

To: Lian-Sheng Ma

Science Editor, Company Editor-in-Chief, Editorial Office of World Journal of Orthopedics

Dear Dr. Lian-Sheng Ma,

We would like to thank you and the World Journal of Orthopedics for the opportunity to revise this manuscript.

We would also like to thank the Reviewer and the Science editor and Company editor-in-chief for their insightful and constructive comments on the text, which shed light on some deficiencies that needed to be addressed. We believe this has helped us improve the manuscript substantially.

We have made every effort to incorporate the reviewers' suggestions in the revised version, making other related changes where necessary. These "other changes" are summarized at the end of this document.

Our responses are given below. New and revised text is highlighted for your convenience.

We hope you will now find the manuscript NO: 67869 acceptable for further review.

Kind regards,

Dr. Sophia Stasi

**Name of Journal:** World Journal of Orthopedics

**Manuscript Type:** ORIGINAL ARTICLE

### *Clinical Trials Study*

## **Direct Anterior Approach vs Hardinge in obese and nonobese osteoarthritic patients: a randomized controlled trial**

Macheras G *et al.* Stasi S DAA vs Hardinge in obese & nonobese OA patients

George Macheras, Sophia Stasi, Michail Sarantis, Athanasios Triantafyllou, Dimitrios Tzeferonis, Stamatios Papadakis

### **Addressing Comments**

#### **Reviewer's comments:**

- All DAA-patients showed 12.2 % less pain, more functionality.....
- Over the past decade, direct anterior approach (DAA) has sparked scientific interest due to its soft-tissue-preserving nature (intramuscular and internervae technique), coupled with the relatively lower risk of dislocation [4].
- On the other hand, THA is an effective treatment for most patients who suffer from pain and decreased functionality due to end-stage symptomatic hip osteoarthritis....
- Other studies have shown that, obese patients do not differentiate from the nonobese in terms of postoperative outcomes [13-15].
- All measurements were carried out by the same examiner, who was not involved in any part of the study.
- In the case that there was no statistically significant interaction, we compared the factor "Surgical Approach" regardless of "BMI" factor and the factor "BMI" regardless of "Surgical Approach" factor.
- All analyses were carried out using the statistical package SPSS v21.00 (IBM Corporation, Somers, NY, USA).

**批注 [R1]:** As 12.2% is an average not each and every patient did have 12.2% less pain

**批注 [R2]:** Do you mean intermuscular?

**批注 [R3]:** Suggestion: internervae

**批注 [R4]:** Spelling: decreased

**批注 [R5]:** Language style: Other studies have shown that obese patients do not differ from the nonobese in terms of postoperative outcomes.

**批注 [R6]:** Suggestion: "... any other part ..."

**批注 [R7]:** Language style: "... there was no statistically interaction ..."

**批注 [R8]:** Suggestion: SPSS v21.00

- At the 6th postoperative week's measurements, ~~all~~ DAA patients reported 12.2 % lesser pain (FPS-R), more functional ability (14.8% faster TUG test performance time and 21.5% higher MHHS-Gr score), and 38.16% better quality-of-life (iHOT12-Gr) compared to Hardinge patients, with statistically significant differences (all  $p$ -values  $<0.001$ ) (Table 4-grey columns).
- At 12th postoperative week's measurements these differences of ~~all~~ DAA groups' outcomes were further increased [FPS-R: 9.9% ( $p<0.001$ ), TUG test: 21.17 % ( $p<0.001$ ), MHHS-Gr: 22.54% ( $p=0.05$ ), and iHOT12-Gr: 40.51% ( $p<0.001$ )] (Table 4-grey columns). The DAA resulted in less postoperative pain, and offered faster and increased functional ability and better quality-of-life compared to the Hardinge.
- At the 6th postoperative week's measurements the DAA-nonobese group had better % percentage of change of all outcomes
- At the 12th postoperative weeks' measurements, only the TUG test performance time of Hardinge-nonobese patients ~~were-revealed~~ significantly shorter (5.5%,  $p=0.001$ ) compared to Hardinge-obese patients (Table 5).
- In addition, the measured outcomes of the aforementioned parameters did not differ between obese and nonobese patients. DAA similarly benefited both obese and nonobese patients.
- DAA is gaining popularity as its intramuscular pathway
- Several studies have shown that obese patients do not differentiate from the nonobese ones in terms of postoperative outcomes [13-15].

批注 [R9]: See previous remark

批注 [R10]: Suggestion:  
"both"  
, as far as I understand you had two DAA groups

批注 [R11]: Please consider language syntax for better understanding

批注 [R12]: Language syntax:  
"... was significantly ..."

批注 [R13]: Suggestion:  
"... between obese and nonobese DAA-patients."

批注 [R14]: It is an intermuscular pathway (!) otherwise you perform a different approach

批注 [R15]: Suggestion:  
"differ"

**Authors' actions:** In response to the reviewer's comments, all the suggested changes have been made.

**Reviewer's comment:**

- **Comparative Results**

批注 [R16]: General remark:  
Please report %-results only up to the precision of a "tenth", not to a "hundredth", i.e. 21.2% instead of 21.17%

**Authors' actions:** We have made the corrections in the main text and the Tables 4 and 5.

**Reviewer's comment:**

- Overall, it seems that Hardinge-nonobese reached in higher functionality, as expressed by TUG test, than Hardinge-obese patients.

**Author's response:** Indeed this is only an impression.

**Authors' actions:** Taking into account the reviewer's comment the sentence has been written as follow: "Overall, Hardinge-nonobese reached in higher functionality, as expressed by TUG test, than Hardinge-obese patients."

**批注 [R17]:** Please explain if it is an impression only or a trend that is seen in your data but may be not significantly different

**Reviewer's comment:**

- To our knowledge, this is the first four-group comparative study .....

**Authors' actions:** Taking into account the reviewer's constructive comment we have made the following changes: "In the present study, the effect of two different THA surgical approaches (DAA versus Hardinge) on postoperative pain levels, functionality and quality-of-life in both obese and nonobese hip OA patients was explored....."

**批注 [R18]:** Comment:  
This is CNN-style ("Be the first to know") and should not be highlighted in science; scientific content is much more important than "be the first"

**Reviewer's comment:**

- ..... In other studies, it had been reported that postoperative wound infection rate is higher in obese patients subjected to DAA, mainly due to the overlying abdominal adipose tissue that may disturb wound healing [33, 34].

**Author's response:** Thank you for your suggestion. One of the most important actions taken has been the rewriting of the paragraph to incorporate the "bikini incision".

**Authors' actions:** "In the present study, most cases with wound healing problems were reported in Hardinge-obese patients (four out of 35 patients, 11.4%), as shown in our flow diagram. This rate was lower than the rates reported in the literature for obese patients, on other classical surgical approaches, ranging from 14.5% to 22%

**批注 [R19]:** Please consider commenting the "bikini-incision" that is recommended in DAA for obese patients as a mean to reduce wound healing complications

[34,35]. Regarding DAA, one incidence in nonobese and two incidences in obese participants were found (3.5 % and 5.7%, respectively). The study's results are within the rates reported in the literature: for DAA-nonobese ranging between 0.8% and 3%, while for DAA-obese patients ranging from 4.46% to 10.0% [36-38]. It is worth to be noted that the horizontal (bikini) incision was shown to facilitate even more wound healing in obese patients. In the retrospective comparative study by Manrique et al [39], involving obese patients (BMI >30 kg/m<sup>2</sup>) it was reported that patients with horizontal incision had significant lower rates of wound healing problems compared to patients with vertical incision (0.00% versus 16.6%, p=0.04)[39]. Nevertheless, the current evidence is limited, and further trials are warranted to identify differences between the two DAA skin incisions regarding wound healing in obese patients."

**Reviewer's comment:**

- While the risks associated with THA in obese patients are well documented [10, 36], the present study results show that DAA would be a preferable THA approach for obese patients.

**Author's response:** Taking into account the reviewer's comment, a sentence with the appropriate references has been added.

**Authors' actions:** "While the risks associated with THA in obese patients are well documented [11,34], the present study results show that DAA would be a preferable THA approach for obese patients. Since it is a minimally invasive surgical technique that provides the most direct access to the hip joint, DAA can be safely performed, by an experienced surgeon and under certain precautions, without an increased and adverse risk for obese patients [4, 40]."

**Reviewer's comment:** Tables 4 and 5

**批注 [R20]:** You did also not mention what is known in the literature that the DAA is the shortest way to get to the hip joint; this detail by itself helps to reduce the risk for wound complications in obese patients; please add this point to your discussion

**批注 [R21]:** Tables not readable

**Authors' actions:** Taking into account the reviewer's comment, we change the orientation of the Tables' pages from "Portrait" with vertical text direction to "Landscape".

### Science editor comments

- (5) Self-cited references: There are 4 self-cited references. The self-referencing rates should be less than 10%. Please keep the reasonable self-citations that are closely related to the topic of the manuscript, and remove other improper self-citations. If the authors fail to address the critical issue of self-citation, the editing process of this manuscript will be terminated.

**Authors' actions:** Taking into account the Science editor comment, in a total of 44 references, two out of four self-cited references have been changed as follow:

(20) **Matta JM**, Shahrदार C, Ferguson T. Single-incision anterior approach for total hip arthroplasty on an orthopaedic table. *Clin Orthop Relat Res.* 2005; **441**: 115-124. [PMID: 16330993 DOI: 10.1097/01.blo.0000194309.70518.cb]

(33) **Cinnamon CC**, Longworth JA, Brunner JH, Chau VK, Ryan CA, Dapiton KR, Chmell SJ, Foucher KC. Static and dynamic abductor function are both associated with physical function 1 to 5 years after total hip arthroplasty. *Clin Biomech (Bristol, Avon)* 2019; **67**: 127-133. [PMID: 31103962 DOI: 10.1016/j.clinbiomech.2019.05.009]

- Issues raised: (1) The title is too long, and it should be no more than 18 words;

**Author's response:** The manuscript NO: 67869 entitled "Direct Anterior Approach vs Hardinge in obese and nonobese osteoarthritic patients: a randomized controlled trial" counting for 15 words. Therefore, no action has been made.

- (2) The authors did not provide original pictures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to

ensure that all graphs or arrows or text portions can be reprocessed by the editor;

**Authors' actions:** In the revised file, the figure of the flow diagram of the study is provided in a Power Point.

- (3) The "Article Highlights" section is missing. Please add the "Article Highlights" section at the end of the main text.

**Authors' actions:** The section "Article Highlights" has been added at the end of the main text as follow:

## ARTICLE HIGHLIGHTS

### *Research background*

Total hip arthroplasty (THA) is an effective treatment for most patients who suffer from pain and decreased functional ability due to hip osteoarthritis (OA). The main risk factors for developing hip OA are advanced age, family history of OA, previous hip injury, hip dysplasia, and obesity. The increased prevalence of obesity has resulted in orthopedic surgeons being likely to face many patients with a high body mass index (BMI) who warrant THAs over the coming years. On the other hand, there has been growing interest in the direct anterior approach (DAA) in recent years because of its soft-tissue-preserving nature.

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### *Research motivation*

In the literature, it has been reported that obesity is significantly associated with a greater need for joint replacement and that compared to patients with normal body mass index (BMI), obese patients may require a THA up to ten years earlier. Some studies indicate that obesity is associated with poorer clinical, functional outcomes, while others have shown that obese patients do not differ from the nonobese in this respect. The data are considered controversial, and further studies need to be performed on obese patients, especially comparative evaluations that compare minimally invasive techniques such as DAA with classical surgical techniques, such as the Hardinge approach. Compared to other classical surgical approaches used in obese patients, the Hardinge was chosen because it offers better access to the hip joint and achieves a lower dislocation rate by preserving its posterior stabilizer muscles.

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#### ***Research objectives***

We aimed to compare DAA and Hardinge in hip OA patients who have undergone primary THA regarding postoperative pain levels, functional status, and quality-of-life. In addition, it was investigated whether these parameters differ between obese and nonobese patients.



### **Research methods**

The present study was a prospective, four-group randomized controlled trial (Clinical Trial Identifier: ISRCTN15066737). One hundred twenty participants were divided into four groups (30 patients per group) according to both the surgical approach used and their body mass index (BMI) as follow: DAA-nonobese group (BMI<30 Kg/m<sup>2</sup>), DAA-obese group (BMI ≥ 30 Kg/m<sup>2</sup>), Harginge-nonobese group (BMI<30 Kg/m<sup>2</sup>) and Harginge-obese group (BMI ≥ 30 Kg/m<sup>2</sup>). Measurements were carried out prior to surgery (baseline) and postoperatively (at the end of the 6<sup>th</sup> week and 12<sup>th</sup> week). Pain levels were measured with the Face Pain Scale - Revised (FPS-R). Functional ability was evaluated with the Timed Up & Go (TUG) test and the Greek version of the Modified Harris Hip Score (MHHS-Gr). Quality-of-life was measured with the Greek version of the International Hip Outcome Tool -12 items (iHOT12-Gr).

### **Research results**

DAA versus Hardinge regardless of BMI: The DAA resulted in less postoperative pain and offered faster and increased functional ability and better quality-of-life than the Hardinge.

DAA-nonobese versus Hardinge-nonobese: The DAA leads faster to better functional ability and quality-of-life compared to the Hardinge in nonobese patients.

DAA-obese versus Hardinge-obese: DAA leads faster to better functional ability and quality-of-life of obese patients than the Hardinge; at 12 weeks, statistically significant differences between groups were narrowed.

Nonobese versus obese regardless of surgical approach: the only statistically significant difference between obese and nonobese patients was revealed in the self-reported functional ability.

DAA-nonobese versus DAA-obese: no statistically significant differences were observed in comparing postoperative outcomes. The DAA similarly benefited both obese and nonobese patients.

Hardinge-nonobese versus Hardinge-obese: Hardinge-nonobese reached higher functionality than Hardinge-obese patients.

#### ***Research conclusions***

DAA patients reported less pain, more functionality, and quality-of-life improvements compared to the Hardinge. Moreover, DAA exhibits equivalent postoperative outcomes in obese and nonobese patients, suggesting a better-suited THA surgical approach for patients with increased BMI.

#### ***Research perspectives***

Further research based on well-designed studies with longer follow-up and larger samples need to be performed to elucidate the efficacy of DAA on functionality and quality of life of hip OA obese patients.

#### ***Company editor-in-chief comment***

- ..... However, the quality of the English language of the manuscript does not meet the requirements of the journal. Before final acceptance, the author(s) must provide the English Language Certificate issued by a professional English language editing company. Please visit the following website for the professional English language editing companies we recommend:  
<https://www.wjgnet.com/bpg/gerinfo/240>.

**Author's response:** Before final acceptance, authors intent to send the manuscript to one of the professional English language editing companies, recommended by the World Journal of Orthopedics, in order to provide the required English Language Certificate.

#### **Other changes**

- In order to commenting the “bikini-incision” in the Discussion section the word “vertical” has been added in the **INTRODUCTION** section and the *Participants* paragraph as follow:
  - **INTRODUCTION:** In recent years, there has been a growing interest in minimally invasive surgical techniques that are used for the performance of total hip arthroplasty (THA). The advantages of these techniques include lesser soft tissue trauma, lesser amount of blood loss, minor postoperative pain, shorter hospital stay, better aesthetic appearance of the incision and a faster recovery time [1-3]. Over the past decade, the direct anterior approach (DAA) has sparked scientific interest due to its soft-tissue-preserving nature (intermuscular and internerval technique), coupled with the relatively lower risk of dislocation [4]. The DAA approach can be performed through a vertical or a horizontal (bikini) incision [5].
  - *Participants:* Participants were selected from patients who have chosen to be operated by either of the two chief orthopedic surgeons/co-researchers of the present trial. One of the head-orthopedic surgeons (GM) performs primary THA using DAA technique -through a single vertical incision- [20], whilst the other (SP) prefers the Hardinge [21].
- In order to commenting the “bikini-incision” and the “reduced risk for wound complications in obese patients who have been undergone a DAA-THA through a bikini-incision”, the references No 5, 35, 39 and 40 has been added.