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Cemented vs. uncemented total knee arthroplasty in obese patients: A systematic review of implant survival, complications, and clinical outcomes

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A R T I C L E I N F O

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A B S T R A C T

Introduction: Obesity is a primary global health concern that negatively affects the outcomes of total knee arthroplasty (TKA). To mitigate complications, both cemented and uncemented fixation techniques have been considered. However, there remains no consensus in the literature regarding the optimal fixation method for obese patients despite the renewed interest in uncemented fixation. This systematic review aims to compare the survival rates, causes of failure, and patient-reported outcome measures (PROMs) between cemented TKA (cTKA) and uncemented TKA (uTKA) in the obese population.

Materials and methods: A comprehensive literature search was conducted according to PRISMA guidelines across five databases—PubMed, Scopus, Embase, Medline, and Cochrane—focusing on studies directly comparing cTKA and uTKA in obese patients. The ROBINS-I tool was used to assess the risk of bias, while the PRISMA flow diagram guided the study selection process based on predefined inclusion and exclusion criteria. This systematic review was registered on PROSPERO.

Results: Four retrospective studies encompassing 1622 patients met the inclusion criteria and were included in the final qualitative analysis. Among these, 50 % of patients underwent uTKA, with three studies exclusively analyzing individuals with at least class II obesity (BMI $\geq$35 kg/m^2). All four studies reported higher rates of aseptic loosening in the cemented fixation group. However, only two studies demonstrated a statistically significant improvement in implant survival, reduced aseptic loosening, and lower revision rates with cementless fixation in the short-to mid-term follow-up. Regarding clinical outcomes, only one study reported a significant improvement in Knee Society Score (KSS) function, range of motion (ROM), and pain scores in the cementless group compared to the cemented group, particularly in the subgroup analysis of posterior-stabilized constrained TKA.

Conclusion: This systematic review suggests that in obese patients, particularly those with BMI $\geq$35 kg/m^2, cementless fixation offers comparable or superior implant survival rates and lower rates of aseptic loosening compared to cemented fixation in the short-to mid-term follow-up. Furthermore, cementless fixation may provide similar or enhanced clinical outcomes in this high-risk and growing patient population.

1. Introduction

Obesity is a growing global health concern,[1] with projections indicating that by 2030, one in two adults in the United States will have a body mass index (BMI) $\geq$ 30 kg/m^2.[2] While no definitive BMI threshold has been established to identify patients at higher risk for knee osteoarthritis (OA),[3,4] extensive evidence correlates a progressive increase in BMI with a higher incidence of knee OA.[3,4] Consequently, the demand for total knee arthroplasty (TKA) is expected to rise exponentially.[5]

Obesity has been widely recognized as an adverse prognostic factor

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for primary TKA, contributing to higher failure and revision rates in this population.[6–10] Among the causes of implant failure, aseptic loosening—particularly of the tibial component—represents the primary mode of failure in cemented TKA (cTKA) due to the increased mechanical stress exerted by excess body weight on the bone-implant interface.[11] In response to this challenge, uncemented TKA (uTKA) has regained popularity as an alternative fixation strategy.[12–18] Recent advancements in implant design have improved the potential for stable, long-term fixation through osteointegration, reducing the risk of loosening and implant failure.[12–18] This biological fixation is primarily facilitated using highly porous titanium and hydroxyapatite coatings, which enhance initial stability, minimize micromotion, and promote bone ingrowth.[12,19–21]

Beyond improving fixation, uTKA offers potential advantages in obese patients, including shorter operative times and a reduced risk of periprosthetic joint infection, a particularly relevant concern in this high-risk population.[22] Conversely, cTKA may be prone to progressive deterioration of the cement-bone interface, increasing the risk of osteolysis and component migration over time.[23–25] Recent literature has supported using uTKA, demonstrating non-inferior implant survival and radiographic outcomes compared to cTKA.[26–28] However, despite the increasing interest in cementless fixation, no definitive consensus exists on the optimal fixation method for obese patients undergoing TKA.[11,16,22]

This systematic review aims to compare the survival rate, the incidence of aseptic loosening as the primary cause of revision, other failure mechanisms, and patient-reported outcome measures (PROMs) between cTKA and uTKA in obese patients, providing an evidence-based perspective on the most effective fixation strategy for this high-risk population.

2. Materials and methods

2.1. Research question

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines[29–31] and was registered on PROSPERO (CRD42024583705) in September 2024.[32] The study aimed to compare clinical, radiographic, and complication outcomes in obese patients undergoing cemented (cTKA) or uncemented total knee arthroplasty (uTKA). The Patient, Intervention, Comparison, Outcome, and Study design (PICOS) framework was used to define the research question: Population (P): Obese patients (BMI $\geq$30 kg/m^2); Intervention (I): TKA in obese patients; Comparison (C): Cemented vs. uncemented fixation; Outcomes (O): Implant survival, aseptic loosening, complications, and PROMs; Study Design (S): Randomized controlled trials (RCTs), prospective, and retrospective studies (LoE 1–4).

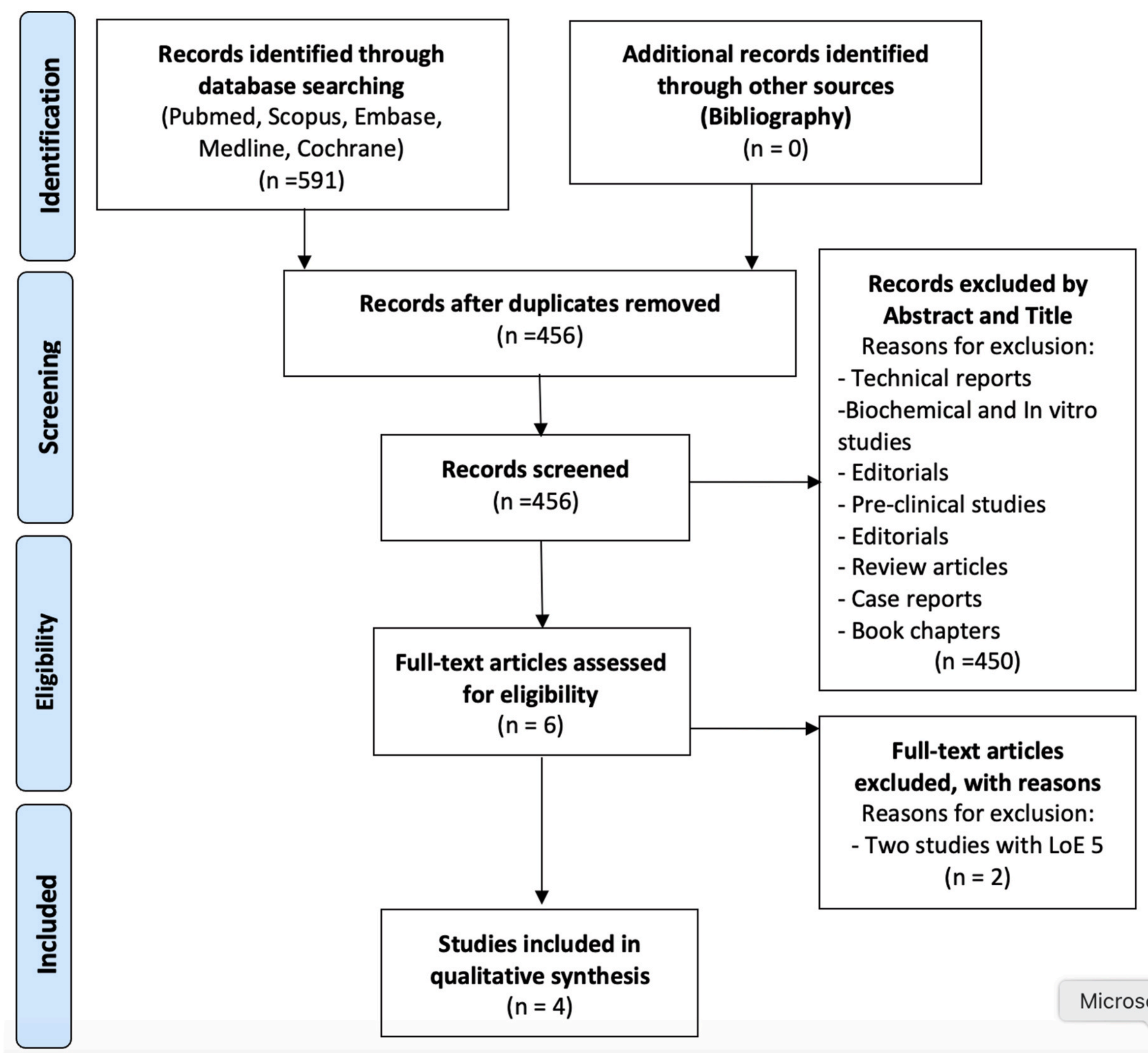

Fig. 1. Preferred reporting items for systematic review and meta-analyses (PRISMA) flow diagram of the studies included in the analysis.

2.2. Search strategy and study screening

A comprehensive literature search was conducted in PubMed, Scopus, Embase, Medline, and Cochrane for studies published between 2004 and May 2024, using the following MeSH terms: ((Cementless) OR (Cement)) AND ((Total Knee Arthroplasty) OR (TKA)) AND ((Obesity) OR (BMI) OR (Body Mass Index)). The initial search retrieved 591 studies, of which 456 remained after duplicate removal. After screening titles and abstracts, 450 studies were excluded, leaving six for full-text evaluation. Four studies were selected for qualitative analysis based on inclusion and exclusion criteria. The reference lists of included studies were reviewed to identify any additional relevant articles. The PRISMA flowchart illustrating the study selection process is shown in Fig. 1.

2.3. Inclusion and exclusion criteria

Inclusion criteria comprised studies comparing cemented and uncemented TKA in obese patients (BMI ≥30 kg/m^2), published in English, from 2004 to May 2024, and reporting a mean follow-up of at least six months. Only RCTs, prospective, and retrospective studies with LoE 1–4 were included. Exclusion criteria encompassed biomechanical, preclinical, or in vitro studies, case reports, editorials, book chapters, technical reports, and review articles. Studies classified as LoE 5 or lower were excluded from the quality analysis.

2.4. Methodological quality assessment

The methodological quality of the selected studies was assessed using the Oxford Centre for Evidence-Based Medicine (LoE 2011) classification. The Risk of Bias in Non-Randomized Studies of Interventions (ROBINS-I) tool was employed to evaluate study bias (Fig. 2). Two independent reviewers (LLC and FO) performed the quality assessment, with a third reviewer (FB) consulted in case of discrepancies. All authors contributed to the study design, data evaluation, manuscript drafting, and final editing.

2.5. Data extraction

Data extraction was performed systematically and recorded in a structured spreadsheet. The extracted variables included study characteristics (author, publication year, study design, sample size), patient demographics (mean age, BMI, follow-up duration, number of patients lost to follow-up), implant survival rates, radiographic features, failure mechanisms, complications, and revision rates, along with details of the implant type and level of constraint used. Additionally, clinical outcomes were analyzed using PROMs, including the Knee Society Score (KSS), Knee Injury and Osteoarthritis Outcome Score for Joint Replacement (KOOS-JR), Lower Extremity Activity Scale (LEAS), Short Form-12 (SF-12) for mental and physical health, and range of motion (ROM) evaluation.

2.6. Data analysis

A descriptive qualitative analysis was performed to synthesize the extracted data. Continuous variables were expressed as means ± standard deviations (SD) or medians with interquartile ranges (IQR), assessed using the Shapiro-Wilk test, depending on data distribution. Categorical variables were presented as absolute frequencies and percentages. All statistical analyses were conducted using R software (version 4.1.3, R Core Team, Vienna, Austria).

3. Results

Based on the predefined inclusion and exclusion criteria, four retrospective studies were included in the final qualitative analysis,[22,33–35] comprising 1622 obese patients who underwent 1818 TKAs. Within this cohort, 811 patients (50 %) received uncemented TKA (uTKA), while the remaining underwent cemented TKA (cTKA). Three studies,[33–35] except Boyle et al.,[22] specifically analyzed patients with at least class II obesity (BMI ≥35 kg/m^2). Notably, Bagsby et al.[33] and Sinicrope et al.[34] included only patients with a BMI ≥40, further refining the analysis of outcomes in the severely obese population.

Regarding implant design, Boyle et al.[22] focused exclusively on Cruciate Retaining (CR) TKA, whereas Sinicrope et al.[34] analyzed outcomes in Posterior Stabilized (PS) implants, providing insights into the impact of different constraint levels in this patient population. Further demographic details are summarized in Table 1.

Across all four studies, higher rates of aseptic loosening were observed in the cemented fixation group. However, only two studies[33,34]

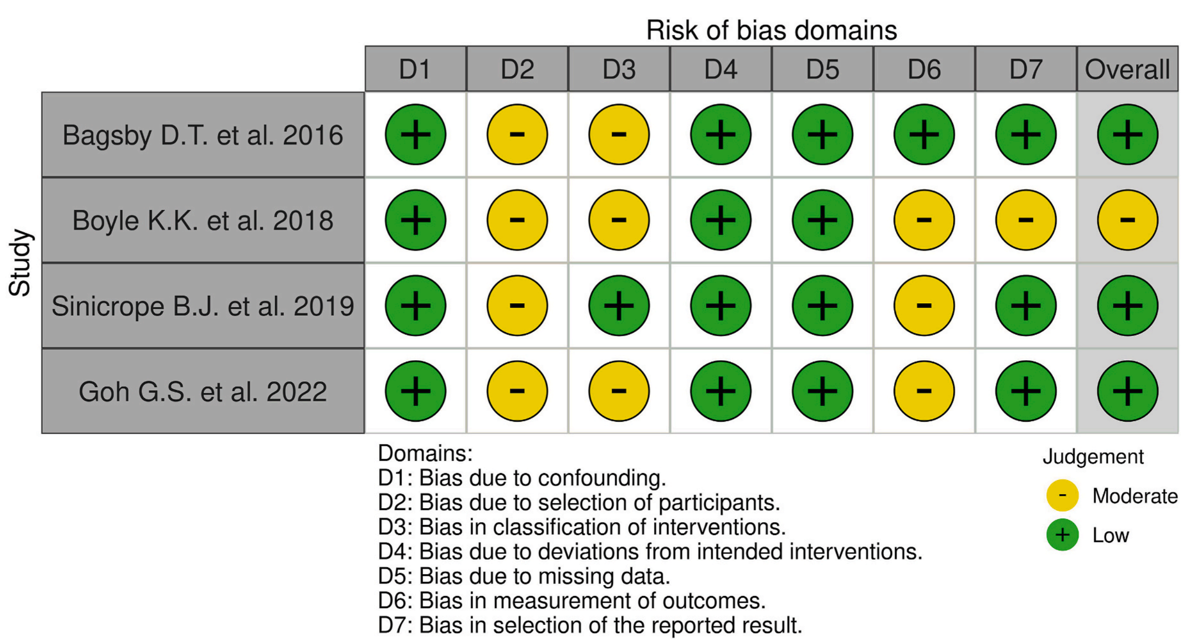

Fig. 2. Assessment of the risk of bias of the individual studies included in the analysis according to the ROBINS-I tool.

Table 1
Demographic details of the included studies.

Study and publication year	Study design	Patients, N		Number of Knees, N		Side R/L, N		Male, N		Female, N		Age, Mean (Range/SD)		BMI, kg/m^2 Mean (Range/SD)		TKA Insert, (%)		Lost to Follow-up, N	Follow-up, months, Mean (Range/SD)	
		C	UC	C	UC	C	UC	C	UC	C	UC	C	UC	C	UC	C	UC	Total	C	UC
Bagsby D.T. et al., 2016[33]	Retrospective Multicenter	149	143	154	145	75/79	59/85	32	43	122	102	58.8 (52–66)	62.7 (56–70)	45.6 (40.7–50.5)	44.7 (40.3–49.1)	CR 37.7 PS 62.3 CS 0	CR 0.7 PS 99.3 CS 0	\	73.6 (SD 37.1)	43.8 (SD 14.5)
Boyle K.K. et al., 2018[22]	Retrospective Monocenter	171	154	171	154	85/86	80/74	43	57	128	97	64.9 (SD 10.0)	59.6 (SD 7.5)	37.4 (30.1–56.1)	37.4 (30.1–56.9)	CR 100 PS 0 CS 0	CR 100 PS 0 CS 0	43	61.2 (SD 8.5)	62.0 (SD 9.5)
Sinicrope B.J. et al., 2019[34]	Retrospective Multicenter	85	108	85	108	\		18	26	67	82	60 (45–80)	62 (39–79)	45 (40–66.1)	45.6 (40–64.5)	CR 0 PS 100 CS 0	CR 0 PS 100 CS 0	\	99.5 (60–171)	71.7 (60–96)
Goh G.S. et al., 2022[35]	Retrospective Monocenter	406	406	489	512	\	\	221	232	185	174	59.4 (SD 8.1)	60 (SD 7.9)	38.6 (35–60)	38.7 (35–54)	CR 3.7 PS 47.5 CS 48.8	CR 4.4 PS 48.0 CS 47.5	136	48 (24–94)	48 (24–93)

N: Number of evaluation cases, C: Cement fixation, UC: Uncemented fixation, BMI: Body Mass Index, SD: Standard Deviation, CR: Cruciate retaining, PS: Posterior stabilized, CS: condylar stabilizing; TKA: Total Knee Arthroplasty, R: Right, L: Left, \: Data not reported. All the numbers are abbreviated at one decimal.

reported a statistically significant advantage in implant survival and lower revision rates for uncemented fixation at short-to mid-term follow-up. Regarding infectious complications, two studies[34,35] noted a higher incidence of infections in the uncemented group, but these findings did not reach statistical significance. The occurrence of instability and arthrofibrosis was comparable between the two fixation techniques across all included studies.[22,33–35]

In terms of clinical outcomes, Bagsby et al.[33] found significantly more significant improvements in Knee Society Score (KSS) in the uncemented group, while two other studies[22,35] reported no significant differences in postoperative PROMs between cTKA and uTKA. Sinicrope et al.[34] did not assess PROMs. Additionally, Bagsby et al.[33] conducted a subgroup analysis on PS implants, revealing that the uncemented PS cohort exhibited superior postoperative ROM, KSS function, and pain scores compared to the cemented counterpart.

A detailed summary of the significant clinical outcomes, complications, and frequency of radiolucent lines (RLLs) reported across the studies is presented in Table 2.

4. Discussion

The main finding of this systematic review is that in obese patients—particularly those with BMI ≥35 kg/m^2—cemented fixation demonstrates equivalent or lower implant survival rates and higher revision rates compared to cementless fixation in the short-to medium-term follow-up.[22,33–35] Two of the four included studies[33,34] reported significantly higher rates of aseptic loosening in the cemented fixation group, reinforcing concerns about its long-term stability in this high-risk population. Additionally, in terms of clinical outcomes, only one study[33] demonstrated a significant improvement in Knee Society Score (KSS), range of motion (ROM), and pain scores in the uncemented group, both overall and in the subgroup analysis focusing on posterior-stabilized (PS) constrained TKA.

Obesity is a growing public health challenge, with an increasing prevalence in industrialized nations.[1,2] Given the well-established correlation between elevated BMI and the incidence of knee osteoarthritis (OA), the global rise in obesity is expected to drive a proportional increase in the demand for total knee arthroplasty (TKA).[3,4] Previous studies analyzing outcomes in patients with BMI ≥35 kg/m^2 have demonstrated more significant PROM improvements than those with lower BMI, emphasizing the clinical relevance of TKA in this population.[9–11,36] However, obesity remains a key risk factor for postoperative complications, higher revision rates, and reduced implant survival, raising concerns about the optimal fixation method in these patients.[6–10]

Cemented fixation has traditionally been considered the gold standard in obese patients, as it provides immediate mechanical stability and may be perceived as more reliable in the setting of increased joint stress.[10–12] However, advancements in implant technology and improved biomaterials have led to a growing preference for uncemented TKA, which is designed to achieve long-term fixation through osteointegration.[14–18] Highly porous titanium and hydroxyapatite-coated implants have demonstrated superior bone-implant integration, potentially reducing the risk of implant loosening and failure.[19–21] Despite promising clinical outcomes and growing evidence supporting cementless fixation, the literature lacks a definitive consensus on the most appropriate fixation strategy for obese patients undergoing TKA.[11,16,22]

In this review, the reported implant survival rate was comparable to or higher in the uncemented group. Bagsby et al.[33] documented an 8-year survival rate of 99.3 % in the uncemented group, significantly superior to 89.7 % in the cemented cohort. Similarly, Sinicrope et al.[34] reported an uncemented implant survival rate of 99.1 % versus 88.2 % in the cemented group at 8 years of follow-up. These findings suggest a statistically significant advantage for uncemented fixation in severely obese patients. Conversely, the remaining two studies[22,35] did not

Table 2
TKA complications with cemented and uncemented fixation techniques.

Study and publication year	Aseptic Loosening, %		Infection, %		Instability, %		Arthrofibrosis, %		Frequency of RLLs on post-op x-rays, %		Revision rate, %		Survival rate, %		
Fixation type	C	UC	C	UC	C	UC	C	UC	C	UC	C	UC	C	UC	p value
Bagsby D.T et al., 2016[33]	5.8 %	0 %	1.3 %	0.7 %	1.9 %	0 %	1.3 %	0 %	/	/	13 %	0.7 %	89.7 % 8y	99.3 % 8y	$p < 0.001$
Boyle K.K. et al., 2018[22]	0.7 %	0.6 %	1 %	0.6 %	/	/	4.7 %	1.9 %	11.1 %	16.8 %	0.7 %	0.6 %	98.3 % 5y	98.1 % 5y	$p > 0.05$
Sinicrope B.J et al., 2019[34]	18.8 %	0.9 %	1.2 %	3.7 %	0 %	1.9 %	1.2 %	2.8 %	2.4 %	0.9 %	25.9 %	5.9 %	88.2 % 8y	99.1 % 8y	$p = 0.02$
Goh G.S. et al., 2022[35]	0.5 %	0 %	1 %	1.7 %	0 %	0.5 %	0 %	0 %	1 %	0.5 %	1.7 %	2.5 %	99.3 % 7y	99.5 % 7y	$p > 0.05$

C: Cement fixation, UC: Uncemented fixation, RLLs: Radiolucent lines, y: year, %: percentage,/: data not reported. All numbers are abbreviated at one decimal and expressed in percentual (%).

observe a significant difference in survival rates between the two fixation methods. A possible explanation for this discrepancy lies in the lower BMI of the patients included in these studies, suggesting that the impact of fixation type may be more pronounced in individuals with severe obesity (BMI $\geq$40 kg/m^2).

4.1. Aseptic loosening

Aseptic loosening remains one of the most common causes of TKA failure in obese individuals due to the excessive mechanical stress on the bone-implant interface.[5–10] Consistent with existing literature, this review identified aseptic loosening as the leading cause of implant failure and the primary reason for revision surgery in two of the four included studies.[33,34] Both studies also reported a significantly higher incidence of aseptic loosening in the cemented group compared to the uncemented cohort. Specifically, Bagsby et al.[33] found an aseptic loosening rate of 5.8 % in the cemented group, compared to 0 % in the uncemented group, while Sinicrope et al.[34] documented an aseptic loosening rate of 18.8 % in cemented TKA, compared to only 0.9 % in uncemented TKA. Moreover, Sinicrope et al.[34] noted that both the tibial and femoral components were affected by loosening, with a slightly higher incidence in the tibial component, a finding commonly described in the literature.[11]

The reduced incidence of aseptic loosening in the uncemented group underscores the potential advantages of modern cementless implants, particularly in highly porous titanium and hydroxyapatite coatings, which enhance initial stability and long-term bone ingrowth.[19–21] These findings highlight the growing interest in uncemented fixation as a biologically superior and mechanically durable alternative in obese patients undergoing TKA.

4.2. Infection

Increased BMI is a well-documented risk factor for systemic and periprosthetic joint infections.[8–10] In this systematic review, infection was identified as the leading cause of revision in two studies.[22,35] However, when comparing the two fixation methods, no statistically significant difference in infection rates was observed between cemented and uncemented TKA.[22,33–35] Interestingly, Sinicrope et al.[34] and Goh et al.[35] reported higher infection rates in the uncemented group. In contrast, Bagsby et al.[33] and Boyle et al.[22] found a greater incidence in the cemented group. These conflicting results suggest a lack of clear consensus regarding the influence of fixation type on infection predisposition in obese patients undergoing TKA. Given that obesity is associated with impaired immune function, increased surgical time, and compromised soft tissue healing, further studies are warranted to understand better the impact of fixation methods on periprosthetic infection risk in this high-risk population.

4.3. Instability and arthrofibrosis

Obesity (BMI >30 kg/m^2) has been recognized as a significant risk factor for both knee instability and arthrofibrosis following TKA.[37,38] Arthrofibrosis, a common complication after knee arthroplasty, has been reported with an incidence ranging from 1 % to 15 % in TKA patients.[37] While the relationship between high BMI and arthrofibrosis remains controversial,[38] increased knee instability in obese individuals is likely due to greater mechanical stress on the joint and reduced muscle quality, which may contribute to functional impairment.[37]

This systematic review identified inconsistent rates of instability and arthrofibrosis between cemented and uncemented fixation techniques.[22,33–35] Three of the four included studies reported instability rates, with two studies noting a higher instability rate in the uncemented group[34,35] and one study reporting a higher rate in the cemented group.[33] However, none of the studies found statistically significant differences between the fixation methods. Arthrofibrosis was reported in all included studies, but only Boyle et al.[22] identified a statistically significant difference, documenting nine cases of flexion contracture (4.7 %) in the cemented group compared to three cases (1.9 %) in the uncemented group. Notably, Goh et al.[35] reported two instability cases but no arthrofibrosis cases at the final follow-up. These findings suggest that both fixation methods may carry similar risks for instability and arthrofibrosis. However, further high-quality studies are necessary to determine whether fixation type plays a significant role in these complications.

4.4. Radiolucent lines on postoperative X-ray

Radiolucent lines (RLLs) in postoperative X-rays of cemented and uncemented TKA implants remain a controversial clinical finding.[22] While RLLs have been associated with early implant loosening, their clinical significance remains uncertain, particularly in obese patients, where implant fixation is crucial.[22]

This systematic review found that three of the four included studies reported RLL incidence.[22,34,35] Two studies[34,35] noted a higher prevalence of RLLs in the cemented group, while one[22] identified a greater occurrence in the uncemented cohort. However, none of the studies reported statistically significant differences.[22,33–35] Interestingly, Boyle et al.[22] observed 26 cases of RLLs (16.8 %) in the uncemented group, compared to 19 cases (11.1 %) in the cemented group. Further subgroup analysis using the PBS classification system revealed that two patients in each group had tibial component RLLs classified as concerning for loosening.[22] These findings suggest that while RLLs are frequently observed in both cemented and uncemented TKA, their clinical impact and potential correlation with early implant failure remain inconclusive.

4.5. Clinical outcomes

Obese patients with knee OA typically present with lower preoperative PROM scores, reflecting greater functional impairment and higher pain levels compared to non-obese individuals.[8–10] However, several studies have suggested that obese patients may experience greater pre-postoperative improvements in clinical outcomes, highlighting the significant functional benefit of TKA in this population.[8–10,36,39]

In this systematic review, only one study[33] found a statistically significant improvement in clinical outcomes favoring the uncemented group, reporting better KSS function, ROM, and pain scores in the cementless cohort, both overall and in the subgroup analysis of posterior-stabilized (PS) constrained TKA. Conversely, the remaining studies[33,35] found no significant differences in postoperative PROMs between cemented and uncemented fixation methods, with both groups demonstrating comparable functional outcomes and improvements from baseline. These findings suggest that while uncemented fixation may offer advantages in specific patient subgroups, the overall clinical benefit between the two fixation techniques remains similar in the obese population. Further research is needed to explore whether specific implant designs, constraint levels, or patient characteristics influence functional outcomes following cemented and uncemented TKA in obese patients.

4.6. Strengths and limitations

This systematic review presents several strengths. First, it is one of the few studies comparing cemented and uncemented TKA in obese patients, providing a focused analysis of a growing and clinically relevant population. Additionally, it highlights key implant survival trends, complication rates, and clinical outcomes, offering valuable insights into the long-term fixation performance in high-BMI patients. Furthermore, including multiple studies with mid to long-term follow-up strengthens the reliability of findings regarding aseptic loosening and implant survival.

However, some limitations must be acknowledged. Only four studies met the inclusion criteria, all of which were retrospective in design, inherently limiting the LoE and increasing the risk of selection bias. The included studies exhibited considerable heterogeneity in patient characteristics, BMI classifications, implant designs, and reported outcome measures, making direct comparisons challenging. Proms varied between studies, and Sinicrope et al.[34] did not report PROMs at all, limiting the ability to draw robust conclusions on functional outcomes. Furthermore, only three studies specifically analyzed Class II obesity (BMI $\geq$35 kg/m^2), reducing generalizability across different obesity subgroups. The heterogeneity in follow-up durations further restricted comparative analysis. Due to insufficient standardized data and incomplete reporting of variables, performing a meta-analysis, sensitivity analyses, or GRADE assessment was not feasible. These limitations emphasize the need for high-quality, prospective studies and randomized controlled trials (RCTs) to establish the optimal fixation strategy for obese patients undergoing TKA. Future research should aim to standardize outcome reporting, stratify patients based on BMI categories, and assess long-term implant performance to enhance clinical decision-making in this high-risk population.

5. Conclusions

This systematic review highlights that in obese patients, particularly those with BMI $\geq$35 kg/m^2, cementless fixation demonstrates equivalent or superior implant survival rates and lower rates of aseptic loosening than cemented fixation over the short-to mid-term follow-up. Moreover, uncemented TKA offers comparable or improved functional outcomes, particularly in implant durability and long-term osteointegration. Given the increasing prevalence of obesity and the growing demand for TKA, further high-quality prospective studies and randomized trials are essential to determine the optimal fixation method for this expanding patient population.

CRediT authorship contribution statement

Lorenzo Lo Carmine: Conceptualization, Writing – original draft, Resources. **Francesco Onorato:** Writing – original draft, Methodology, Software. **Carmelo Burgio:** Writing – original draft, Data curation, Methodology, Software, Investigation, Supervision. **Zepeda Karlos:** Data curation, Methodology, Investigation. **Virginia Masoni:** Methodology, Resources, Writing – review & editing, Supervision. **Marcello Capella:** Validation, Visualization, Supervision. **Lawrence Camarda:** Validation, Supervision. **Danilo Francesco Chirillo:** Conceptualization, Supervision. **Alessandro Massè:** Validation, Supervision. **Francesco Bosco:** Writing – review & editing, Formal analysis, Project administration, Supervision.

Guardian/patient's consent

Not Applicable.

Ethical statement

The study was conducted following the ethical standards of the Declaration of Helsinki (1964).

Funding/sponsorship

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Funding statement

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Declaration of competing interest

On behalf of all authors, the corresponding author states that there is no conflict of interest.

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