Incidence and Risk Factors of Postoperative Delirium Following Total Knee Arthroplasty: A Retrospective Nationwide Inpatient Sample Database Study

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Abstract

Background

Postoperative delirium is a common complication following major surgeries, causing a variety of adverse effects. However, the incidence and risk factors of delirium after total knee arthroplasty (TKA) has not been well studied 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. Patient demographics, comorbidities, length of stay (LOS), total charges, type of insurance, in-hospital mortality, and medical and surgical perioperative complications were evaluated.

Results

A total of 1,228,879 TKAs were obtained from the NIS database. The general incidence of delirium after TKA was 1.00%, which peaked in the year 2008. Patients with delirium after TKA presented more comorbidities, increased LOS, extra hospital charges, wider coverage of medicare, and higher in-hospital mortality (P<0.0001). Delirium following TKA was associated with medical complications during hospitalization including acute renal failure, acute myocardial infarction, pneumonia, pulmonary embolism, stroke, and urinary tract infection. Risk factors of postoperative delirium included advanced age, neurological disorders, alcohol and drug abuse, depression, psychoses, fluid and electrolyte disorders, diabetes, weight loss, deficiency and chronic blood loss anemia, coagulopathy, congestive heart failure, chronic pulmonary disease and pulmonary circulation disorders, peripheral vascular disorders, renal failure, and teaching hospital.

Conclusions

A relatively low incidence of delirium after TKA was identified. Postoperative delirium of TKA was associated with increased comorbidities, LOS, total charges, coverage of medicare, mortality and medical perioperative complications. It is of benefit to study risk factors of postoperative delirium to ensure the appropriate management and moderate its consequences.

Background
Total knee arthroplasty (TKA) remains one of the most successful procedures in alleviating pain and restoring function of the knee [1]. 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 2030 [2]. However, quite a few postoperative patients suffer from postoperative complications.

Postoperative delirium is one of the common complications after TKA, resulting in heavy burdens on individuals and society [1]. Delirium is an acute and fluctuating alteration of mental state characterized by the disturbance of consciousness, cognitive function, or perception. It is regarded to be caused by maladaptation of the brain to the surgical stress [3, 4]. Postoperative delirium is a common complication in geriatric patients after major operations [5, 6]. The reported incidence of delirium after TKA ranges from 0.59–25%, which varied among studies depending on the patient population [1, 7-13]. It has become a heavy burden on healthcare resources because it prolongs hospitalization and increases medical costs [1, 4, 9, 11-14]. About 2.4 million hospitalized elderly patients suffer from delirium and the annual cost ranges from $143 billion to $152 billion [15].

Additionally, postoperative delirium has an adverse impact on patients, family members, and health care practitioners, as it had been shown to be associated with higher mortality, progressive functional impairment, long-term cognitive disorder and other complications such as pneumonia, acute renal failure, pulmonary edema, and myocardial infarction [4, 7, 11-14, 16-20].

In order to optimize postoperative outcomes and prevent complications, it is critical to identify preoperatively whether patients are at high risk of postoperative delirium [1, 4, 11-13, 21]. Several risk factors of postoperative delirium had been reported in previous literatures, among which advanced age is the most frequently acknowledged [1, 4, 9, 11-13, 21-25]. Other risk factors, including a history of dementia, depression, psychiatric illness, cognitive impairment, stroke, polypharmacy, postoperative electrolyte disorders, peripheral vascular diseases, infection during admission (pneumonia and urinary tract infection), anemia, and diabetes had also been identified [1, 4, 9, 11-13, 21-25]. However, currently there is no study based on large-scale national database analysis, especially for the incidence and risk factors of postoperative delirium associated with TKA [1, 7, 9, 11-13, 22, 23].
The purpose of this study was to investigate the incidence and risk factors of delirium after TKA, based on a national database, with the hypothesis that postoperative delirium has a relatively lower incidence and numerous risk factors to highlight patient groups that might require preoperative optimization. The incidence, patient demographics, Charlson Comorbidity Index (CCI), length of stay (LOS), total charges, type of insurance, in-hospital mortality, medical and surgical perioperative complications, and risk factors of postoperative delirium after TKA were evaluated.

Methods

Data Source
The Nationwide Inpatient Sample (NIS) database is part of the Healthcare Cost and Utilization Project, Agency for Healthcare Research and Quality, and was the data source for this study. In the United States, the NIS represents the largest all-payer database of hospital admissions. The NIS collects a stratified sample from more than 1,000 hospitals, of approximately 20% of the hospitalizations in the United States each year [16, 26]. The information, including patient demographics, LOS, total hospital charges, type of insurance, diagnostic and procedural codes from International Classification of Diseases (ninth revision) Clinical Modification (ICD-9-CM) were extracted from this database.

Data Collection
Data was obtained from the NIS database from 2005 to 2014. Patients were identified according to ICD-9-CM procedural codes of TKA (81.54). Patients with a diagnosis of delirium were defined by ICD-9-CM diagnostic codes and selected, including transient mental disorders, acute and subacute delirium (293, 293.0, 293.1, 293.8, 293.9, 293.81–84, 293.89), drug-induced delirium (292.81), and altered mental status (780.97). Patients who were less than 18 years of age, were non-elective admission, had osteomyelitis, or had pathologic fracture were excluded from this study.

The recruited cases were divided into two groups according to the occurrence of postoperative delirium. Patient demographics, including age, sex, and race, were evaluated. Outcome measures such as LOS, total charges during hospitalization, type of insurance, and in-hospital mortality were analyzed. Medical and surgical perioperative complications before discharge were searched from the database by ICD-9-CM diagnostic code. Medical perioperative complications were defined as acute renal failure, acute myocardial infarction, pneumonia, pulmonary embolism, stroke, urinary tract
infection, deep vein thrombosis, transfusion of blood, sepsis, and death. Surgical perioperative complications included dislocation of prosthetic joint, seroma/hematoma, wound infection, injury to peripheral nerve, wound dehiscence, and irrigation and debridement [26]. The included covariates were comorbidities given a numerical score according to the CCI. There were 17 comorbid conditions assigned with specific point values, where higher score means more comorbidities [16, 27]. As comorbidity definitions in the NIS database vary slightly from the CCI, several modifications were made for analysis: A history of coronary heart disease or leukemia was omitted from the CCI score; liver disease got a weighted value of 2 points instead of 1 point for mild chronic liver disease and 3 points for moderate to severe liver disease [11, 16]. Other comorbid conditions and their point values were: age (age ≤ 50 yrs.=1, age 51-60 yrs.=2, age 61-70 yrs.=3, age ≥ 71 yrs.=4), congestive heart failure (1), peripheral vascular disorders (1), neurological disorders (1), psychoses (2), chronic pulmonary disease (1), rheumatoid arthritis/collagen vascular diseases (1), peptic ulcer disease (1), diabetes without complications (1), diabetes with complications (2), paralysis(2), renal disease (2), lymphoma (2), liver disease(2), solid tumor without metastasis(2), metastatic cancer (6), and AIDS/HIV (6).

Data Analysis
The statistical software, R version 3.5.3 was used to perform statistical analysis. Significant differences between two groups were determined by Wilcoxon rank test for continuous data and chi-square test for categorical data. Univariate and multivariate logistic regression models were constructed to assess the association of delirium with medical and surgical perioperative complications. To identify independent risk factors for postoperative delirium, binary logistic regression with the stepwise method was performed. All variables, including demographics, hospital characteristics, and comorbidities which were provided by the NIS were entered into the regression analysis (Table 1). Statistical significance was defined by an alpha level of $P \leq 0.001$ because of the large-scale sample volume, which has been utilized by other NIS-researches [16, 28].
| Variables Categories                  | Specific Variables                                                                 |
|--------------------------------------|-------------------------------------------------------------------------------------|
| Patient demographics                 | Age (≤ 70 yrs. and ≥ 71 yrs.), sex (male and female), race (White, Black, Hispanic, Asian or Pacific Islander, Native American and Other) |
| Hospital characteristics             | Bed size of hospital (small, medium, large), teaching status of hospital (nonteaching, teaching), location of hospital (rural, urban), type of insurance (medicare, medicaid, private insurance, self-pay, no charge, other) |
| Comorbidities                        | AIDS, alcohol abuse, deficiency anemia, rheumatoid arthritis/collagen vascular 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 Postoperative Delirium in Patients Undergoing TKA**

A total of 1,228,879 TKAs were identified in the NIS database from 2005 to 2014. Overall, there were 12,339 cases of postoperative delirium with an incidence of 1.00% (Table 2). It was found that the incidence of postoperative delirium was approximately increasing from 2005 to 2008 (from 1.12-1.21%) (Fig. 1), while annually decreasing from 2008 to 2014 (from 1.21-0.71%) (Fig. 1).
Table 2
Patient Characteristics and Outcomes of Delirium after TKA (2005–2014)

| Parameter                        | No delirium | Delirium   | P     |
|----------------------------------|-------------|------------|-------|
| Total (n = count)                | 1,216,540   | 12,339     |       |
| Total incidence (%)              | 1.00        |            |       |
| Age (yrs.)                       | 66 (59–73)  | 75 (69–81) | < 0.0001 |
| Age group (%)                    |             |            |       |
| ≤ 50                             | 6.46        | 1.13       | < 0.0001 |
| 51–60                            | 23.01       | 6.50       |       |
| 61–70                            | 35.43       | 22.35      |       |
| ≥ 71                             | 35.10       | 70.02      |       |
| Sex (% female)                   |             |            | < 0.0001 |
| White                            | 83.35       | 86.62      |       |
| Black                            | 7.37        | 5.72       |       |
| Hispanic                         | 5.32        | 4.20       |       |
| Asian or Pacific Islander        | 1.25        | 1.05       |       |
| Native American                  | 0.48        | 0.39       |       |
| Other                            | 2.22        | 2.02       |       |
| CCI a                            | 4 (3–4)     | 5 (4–6)    | < 0.0001 |
| LOS b (d)                        | 3 (3–4)     | 4 (3–6)    | < 0.0001 |
| Total charges ($)                | 41,244 (30,546 – 57,281) | 46,394 (33,706.75–66,750.50) | < 0.0001 |
| Type of insurance (%)            |             |            |       |
| Medicare                         | 55.14       | 82.50      | < 0.0001 |
| Medicaid                         | 2.92        | 1.70       |       |
| Private insurance                | 38.12       | 14         |       |
| Self-pay                         | 0.44        | 0.26       |       |
| No charge                        | 0.08        | 0.06       |       |
| Other                            | 3.30        | 1.47       |       |
| In-hospital mortality (%)        | 0.07        | 0.24       | < 0.0001 |

CCI a: Charlson Comorbidity Index; LOS b: length of stay.

Patient Demographics between Two Surgical Groups

Significant difference of the incidence of postoperative delirium between two genders was observed with the female demonstrating a smaller proportion in patients affected by delirium than in the nonaffected population (P < 0.0001) (Table 2). Patients suffered from postoperative delirium (75 yrs.) were significantly older than those without postoperative delirium (66 yrs.) (P < 0.0001). Consistently, there was significant difference of the age distribution between the two groups, with a significant higher incidence among patients older than 71 years (P < 0.0001) (Table 2). Meanwhile, significant difference was detected in races, with the Whites occupying a larger proportion in the postoperative delirium group (P < 0.0001) (Table 2).

Adverse Effects of Postoperative Delirium after TKA

Patients with postoperative delirium demonstrated significant greater CCI scores (5 vs. 4, P < 0.0001), which as mentioned previously, represented more comorbidities. Not surprisingly, in-hospital mortality was increased from 0.07–0.24% with the presence of postoperative delirium (P < 0.0001) (Table 2). The mean LOS of patients with delirium was longer than those without delirium (4 d vs. 3 d;
P < 0.0001) (Table 2). Consequently, postoperative delirium increased medical cost. There was an average increase of $5150 in total hospital charges, with the presence of postoperative delirium ($46,394 vs. $41,244, P < 0.0001) (Table 2). Correspondingly, it was observed that the medicare occupied an obviously larger proportion while private insurance took a relatively smaller proportion in the postoperative delirium group in terms of the type of insurance (P < 0.0001) (Table 2).

Those with delirium were more likely to have medical perioperative complications including acute renal failure, acute myocardial infarction, pneumonia, pulmonary embolism, stroke, urinary tract infection, deep vein thrombosis, transfusion of blood, sepsis, death, and overall medical perioperative complications compared with patients without delirium (P < 0.0001) (Table 3). Postoperative delirium was found to be associated with acute renal failure (odds ratio [OR] = 2.27; 95% confidence interval [CI] = 2.10–2.46), acute myocardial infarction (OR = 1.60; CI = 1.41–1.83), pneumonia (OR = 2.64; CI = 2.34–2.97), pulmonary embolism (OR = 1.35; CI = 1.14–1.60), stroke (OR = 1.69; CI = 1.46–1.96), and urinary tract infection (OR = 1.69; CI = 1.56–1.82). Regarding to the surgical perioperative complications, patients with delirium were more likely to have seroma/hematoma, wound infection, wound dehiscence and overall surgical complications compared with those without delirium (P < 0.0001) (Table 3). However, delirium was not associated with any surgical perioperative complications on multivariate analysis (Table 3).
## Table 3
Complications Associated with Postoperative Delirium Following TKA (2005–2014)

| Complication                        | Univariate Analysis | Multivariate Logistic Regression |
|-------------------------------------|---------------------|----------------------------------|
|                                     | No delirium         | Delirium                          | P       | Odds Ratio | 95% Confidence Interval | P     |
| Medical complication                |                     |                                  |         |            |                       |       |
| Acute renal failure                 | 18,502 (1.52%)      | 889 (7.20%)                      | < 0.0001| 2.27       | 2.10–2.46             | < 0.0001|
| Acute myocardial infarction         | 7824 (0.64%)        | 264 (2.14%)                      | < 0.0001| 1.60       | 1.41–1.83             | < 0.0001|
| Pneumonia                           | 5428 (0.45%)        | 333 (2.70%)                      | < 0.0001| 2.64       | 2.34–2.97             | < 0.0001|
| Pulmonary embolism                  | 5100 (0.42%)        | 153 (1.24%)                      | < 0.0001| 1.35       | 1.14–1.60             | < 0.0001|
| Stroke                              | 6379 (0.52%)        | 204 (1.65%)                      | < 0.0001| 1.69       | 1.46–1.96             | 0.0005|
| Urinary tract infection             | 31,588 (2.60%)      | 1050 (8.51%)                     | < 0.0001| 1.69       | 1.56–1.82             | < 0.0001|
| Deep vein thrombosis                | 5023 (0.41%)        | 102 (0.83%)                      | < 0.0001| 0.94       | 0.76–1.15             | < 0.0001|
| Transfusion of blood                | 131,814 (10.84%)    | 3293 (26.69%)                    | < 0.0001| 1.44       | 1.33–1.55             | 0.52  |
| Sepsis                              | 1062 (0.09%)        | 62 (0.50%)                       | < 0.0001| 0.99       | 0.75–1.31             | < 0.0001|
| Death                               | 871 (0.07%)         | 29 (0.24%)                       | < 0.0001| 0.77       | 0.52–1.14             | 0.95  |
| Any medical complicationa           | 187,343 (15.41%)    | 4910 (39.82%)                    | < 0.0001| 2.07       | 1.91–2.24             | 0.19  |
| Surgical complication               |                     |                                  |         |            |                       |       |
| Dislocation of prosthetic joint     | 274 (0.02%)         | 7 (0.06%)                        | 0.02    | 1.41       | 0.60–3.31             | 0.43  |
| Seroma/hematoma                     | 3286 (0.27%)        | 108 (0.88%)                      | < 0.0001| 1.44       | 0.95–2.17             | 0.09  |
| Wound infection                     | 3552 (0.29%)        | 115 (0.93%)                      | < 0.0001| 1.41       | 0.92–2.17             | 0.11  |
| Injury to peripheral nerve           | 245 (0.02%)         | 1 (0.01%)                        | 0.53    | 0.26       | 0.04–1.92             | 0.19  |
| Wound dehiscence                    | 1067 (0.09%)        | 31 (0.25%)                       | < 0.0001| 1.64       | 1.02–2.64             | 0.04  |
| Irrigation and debridement          | 1864 (0.15%)        | 29 (0.24%)                       | 0.03    | 0.71       | 0.46–1.11             | 0.14  |
| Any surgical complicationb          | 9327 (0.77%)        | 258 (2.09%)                      | < 0.0001| 1.37       | 0.89–2.11             | 0.15  |

Any medical complication or surgical complications: patients with more than one complication are counted only once.

### Risk Factors of Postoperative Delirium after TKA

Logistic regression analysis was applied to investigate risk factors of postoperative delirium (Table 4), and the following indicators were identified: advanced age (≥ 71 years, odds ratio [OR] = 3.07; 95% confidence interval [CI] = 2.92–3.23; P < 0.0001), teaching hospital (OR = 1.13; CI = 1.09–1.18), alcohol abuse (OR = 2.79; CI = 2.44–3.19), deficiency anemia (OR = 1.36; CI = 1.29–1.43), chronic blood loss anemia (OR = 1.54; CI = 1.36–1.74), congestive heart failure (OR = 1.59; CI = 1.47–1.72), chronic pulmonary disease (OR = 1.14; CI = 1.08–1.20), coagulopathy (OR = 1.53; CI = 1.39–1.69), depression (OR = 1.43; CI = 1.35–1.51), uncomplicated diabetes (OR = 1.20; CI = 1.14–1.26), diabetes with chronic complications (OR = 1.87; CI = 1.68–2.07), drug abuse (OR = 1.90; CI = 1.53–2.36), fluid
and electrolyte disorders (OR = 2.41; CI = 2.30–2.54), neurological disorders (OR = 8.35; CI = 7.97–8.76), peripheral vascular disorders (OR = 1.29; CI = 1.17–1.42), psychoses (OR = 2.18; CI = 1.98–2.40), pulmonary circulation disorders (OR = 1.48; CI = 1.29–1.69), renal failure (OR = 1.36; CI = 1.27–1.47), and weight loss (OR = 2.02; CI = 1.65–2.49). Interestingly, there were several protective factors for postoperative delirium including female (OR = 0.79; CI = 0.76–0.83; \( P < 0.0001 \)), the Hispanic (OR = 0.83; CI = 0.75–0.91; \( P = 0.0002 \)), urban hospital (OR = 0.87; CI = 0.82–0.93; \( P < 0.0001 \)), medicaid (OR = 0.71; CI = 0.61–0.83; \( P < 0.0001 \)), private insurance (OR = 0.56; CI = 0.53–0.60; \( P < 0.0001 \)), other type of insurance (OR = 0.64; CI = 0.54–0.76; \( P < 0.0001 \)), and obesity (OR = 0.85; CI = 0.80–0.90; \( P < 0.0001 \)).
### Table 4
#### Risk Factors for Postoperative Delirium (2005–2014)

| Variable                        | Odds Ratio | 95% Confidence Interval | P      |
|---------------------------------|------------|--------------------------|--------|
| Age ≥ 71 yr                     | 3.07       | 2.92–3.23                | < 0.0001|
| Female                          | 0.79       | 0.76–0.83                | < 0.0001|
| Race                            |            |                          |        |
| Black                           | 0.92       | 0.84–1.00                | 0.06   |
| Hispanic                        | 0.83       | 0.75–0.91                | 0.0002 |
| Asian or Pacific Islander       | 0.83       | 0.68–1.01                | 0.07   |
| Native American                 | 0.88       | 0.64–1.22                | 0.44   |
| Other                           | 0.95       | 0.83–1.10                | 0.49   |
| Bed size of hospital            |            |                          |        |
| Small                           | 0.93       | 0.88–0.99                | 0.02   |
| Medium                          | 0.92       | 0.87–0.97                | 0.0015 |
| Large                           |            |                          |        |
| Teaching hospital               | 1.13       | 1.09–1.18                | < 0.0001|
| Urban hospital                  | 0.87       | 0.82–0.93                | < 0.0001|
| Type of insurance               |            |                          |        |
| Medicare                        | 0.71       | 0.61–0.83                | < 0.0001|
| Private insurance               | 0.56       | 0.53–0.60                | < 0.0001|
| Self-pay                        | 0.83       | 0.88–1.18                | 0.30   |
| No charge                       | 1.17       | 0.58–2.37                | 0.66   |
| Other                           | 0.64       | 0.54–0.76                | < 0.0001|
| Alcohol abuse                   | 2.79       | 2.44–3.19                | < 0.0001|
| Deficiency anemia               | 1.36       | 1.29–1.43                | < 0.0001|
| Chronic blood loss anemia       | 1.54       | 1.36–1.74                | < 0.0001|
| Congestive heart failure        | 1.59       | 1.47–1.72                | < 0.0001|
| Chronic pulmonary disease       | 1.14       | 1.08–1.20                | < 0.0001|
| Coagulopathy                    | 1.53       | 1.39–1.69                | < 0.0001|
| Depression                      | 1.43       | 1.35–1.51                | < 0.0001|
| Diabetes, uncomplicated         | 1.20       | 1.14–1.26                | < 0.0001|
| Diabetes with chronic complications | 1.87   | 1.68–2.07                | < 0.0001|
| Drug abuse                      | 1.90       | 1.53–2.36                | < 0.0001|
| Hypertension                    | 1.08       | 1.03–1.13                | 0.0026 |
| Fluid and electrolyte disorders | 2.41       | 2.30–2.54                | < 0.0001|
| Metastatic cancer               | 1.85       | 1.16–2.95                | 0.0095 |
| Neurological disorders          | 8.35       | 7.97–8.76                | < 0.0001|
| Obesity                         | 0.85       | 0.80–0.90                | < 0.0001|
| Peripheral vascular disorders   | 1.29       | 1.17–1.42                | < 0.0001|
| Psychoses                       | 2.18       | 1.98–2.40                | < 0.0001|
| Pulmonary circulation disorders | 1.48       | 1.29–1.69                | < 0.0001|
| Renal failure                   | 1.36       | 1.27–1.47                | < 0.0001|
| Valvular disease                | 1.14       | 1.05–1.24                | 0.0015 |
| Weight loss                     | 2.02       | 1.65–2.49                | < 0.0001|

### Discussion

This study has provided a large-scale and health-economic analysis of postoperative delirium after TKA. From the year 2005 to 2008, the incidence of postoperative delirium was increasing nearly from 1.12–1.21%. Then, the incidence of postoperative delirium decreased annually to 0.71% in 2014 (Fig. 1). Interestingly, this trend had never been reported in previous studies. Although there was no change of the definition of delirium over this decade, according to ICD-9-CM, the diagnosis of delirium...
may vary among institutions [16]. One possible explanation for this trend may be that the number of TKA performed was increased with aging of population, however, the lack of recognition and medical interventions led to a higher incidence of postoperative delirium. Then postoperative delirium received more and more attention and this trend was reversed after 2008. We identified an overall incidence of 1.00% after TKA procedures, which is much lower compared with most of the previous studies ranging from 3.1–25% [1, 8-13], with the exception of an Asian study by Huang et al. reporting the incidence of 0.59% [7]. There are two possible reasons accounting for the former obvious difference. First, most of previous literatures observed small-scale and selected senior patients, resulting in an over-reported incidence. Second, the diagnostic accuracy varied between institutions may also contributed to the difference [16, 29]. Huang et al. observed the Asian population with a lower incidence while our study observed a diverse race mainly in the Whites indicating a racial difference in the occurrence of postoperative delirium. It was also found that patients with delirium were less likely in Asian or Pacific Islander compared with those without delirium (P < 0.0001) (Table 2). Interestingly, another significant difference of race distribution between the two groups was found, the Whites occupying a larger proportion in the postoperative delirium group. This is consistent with the previous report that the Whites undergoing general or orthopedic surgery were more likely to develop postoperative delirium [30]. Additionally, in logistic regression analysis, the Hispanics was a protective factor for postoperative delirium in comparison with the Whites, which was never been found before. However, very few studies have focused on racial difference in postoperative delirium.

Regarding to another demographic characteristic, patients with postoperative delirium were significantly 9 years older than those without. Besides, in terms of age distribution, as observed in clinical practice, elderly patients take a greater proportion in the postoperative delirium group. Further, in logistic regression analysis, older than 71 yrs. was identified as an independent risk factor of postoperative delirium (Table 4). This was highly consistent with previous studies which had identified advanced age as a common independent predictor of postoperative delirium [1, 4, 9, 11-13, 21-25].
The CCI score of patients with postoperative delirium was significantly higher. This is reasonable as higher CCI score means relatively worse healthy condition before surgery, and may increase postoperative complications including delirium. Postoperative delirium has been reported to increase hospitalization duration, medical cost, and mortality [1, 4, 9, 11-14]. Similar findings were observed in our study (Table 2). With the presence of postoperative delirium, the average LOS was 1 day longer and the total hospital charges was $5150 more per admission. This may be due to that patients with postoperative delirium can not follow instructions of nursing and rehabilitation [16, 31]. Another explanation is that, postoperative delirium may be associated with medical perioperative complications, including acute renal failure, acute myocardial infarction, pneumonia, pulmonary embolism, stroke, and urinary tract infection (Table 3), which commonly delay discharge and prolong hospital stay [18, 26]. Consistently, patients with delirium were more commonly pay the charges through the medicare than those without delirium. Further, the medicaid, the private insurance, and the other type of insurance were protective factors for postoperative delirium in logistic regression analysis, illustrating that the medicare played a major role among the type of insurance. Thus, the in-hospital mortality of patients affected by delirium was more than three times to those unaffected.

Several studies on postoperative delirium after total joint arthroplasty suggested that pre-screening, risk stratification and appropriate management is essential to improve outcomes [1, 4, 11-13, 21]. Consequently, in order to prevent postoperative delirium, it is critical to understand the risk factors before surgery. Logistic regression was applied and the results were consistent with previous publications [1, 4, 9, 11-13, 21-25]. As expected, neurological disorders before surgery introduced the highest odds ratio (OR, 8.35) for delirium (Table 4). Age greater than 71 years had a considerably high OR (3.07). Patients with a history of the other neuropsychiatric disorders such as drug abuse (OR = 1.90), psychosis (OR = 2.18), alcohol abuse (OR = 2.79) and depression (OR = 1.43) were at increased risk of postoperative delirium [1, 4]. A diagnoses of either chronic deficiency (e.g., iron, Vitamin B12) anemia (OR = 1.36) or chronic blood loss anemia (OR = 1.54) were independent risk factors, confirming previous findings that patients with perioperative anemia were more likely to experience delirium [4, 16, 23, 32-34]. Other comorbidities such as fluid and electrolyte disorders
(OR = 2.41), congestive heart failure (OR = 1.59), coagulopathy (OR = 1.53), renal failure (OR = 1.36), peripheral vascular disorders (OR = 1.29), uncomplicated diabetes (OR = 1.20) and diabetes with chronic complications (OR = 1.87) had also been previously reported as risk factors of delirium [4, 14, 22, 23]. Furthermore, to the best of the author's knowledge, for the first time chronic pulmonary disease (OR = 1.14), weight loss (OR = 2.02), pulmonary circulation disorders (OR = 1.48), and teaching hospital (OR = 1.13), were identified as independent risk factors of postoperative delirium. Interestingly, female (OR = 0.79), obesity (OR = 0.85), and urban hospital (OR = 0.87) were found to be protective factors. Additionally, female patients with delirium occupied smaller proportion indicating that whether female sex hormone has an effect on postoperative delirium will need further study.

Several limitations exist in utilizing the NIS database. First, information of each patient is only recorded before discharge, meaning any complication that occurs after discharge will not be included in the NIS database. This limitation might contribute to the lower incidence of postoperative delirium as only early period medical records were analyzed. Second, only risk factors recorded in the NIS database could be analyzed. There are other known risk factors that were not available in the NIS database, such as a history of dementia, type of anaesthesia, commonly used perioperative medications (opioids, benzodiazepines, and ketamine), sedation during anesthesia recovery, vision impairment, functional impairment, and so on [4, 16, 23, 24, 35]. Further more, as a retrospective database analysis, the results obtained need clarification to confirm their etiology.

Conclusions
Postoperative delirium is a common complication typically occurring in the elderly after TKA, with an overall incidence of 1.00%. The annual incidence of postoperative delirium was increasing almost from 2005 to 2008 while decreasing gradually from 2008 to 2014. Numerous risk factors were identified in this study including advanced age (≥ 71 yrs.), a history of neurological and psychiatric diseases, alcohol and drug abuse, fluid and electrolyte disorders, complicated and uncomplicated diabetes, weight loss, deficiency and chronic blood loss anemia, coagulopathy, congestive heart failure, chronic pulmonary disease and pulmonary circulation disorders, peripheral vascular disorders,
renal failure, and teaching hospital. Female, obesity, the Hispanics, urban hospital, medicaid, private insurance, and other type of insurance, however, were found to be protective factors. The occurrence of delirium after TKA was associated with an increased LOS, extra total hospital charges, wider coverage of medicare, higher inpatient mortality and medical perioperative complications (acute renal failure, acute myocardial infarction, pneumonia, pulmonary embolism, stroke, and urinary tract infection), but not surgical complications.

Abbreviations
TKA
Total knee arthroplasty
NIS
Nationwide Inpatient Sample
LOS
Length of stay
CCI
Charlson Comorbidity Index
OR
Odds ratio
CI
Confidence interval

Declarations

**Ethics approval and consent to participate**

This article does not contain any studies with human participants or animals performed by any of the authors. This observational study was deemed exempt because it used deidentified publicly available data.

**Consent for publication**

Not applicable.

**Availability of data and materials**

This study is based on data provided by Nationwide Inpatient Sample (NIS) database, part of the Healthcare Cost and Utilization Project, Agency for Healthcare Research and Quality. The NIS database is a large publicly available all-payer inpatient care database in the United States.
Therefore, individual or grouped data cannot be shared by the authors.

**Competing interests**

The authors declare that they have no competing interest.

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**Authors' contributions**

JW and QY contributed to the study design, data acquisition and analysis, interpretation of results, and writing and revising the manuscript. YX contributed to the study design, interpretation of results, and reviewing the manuscript. YC and QL contributed to data acquisition, data analysis, and reviewing of the manuscript. YZ contributed to the study design, interpretation of results, and reviewing the manuscript. All authors read and approved the final manuscript.

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Figures
Figure 1

Annual Incidence of Postoperative Delirium in Patients Undergoing TKA