The Influence of Abdominal Obesity on Hip Pain, Function, and Walking Ability after Three Years of THA: A Prospective Cohort Study

Xiang Wang
The First Clinical Medical College, Zhejiang Chinese Medical University
Ze Yang
The First Clinical Medical College, Zhejiang Chinese Medical University
Yang Zhang
Traditional Chinese Medicine Hospital of Zhuji
Yuan Tian
Hangzhou TCM Hospital Affiliated to Zhejiang Chinese Medical University
Jing Shen
The First Affiliated to Zhejiang Chinese Medical University
Weifeng Ji (jiweifeng1230@163.com)
The First Affiliated to Zhejiang Chinese Medical University

Research Article

Keywords: Abdominal obesity, waist circumference, THA, hip joint function, outcome

Posted Date: December 20th, 2021

DOI: https://doi.org/10.21203/rs.3.rs-1119061/v1

Abstract

Background: There are many clinical studies about the impact of obesity on postoperative function following THA, but their conclusions are different and even contradictory. Abdominal obesity is closely related to obesity, while its impact on postoperative function following THA remains to be elucidated.

Methods: Four hundred and thirteen patients were included in this study. They were divided into an AO group (waist circumference ≥ 90 cm for men and ≥ 85 cm for women) and a non-AO group (waist circumference ≤ 90 cm for men and ≤ 85 cm for women). Preoperative assessments including numerical pain rating, the Oxford Hip Score, and 6-minute walk test were repeated at 1,2, and 3 years postoperatively. Postoperative assessments included the anteversion and inclination of the acetabular prosthesis and satisfaction survey.

Results: At a mean follow-up of 48±1.3 months, there was a significant difference in the improvement of the 6-minute walk test (251.22 to 387.46, 410.34, 410.07 vs 207.79 to 362.17, 395.82, 403.36; $p < 0.001$) at 1, 2 and 3 years and the numerical pain rating scale (6.00 to 0.39 vs 5.76 to 0.80; $p < 0.001$) at 1 year between the non-AO group and AO group. There was no difference between both groups in inclination, anteversion, OHS, and satisfaction.

Conclusion: AO does not increase the complications after THA, nor does it have a significant impact on the function after THA, but it seems to have a negative effect on the improvement of walking ability and the relief of hip pain.

Introduction

In the past 50 years or so, the prevalence of obesity has increased worldwide, reaching epidemic levels[1]. Obesity is an influencing factor that has been discussed in total hip arthroplasty (THA). However, there has been controversy over whether obesity has impact on THA. We reviewed many works of literature on the effects of obesity on THA, the conclusions of which are not uniform or even contradictory, holding opposite views[2–7].

Abdominal obesity (AO) is closely related to obesity, but it can also occur in people with normal body mass index (BMI)[8]. The incidence of AO is increasing worldwide, and it is a close factor of metabolic syndrome and cardiovascular disease that will increase the risk of hip fractures[9–11]. Therefore, increasing numbers of THA have been performed on AO patients clinically. Based on this, we put forward a question: is there a factor closely related to obesity but not the same that causes the contradiction in the above studies?

As far as we know, AO is still a neglected factor in THA, and there has been no research on AO and THA. To explore the impact of abdominal obesity on THA, we conduct this research.

Method

Study design and population setting

The study design was a prospective study, which was approved by the Ethics committee at The First Affiliated Hospital of Zhejiang Chinese Medical University (Zhejiang, Hangzhou, China; No. 2019-K-306-01). All cases were performed from January 2014 to June 2018, with direct anterior THA under the assistance of direct anterior approach (DAA) table attachment (Fig. 1). All patients were informed about the study and given written consent. Inclusion criteria: In line with the diagnostic criteria of "Guidelines for the diagnosis and treatment of adult femoral head necrosis 2019", hip osteoarthritis. Exclusion criteria: Patients with Parkinson's and other related neurological diseases that affect limb function activity, malignant tumors, stroke, other operations before or within three years after THA, scoliosis, sagittal plane pelvic tilt[12], death, or incomplete data. All operations were performed by an orthopedic surgeon and his team, who had experience in more than 500 DAA THA operation experience. Preoperatively, patients' waist circumference (WC) will be measured by a special training doctor. AO was defined as WC ≥ 90 cm for men and ≥ 85 cm for women[13]. Among them, there has been no consensus on the best anatomical position for measuring the abdominal circumference, WHO recommends the midpoint between the last palpable rib and the iliac crest, while the National Institutes of Health recommends it at the height of the navel[10]. This study adopted the recommendations of the WHO. Two groups were formed for the study: non-AO group and AO group. The follow-up was for 48 months (mean and standard deviation,48±1.3months), with a minimum follow-up of 38 months and a maximum follow-up of 75 months.

Outcomes

The main outcome of this study was the hip joint function, which was measured by the reliable and validated Oxford hip score (OHS)[14]; the anteversion and inclination of the acetabular prosthesis (both the forward tilt angle and the inclination are measured by X-ray radiography[15]). Secondary results included a numerical pain rating scale [16](with anchors of 0 being no pain and 10 being severe pain), walking capacity assessed[17](via a 6-minute walk test (6 mwt), and patients' satisfaction. Walking assessments were undertaken along a 50-metre corridor by a physiotherapist blinded to the purpose of study. Patients were deemed walking aid dependent if they used any walking assistive device most of the time. A 5-point Likert scale measured satisfaction with surgery. Responses of 'Very Satisfied' and 'Satisfied' were grouped and reported as a percentage. Preoperative assessment included numerical pain rating, the Oxford Hip Score, and 6-minute walk test were repeated at 1,2, and 3 years postoperatively. Postoperative assessments included the anteversion and inclination of the acetabular prosthesis, and satisfaction at 3 years.

Surgical methods and materials

All THAS were completed by the same orthopedic surgeon with the assistance of DAA surgical stents. With the assistance of DAA table attachment, the patient adopted a supine position during the operation, and the patient's abdominal fat was squeezed on the opposite side with tape to prevent it from affecting the surgical field of view (Fig. 2). The surgical approach was to start at 2cm from the distal and lateral

sides of the anterior superior iliac spine, and the direct anterior approach was incised in the direction of the fibula head. The incision length was 8±1cm. All patients received perioperative antibiotic treatment (unified Cefotiam Hydrochloride for Injection) before and 24 hours after the skin incision. The surgical incisions were sutured intracutaneously, with no drainage tube. Early postoperative exercises were recommended (routine exercises can be performed on the first day after surgery) to prevent the formation of deep vein thrombosis.

Statistical analysis

The data was collected by two people who did not know the purpose of the experiment and then transferred to a Microsoft Excel spreadsheet. All measurements were compared after testing to confirm a normal distribution, using the unpaired t-test and chi-square test at a significance level of 0.05(IBM SPSS Statistics version 25 and JASP 0.10.2). For the calculation of the sample size, G * Power 3.1.9.7 was used, and a priori power analysis was calculated to achieve a statistical power of 95% with a level of significance α = 5%.

Results

Patient flow

A total of 932 cases were collected, of which 519 cases did not meet the inclusion criteria and were excluded, thus 519 cases were excluded. Four-hundred thirteen patients were included, 35 of whom were lost to follow-up; therefore, 378 patients (378 hips) were analyzed. The Non-AO group included 181 patients and the AO group was 197. Patient flow was depicted in Figure 3.

Patient Demographics

The study included 243 men and 135 women. The average duration of surgery was 61±11 minutes in the non-AO group and 63±10 minutes in the AO group(p=0.540). The right hip was operated in 267 times and the left hip in 111 times. The average patient height was 165±10cm in the non-AO group and 168±8cm in the AO group(p=0.732). The average patient weight was 69.2±15.4kg in the non-AO and 73.5±17.1kg in the AO(p=0.452). Demographics prior to surgery were similar, apart from the dependent variable of WC (p<0.001). (Table 1)

Table 1
Patient Demographics

	AO n=197	non-AO n=181	Cohen's d with 95%CI	P value
BMI (kg/m^2)	26.64±2.00	25.37±3.40	0.43(-0.07-0.93)	0.077
Age (years)	57.39±9.71	59.00±9.79	-	0.513
Gender (Male)	25	18	-	0.132
Abdominal circumference (cm) male	104.40±7.83	85.22±3.24	-	<0.001
Abdominal circumference (cm) female	93.00±8.76	57.81±7.86	-	<0.001
Oxford Hip Score (0-48)	36.15±3.41	34.48±3.31	-0.38(-0.58–0.17)	0.052
Pain (0-10)	5.76±0.97	6.00±1.00	0.29(-0.78-0.21)	0.329
6 Minute Walk Distance (m)	207.79±16.24	209.55±20.74	-0.04(-0.24-0.16)	0.694
infection	0	1	-	-
Mean (Standard Deviation) unless stated otherwise				

Comparison of postoperative recovery between the two groups

Inclination was 43.00°±4.01°in the non-AO group and 42.37°±3.53°in the AO group(p=0.502). Anteversion was 23.01°±4.53°in the non-AO group and 21.01°±2.99°in the AO group(p=0.404). (Fig. 4) In the non-AO group, the OHS improved from 36.15±3.41(range,28 to 42points) to 12.09±0.29 (range,12 to 13points) at 3-year postoperatively. The OHS in the AO group improved from 34.48±3.31 (range,29 to 40 points) to 12.48±2.69 (range,12 to 27 points) at 3 years postoperatively. There was no difference in the improvement of the OHS between the groups (p = 0.408). (Fig. 5) No difference between the two groups was found in terms of whether to revision or whether to readmission. At 1 year postoperatively, the numerical pain rating scale in the non-AO group improved from 6.00±1.00(range,4 to 7 points) to 0.39±0.59(range,0 to 2 points); the numerical pain rating scale in the AO group improved from 5.76±0.97(range,4 to 7 points) to 0.80±0.85(range,0 to 2 points), a value of p< 0.001 was considered statistically significant between both groups. However, not statistically significant at 2 and 3 years. (Fig. 6) The 6 mwt in the non-AO group improved from 251.22±31.36m (range, 140 to 321m) to 387.46±26.70m (range, 223 to 430m), 410.34±12.04m (range, 234 to 437m),410.07±16.81m (range, 352 to 428m) at 1,2 and 3 years postoperatively. The 6 mwt in the AO group improved from 207.79±16.24m (range, 186 to 245m) to 362.17±26.20m (range, 293 to 450m),395.82±14.72m (range, 310 to 453m),403.36±13.34m (range, 311 to 435m) at 1,2 and 3 years postoperatively. There was a difference in

the improvement of 6 mwt between the groups at 1,2, and 3 years postoperatively ($p < 0.001$). (Fig. 7) The average patient satisfaction was 97.42±8.55 in the non-AO group and 97.58±6.63 in the AO group($p=0.935$). It seemed that everyone expressed great satisfaction with the operation. (Fig. 8)

The only complication was the occurrence of revision in one male patient in the non-AO group because of periprosthetic infection. No vascular and/or nerve lesions or dislocations occurred.

Discussion

There were many clinical studies on the relationship between obesity and THA, in which several different perspectives have been proposed[18–25]. However, there was still no unified conclusion on whether obesity had a negative impact on THA. This was conflicting evidence as to whether, how, and to what degree obesity may negatively influence the outcomes of THA. For a more in-depth discussion, we have provided this idea as to whether there was a factor closely related to but not absolutely consistent with, obesity that led to this result. Our prospective study explored the factor of AO to prove it.

Our research identified no significant difference between AO and non-AO patients in terms of their hip function 3-year following their THA, the preoperative scores of the two groups were significantly improved. There was no significant difference between the two groups in acetabular anteversion, inclination and patients' satisfaction. However, there were significant differences in the improvement of walking ability and the relief of hip pain between the two groups. The improvement of walking ability in non-AO group was significantly higher than that in AO group. In terms of walking ability, AO had a certain impact on patients after THA. This was the same as Samantha Haebich's conclusion[7] on the impact of obesity on THA in 2019. This seemed to corroborate the hypothesis proposed in this article. The relationship between AO index and degree of influence has not been discussed in depth in this study. The patient mentioned in our results who underwent revision surgery due to prosthesis infection was in non-AO group, the cause may be postoperative trauma infection. There was no significant difference in BMI between the two groups in this study, and the influence of obesity on the experimental results was ruled out.

A study by Purcell in 2016 showed that the infection rate of deep and superficial wounds in obese patients increased during THA[26]. In this study, there was no significant relationship between the occurrence of infection and AO, which seemed to indicate that the increase in the infection rate in obese patients was not related to AO. However, it was worth noting that the surgical method used a direct anterior approach with a specific surgical auxiliary machine. During the operation, we took some approaches to the abdomen of patients with AO to reduce the influence of abdominal fat on the operation and prevent it from affecting the surgical field of vision. This may be the reason we had fewer complications.

In a large cohort study[27] of 124368 patients undergoing THA, the authors found that in patients undergoing total hip replacement surgery, obesity increased the risk of various complications and correction rates. For overall complications, 1-year revision surgery, and 90-day surgery complications, the

risk increased with increasing body mass index (BMI). In a prospective study, Chee et al.[28]compared the matching of 55 consecutive THAs in morbidly obese patients with a set of 55 THAs in non-obese patients. The authors found that the incidence of all types of complications was significantly higher in obese patients. However, there were no significant differences in the risk of superficial and deep wound infection and dislocation between the two groups[28]. In our study, AO did not significantly add the incidence of pulmonary complications. All patients have achieved satisfactory results, and postoperative pain, hip joint function, and walking ability have all been greatly improved.

AO was a component of the metabolic syndrome and was a predictor of exercise performance during the 6-minute walk test[29]. AO had a significant impact on sports performance and physical activity. The blood flow of the calf was significantly reduced, which increased the risk of thrombosis in surgical patients. However, there was no significant statistical difference in the 6wt preoperative baseline data of the two groups in this study. The specific reason is not yet clear. Perhaps the pain of the hip and limited movement of the lower limbs covered the impact of AO on walking ability. This requires further research. In terms of the 6wt improvement of the two groups, the AO group was significantly lower than the non-AO group, and the two groups' data were statistically significant($p<0.001$). However, it cannot be ruled out that the impact of AO on walking ability would appear after the elimination of hip pain and limited movement of lower limbs. No patient with thrombosis was found in this study. The specific reason may be the current general use of "Low Molecular Weight Heparin Sodium Injection" in THA. The impact of the reduction of peripheral circulation on the recovery of the soft tissues of the lower extremity wounds was not mentioned in this study due to the long follow-up time.

As far as we know, there are few studies on AO for the prognosis of THA. The surgical method used in this study was a direct anterior approach, and some additional measures were taken during the operation for patients with AO. This is not shown in other studies, which may be the reason our results conflict with other studies. The follow-up time of this study was about 3 years, which is relatively short compared with other studies. To understand the long-term effects of AO on THA surgery, longer follow-up is needed. This study only counted the patient's weight and abdominal circumference before surgery but did not consider the patient's weight and abdominal circumference changes during the follow-up period.

In conclusion, AO does not increase the complications after THA, nor does it have a significant impact on the function after THA. However, it seems to have a negative effect on the improvement of walking ability and the relief of hip pain, slowing down the time to recover from pain and reducing the patient's postoperative walking speed. However, multicentre study with larger sample sizes is needed to further confirm the impact of AO on THA.

Abbreviations

Abdominal obesity (AO), waist circumference (WC), total hip arthroplasty (THA), Oxford hip score (OHS), 6-minute walk test (6 mwt)

Declarations

Ethics approval and consent to participate

The research project obtained approval of the Ethics committee at The First Affiliated Hospital of Zhejiang Chinese Medical University. No. 2019-K-306-01. The procedures used in this study adhere to the tenets of the Declaration of Helsinki. Prior to participation in the study all patients signed informed consent.All methods were carried out in accordance with relevant guidelines and regulations.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests

Funding

This project was supported by the “National Natural Science Foundation of China(81974576)”.

Authors' contributions

XW prepared the manuscript, tables and figures. WFJ and JS designed this study, approved the final manuscript. ZY, YZ, YT collected and/or rated the data, read and approved the final manuscript.

Acknowledgements

We would like to gratefully acknowledge Imaging Centre and The Recovery Room for their support.

References

1. Bluher M: **Obesity: global epidemiology and pathogenesis**. *Nat Rev Endocrinol* 2019, **15**(5):288–298.

2. Haynes J, Nam D, Barrack RL: **Obesity in total hip arthroplasty**: **does it make a difference?** *The bone & joint journal* 2017, **99-b**(1 Supple A):31-36.
3. Pietrzak J, Maharaj Z, Mokete L, Sikhauli N, van der Jagt DR: **Total hip arthroplasty in obesity**: **separating 'fat' from fiction**. *British journal of hospital medicine (London, England*: 2005) 2019, **80**(6):325-330.
4. Roger C, Debuyzer E, Dehl M, Bulaïd Y, Lamrani A, Havet E, Mertl P: **Factors associated with hospital stay length, discharge destination, and 30-day readmission rate after primary hip or knee arthroplasty: Retrospective Cohort Study**. *Orthop Traumatol Surg Res* 2019, **105**(5):949–955.
5. Pozzobon D, Ferreira PH, Blyth FM, Machado GC, Ferreira ML: **Can obesity and physical activity predict outcomes of elective knee or hip surgery due to osteoarthritis? A meta-analysis of cohort studies**. *BMJ open* 2018, **8**(2):e017689.
6. Bookman JS, Schwarzkopf R, Rathod P, Iorio R, Deshmukh AJ: **Obesity: The Modifiable Risk Factor in Total Joint Arthroplasty**. *The Orthopedic clinics of North America* 2018, **49**(3):291–296.
7. Haebich SJ, Mark P, Khan RJK, Fick DP, Brownlie C, Wimhurst JA: **The Influence of Obesity on Hip Pain, Function, and Satisfaction 10 Years Following Total Hip Arthroplasty**. *J Arthroplasty* 2020, **35**(3):818–823.
8. Dhawan D, Sharma S: **Abdominal Obesity, Adipokines and Non-communicable Diseases**. *The Journal of steroid biochemistry and molecular biology* 2020, **203**:105737.
9. Lukacs A, Horvath E, Mate Z, Szabo A, Virag K, Papp M, Sandor J, Adany R, Paulik E: **Abdominal obesity increases metabolic risk factors in non-obese adults: a Hungarian cross-sectional study**. *BMC Public Health* 2019, **19**(1):1533.
10. Fang H, Berg E, Cheng X, Shen W: **How to best assess abdominal obesity**. *Curr Opin Clin Nutr Metab Care* 2018, **21**(5):360–365.
11. Sadeghi O, Saneei P, Nasiri M, Larijani B, Esmaillzadeh A: **Abdominal Obesity and Risk of Hip Fracture: A Systematic Review and Meta-Analysis of Prospective Studies**. *Adv Nutr* 2017, **8**(5):728–738.
12. Fritz JK, Waddell BS, Kitziger KJ, Peters PC, Jr., Gladnick BP: **Is Dislocation Risk due to Posterior Pelvic Tilt Reduced With Direct Anterior Approach Total Hip Arthroplasty?** *J Arthroplasty* 2021.
13. Hu L, Huang X, You C, Li J, Hong K, Li P, Wu Y, Wu Q, Bao H, Cheng X: **Prevalence and Risk Factors of Prehypertension and Hypertension in Southern China**. *PLoS One* 2017, **12**(1):e0170238.
14. Murray DW, Fitzpatrick R, Rogers K, Pandit H, Beard DJ, Carr AJ, Dawson J: **The use of the Oxford hip and knee scores**. *The Journal of bone and joint surgery British volume* 2007, **89**(8):1010–1014.
15. Loitsch T, Freitag T, Leucht F, Reichel H, Bieger R: **[Measurement of acetabular cup inclination in anteroposterior pelvic radiogram: An indicator of quality after primary total hip arthroplasty?]**. *Orthopade* 2018, **47**(12):1003–1008.
16. Hawker GA, Mian S, Kendzerska T, French M: **Measures of adult pain: Visual Analog Scale for Pain (VAS Pain), Numeric Rating Scale for Pain (NRS Pain), McGill Pain Questionnaire (MPQ), Short-Form McGill Pain Questionnaire (SF-MPQ), Chronic Pain Grade Scale (CPGS), Short Form-36 Bodily Pain

Scale (SF-36 BPS), and Measure of Intermittent and Constant Osteoarthritis Pain (ICOAP). *Arthritis care & research* 2011, **63 Suppl 11**:S240-252.

17. Unver B, Kahraman T, Kalkan S, Yuksel E, Karatosun V: **Reliability of the six-minute walk test after total hip arthroplasty**. *Hip international: the journal of clinical and experimental research on hip pathology and therapy* 2013, **23**(6):541–545.
18. Davidovitch R, Riesgo A, Bolz N, Murphy H, Anoushiravani A, Snir N: **The Effect of Obesity on Fluoroscopy-Assisted Direct Anterior Approach Total Hip Arthroplasty**. *Bulletin of the Hospital for Joint Disease (2013)* 2020, **78**(3):187–194.
19. Sali E, Marmorat JL, Gaudot F, Nich C: **Perioperative complications and causes of 30- and 90-day readmission after direct anterior approach primary total hip arthroplasty**. *Journal of orthopaedics* 2020, **17**:69–72.
20. Sprowls GR, Allen BC, Lundquist KF, Sager LN, Barnett CD: **Incision site fat thickness and 90-day complications for direct anterior and posterior approach total hip arthroplasty**. *Hip international: the journal of clinical and experimental research on hip pathology and therapy* 2020:1120700020977166.
21. Hartford JM, Graw BP, Frosch DL: **Perioperative Complications Stratified by Body Mass Index for the Direct Anterior Approach to Total Hip Arthroplasty**. *J Arthroplasty* 2020, **35**(9):2652–2657.
22. Jahng KH, Bas MA, Rodriguez JA, Cooper HJ: **Risk Factors for Wound Complications After Direct Anterior Approach Hip Arthroplasty**. *J Arthroplasty* 2016, **31**(11):2583–2587.
23. Antoniadis A, Dimitriou D, Flury A, Wiedmer G, Hasler J, Helmy N: **Is Direct Anterior Approach a Credible Option for Severely Obese Patients Undergoing Total Hip Arthroplasty? A Matched-Control, Retrospective, Clinical Study**. *J Arthroplasty* 2018, **33**(8):2535–2540.
24. Russo MW, Macdonell JR, Paulus MC, Keller JM, Zawadsky MW: **Increased Complications in Obese Patients Undergoing Direct Anterior Total Hip Arthroplasty**. *J Arthroplasty* 2015, **30**(8):1384–1387.
25. Purcell RL, Parks NL, Cody JP, Hamilton WG: **Comparison of Wound Complications and Deep Infections With Direct Anterior and Posterior Approaches in Obese Hip Arthroplasty Patients**. *J Arthroplasty* 2018, **33**(1):220–223.
26. Purcell RL, Parks NL, Gargiulo JM, Hamilton WG: **Severely Obese Patients Have a Higher Risk of Infection After Direct Anterior Approach Total Hip Arthroplasty**. *J Arthroplasty* 2016, **31**(9 Suppl):162–165.
27. Jeschke E, Citak M, Günster C, Halder AM, Heller KD, Malzahn J, Niethard FU, Schräder P, Zacher J, Gehrke T: **Obesity Increases the Risk of Postoperative Complications and Revision Rates Following Primary Total Hip Arthroplasty: An Analysis of 131,576 Total Hip Arthroplasty Cases**. *J Arthroplasty* 2018, **33**(7):2287-2292.e2281.
28. Chee YH, Teoh KH, Sabnis BM, Ballantyne JA, Brenkel IJ: **Total hip replacement in morbidly obese patients with osteoarthritis: results of a prospectively matched study**. *The Journal of bone and joint surgery British volume* 2010, **92**(8):1066–1071.

29. Gardner AW, Montgomery PS: **The effect of metabolic syndrome components on exercise performance in patients with intermittent claudication**. *Journal of vascular surgery* 2008, **47**(6):1251–1258.

Figures

Figure 1

Auxiliary traction bracket for direct anterior THA in the supine position.

Figure 2

DAA surgery assisted by DAA stent

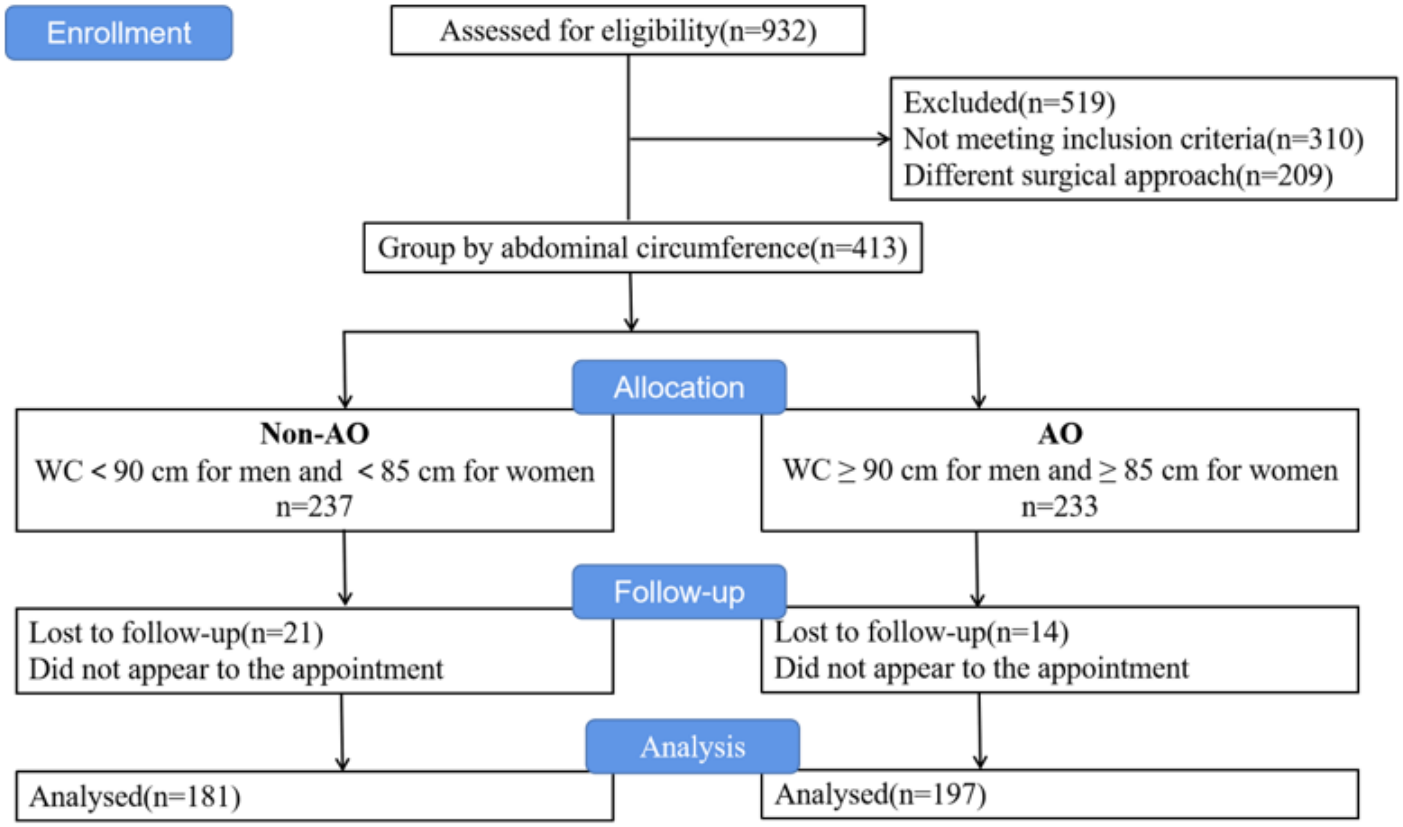

Figure 3

CONSORT (Consolidated Standards of Reporting Trials) flow diagram for the study.

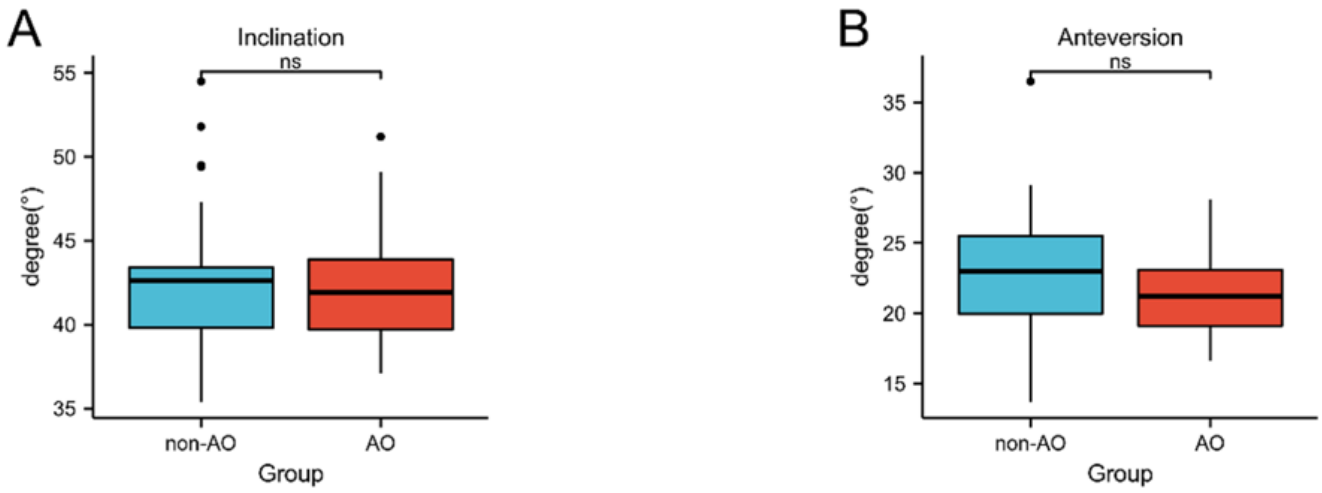

Figure 4

AO and non-AO Inclination and Anteversion. **A** Comparison of inclination between AO group and non-AO group. **B** Comparison of anteversion between AO group and non-AO group. NS, no significance.

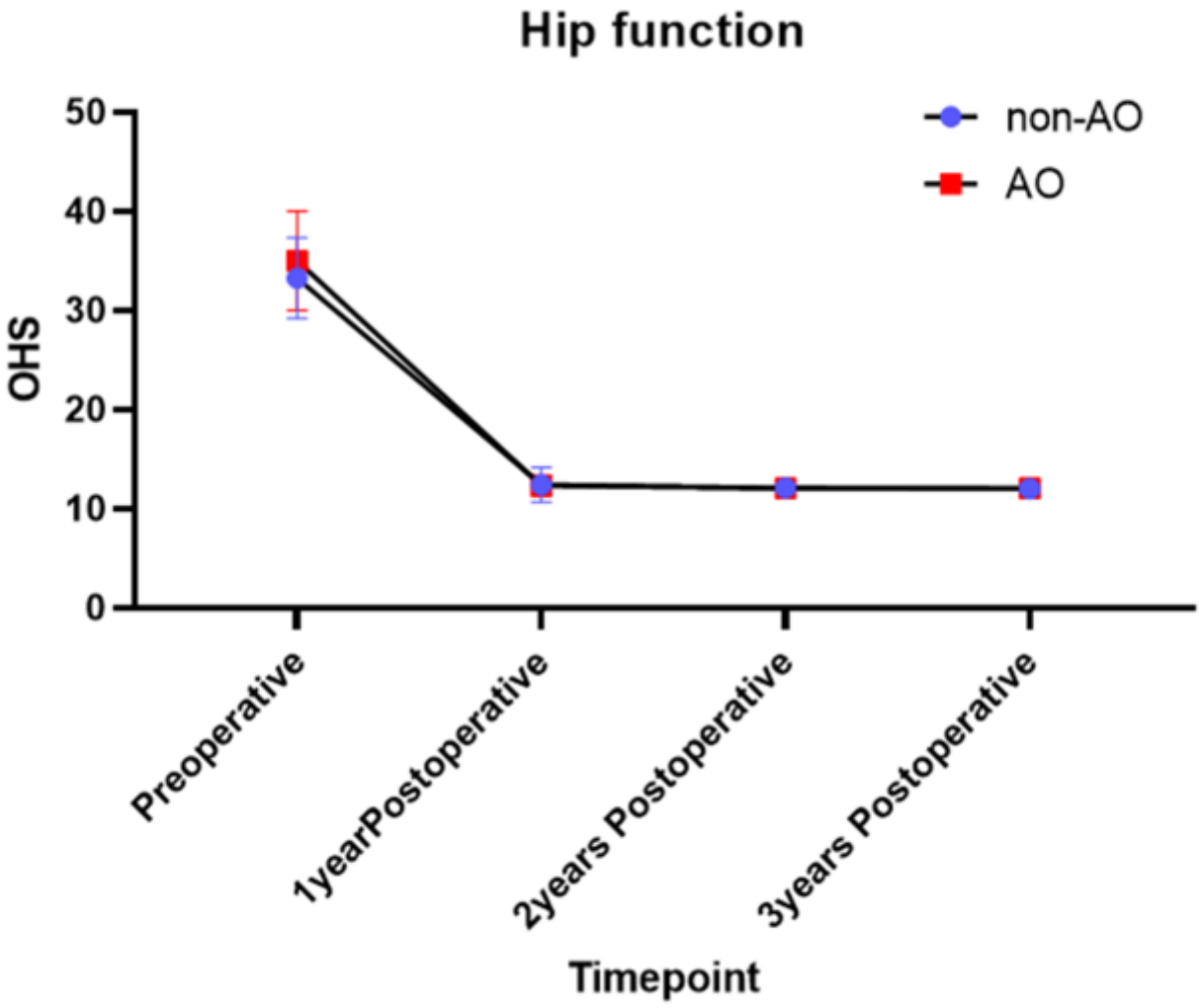

Figure 5

The comparison of Hip function between AO Group and non-AO Group.

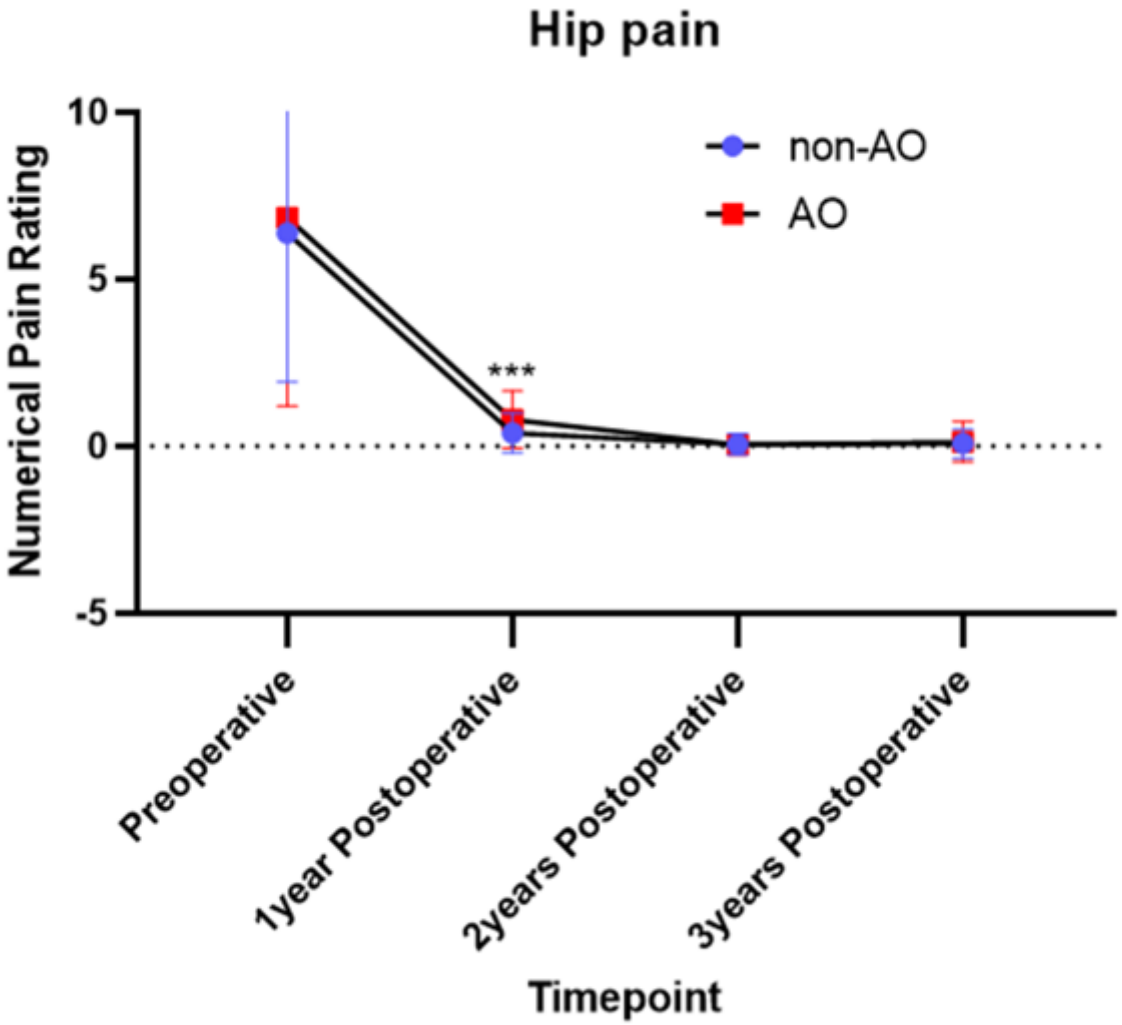

Figure 6

The comparison of Hip pain between AO Group and non-AO Group.***, p<0.001.

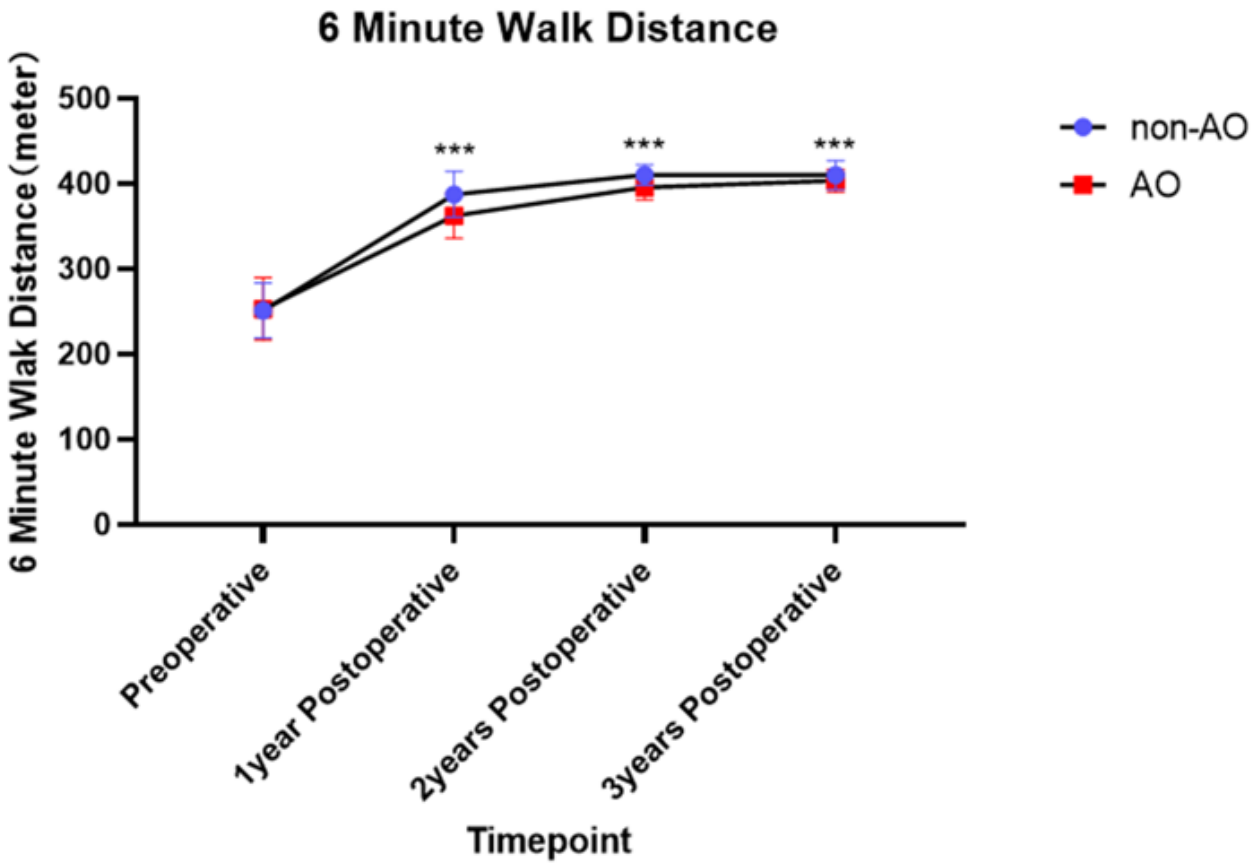

Figure 7

The comparison of 6 Minute Walk Test Distance between AO Group and non-AO Group. ***, p<0.001.

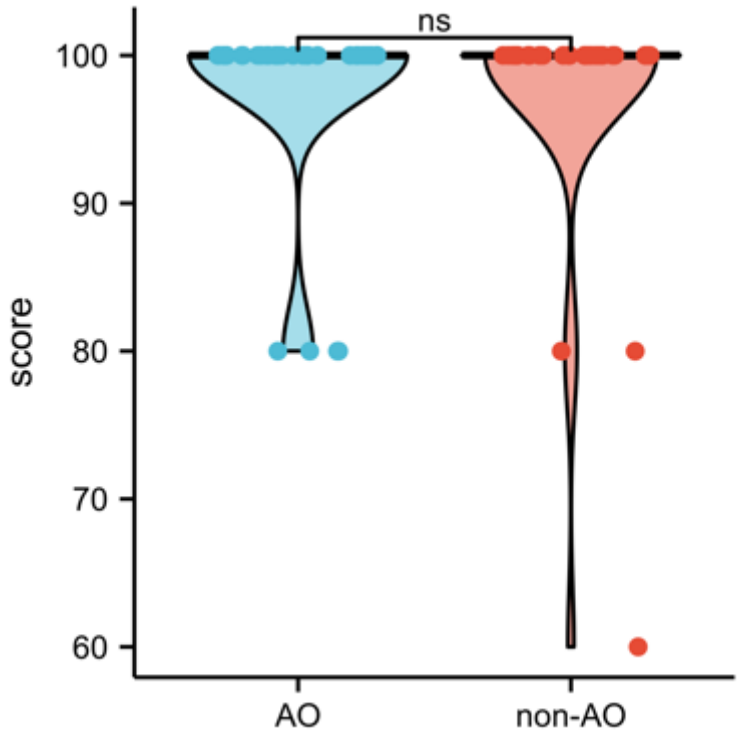

Figure 8

Comparison of Satisfaction between AO group and non-AO group. NS, no significance.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- file.xlsx