SYSTEMATIC REVIEW

Staged Bilateral Total Knee Arthroplasty: When Should the Second Knee be Replaced?

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Abstract

Background: Bilateral total knee arthroplasty (BTKA) under the same anesthesia (simultaneous) or staged are options for patients with end-stage arthritis of the knee that carries advantages and limitations. Not all patients are candidates for simultaneous BTKA, and therefore, surgeons prefer to stage the two TKAs. The optimal safe interval between two TKAs is not known. The present systematic review aimed to determine the optimal time interval between the two stages of BTKA.

Methods: Pubmed and Scopus databases were searched to identify publications from January 1979 to November 2017 in English that compared the outcomes of staged BTKA performed using various time intervals between the two TKAs. Data on systemic and local complications following staged BTKA were extracted, and the pooled data were analyzed to adjust for age.

Results: In total, 23 studies that enrolled 117,090 patients undergoing staged BTKA were included in this systematic review. A significant increase was observed in the incidence of myocardial infarction (OR=8.4 and 8.32), other cardiac complications (OR=17.71 and 18.18), deep vein thrombosis (OR=4.72 and 4.89), pneumonia (OR=3.37 and 3.45), and knee revision (OR=3.73 and 4.14) in patients undergoing the second TKA within 30 days or 90 days of the first TKA. However, the replacement of the second knee within this time interval was associated with a significantly lower risk of pulmonary embolism (OR=0.145 and 0.128), superficial (OR=0.14 and 0.79) and deep knee infection (OR=0.0 and 0.0), as well as vascular complications (OR=0.0 and 0.42).

Conclusion: Time interval of less than 30 or 90 days between two TKAs performed in patients with BTKA was associated with a higher risk of systematic complications. However, the shorter time intervals between the two TKA may reduce the risk of other complications. This information may help surgeons' council patients better when deciding on the optimal time interval between two TKAs.

Level of evidence: I

Keywords: Bilateral Total Knee Arthroplasty, Systematic review, Two-stage procedure

Introduction

Over 9 million adults in the U.S. have been estimated to have symptomatic knee osteoarthritis (1). Among these, the prevalence of bilateral osteoarthritis is estimated to be about 5% (2). Considerable numbers of patients with symptomatic knee osteoarthritis eventually undergo total knee arthroplasty (TKA). The prevalence of TKA among the total U.S. population was 1.52% in 2010, which corresponds to 4.7 million individuals (3). It is predicted that by 2030, the annual rate of TKA will increase to over 3.4 million in the U.S. population (4). There are two surgical options available for patients with bilateral knee osteoarthritis, namely simultaneous or staged bilateral TKA (BTKA) (5). There are numerous advantages to simultaneous BTKA that include the need for one preoperative medical clearance, one hospital admission, administration of one anesthesia, and shorter overall length of hospital stay (6, 7). However, some studies have detected a higher

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incidence of serious complications, including mortality, following simultaneous BTKA (8-12). Therefore, in patients with multiple underlying co-morbidities, staged BTKA is considered to be a safer approach. However, the optimal time interval between the two TKAs in these patients is not known (13). A consensus group on the management of BTKA recommended that TKAs should be staged by 90 days or more in an effort to reduce the risk of complications. . The latter recommendation was based on minimal evidence as this issue has not been investigated by high-level studies. The objective of the current systematic review was to determine the optimal time interval between the two TKAs in patients undergoing staged BTKA. Using serious complications as the end point, we evaluated the available literature to determine the optimal time interval between two TKAs.

Materials and Methods

PubMed and Scopus were searched to identify all relevant articles published in English between January 1st, 1979 and December 9th, 2017 using MeSH with the search strings of knee, arthroplasty, replacement, bilateral, stage, and complication. Two medically qualified individuals read the titles and abstracts of all eligible studies, and those comparing the outcomes of staged BTKA were retained. On the other hand, review articles, surgical techniques, abstracts from the scientific meetings, and expert opinions were excluded. In the next step, the full-texts of the remaining studies were read, and those comparing the outcome of staged BTKA were retained for data extraction [Figure 1].

In total, two independent reviewers read the full texts of the included studies to extract data from each eligible study using a pre-specified data extraction form. Additionally, the reference list of the included studies was searched to identify additional relevant studies that may have been missed during the primary literature search. Extracted data included demographic characteristics, methodology, the time interval between the two TKAs, incidence of reported complications that included mortality, myocardial infarction (MI), deep vein thrombosis (DVT), pulmonary embolism (PE), wound complications, infection, revision, urinary complications (urinary retention and urinary tract infection), respiratory complications (pneumonia, adult respiratory distress syndrome), neurological complications (cerebrovascular accident), and gastrointestinal complications, as well as the length of hospital stay, intensive care unit admission, and costs of hospitalization, if disclosed. Forms were then reviewed for completeness and agreement. Disagreements were resolved by consensus and discussion with the senior authors. Eventually, complications and mortality across the studies were compared using two-time intervals of 30 and 90 days between the two TKAs. It was also assumed that patients who were younger and healthier might be scheduled in a shorter time interval for the second-knee replacement. Therefore, it was tried to adjust the results for age and co-morbidities.

Statistical analysis

For analysis, the number of events (complications and mortality) in a set of trials for each study was analyzed using a generalized linear model, which specified a binomial distribution, a logit link function, and covaried out age. As reported, co-morbidities varied between the studies, we could not adjust the results for co-morbidities. A p-value less than 0.05 was considered statistically significant.

Results

Search results

The literature search provided 820 articles, of which 23 studies fulfilled the criteria through the scrutiny of the titles, abstracts, and full-texts. These 23 studies collectively included 117,090 patients undergoing staged BTKA [Figure1] [Table 1].

Outcomes and complications of BTKA with 30 days interval between stages

As can be seen in [Figure 2], a significant increase is observed in the incidence of MI (OR=8.4, 95% CI: 7-10.08; P<0.001), other cardiac complications (OR=17.71, 95% CI: 6.64-47.26; P<0.001), DVT (OR=4.72, 95% CI: 3.23-6.88; P<0.001), pneumonia (OR=3.37, 95% CI: 1.86-6.1; P<0.001), and knee revision (OR=3.73, 95% CI: 1.99-6.97; P<0.001) in 35,939 patients undergoing staged BTKA with a time interval of fewer than 30 days between two TKAs after adjusting for age. However, the replacement of the second knee within 30 days from the first knee was associated with a lower risk of PE (OR=0.145, 95% CI: 0.08-0.24; P<0.001), wound infection or superficial surgical site infection (OR=0.14, 95% CI: 0.02-0.78; P=0.025), deep knee infection (OR=0.0, 95% CI: 0.0-0.0; P<0.001), and vascular complications (OR=0.0, 95% CI: 0.0-0.0; P<0.001).

Outcomes and complications of BTKA with 90 days interval between stages

Pooled data analysis comparing outcomes and complication rates between 90-day and more than 90-day groups (including 47,269 Patients) similarly showed unfavorable results in MI (OR=8.32, 95% CI: 7.04-9.8; P<0.001), other cardiac complications (OR=18.18, 95% CI: 6.6-50.08; P<0.001), DVT (OR=4.89, 95% CI: 3.55-6.75; P<0.001), pneumonia (OR=3.45, 95% CI: 1.99-5.97; P<0.001), and knee revision (OR=4.14, 95% CI: 2.38-7.17; P<0.001) in patients who underwent the second TKA within 90 days of the first TKA [Figure 3]. Similar to a 30-day cut-off point, the replacement of the second knee within 90 days of the first knee was associated with a lower risk of PE (OR=0.128, 95% CI: 0.06-0.24; P<0.001), superficial surgical site infection (OR=0.79, 95% CI: 0.67-0.93; P<0.05), deep knee infection (OR=0.0, 95% CI: 0.0-0.0; P<0.001), and vascular complications (OR=0.42, 95% CI: 0.3-0.58; P<0.001). There was no significant difference in mortality rate, neurologic, gastrointestinal, and urinary complications through either cut-off points of 30-day and 90-day.

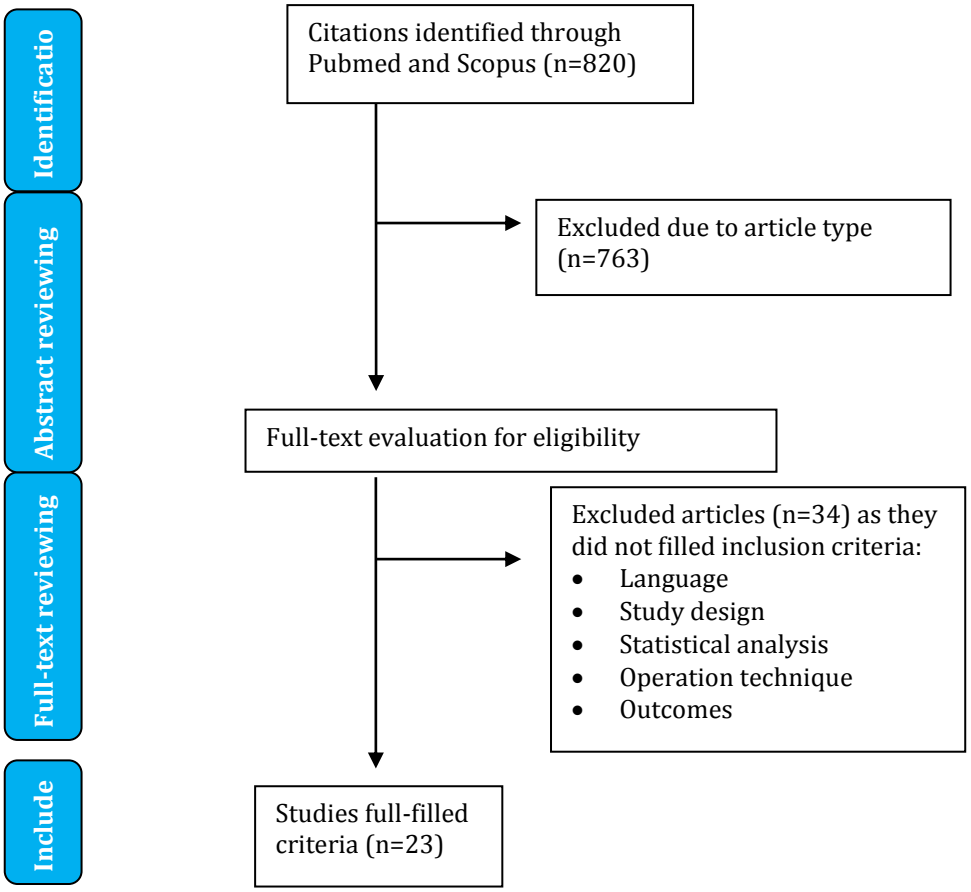

Figure 1. Flowchart of the systematic review

Table 1. List of included studies

Author (year)	Number of patients	Time interval	Follow-up	Co-morbidities	Outcomes and complications
Sobh et al. (2018) (23)	337	<1yaer	90days	Undetermined	Transfusion, DVT, Wound infection
Sarzaeem et al. (2017) (24)	60	2.5-4months	38months	Undetermined	DVT
Seol et al. (2016) (25)	315	36.6days	53months	Coronary artery disease, Congestive heart failure, Chronic obstructive pulmonary disease, DM, Hypertension, Renal disease, Hypothyroidism	MI, DVT, Pneumonia, Neurologic, Urinary, Wound infection, Deep knee infection
Sheth et al. (2016) (26)	14370	3-12months	_	Undetermined	Mortality, MI, DVT, Neurologic, Deep knee infection, Knee revision
Zhao et al. (2015) (27)	39	2-36months	39months	Coronary artery disease, Hypertension, DM	Transfusion, DVT, PE, Wound infection

Liu et al. (2015) (28)	1075 1496	1-3days 4-7days	–	Cancer, Congestive heart failure, Chronic obstructive pulmonary disease, DM, Obesity, Liver dysfunction, Renal disease, Cardiac valvular disease	Transfusion, Mortality, MI, DVT, Other cardiac, Pneumonia, PE, Neurologic, Respiratory, Digestive, Urinary, Wound infection
Lindberg-Larsen et al. (2015) (29)	346 292	0-6months 7-18months	90days	Undetermined	DVT, Other cardiac, Urinary, Wound infection, Deep knee infection, Knee revision, Surgical complication
Courtney et al. (2014) (30)	131	7days	1year	Cardiac disease, Chronic obstructive pulmonary disease, DM, Chronic Renal insufficiency	Transfusion, Mortality, DVT, Other cardiac, PE, Neurologic, Wound infection, Knee revision, Surgical complication
Niki et al. (2014) (16)	58	8.2months	38months	Undetermined	MI, DVT, Other cardiac, PE, Neurologic, Surgical complication
Poultsides et al. (2014) (31)	172 1533	<3months 3-12months	30days	Congestive heart failure, Coronary artery disease, Pulmonary disease, DM, Hypercholesterolemia, Hypertension, Liver disease, Renal disease	Mortality, MI, DVT, Pneumonia, PE, Neurologic, Digestive, Hypotension, Urinary, Wound infection, Surgical complications
Alosh et al. (2014) (32)	118	7days	3.5years	BMI, Charlson comorbidity index, ASA classification score	Mortality, MI, Other cardiac, Neurologic, Digestive, Urinary, Wound infection
Memtsoudis et al. (2009) (33)	32691	3.59days	–	Chronic pulmonary disease, DM, Liver disease, Obesity, Peripheral vascular disease, Renal failure, Valvular disease, Congestive heart failure	Mortality, DVT, PE, Neurologic, Respiratory, Digestive, Urinary, Wound infection, Deep knee infection, Vascular
Wu et al. (2008) (34)	46 33	2days 7days	–	Heart disease, Hypertension, DM, Chronic lung disease, Chronic renal insufficiency	Mortality, PE, Hypotension, Urinary
Ersozlu et al. (2008) (35)	68	4-11days	>32months	Hypertension, Diabetes, Chronic obstructive lung disease, Coronary heart disease, Gastrointestinal disease, Urinary tract infections	Mortality, PE, Wound infection
Forster et al. (2006) (36)	36 38	7days 29months	4.1years 3.9yrs	Undetermined	PE, Neurologic, Digestive, Knee revision, Surgical complications
Barrett et al. (2006) (37)	1663 4146 7230	<3months 3-6months 6-12months	–	Undetermined	PE
Stubbs et al. (2005) (38)	38	<12months	–	Undetermined	Transfusion, Mortality, MI, Other cardiac, Neurologic, Respiratory, Digestive, Deep knee infection, Knee revision
Sliva et al. (2005) (39)	241	4-7days	–	Hypertension, Hypercholesterolemia, Obesity, Thyroid disorder, DM, CAD	Transfusion, Mortality, MI, DVT, Other cardiac, Neurologic, Urinary, Wound infection, Knee revision
Gill et al. (2003) (40)	302	<3months	90days	Cardiovascular disease	Mortality
Mangaleshkar et al.	4	15days	30days	Undetermined	Mortality

(2001) (41)	2	3months			
	28	>6months			
Ritter et al. (1997) (42)	4354	<6weeks	>2years	Undetermined	Mortality, wound infection, Vascular, Surgical complication
	4524	6weeks-3months			
	9829	3-6months			
	31401	6-12months			
Jankiewicz et al. (1994) (43)	56	9months	_	Undetermined	Mortality, DVT, PE, Neurologic
Soudry et al. (1985) (44)	18	1week-5months	>2years	Undetermined	Transfusion, MI, DVT, Other cardiac, Pneumonia, PE, Neurologic, Digestive, Urinary, Wound infection, Deep knee infection, Surgical complication

DVT: Deep Vein Thrombosis, MI: Myocardial Infarction, PE: Pulmonary Embolism

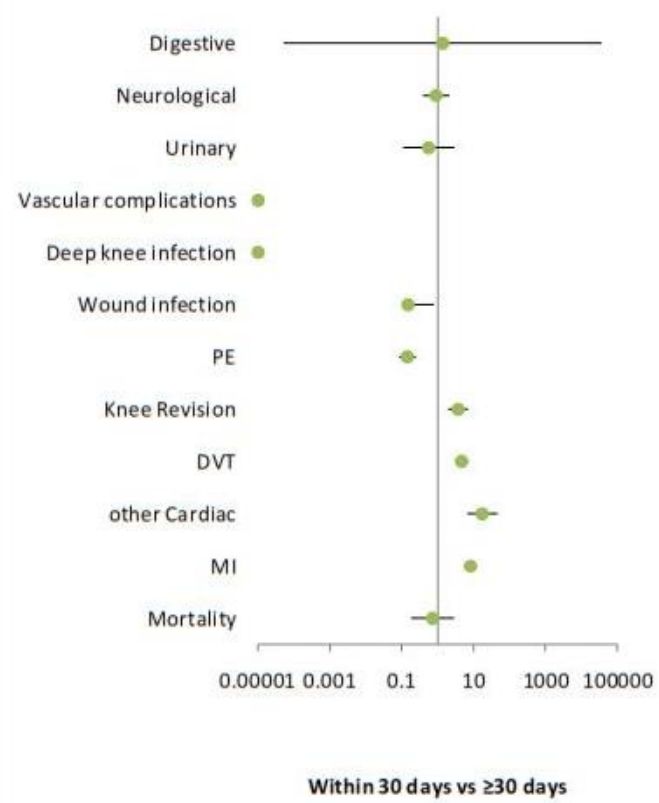

Figure 2. Comparison of complication rate by a 30-day cut-off point

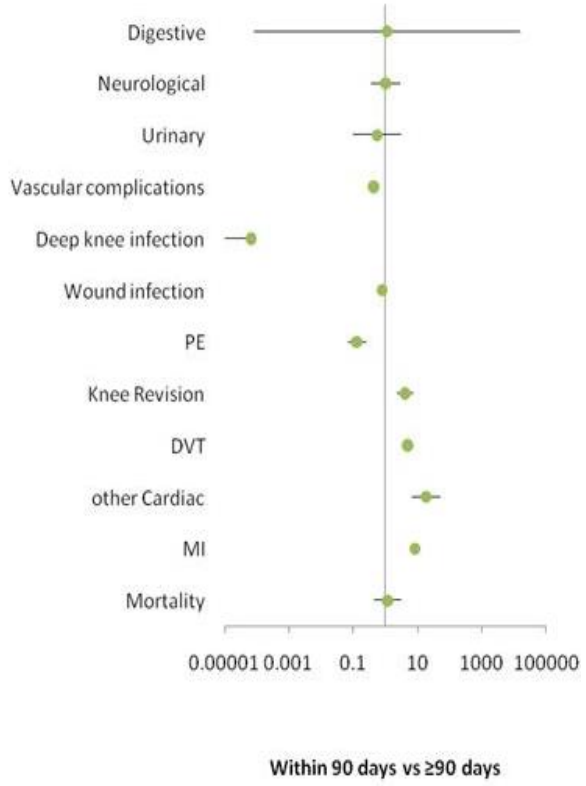

Figure 3. Comparison of complication rate by a 90-day cut-off point

Discussion

This systematic review demonstrated that the rates of major complications, such as pneumonia, knee revision, DVT, MI, and other cardiac complications were higher if the second TKA was performed within 90 days of the first TKA in patients undergoing staged BTKA. Interestingly, and perhaps surprisingly, the incidence of some

complications, such as vascular complications, PE, wound infection or superficial surgical site infection, and deep knee infections were significantly lower when the two TKAs were performed within 30 or 90 days of each other.

Our findings are in line with the prior recommendations by the consensus group and the commonly held belief in that performing the second TKA in less than 3 months of the first TKA is associated with a higher risk of major complications, including mortality (13). The explanation for these findings may reside in the inflammatory or tissue response process. Tissue trauma during surgery leads to a series of inflammatory responses that result in the local and systemic release of cytokines, interleukins, and other inflammatory mediators. The latter explains why the level of non-specific inflammatory markers, such as C-reactive protein (CRP) and erythrocyte sedimentation rates rise rapidly following surgery (14). The level of these markers peaks shortly after surgery and gradually declines (15). The level of these markers may remain elevated for up to 90 days. The tissue inflammatory response is obviously higher when two TKAs are performed under the same anesthesia, which explains the higher complications associated with simultaneous BTKA (14). The rationale for staging BTKA in patients with comorbidities is to reduce the physiological insult and inflammatory process of two TKAs. The fact that the incidence of some major complications, such as MI and other cardiac events, is higher when two TKAs are performed close to each other relates to the persistence of inflammatory or catabolic state in these patients (16).

In support of this assumption, Niki et al. (16) found perioperative changes in laboratory markers, which might be indicative of higher potential surgical complications. They observed that the peak in CRP levels (indicative of surgical invasiveness), creatine phosphokinase index (reflecting the degree of muscle damage), and D-dimer levels (as a parameter for venous thromboembolism) especially occur within the first few days postoperatively with no significant difference among either stage of BTKA. Nonetheless, these parameters are significantly higher following simultaneous BTKA probably due to greater surgical stress which makes the

procedure more susceptible to complications. Accordingly, in a study comprising of 1,410 patients undergoing BTKA, Wood et al. (17) found that clinically significant complications, such as MI, DVT, PE, and death more likely occur within the first few days postoperatively.

Although the level of these inflammatory markers has not been evaluated in different time intervals between two stages of BTKA, it can be assumed that a longer time

interval between two stages may be associated with a lower rate of specific complications since a longer period will provide more time for the normalization of these markers. However, our findings cannot be fully explained based on the available literature.

A study conducted by Lalmohamed et al. (18) attempted to determine the timing of acute MI in TKA patients and concluded that the risk of MI significantly increased during the first two weeks postoperatively and sharply decreased thereafter to the baseline level; moreover, the risk attained the baseline from two to six weeks after surgery. The authors attributed this increased risk of MI to a greater chance of developing marrow embolization due to surgical invasions, as well as hemodynamic stressors, such as anesthesia, blood and fluid disturbances, and hypoxia. In a study performed by Chua et al. (19), rates and causes of revision, as well as 30-day mortality, have been compared between various BTKA groups with different time intervals. The authors found no significant difference between the groups in terms of revision rate and its reasons; however, they found a decreased mortality rate in six weeks to three months interval group and suggested a 6-week delay in stage BTKA to mitigate mortality risk. A longer time interval between stages of BTKA (more than 90 days and less than 270 days) has been suggested by Chen et al. (20) to decrease the risk of complications, particularly periprosthetic joint infection.

There also might be a concern regarding the impact of patient comorbidities associated with the risk of developing postoperative complications since staged BTKA with a short time interval between stages can more likely be performed in healthier patients. Some studies have proposed an association between medical comorbidities and postoperative complications regardless of the type of surgery (21, 22). Another study (16) also noted that cardiovascular comorbidities could be used to determine whether patients were able to undergo TKA, but not for making decision on surgical procedure. In the present study, however, patient comorbidities were not included in the final analysis due to a lack of information in the majority of the studies and considerable variation in the reported comorbidities in other studies.

This systematic review has some limitations that should be highlighted. As comorbidity varied across the studies, our findings could not be adjusted for underlying comorbidities. However, our results were adjusted for age. This systematic review was also limited by the inclusion of studies in English, and none of them were randomized controlled trials. Furthermore, there was not a similar definition for complications in different studies that should be considered one of the limitations of this systematic review. However, the large number of studies included with a variety of different outcomes, using a comprehensive search strategy, is considered the strength of this study. Furthermore, changes in surgical and anesthetic techniques, as well as the use of diagnostic laboratory and imagining modalities for diagnosing complications over time should also be considered.

In conclusion, despite the limitations of this study, the time interval of less than 30 or 90 days between two stages of BTKA was associated with a higher risk of serious systematic complications. However, the shorter time intervals between the stages may reduce the risk of local complications. Based on these findings, at least a 30-day interval is recommended between two stages of TKA. The exact reason that a shorter time interval between two stages is associated with a lower risk of PE and local complications is not clear to us. Further

studies are required to determine a safe and optimal time interval between the two stages of BTKA.

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