RESEARCH ARTICLE

Postoperative Outcomes of Total Knee Arthroplasty in Patients with Alcohol Use Disorders: A Retrospective Propensity-Matched Analysis

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Abstract

Objectives: Alcohol use disorder (AUD) has been associated with post-surgical complications, but previous studies were limited by national, single-database sources. The purpose of this study was to characterize differences in complications of matched cohorts of patients with versus without AUD undergoing primary total knee arthroplasty (TKA) and to evaluate the effect of AUD-associated comorbidities on the hazard of post-operative complications.

Methods: A total of 6,634 patients were extracted from the TriNetX global database for patients undergoing primary TKA from 2015-2025. Univariate analysis was performed to examine the relationship between AUD and postoperative complications. A subgroup analysis was performed using the TKA/AUD cohort with surgical complications compared to AUD patients without surgical complications. Cox proportional hazards modeling evaluated the impact of comorbidities and pre-operative labs on the hazard of post-operative complications.

Results: Patients with AUD had a significantly higher risk of acute renal failure, respiratory failure, delirium, transfusion, joint infection, wound dehiscence, superficial skin and soft tissue infection, infection following procedure, periprosthetic fracture around the knee joint, and revision arthroplasty. The cohort of TKA/AUD patients with surgical complications had a significantly higher percentage of diabetes, tobacco use, essential hypertension, depression, anxiety, bipolar disorder, and atrial fibrillation than the cohort without surgical complications. These patients also had significantly lower preoperative hemoglobin, albumin, and alanine aminotransferase (ALT), and a higher international normalized ratio (INR) than patients without complications. The Cox proportional hazards model showed a significantly increased hazard of post-operative complications for hypertension, hemoglobin of 6 – 10 g/dL, and albumin of 2.5 – 3 g/dL in a cohort of patients with AUD.

Conclusion: AUD has a significant effect on both medical and surgical complications following primary TKA at 30 days, 90 days, 1 year, and 5 years post-operatively. Certain preoperative labs can predict the risk of postoperative complications. This data supports a multidisciplinary approach to optimize care for high-risk individuals.

Level of evidence: III

Keywords: Alcohol-related disorders, Comorbidity, Knee arthroplasty, Postoperative complications, Propensity score, Treatment Outcome

Introduction

Alcohol is one of the most widely used substances in the world.[1] It is a risk factor for diseases contributing to poor bone health, such as osteoporosis, increased fractures, and impaired osteointegration. Alcohol influences bones and soft tissues in a variety of ways through altering hormonal release and changing innate and adaptive immune responses.[2] It is estimated that about 2.3 billion adults consume alcohol at least once per year, and that 1/20 adults globally have an alcohol use disorder (AUD).[3] AUD is defined by the Diagnostic and Statistical Manual of Mental Disorders as "a problematic pattern of alcohol use leading to clinically

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significant impairment or distress."[4] Alcohol use has been associated with increased medical and surgical postoperative complications such as acute infection, thrombocytopenia, convulsion, and pulmonary insufficiency after arthroplasty, but there is limited data suggesting AUD increases healing time.[5,6]

These risks are particularly relevant to patients undergoing total knee arthroplasty (TKA), one of the most common and successful joint replacement procedures, as it can reduce pain and improve joint function. With increasing obesity rates worldwide and a predicted doubling of the global population over 60 between 2013 and 2050, it is expected that the incidence of primary TKA procedures will increase by 265%.[7,8] This momentous increase in case volume, as well as the prevalence of AUD in the population, underscores the importance of investigating the effects of AUD on post-operative complications. In the context of TKA, where successful outcomes depend on proper rehabilitation, wound healing, and pain management, AUD may significantly increase the risk of adverse events detrimental to the procedure's success.[9]

While a few studies have investigated the effect of AUD in the context of total joint arthroplasty, the evidence was derived from national database studies evaluating unmatched cohorts. These studies examined the effect of AUD in arthroplasty cases. They found an increased risk of revision arthroplasty after two years, hospital readmission, more frequent ER visits, and multiple complications, including renal failure, dislocations, and post-operative anemia.[10-12] Research, such as Best *et al.* and Luo T *et al.,* analyzed alcohol's effect on TKA using data from 1990 to 2014 and relied on a national patient database.[5,13] These studies may not reflect contemporary trends in primary TKA and perioperative care and were limited by the use of non-global, single-database data sources. The purpose of our study is to identify the medical and surgical complications of AUD on primary TKA using a global database with matched cohorts that reflect more current surgical practices and limit confounding variables.

Materials and Methods

Data Acquisition

The data used in this study were acquired from TriNetX, a global patient database with over 130 million patients. This data is obtained from 153 health care organizations (HCOs) and accesses de-identified patient data from both inpatient and outpatient facilities. TriNetX is health insurance portability and accountability act (HIPAA-), general data protection regulation (GDPR-), and general data protection law (LGPD-) compliant due to the de-identification of patient information and strict security practices.[14]

Cohort Construction

Two cohorts were created in TriNetX using the query builder function. The Global Collaborative Network was used, which contains over 180 million patients from 153 HCOs worldwide. Patients aged 18 years and older who underwent primary TKA were selected using current procedural terminology (CPT) 27447 between January 1, 2015, and January 1, 2025. To select for patients with AUD (AUD), the international classification of diseases 10th revision (ICD-10) code for alcohol dependence, F10.2, was used. Using these codes, patients were put into two cohorts: TKA with AUD and TKA without AUD. The TKA and AUD cohort included 6,634 patients, and the TKA-only cohort included 306,412 patients. ICD-10 codes were used to define diagnoses: essential hypertension I10, hyperlipidemia E78.5, tobacco use Z72.0, diabetes mellitus E08-E13, atherosclerotic heart disease of native coronary artery I25.1, depression F32.A, anxiety disorder F41.9, bipolar disorder F31, atrial fibrillation I48.91. These codes were also used to identify postoperative complications: acute myocardial infarction I21, pulmonary embolism I26, acute embolism and thrombosis of deep veins of lower extremity I82.9, injury of unspecified body region T14, transfusion of blood or components CPT 36430, acute kidney failure N17, pneumonia J18, respiratory failure J96, delirium R41, urinary tract infection N39, cerebral infarction I63, infection and inflammatory reaction due to internal joint prosthesis T84.50, disruption of wound T81.30, infection following a procedure, superficial incisional site T81.41, infection following a procedure T81.4, periprosthetic fracture around internal prosthetic knee joint M97.1, fracture of bone following insertion of orthopedic implant M96.6, manipulation under anesthesia CPT 27570, revision arthroplasty CPT 27486 and 27487.

Pre-Match Characteristics

The pre-match characteristics of the cohorts are presented in [Table 1], and the post-match characteristics are shown in [Table 2]. TKA patients with AUD were more likely to be younger at the time of surgery, with an average age of 63.5 versus 68.1 for patients without AUD. In the AUD cohort, patients were more likely to be male (59.2%) than patients without AUD (37.6%). The AUD cohort had significantly higher percentages of common comorbidities associated with AUD: hypertension (75.445% vs 58.03%), hyperlipidemia (54.70% vs 41.70%), tobacco use (12.80% vs 2.80%), diabetes mellitus (24.90% vs 20.80%), atherosclerotic heart disease (21.30% vs 13.40%) and atrial fibrillation (11.90% vs 7.00%). The AUD group also had significantly higher percentages of mental health disorders such as depression (23.70% vs 9.00%), anxiety (39.10% vs 16.10%), and bipolar disorder (9.60% vs 1.60%). TKA patients with AUD had a slightly lower body mass index (BMI) at 31.5 vs 32.3 kg/m^2.

Propensity Matching

Propensity matching was performed to make the characteristics and comorbidities of the cohorts as similar as possible. Matched variables included age at index surgery, race, sex, and BMI. Before matching, patients with AUD had significantly higher percentages of essential hypertension, hyperlipidemia, anxiety disorder, diabetes mellitus, depression, atherosclerotic heart disease of native artery, tobacco use, atrial fibrillation, and bipolar disorder. After matching, there were no significant differences in the percentages of these comorbidities between the two cohorts, and each group contained a total of 6,634 patients. All characteristics and comorbidities did not differ significantly between the cohorts, except for BMI, which was 31.5 in the AUD cohort and 32.5 in the non-AUD cohort. After matching, the mean age at surgery was 63.5 years. The cohort included 59.20% males, with comorbidities as follows: hypertension (75.40%), hyperlipidemia (54.70%),

tobacco use (12.80%), atherosclerotic heart disease (21.30%), depression (23.70%), anxiety (39.10%), bipolar disorder (9.60%), and atrial fibrillation (11.90%).

Postoperative Outcomes

This study aimed to analyze both medical and surgical outcomes after primary TKA. Medical outcomes were assessed at 1 month and 3 months postop, and surgical outcomes were assessed at 1 month, 3 months, 1 year, and 5 years post op. Medical outcomes analyzed were as follows: acute myocardial infarction, pulmonary embolism, deep vein thrombosis, injury of unspecified body region, transfusion, acute renal failure, pneumonia, respiratory failure, delirium, urinary tract infection, stroke, and death. Surgical outcomes analyzed included: joint infection, wound dehiscence, superficial SSI, infection following procedure, periprosthetic fracture around the knee joint, manipulation under anesthesia, and revision arthroplasty. Primary TKA was used as the index event for the analysis, with outcomes starting on post-operative day one after the index surgery.

Table 1. Pre-Match Characteristics

	AUD (N=6,634)	Without AUD (N=306,412)	
Characteristic	**Number (%)**	**Number (%)**	**P**
Age at index in years	63.5 +/- 9.1	67.0 +/- 9.4	<0.001
Sex			
Male	3,926 (59)	115,193 (38)	<0.001
Female	2,473 (37)	177,690 (58)	<0.001
Race and Ethnicity			
Black or African American	772 (12)	31,787 (10)	0.001
White	5,201 (78)	231,899 (76)	<0.001
Hispanic or Latino	290 (4)	15,206 (5)	0.028
Asian	36 (1)	8,763 (3)	<0.001
American Indian or Alaska Native	54 (1)	1,124 (0.4)	<0.001
Other race	140 (2)	6,951 (2)	0.392
Diagnosis			
Essential hypertension	5,005 (75)	177,810 (58)	<0.001
Hyperlipidemia	3,630 (55)	127,672 (42)	<0.001
Tobacco use	851 (13)	8,709 (3)	<0.001
Diabetes mellitus	1,651 (25)	63,754 (21)	<0.001
Atherosclerotic heart disease	1,412 (21)	41,074 (13)	<0.001
Depression	1,570 (24)	27,496 (9)	<0.001
Anxiety disorder	2,593 (39)	49,330 (16)	<0.001
Bipolar disorder	639 (10)	5,039 (2)	<0.001
Atrial Fibrillation	791 (12)	21,503 (7)	<0.001
Mean BMI	31.5 +/- 6.0	32.3 +/- 6.2	<0.001

Table 2. Post-Match Characteristics

	AUD (N=6,634)	Without AUD (N=306,412)	
Characteristic	**Number (%)**	**Number (%)**	**P**
Age at index in years	63.5 +/- 9.1	63.5 +/- 9.2	0.703
Sex			
Male	3,926 (59)	3,930 (59)	0.944
Female	2,473 (37)	2,468 (37)	0.928
Race and Ethnicity			
Black or African American	772 (12)	772 (12)	1
White	5,201 (78)	5,199 (78)	0.966

Table 2. Continued			
Hispanic or Latino	290 (4)	290 (4)	1
Asian	36 (1)	37 (1)	0.907
American Indian or Alaska Native	54 (1)	54 (1)	1
Other race	140 (2)	140 (2)	1
Diagnosis			
Essential hypertension	5,005 (75)	5,029 (76)	0.627
Hyperlipidemia	3,630 (55)	3,617 (55)	0.821
Tobacco use	851 (13)	851 (13)	1
Diabetes mellitus	1,651 (25)	1,655 (25)	0.936
Atherosclerotic heart disease	1,412 (21)	1,408 (21)	0.932
Depression	1,570 (24)	1,568 (24)	0.967
Anxiety disorder	2,593 (39)	2,592 (39)	0.986
Bipolar disorder	639 (10)	638 (10)	0.977
Atrial Fibrillation	791 (12)	790 (12)	0.979
Mean BMI	31.5 +/- 6.0	32.5 +/- 6.1	<0.001

Subgroup analysis

After analysis of the two cohorts, surgical outcomes that reached significance (P<0.05) at 1 year and 5 years were selected for subgroup analysis. In this analysis, two cohorts were created within the AUD patient cohort. One cohort contained patients with AUD who had adverse surgical outcomes, and the second cohort contained patients with AUD who did not have any of these outcomes. The characteristics and comorbidities of the two groups were analyzed. The comorbidities that were analyzed were the same as those used in the propensity matching: diabetes mellitus, tobacco use, hypertension, atherosclerotic heart disease, depression, anxiety, bipolar disorder, and atrial fibrillation. Additionally, preoperative hemoglobin, albumin, AST, ALT, and INR were analyzed between the two groups.

Cox Proportional Hazards Model

To assess the effect of covariates on the likelihood of postoperative complications, a Cox proportional hazards analysis was conducted in TriNetX. Patients with AUD who underwent primary TKA were included in the analysis. Primary TKA was set as the index event, and covariates were added based on the comorbidities used for propensity score matching. Additionally, stratified laboratory values were added as covariates: hemoglobin (6-10 g/dL, 10-14 g/dL, 14-18 g/dL) and albumin (1.5-3.5 g/dL, 3.5-5.5 g/dL). Postoperative complications, including revision arthroplasty, wound disruption, periprosthetic fracture around the knee joint, and infection of the joint prosthesis, were set as the primary outcome and measured at 1 year and 5 years after the index event.

Results

Post-Operative Outcomes at 30 Days

Medical and surgical outcomes were measured at 30 days following the primary TKA [Table 3]. At 30 days, the AUD cohort had a significantly higher risk of acute renal failure (relative risk (RR): 1.552), needing transfusion (RR: 2.067), respiratory failure (RR: 1.538), delirium (RR: 1.611), and infection following a procedure (RR: 1.585). There was no significant difference between the cohorts for acute myocardial infarction, pulmonary embolism, deep vein thrombosis, injury of unspecified body region, pneumonia, urinary tract infection, cerebral vascular accident, death, joint infection, wound dehiscence, superficial skin and soft tissue infection (SSI), periprosthetic fracture around knee joint, manipulation under anesthesia (MUA), or revision arthroplasty.

Table 3. Medical and Surgical Complications						
	30 Days			90 Days		
	Risk ratio	95% Confidence Interval	P Value	Risk ratio	95% Confidence Interval	P Value
Acute Myocardial Infarction	0.787	0.47 - 1.32	0.3611	0.772	0.52 - 1.14	0.1941
Pulmonary Embolism	1.083	0.77 - 1.53	0.6557	1.046	0.78 - 1.4	0.7628
DVT	1.053	0.82 - 1.36	0.6923	1.077	0.87 - 1.34	0.4984
Injury of unspecified body region	1.341	0.91 - 1.98	0.1379	1.205	0.89 - 1.62	0.2195
Transfusion	2.067	1.34 - 3.19	0.0008	1.900	1.3 - 2.78	0.0008
Acute Renal Failure	1.552	1.23 - 1.95	0.0002	1.438	1.19 - 1.74	0.0002

Table 3. Continued						
Pneumonia	1.111	0.77 - 1.6	0.5725	1.119	0.84 - 1.50	0.4505
Respiratory Failure	1.538	1.16 -2.04	0.0026	1.381	1.09 - 1.75	0.0067
Delirium	1.611	1.25 -2.08	0.0002	1.543	1.26 - 1.89	<0.0001
UTI	1.262	0.91 - 1.74	0.1585	1.021	0.81 - 1.29	0.8569
Stroke (CVA)	0.907	0.59 - 1.4	0.6577	1.058	0.76 - 1.47	0.7358

	30 Days			*90 Days*			*1 Year*			*5 Years*		
	Risk ratio	**95 % Confidence Interval**	**P Value**	**Risk ratio**	**95 % Confidence Interval**	**P Value**	**Risk ratio**	**95 % Confidence Interval**	**P Value**	**Risk ratio**	**95 % Confidence Interval**	**P Value**
Joint Infection	1.526	0.86 - 2.72	0.1482	1.405	0.95 - 2.08	0.0895	1.292	0.95 - 1.75	0.0999	1.392	1.08 - 1.79	0.0097
Wound dehiscence	1.292	0.76 - 2.20	0.3442	1.641	1.10 - 2.44	0.0134	1.583	1.15 - 2.18	0.0047	1.500	1.16 - 1.93	0.0016
Superficial SSI	1.500	0.67 - 3.34	0.3169	1.478	0.87 - 2.51	0.1443	1.316	0.86 - 2.00	0.1993	1.429	1.04 - 1.97	0.0281
Infection following procedure	1.585	1.07 - 2.34	0.0193	1.470	1.11 - 1.94	0.006	1.392	1.11 -1.74	0.0034	1.567	1.32 - 1.86	<0.0001
Periprosthetic fracture around knee joint	1.100	0.47 -2.59	0.8271	1.500	0.76 - 2.95	0.2361	1.387	0.88 - 2.20	0.1618	1.458	1.07 - 2.03	0.0242
Manipulation under anesthesia	1.300	0.57 - 2.96	0.5313	0.885	0.71 - 1.11	0.29	0.842	0.69 - 1.02	0.0828	0.848	0.70 - 1.02	0.0851
Revision arthroplasty	1.375	0.87 - 2.17	0.1674	1.429	1.05 -1.94	0.023	1.345	1.09 - 1.66	0.006	1.232	1.05 - 1.44	0.0100

Post Operative Outcomes at 90 Days

Medical and surgical outcomes were also measured at 90 days following primary TKA. There was a significant increase in the risk of transfusion (RR: 1.9), acute renal failure (RR: 1.438), respiratory failure (RR: 1.381), delirium (RR: 1.543), wound dehiscence (RR:1.641), and infection following procedure (RR: 1.47). There was no significant difference between the cohorts for acute myocardial infarction, pulmonary embolism, deep vein thrombosis, injury of unspecified body region, pneumonia, urinary tract infection, cerebral vascular accident, death, joint infection, superficial SSI, periprosthetic fracture around the knee joint, MUA, or revision arthroplasty.

Post Operative Outcomes at 1 Year

Surgical outcomes were measured 1 year after primary TKA. There was a significantly increased risk of wound dehiscence (RR: 1.583), infection following the procedure (RR: 1.392), and revision arthroplasty (RR: 1.345). There was no significant risk of joint infection, superficial SSI, periprosthetic fracture around the knee joint, or MUA.

Post Operative Outcomes at 5 Years

Surgical outcomes were measured at 5 years following primary TKA. There was a significantly increased risk of joint infection (RR: 1.392), wound dehiscence (RR: 1.5), superficial SSI (RR: 1.429), infection following a procedure (RR: 1.567), periprosthetic fracture around the knee joint (RR: 1.458), and revision arthroplasty (RR: 1.232). There was no significant risk of manipulation under anesthesia.

Subgroup Analysis at 1 Year

Two cohorts were created from primary TKA patients with AUD and the surgical complications that reached significance at 1 year and 5 years, respectively. For patients with adverse outcomes at 1 year with AUD, there was a significantly increased percentage of the cohort with diabetes mellitus (41% vs 33%), tobacco use (20% vs 16%), essential hypertension (91% vs 86%), depression (45% vs 40%), anxiety (62% vs 52%) and atrial fibrillation (25% vs 20%). There was no significant difference in the percentage of the cohort with hyperlipidemia (67% vs 69%) or atherosclerotic heart disease (38% vs 34%). Preoperative labs were also analyzed, and patients with complications had significantly lower hemoglobin (11.4 g/dL vs 13.7 g/dL), albumin (3.69 g/dL vs 4.19 g/dL), and alanine aminotransferase (24.2 U/L vs 27.6 U/L), and higher international normalized ratio (1.23 vs 1.08). There was no significant difference in aspartate aminotransferase levels (31.6 U/L vs 29.8 U/L) between the two cohorts [Table 4].

Subgroup Analysis at 5 Years

The subgroup analysis was duplicated and analyzed 5 years after primary TKA. For AUD patients with adverse outcomes after primary TKA, there was a significantly higher percentage of the cohort with diabetes mellitus (85% vs 83%), tobacco use (24% vs 18%), hypertension (91% vs 86%), atherosclerotic heart disease (39% vs 33%), depression (48% vs 41%), anxiety (61% vs 52%), bipolar disorder (16% vs 11%), and atrial fibrillation (26% vs 19%). There was no significant difference in the hyperlipidemia rate between the two cohorts (68%). The cohort with adverse outcomes had significantly different hemoglobin (11.5 g/dL vs 13.8 g/dL), albumin 3.65 (g/dL vs 4.18 g/dL), ALT (24.3 U/L vs 27.8 U/L), and INR (1.22 vs 1.08)

(p<0.0001). There was no significant difference between AST (32 U/L vs 29.8 U/L) between cohorts.

Cox Proportional Hazards Model

A Cox proportional hazards model was performed to analyze covariates for the hazard of developing post-operative complications at 1 year and 5 years in patients with AUD. Of the common comorbidities associated with alcohol use disorder, only hypertension showed a significant increase in hazard of complications after 5 years (HR: 1.399, 95% CI [1.074 – 1.822]). The age at index surgery significantly reduced the hazard of complications at 1 year (HR: 0.966, 95% CI [0.953, 0.979]) and 5 years (HR: 0.965, 95% CI [0.955, 0.976]). Lab values were also shown to be predictive of increased hazard for post-operative complications: hemoglobin 6 – 10 g/dL (HR: 1.381, 95% CI [1.043 – 1.828]) at 1 year and (HR: 1.363, 95% CI [1.092 – 1.701]) at 5 years, and albumin 2.5 – 3 g/dL (HR: 1.769, 95% CI [1.252 – 2.5]) at 1 year and (HR: 1.449, 95% CI [1.098 – 1.914]) at 5 years. No other covariates had a significant impact on the hazard of post-operative complications [Table 5].

Table 4. Comorbidity and Characteristics of AUD Patients with Surgical Complications

	1 Year			5 Years		
Comorbidity	**Comp + Cohort %**	**Comp - Cohort %**	**P value**	**Comp + Cohort %**	**Comp - Cohort %**	**P value**
Diabetes mellitus	41	33	0.0006	42	33	<0.0001
Tobacco use	20	16	0.0101	24	18	<0.0001
Essential hypertension	91	86	0.0003	91	86	<0.0001
Hyperlipidemia	67	69	0.3453	68	68	0.9346
Atherosclerotic heart disease	38	34	0.0609	39	33	0.0025
Depression	45	40	0.0201	48	41	0.0002
Anxiety	62	52	<0.0001	61	52	<0.0001
Bipolar disorder	15	11	0.0095	16	11	0.0002
Atrial Fibrillation	25	20	0.008	26	19	<0.0001

Comparison Stats at 1yr	**Lab Value w/ Complications**	**Lab Value w/o Complications**	**P value**	***Comparison Stat at 5yr***	***Lab Value w Complications***	***Lab Value w/o Complications***	***P value***
Hemoglobin	11.4 +-2.08	13.7 +-1.56	<0.0001	*Hemoglobin*	11.5 +-2.19	13.8 +- 1.54	<0.0001
Albumin	3.69 +-0.689	4.19 +-0.403	<0.0001	*Albumin*	3.65 +-0.697	4.18 +-0.402	<0.0001
AST	31.6 +- 24.8	29.8 +- 23.6	0.3428	*AST*	32 +-24.8	29.8+-23.6	0.121
ALT	24.2 +- 17.6	27.6 +- 21.8	0.0439	*ALT*	24.3+-18.6	27.8+-22.1	0.0083
INR	1.23 + 0.449	1.08 +-0.312	<0.0001	*INR*	1.22 +-0.425	1.08 +-0.313	<0.0001

Table 5. Cox Proportional Hazards Model for AUD Patients with Surgical Complications

Covariate	**Hazard Ratio**	**P > |z|**	**95% Confidence Interval**	**Covariate**	**Hazard Ratio**	**P > |z|**	**95% Confidence Interval**
Male Sex	1.02	0.882	(0.788, 1.319)	*Male Sex*	1.067	0.5349	(0.869, 1.311)
Diabetes mellitus	1.023	0.8682	(0.785, 1.333)	*Diabetes mellitus*	0.997	0.9802	(0.807, 1.233)
Tobacco use	1.199	0.2453	(0.883, 1.628)	*Tobacco use*	1.068	0.6138	(0.828, 1.377)
Essential (primary) hypertension	1.259	0.1649	(0.91, 1.742)	*Essential (primary) hypertension*	1.399	0.0127	(1.074, 1.822)
Hyperlipidemia, unspecified	0.984	0.8989	(0.762, 1.269)	*Hyperlipidemia unspecified*	0.947	0.5967	(0.773, 1.159)
Atherosclerotic heart disease of native coronary artery	0.904	0.5042	(0.672, 1.216)	*Atherosclerotic heart disease of native coronary artery*	0.96	0.7355	(0.759, 1.215)
Depression, unspecified	1.18	0.2256	(0.903, 1.541)	*Depression, unspecified*	1.178	0.1346	(0.951, 1.46)
Bipolar disorder	0.789	0.2326	(0.534, 1.165)	*Bipolar disorder*	0.918	0.5723	(0.682, 1.236)

Table 5. Continued							
Anxiety disorder, unspecified	0.834	0.1632	(0.646, 1.077)	*Anxiety disorder, unspecified*	0.855	0.1301	(0.698, 1.047)
Unspecified atrial fibrillation	1.185	0.3243	(0.846, 1.659)	*Unspecified atrial fibrillation*	1.257	0.0919	(0.963, 1.639)
Age at Index	0.966	<0.0001	(0.953, 0.979)	*Age at Index*	0.965	< 0.0001	(0.955, 0.976)
Hemoglobin [Mass/volume] in Blood				*Hemoglobin [Mass/volume] in Blood*			
6 - 10 g/dL	1.381	0.0242	(1.043, 1.828)	*6 - 10 g/dL*	1.363	0.0062	(1.092, 1.701)
10 - 14 g/dL	1.054	0.7915	(0.713, 1.559)	*10 - 14 g/dL*	1.2	0.2582	(0.875, 1.648)
14 - 18 g/dL	0.835	0.2052	(0.633, 1.103)	*14 - 18 g/dL*	0.823	0.0847	(0.66, 1.027)
Albumin [Mass/volume] in Blood				*Albumin [Mass/volume] in Blood*			
1.5 - 2 g/dL	0.889	0.6755	(0.512, 1.542)	*1.5 - 2 g/dL*	0.773	0.2895	(0.479, 1.245)
2 - 2.5 g/dL	1.106	0.6187	(0.745, 1.641)	*2 - 2.5 g/dL*	1.194	0.2842	(0.863, 1.654)
2.5 - 3 g/dL	1.769	0.0012	(1.252, 2.5)	*2.5 - 3 g/dL*	1.449	0.0089	(1.098, 1.914)
3 - 3.5 g/dL	1.11	0.5244	(0.805, 1.529)	*3 - 3.5 g/dL*	1.13	0.3402	(0.879, 1.452)
3.5 - 4 g/dL	1.005	0.9728	(0.741, 1.364)	*3.5 - 4 g/dL*	0.984	0.8989	(0.774, 1.253)

Discussion

Our data suggests that patients with AUD who undergo a primary TKA are at a significantly higher risk of medical and surgical complications compared to patients without AUD undergoing a primary TKA. Propensity matching was done to control for common comorbidities that are associated with AUD; our data suggest that alcohol is an independent risk factor for post-surgical complications, in addition to the effects of the comorbidities that it predisposes patients to. The detrimental effects were seen at all time periods analyzed, from 30 days to 5 years after surgery.

Within 30 days and 90 days after surgery, patients with AUD had a greater risk of complications, including transfusion requirements, renal failure, respiratory failure, and delirium. These results are similar to those of Best MJ *et al.,* which found that there was an increased risk of acute renal failure (OR: 2.272) and transfusion (OR: 1.237) in patients with AUD who underwent either TKA or total hip arthroplasty.[5] Our findings that AUD patients have higher rates of postoperative delirium are similar to a prospective cohort study, which found patients with alcohol abuse have a significantly higher risk of delirium after surgery (OR: 4.2, [95% CI: 1.4 – 12.9]).[15] Chronic alcohol use has been consistently linked with postoperative complications in surgical patients, including infection, cardiac complications, and hemorrhage requiring transfusion.[16] An increased risk of systemic disease is expected in AUD due to the numerous deleterious effects that it has on the body, such as malnutrition, liver and kidney dysfunction.[17] While AUD is associated with comorbidities such as cirrhosis, hypertension, hyperlipidemia, tobacco use, mental health disorders, and atrial fibrillation,[18-20] our results show that even after propensity matching for these comorbidities, alcohol remains an independent risk factor for postoperative complications.

Surgical complications in the matched cohorts were analyzed from 30 days to 5 years after the index surgery and showed that AUD is associated with complications, including infections, wound dehiscence, periprosthetic fractures, and increased risk for revision arthroplasty. Alcohol use can suppress proinflammatory cytokines crucial for wound healing, change bone remodeling dynamics leading to decreased bone formation, and cause alcohol-induced osteopenia.[6] In both mice and humans, alcohol has shown to inhibit Wnt signaling pathways critical for fracture healing, leading to decreased quantity and quality of bone healing.[21] Other studies have found adverse surgical outcomes such as acute postoperative infection and complications of internal joint prosthesis in AUD patients who underwent TKA or THA[5] as well as periprosthetic fracture and periprosthetic joint infection in TKA patients with AUD.[13]

In addition to the Cox model, a subgroup analysis was done to evaluate the relationship between surgical complications in patients with AUD and their comorbidities. The cohort with surgical complications had a significantly increased percentage with comorbidities such as diabetes, tobacco use, atrial fibrillation, and psychiatric conditions. Within the TKA subgroup with surgical complications, pre-operative hemoglobin and albumin were significantly lower, and INR was significantly higher than in the cohort without complications. The Cox model showed that a hemoglobin of 6 – 10 g/dL had a hazard ratio of 1.406 (95% CI 1.282 – 1.542) while a hemoglobin of 14 – 18 g/dL had a hazard ratio of 0.903 (95% CI 0.837 – 0.973) for needing revision arthroplasty after one year. The same trend is seen in plasma albumin: an albumin of 1.5–3.5 g/dL showed a hazard of 1.37, whereas 3.5–5.5 g/dL showed a hazard of 0.792. These lab values are similar to those in a study that found TKA revision was higher in patients with deficiency anemia and liver disease.[22] This points to a significant reduction in the hazard of needing revision surgery based on pre-operative labs and demonstrates the importance of pre-operative screening for patients with AUD.

Various studies have evaluated management strategies for patients with AUD, recommending preoperative screening with the Alcohol Use Disorder Identification Test (AUDIT), which can quantify harmful alcohol intake with good sensitivity and specificity.[6,23] This test can help stratify the severity of alcohol use and determine whether a multidisciplinary approach should be used. A systematic review of 3 RCTs assessed whether alcohol cessation prior to surgery decreases postoperative complications compared with controls and found a decrease in

postoperative complications in the intervention group (RR: 0.62 [95% CI: 0.40 -0.96]). It also found that patients in the intervention group successfully quit drinking at a much higher rate compared to the control (RR: 8.22 [95% confidence interval (CI): 1.67 – 40.44]),[24] which is important as this could alleviate some of the long-term effects that alcohol has in the post-operative period. While alcohol cessation has its benefits of decreasing post-operative complications, it is not without its risks. Acute alcohol withdrawal can occur, which poses serious health complications; patients should be monitored using the Clinical Institute Withdrawal Assessment Alcohol (CIWA) or shortened CIWA-Ar[6,23] both if cessation is attempted and in the perioperative period. Overall, AUD affects the body through its multi-factorial activities on cellular functions and molecular pathways, leading to adverse post-surgical outcomes. This data underscores the importance of patient selection and counseling to address modifiable risk factors in the pre-operative period and improve post-operative outcomes.

This study has some potential limitations as it is a retrospective study based on medical coding from large academic institutions. Propensity matching was used to balance cohorts and reduce confounding variables, but not all variables can be matched, and residual confounding remains possible. Due to reliance on ICD-10 and CPT coding, there could be errors in the data collected and used for analysis. AUD was defined as alcohol dependence (ICD-10 F10.2), which may not truly encompass all people with AUD. There is a large stratification between the amount of alcohol patients consume with AUD, and the ICD codes do not allow for such granularity.

Conclusion

Our data shows that AUD is an independent risk factor for medical and surgical complications after primary TKA, including but not limited to transfusion, acute renal failure, respiratory failure, delirium, perioperative infections, and revision arthroplasty. Additionally, preoperative hemoglobin, albumin, and INR can serve as important markers of the risk of revision knee arthroplasty. More research is needed to stratify the risk of complications in the varying severities of AUD to better determine the best perioperative management for TKA.

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