# Impact of chronic kidney disease on outcomes after total joint arthroplasty: A meta-analysis & systematic review.

**Jiang Chen**
Beijing University of Chinese Medicine Affiliated Dongzhimen Hospital
**Fan Zhang**
Beijing University of Chinese Medicine Affiliated Dongzhimen Hospital
**Chu-Yin Liu**
Beijing University of Chinese Medicine Affiliated Dongzhimen Hospital
**Qiao-Mei Yuan**
Beijing University of Chinese Medicine Affiliated Dongzhimen Hospital
**Xue-Shi Di**
Beijing University of Chinese Medicine Affiliated Dongzhimen Hospital
**Shui-Wen Long**
Beijing University of Chinese Medicine Affiliated Dongzhimen Hospital
**Hong-Cai Shang** ( cjdzmhp@163.com )
Beijing University of Chinese Medicine Affiliated Dongzhimen Hospital
**Yu-Song Jia**
Beijing University of Chinese Medicine Affiliated Dongzhimen Hospital

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# Abstract

Background Comorbidities in patients undergoing total hip arthroplasty (THA) and total knee arthroplasty (TKA) may compromise outcomes with increased hospital stays, readmission and mortality rates. We aimed to determine whether chronic kidney disease (CKD) affects postoperative outcomes of patients undergoing total joint arthroplasty (TJA).

Methods To identify studies for this review and meta-analysis, two independent reviewers searched PubMed, Cochrane, EMBASE and Google Scholar until April 1, 2019, and identified additional studies by manual search of reference lists. Prospective or retrospective studies with quantitative outcomes for patients undergoing TJA were selected. Outcomes were compared between patients with underlying CKD stage >=3 or eGFR< 60 mL/min/1.73 m2 versus mild/non-CKD as controls. Main endpoints were mortality, re-operation and re-admission rates.

Results Among 59 studies reviewed, 19 meeting the eligibility criteria were included, providing data of 2,141,393 patients. After THA or TKA, CKD was associated with higher mortality risk than non-CKD (pooled OR 2.20, 95%CI = 1.90 to 2.54; P < 0.001); no significant differences were seen in re-operation between CKD and non-CKD patients (pooled OR 1.26, 95%CI = 0.84 to 1.88; P=0.266); and CKD patients had higher any-cause re-admission rates (pooled OR= 1.57, 95%CI = 1.27 to 1.94, P<0.001).

Conclusion Underlying CKD predicts adverse outcomes after elective TJA with increased risk of mortality, re-admission, surgical site infection, and perioperative transfusion. Findings of this review and meta-analysis highlight CKD as a critical contributor to complications after TJA and may be helpful to surgeons when advising patients about associated risks of TJA.


# Background

Comorbidities in patients undergoing total hip arthroplasty (THA) and total knee arthroplasty (TKA) are known to result in poor outcomes with longer hospital stays, increased hospital readmission rates and higher mortality rates [1]. Comorbidities previously reported for poor surgical outcomes in the setting of joint replacement surgery include obesity [2], cardiovascular disease [3], depression and other mental health disorders [4-6], diabetes mellitus [7-9], hepatic disease [10-12], and frailty [13]. Studies on joint replacement also show variations in the definitions and severity of comorbid disease [1], which may yield conflicting results, and consensus is still lacking among clinicians about the clinical indications for joint replacement surgeries [14], which may lead to differences in outcomes based on severity levels of associated comorbidities.

Chronic kidney disease (CKD) is associated with age-related decline in renal function and more rapid decline in the presence of hypertension, diabetes, obesity and primary renal disorders [15]. It is also an established independent predictor of mortality and cardiovascular events in the nonsurgical setting [16-18]. Previous studies have also shown that CKD is an independent risk factor for postoperative death and cardiovascular events in elective noncardiac surgeries, including elective orthopedic surgeries [19, 20]. Patients undergoing total joint arthroplasty (TJA) are commonly affected by CKD; reported incidence is 17% in TJA patients, which is higher than that of the general population [21]. Among TJA patients, risk

was markedly higher for overall complications and mortality in patients with moderate to severe CKD than in those without CKD [21].

To date, the influence of CKD on postoperative outcomes after hip or knee replacement is still not well characterized. Although the medical literature has focused increasingly on the potential impact of CKD and various postoperative outcomes, no comprehensive systematic review and meta-analysis has yet been published. In addition, given that interest in elective TJA is growing and the volume of these surgeries is rising correspondingly [22], orthopedic surgeons need to recognize the healthcare burden of this population and must assess outcomes of TJA in patients with CKD or other comorbid conditions in order to optimize treatment strategies and improve outcomes [1].

We hypothesized that underlying CKD would negatively influence the outcomes of patients undergoing TJA. Therefore, the purpose of this systematic review and meta-analysis was to determine whether and how CKD impacts postoperative outcomes in patients undergoing TJA.

# Methods

This meta-analysis and systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).

### Search strategy

To find timely and appropriate studies for review and meta-analysis, we searched the following databases: PubMed, Cochrane, EMBASE and Google Scholar until April 1, 2019. Additional studies were identified by hand-search of reference lists from the relevant studies. The following combinations of keywords were used to maximize the search results: (arthroplasty) AND ((chronic kidney disease) OR renal).

### Study selection and data extraction

Studies were identified by two independent reviewers. Where there was uncertainty regarding eligibility, a third reviewer was consulted. Inclusion criteria were: prospective or retrospective studies comparing outcomes after TJA between patients with underlying CKD (defined as CKD stage >=3 or eGFR< 60 mL/min/1.73 m2) as case group versus mild/non-CKD as control group; quantitative outcomes; and patients undergoing total joint arthroplasty (TJA) of lower-extremities, including total hip arthroplasty (THA) or total knee arthroplasty (TKA). Studies designed only for comparing outcomes between

dialysis-dependent versus non-dialysis-dependent patients were excluded. Letters, comments, editorials, case reports, proceedings and personal communications were also excluded as well as studies with no quantitative outcomes. The following data were extracted from studies that met the inclusion criteria: the name of the first author, year of publication, data source, CKD stage and eGFR level, type of arthroplasty (THA or TKA), number of patients, major comorbidities, length of follow-up and major outcomes.

### Quality assessment

The Quality In Prognosis Studies (QUIPS) tool was used to assess bias in any of the included studies, as previously described [23]. This tool evaluates bias in any of six domains within a study, including: study participants; study attrition; prognostic factor measurement; outcome measurement; study confounding; and statistical analysis and reporting. Assessed outcomes for the included studies are shown in Figure 4.

### Outcome measures

For this meta-analysis, the endpoints were all-cause mortality (at the end of follow-up), re-operation rate, re-admission rate, surgical site infection, deep vein thrombosis (DVT) and perioperative blood transfusion rate. Re-operation was defined as any revision surgery after the primary THA/TKA during which an implant was removed or replaced during the following period. Re-admission was defined as any subsequent hospital inpatient visit due to any cause within 90 days. Surgical site infection was defined as any superficial or deep surgical site infection using the Centers for Disease Control and Prevention (CDC)/National Healthcare Safety Network definitions [24].

### Statistical analysis

Odds ratios (OR) with 95% confidence intervals (CI) were extracted from the selected publications. In addition, ORs were calculated from the 2 x 2 table if OR was not otherwise available. A $\chi$2-based test of homogeneity was performed and the inconsistency index ($I^2$) and Q statistics were determined. If $I^2$ statistic was > 50%, a random-effects model (DerSimonian–Laird method) was used. Otherwise, fixed-effects models (Mantel-Haenszel method) were employed. Pooled effects were calculated and a 2-sided P value < 0.05 was established as statistical significance. Sensitivity analysis was carried out using the leave-one-out approach to determine the robustness of outcomes data. Publication bias was assessed by constructing funnel plots using Egger's test. The absence of publication bias was indicated by the data points forming a symmetric funnel-shaped distribution and one-tailed significance level P > 0.05. Analysis of publication bias was not performed because the number of studies was too few (less than 10 studies) to detect an asymmetric funnel, as described

previously [25]. All analyses were performed using Comprehensive Meta-Analysis statistical software, version 2.0 (Biostat, Englewood, NJ, USA).

# Results

Selected studies Among 59 research articles that underwent full-text review, 40 were excluded and 19 retrospective studies that met the eligibility criteria were included in this review and meta-analysis [21, 26-39]. The full search results and presentation of the characteristics of the included 19 studies are summarized in Table 1. Overall, the eligible studies reported data of 2,141,393 patients (range 270 to 1,016,686) who underwent either THA or TKA. The mean age of patients ranged from 65 to 76 years and the percentage of males ranged from 14% to 77%. Meta-analyses Mortality Four studies [26, 28, 30, 36] provided ORs, and eight studies [21, 27, 29, 31-35] provided simple 2 x 2 tables and were included in the meta-analysis to determine whether CKD was associated with mortality. Evidence of heterogeneity was found among the 12 studies (Q statistic = 25.878, I2 = 53.63%, P =0.011), therefore, a random-effects model of analysis was used. The pooled OR (2.20, 95%CI = 1.90 to 2.54) indicated that CKD was associated with higher risk of mortality than non-CKD patients (P < 0.001) after THA or TKA (Figure 2A). Re-operation Six studies [21, 28, 31, 33, 34, 37] provided enough data to calculate ORs and were included in the meta-analysis. Evidence of heterogeneity was found among the studies (Q statistic = 27.939, I2 = 78.53%, P < 0.001), therefore, a random-effects model of analysis was used. The pooled OR (1.26, 95%CI = 0.84 to 1.88, P=0.266) indicated that no significant differences were seen in re-operation between non-CKD patients and CKD patients after THA or TKA (Figure 2B). Re-admission Eight studies [29, 31, 33, 34, 37, 38, 40, 41] provided enough information to calculate pooled ORs and were included in the meta-analysis. Evidence of heterogeneity was found among the studies (Q statistic = 154.130, I2 = 95.46%, P < 0.001), therefore, a random-effects model of analysis was used. The result of meta-analysis indicated that the CKD group had a higher re-admission rate due to any cause after THA or TKA (pooled OR= 1.57, 95%CI = 1.27 to 1.94, P<0.001) (Figure 2C). Deep Vein Thrombosis Six studies [21, 26, 29, 33, 34, 42] provided enough information to calculate ORs and were included in the meta-analysis. Evidence of heterogeneity was found among the studies (Q statistic = 10.325, I2 = 51.57%, P =0.067), therefore, a random-effects model of analysis was used. The pooled OR (1.29, 95%CI = 0.99 to 1.68) demonstrated no significant differences in DVT between patients with and without CKD (P = 0.057, Figure 2D). Transfusion Seven studies [21, 26, 28, 32, 37, 43, 44] were included in the meta-analysis. The random-effects model was applied to calculate ORs since evidence of heterogeneity was found among the studies (Q statistic = 118.678, I2 = 94.10%, P < 0.001). The pooled ORs (2.41, 95%CI = 1.90 to 3.06, P < 0.001) indicated that CKD was significantly associated with blood transfusion (Figure 2E). Surgical site infection Nine studies [21, 26, 28-31, 33, 36, 38] provided enough information to calculate ORs and were included in the meta-analysis. Moderate heterogeneity was noted among the studies (Q statistic =17.558, I2 = 48.74%, P =0.041), therefore, a fixed-effect model of analysis was used. The pooled OR (1.32, 95%CI = 1.21 to 1.44) indicated that CKD patients had higher odds of surgical site infection than non-CKD patients (P < 0.001) after THA or TKA (Figure 2F). Sensitivity analysis and publication bias Sensitivity analyses were performed using the leave-one-out approach in which the meta-analysis was performed with each study removed in turn (Table 2). The direction of combined estimates did not vary markedly with the removal of the studies, indicating that the meta-analysis was robust and the data were not overly influenced by any single study except for DVT results of Kuo (2017) [29], Li (2017) [42] and Miric (2014b) [34]. Pooled ORs of DVT remained > 1 after each study was removed in turn; although results of Kuo (2017) [29], Li (2017) [42] and Miric (2014b) [34] studies became significant (P values were borderline) and most remained non-significant, indicating no obvious influence of any individual study on the pooled estimate. In addition, no publication bias was found for mortality (t = 0.545, one-tailed, P= 0.298, Figure 3). Quality assessment The results of quality assessment for the included studies are shown in Figure 4. All 19 included studies had low risk of bias in study attrition, outcome measurement, and statistical analysis and reporting. Most studies had low risk of bias for study participation, prognostic factor measurement and study confounding.

# Discussion

This review and meta-analysis investigated whether CKD has an adverse impact on the outcomes of TJA based on recently published evidence with data of over two million patients. Our analysis determined that patients with baseline moderate to severe CKD had a significantly increased risk of mortality (two-fold or more) compared to those with mild/non-CKD. CKD was also significantly associated with more than twice the increased risk of receiving blood transfusion and was significantly associated with increased risk of re-admission and surgical site infection compared to those without CKD. No significant associations were found between CKD and reoperation or DVT in patients undergoing TJA.

Studies included in the present meta-analysis were selected based on inclusion of patients with a range of severity from stage 3, or "moderate," to severe, defining CKD as stage >=3 or eGFR < 60 mL/min/1.73 $m^2$. Studies designed only for comparing outcomes between dialysis-dependent versus non-dialysis-dependent patients were excluded. Our selection strategy was to extend the range of investigation to cover patients with less advanced CKD who were more likely to undergo TJA compared to those with end-stage renal disease (ESRD) and/or were on maintenance dialysis who may not be candidates for surgery. Multiple previous studies have examined outcomes of TJA specifically in patients who were either dialysis-dependent or renal transplant recipients, which led to noticeably higher risk of increased length of stay, readmission and mortality in those study populations [45-48]. In one such study [45], the results revealed that kidney transplant increased risk of surgical site infection and wound infections, systemic infection, deep venous thrombosis, acute renal failure, respiratory, and cardiac complications in patients undergoing TJA. And dialysis dependence was found to be independently associated with higher risk for 30-day adverse events [46, 48], ICU care, longer admission, rehabilitation needs [46], and inpatient mortality [47, 48].

### Mortality

In the present review and meta-analysis, CKD was associated with a significantly higher risk of mortality than that among non-CKD patients who had undergone THA or TKA. CKD is a known risk factor for mortality in the nonsurgical setting [16-18], and in the setting of noncardiac surgeries, CKD is also predictive of postoperative death as reported in the previous studies [19, 20]. In elective primary total knee and hip arthroplasty, dialysis-dependent patients present with inpatient mortality rates 10-20 times greater than in non-dialysis-dependent patients [47]. Given our findings and those of other studies reporting higher mortality risk among patients with varying stages of CKD, this risk should be of the main concern in the selection of TJA candidates who had underlying CKD, even if not yet considered ESRD.

### Reoperation and readmission

Results of the present meta-analysis found no significant differences in the occurrence of re-operation between CKD and non-CKD patients undergoing TJA; however, CKD patients who received TJA had higher any-cause readmission rates than

non-CKD patients. Although outcomes of TJA are generally reported to be excellent, implant failure and increased risk of revision surgery continues to be of concern [49-51]. Revision surgery may be the result of infection, dislocation, osteolysis or loosening of the component; after THA, dislocation and mechanical loosening are the main risk factors reported for revision surgery [49]. For TKA, the main etiology reported for re-operation are infection and mechanical loosening [50]. A scoping review determined that risk of revision surgery was associated mainly with demographic factors such as age and African-American ethnicity, as well as surgical factors such as uncemented procedure, implant malalignment and longer operative times [51]. A systematic review evaluating results of 86 studies reported that risk factors for revision surgery included younger age, more comorbidities, avascular necrosis as an indication (rather than osteoarthritis) and larger femoral head size in revision performed due to dislocation [52]. However, in that study, younger age was associated with fewer dislocations. Perhaps not all studies had adjusted for confounders when determining risk factors, and clearly, not enough is known about the causes of revision surgery. Further study is needed to identify modifiable and non-modifiable risk factors related to the need for revision.

As mentioned above, readmission rates after TJA in the present meta-analysis were significantly higher among CKD patients than among those without CKD. Another review and meta-analysis reported that the overall readmission rates after THA were 5.6% at 30 days and 7.7% at 90 days, and for TKA were 3.3% at 30 days and 9.7% at 90 days; the leading reason for readmission were joint-specific for THA and surgical site infection for TKA, followed by DVT, pulmonary embolism, and cardiac dysrhythmia [53]. The early successes commonly associated with TJA are compromised by such postoperative complications, and readmission is often considered an indictment of surgical management; however, no consensus has been reached on the main reasons for readmission after primary TJA [53], and further research is essential to determine trends in readmission rates and reasons for readmission.

### Deep vein thrombosis (DVT)

In the present study, no significant differences were found in the presence of DVT between patients with and without CKD who underwent TJA. Although DVT has been shown to occur commonly after joint replacement surgeries, and has been reported to cause unfavorable outcomes after TJA, a recent study of national trends in the United States showed that DVT incidence actually declined for TKA (0.86% to 0.45%) and THA (0.55% to 0.24%) over a 10-year period from 2001 to 2011 [54]. The explanation for this trend is that DVT prophylaxis has been the focus of surgeons performing TJA, along with the recognition of higher risk for DVT among older patients, African Americans and patients with comorbidities [54]. This may, at least in part, explain our result in conjunction with the characteristics of our CKD patient population. A systematic review and meta-analysis conducted in 2015 examined evidence from 54 studies across ten previous years and identified several potential factors associated with venous thromboembolism (VTE) occurring after THA and TKA including older age, female, history of VTE, higher body mass index (BMI), longer surgeries and bilateral surgeries [55]. Decreased kidney function is associated with an increased risk of venous thrombosis and, in particular, in combination with arterial

thrombosis, is increased additionally in patients with moderate and severe reduction in kidney function undergoing surgery [56], however, the types of surgical setting were not specified. In the present study, the database lacked information about DVT prophylaxis, therefore, our estimation of associations between CKD and DVT may include bias. Nevertheless, continued focus on DVT prophylaxis and perhaps applying more aggressive management strategies may help to reduce the rate of DVT among those at increased risk [54].

### Transfusion

CKD was found significantly associated with perioperative blood transfusion in the present review and meta-analysis. A previous study analyzing a large statewide database from the year 2006 to 2011 reported that overall utilization of blood transfusion in TJA remained high over time, with nearly 25% of their study cohort [57]. It is also found that hip arthroplasty more often required transfusion during surgery than knee arthroplasty, and risk was even greater in bilateral procedures. Transfusion was more common among females, older patients and those with a higher burden of comorbidities [57]. CKD is commonly associated with both lower hemoglobin levels and elevated risks of bleeding, which may explain the greater risk of blood transfusion in CKD after TJA.

### Surgical site infection

The result in this review and meta-analysis indicated that CKD patients had higher risk of surgical site infection than non-CKD patients after TJA. Surgical site infection is previously estimated to occur in 1% to 2.5% of cases annually after TJA [58]. It is thought to pose a great challenge on the joint replacement, and also place a substantial burden on the healthcare system. A recent review documented that advances in surgical technique, sterile protocol, and operative procedures have been instrumental in minimizing surgical site infections and may account for the recent plateau in rising rates after TKA and THA [59]. In the present review and meta-analysis, CKD group might contain ESRD patients who are susceptible to infections, thus explains the excess risk of surgical site infection compared to non-CKD. Also, the fact that CKD patients are more prone to surgical site infections might attribute to increased related conditions such as diabetes or poor nutrition.

### Cardiovascular complications

## Strengths And Limitations

The present review and meta-analysis are the first to be conducted on comorbid CKD and outcomes after elective TJA. The analysis was strengthened by using the data of a large number of patients (2,141,393) from the 19 included studies. In addition, the analyses in this meta-analysis were based on the most recent studies; the clinical reports included were all

published within last 10 years and most were within the recent three years, which may avoid the possible influence of progress in aftercare or surgical technique.

Nevertheless, this study still has several limitations, including that the data of all included studies had been analyzed retrospectively, which means that the level of evidence is moderate, as noted in guidelines for systematic reviews [68], and also that causation cannot be inferred. Although CKD might impact the outcomes differently in TKA and THA, the majority of included studies reported findings without separating TKA from THA, so they were not analyzed separately in the present meta-analysis. Also, CKD is often associated with multiple comorbid conditions such as obesity, diabetes mellitus, cardiovascular disease, etc., each of which is known as an independent risk factor in patients undergoing TJA. However, not all included studies were controlled for such factors and therefore possible confounding cannot be fully excluded. Consequently, the potential interaction of these factors may over-emphasize our results. Future prospective study is highly warranted to more accurately investigate the impact of CKD on each total arthroplasty procedure separately, and to also address the prognostic roles of different CKD stages.

## Conclusions

Underlying CKD predicts adverse outcomes after elective TJA with increased risk of mortality, re-admission, surgical site infection and blood transfusion. The findings of this review and meta-analysis highlight CKD as a critical contributor to complications after TJA and may be helpful to surgeons when advising patients about associated risks of TJA.

## Declarations

### List of Abbreviations

hip arthroplasty (THA)

total knee arthroplasty (TKA)

chronic kidney disease (CKD)

total joint arthroplasty (TJA)

deep vein thrombosis (DVT)

Centers for Disease Control

confidence intervals (CI)

### Ethics approval and Patient consent

Ethical approval and patient consent are not required for the meta-analysis.

## Consent for publication

Not applicable

## Availability of data and materials

All data relevant to the study are included in the article.

## Conflict of interests

The authors declare they have no conflicts of interest associated with this study.

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## Tables

Table 1. The characteristics of the studies included in this study

| First author (year) | Data Source | Total no. of pts | Group | CKD stage | Criteria | No. of pts | Type of arthroplasty (THA/TKA) (%) | Age (yr) | Male (%) | DM (%) | CAD/MI/CHF (%) | Anemia (%) | Length of follow up |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Jamsa (2018) | Institutional database | 18575 | Severe CKD | 5 | eGFR < 15 | 35 | 47.5%/52.5% | 69^ | 37% | 8% | 11% | 11% | 7.8 Y^ |
| | | | Severe CKD | 4 | eGFR 15-29 | 81 | | | | | | | |
| | | | Moderate CKD | 3 | eGFR 30-59 | 2023 | | | | | | | |
| | | | Mild CKD | 2 | eGFR 60-89 | 9917 | | | | | | | |
| | | | Normal | 1 | eGFR > 90 | 6519 | | | | | | | |
| Kaiser (2018) | Institutional data | 3301 | Moderate to Severe CKD | 3b-4 | eGFR 15–45 | 166 | 61.9%/38.1% | 76 | 36% | 24% | NA | NA | in-hospital |
| | | | Control | 1-3a | eGFR > 45 | 3135 | | 68 | 34% | 12% | | | |
| Rhee (2018) | CIHI-DAD 2000-2014 | 10123 | CKD | NA | NA | 217 | 100%/0% | 66 | 44% | | NA | NA | 1 Y |
| | | | Control | | | | | | | | | | |
| | | 17243 | CKD | NA | NA | 370 | 0%/100% | 67 | 40% | | NA | NA | |
| | | | Control | | | | | | | | | | |
| Urish (2018) | Nationwide Readmission Database 2014 | 224465 | CKD | NA | NA | 10959 | 0%/100% | NA | 37% | 22% | 2% | NA | 30 day |
| | | | Control | | | 213506 | | | | | | | |
| Kuo (2017) | NHIRD of Taiwan | 13844 | CKD | 3-5 | eGFR <60 | 1459 | 100%/0% | 72 | 33% | 100% | 29% | NA | 1.9 Y |
| | | | Control | 1-2 | eGFR >=60 | 12385 | | 70 | 22% | | 22% | NA | 2.1 Y |
| Li (2017) | Institutional data | 1274 | Moderate to Severe CKD | 3-5 | eGFR <60 | 32 | 61%/39% | 65 | NA | NA | 10% | NA | in-hospital |
| | | | Mild CKD | 2 | eGFR 60-89 | 103 | | | | | | | |
| | | | Normal | 1 | eGFR >90 | 1139 | | | | | | | |
| Siracuse (2017) | State Inpatient Database, 2006-2011 | 433638 | CKD | NA | NA | 14756 | 0%/100% | 67 | 36% | 20% | 2% | 15% | 30 day |
| | | | Control | | | 418882 | | | | | | | |
| Cavanaugh (2016) | NIS 2007 -2011 | 1016686 | CKD | 3-5 | eGFR <60 | 38308 | THA & TKA | 72 | 49% | 10% | 13% | NA | in-hospital |
| | | | Control | 1-2 | eGFR >=60 | 978378 | | 66 | 39% | 1% | 2% | NA | |
| Erkocak (2016) | Institutional database | 1077 | CKD | 3-5 | eGFR <60 | 359 | 52.9%/47.1% | 68 | 55% | NA | NA | NA | in-hospital |
| | | | Control | 1-2 | eGFR >=60 | 718 | 52.9%/47.1% | 67 | 55% | NA | NA | NA | |
| Kuo (2016) | Institutional registry | 615 | CKD | 3-5 | eGFR <60 | 205 | 100%/0% | 72 | 14% | 30% | 15% | NA | 2.7 Y |
| | | | Control | 1-2 | eGFR >=60 | 410 | | 71 | 18% | 13% | 6% | NA | |
| Siracuse (2016) | State Inpatient Database, 2006-2011 | 268518 | CKD | NA | NA | 9828 | 100%/0% | | | 11% | 2% | 16% | 30 day |
| | | | Control | | | 258690 | | | | | | | |
| Warth | ACS NSQIP 2006-2012 | 25116 | CKD | 3-5 | eGFR <60 | 12558 | Primary THA & TKA | 73 | 30% | 24%% | 1% | NA | 30 day |

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| (2015) | | | Control | 1-2 | eGFR >=60 | 12558 | | 71 | 32% | 23% | 1% | NA | |
| Deegan (2014) | Institutional database | 779 | CKD | 3 | eGFR 30-59 | 377 | 29%/71% | 72 | 29% | 17% | 5% | NA | 2.9 Y |
| | | | Control | 1-2 | eGFR >=60 with proteinuria | 402 | 29%/71% | 72 | 43% | 20% | 3% | NA | 2.6 Y |
| Graves (2014) | Institutional database | 380 | Severe CKD | 4-5 | eGFR <30 | 13 | 35.5%/61.5% | 73 | 77% | | NA | 85% | 1 Y |
| | | | Moderate CKD | 3 | eGFR 30-59 | 73 | 45.2%/54.8% | 75 | 42% | | NA | 37% | |
| | | | Control | 1-2 | eGFR >=60 | 294 | 63.3%/36.7% | 67 | 46% | | NA | 13% | |
| Miric (2014)a | TJRR | 20720 | CKD | 3-5 | eGFR <60 | 1269 | 100%/0% | 75^ | 43% | 40% | 11% | NA | |
| | | | Control | 1-2 | eGFR >=60 | 17394 | | 65^ | 42% | 17% | 2% | NA | |
| Miric (2014)b | TJRR | 41852 | CKD | 3-5 | eGFR <60 | 2686 | 0%/100% | 73^ | 40% | 46% | 12% | NA | 2.1 Y^ |
| | | | Control | 1-2 | eGFR >=60 | 34196 | | 67^ | 37% | 25% | 3% | NA | |
| Augustin (2013) | Institutional Total Joint Registry | 270 | Severe CKD | 4-5 | eGFR <30 | 90 | 38.9%/ 61.1% | 72 | 41% | NA | 60% | NA | in-hospital |
| | | | Control | 1-2 | eGFR >=60 | 180 | 38.9%/61.1% | 72 | 41% | NA | 22% | NA | |
| Jamsen (2013) | Institutional database | 1998 | Severe CKD | 4-5 | eGFR <30 | 9 | Primary THA & TKA | NA | 27% | NA | NA | 15% | 4.4 Y^ |
| | | | Moderate CKD | 3 | eGFR 30-59 | 304 | | | | | | | |
| | | | Mild CKD | 2 | eGFR 60-89 | 467 | | | | | | | |
| | | | Normal | 1 | eGFR >=60 | 106 | | | | | | | |
| Bozic (2012) | Medicare 1998-2007 | 40919 | CKD | NA | NA | NA | 100%/0% | NA | NA | NA | NA | NA | 10 Y |
| | | | Control | | | NA | | NA | NA | NA | NA | NA | |

CKD: chronic kidney disease; DM: diabetes mellitus; CAD: coronary artery disease; MI: myocardial infarction; CHF: congestive heart failure

TKA: total knee arthroplasty; THA: total hip arthroplasty

CIHI-DAD: Canadian Institute for Health Information Discharge Abstract Database

NHIRD: National Health Insurance Research Database

NIS: National Inpatient Sample

TJRR: Total Joint Replacement Registry

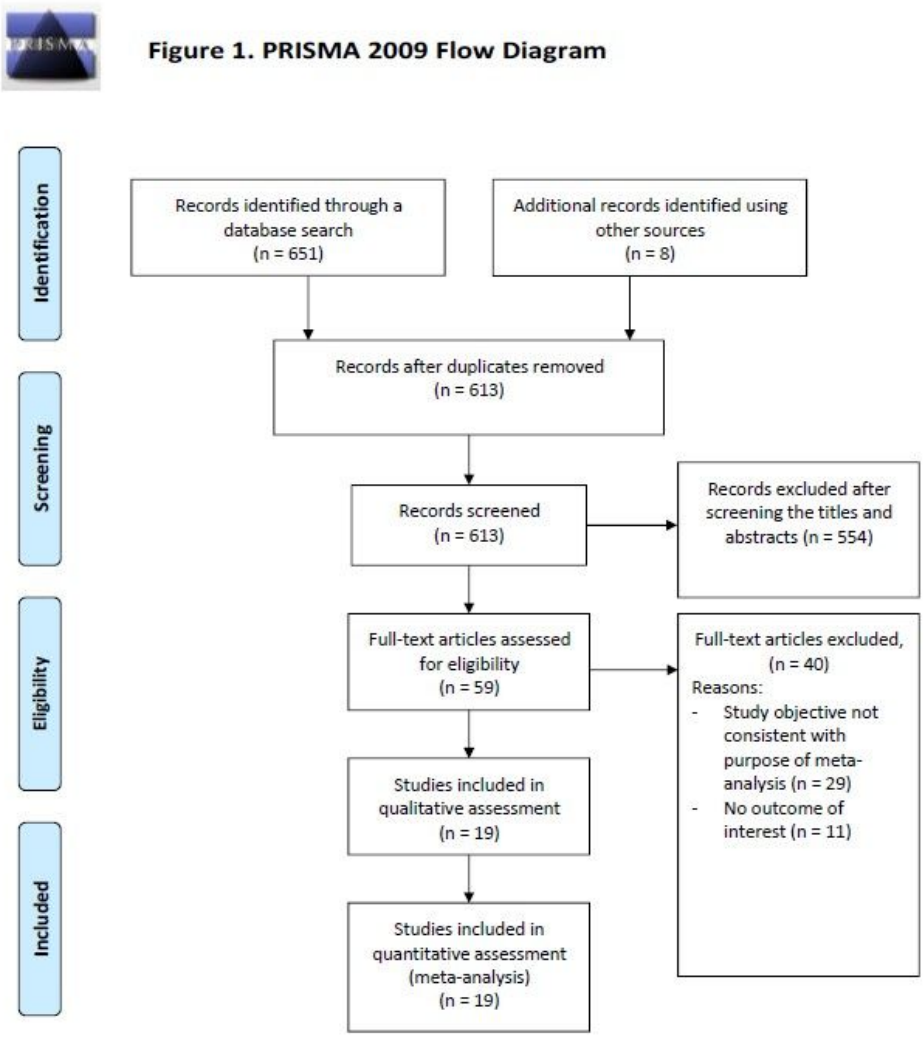
ACS NSQIP: American College of Surgeons National Surgical Quality Improvement Program

Table 2

| First author (year) | Statistics with study removed | | | | |
|---|---|---|---|---|---|
| | Points | Lower limit | Upper limit | Z-Value | P-Value |
| **Mortality** | | | | | |
| Jamsa (2018) | 2.13 | 1.83 | 2.49 | 9.68 | <0.001 |
| Rhee (2018) | 2.21 | 1.90 | 2.56 | 10.33 | <0.001 |
| Rhee (2018) | 2.18 | 1.87 | 2.54 | 10.06 | <0.001 |
| Kuo (2017) | 2.18 | 1.84 | 2.58 | 9.07 | <0.001 |
| Cavanaugh (2016) | 2.20 | 1.84 | 2.62 | 8.79 | <0.001 |
| Erkocak (2016) | 2.21 | 1.91 | 2.56 | 10.59 | <0.001 |
| Warth (2015) | 2.22 | 1.91 | 2.59 | 10.17 | <0.001 |
| Deegan (2014) | 2.19 | 1.88 | 2.55 | 10.03 | <0.001 |
| Graves (2014) | 2.20 | 1.90 | 2.56 | 10.37 | <0.001 |
| Miric (2014)a | 2.30 | 2.01 | 2.64 | 11.98 | <0.001 |
| Miric (2014)b | 2.23 | 1.89 | 2.63 | 9.52 | <0.001 |
| Jamsen (2013) | 2.20 | 1.90 | 2.56 | 10.32 | <0.001 |
| Bozic (2012) | 2.08 | 1.90 | 2.27 | 16.26 | <0.001 |
| **Re-operation** | | | | | |
| Rhee (2018) | 1.27 | 0.81 | 1.98 | 1.05 | 0.295 |
| Rhee (2018) | 1.26 | 0.80 | 1.97 | 0.99 | 0.322 |
| Kuo (2016) | 1.07 | 0.91 | 1.26 | 0.85 | 0.396 |
| Warth (2015) | 1.29 | 0.73 | 2.30 | 0.88 | 0.380 |
| Deegan (2014) | 1.35 | 0.85 | 2.13 | 1.27 | 0.202 |
| Miric (2014)a | 1.39 | 0.89 | 2.18 | 1.43 | 0.152 |
| Miric (2014)b | 1.34 | 0.82 | 2.20 | 1.18 | 0.237 |
| **Re-admission** | | | | | |
| Urish (2018) | 1.44 | 1.24 | 1.67 | 4.81 | <0.001 |
| Kuo (2017) | 1.54 | 1.22 | 1.95 | 3.58 | <0.001 |
| Siracuse (2017) | 1.63 | 1.25 | 2.13 | 3.61 | <0.001 |
| Kuo (2016) | 1.45 | 1.18 | 1.79 | 3.50 | <0.001 |
| Siracuse (2016) | 1.64 | 1.28 | 2.11 | 3.90 | <0.001 |
| Deegan (2014) | 1.66 | 1.33 | 2.06 | 4.51 | <0.001 |
| Miric (2014)a | 1.61 | 1.28 | 2.02 | 4.04 | <0.001 |
| Miric (2014)b | 1.62 | 1.28 | 2.04 | 4.03 | <0.001 |
| **Deep Vein Thrombosis** | | | | | |
| Kuo (2017) | 1.35 | 1.00 | 1.82 | 1.96 | 0.049 |
| Li (2017) | 1.19 | 1.01 | 1.41 | 2.02 | 0.043 |
| Cavanaugh (2016) | 1.28 | 0.90 | 1.84 | 1.38 | 0.169 |
| Warth (2015) | 1.36 | 0.96 | 1.94 | 1.72 | 0.085 |
| Miric (2014)a | 1.30 | 0.96 | 1.78 | 1.68 | 0.092 |
| Miric (2014)b | 1.36 | 1.01 | 1.82 | 2.05 | 0.041 |
| **Transfusion** | | | | | |
| Kaiser (2018) | 2.18 | 1.73 | 2.74 | 6.58 | <0.001 |
| Rhee (2018) | 2.48 | 1.92 | 3.21 | 6.94 | <0.001 |
| Rhee (2018) | 2.48 | 1.92 | 3.21 | 6.94 | <0.001 |
| Cavanaugh (2016) | 3.03 | 1.74 | 5.27 | 3.92 | <0.001 |
| Kuo (2016) | 1.98 | 1.61 | 2.42 | 6.56 | <0.001 |
| Warth (2015) | 3.06 | 1.82 | 5.14 | 4.24 | <0.001 |
| Graves (2014) | 2.19 | 1.73 | 2.76 | 6.62 | <0.001 |
| Augustin (2013) | 2.38 | 1.87 | 3.03 | 7.00 | <0.001 |
| **Surgical Site Infection** | | | | | |

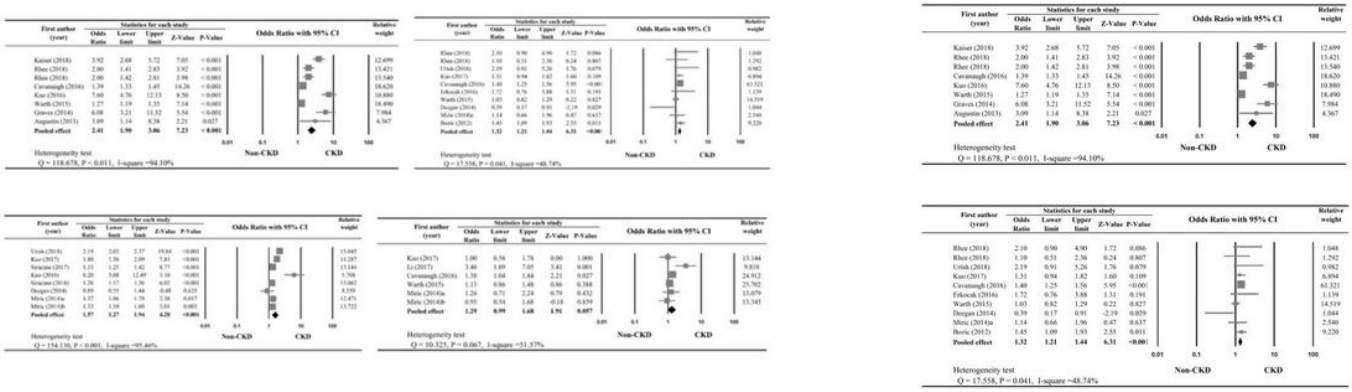
| | | | | | |
|---|---|---|---|---|---|
| Rhee (2018) | 1.32 | 1.21 | 1.44 | 6.17 | <0.001 |
| Rhee (2018) | 1.33 | 1.21 | 1.45 | 6.32 | <0.001 |
| Urish (2018) | 1.32 | 1.21 | 1.44 | 6.17 | <0.001 |
| Kuo (2017) | 1.32 | 1.21 | 1.45 | 6.10 | <0.001 |
| Cavanaugh (2016) | 1.21 | 1.05 | 1.39 | 2.65 | 0.008 |
| Erkocak (2016) | 1.32 | 1.21 | 1.44 | 6.21 | <0.001 |
| Warth (2015) | 1.38 | 1.26 | 1.52 | 6.73 | <0.001 |
| Deegan (2014) | 1.34 | 1.23 | 1.46 | 6.57 | <0.001 |
| Miric (2014)a | 1.33 | 1.22 | 1.45 | 6.31 | <0.001 |
| Bozic (2012) | 1.31 | 1.20 | 1.43 | 5.81 | <0.001 |

## Figures



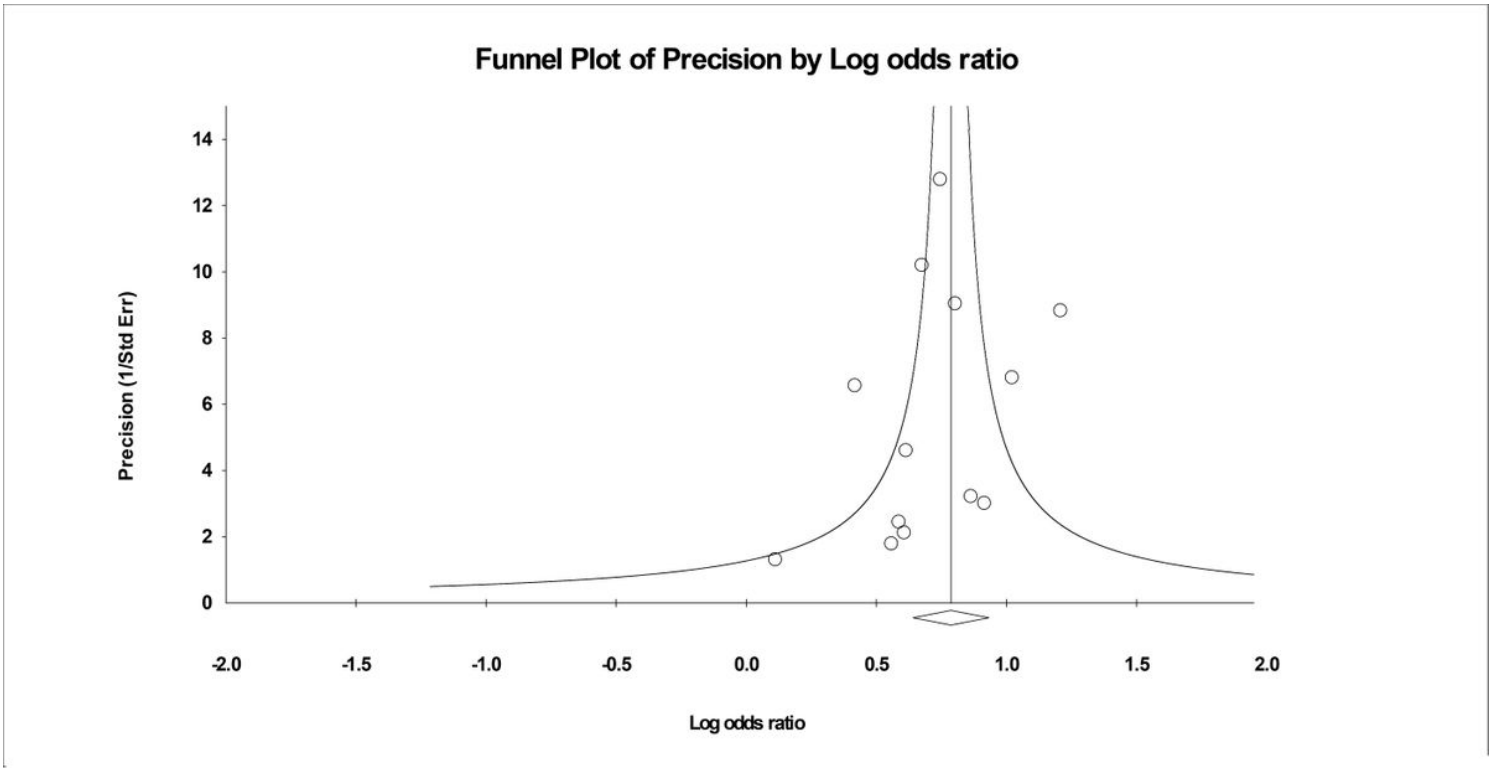

## Figure 1

PRISMA Flow Diagram



## Figure 2

Meta-analysis for outcomes




## Figure 3

Analysis of publication bias for mortality

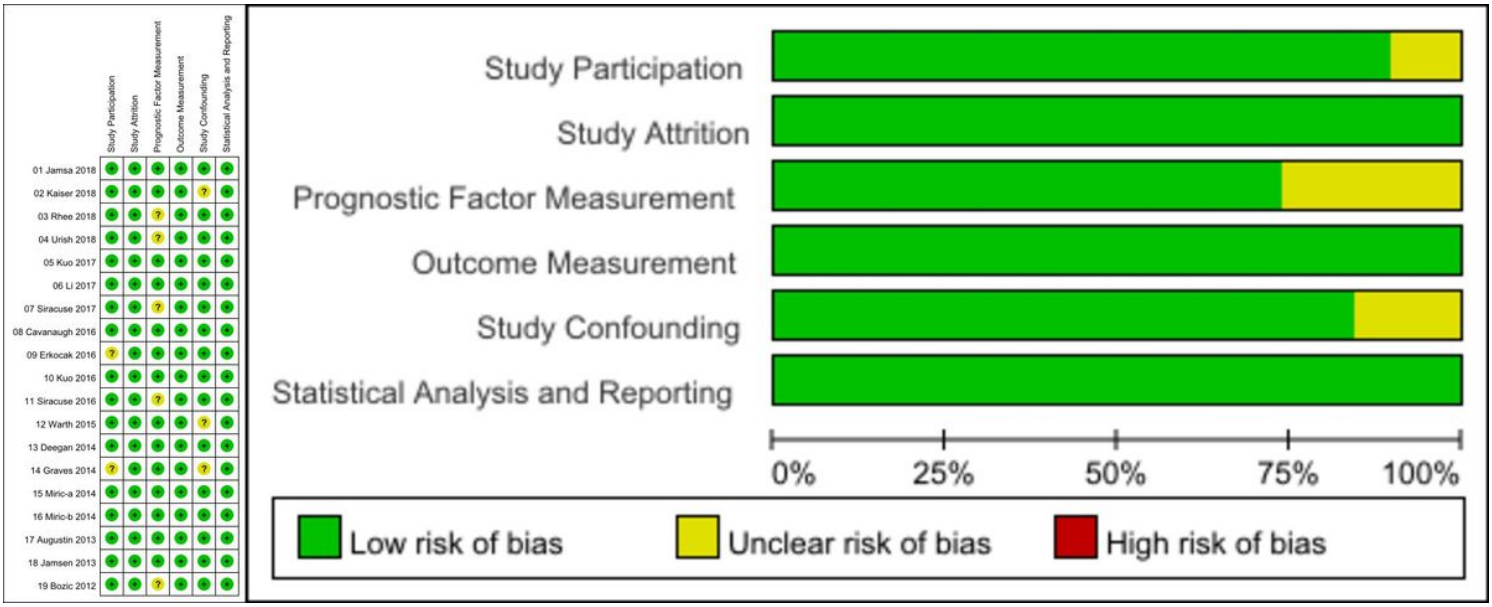



**Figure 4**

Quality Assessment

## Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- PRISMA2009Checklistr.doc