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**Impact of being underweight on peri-operative and post-operative outcomes of total knee or hip arthroplasty: A meta-analysis**

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**Abstract**

**BACKGROUND**

Many systematic reviews have been focused to assess the effect of Body mass index (BMI) on the outcomes and complications associated with total hip arthroplasty (THA) and total knee arthroplasty (TKA), but primarily dealt with obesity about normal weight (NW). None of the reviews ever attempted to assess the effect of low BMI or underweight (UW) compared to NW on patients undergoing THA or TKA.

**AIM**

This review aims to compare the specific operative outcomes like operation duration, length of hospital stays, and postoperative complications like mortality (death), infections, deep vein thrombosis (DVT), etc. along with re-hospitalization and reoperation rates between UW and NW patients undergoing THA, TKA or both.

**METHODS**

An electronic search was performed in PubMed, Scopus, Excerpta Medica database (EMBASE), Web of Science (WoS), and Cochrane Central Register of Controlled Trials (CENTRAL) along with a manual search. The quality of the studies was assessed using the new castle Ottawa scale for cohort studies. The data were subjected to both qualitative and quantitative analysis.
RESULTS
Thirteen retrospective and five prospective cohort studies were included. The quality of included studies was assessed to be good to fair. The length of hospital stays after TKA or THA was found to be significantly higher for UW patients when compared to NW patients. Mean Difference (MD) 0.39 95% CI [0.06, 0.72], $P = 0.02$ (in days). Studies presenting both THA and TKA together as total joint arthroplasty (TJA) showed an increased incidence of mortality in patients treated with THA or TKA alone, Odds ratio (OR) 4.18 95% CI [2.88, 6.07]. A higher incidence of postoperative complications was also observed with UW patients undergoing THA.

CONCLUSION
UW patients undergoing THA or TKA presented with a higher incidence of postoperative complications and were associated with a higher readmission rate. Moreover, UW patients were associated with an increased incidence of mortality in the studies that report THA and TKA together.

INTRODUCTION
BMI plays a pivotal role in predicting the outcomes and associated complications after THA and TKA [1]. BMI among the population is majorly divided into 5 categories: underweight (score of <18.5); normal weight (18.5-24.9); overweight (25-29.9); obese (30-34.9) and morbidly obese (>40). This score is defined by weight in kilograms per square meter of height [2].

Extreme values of BMI are regarded as a risk factor for various systemic diseases like diabetes, cardiovascular diseases, pulmonary diseases, dementia, and notable osteoarthritis in the elderly.[3] Obesity has already been proved to be associated with poor clinical outcomes, and lower success rates in patients undergoing TJA.[4,5] Obese patients present with a higher incidence of infection, and complications compared to NW individuals.[6] However, the results were conflicting. Despite this negative relation
between obesity on the success of THA or TKA, some studies established the fact that no difference was observed between obese and non-obese patients in terms of clinical outcomes, survival rate, and complications [7-9].

Underweight (UW) patients suffer from poor nutrition, anaemia, vitamin deficiencies, and most importantly osteoporosis due to calcium and vitamin D deficiency. Osteoporosis is a major risk factor for patients with osteoarthritis requiring THA or TKA. The understanding of prognosis post-THA or TKA in UW patients is less studied and not clearly understood. The literature which focused on evaluating the effect of BMI also presented with outcomes of UW patients undergoing arthroplasty. It was interesting to find that UW patients may also lead to poor postoperative outcomes, including increased rates of post-operative infection, transfusion, cardiovascular events, and renal complications [10,11]. UW patients have also been shown to potentially delay mobilization, and increase lengths of stay and hospital expenditures [12,13]. However, the evidence is scarce, and very few studies directly attempted to assess the effect of UW compared on NW individuals.

Many systematic reviews have been focused to assess the effect of BMI on the outcomes and complications associated with TJA [14-17], but primarily dealt with obesity about to NW. None of the reviews ever attempted to assess the effect of low BMI or UW on patients undergoing THA or TKA. The risk of UW patients undergoing TJA is rather debatable and no substantial evidence has been put forth. This is the first of its kind review that aims to compare operative and postoperative complications between UW and NW patients undergoing THA or TKA. The objective of this review is to compare the specific operative outcomes like operation duration, length of hospital stays, and postoperative complications like mortality (death), infections, deep vein thrombosis (DVT), etc. along with rehospitalization and reoperation rates between UW and NW patients undergoing THA, TKA or both.

MATERIALS AND METHODS
This systematic review and meta-analysis were performed according to preferred reporting items for systematic review and meta-analysis (PRISMA) guidelines [18]. The protocol for conducting this review was predefined and employed for conducting the systematic review efficiently in a smooth manner. The ethics approval was not required for this review.

Research Question:
What is the impact of UW compared to NW on operative outcomes, rehospitalization and reoperation rates, and postoperative complications in patients undergoing THA or TKA?

The following PICO strategy was employed to formulate the research question and search strategy to identify eligible articles: Patients (P): Patients undergoing THA or TKA; Exposure (E): UW patients with BMI <18.5 kg/m²; Comparison (C): NW patients with BMI between 18.5-24.9 Kg/m²; Outcome (O): operation duration (in minutes), length of hospital stays (in days), and postoperative complications like mortality (death), infections, deep vein thrombosis (DVT), pulmonary embolism, Genito-urinary complications, dislocation/ subluxation, fracture along with rehospitalization and reoperation rates expressed as a proportion (event/total); Study design (S): All observational studies comparing outcomes of UW vs NW patients undergoing THA or TKA or TJA

Search strategy:
A comprehensive search strategy was developed to identify the relevant articles to answer the question. An electronic search was performed in PubMed, Scopus, Excerpta Medica database (EMBASE), Web of Science (WoS), and Cochrane Central Register of Controlled Trials (CENTRAL). The search strategy was framed using the following relevant keywords: underweight; "low body mass index"; malnourished; "Total knee arthroplasty"; "Total joint arthroplasty"; "Total hip arthroplasty"; mortality; complications; rehospitalization; readmissions; “length of hospital stay”. The details of the search strategy are provided in Table 1. No limits or restrictions were applied to the
electronic search. The last electronic search was carried out till June 2021. An additional manual search was also carried out in peer-reviewed relevant journals like the Journal of orthopedics; Journal of arthroplasty; Journal of orthopedic surgery and research; and Journal of knee surgery, sports traumatology, and arthroscopy. The reference list of previously conducted relevant systematic reviews and other relevant studies were screened for possible inclusion of eligible articles. The identified reports along with electronic search results were imported into a citation manager (ENDNOTE) for discarding the duplicates obtained from multiple databases.

**Study Selection:**

The reports were screened by two independent reviewers based on the below-mentioned inclusion and exclusion criteria:

**Inclusion criteria:**

All studies comparing outcomes of UW vs NW patients undergoing THA or TKA or TJA. Studies report outcomes like operation duration, length of hospital stays, and postoperative complications like mortality (death), infections, DVT, pulmonary embolism, Genito-urinary complications, dislocation/subluxation, fracture along with rehospitalization and reoperation rates.

Studies attaining a minimum score of 7 assessed using the New Castle-Ottawa scale of quality assessment were included.

**Exclusion criteria:**

Studies published in other than the English language.

Studies do not report relevant outcomes.

Studies recruiting patients with other systemic diseases, immune-compromised patients.

Studies with a score less than 7 assessed using the New Castle-Ottawa scale of quality assessment were excluded.

**Data extraction:**
The data extraction was performed by two independent reviewers (YM, and QS) using an excel spreadsheet. The demographic characteristics and details of outcomes like operation duration, length of hospital stays, and postoperative complications like mortality (death), infections, DVT, pulmonary embolism, Genito-urinary complications, dislocation/ subluxation, fracture along with rehospitalization and reoperation rates were extracted. The authors were contacted through a corresponding email for clarification about any missing data or unclear information.

Data synthesis:
The extracted data were subjected to both qualitative and quantitative analysis. The outcomes which could not be combined for quantitative analysis were summarized. The continuous data of the extracted outcomes were expressed as mean and standard deviation. The dichotomous outcomes were expressed as an absolute number of events, ratio, and proportion. The outcome effect was calculated between UW and NW patients as the mean difference for continuous outcomes and odd’s ratio for dichotomous outcomes. The quantitative data were subjected to meta-analysis using RevMan 5.4 v software. The meta-analysis was carried out only if two or more studies with similar outcomes were available. A p-value <0.05 for assessing the outcome effect was considered significant. A random effect was chosen as the included studies presented with a varied population. The heterogeneity among the studies was assessed using i2 statistics. The heterogeneity was considered low if the i2 value was found to be <40%, moderate for a value of 40-70%, and high for a value more than 70%. The studies presented the data on THA or TKA alone and also reported both THA and TKA data together. Hence, a sub-group analysis was carried out based on the type of joint arthroplasty reported. For outcomes like Mortality, a sub-group analysis was carried out based on the time frame.

Quality of included studies:
The methodological quality of included studies was assessed by two independent reviewers using the Newcastle-Ottawa Scale (NOS). The NOS consists of eight items grouped into three categories, namely: selection, comparability, and outcome. A scoring
system, ranging from zero to nine stars, was used to classify the quality of the study being reviewed. Each included study received the following categorical scores representing its quality: good (three or four scores in the selection domain AND one or two scores in the comparability domain AND two or three scores in the outcome domain), fair (two scores in selection domain AND one or two scores in comparability domain AND two or three scores in outcome domain) or poor (zero or one score in selection domain OR zero score in comparability domain OR zero or one score in outcome domain).

RESULTS
A total of eighteen studies \[10,11,19-34\] were included in this review. Twenty-two eligible studies \[4,35-37\] were screened from a pool of 671 records identified from both electronic and manual searches, purely based on title and abstract. The inclusion and exclusion were strictly applied for carrying out the full-text assessment of eligible studies. Finally, eighteen studies were deemed inclusive after satisfying the pre-defined criteria. The complete study selection process is provided. (Figure 1) And, the detailed search strategy employed in all databases is provided in Table 1.

Demographic characteristics
Thirteen retrospective cohort studies \[10,11,19-23,25,26,28,31,33\] and five prospective cohort studies \[24,27,30,32,34\] were included. The studies included a total of 11,36,506 subjects undergoing TKA or THA with a mean age of 65.32 years. The subjects comprised 469387 males and 667119 females. Out of these recruited subjects undergoing TKA or THA, 213028 subjects were NW individuals with BMI ranging between 18.5-24.9, and only 10785 subjects were UW individuals with BMI <18.5. Sixteen studies \[10,19,21-34\] assessed the outcomes for THA and nine studies \[11,19,20,23,26,28,30,31,33\] for TKA. Only seven studies \[19,23,26,28,30,31,33\] presented data with both THA and TKA. The demographic characteristics of the included studies are provided in Table 2. The quality of studies assessed using NOS is found to have good to fair quality. The details of Newcastle-Ottawa scoring criteria according to domains are well presented and shown in Table 3.
**Meta-analysis**

**Operative duration (in minutes)**

The operative duration between UW (n = 2102) and NW (n = 55701) patients undergoing THA or TKA, was found to have no significant difference with MD 1.66 95%CI [-1.89, 5.21], \( P = 0.36 \). A subgroup analysis was carried out based on the type of procedure to analyze the heterogeneity (\( i^2 = 75\% \)). No difference in the result was observed in patients undergoing THA MD 0.73 95%CI [-3.31, 4.77], \( P = 0.72 \) and TJA MD 2.54 95%CI [-3.59, 8.66], \( P = 0.42 \). (Figure 2)

**Length of hospital stay (in days)**

The length of hospital stay after arthroplasty was found to be significantly higher for UW patients (n = 4555), when compared to NW patients (n = 58890). MD 0.39 95%CI [0.06, 0.72], \( P = 0.02 \), \( i^2 = 81\% \).

The subgroup analysis showed no significant differences were observed between UW and NW patients undergoing THA or TKA. However, in patients undergoing both THA and TKA, the length of hospital stay was found to be significantly higher for UW patients (n = 2207) MD 0.76 95%CI [0.43, 1.09], \( P < 0.0001 \). A low heterogeneity was also observed with an \( i^2 \) value of 31%. (Figure 3)

**30–90-day Readmission rate**

No significant difference in association of readmission rate was observed between UW and NW patients undergoing THA or TKA with OR 1.42 95%CI [0.71, 2.87], \( P = 0.32 \); \( i^2 = 36\% \). No subgroup differences were observed. UW patients (n = 408) undergoing THA presented with an increased odds OR 1.75 95%CI [0.58, 5.27], \( P = 0.32 \), \( i^2 = 49\% \) (not significant) of 30-90 day readmission compared to NW patients. (Figure 4)

**Re-operation rate**

No significant difference in the association of reoperation rate was observed between UW and NW patients undergoing THA with OR 1.22 95%CI [0.43, 3.42], \( P = 0.71 \); \( i^2 = 0\% \).

No subgroup differences were observed. (Figure 5)

**Post-operative mortality**
UW patients \((n = 6880)\) had a higher odds of postoperative mortality than NW patients \((126040)\) with OR 2.20 95%CI [1.43, 3.37], \(P = 0.0003\). However, a high heterogeneity with an \(i^2\) value of 91% was observed. On subgroup analysis, it was found that studies reporting THA and TKA together showed an increased incidence of mortality with UW patients \((n = 438)\) OR 4.18 95%CI [2.88, 6.07], \(p<0.0001\) with \(i^2 = 0\%\). Although not significant, the incidence of postoperative mortality is less likely to be observed in UW patients, compared to NW patients. (Figure 6)

A subgroup analysis carried out based on timeframe showed higher 31-365 day mortality than in UW patients with OR 2.35 95%CI [1.31, 3.54], \(p<0.0001, i^2=29\%\), than NW patients. (Supplementary Figure 1)

**Post-operative infection**

No significant difference in incidence of postoperative infection was observed between UW \((n = 2955)\) and NW patients \((n = 8261)\) undergoing THA or TKA with OR 0.68 95%CI [0.20, 1.29], \(P = 0.54; i^2=51\%\). No subgroup differences were observed. (Figure 7) The incidence of post-operative infection presented with lesser odds (not significant) when observed in UW patients, compared to NW patients.

**Total complications**

No significant difference in hazard ratios computing total complications was observed between UW and NW patients. The incidence of total or overall complications observed between the two groups of patients undergoing arthroplasty was similar with HR 1.27 95%CI [0.50, 3.22], \(P = 0.61, i^2=27\%\). (Figure 8)

**Post-operative complications in patients undergoing THA**

UW patients \((n = 31619)\) showed higher odds for incidence of post-operative complications with OR 1.44 95%CI [1.10, 1.88], \(P = 0.008, i^2=58\%\), in patients undergoing THA. Subsequently, a significantly higher incidence of DVT and cardiac infarction among the post-operative complications are observed with UW patients undergoing THA. (Figure 9)

**Post-operative complications in patients undergoing TKA**
No significant difference in association of post-operative infection, DVT and pulmonary embolism (PE) was observed in UW ($n = 2134$) compared to NW ($n = 3424$) patients undergoing TKA with OR 1.88 95%CI [0.34, 10.41], $P = 0.47$, $I^2=56\%$. (Figure 10)

**DISCUSSION**

This systematic review and meta-analysis included thirteen retrospective and five prospective cohort studies to compare UW and NW patients undergoing THA or TKA or TJA in terms of specific outcomes like operation duration, length of hospital stays, and postoperative complications like mortality (death), infections, (DVT, pulmonary embolism, Genito-urinary complications, dislocation/subluxation, fracture along with rehospitalization and reoperation rates. The quality of the studies included was good to fair. UW patients undergoing THA or TKA presented with a higher incidence of postoperative complications and readmission rate. Moreover, studies reporting THA and TKA were associated with increased incidence of mortality. Also, a higher incidence of DVT and cardiac infarction was evident among all the post-operative complications associated with UW patients undergoing THA. No difference in the association of postoperative complications could be found in UW patients undergoing TKA.

Knee and Hip osteoarthritis (OA) is a kind of degeneration of articular cartilage, and bone hyperplasia of joint disease, is a kind of common chronic disabling disease, causing physiological and psychological pain to the patient [38]. OA is a common disease among the elderly. Elderly patients suffering from OA opt for arthroplasty for improved quality of life and morbidity free life [39,40]. Modern-day arthroplasty includes the replacement of joints with a metal prosthesis, compatible and restoring function. TKA involves replacing the articular surfaces (femoral condyles and tibial plateau) of the knee joint with smooth metal and highly cross-linked polyethylene plastic [41,42]. And THA involves the replacement of the acetabulum or hip socket, and the head of the femur is removed and replaced with metal replicas [43]. TJA involves both THA and TKA carried out simultaneously to deal which OA complications. The prognosis of
undergoing both procedures is good and is considered to improve the quality of life by reducing pain and increasing function [44].

BMI is considered one of the key predictive tools for assessing the outcomes after TKA or THA. An extreme BMI level is believed to worsen the prognosis and is associated with increased complications after TKA or THA. Many systematic reviews have assessed the effect of BMI on these procedures. According to a recent systematic review [45], BMI higher than normal can affect the intra-operative risk of TKA and postoperative recovery, and increase the risk of complications. Another review [46] concluded increased BMI was associated with an increased risk for peri-prosthetic joint infection (PJI) after primary THA or TKA. Patients following THA were more likely to suffer from PJI than patients following TKA. All the systematic reviews and meta-analysis conducted focused on the effect of obesity or patients with high BMI on various outcomes after undergoing THA or TKA. However, some studies have shown that even low BMI or UW patients have shown both peri-operative morbidity and poor post-operative recovery with complications. A study [47] that evaluated the readmission rate and postoperative infection in UW patients undergoing THA, demonstrated that patients with BMI <18.5 kg/m² were more likely to be associated with post-discharge infections and thereby increased readmission rates.

Most of the included studies classified underweight patients with BMI <18.5 kg/m²; however few studies like Katakam et al 2020 (19) and Anoushiravani et al 2016 (31) used an up-bound cut-off of <20 kg/m² and <19.5 kg/m² to justify the fact that the present WHO classification of BMI was set based on the findings in a young population and the included patients were elderly over a mean age of 60 years.

The peri-operative outcomes assessed after undergoing arthroplasty include the operative duration and length of hospital stay. Our meta-analysis showed no significant difference in operative duration between UW and NW patients, however, the length of hospital stays after THA or TKA was found to be significantly higher for UW patients when compared to NW patients with MD of 0.39 days 95%CI [0.06, 0.72], P = 0.02. Poor nutritional status among UW patients leads to musculoskeletal degeneration
characterized by less muscle mass, less soft tissue, and a greater probability of osteoporosis. A study in 2016 [30] showed a higher proportion of UW patients with a length of hospital stay of more than 4 days compared to normal and obese patients. However, the mean difference of 0.39 days (=9.4 h) for the length of hospital stay between UW and NW patients undergoing THA or TKA, though statistically significant, but not clinically significant. This negligible difference in hours may be due to delay in discharge related to system-level reason or inadequate staff availability.”

Our systematic review did not find any significant difference in readmission and re-operation rate for both UW and NW patients undergoing THA or TKA or TJA. Although not significant, the association of 30-90 readmission rates is more likely to be observed in UW patients, compared to NW patients. The result of the same cannot be regarded as sufficient certainty as the readmission rate is positively affected by various independent risk factors like age, male sex, black race, presence of pre-operative co-morbidities, and increased operative time following TKA [48].

Our meta-analysis showed a significant association with postoperative mortality was observed in UW patients OR 2.20 95%CI [1.43, 3.37]. UW patients are supposed to be malnourished, and often present with poor nutritional reserve. This may lead to a less pronounced immunological response. This may be a reasonable explanation for the higher incidence of postoperative mortality. The compromised immune response among these patients could trigger numerous debilitating diseases, leading to death. Additionally, patients undergoing both THA and TKA together showed an increased incidence of mortality with UW patients OR 4.18 95%CI [2.88, 6.07]. This could be explained by the fact that total joint arthroplasty (THA and TKA) is a more morbid and complicated surgery, presenting with a higher incidence of complications than THA or TKA alone. A registry study [33] found U-shaped risk associations between BMI and perioperative cardiovascular events and mortality, which were highest in the UW group, in THA and TKA, suggesting that this was a subpopulation at risk.
Several authors have evaluated complications of underweight patients, however, some of the reported data is controversial. Many authors contend that underweight patients have a higher complication rate than their normal weight or even obese counterparts. Our meta-analysis of included studies regarding post-operative complications showed a significantly higher incidence of DVT and cardiac infarction among the post-operative complications observed with UW patients undergoing THA alone. Three studies [11,24,31] showed that underweight patients undergoing THA or TKA have increased risks for infection, cardiac complications, and Venous thromboemboli. The reason for the contention is not entirely clear, however, in their studies, it appears that the underweight group tends to have lower preoperative haematocrit and albumin which are markers of malnutrition and predispose patients to medical complications. Nowadays, autologous platelet concentrates [40-51] prove to be beneficial in the management of bone-related disorders [52-55]. It has also found its use in adjunct to arthroplasty [56,57]. Many studies have opted for it as an alternative to arthroplasty [58,59]. This can be indicated as an alternative to arthroplasty in less severe cases for improving the quality of life in UW patients [60].

Our systematic review and meta-analysis are the first of their kind to assess the impact of being underweight on peri-operative and postoperative outcomes of THA or TKA. Our review also presents certain limitations. The confounding factors like age, presence of comorbidities like anaemia, diabetes, hypertension, patients using anticoagulants, and preoperative use of any walking aids, were not taken into consideration to assess the peri-operative outcomes and readmission or reoperation rates. Moreover, no subgroup analysis could be performed based on follow-up time, especially on 30-day and 90-day readmission rates. The exclusion of articles other than the English language could also be a possible limitation as little good evidence could have been missed out.

CONCLUSION
UW patients undergoing THA or TKA presented with a higher incidence of postoperative complications and readmission rate. Moreover, UW patients undergoing TJA were associated with an increased incidence of mortality between the 31-365-day time frame. Also, a higher incidence of DVT and cardiac infarction was evident among all the post-operative complications associated with UW patients undergoing THA. No difference in the association of postoperative complications could be found in UW patients undergoing TKA. Hence, careful clinical judgment needs to be made by the clinicians before treating UW patients with THA or TKA.

ARTICLE HIGHLIGHTS

Research background
The effect of Body mass index (BMI) on the outcomes and complications associated with total hip arthroplasty (THA) and total knee arthroplasty (TKA) is less studied and believed to be a determent factor.

Research motivation
The systematic reviews on the same primarily dealt with obesity about normal weight (NW). None of the reviews ever attempted to assess the effect of low BMI or underweight (UW) compared to NW on patients undergoing THA or TKA.

Research objectives
The objective of this review is to compare the specific operative outcomes like operation duration, length of hospital stays, and postoperative complications like mortality (death), infections, deep vein thrombosis (DVT), etc. along with rehospitalization and reoperation rates between UW and NW patients undergoing THA or TKA or both.

Research methods
An electronic search was performed in PubMed, Scopus, Excerpta Medica database (EMBASE), Web of Science (WoS), and Cochrane Central Register of Controlled
Trials (CENTRAL) along with a manual search. The quality of the studies was assessed using the Newcastle Ottawa scale for cohort studies. The data were subjected to both qualitative and quantitative analysis.

Research results

Thirteen retrospective and five prospective cohort studies were included. The quality of included studies was assessed to be good to fair. The length of hospital stays after TKA or THA was found to be significantly higher for UW patients when compared to NW patients. Mean Difference (MD) 0.39 95%CI [0.06, 0.72], $P = 0.02$ (in days). Studies presenting both THA and TKA together as total joint arthroplasty (TJA) showed an increased incidence of mortality in patients treated with THA or TKA alone Odds ratio (OR) 4.18 95%CI [2.88, 6.07]. A higher incidence of postoperative complications was also observed with UW patients undergoing THA.

Research conclusions

UW patients undergoing THA or TKA presented with a higher incidence of postoperative complications and were associated with a higher readmission rate. Moreover, UW patients were associated with an increased incidence of mortality in the studies that report THA and TKA together.

Research perspectives

Careful clinical judgment needs to be made by the clinicians before treating UW patients with THA or TKA for attaining better outcomes.
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