Bleeding Risk Following Total Shoulder Arthroplasty in Patients Using Selective Serotonin Reuptake Inhibitors

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ABSTRACT

BACKGROUND: The purpose of the current study is to evaluate the association between selective serotonin reuptake inhibitor (SSRI) use and the risk of perioperative bleeding and blood transfusion following total shoulder arthroplasty.

METHODS: The PearlDiver (PearlDiver Technologies, Colorado Springs, CO, USA) Mariner170 database was queried to conduct this retrospective cohort study. Patients were included if they were over 18 years, had anxiety or depression, and underwent primary TSA. Eligible patients were stratified by SSRI use and 1:1 case-control matched by age, gender, Charlson Comorbidity Index (CCI), and relevant comorbidities. Patient demographics and 30-day postoperative outcomes, including bleeding, transfusion, deep venous thrombosis, or pulmonary embolism, were extracted and compared across cohorts.

RESULTS: The SSRI and control groups each contained 3,346 patients who underwent anatomic or reverse TSA. For each group, the mean age was 67.45 ± 7.44 years with 2,410 (72.03%) males and a mean CCI of 1.04 ± 1.07. There were no significant differences ($p < 0.05$) in the risk of postoperative bleeding, transfusion, deep venous thrombosis, or pulmonary embolism between patients with anxiety and/or depression on SSRIs and those not using SSRIs.

CONCLUSION: The current study determined that there was no increased bleeding or thrombotic risk in patients with anxiety or depression on SSRIs undergoing TSA compared to those not using SSRIs. These findings do not provide support for the alteration of SSRI regimens in the TSA perioperative period due to bleeding or thrombotic risk. However, caution should still be used in patients on SSRIs undergoing TSA.

KEYWORDS: total shoulder arthroplasty; bleeding risk; SSRI; anxiety; depression

INTRODUCTION

Total shoulder arthroplasty (TSA), including both anatomic and reverse techniques, is a procedure that is being performed with increasing incidence across both older and younger populations.[1,2] While TSA is widely regarded as a safe and effective intervention for various shoulder pathologies, it carries the risk of bleeding-related complications.[3] Increased blood loss and the need for transfusions have been linked to longer hospital stays, dislocations, periprosthetic fractures, mechanical loosening, and periprosthetic joint infections.[4,5] Furthermore, blood transfusions following TSA have been associated with higher rates of sepsis, pneumonia, myocardial infarction, cerebrovascular accident, and venous thromboembolic events.[6] However, the studies also suggest that patients requiring transfusion often have a greater preoperative comorbidity burden, which may partly account for these associations.[6] Established risk factors for perioperative bleeding complications and transfusions in TSA include a higher Charlson-Deyo Comorbidity Index (CCI), low preoperative hemoglobin, coagulation disorders, and ischemic heart disease, among others.[7–9] Additionally, selective serotonin reuptake inhibitors (SSRIs) have been shown to increase the risk of transfusion in patients undergoing total hip (THA) or knee arthroplasty (TKA).[10-12] However, the hematologic effects of SSRIs in the setting of TSA remain poorly understood and underexplored in the existing literature.

SSRIs are among the most commonly prescribed medications nationally and represent the most frequently used class of antidepressants, with usage steadily increasing over the past 30 years.[13,14] While SSRIs are effective and widely used for a variety of psychiatric conditions, they are not without side effects—most notably, their impact on platelet function. SSRIs exert their antiplatelet effects by depleting serotonin levels within platelet dense granules, thereby impairing primary homeostasis and increasing the risk of bleeding.[15-17] In the orthopaedic setting, perioperative SSRI use has been linked to higher rates of both aseptic and all-cause revision following TSA.[18]

Despite SSRIs demonstrating an association with an increased risk of bleeding following both THA and TKA, the effect of SSRIs on the risk of perioperative transfusions and bleeds following TSA has not been previously investigated to our knowledge.[10–12] The purpose of the current study is to evaluate the association between SSRI use and the risk of perioperative bleeding and blood transfusion following TSA. We hypothesized that SSRI use during the perioperative period would be associated with an increased risk of bleeding and/or need for blood transfusion.

METHODS

Study Design

The PearlDiver (PearlDiver Technologies, Colorado Springs, CO, USA) Mariner170 dataset was queried as part of this retrospective cohort study. The Mariner170 dataset contains over 170 million United States (U.S.) patients receiving health coverage under commercial insurance, Medicare, Medicaid, government insurance, and self-pay between 2010 and 2023. Patient records were retrieved using procedural and diagnostic codes from the International Classification of Diseases Ninth (ICD-9) and Tenth (ICD-10) Revision, and Current Procedural Terminology (CPT). Institutional review board approval was waived since the dataset has been de-identified for public access.

Study Population

Adult patients over the age of 18 years with a history of anxiety or depression who underwent primary TSA (CPT-23472) and had 30-day postoperative outcomes data available were included. Patients with a history of coagulation or hemorrhagic disorder, thromboembolic disease, anemia, tumor or metastasis, trauma about the shoulder, or infection of the shoulder joint were excluded.

Data Extraction

Demographic variables included age, gender, Charlson Comorbidity Index (CCI), and history of diabetes, chronic kidney disease (CKD), obesity, hypertension (HTN), coronary artery disease (CAD), congestive heart failure (CHF), rheumatoid arthritis (RA), depression, alcohol use, tobacco use, anemia, coagulopathy, anticoagulant use, coagulation factor use, prothrombotic agent use, and SSRI use were extracted. Postoperative outcomes within the first 30 days of surgery included bleeding, transfusion needs, deep venous thrombosis (DVT), and pulmonary embolism (PE). Medication exposure was identified at the SSRI class level. Although individual agents can be identified within the database, overlapping treatment windows and transitions between antidepressants limit the accuracy of agent-specific classification.

Statistical Analysis

Eligible patients were stratified by SSRI use and case-control matched 1:1 by age, gender, CCI, and history of diabetes, CKD, obesity, HTN, CHF, RA, depression, alcohol use, tobacco use, anemia, coagulopathy, anticoagulant use, coagulation factor use, and prothrombotic agent use. Patient demographics and 30-day postoperative outcomes were compared across cohorts using student's t-tests for continuous variables and chi-square analyses for categorical variables. All analyses were conducted using the built-in R statistical software within PearlDiver, with p-value of <0.05 indicating statistical significance.

RESULTS

Demographics

After matching, a total of 3,340 patients undergoing TSA were included in the study, with 2,630 patients (78.60%) in both the SSRI and control group having a documented history of depression, with the remaining patients having anxiety [**Table 1**]. The mean age was 67.45 ± 7.44 years with 2,410 (72.03%) males and a mean CCI of 1.04 ± 1.07 were identical between SSRI and control group. [**Table 1**]

Outcomes

There were no statistically significant differences (p <0.05) in the risk of bleeding, transfusion, deep venous thrombosis, or pulmonary embolism 30 days following TSA between patients with anxiety and/or depression on SSRIs and those not on SSRIs [**Table 2**].

Table 1. Demographics of patients with anxiety/depression who underwent total shoulder arthroplasty

	SSRI n (%)	Control n (%)	p-value
Age (mean ± SD)	67.45 ± 7.44	67.45 ± 7.44	1
CCI (mean ± SD)	1.04 ± 1.07	1.04 ± 1.07	1
Gender	2,410 (72.03)	2,410 (72.03)	1
Diabetes	541 (16.17)	541 (16.17)	1
CKD	41 (1.23)	41 (1.23)	1
Obesity	967 (28.90)	967 (28.90)	1
HTN	2,542 (75.97)	2,542 (75.97)	1
CAD	328 (9.80)	328 (9.80)	1
CHF	16 (0.48)	16 (0.48)	1
RA	65 (1.94)	65 (1.94)	1
Depression	2,630 (78.60)	2,630 (78.60)	1
Alcohol Use	46 (1.37)	46 (1.37)	1
Tobacco Use	755 (22.56)	755 (22.56)	1
Anemia	26 (0.78)	26 (0.78)	1
Coagulopathy	0 (0)	0 (0)	1
Anticoagulation Use	41 (1.23)	41 (1.23)	1
Coagulation Factor	42 (1.23)	42 (1.23)	1
Prothrombotic	0 (0)	0 (0)	1

SSRI = selective serotonin reuptake inhibitor; SD = standard deviation;
SSRI = selective serotonin reuptake inhibitor; CCI = Charlson Comorbidity Index; CKD = chronic kidney disease; HTN = hypertension; CAD = coronary artery disease; CHF = congestive heart failure

Table 2. Bleeding and thrombotic risk in patients with anxiety or depression within 30 days following total shoulder arthroplasty

	SSRI n (%)	Control n (%)	p-value
Bleeding	7 (0.21)	10 (0.30)	0.627
Transfusion	10 (0.30)	14 (0.42)	0.539
DVT	7 (0.21)	3 (0.09)	0.342
PE	1 (0.03)	2 (0.06)	1

SSRI = selective serotonin reuptake inhibitor; DVT = deep vein thrombosis; PE = pulmonary embolism

DISCUSSION

The purpose of the present study was to evaluate the impact of SSRIs on the risk of perioperative bleeding and transfusions following TSA. Contrary to our initial hypothesis, the findings of this study did not demonstrate a significant increase in bleeding-related complications among patients with anxiety and/or depression on SSRIs undergoing TSA. Given the widespread and increasing use of SSRIs,[13,14] along with the rising incidence of TSA procedures,[1,2] it is important to understand the potential implications of SSRI use in the surgical context. The present findings contrast with prior studies that reported increasing bleeding risk associated with SSRIs in THA and TKA.[10-12] Thus, the current study does not provide support for the alteration of SSRI regimens in the TSA perioperative period due to bleeding or thrombotic risk. However, caution should still be used for patients undergoing TSA who are using SSRIs in the perioperative period.

Understanding whether SSRI use increases perioperative bleeding risk is important for guiding medication management in a growing surgical population with high rates of mental health comorbidity. SSRIs have been linked to impaired platelet aggregation by decreasing serotonin content in platelet dense granules,[15-17] which may account for increased bleeding risk reported in TKA and THA.[10-12] Bismuth-Evanzal et al demonstrated that in a clinical setting, SSRIs depleted platelet serotonin stores and reduced aggregation in response to ADT, collagen, and epinephrine.[15] Additionally, in-vitro studies have demonstrated that sertraline and its inactive metabolite, N-desmethylsertraline, inhibit platelet aggregation and down regulate surface markers of activation.[17] However, these effects did not translate into increased bleeding or transfusion requirements in our TSA cohort. These differences may reflect a gap between in-vitro models and differing clinical settings, where compensatory mechanisms and surgical factors influence outcomes. This discrepancy may also be due to anatomical and procedural differences between lower extremity arthroplasty and TSA. Additionally, although antiplatelet agents have been associated with increased blood loss in TSA,[19] this increase is not clinically significant and rarely necessitates transfusions.[19,20] It is possible that SSRIs exert a similar mild antiplatelet effect that does not result in significant clinical consequences in TSA.

Although thrombotic events following TSA are uncommon, certain patients—such as those with prolonged operative times, elevated BMI, or older age—are at increased risk.[19,20] Therefore, individualized risk stratification for potential venous thromboembolism (VTE) prophylaxis remains critical.[21] Given the role of SSRIs in modulating platelet function, their potential effect on thrombotic risk also warrants consideration. Prior work by Bruun et al did not find a significant difference in the rate of VTE between SSRI and non-SSRI patients who underwent operative repair of hip fractures.[22] In alignment with these findings, the current results did not demonstrate a significant difference in VTE rates post-TSA between SSRI and non-SSRI users. This mirrors findings with other antiplatelet medications, such as aspirin and clopidogrel, which also do not increase VTE risk after TSA.[23]

Limitations

The most significant limiting factor of this study is that the data source was an administrative claims database. This introduces potential inaccuracies due to coding variability in ICD or CPT codes, upon which the analysis relied. In addition, the data source lacked clinical granularity and patient-level details. Prior studies have reported variability in bleeding risk among specific SSRIs.[24,25] However, specific SSRI, dosage, treatment duration, and overlap between agents were not assessed in the present study. Important perioperative variables such as operative times, known to influence bleeding and VTE risk,[20,21,26] could not be measured. Additionally, estimated blood loss was also unavailable, as were patient-specific risk factors such as prolonged immobility or bed confinement.[27] These limitations reduce the ability to control for potential confounders.

CONCLUSION

The current study determined that there was no increased bleeding or thrombotic risk in patients with anxiety or depression on SSRIs undergoing TSA compared to those not using SSRIs. These findings do not provide support for the alteration of SSRI regimens in the TSA perioperative period due to bleeding or thrombotic risk. However, caution should still be used in patients on SSRIs undergoing TSA.

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