


CLINICAL ARTICLE

Incidence and Risk Factors of In-Hospital Prosthesis-Related Complications Following Total Knee Arthroplasty: A Retrospective Nationwide Inpatient Sample Database Study

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Objective: To examine the incidence and risk factors of in-hospital prosthesis-related complications (PRCs) following total knee arthroplasty (TKA) using a large-scale national database.

Methods: A retrospective database analysis was performed based on Nationwide Inpatient Sample (NIS) from 2005–2014. Patients who underwent TKA were included. The recruited cases were divided into two groups according to the occurrence of PRCs. Patient demographics (age, sex, and race), hospital characteristics (type of admission and payer, and bedsize, teaching status, location, and region of hospital), length of stay (LOS), total charges during hospitalization, in-hospital mortality, comorbidities, and perioperative complications were analyzed.

Results: A total of 1,227,244 TKAs were captured from the NIS database. There were 8484 cases of in-hospital PRCs after TKA and the overall incidence was 0.69%, with a slight downward trend annually. Periprosthetic joint infection (PJI) was the main category among PRCs (0.20%), followed by mechanical loosening (0.04%), dislocation (0.02%), and periprosthetic fracture (PPF) (0.01%). Patients suffered from in-hospital PRCs were 3 years younger (64 years vs 67 years) and 6.51% more likely to be male (43.60% vs 37.09%) compared to the nonaffected population ($P < 0.0001$). Additionally, patients experiencing in-hospital PRCs after TKA were 2.11% less likely through elective admission (92.07% vs 94.18%) while 2.34% more likely in teaching hospital (45.53% vs 43.19%) than those without these complications ($P < 0.0001$). Furthermore, the occurrence of in-hospital PRCs was associated with longer LOS (4 days vs 3 days; $P < 0.0001$), more total charges (\$53,418 vs \$41,204, $P < 0.0001$), and higher in-hospital mortality (0.30% vs 0.07%; $P < 0.0001$). Multivariate logistic regression was performed to identify independent risk factors of in-hospital PRCs after TKA which included younger age, male, non-elective admission, teaching hospital, deficiency and chronic blood loss anemia, coagulopathy, congestive heart failure, depression, diabetes with chronic complications, fluid and electrolyte disorders, pulmonary circulation disorders, metastatic cancer, and weight loss. Besides, in-hospital PRCs after TKA were associated with secondary osteoarthritis, inflammatory arthritis, prior knee arthroscopy, acute renal failure, acute myocardial infarction, deep vein thrombosis, sepsis, transfusion, and wound dehiscence.

Conclusion: It is beneficial to study the risk factors of in-hospital PRCs after TKA to ensure the appropriate management and optimize consequences although a relatively low incidence was identified.

Key words: Arthroplasty; Complications; Database; Knee; Prostheses and Implants; Replacement

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Introduction

Total knee arthroplasty (TKA) has been proven to be one of the most successful and effective procedures for alleviating pain, restoring function, and improving quality of life in patients with severe knee diseases¹⁻³. Currently, more than 1,000,000 TKAs are performed each year in the United States, which is expected to increase up to 3,480,000 by 2030⁴. However, implant failure and total knee revision (TKR) procedures may occur, most commonly as a result of prosthesis-related complications (PRCs), such as periprosthetic joint infection (PJI), mechanical loosening, dislocation, and periprosthetic fracture (PPF)^{3,5-9}.

PRCs are a series of catastrophic events that place heavy burdens on the patients as well as healthcare system^{1-3,8-11}. They have been found to be associated with severe pain, poor function of joint or even postoperative disability, prolonged length of stay (LOS), increased rates of readmission, and higher mortality^{1,2,10,12-14}. Most PRCs will result in TKR surgeries. Currently, the demand for TKR procedures continues to rise, despite of great advancements in surgical techniques and component design^{3,4,8}. It is estimated that the number of TKR procedures performed annually surpasses 100,000 in the United States, with a direct medical cost nearly \$2.7 billion^{4,8}.

The reported incidence of PRCs after TKA varies mainly according to the category and the corresponding follow-up period of specific adverse events, such as PJI (0.50%–3.73%), PPF (0.30%–2.50%), mechanical loosening (0.98%), and dislocation (0.15%–0.50%)^{1,2,5,10,12,15-22}. Consequently, preoperative identification of patients at increased risk of early PRCs allows for development of strategies with purpose of moderating postoperative outcomes and mitigating the need for TKR^{2,5,8-14,18,22}. Numerous risk factors of PJI after TKA have been reported in prior literatures including younger age, male, diabetes, rheumatoid arthritis, corticosteroid therapy, blood transfusion, alcohol abuse, drug abuse, smoking, posttraumatic arthritis, prior knee arthroscopy (PKA), chronic pulmonary disease, liver disease, peripheral vascular disease, coagulopathy, malignancy, myocardial infarction, urinary tract infection, and wound dehiscence^{1,2,11,12,14-16,21,23-27}. Furthermore, the patient-related risk factors of PPF include advanced age, female, osteoporosis, rheumatoid arthritis, corticosteroid therapy, and Parkinson's disease^{5,10,20,28}. Additionally, the risk factors of mechanical loosening such as younger age, PKA, diabetes, and hyperglycemia also have been identified^{17,23,26}. Previous findings suggest that obesity, female, and neuropsychiatric disorders may increase the risk of dislocation^{18,19}.

However, there is no study so far discussing the incidence and risk factors of the in-hospital PRCs following TKA, based on a large-scale sample. Therefore, the aim of this study was to: (i) analyze the overall and annual incidence of in-hospital PRCs after TKA during a decade; (ii) clearly describe the adverse outcomes in inpatients suffered from PRCs undergoing TKA; and (iii) identify the risk factors of in-hospital PRCs following TKA. Patient demographics, hospital characteristics, length of stay (LOS), total charges during hospitalization, in-hospital mortality, comorbidities, and perioperative complications were analyzed using a national database.

Methods

Data Source

The Nationwide Inpatient Sample (NIS) database, conducted by the Healthcare Cost and Utilization Project, and sponsored by the Agency for Healthcare Research and Quality, was the data source of this study. In the United States, NIS represents the largest all-payer database of hospital admissions. NIS collects a stratified sample from more than 1000 hospitals, of approximately 20% of the hospitalizations in the United States each year^{8,29}. The information, including patient demographics, hospital characteristics, LOS, total charges, type of payer, in-hospital mortality, and diagnostic and procedural codes from International Classification of Diseases (ninth revision) Clinical Modification (ICD-9-CM) were obtained from this database. This observational study utilized deidentified publicly available data, thus it was deemed exempt.

Data Collection

Patients who satisfied the following inclusion criteria were included in this study: (i) patients with available hospitalized information registered in NIS database from 2005 to 2014; (ii) patients undergoing TKA with the ICD-9-CM procedural code 81.54 (n = 1,228,879). Patients were excluded from the study if they were: (i) less than 18 years of age; (ii) diagnosed with osteomyelitis; or (iii) diagnosed with pathologic fracture (n = 1635)³⁰. Depending on the occurrence of PRCs, the selected cases were divided into two groups. In-hospital PRCs were defined by ICD-9-CM diagnostic codes including PJI (996.66/996.67/998.5/998.51/998.59), PPF (996.44), mechanical loosening (996.41/996.43/996.45), dislocation (996.42), and other prosthesis-related complications (996.4/996.40/996.46/996.47/996.49/996.77/996.78/996.79)⁶⁻⁸.

Patient demographics, hospital characteristics, outcome measures (LOS, total charges, and in-hospital mortality) were assessed. Perioperative complications during hospitalization were obtained from the database by ICD-9-CM diagnostic code. Medical complications were defined as acute renal failure, acute myocardial infarction, pneumonia, pulmonary embolism, stroke, postoperative delirium, urinary tract infection, deep vein thrombosis, sepsis, postoperative shock and blood transfusion. Surgical complications included wound dehiscence, hemorrhage/seroma/hematoma, non-healing surgical wound, and nerve injury^{7,30}. Additional comorbidities were analyzed at the author's discretion if they had been determined as significant risk factors for any one of the PRCs in previous studies^{1,2,5,6,11,12,14,15,28-20,24-26,28}.

Outcome Measures

LOS

LOS is calculated by subtracting the admission date from the discharge date. Same-day stays are therefore coded as 0. Patients received operations with longer LOS commonly means adverse outcomes.

Total Charges

Total charges contain the total charges of inpatient and do not include professional fees and non-covered charges. Values are rounded to the nearest dollar. Patients received operations with more total charges commonly means adverse consequences.

In-Hospital Mortality

In-hospital mortality is the number of patients died in the hospital divided by the total number of inpatients. Patients received operations with higher in-hospital mortality commonly means adverse effects.

Data Analysis

All the statistical analyses were conducted *via* the statistical software, R version 3.5.3 (The R Foundation Inc., Auckland, New Zealand). Significant differences between two groups were determined by independent t test for continuous data and chi-square test for categorical data. Multivariate logistic regression with the stepwise method was applied to investigate independent risk factors of PRCs. All variables, including demographics, hospital characteristics, type of payer, and comorbidities that were provided by the NIS were simultaneously entered into the regression analysis (Table 1). Univariate and multivariate logistic regression models were established to evaluate the association of additional comorbidities or perioperative complications with PRCs. Statistical significance was defined by an alpha value of $P \leq 0.001$ because of the large sample size²⁹.

TABLE 1 Variables entered into the logistic regression analysis

Variables categories	Specific variables
Patient demographics	Age (18–44 years, 45–64 years, 65–74 years, and ≥ 75 years), sex (male and female), race (White, Black, Hispanic, Asian or Pacific Islander, Native American and Other)
Hospital characteristics	Type of admission (non-elective, elective), bedsize of hospital (small, medium, large), teaching status of hospital (nonteaching, teaching), location of hospital (rural, urban), region of hospital (Northeast, Midwest or North Central, South, West), type of payer (Medicare, Medicaid, Private insurance, Self-pay, No charge, Other)
Comorbidities	AIDS, alcohol abuse, deficiency anemia, rheumatoid diseases, chronic blood loss anemia, congestive heart failure, chronic pulmonary disease, coagulopathy, depression, diabetes (uncomplicated), diabetes (with chronic complications), drug abuse, hypertension, hypothyroidism, liver disease, lymphoma, fluid and electrolyte disorders, metastatic cancer, neurological disorders, obesity, paralysis, peripheral vascular disorders, psychoses, pulmonary circulation disorders, renal failure, solid tumor without metastasis, peptic ulcer disease, valvular disease, weight loss

Results

Incidence of In-Hospital PRCs in Patients Undergoing TKA

A total of 1,227,244 TKAs were obtained from the NIS database during the period of 2005 to 2014. Totally, there were 8484 cases of in-hospital PRCs with an incidence of 0.69%

TABLE 2 Patient characteristics and outcomes of PRCs after TKA (2005–2014)

Parameter	No PRCs	PRCs	P
Total (n = count)	1,218,760	8484	–
Total incidence (%)	0.69		
Age (median, years)	67 (59–74)	64 (56–72)	<0.0001
Age group (%)			
18–44	1.73	4.93	<0.0001
45–64	40.85	47.49	
65–74	34.83	28.23	
≥ 75	22.58	19.35	
Sex (% female)	62.91	56.40	<0.0001
Race (%)			
White	83.40	82.50	0.01
Black	7.35	7.51	
Hispanic	5.30	6.14	
Asian or Pacific Islander	1.25	1.03	
Native American	0.48	0.59	
Other	2.22	2.24	
Type of admission (% elective)	94.18	92.07	<0.0001
Bedsize of hospital (%)			
Small	19.40	19.54	0.58
Medium	25.72	25.22	
Large	54.89	55.24	
Teaching status of hospital (% teaching)	43.19	45.53	<0.0001
Location of hospital (% urban)	87.85	88.26	0.26
Region of hospital (%)			
Northeast	16.40	17.08	<0.0001
Midwest or North Central	27.48	24.30	
South	36.80	38.14	
West	19.33	20.47	
LOS (median, d)	3 (3–4)	4 (3–6)	<0.0001
Total charges (median, \$)	41,204 (30,532-57,187)	53,418 (37,080-80,637)	<0.0001
Type of payer (%)			
Medicare	55.48	49.05	<0.0001
Medicaid	2.88	4.38	
Private insurance	37.85	40.93	
Self-pay	0.44	0.48	
No charge	0.08	0.12	
Other	3.27	5.03	
In-hospital mortality (%)	0.07	0.30	<0.0001

LOS, length of stay; PRCs, prosthesis-related complications; TKA, total knee arthroplasty.

TABLE 3 Risk factors of PRCs after TKA (2005–2014)

Variable	OR	95% CI	P
Age (years)			
18–44	Ref.	–	–
45–64	0.44	0.40–0.50	<0.0001
65–74	0.30	0.27–0.34	<0.0001
≥75	0.30	0.26–0.34	<0.0001
Female	0.76	0.72–0.80	<0.0001
Race			
White	Ref.	–	–
Black	0.92	0.84–1.01	0.07
Hispanic	1.07	0.97–1.18	0.18
Asian or Pacific Islander	0.84	0.66–1.06	0.14
Native American	1.20	0.88–1.63	0.24
Other	1.00	0.86–1.18	0.97
Elective admission	0.70	0.64–0.76	<0.0001
Bedsize of hospital			
Small	Ref.	–	–
Medium	1.01	0.94–1.08	0.84
Large	1.01	0.95–1.08	0.66
Teaching hospital	1.14	1.09–1.20	<0.0001
Urban hospital	0.96	0.89–1.04	0.30
Region of hospital			
Northeast	Ref.	–	–
Midwest or North Central	0.80	0.74–0.87	<0.0001
South	1.01	0.94–1.08	0.82
West	1.04	0.97–1.13	0.26
Type of payer			
Medicare	Ref.	–	–
Medicaid	1.16	1.02–1.32	0.03
Private insurance	0.93	0.87–1.00	0.05
Self-pay	1.03	0.75–1.43	0.84
No charge	1.15	0.61–2.15	0.66
Other	1.22	1.08–1.38	0.002
Deficiency anemia	1.33	1.24–1.42	<0.0001
Chronic blood loss anemia	1.39	1.18–1.64	0.0001
Congestive heart failure	1.59	1.41–1.80	<0.0001
Coagulopathy	1.47	1.28–1.69	<0.0001
Depression	1.15	1.08–1.24	0.0001
Diabetes with chronic complications	1.31	1.12–1.54	0.0008
Hypertension	0.80	0.76–0.84	<0.0001
Hypothyroidism	0.88	0.82–0.94	0.0004
Fluid and electrolyte disorders	1.61	1.49–1.73	<0.0001
Metastatic cancer	3.53	2.25–5.56	<0.0001
Obesity	0.85	0.80–0.91	<0.0001
Pulmonary circulation disorders	1.71	1.43–2.05	<0.0001
Weight loss	3.24	2.53–4.15	<0.0001

Only significant comorbidities are presented.; CI, confidence interval; OR, odds ratio; PRCs, prosthesis-related complications; TKA, total knee arthroplasty.

(Table 2). It was observed that the incidence of PRCs, including PJI, mechanical loosening, dislocation, PPF, and others, decreased from 0.86% to 0.53% (Fig. 1). PJI (0.20%) was the most common PRCs after TKA, followed by mechanical loosening (0.04%), dislocation (0.02%), and PPF (0.01%), except for the miscellaneous (0.43%) (Fig. 2).

Patient Demographics of Two Groups

Patients affected by in-hospital PRCs were 3 years younger (64 years vs 67 years) and 6.51% more likely to be male

(43.60% vs 37.09%) compared to the nonaffected population ($P < 0.0001$) (Table 2). Consistently, there was significant difference of the age distribution between the two groups, patients suffered from PRCs after TKA with a 12.84% higher incidence among patients younger than 64 years (55.42% vs 42.58%, $P < 0.0001$) (Table 2). However, no significant difference was detected in races between two cohorts at our defined level ($P = 0.01$) (Table 2).

Hospital Characteristics of Two Groups

Not surprisingly, patients suffered from PRCs after TKA were 2.11% less likely through elective admission compared to those without these complications (92.07% vs 94.18%, $P < 0.0001$) (Table 2). Additionally, in-hospital PRCs tended to occur in teaching hospital (45.53% vs 43.19%, $P < 0.0001$) (Table 2). Regarding to the region of hospital, the occurrence of in-hospital PRCs was 3.18% less likely in the Midwest or North Central (24.30% vs 27.48%, $P < 0.0001$) (Table 2). Nevertheless, neither the difference of the hospital bedsize ($P = 0.58$) nor location ($P = 0.26$) between two groups was significant statistically (Table 2).

Adverse outcomes of In-Hospital PRCs Following TKA

As expected, in-hospital mortality of patients with PRCs was significantly higher exceeding four times than patients without a diagnosis of PRCs (0.30% vs 0.07%; $P < 0.0001$) (Table 2). The median LOS with the presence of PRCs was 1 day longer (4 days vs 3 days; $P < 0.0001$) (Table 2). Hence, PRCs increased medical expenditure. It was found that there was an obvious increase of \$12,214 in total hospital charges, with the occurrence of in-hospital PRCs (\$53,418 vs \$41,204, $P < 0.0001$) (Table 2). With regard to the type of payer, the Medicare was observed to took a 6.43% smaller proportion (49.05% vs 55.48%) while Private insurance occupied a 3.08% larger proportion in the PRCs group (40.93% vs 37.85%) ($P < 0.0001$) (Table 2).

Risk Factors of In-Hospital PRCs Following TKA

Logistic regression analysis was performed to identify risk factors of PRCs (Table 3), and the following indicators were determined: teaching hospital (odds ratio [OR] = 1.14; CI = 1.09–1.20), deficiency anemia (OR = 1.33; CI = 1.24–1.42), chronic blood loss anemia (OR = 1.39; CI = 1.18–1.64), congestive heart failure (OR = 1.59; CI = 1.41–1.80), coagulopathy (OR = 1.47; CI = 1.28–1.69), depression (OR = 1.15; CI = 1.08–1.24), diabetes with chronic complications (OR = 1.31; CI = 1.12–1.54), fluid and electrolyte disorders (OR = 1.61; CI = 1.49–1.73), metastatic cancer (OR = 3.53; CI = 2.25–5.56), pulmonary circulation disorders (OR = 1.71; CI = 1.43–2.05), and weight loss (OR = 3.24; CI = 2.53–4.15). Surprisingly, there were several protective factors of PRCs including patients aged 45 years to 64 years (OR = 0.44; CI = 0.40–0.50), patients aged 65 years to 74 years (OR = 0.30; CI = 0.27–0.34), patients older than 75 years (OR = 0.30; CI = 0.26–0.34), female (OR = 0.76; CI = 0.72–0.80), elective admission (OR = 0.70; CI = 0.64–

TABLE 4 Additional comorbidities associated with PRCs after TKA (2005–2014)

Comorbidities	Univariate analysis			Multivariate logistic regression		
	No PRCs	PRCs	P	OR	95% CI	P
Indications for TKA						
Primary osteoarthritis	1,185,426 (99.18%)	6,960 (96.96%)	0.0005	Ref.	–	–
Secondary osteoarthritis	3865 (0.32%)	131 (1.83%)	0.0005	5.48	4.59–6.54	<0.0001
Avascular necrosis	597 (0.05%)	6 (0.08%)	0.0005	1.61	0.72–3.59	0.25
Inflammatory arthritis	5366 (0.45%)	81 (1.13%)	0.0005	2.35	1.89–2.94	<0.0001
Other comorbidities						
Parkinson disease	6545 (0.54%)	46 (0.54%)	1	1.05	0.77–1.44	0.75
Dementia	5515 (0.45%)	60 (0.71%)	0.0007	1.50	1.13–2.00	0.005
Frailty	3230 (0.27%)	27 (0.32%)	0.40	1.27	0.85–1.90	0.25
Smoking	210,597 (17.28%)	1584 (18.67%)	0.0008	1.08	1.02–1.15	0.01
Osteoporosis	58,771 (4.82%)	459 (5.41%)	0.01	1.04	0.94–1.16	0.43
Prior knee arthroscopy	28,330 (2.32%)	788 (9.29%)	<0.0001	4.16	3.83–4.51	<0.0001

CI, confidence interval; OR, odds ratio; PRCs, prosthesis-related complications; TKA, total knee arthroplasty.

TABLE 5 Complications associated with PRCs following TKA (2005–2014)

Complications	Univariate analysis			Multivariate logistic regression		
	No PRCs	PRCs	P	OR	95% CI	P
Medical complications						
Acute renal failure	19,013 (1.56%)	347 (4.09%)	<0.0001	1.30	1.14–1.48	0.0001
Acute myocardial infarction	7955 (0.65%)	125 (1.47%)	<0.0001	1.36	1.13–1.64	0.001
Pneumonia	5611 (0.46%)	134 (1.58%)	<0.0001	1.29	1.06–1.57	0.01
Pulmonary embolism	5140 (0.42%)	107 (1.26%)	<0.0001	1.27	1.03–1.57	0.02
Stroke	6539 (0.54%)	40 (0.47%)	0.46	0.59	0.43–0.81	0.001
Postoperative delirium	12,168 (1%)	159 (1.87%)	<0.0001	1.22	1.03–1.45	0.02
Urinary tract infection	32,165 (2.64%)	418 (4.93%)	<0.0001	1.19	1.06–1.33	0.004
Deep vein thrombosis	5337 (0.44%)	231 (2.72%)	<0.0001	3.99	3.43–4.63	<0.0001
Sepsis	933 (0.08%)	184 (2.17%)	<0.0001	13.29	11.02–16.02	<0.0001
Postoperative shock	105 (0.01%)	7 (0.08%)	<0.0001	1.53	0.64–3.66	0.34
Blood transfusion	183,660 (15.07%)	2298 (27.09%)	<0.0001	1.42	1.28–1.57	<0.0001
Any medical complication*	244,202 (20.04%)	3041 (35.84%)	<0.0001	–	–	–
Surgical complications						
Wound dehiscence	1013 (0.08%)	79 (0.93%)	<0.0001	3.62	2.12–6.17	<0.0001
Hemorrhage/seroma/hematoma	8214 (0.67%)	357 (4.21%)	<0.0001	1.86	1.05–3.32	0.03
Non-healing surgical wound	42 (0%)	5 (0.06%)	<0.0001	2.47	0.81–7.54	0.11
Nerve injury	236 (0.02%)	9 (0.11%)	0.0001	2.16	0.90–5.20	0.09
Any surgical complication†	9379 (0.77%)	431 (5.08%)	<0.0001	–	–	–

* Any medical complication patients with more than one complication are counted only once.; † Any surgical complication patients with more than one complication are counted only once.; CI, confidence interval; OR, odds ratio; PRCs, prosthesis-related complications; TKA, total knee arthroplasty.

0.76), hospital in the Midwest or North Central (OR = 0.80; CI = 0.74–0.87), hypertension (OR = 0.80; CI = 0.76–0.84), hypothyroidism (OR = 0.88; CI = 0.82–0.94), and obesity (OR = 0.85; CI = 0.80–0.91).

Additional Comorbidities and Complications Associated with In-Hospital PRCs Following TKA

In terms of the indications for TKA, patients diagnosed with primary osteoarthritis (POA) were less likely to experience in-hospital PRCs ($P = 0.0005$) (Table 4). However, those diagnosed with secondary osteoarthritis (SOA), avascular

necrosis (AVN), or inflammatory arthritis (IA) undergoing TKA were more likely to suffer in-hospital PRCs ($P = 0.0005$) (Table 4). Additionally, PRCs after TKA tended to occur in patients with histories of dementia, smoking or PKA ($P < 0.001$) (Table 4). In multivariate analysis, SOA (OR = 5.48; CI = 4.59–6.54), IA (OR = 2.35; CI = 1.89–2.94) compared with POA, and PKA (OR = 4.16; CI = 3.83–4.51) were independent risk factors for PRCs after TKA ($P < 0.0001$) (Table 4).

Univariate analysis presented that patients with in-hospital PRCs were more likely to have either medical

perioperative complications during hospitalization including acute renal failure, acute myocardial infarction, pneumonia, pulmonary embolism, postoperative delirium, urinary tract infection, deep vein thrombosis, sepsis, postoperative shock, and blood transfusion, or surgical perioperative complications during hospitalization including wound dehiscence, hemorrhage/seroma/hematoma, non-healing surgical wound, and nerve injury compared with patients without PRCs ($P < 0.0001$) (Table 5). Multivariate analysis showed that in-hospital PRCs after TKA was independently associated with acute renal failure (OR = 1.30; CI = 1.14–1.48), acute myocardial infarction (OR = 1.36; CI = 1.13–1.64), deep vein thrombosis (OR = 3.99; CI = 3.43–4.63), sepsis (OR = 13.29; CI = 11.02–16.02), blood transfusion (OR = 1.42; CI = 1.28–1.57), and wound dehiscence (OR = 3.62; CI = 2.12–6.17).

Discussion

This study provides a large-scale and health-economic analysis of in-hospital PRCs after TKA. With more attention on improving surgical techniques and component design, the incidence of PRCs decreased gradually from 2005 to 2014^{3,4,8} (Fig. 1). An overall incidence of 0.69% of in-hospital PRCs after TKA was firstly identified because prior studies focused on the specific categories of PRCs^{1,2,5,10,12,15–22}. It was observed that PJI was the main complication among PRCs after TKA, followed by mechanical loosening, dislocation, and PPF (Fig. 2). This is totally consistent with the study which was focusing on the analysis of the epidemiology of TKR using the same database⁸. However, the study conducted by our authors identified an overall incidence of 1.96% of in-hospital PRCs after total hip arthroplasty (THA) and found that dislocation was the most common PRCs, followed by PJI, PPF and mechanical loosening. This disparities between TKA and THA reflect their intrinsic features respectively³¹.

It has been proven that both younger age and male are associated with increased risk of PJI or revision after TKA^{1,9,12,23,27,32}. Similar results could also be observed in this study. Approximately, patients affected by PRCs were 3 years younger than those unaffected. Besides, regarding to age distribution, patients younger than 65 years occupied a larger proportion in the PRCs group. Furthermore, in logistic regression analysis, compared with patients aged 18 years to 44 years, patients aged 45 years to 64 years, patients aged 65 years to 74 years, and patients older than 75 years were identified as protective factors of PRCs after TKA. Additionally, it was found that female accounted for a smaller proportion in patients with PRCs and also was identified as a protective factor in logistic regression analysis. On the contrary, younger age and male could statistically be identified as risk factors of PRCs following TKA. One possible explanation accounting for this is that younger and male patients are generally more active than older and female patients and further cause cumulative stresses on the implant, bone, and soft-tissue interfaces over many years, which may lead to higher odds of PJI or mechanical loosening^{1,23}. Another potential explanation may be that younger patients are more

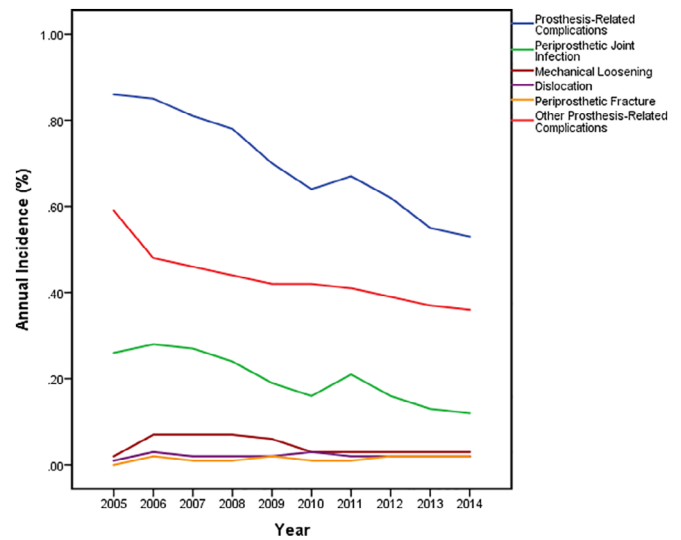


Fig 1 Annual incidence of in-hospital prosthesis-related complications (PRCs) following total knee arthroplasty during a decade. This indicates that the incidence of in-hospital PRCs which include periprosthetic joint infection, mechanical loosening, dislocation, periprosthetic fracture, and others, decreases from 2005 (0.86%) to 2014 (0.53%).

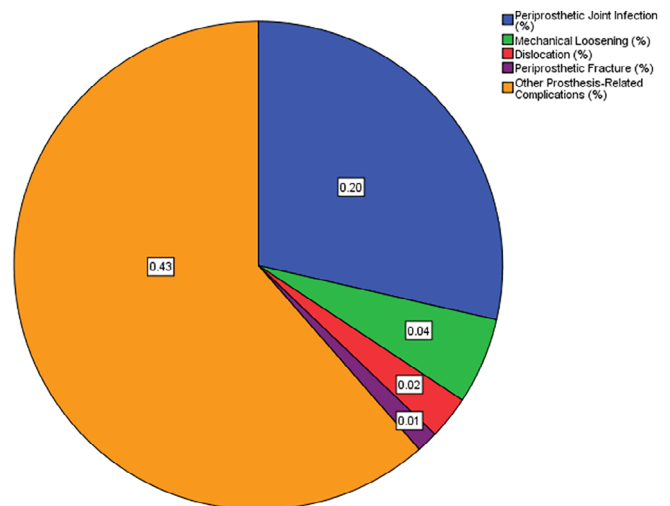


Fig 2 Incidence of specific categories among prosthesis-related complications (PRCs) following total knee arthroplasty. This shows that except for the miscellaneous (0.43%), periprosthetic joint infection (0.20%) is the most common PRCs, followed by mechanical loosening (0.04%), dislocation (0.02%), and periprosthetic fracture (0.01%).

likely to have IA (e.g., rheumatoid arthritis) or SOA (e.g., post-traumatic arthritis) rather than POA. These indications for TKA which were also detected as risk factors of PRCs in this study may be associated either with poor immune response (e.g., corticosteroid therapy) or with multiple prior surgeries (e.g., arthrotomy with open reduction and

internal fixation of the traumatic injury) that increase risk of PJI or PPF^{1,5,12,23,25,27,33}. Considering the context that TKA will be performed more frequently in younger patients, this finding suggests a demand for continued efforts to optimize outcomes in this population. Surgeons may find this information important in counseling their younger patients about the risk of PRCs after TKA^{9,23}.

Not surprisingly, patients undergoing TKA through elective admission were less likely to suffer PRCs. This may be due to that most elective cases have either well healthy conditions or adequate evaluations and preparations preoperatively³⁴. Elective admission was found as a protective factor of PRCs further confirmed this finding. A possible reason for teaching hospital as risk predictors of in-hospital PRCs is that cases in these facilities are commonly challenging with complex comorbidities³⁵. In terms of region of hospital, hospital in the Midwest or North Central was associated with decreased risk of PRCs. However, the reason for this remains unclear but is likely multifactorial⁸.

The occurrence of in-hospital PRCs after TKA was found to be associated with prolonged LOS, extra total charges and higher in-hospital mortality (Table 2). A longer LOS is possibly attributed to several postoperative factors including complications, pain management, ambulatory ability, and family support^{10,36}. The increased total charges are due to not only the extended hospitalization, but also the presence of costly PRCs, such as PJI and PPF^{10,12,15,21,22,36}. PJI, PPF, and revision after TKA that increase rates of mortality have been reported by many researchers^{1,10,16,20,21,22,27,35}.

In order to reduce and ameliorate these challenging events, it is imperative to identify preoperatively whether patients are at high risk of in-hospital PRCs after TKA^{2,5,8-14,18,22}. Logistic regression was performed and a series of risk factors of in-hospital PRCs after TKA were identified (Tables 3-5). It was found that deficiency anemia, chronic blood loss anemia, weight loss, and blood transfusion were risk factors of PRCs. Low level of hemoglobin typically relates to poor nutritional status, and patients undergoing arthroplasty with preoperative anemia are more likely to receive blood transfusion. In line with prior findings, all of these factors are associated with an increased risk of postoperative infection^{1,2,11,14,16,27,31}. Besides, the association between blood transfusion and postoperative infection is probably caused by immunomodulation effect from allogenic blood products^{2,27}. Patients with coagulopathy, acute myocardial infarction or deep vein thrombosis commonly signify coagulation disorder and receive more aggressive anticoagulation or antiplatelet therapy, which may be associated with an increased risk for superficial infections, prolonged drainage, and subsequent deep infections^{2,14,31,37}. In terms of the association between wound dehiscence and PJI, it is possibly mutual and co-existing^{1,14,31}.

In this study, depression was determined as a risk factor of PRCs following TKA, although the underlying mechanisms for this phenomenon remain unknown. It was reported that depressed patients undergoing TKA were prone to suffer revision and PJI, and tended to experience

worse functional outcomes, more surgical complications, increased rates of readmission, and even higher mortality³⁸. Both diabetes with chronic complications and metastatic cancer commonly mean at respective ending stage of diseases, which predispose patients to PJI as a result of their immunosuppressive conditions and impaired defenses against bacteria. Furthermore, microangiopathic changes of diabetic patients reduce the tissue concentrations of antibiotics and cause local tissue ischemia, which consequently affect wound healing^{1,11,12,14,31}. Intriguingly, patients undergoing PKA were at high risk of PRCs, in accordance with the study found that PKA was associated with increased revision rate, postoperative stiffness, PJI, and aseptic loosening after TKA²⁶.

Consistent with previous studies, congestive heart failure, pulmonary circulation disorders, fluid and electrolyte disorders, acute renal failure, and sepsis have also been found to be associated with in-hospital surgical site infections or PRCs following arthroplasty^{31,39}. Interestingly, the results that hypertension, hypothyroidism, and obesity commonly at increased risk of numerous diseases or complications were detected as protective factors of PRCs will warrant further investigate^{1,2,7,25,31}.

The main strengths of our study include its large sample size and national representativeness, and the application of multivariable regression modeling to mitigate confounding. Nevertheless, we acknowledge several limitations inherent to the utilization of the NIS database. First, as with any large administrative data, discrepancy or misclassification in coding and documentation may occur^{6,7,29,31,40}. Second, information of each patient is only recorded during hospitalization, suggesting any complication or outcome that occurs after discharge such as rates of readmission and long-term follow-up will not be captured in this database. This limitation might lead to underestimating the incidence of PRCs because only early period in-hospital cases were included^{8,29,31,39,40}. Additionally, only variables recorded in the NIS database could be evaluated. There are other known procedural and component characteristics that might influence PRCs were unavailable in the NIS database, such as surgical approach, length of operation, cemented or uncemented components, and implant choice^{6,31,39,40}.

In conclusion, in-hospital PRCs are devastating and costly complications occurring after TKA with a general incidence of 0.69%. The annual incidence of PRCs was gradually decreasing from 2005 to 2014. PJI was the most common PRCs, followed by mechanical loosening, dislocation, and PPF. Several risk factors of PRCs following TKA were identified in this study including younger age, male, non-elective admission, teaching hospital, deficiency and chronic blood loss anemia, coagulopathy, congestive heart failure, depression, diabetes with chronic complications, fluid and electrolyte disorders, pulmonary circulation disorders, metastatic cancer, and weight loss. Furthermore, PRCs were associated with secondary osteoarthritis, inflammatory arthritis, prior knee arthroscopy, acute renal failure, acute myocardial infarction, deep vein thrombosis, sepsis, transfusion, and wound dehiscence. Advanced age, female, elective admission, hospital in the Midwest or North Central, hypertension,

hypothyroidism, and obesity were detected to be protective factors. Patients with PRCs after TKA demonstrated extended LOS, more total charges, and higher in-hospital mortality.

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Authorship Declaration

All authors listed meet the authorship criteria according to the latest guidelines of the International Committee of Medical Journal Editors, and all authors are in agreement with the manuscript.

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