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Editorial Board Member of World Journal of Clinical Cases, Rajeev Gurunath Redkar, FRCS, FRCS (Ed), FRCS (Gen Surg), MBBS, MCh, MS, Dean, Professor, Surgeon, Department of Pediatric Surgery, Lilavati Hospital and Research Centre, Mumbai 400050, Maharashtra, India. rajeev.redkar@gmail.com

AIMS AND SCOPE
The primary aim of World Journal of Clinical Cases (WJCC, World J Clin Cases) is to provide scholars and readers from various fields of clinical medicine with a platform to publish high-quality clinical research articles and communicate their research findings online.

WJCC mainly publishes articles reporting research results and findings obtained in the field of clinical medicine and covering a wide range of topics, including case control studies, retrospective cohort studies, retrospective studies, clinical trials studies, observational studies, prospective studies, randomized controlled trials, randomized clinical trials, systematic reviews, meta-analysis, and case reports.

INDEXING/ABSTRACTING
The WJCC is now abstracted and indexed in Science Citation Index Expanded (SCIE, also known as SciSearch®), Journal Citation Reports/Science Edition, Current Contents/Clinical Medicine, PubMed, PubMed Central, Scopus, Reference Citation Analysis, China National Knowledge Infrastructure, China Science and Technology Journal Database, and Superstar Journals Database. The 2022 Edition of Journal Citation Reports® cites the 2021 impact factor (IF) for WJCC as 1.534; IF without journal self cites: 1.491; 5-year IF: 1.599; Journal Citation Indicator: 0.28; Ranking: 135 among 172 journals in medicine, general and internal; and Quartile category: Q4. The WJCC’s CiteScore for 2021 is 1.2 and Scopus CiteScore rank 2021: General Medicine is 443/826.

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Meta-analysis

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

Yun-Ping Ma, Qiu Shen

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Peer-review report's scientific quality classification
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BACKGROUND
Many systematic reviews have focused on assessing 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 compared to normal weight (NW). None of these reviews attempted to assess the effect of low BMI or underweight (UW) compared to NW in patients undergoing THA or TKA.

AIM
This review aims to compare specific operative outcomes such as operation duration, length of hospital stay, and post-operative complications including mortality, infections, deep vein thrombosis, etc. along with re-hospitalization and reoperation rates between UW and NW patients undergoing THA or TKA.

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.

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 stay after TKA or THA was found to be significantly higher for UW patients when compared to NW patients, with a mean difference: 0.39 95%CI: [0.06, 0.72], P = 0.02 (in days). Studies presenting both THA and TKA together as total joint arthroplasty showed an increased incidence of mortality in patients treated with THA or TKA alone, Odds ratio: 4.18 95%CI: [2.88, 6.07]. A higher incidence of post-operative complications was also observed in UW patients undergoing THA.
CONCLUSION
UW patients undergoing THA or TKA had a higher incidence of post-operative complications and were associated with a higher readmission rate. Moreover, UW patients were associated with an increased incidence of mortality in the studies that reported THA and TKA together.

Key Words: Underweight; Total knee arthroplasty; Total hip arthroplasty; Systematic review; Meta-analysis

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Core Tip: Many systematic reviews have focused on assessing 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 compared to normal weight (NW) patients. None of these reviews attempted to assess the effect of low BMI or underweight (UW) compared to NW in patients undergoing THA or TKA. The present analysis found that UW patients undergoing THA or TKA had with a higher incidence of post-operative complications and were associated with a higher readmission rate.

INTRODUCTION
Body mass index (BMI) plays a pivotal role in predicting the outcomes and associated complications after total hip arthroplasty (THA) and total knee arthroplasty (TKA)[1]. BMI in the population is mainly 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[2].

Extreme values of BMI are regarded as a risk factor for various systemic diseases such as 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 total joint arthroplasty (TJA)[4,5]. Obese patients present with a higher incidence of infection, and complications compared to normal weight (NW) individuals[6]. However, the results were conflicting. Despite this negative relation between obesity and the success of THA or TKA, some studies established 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, anemia, 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 showed the outcomes of UW patients undergoing arthroplasty. It was interesting to note that UW patients may also lead to poor post-operative 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, increase length 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 to NW individuals.

Many systematic reviews have focused on assessing the effect of BMI on the outcomes and complications associated with TJA[14-17], but primarily dealt with obesity compared to NW. None of the reviews attempted to assess the effect of low BMI or UW in patients undergoing THA or TKA. The risk of UW patients undergoing TJA is debatable and no substantial evidence has been put forth. This is the first review to compare operative and post-operative complications between UW and NW patients undergoing THA or TKA. The objective of this review is to compare the specific operative outcomes such as operation duration, length of hospital stay, and post-operative complications including mortality, infections, deep vein thrombosis (DVT), etc. along with rehospitalization and reoperation rates between UW and NW patients undergoing THA, TKA or both.
Table 1 Search strategy

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<th>Search strategy</th>
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<td>PubMed</td>
<td>(((&quot;Under-weight&quot;) OR (Low body mass index)) OR (malnourished)) AND (((&quot;total knee arthroplasty&quot;[All Fields]) OR (&quot;total joint arthroplasty&quot;[All Fields])) OR (&quot;total knee replacement&quot;[All Fields])) AND (((mortality OR (complications)) OR (readmissions)) OR (rehospitalization)) OR (length of hospital stay))</td>
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<tr>
<td>CENTRAL</td>
<td>#1 Underweight</td>
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<td></td>
<td>#2 Low body mass index</td>
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<td>#3 Malnourished</td>
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<td>#4 #1 OR #2 OR #3</td>
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<td>#5 MeSH descriptor: [Arthroplasty, Replacement, Knee] explode all trees</td>
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<td>#6 MeSH descriptor: [Arthroplasty, Replacement, Hip] explode all trees</td>
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<td>#8 #5 OR #6 OR #7</td>
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<td>#9 #4 AND #8</td>
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<td>(((&quot;Under-weight&quot;) OR (Low body mass index)) OR (malnourished)) AND (((&quot;total knee arthroplasty&quot;[All Fields]) OR (&quot;total joint arthroplasty&quot;[All Fields])) OR (&quot;total knee replacement&quot;[All Fields])) AND (((mortality OR (complications)) OR (readmissions)) OR (rehospitalization)) OR (length of hospital stay))</td>
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MeSH: Medical subheadings; TS: Topic; WoS: Web of science.

MATERIALS AND METHODS

This systematic review and meta-analysis were performed according to the preferred reporting items for systematic review and meta-analysis (PRISMA) guidelines[18]. The protocol for conducting this review was predefined and employed to conduct the systematic review efficiently in a smooth manner. 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 post-operative 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 min), length of hospital stay (in days), and post-operative complications such as mortality, infections, 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 in June 2021. An additional manual search was also carried out in peer-reviewed relevant journals such as 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) in order to discard 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 reporting outcomes such as operation duration, length of hospital stay, and post-operative complications including mortality, 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 Newcastle-Ottawa scale (NOS) of quality assessment were included.

**Exclusion criteria:** Studies published in other than the English language. Studies not reporting relevant outcomes. Studies recruiting patients with other systemic diseases, and immune-compromised patients. Studies with a score less than 7 assessed using the NOS of quality assessment were excluded.

**Data extraction**
Data extraction was performed by two independent reviewers (YM, and QS) using an Excel spreadsheet. The demographic characteristics and details of outcomes such as operation duration, length of hospital stay, and post-operative complications including mortality, infections, DVT, pulmonary embolism, genito-urinary complications, dislocation/subluxation, fracture along with rehospitalization and reoperation rates were extracted. The authors were contacted by email for clarification on 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 odds ratio for dichotomous outcomes. The quantitative data were subjected to meta-analysis using RevMan v 5.4 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 model was chosen if the included studies presented a varied population. The heterogeneity among the studies was assessed using $I^2$ statistics. The heterogeneity was considered low if the $I^2$ 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 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 such as 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 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\cite{10, 11, 19-34} were included in this review. Twenty-two eligible studies\cite{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 criteria were strictly applied to carry 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 described in Figure 1, and the detailed search strategy employed in all databases is provided in Table 1.

**Demographic characteristics**
Thirteen retrospective cohort studies\cite{10, 11, 19-23, 25, 26, 28, 29, 31, 33} and five prospective cohort studies \cite{24, 27, 30, 32, 34} were included. The studies included a total of 1136506 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 a BMI between 18.5 and 24.9, and only 10785 subjects were UW individuals with a 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 was found to be good to fair quality. Details of the Newcastle-Ottawa scoring criteria according to domains were well presented and are shown in Table 3.

**Meta-analysis**

**Operation duration (in min):** The operation duration between UW (n = 2102) and NW (n = 55701) patients undergoing THA or TKA, was found to be not significantly different 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 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], $P < 0.0001$. Low heterogeneity was also observed with an $I^2$ value of 31% (Figure 3).

**30-90-day readmission rate:** No significant difference in 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 OR: 1.75 95%CI: [0.58, 5.27], $P = 0.32$, $I^2 = 49\%$ (not significant) of 30-90 d readmission compared to NW patients (Figure 4).

**Re-operation rate:** No significant difference in 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).
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<td>Hartford et al[20], 2020</td>
<td>Retrospective</td>
<td>1774</td>
<td>67.08</td>
<td>3 mo</td>
<td>1078/696</td>
<td>THA</td>
<td>Underweight</td>
<td>13</td>
</tr>
<tr>
<td>Katakam et al[18], 2021</td>
<td>Retrospective</td>
<td>4802</td>
<td>65.9</td>
<td>2 yr</td>
<td>2698/2104</td>
<td>THA and TKA</td>
<td>Underweight2</td>
<td>463</td>
</tr>
<tr>
<td>Kwon et al[19], 2020</td>
<td>Retrospective</td>
<td>118</td>
<td>70.75</td>
<td>2 yr</td>
<td>118/0</td>
<td>TKA</td>
<td>Underweight</td>
<td>85</td>
</tr>
<tr>
<td>Sloan et al[22], 2019</td>
<td>Retrospective</td>
<td>378775</td>
<td>65.7</td>
<td>1 mo</td>
<td>224912/153863</td>
<td>THA and TKA</td>
<td>Underweight</td>
<td>1846</td>
</tr>
<tr>
<td>Hung et al[24], 2019</td>
<td>Retrospective</td>
<td>1565</td>
<td>54.46</td>
<td>1 mo</td>
<td>830/735</td>
<td>THA</td>
<td>Underweight</td>
<td>77</td>
</tr>
<tr>
<td>Sayed-Noor et al [23], 2019</td>
<td>Prospective</td>
<td>83146</td>
<td>69</td>
<td>2 yr (90 d mortality)</td>
<td>47210/35936</td>
<td>THA</td>
<td>Underweight</td>
<td>51130</td>
</tr>
<tr>
<td>Woo et al[21], 2019</td>
<td>Retrospective</td>
<td>3672</td>
<td>78.06</td>
<td>1 yr</td>
<td>2620/1007</td>
<td>THA</td>
<td>Underweight</td>
<td>550</td>
</tr>
<tr>
<td>Dowsey et al[27], 2018</td>
<td>Retrospective</td>
<td>172767</td>
<td>67.65</td>
<td>5 yr</td>
<td>104742/68024</td>
<td>THA and TKA</td>
<td>TK + Underweight</td>
<td>268</td>
</tr>
<tr>
<td>Shohat et al[25], 2018</td>
<td>Retrospective</td>
<td>18173</td>
<td>61.33</td>
<td>3 mo</td>
<td>9986/8187</td>
<td>THA and TKA</td>
<td>Underweight</td>
<td>96</td>
</tr>
<tr>
<td>Zusmanovich et al [9], 2018</td>
<td>Retrospective</td>
<td>840</td>
<td>72.05</td>
<td>1 mo</td>
<td>660/180</td>
<td>THA</td>
<td>Underweight</td>
<td>3266</td>
</tr>
<tr>
<td>Mouchti et al[26], 2018</td>
<td>Prospective</td>
<td>415598</td>
<td>67.75</td>
<td>3 mo</td>
<td>246780/168818</td>
<td>THA</td>
<td>Underweight</td>
<td>539</td>
</tr>
<tr>
<td>Manrique et al[10], 2017</td>
<td>Retrospective</td>
<td>108</td>
<td>69.7</td>
<td>3.8 yr</td>
<td>93/24</td>
<td>TKA</td>
<td>Underweight</td>
<td>86336</td>
</tr>
<tr>
<td>Anoushirvani et al [30], 2016</td>
<td>Retrospective</td>
<td>4864</td>
<td>70.54</td>
<td>NA</td>
<td>4064/800</td>
<td>THA and TKA</td>
<td>THA + Underweight1</td>
<td>1762</td>
</tr>
<tr>
<td>Husted et al[29], 2016</td>
<td>Prospective</td>
<td>13730</td>
<td>NR</td>
<td>3 mo</td>
<td>NR</td>
<td>THA and TKA</td>
<td>THA + Underweight</td>
<td>1787</td>
</tr>
<tr>
<td>Shaparin et al[28], 2016</td>
<td>Retrospective</td>
<td>880</td>
<td>61.33</td>
<td>1 mo</td>
<td>541/339</td>
<td>THA</td>
<td>Underweight</td>
<td>645</td>
</tr>
</tbody>
</table>
Underweight and total joint arthroplasty

Zhao et al[31], 2014  Prospective  236  36.5  NA  34/202  THA  Underweight  91  Normal  145
Thornqvist et al [32], 2014  Retrospective  34744  70.6  1 mo  20438/14306  THA and TKA  Underweight  353  Normal  9859
Zhang et al[33], 2012  Prospective  714  62.17  5-20 yr  315/399  THA  Underweight  62  Normal  413

1Underweight < 19.5 kg/m².
2Underweight < 20 kg/m².
Underweight < 18.5 kg/m², Normal = 18.5 – 24.9 kg/m². THA: Total hip arthroplasty; TKA: Total knee arthroplasty; NA: Not available; NR: Not reported.

Post-operative mortality: UW patients (n = 6880) had higher odds of post-operative mortality than NW patients (12604) with OR: 2.20 95%CI: [1.43, 3.37], P = 0.0003. However, a high heterogeneity with an I² value of 91% was observed. Following subgroup analysis, it was found that studies reporting THA and TKA together showed an increased incidence of mortality in UW patients (n = 438) OR: 4.18 95%CI: [2.88, 6.07], P < 0.0001 with I² = 0%. Although not significant, the incidence of post-operative mortality was 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 d mortality in UW patients with OR: 2.35 95%CI: [1.31, 3.54], P < 0.0001, I² = 29%, than NW patients (Supplementary Figure 1).

Post-operative infection: No significant difference in the incidence of post-operative infection was observed between UW (n = 2955) and NW patients (n = 8261) undergoing THA or TKA with OR: 0.68 95%CI: [0.20, 1.69], P = 0.54; I² = 75%. No subgroup differences were observed (Figure 7). The incidence of post-operative infection was lower (not significant) 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, I² = 27% (Figure 8).

Post-operative complications in patients undergoing THA: UW patients (n = 31619) showed higher odds for the incidence of post-operative complications with OR: 1.44 95%CI: [1.10, 1.88], P = 0.008, I² = 58%, in patients undergoing THA. Subsequently, a significantly higher incidence of DVT and cardiac infarction among the post-operative complications were observed in UW patients undergoing THA (Figure 9).

Post-operative complications in patients undergoing TKA: No significant difference in post-operative infection, DVT and pulmonary embolism 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, I² = 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 such as operation duration, length of hospital stay, and post-operative complications including mortality, 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 had a higher incidence of post-operative complications and readmission rates. Moreover, studies reporting THA and TKA were associated with an increased incidence of mortality. Also, a higher incidence of DVT and cardiac infarction was evident among the post-operative complications in UW patients undergoing THA. No difference in post-operative complications was found in UW patients undergoing TKA.
Knee and hip osteoarthritis (OA) involves degeneration of articular cartilage, and bone hyperplasia of joint disease, is a common chronic disabling disease, causing physiological and psychological pain in patients[38]. OA is a common disease among the elderly, and 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 compatible metal prosthesis to restore 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]. TKA involves the replacement of the acetabulum or
Ma YP et al. Underweight and total joint arthroplasty

3.2.1 THA
Zusmanovich et al., 2018 4 301 5 539 61.40% 1.44 [0.38, 5.40] 2018
Hartford et al., 2020 0 13 8 463 12.70% 1.98 [0.11, 36.18] 2020
Subtotal (95%CI) 314 1002 74.10% 1.52 [0.46, 5.06]
Total events 4 13
Heterogeneity: Tau² = 0.00; Chi² = 0.04, df = 1 (P = 0.84); I² = 0%
Test for overall effect: Z = 0.68 (P = 0.50)

3.2.2 TKA and TKA
Katakam et al., 2020 1 85 15 821 25.90% 0.64 [0.08, 4.90] 2020
Subtotal (95%CI) 85 821 25.90% 0.64 [0.08, 4.90]
Total events 1 15
Heterogeneity: Not applicable
Test for overall effect: Z = 0.43 (P = 0.67)

Total (95%CI) 399 1823 100% 1.22 [0.43, 3.42]
Total events 5 28
Heterogeneity: Tau² = 0.00; Chi² = 0.56, df = 2 (P = 0.75); I² = 0%
Test for overall effect: Z = 0.37 (P = 0.71)
Test for subgroup differences; Chi² = 0.51, df = 1 (P = 0.47), I² = 0%

Figure 5 Re-operation rate. CI: Confidence intervals; P: Heterogeneity; M-H: Mantel-Haenszel; NW: Normal weight; THA: Total hip arthroplasty; TKA: Total knee arthroplasty; UW: Underweight.

4.1.1 THA
Amouzegarvand et al., 2016 10 1762 10 1387 10.30% 1.01 [0.42, 2.44] 2016
Dowsey et al., 2018 87 492 1233 13266 17.10% 2.09 [1.65, 2.65] 2018
Mouche et al., 2018 185 3588 3963 86330 17.70% 1.13 [0.97, 1.31] 2018
Woo et al., 2019 49 332 48 750 15.40% 2.53 [1.66, 3.86] 2019
Subtotal (95%CI) 6174 102099 60.50% 1.63 [1.03, 2.59]
Total events 331 5254
Heterogeneity: Tau² = 0.18; Chi² = 26.69, df = 3 (P < 0.00001); I² = 89%
Test for overall effect: Z = 2.07 (P = 0.04)

4.1.2 TKA
Dowsey et al., 2018 58 268 1325 13261 16.70% 2.49 [1.85, 3.35] 2018
Subtotal (95%CI) 268 1325 16.70% 2.49 [1.85, 3.35]
Total events 58 1325
Heterogeneity: Not applicable
Test for overall effect: Z = 6.03 (P < 0.00001)

4.1.2 THA and TKA
Thomassian et al., 2014 31 353 229 9859 15.70% 4.05 [2.74, 5.99] 2014
Katakam et al., 2020 4 85 7 821 7.10% 5.74 [1.65, 20.03] 2020
Subtotal (95%CI) 438 10680 22.80% 4.18 [2.88, 6.07]
Total events 35 236
Heterogeneity: Tau² = 0.00; Chi² = 0.27, df = 1 (P = 0.60); I² = 0%
Test for overall effect: Z = 7.51 (P < 0.00001)

Total (95%CI) 6880 126040 100% 2.20 [1.43, 3.37]
Total events 424 6815
Heterogeneity: Tau² = 0.26; Chi² = 65.31, df = 6 (P < 0.00001); I² = 91%
Test for overall effect: Z = 3.62 (P = 0.0003)
Test for subgroup differences; Chi² = 10.09, df = 2 (P = 0.006), I² = 80.2%

Figure 6 Mortality. CI: Confidence intervals; P: Heterogeneity; M-H: Mantel-Haenszel; NW: Normal weight; THA: Total hip arthroplasty; TKA: Total knee arthroplasty; UW: Underweight.

BMI is considered one of the key predictive tools for assessing 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 post-operative recovery, and increase the risk of complications. Another review[46] concluded that increased BMI was associated with an increased risk of peri-prosthetic joint infection (PJI) after primary THA or TKA. Following THA, patients were more likely to suffer from PJI than TKA.
patients. All the systematic reviews and meta-analyses conducted have 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 post-discharge infections 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 a BMI < 18.5 kg/m²; however, a few studies such as those by Katakam et al.[18] 2021 and Anoushiravani et al.[30] 2016, used an up-bound cut-off of < 20 kg/m² and < 19.5 kg/m² to justify the fact that the present World Health Organization classification of BMI was set based on the findings in a young population and the included patients were elderly with a mean age of over 60 years.

The peri-operative outcomes assessed after undergoing arthroplasty include the operation duration and length of hospital stay. Our meta-analysis showed no significant difference in operation duration between UW and NW patients; however, the length of hospital stay after THA or TKA was found to be significantly higher for UW patients compared to NW patients with MD of 0.39 d 95%CI: [0.06, 0.72], P = 0.02. Poor nutritional status among UW patients leads to musculoskeletal degeneration characterized by
Figure 9 Post-operative complications in patients undergoing total hip arthroplasty. CI: Confidence intervals; DVT: Deep vein thrombosis; I²:
Heterogeneity; IV: Inverse variance; NW: Normal weight; PE: Pulmonary embolism; UW: Underweight.

Table 1: Odds ratios for post-operative complications in patients undergoing total joint arthroplasty.

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>UW Events</th>
<th>NW Events</th>
<th>Total</th>
<th>Weight</th>
<th>Odds ratio M-H random 95%CI Year</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Total</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>5.2.1 Infection</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anoushvariravani et al., 2016</td>
<td>0</td>
<td>670</td>
<td>10</td>
<td>645</td>
<td>15.10% 0.05 [0.00, 0.77] 2016</td>
</tr>
<tr>
<td>Husted et al., 2016</td>
<td>0</td>
<td>29</td>
<td>3</td>
<td>1250</td>
<td>14.40% 6.04 [0.31, 119.60] 2016</td>
</tr>
<tr>
<td>Know et al., 2020</td>
<td>0</td>
<td>41</td>
<td>1</td>
<td>77</td>
<td>13.50% 0.61 [0.02, 35.42] 2020</td>
</tr>
<tr>
<td><strong>Total (95%CI)</strong></td>
<td>740</td>
<td>1972</td>
<td></td>
<td>43.00%</td>
<td>0.54 [0.02, 13.43]</td>
</tr>
<tr>
<td><strong>Total events</strong></td>
<td>10</td>
<td>14</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Heterogeneity: Tau^2 = 5.72; Chi^2 = 6.85, df = 2 (P = 0.03); P = 71%</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 0.38 (P = 0.71)</td>
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<td></td>
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<td></td>
</tr>
</tbody>
</table>

**5.2.2 DVT**

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>UW Events</th>
<th>NW Events</th>
<th>Total</th>
<th>Weight</th>
<th>Odds ratio M-H random 95%CI Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anoushvariravani et al., 2016</td>
<td>10</td>
<td>670</td>
<td>0</td>
<td>645</td>
<td>15.10% 20.52 [1.20, 350.96] 2016</td>
</tr>
<tr>
<td>Manrique et al., 2017</td>
<td>0</td>
<td>27</td>
<td>1</td>
<td>81</td>
<td>13.40% 0.98 [0.04, 24.66] 2017</td>
</tr>
<tr>
<td><strong>Total (95%CI)</strong></td>
<td>697</td>
<td>726</td>
<td></td>
<td>28.50%</td>
<td>4.91 [0.21, 111.96]</td>
</tr>
<tr>
<td><strong>Total events</strong></td>
<td>10</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Heterogeneity: Tau^2 = 2.70; Chi^2 = 2.12, df = 1 (P = 0.15); P = 53%</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 1.00 (P = 0.32)</td>
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<td></td>
</tr>
</tbody>
</table>

5.2.3 PE

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>UW Events</th>
<th>NW Events</th>
<th>Total</th>
<th>Weight</th>
<th>Odds ratio M-H random 95%CI Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anoushvariravani et al., 2016</td>
<td>10</td>
<td>670</td>
<td>0</td>
<td>645</td>
<td>15.10% 20.52 [1.20, 350.96] 2016</td>
</tr>
<tr>
<td>Manrique et al., 2017</td>
<td>0</td>
<td>27</td>
<td>1</td>
<td>81</td>
<td>13.40% 0.98 [0.04, 24.66] 2017</td>
</tr>
<tr>
<td><strong>Total (95%CI)</strong></td>
<td>697</td>
<td>726</td>
<td></td>
<td>28.50%</td>
<td>4.91 [0.21, 111.96]</td>
</tr>
<tr>
<td><strong>Total events</strong></td>
<td>10</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Heterogeneity: Tau^2 = 2.70; Chi^2 = 2.12, df = 1 (P = 0.15); P = 53%</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 1.00 (P = 0.32)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Total (95%CI)

| Total (95%CI) | 2134 | 3424 | 100% | 1.88 [0.34, 10.41] |
| Total events | 20   | 16   |      |                   |
| Heterogeneity: Tau^2 = 2.96; Chi^2 = 13.50, df = 6 (P = 0.04); P = 56% |
| Test for overall effect: Z = 0.72 (P = 0.47) |
| Test for subgroup differences: Chi^2 = 1.23, df = 2 (P = 0.54), P = 0% |

Figure 10: Post-operative complications in patients undergoing total knee arthroplasty. CI: Confidence intervals; DVT: Deep vein thrombosis; I^2: Inverse variance; NW: Normal weight; PE: Pulmonary embolism; UW: Underweight.

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 d compared to normal and obese patients. However, the mean difference of 0.39 d (= 9.4 h) for the length of hospital stay between UW and NW patients undergoing THA or TKA, though statistically significant, was not clinically significant. This negligible difference may be due to delay in discharge related to a system-level reason or inadequate staff availability.

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

Our meta-analysis showed a significant association with post-operative mortality in UW patients OR: 2.20 95%CI: [1.43, 3.37]. UW patients can 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 post-operative mortality. The compromised immune response in 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 TJA (THA and TKA) is a more complicated surgery, 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 undergoing THA and TKA, suggesting that this was a subpopulation at risk.

Several authors have evaluated complications in UW patients; however, some of the reported data is controversial. Many authors suggest that UW patients have a higher complication rate than their NW 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 in UW patients undergoing THA alone. Three studies[11,24,31] showed that UW patients undergoing THA or TKA had increased risks for infection, cardiac complications, and venous thrombo-emboli. The reason for this is not entirely clear; however, in their studies, it appears...
that the UW group tended to have lower preoperative hematocrit and albumin which are markers of malnutrition and predispose patients to medical complications. Nowadays, autologous platelet concentrates[49-51] have been proved to be beneficial in the management of bone-related disorders[52-55]. They have also been used as an adjunct to arthroplasty[56,57]. Many studies have opted for this as an alternative to arthroplasty[58,59]. This can be used as an alternative to arthroplasty in less severe cases to improve the quality of life in UW patients.

Our systematic review and meta-analysis are the first to assess the impact of UW on peri-operative and post-operative outcomes of THA or TKA. However, our review also has certain limitations. Confounding factors such as age, presence of comorbidities including anemia, 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-d and 90-d readmission rates. The exclusion of articles other than the English language could also be a possible limitation as good evidence could have been missed.

CONCLUSION

UW patients undergoing THA or TKA had a higher incidence of post-operative complications and readmission rates. Moreover, UW patients undergoing TJA were associated with an increased incidence of mortality in the 31-365-d time frame. Also, a higher incidence of DVT and cardiac infarction was evident among all the post-operative complications in UW patients undergoing THA. No difference in post-operative complications was found in UW patients undergoing TKA. Hence, careful clinical judgment is needed by clinicians before UW patients undergo 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 is believed to be a determining factor.

Research motivation
Systematic reviews on this issue have primarily focused on obesity compared to normal weight (NW). None of these reviews attempted to assess the effect of low BMI or underweight (UW) compared to NW in patients undergoing THA or TKA.

Research objectives
The objective of this review was to compare specific operative outcomes such as operation duration, length of hospital stay, and post-operative complications including mortality, infections, deep vein thrombosis, 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 stay after TKA or THA was found to be significantly higher for UW patients when compared to NW patients. Mean difference: 0.39 95%CI: [0.06, 0.72], \( P = 0.02 \) (in days). Studies presenting both THA and TKA together as total joint arthroplasty showed an increased incidence of mortality in patients who underwent THA or TKA alone with an odds ratio: 4.18 95%CI: [2.88, 6.07]. A higher incidence of post-operative complications was also observed in UW patients undergoing THA.

Research conclusions
UW patients undergoing THA or TKA had a higher incidence of post-operative complications and were associated with a higher readmission rate. Moreover, UW patients were associated with an increased incidence of mortality in the studies that reported THA and TKA together.
**Research perspectives**
Careful clinical judgment is needed by clinicians before UW patients undergo THA or TKA to attain better outcomes.

**FOOTNOTES**

**Author contributions:** Ma YP conceived and designed the study; Ma YP and Shen Q were involved in the literature search and data collection; Ma YP analyzed the data; Ma YP and Shen Q wrote the paper; Ma YP edited the manuscript; all authors read and approved the final manuscript.

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