraoperative extensive impairment of periarticular soft tissue, especially the external rotators and joint capsules (12-14).*” (page 5, lines 83-86)

Comment 2: Line 102. Why do you make this hypothesis? In your previous study, Super path had not superior outcomes. Why do you think that maybe in this study, outcomes would be better?

Reply 2: The reasons why we make the hypothesis of the present study are as follows: Firstly, previous published studies (1-5) on the SuperPath majorly indicate that SuperPath is associated with better outcomes than conventional approaches of total hip arthroplasty (THA). Patient cohorts evaluated in most available studies are subjectives with various preoperative indications in one study, including osteoarthritis (OA) (6,7) osteonecrosis of the femoral head (ONFH) (6,7) femoral neck fracture (2,6), post-septic arthritis (7), ankylosing spondylitis (7), and developmental dysplasia of the hip (7). Such a mixed study design might hold patient selection and sampling bias.

Secondly, it has been recognized that the clinical outcomes of THA are influenced by the preoperative hip pathologies. For example, end-staged ONFH and OA are two major indications of THA. Saito S *et al.* (8), comparing long-term outcomes of unilateral or bilateral THA between ONFH (n = 29) and osteoarthritis (n = 63) treated, reported significantly more unsatisfactory results (48%) and femoral component loosening (28%) in ONFH group than in OA group (33% and 5%, respectively). Similarly, Ritter MA *et al.* (9), comparing THA outcomes in ONFH (n = 82) and OA (n = 706) patients, reported

a much higher death rate in ONFH patients (24%) than in OA patients (15%). These data indicate that ONFH patients are highly risky, compared with OA patients, for THA in terms of long-term implant durability and patient mortality, which might arise a requirement to separately analyze the efficacy of SuperPath techniques only within hip OA surgical candidates.

Furthermore, our previous published study (10), regarding outcomes of staged THA with the SuperPath or PLA for bilateral ONFH patients, shows less favorable short-term outcomes in SuperPath group than in PLA THA group. Of note, there is a possibility that these relative negative outcomes of SuperPath are due to the disease characteristics of ONFH, while positive favorable results of SuperPath can be possibly witnessed in surgical candidates with other preoperative diseases (e.g. hip OA). Taken together, based on the aforementioned preconditions and evidences and to further validate evidences from other available studies, the present study aims to compare the outcomes between the SuperPath and PLA THA for unilateral end-stage primary OA patients with a hypothesis that the SuperPath would yield superior outcomes over the PLA THA for OA patients with better perioperative status and improved postoperative function.

Changes in the text: To avoid possible misunderstanding, we rewrote the hypothesis in the end of Introduction section to read as “*We hypothesized that the SuperPath would yield superior outcomes over the PLA THA for OA patients with better perioperative status (operation time, incision length, intraoperative blood loss, soft tissue damage, and length of hospital stay) and improved postoperative function (range of motion, pain, and hip function).*” (page 6, lines 103-107)

Comment 3: Patient selection - Correct

Reply 3: Thank you very much for this positive comment.

Changes in the text: None

Comment 4: Surgical approach - to eliminate the learning curve, authors accomplished over 50 cases. Did the authors study the outcomes of this cohort? I understand that these patients were operated before March 2017. So, all of them have a minimum 2-year follow-up. Did the authors have published these outcomes? Standardized postoperative care did not include pain management?

Reply 4: We would like to thank the Reviewer B for these useful comments. Those first 50 cases of patients with various preoperative conditions (e.g. OA, ONFH, DDH, and revision) have been attributed into another ongoing large-scale, long-term project to comprehensively investigate the efficacy of SuperPath technique for all spectrum of primary or revision THA. As it is an ongoing project, these data were not yet published. Moreover, we sincerely apologize for the omission of the information of pain management in the manuscript, which is indeed utilized routinely in our Center as published elsewhere (11).

Changes in the text: We added an additional paragraph about the pain management issue in the Methods section to read as “*Multimodal pain management as part of the standardized postoperative care were applied to all patients (23). Patients received preoperative femoral nerve block and a prophylactic oral celecoxib (200 mg). Intraoperatively, a periarticular cocktail injection (100 ml) was delivered into the surgical site with ropivacaine 0.5% (49.25 mL), epinephrine 0.5 mg (0.5 mL), ketorolac 30 mg (1 mL), clonidine 80 mcg (0.8 mL), and sterile water (48.45 mL). Postoperatively, intravenous patient-controlled morphine pump and oral celecoxib were applied for pain control depending on intensity of pain. After discharge, oral celecoxib or other nonsteroidal anti-inflammatory drugs were ordered and used as appropriate.*” (pages 8-9, lines 151-159)

Comment 5: Postoperative rehabilitation - Which criteria did the authors have for patients discharge? if patients were discharged on a postoperative day 3, why mean LOS was 2.7 in the PLA group?

Reply 5: Thank you very much for this helpful comment. Our discharge standards are,

as published elsewhere (12), as follows: (1) good spirit and diet; (2) stable surgical wounds; (3) hip flexion > 100 degrees, hip abduction > 35 degrees; (4) hemoglobin > 100 g/L, (5) albumin > 35 g/L. Our initial plan was to discharge all patients after taking the serologic tests. Of note, 2 patients in the PLA group, who were living close to the hospital, chose to be discharged at the postoperative day 2 after surgery after reaching the mentioned criteria. The serologic tests of these 2 patients were undertaken in the outpatient clinic at the postoperative day 3. Therefore, the mean LOS was calculated to be 2.7 in the PLA group.

Changes in the text: None.

Comment 6: Pain, range of motion, and hip function - how the authors measured the range of motion (a goniometer?). All measurements were made by the same person?

Reply 6: We thank the Reviewer B for this kind comment. The ROMs was measured using a goniometer, as previously described (13), by the junior author (W.M.) and verified by the senior author (Z.Z.).

Changes in the text: We rewrote the sentence to read as “*The ROMs was measured using a goniometer at the day before surgery, postoperative 3 months, 6 months, and 12 months (28).*” (page 10, lines 193-195)

Comment 7: Statistical analysis - Did the authors determine normal distribution in data? A power analysis of the study has not been made.

Reply 7: Thank you very much for this useful comment. We tested the normal distribution of 47 variables with our data. Fifteen variables were found to be normally distributed, including operation time, incision length, blood loss, C-reactive protein post-3d, ESR post-3d, ESR post-14d, creatine kinase postoperative post-1d, creatine kinase postoperative post-3d, cup ante version angle, flexion preoperative, HHS preoperative, HHS post-1d, HHS post-3d, HHS post-14d, and HHS post-6m.

As a pilot study, the relatively small sample size is a potential problem to undermine the study power, which has been already underlined in the limitation section

of the Discussion. However, we chose to omit a power analysis in the present study mainly due to three reasons. Firstly, the initial purpose of the present research is to test the possible difference between two procedures rather than obtaining a precise estimate of specific parameters (i.e., minimizing the standard errors). Therefore, in theory, a relatively small sample size is needed in such studies. Secondly, our major variables of postoperative joint functions are patient-reported outcomes, which are generally subjective and indirect measures and make a power analysis unpractical in this case. Thirdly, the sample size of our study was also restricted by the limited funding covering the radiographic and serological assessment, which practically did not allow us to include more subjects. Considering these critical preconditions and potential drawbacks, we took some means to increase our power and to diminish the measurement errors as much as possible. For example, in pain VAS assessments, an experienced senior nurse was trained specifically in charge of these scheduled measurements with clear oral instructions to patients. Similarly, for continuous data (e.g. ROMs) and Harris hip score measurements, they were always performed by the junior authors first and then confirmed by senior authors again. Finally, a robust and flexible combination of statistical methods was applied to analyse our data, where appropriate, including Student's t-test, one-way ANOVA, and nonparametric Mann-Whitney U test.

Changes in the text: We underlined this issue in the limitation section of Discussion, reading as “First, the sample size is relatively limited without a power analysis performed in the research planning phase, and the postoperative follow-up is relatively short.” (page 19, lines 363-365)

Comment 8: Patient demographics and surgical details - do not repeat data in text and table. What is the meaning of n.a. in the table? Obviously, if it is not applicable, groups achieve comparability.

Reply 8: We would like to thank the Reviewer for this helpful comment. We deleted the repeat data. n.a. means zero or not applicable in Table 1.

Changes in the text: We rewrote the text about patient demographics and surgical details to read as “*The incision length in the SuperPath group was significantly shorter than the PLA group (Table 1). However, the SuperPath group was associated with a significantly longer operation time than the PLA group. Similarly, the mean blood loss was significantly higher in the SuperPath group than in the PLA group. However, both groups achieved the comparability in terms of LOS, blood transfusion rate, postoperative complication, and hospital readmission/reoperation rate within 12 months postoperatively.*” (Page12, Line 216-221) The meaning of n.a. in the Table 1 was provided (page 27, line 519).

Comment 9: Line 282. Are you sure that the increases CK level was related to the trocar cannula? Maybe authors have to find another reason for this CK results.

Reply 9: Thanks a lot for this helpful comment. We totally agree with the Reviewer B that associations have been established between increased CK level after orthopedic surgeries and the soft tissue (mainly muscle) damage from many sources (14), including intraoperative stretching (15), unintentional detachment (15), and varied retraction with instruments (16). The application of trocar cannula might be a possible source for the additional soft tissue damage.

Changes in the text: To be more accurate, we rewrote these texts to read as “*Such unexpected results are possibly attributed to the additional intraoperative soft tissue (mainly muscle) damage from many sources (37), including intraoperative stretching (38), unintentional detachment (38), and varied instrument retraction (39,40) within the significantly elongated operation time during the SuperPath procedure (33,41-43).*” (page 16, lines 295-299)

Comment 10: Line 285. The most important hip flexor is iliopsoas. And in a SuperPath approach, it has not been damaged. Maybe the reason for the less hip flexion was the postoperative pain and not the muscle damage.

Reply 10: We would like to thank the Reviewer for this great comment. Indeed, the

iliopsoas is not cut in the SuperPath procedure, however a validated study to specifically investigate the soft tissue/muscle damage is currently lacking for SuperPath procedure. A good example is the direct anterior approach (DAA) THA, as another tissue-sparing technique, which has been widely used in the past decade. Many existing studies, comparing the DAA THA with traditional approaches, have showed that this tissue-sparing approach, using intramuscular and internervous planes without muscle dissections, did not significantly alleviate the soft tissue damage (15,17,18). In good agreement with our data, we conclude that, as we already stated in Replay#9, the soft tissue damage might not be relieved by specific muscle (e.g. iliopsoas) preservation but be increased by additional tissue stretching and instrument retraction. Therefore, we totally agree with Reviewer B that more studies are needed to further investigate these tissue-sparing procedures and to boost their possible superiorities over traditional techniques. Moreover, we also agree that the postoperative pain might be also a reason for less hip flexion.

Changes in the text: Per the kind suggestions, we added the information in the Discussion to read to as “*Therefore, more studies are needed to identify the attributing factors of soft tissue damages during the SuperPath technique and to boost its possible superiorities over traditional techniques.*” (page 16, lines 299-301) and “*Such a temporary aggravated ROM restriction in the SuperPath group might be attributed to both intraoperative soft tissue damage and postoperative pain. As stated by other authors, the clinical importance of postoperative CK values and associations between hip function with other clinical outcomes (e.g. soft tissue damage, pain symptom, and blood loss) warrants further studies (20,33).*” (pages 16-17, lines 307-312)

Comment 11: Line 297. How did the authors calculate HHS at 1-day, 3-day, or 14-day postoperative? HHS includes daily activities as put socks or shoes on, go up and downstairs, ability to walk distances. It is difficult to understand this point.

Reply 11: Thank you very much for this important comment. With the application of enhanced recovery after surgery (ERAS) in our Center, the hospital stay after THA is

getting shorter and postoperative functional rehabilitation is accelerated (19). Indeed, not all patients can perform satisfactory activities. However, as a routine postoperative assessment in our Center, we faithfully utilize the HHS (**Table 1**) to evaluate the postoperative joint function of THA patients (20). For example, regarding Item #4 of HHS (walking distance with or without a support aid), normally patients are only able to amble indoor at postoperative day 1, then a score of 2 is recorded (if patients cannot walk, then a score of 0 is recorded).

Table 1. Harris hip score.

Question	Score
1. Please describe any pain in your hip:	
A. No pain	44
B. Slight pain or occasional pain	40
C. Mild, no effect on ordinary activity, pain after unusual activity, uses aspirin or similar medication	30
D. Moderate pain that requires pain medicine stronger than aspirin/similar medications. I'm active but have had to make modifications and/or give up some activities because of pain	20
E. Marked or severe pain that limits activity and requires pain medicine frequently	10
F. Totally disabled—wheelchair or bed ridden	0
2. Amount and type of support used:	
A. None	11
B. Cane for long walks	7
C. Cane all the time	5
D. 2 canes	2
E. 1 crutch	3
F. 2 crutches or walker	0
G. Unable to walk	0
3. Limp. This should be judged at the end of a long walk using the <i>type</i> of support chosen in question 2.	
A. None	11
B. Slight	8
C. Moderate	5
D. Severe	0
4. Distance that you can walk. This should be judged with the aid of a support if you use one.	
A. Unlimited	11
B. 5–6 blocks	8
C. 1–4 blocks	5
D. In the house only	2
E. Unable to walk	0
5. Climbing stairs:	
A. Normally	4
B. Need a banister or cane or crutch	2
C. Must put both feet on each step/severe trouble climbing stairs	1
D. Unable to climb stairs	5
6. Shoes and socks:	
A. Can put on socks and tie a shoe easily	4
B. Can put on socks and tie a shoe with difficulty	2
C. Cannot put on socks and shoes	0
7. Sitting:	
A. Comfortable in any chair	5
B. Comfortable only in high chair, or can sit comfortably for only 0.5 hour	3
C. Cannot sit for 0.5 hour because of pain	0

Changes in the text: None.

Comment 12: Line 314. The authors performed over 50 superpath approach before this study. In all these cases, did they check if the position of the acetabular component was unsatisfactory?

Reply 12: We would like to thank the Reviewer B for this comment. As we mentioned in *Reply #4*, those first 50 cases have been included into another ongoing large-scale, long-term project to comprehensively investigate the efficacy of SuperPath technique for all spectrum of primary or revision THA. As it is an on-going project, we cannot here provide an exact result regarding their angles of acetabular component. However, we would state that not all cases are of satisfactory radiographic positions. We hope to report these data as soon as possible.

Comment 13: In my opinion, this study maybe has several flaws. It is interesting the preoperative serum markers. But it is difficult to understand the results related to pain, acetabular position, range of motion, and hip function. It needs major revision or reject.

Reply 13: We would like to thank the reviewer very much for these important and helpful comments. In the present study, we choose to faithfully report our data, rather than to excessively discuss possible implications with our data based on the following two reasons. Firstly, the original purpose of our study aimed to compare the short-term outcomes between the SuperPath and PLA THA for unilateral end-stage primary OA patients in terms of perioperative status and postoperative function, however, exploring possible associations between serum makers and other clinical outcomes/parameters are not within the scope of this study. Secondly, the current evidence regarding associations between serum markers and clinical parameters are greatly controversial (even with large sample size in several studies) and are largely obtained from traditional THA approaches. Therefore, such attempts would be practically inappropriate and also of limited clinical significance in our pilot study, which have been avoided in the initial study design. The details about these issues are also within the replies to comments

from Reviewers A and B:

(1) Serum markers, including serum creatine kinase (CK), C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR), are previously validated and widely accepted indicators of intraoperative soft tissue/muscle damage and trauma-related acute phase response following orthopedics surgeries (16,21-26).

(2) The associations between serum markers and postoperative pain were not yet established. As we already stated in *Reply #10*, a validated study to specifically investigate the soft tissue/muscle damage is currently lacking for SuperPath procedure, while pain related to the surgery itself can be associated with the implant, bone alterations and soft tissue or nerve injuries (27). If we look at the direct anterior approach (DAA) THA, as another tissue-sparing technique, which has been widely used in the past decade (Literature about this issue in SuperPath are very limited, so we use DAA as example). Many existing studies, comparing the DAA THA with traditional approaches, have showed that this tissue-sparing approach, using intramuscular and internervous planes without muscle dissections, did not significantly alleviate the soft tissue damage (15,17,18). For example, Mjaaland et al. reported that DAA THA yielded less pain but higher postoperative levels of CK at postoperative day 4 than the lateral approach THA (18).

(3) Poor acetabular component position is believed to associated with inadequate visualization of the acetabulum and surrounding anatomy (28), increased body mass index (29), surgery volume (30), inherent inaccuracies of external positioning guides (31), and the inability to consistently obtain and maintain precise patient positioning during the procedure (32). There are current no evidence showing that it is associated with serum marker changes (33).

(4) Restricted range of motion is believed to associated with pain (34), improper

implant positioning (35), and soft tissue/muscle damage (36). Sascha *et.al* (37) demonstrated that better postoperative pain relief led to an earlier achievement of a definite range of motion. As mentioned by the Reviewer B's Comment#10, one possible reason for the less hip flexion was the postoperative pain. Serum markers, as indicators of muscle damage, can also be related with hip range of motion after THA, however, direct evidences are not available in literature.

(5) A consensus statement about the possible association between serum markers and hip function is also not yet established. Here, we reviewed the literature about DAA again. Rykov *et al.* reported that no significant differences of CK, CRP and hip functions (Hip disability and Osteoarthritis Outcome Score and the Harris Hip Score) between DAA THA and PLA THA (15). In contrast, Zhao *et al.* compared DAA with PLA THA and reported that lower levels of CRP and ESR at the first postoperative days 1-4 in DAA group as well as better HHS and University of California Los Angeles activity score at the 3 months postoperatively (38).

Changes in the text: Additional information were provided in the Discussion section reading as “*Such unexpected results are possibly attributed to the additional intraoperative soft tissue (mainly muscle) damage from many sources (37), including intraoperative stretching (38), unintentional detachment (38), and varied instrument retraction (39,40) within the significantly elongated operation time during the SuperPath procedure (33,41-43). Therefore, more studies are needed to identify the attributing factors of soft tissue damages during the SuperPath technique and to boost its possible superiorities over traditional techniques.*” (page 16, lines 295-301) and “*Such a temporary aggravated ROM restriction in the SuperPath group might be attributed to both intraoperative soft tissue damage and postoperative pain. As stated by other authors, the clinical importance of postoperative CK values and associations between hip function with other clinical outcomes (e.g. soft tissue damage, pain symptom, and blood loss) warrants further studies (20,33).*” (pages 16-17, lines 307-312)

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