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ORIGINAL ARTICLE

Staggered bilateral total knee arthroplasty during a single hospitalization: is it still an option? a systematic review

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Abstract

Background Bilateral knee osteoarthritis requiring total knee arthroplasty (TKA) can be addressed simultaneously in one surgical setting, staggered a few days apart during a single hospitalization, or staged several weeks to months apart. Several studies have reported on the complications and clinical outcomes of staggered bilateral TKA (BTKA) in a single hospitalization. However, there is no consensus regarding the safety and efficacy of this practice.

Materials and methods We performed a systematic review of the literature, utilizing the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and identifying articles that reported the clinical outcomes and postoperative complications following staggered BTKA.

Results Overall, six articles were included for analysis, including 43,892 patients in total. Females ($n = 25{,}931$; 59% of all patients) outnumbered males ($n = 17{,}961$; 40.1% of all patients), and most patients were middle-aged or elderly (mean age: 68.0 years). The majority of studies (83%) used a 1-week interval as the maximum time for single-hospitalization staggered BTKA. Five studies (83%) reported no difference in mortality rates between staggered, simultaneous, or staged BTKA. Compared to staged BTKA, staggered BTKA conferred an increased rate of blood transfusions. There was no consensus that staggered BTKA led to reduced complications rates, compared to simultaneous or staged BTKA.

Conclusions Single-hospitalization staggered BTKA does not appear to be safer than the well-established simultaneous or staged procedures. Overall, the data suggest that staggered BTKA will continue to decline in utilization, as staggered BTKA does not appear to yield clinical advantage over simultaneous BTKA in a medically appropriate patient.

Level of evidence III systematic review (lowest level of studies included)

Keywords Staggered total knee arthroplasty · Staged bilateral knee arthroplasty · Simultaneous knee arthroplasty · Same-admission · Single hospitalization · Systematic review

Introduction

As the population continues to age, the incidence of knee osteoarthritis and, concomitantly, total joint replacement has increased [1]. Bilateral knee osteoarthritis is also increasing in prevalence with up to one-third of patients developing bilateral disease within 2 years of initial unilateral diagnosis [2]. Total knee arthroplasty (TKA) has been shown to be a successful treatment modality for end-stage knee osteoarthritis [2]. For patients with bilateral disease, TKA can be accomplished in a simultaneous (one anesthesia), staggered (single-admission, procedures separated by several days), or staged (separate admissions, procedures weeks or months apart) fashion [3]. Compared to staged bilateral TKA (BTKA), a simultaneous procedure has several advantages: 1) patient preference to undergo a single operation; 2) decreased total recovery time; and 3) reduced perioperative cost [4]. However, some studies have demonstrated higher complication rates associated with simultaneous BTKA, including increased intraoperative blood loss, greater need for perioperative blood transfusion, and increased rates of venous thromboembolism (VTE), cardiorespiratory complications, neurologic complications, wound breakdown,

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deep infection, and mortality [5–8]. Careful patient selection has been shown to reduce perioperative complications with simultaneous BTKA [9]. Patients with coronary artery disease with inducible ischemia, congestive heart failure, advanced chronic obstructive pulmonary disease, uncontrolled diabetes, peripheral vascular disease, renal failure, morbid obesity, history of VTE, or those who are older than 75 years are usually not considered eligible for simultaneous BTKA [10]. In such cases, treatment options include single-admission staggered BTKA (managed as two separate procedures performed on different days during a single hospitalization) or staged BTKA during two separate hospitalizations, usually performed within 1 year [11]. Staggered BTKA confers many of the same advantages as simultaneous BTKA, including 1) patient preference for single hospitalization; 2) decreased overall recovery time [10]. For medically complex patients who are contraindicated for simultaneous BTKA, staggered BTKA may offer a compromise to correct severe bilateral knee deformities in quick succession [10]. Meanwhile, staged BTKA may not be preferred by patients due to lengthier overall recovery time and multiple hospital admissions, but staged BTKA demonstrates the lowest complication rates of all BTKA options [12].

Recently, several clinical trials have been published in relation to staggered BTKA performed during a single hospitalization [10, 13–17]. However, no systematic or comprehensive review of the literature has been published to date. For this reason, the aims of this study were threefold: 1) to characterize the methodological quality of the relevant, available literature, 2) to summarize early postoperative complication rates and clinical outcomes associated with the use of staggered BTKA, and 3) to compare the early postoperative outcomes of staggered BTKA with those of simultaneous BTKA and staged BTKA.

Methods

Two reviewers (AG, NS) independently conducted the search in a systematic way according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [18] using the MEDLINE/PubMed database, Embase, and the Cochrane Database of Systematic Reviews without any publicly registered systematic review protocol (Fig. 1). These databases were searched using terms defined in detail in Table 1. To maximize the search, backward chaining of reference lists from retrieved papers was also undertaken. A preliminary assessment of only the titles and abstracts of the search results was performed. The second stage involved a careful review of the full-text publications.

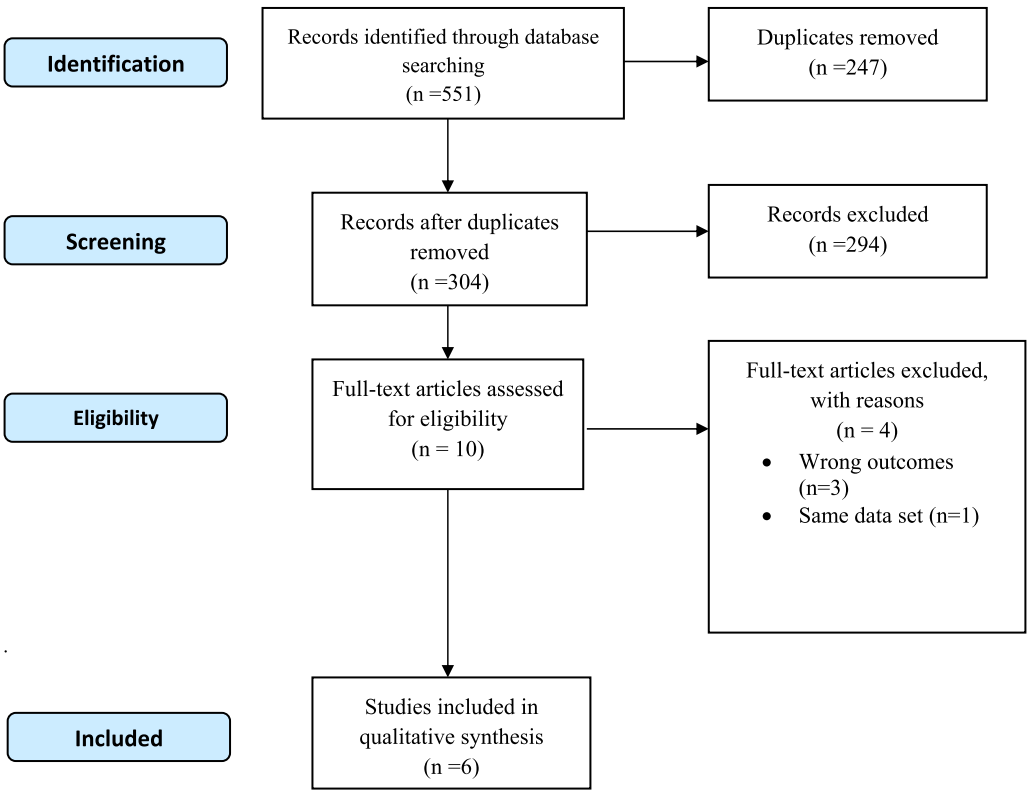

Fig. 1 Systematic review flow diagram

Table 1 Search strategy

Database	PubMed, Cochrane, Embase
Date	October 2018
Strategy	#1 AND #2 AND #3
Limit	Human AND English
#1	("Arthroplasty, Replacement, Knee"[Mesh] AND bilateral[tw]) OR (total knee arthroplasty[tw] AND bilateral[tw]) OR (tka[tw] AND bilateral[tw]) OR (Total knee replacement[tw] AND bilateral[tw]) OR (TKR[tw] AND bilateral[tw])
#2	Simultaneous[tw] OR Staggered[tw] OR Staged[tw] OR non-simultaneous[tw]
#3	Treatment outcome[tw] OR Clinical outcome[tw] OR Pain[tw] OR "Treatment Outcome"[Mesh] OR "Pain"[Mesh] OR "Pain Measurement"[Mesh] OR "Patient Reported Outcome Measures"[Mesh] OR "Patient Outcome Assessment"[Mesh] OR "Outcome Assessment (Health Care)"[Mesh] OR Pain, Postoperative[mesh] OR Pain Threshold[tw]

Inclusion and exclusion criteria

The inclusion criteria were: 1) studies describing human subjects of any age and gender; 2) studies that include a population of at least ten patients who underwent staggered BTKA (managed as separate procedures performed in different days during a single hospitalization); 3) clinical trials investigating the clinical and/or functional and/or radiographic outcomes of staggered BTKA; 4) studies that compared staggered BTKA (managed as separate procedures performed in different days during a single hospitalization) to either simultaneous BTKA (both procedures performed in the same day during one anesthetic session) or staged BTKA (managed as separate procedures during two separate hospitalizations) or studies that compared staggered BTKA various time points; 5) full-text English articles published until October 30, 2018; and 6) perioperative or early postoperative follow-up (no restriction in minimum time, since we planned to examine perioperative and early postoperative complications).

The exclusion criteria were: 1) non clinical study; 2) general review and systematic review; 3) non-English articles; 4) studies stratifying patients based on perioperative management (anesthesia protocol, limitation of blood loss, surgical technique, prosthesis type, etc.); 5) number of cases being less than 10; 6) studies only dealing with staged BTKA (managed as separate procedures during two separate hospitalizations) and/or simultaneous BTKA (same-day, 1-anesthestic session) and/or unilateral TKA; 7) studies reporting on revision unilateral TKA and/or revision BTKA; 8) studies dealing with simultaneous or staged or staggered bilateral unicompartmental knee arthroplasty; 9) editorial comments, corrigenda; 10) non full-text articles; 11) studies without clinical and/or functional and/or radiographic results; and 12) articles published after October 30, 2018.

Data collection

Two authors independently conducted the search. Differences between reviewers were discussed until agreement was achieved. In cases of disagreement, the senior author (PS) had the final decision. The two reviewers independently extracted data from each study and assessed variable reporting of outcome data. Descriptive statistics were calculated for each study and parameters analyzed. The level of evidence in the included studies was determined using the Oxford Centre for Evidence-Based Medicine—Levels of Evidence [19]. The "quality assessment" of the studies for methodological deficiencies, as a common alternative to "risk of bias," was examined by the modified Coleman Methodology Score [20]. The methodological quality of each study and the different types of detected bias were assessed independently by each reviewer and then combined. Selective reporting bias, such as publication bias, was not included in the assessment. Finally, a comprehensive analysis of the eligible studies was performed, focusing on specific questions which were relative to the topic.

During the initial review of the data, the following information was collected for each study: title, author, year of publication, study design, number of patients, number of knees, time between first and second surgery, gender, range of motion changes after the first and second surgeries, postoperative complications, and pre- and post-TKA clinical outcome scores. Early postoperative complications were categorized into mortality rate, systematic complications, orthopedic complications, blood transfusions, length of stay, intensive care unit (ICU) admissions, and hospital re-admissions. The primary outcome measure was the rate of early postoperative complications. Secondary outcome measures included clinical, functional, and radiographic outcomes.

Results

In total, 551 articles were identified utilizing the search criteria (Fig. 1). Following the removal of duplicate articles, 304 articles remained and were subjected to application of the predetermined inclusion and exclusion criteria. Following application of these criteria, 10 articles underwent a full-text screening process. Among those, 7 articles were eligible for analysis [10, 13–17, 21]. However, two articles assessed staggered BTKA utilizing the same dataset [16, 21]. We included one of the two articles that had more comprehensive analysis [16] and subsequently excluded the other [21]. Overall, six articles were included in this analysis [10, 13–17]. Among them, only one study was published after 2015 [14].

Study design, level of evidence

All papers included in this review were retrospective case–control studies (Table 2). In total, four out of six studies (66%) [13–16] made comparisons between the outcome of single-hospitalization staggered BTKA and simultaneous BTKA, whereas three studies [10, 13, 14] compared staggered BTKA (single hospitalization) with staged BTKA (different admissions). Furthermore, a comparison between staggered BTKA and unilateral TKA was conducted in one paper (16.7%) [15]. Two studies (33%) [16, 17] analyzed the impact of different time intervals in the same-admission staggered BTKA. In this analysis, all studies were level of evidence III [10, 13–17]. Four papers (66%) were 3-arm studies [13–16], while two papers (33.3%) were 2-arm trials [10, 17]. Finally, one paper was based on data extracted from a nationwide registry [16]. (Table 2).

Quality of the studies and possible high risk of bias

The "quality assessment" of the studies for methodological deficiencies, as a common alternative to "risk of bias" [22], was examined by the modified Coleman Methodology Score [23]. The total mean modified Coleman Score of the review was 55/100, ranging from 38 [17] to 62 [10, 13] (Table 2). All studies which were included in this review had a high risk of possible selection, performance, detection, and reporting bias [10, 13–17]. Furthermore, one study had high risk of potential other types of bias [16] (Table 2).

Demographics

In total, the review included 43,892 patients: 2,042 (4.7%) single-hospitalization staggered BTKA, 39,962 (91.6%) simultaneous BTKA, and 1,887 (4.3%) staged BTKA during different hospitalizations. Females ($n = 25{,}931$; 59.1% of all patients) outnumbered males ($n = 17{,}961$; 40.1% of all patients), and mean age of the staggered BTKA patients was 68.0 years. Additional patient demographics are listed in Table 3. Patient follow-up varied from 0 months (only perioperative follow-up [17]) to 12 months postoperatively [14, 15] (Table 2). For same-admission staggered BTKA, the time between the first and the second operation ranged from 1 [16] to 14 days [10], with the majority of the studies (83%) using a 1-week interval between surgeries [13–17] (Table 3).

All studies comparing simultaneous and staggered procedures reported significantly increased rates of preoperative comorbidities or higher ASA score in the patients who were treated with staggered BTKA [13–16]. In these studies, simultaneous BTKA patients were predominantly male, younger, and healthier, as compared to staggered BTKA patients [13–16]. Finally, one study noted that patients contraindicated for simultaneous BTKA (due to medical comorbidities), but presenting with major bilateral knee deformities requiring simultaneous correction (for accelerated

Table 2 Type of study, level of evidence, follow-up, early clinical evaluation, modified Coleman methodology score (MCMS), and potential risk of bias

Author	Type of study	Level of Evidence	Follow-up Period	Early first week evaluation	MCMS 0–100	Potential Bias (Selection, Performance, Attrition, Detection, Reporting, Other)
Courtney et al. [14]	Retrospective	III	12 months	No	54/100	Selection, Performance, Detection, Reporting
Koh et al. [13]	Retrospective	III	12 Months	No	59/100	Selection, Performance, Detection, reporting
Liu et al. [15]	Retrospective	III	12 months	No	56/100	Selection, Performance, Detection, Reporting, Other (national database)
Poultsides et al. [10]	Retrospective	III	30 Days	No	62/100	Selection, Performance, Detection, Reporting
Sliva et al. [12]	Retrospective	III	60 Days	No	62/100	Selection, Performance, Detection, Reporting
Wu et al. [16]	Retrospective	III	Perioperative Time period: range: 10–21 days	Yes	38/100	Selection, Performance, Detection, Reporting

Table 3 Number of patients per study, sex, mean age, and time between the first and the second surgery in the patients with staggered bilateral TKA

Author(s)	Number of patients Simultaneous	Number of patients Staggered	Number of patients staged	Sex	Mean age (years)	Time between first and second TKA (staggered)
Courtney et al. [14]	103	131	N/A	108 males 257 females	63	1 week
Koh et al. [13]	820	368	265	786 females (simultaneous) 34 males (simultaneous) 355 females (staggered) 13 males (staggered) 252 females (staged) 13 males (staged)	69.5 (staggered) 68.6 (Simultaneous) 69.9 (staged)	< or = 1 week
Liu et al. [15]	39,013	1,075	N/A	16,005 males (Simultaneous) 23,083 females (simultaneous) 445 males (staggered 1–3 days) 630 females (staggered 1–3) 597 males (staggered 4–7) 899 females (4–7 staggered)	68.3	1–7 days
Poultsides et al. [9]	N/A	149	1557	1023 Females (staged) 534 Males (staged) 72 Females (same admission) 77 Males (same admission)	71.3 (same admission) 69.7 (staged)	6.5 days (1–14 days same admission) 205.5 days (6–365 days staged)
Sliva et al. [11]	26	241	65	92 males (staggered) 149 females (staggered) 14 males (staged) 51 females (staged) 14 males (simultaneous) 12 females (simultaneous)	64 (35–88 staggered) 67.2 (48–90 staged) 59.3 (41–76 simultaneous)	Staggered: 4.5 days (4–7 days) Staged: 79.5 weeks (1.6 to 270.9 weeks)
Wu et al. [16]	N/A	46 (2 day) 33 (7 day)	N/A	10 male (2 day) 36 female (2 day) 5 male (7 day) 28 female (7 day)	70.7 (2 day 70.6 (7 day)	2/7 day

postoperative rehabilitation) were recommended to undergo staggered instead of staged BTKA [10].

Mortality rate

All six trials reported postoperative mortality rate (Table 4). Mortality rate in staggered-treated patients ranged from 0 [17] to 1% [14], while mortality ranged from 0 [15] to 0.24% [14] for the simultaneous-treated patients, and from 0.06 [10] to 6% [13] for the staged-treated patients. Five of six studies (83%) reported no significant difference between staggered, simultaneous, or staged BTKA in regard to mortality rate [10, 14–17]. One study [12] reported that the staged group had an increased mortality rate in comparison with the staggered and the simultaneous groups (Table 4).

Perioperative complications

Medical or systemic complications (not related to the wound or the implant) were reported in all 6 studies [10, 13–17],

Table 4 Complications and outcomes measured as well as mortality rate and major complications' rate per study

Author	Outcomes assessed	Complications assessed	Mortality rate	Major complications' rate in the staggered-treated patients
Courtney et al. [14]	1 Year Complication rate, 90- Day readmission, Mortality	Perioperative complication, Neurologic complication, Cardiovascular, Thromboembolic event, Bleeding, Pulmonary, Renal, Infection, Arthrofibrosis, Extensor mechanism, Revision for instability, Reoperation, 90-day readmission	Staggered: 1% Simultaneous: 0%	15%
Koh et al. [13]	AKI, Major complications*, MACE, ICU admission, 1- year mortality	AKI, Major complications*, MACE (major adverse cardiovascular and cerebral events), ICU admission, 1- year mortality	Staggered: 0.27% Staged: 1.89% Simultaneous: 0.24%	5.4%
Liu et al. [15]	Major Complications, Mortality	Mortality, Major complications, acute myocardial infarction, acute renal failure, all infection, blood transfusion, cardiac complications, cerebrovascular event, gastrointestinal complication, mechanical ventilation, pneumonia, pulmonary compromise, pulmonary embolism, wound infection	Simultaneous: 0.23% 1–3 day BTKA Staggered: 0.09% 4–7 day BTKA Staggered: 0.07%	9.1% (4–7-day interval)—13.2% (1–3-day interval)
Poultsides et al. [10]	Major, Minor, Local Complications, Mortality	Local Complications: peripheral nerve injuries, peripheral vascular complications, hemorrhage complicating a procedure, hematoma complicating a procedure, seroma complicating a procedure, accidental puncture or laceration during a procedure, disruption of operative wound, disruption of internal operation wound, disruption of external operation wound, non-healing surgical wound Minor complications: hypotension, syncope and collapse, tachycardia, delirium, urinary tract infection, urinary retention, superficial incisional surgical site infection and cellulitis, paralytic ileus, pleural effusion Major complications: central nervous system, pulmonary compromise, sepsis, shock/cardiorespiratory arrest, acute myocardial infarction, cardiac complications, pneumonia, pulmonary embolism, deep-vein thrombosis, deep periprosthetic infection	Staggered: 0% Staged: 0.06%	16.1%
Sliva et al. [12]	Major, minor, perioperative complications, Mortality	Major Complications: myocardial infarction, stroke, pulmonary embolism, arrhythmia, return to operating room Perioperative complications: blood transfusion, length of acute inpatient hospitalization, need for placement in a rehabilitation hospital Minor Complications: urinary retention, urinary tract infection, deep-vein thrombosis, pneumonia, superficial infection, early knee manipulation for poor motion, atrial fibrillation, admission to hospital without monitoring in the intensive care unit	Staggered: 0.4% Simultaneous: 0% Staged: 6%	13%
Wu et al. [16]	Length of Stay, Perioperative/ Postoperative Complications	Length of Stay, surgical time, hypotension, desaturation, arrhythmia, stroke, pulmonary embolism, ICU admission	0%	0%

* Major complications defined as greater than or equal to 3a stage according to the Clavien–Dindo classification system

AKI: acute kidney injury; MACE: major adverse cardiovascular and cerebral events; ICU: intensive care unit

but the results were conflicting. Three out of the 6 studies depicted no difference between staggered, simultaneous, or staged BTKA in regard to the rate of medical complications [14, 15, 17]. Another study confirmed these results only when the staggered-treated patients had a 4–7-day interval between operations [16]. Staggered BTKA patients who had the second TKA within a 1–3-day interval showed increased complications rates [16]. In addition, one study reported increased rates of general complications after staggered BTKA compared to staged BTKA with the second operation performed within one year after the first one [10]. However, the two groups were not comparable since the staggered patients were more likely to be male and had a higher overall comorbidity burden than the staged patients [10]. In contrast, one study (16.7%) reported that the staged-treated group (different hospitalizations) experienced increased rates of complications when compared with the single-hospitalization staggered-treated group [13] (Table 4).

The rate of major complications of patients treated with staggered BTKA ranged widely from 0 [17] to 16% [10]. The exact ratios per study can be found in Table 4.

Three studies (50%) separately investigated the rate of acute renal failure [14–16]. Two of these studies (66.7%) depicted that staggered BTKA led to significantly decreased rate of acute renal failure in comparison with simultaneous BTKA [14, 16], while one study (33%) noted that there was not any significant difference among groups [15] (Table 4).

Surgery-related (or orthopedic) complications

Surgery-related (or orthopedic) complications were documented in three studies (50% of all) [10, 15, 16]. Two out of these three studies (66.7%) [10, 16] found that staggered BTKA led to an increased rate of surgery-related complications. One study (33.3% of these specific studies) [15] did not document any significant difference between staggered-treated and simultaneous-treated patients regarding the rate of orthopedic complications (Table 4).

Blood transfusions

Four studies (66.7% of all) assessed the rate of blood transfusion in the different groups of patients [10, 13, 15, 16]. Three studies (75% of these specific studies) compared staggered and simultaneous BTKA [13, 15, 16]. Two of them concluded that there was no difference among groups regarding the requirement for blood transfusion [13, 15], whereas one study noted that staggered BTKA resulted in increased rates of blood transfusion when compared with simultaneous BTKA [16]. Moreover, two studies (50% of these specific studies) compared single-hospitalization staggered and staged BTKA during different hospitalizations [10, 13]. Both studies showed that staggered BTKA led to an increased rate of blood transfusions in comparison with the staged BTKA [10, 13].

Length of stay, intensive care unit (ICU) admissions, and re-admissions

Four out of the six studies (66.7%) measured mean length of stay as an outcome variable [13–15, 17]. All studies which compared staggered and simultaneous BTKA concluded that the mean length of stay after the former was significantly longer [13–15]. The only study which compared single-hospitalization staggered and staged (during different hospitalizations) BTKA suggested that the former resulted in shorter mean length stay [15].

Two studies (33.3%) assessed the ratio of ICU admissions [15, 17]. One of these studies found that patients who were treated with staggered BTKA had lower rates of ICU admission in comparison with those who underwent a simultaneous BTKA [14]. The other study did not use any control group to compare the results of staggered BTKA, since the comparison was carried out between different intervals of single-hospitalization staggered BTKA [17].

Furthermore, two studies (33.3%) investigated readmission rates [13, 15]. Both these studies found that there was not any significant difference in the readmission rate between staggered BTKA and simultaneous BTKA [13, 15]

Staggered BTKA versus simultaneous BTKA: Overall

While four studies made comparisons between staggered BTKA and simultaneous BTKA [13–16], no consensus was found regarding the superiority of either procedure. Two studies [13, 14] noted that the staggered BTKA group had significantly better results in terms of primary outcomes (overall complication rate, acute kidney insufficiency) compared to the simultaneous BTKA group. One study [15] reported that there was not any difference among groups, whereas the final investigation [16] noted that the difference was insignificant in patients undergoing staggered BTKA with 4–7-day interval. Furthermore, the latter study [16] suggested that staggered-treated patients with a 1–3-day interval had inferior results compared to those treated with simultaneous BTKA (Table 5).

Staggered BTKA versus staged BTKA: Overall

Three studies compared single-hospitalization staggered and staged (different admissions) BTKA, but the results were conflicting [10, 13, 14]. Two studies (66.7% of these specific studies) showed better outcomes with the use of staggered BTKA [13, 14], whereas one study (33%) noted that staged BTKA during different hospitalizations led to significantly better results than staggered BTKA [10] (Table 5).

Table 5 Assessment of same-admission staggered BTKA in comparison with: a. simultaneous BTKA and b. staged BTKA (two separate hospitalizations). Take-home-message per study is also illustrated

Author	Significant difference between Simultaneous vs Staggered	Significant difference between Staggered vs Staged	Take-home message
Courtney et al. [14]	No difference was seen between Staggered and Simultaneous BTKA	N/A	There was no difference among staged or staggered BTKA
Koh et al. [13]	Yes, staggered BTKA was associated with decreased risk of AKI. No other differences seen	Yes, staggered BTKA was associated with decreased risk of AKI. No other differences seen	Patients with staggered BTKA were at decreased risk for AKI compared to staged and simultaneous BTKA
Liu et al. [15]	Yes, staggered BTKA at 1–3 days was associated with increased risk of any major complication and Pulmonary Compromise. Staggered BTKA at 4–7 days was no different compared to simultaneous BTKA	N/A	Staggered BTKA offers no benefits in terms of mortality and major morbidity. 1–3-day staggered BTKA is associated with increased risk for major complications, while there was no difference between 4–7-day staggered and simultaneous BTKA
Poultsides et al. [10]	N/A	Patients with Staggered BTKA were at increased risk for minor or major complications. No difference seen for local complications between 2 groups	Patients who received a staggered BTKA were at risk for increased perioperative complications. No difference was seen in Mortality or local complications between Staggered and Staged BTKA
Sliva et al. [12]	Yes, staggered BTKA was associated with fewer overall, minor complications and blood transfusions	Yes, staggered BTKA was associated with fewer overall and minor complications	Patients with staggered BTKA were at less risk of developing complications compared to simultaneous and staged BTKA. Patients receiving staggered BTKA require additional blood transfusions and additional inpatient rehabilitation compared to staged BTKA, but not compared to simultaneous BTKA
Wu et al. [16]	N/A	N/A	No difference in major complications among patients with 2 day versus 7 day staggered BTKA

Timing of staggered BTKA

There was no consensus regarding the optimal interval between surgeries in single-hospitalization staggered BTKA. Two studies (33.3% of all) compared the outcome of two different intervals in patients treated with staggered BTKA [16, 17]. Wu et al. found that there was not any significant difference between the outcomes of 2-day interval and those of 7-day interval [17]. However, Liu et al. noted that the 4–7-day interval conferred better results (comparable to simultaneous BTKA) than the 1–3-day interval [16] (Table 6).

Discussion

Our systematic review of the literature illustrates that controversy continues about the optimal timing of the second surgery for patients with bilateral knee osteoarthritis and whether single-admission staggered bilateral TKA should be performed [13]. Eighty-one percent of participants in a consensus conference agreed that if a patient is not deemed a candidate for the same-day BTKA, a second TKA should be scheduled no sooner than 3 months after the first [9]. The most important finding of our review was that existing evidence regarding the safety and efficacy of staggered BTKA is lacking and further research is required to make more evidence-based conclusions. Particularly, there was no consensus among authors regarding the safety and efficacy of staggered BTKA when compared with staged or simultaneous BTKA. Although single-hospitalization staggered BTKA resulted in satisfactory clinical outcomes with relatively low complication rates in patients who were not considered eligible for the same-day BTKA, we could not conclude that staggered BTKA is superior to the staged procedure.

Regardless of the surgical strategy, bilateral TKA is considered a safe procedure [24, 25]. Staggered BTKA illustrated similar mortality rates as compared to both simultaneous or staged BTKA, in almost all studies [10, 14–17]. Furthermore, the rates of major complications were low, although they varied widely among studies in this review. Some trials showed special interest in the rate of postoperative acute renal failure [14–17]. All of them noted that staggered BTKA led to at least similar or better results regarding postoperative renal insufficiency when compared to simultaneous BTKA [14–17]. Koh et al. [14] reported that the incidence of acute kidney injury (AKI) was lower in the staggered group compared to the staged and simultaneous groups in primary bilateral TKA patients. Even though the preoperative demographic and laboratory data were comparable among groups, the authors suggested that this difference might have been related to the type of anesthesia, favoring spinal anesthesia instead of general anesthesia in order to reduce the occurrence of postoperative AKI [26]. On the other hand, it was not clear whether staggered BTKA resulted in different rates of surgery-related (orthopedic) complications when compared with staged or simultaneous BTKA [10, 15, 16].

As for the comparison between the overall complication rates of staggered and simultaneous BTKA, this systematic analysis showed that there was weak evidence in favor of the staggered procedure. Most studies which dealt with this kind of comparison found that staggered BTKA led to at least similar or better results than simultaneous BTKA [13–15], whereas only one study showed better results with the simultaneous procedure [16]. In addition, Poultsides et al. [10] reported that single-hospitalization staggered BTKA treated patients were more likely to develop minor or major complication compared to different-hospitalization staged BTKA treated patients. These complications included a higher incidence of cardiac and thromboembolic events, likely secondary to increased patient comorbidity in the single-hospitalization group. Finally, no recommendations can be made regarding the comparison of the overall complication rates between staggered and staged BTKA, since the results were conflicting [10, 13, 14]. In brief, it could be argued that staggered BTKA did not show an improved safety and complication profile compared to the well-established simultaneous or staged procedures.

Another point of interest was the requirement of blood transfusions. Increased need of blood transfusion in patients undergoing single-hospitalization staggered BTKA has been previously reported in a nationally representative data analysis including 43,350 patients [21]. In the present analysis, none of the studies depicted lower rates of blood transfusion with the use of staggered BTKA [10, 13, 15, 16]. On the contrary, all studies that compared staggered and staged BTKA patient cohorts showed that staggered BTKA led to increased rates of blood transfusions [13, 15, 16]. A higher rate of

Table 6 Impact of Timing of Staggered BTKA on Postoperative Outcomes

Author	Time Periods Assessed	Significant Difference between time periods
Liu et al. [15]	1–3/4–7 days	Yes, 1–3-day staggered BTKA was associated with increased risk for major complications
Wu et al. [16]	2/7 day	No difference in major complications among patients when comparing 2 day versus 7 day staggered BTKA

perioperative blood-product transfusion is considered a risk factor for the development of AKI [14]. Based on these findings, we suggest the standardized use of intraoperative tranexamic acid [21, 27] in all patients undergoing staggered BTKA, in order to reduce postoperative bleeding and blood transfusions.

In all studies, the mean length stay was longer for staggered compared to simultaneous BTKA [13–15]. As reported by Poultsides et al. [10], extended hospital stay found in patients treated with staggered BTKA may be associated with a higher in-hospital infection rate. Large institutional series have previously shown that longer hospitalization is a significant predictor of periprosthetic joint infection (PJI) [28, 29]. However, readmission rates were similar between staggered and simultaneous BTKA [13, 15]. In addition, recent economic studies have demonstrated a significative reduction of the economic burden with the use of simultaneous BTKA or single-hospitalization staggered BTKA compared to different-hospitalization staged BTKA [30].

The optimal time interval in the single-hospitalization staggered BTKA continues to be debated. The results of the two studies which dealt with this parameter were conflicting [16, 17]. We support the need for further studies to clarify whether "early" staggered BTKA (1–3 days after the first operation) results in different outcomes in comparison with "late" staggered procedures (4–7 days after the first operation).

This systematic review has several limitations. The studies involved in this review had several design limitations including a lack of prospective studies, randomization, and blinding. Specifically, there were no level I and II controlled trials, while all studies were level of evidence III. The quality of the studies ranged from low to moderate based on the modified Coleman Methodology Score, and potential biases related to the retrospective design might have influenced the results. Selection bias was an important issue in the studies. Some patients may have refused to undergo single-hospitalization staggered BTKA for medical reasons, because the perioperative complication risk may have been considered too high. Moreover, the studies varied widely in regard to follow-up, control groups, time interval between stages, and number of patients. In contrast, a strength of this review was the considerably high total number of patients included in analysis. Nonetheless, the number of patients who specifically underwent staggered BTKA was relatively low. Finally, the groups of patients involved in the studies that we review demonstrated heterogeneous baseline characteristics, leading to potential biases in the results when comparing outcomes among different groups.

Conclusions

While the quality of the current literature on the outcomes and complication rates of staggered bilateral TKA during the same-admission is low-to-moderate, same-admission staggered BTKA does not appear to be safer than the well-established simultaneous or staged BTKA. In addition, same-admission staggered BTKA is associated with increased rates of blood transfusions compared to staged BTKA and increased length of stay compared to simultaneous BTKA. Overall, the data suggest that staggered BTKA will probably continue to decline in utilization and does not appear to have much clinical applicability/advantage over simultaneous BTKA in a medically appropriate patient.

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Compliance with ethical standards

Conflict of interest Author A, Author B, Author D, Author E declared no conflict of interests. Author C is paid consultant for Lima Corporate (not related to this study). Author F reported that he had received research support (not related to this study) from Intellijoint, as Primary Investigator, while he is paid consultant for EOS Imaging as well as Lima Corporate (not related to this study).

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. For this type of study, formal consent is not required.

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