Research Article

Do Antidepressant Medications Influence Readmission Rates Following Primary Total Hip Arthroplasty: A Retrospective Study

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Introduction

In 2014, total knee and total hip arthroplasty procedures were, respectively, the third and fourth most frequently performed procedures and accounted for 9% of all inpatient surgical procedures performed in the United States [1]. Numerous studies forecast an increased number of these procedures being performed over the coming decade and beyond [2]. A 25-year projection of TJA volume expects 572,000 total hip arthroplasties (THA) and 3.48 million total knee arthroplasties (TKA) to be performed annually by 2030 [3]. Under these conditions, nearly 1% of the projected 355.1 million Americans will undergo a THA procedure in 2030 [4]. It is crucial we better understand this expanding population to better mitigate risk factors and improve outcomes.

Antidepressant (AD) medications encompass a variety of drug classes (selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibits (SNRIs), tricyclic antidepressants (TCAs), etc.). Much of the literature describing their impact in orthopedic procedures focuses on the role of serotonergic agents, likely because of the presumed effects on platelet aggregation [5-8]. Between 10-15% of older adults experience some clinically significant form of depression and likewise, report the greatest rates of antidepressant medication use among all age groups [9]. Clinically speaking, Gold et al. showed an association between depression and 90-day readmissions following TJA as patients with a recorded history of depression were 21-24% more likely to experience a readmission event [10]. There are potential economic impacts to consider as well. Ahn et al. identified an association between TJA patients with a recorded clinical history of depression, and higher predicted bundle cost than the target price of this procedure [11]. It is prudent we uncover the influence AD medications may play in the clinical success of TJA procedures. The purpose of this analysis was to examine how various classes of AD medication influence readmission rates of primary THA procedures. Readmission events can negatively impact a patient's recovery from THA and create financial strain on the hospitals caring for these patients. Investigation of this patient population is warranted to better inform physicians how best to manage patients taking antidepressant medications.

Methods

Having obtained Institutional Review Board approval, a retrospective review was conducted of all THA procedures at our institution from January 2015 to June 2019. Patients were identified from their THA procedure codes (DRG 469 & 470 w/out fracture) in the hospital's Billing Claims Database. A total of 4,935 subjects were identified. Subjects were excluded for the following: revision or conversion THA, hip resurfacing, bilateral, and hip fracture procedures.

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Patient level data including age, sex, ASA and select comorbidities was abstracted from the hospitals electronic medical record (EMR) system. Outpatient use of AD medication was assumed if any of the specified AD medication was listed in the billings claim database during the index admission. A total of 696 subjects taking AD medication were identified.

Readmission events were identified in the cohort using the hospital EMR. Readmission events were defined by admission to any part of the hospital system following their index procedure date. Readmissions events were classified by the nature of the complication. Admission to the hospital for dislocation/instability, periprosthetic femur or acetabular fracture (PPF), aseptic loosening/failed osseointegration, prosthetic joint infection (PJI) and other instances of hardware failures were considered mechanical complication readmissions. Admission to the hospital for any reason other than those previously stated were considered non-mechanical complication readmission. Diagnosis codes for all potential complications were considered by two reviewers and classified by the nature of the event. Minitab (State College, PA, USA) was used to perform basic and univariate analysis of the data.

Results

A total of 4,935 patients were identified based on our inclusion criteria with 696 having been prescribed antidepressants. Of the patients included, 2,217 (52.30%) were female and 497 (71.41%) were female in the antidepressant cohort. The average age in the total group was 66.562 which was similar to the average age in the antidepressant group of 66.235. There was a significant difference found between the two groups' comorbidities. Specifically, there were differences in lung disease, diabetes mellitus, as well as having a past medical history of smoking, alcohol use and depression as seen in table 1.

The overall readmission rate between 1-30 days was found to be significantly different between the groups (P<0.001) with 110 patients (2.6%) who were not prescribed antidepressants and 37(5.3%) who were prescribed antidepressants. Total readmission rates trended towards statistical significance at 31-60 days (p=0.057) with 31 (0.7%) patients who were not taking antidepressants and 10 (1.4%) who were taking antidepressants. Overall readmission rates from 1-60 days was statistically significant (p<0.05) with 131(3%) to 47(6.8%) for no antidepressants and depressants respectively. At 61-90 days, there was no significant difference between the two groups (P=0.353). Overall readmission rates from 1-90 days was statistically significant (p <0.05) with 180 (4.2%) and 56 (8%) for the non antidepressant and antidepressant group respectively as seen in table 1.

It was found there was a statistically significant difference in overall mechanical complication readmission rates (p=0.014) between the two groups at 30 days as 49 (1.2%) were readmitted who were not taking antidepressants and 16 (2.3%) who were on antidepressants. There was no statistically significant difference in mechanical complication readmission rates between the two groups at the 31-60 days and 61-90 days period. When examining total mechanical readmission from 1-60 days, 56 (1.3%) and 20 (2.9%) there was a statistically significant difference between the non antidepressant and antidepressant group (p<0.05), as well as 1-90 days with 59 (1.4%) and 22 (3.2%) (p<0.05) for the non antidepressant and anti depressant group respectively as seen in table 1.

Regarding overall non-mechanical readmission rates, there was no statistically significant difference at 1-30 days, 1-60 days, 1-90 days, and 61-90 days but there was a difference found at 31-60 days. Thirty-one patients (0.7%) not taking antidepressants were readmitted at 60 days for non mechanical complications and 11(1.6%) while on antidepressants (P=0.024) as shown in table 1.

Sub-analysis by gender of patients in the antidepressant group found there to be 497 females taking antidepressant and 199 males taking antidepressants. There were statistically significant differences between the two groups comorbidities as 73 (14.7%) females had a history of cardiac disease compared to 57 (28.6%) males (p<0.001). Similarly, 57 (11.5%) females had a history of diabetes mellitus compared to 38 (19.1%) males (p=0.015). There was no difference in the two groups regarding history of lung disease, renal disease, smoking history, alcohol use, or history of depression as seen in table 2.

Analysis of overall readmission rates by gender revealed no differences at 1-30, 31-60, 1-60, 61-90 or 90 days. Mechanical complication readmission rates at 30 days were statistically significant and found 16 (3.2%) females taking antidepressants compared to 0 males to be readmitted (p=0.009.) Similarly, there was a statistically significant difference from 1-60 days with 19 (3.8%) females taking antidepressants and 1 (0.5%) male readmitted for mechanical complications (p<0.05). There was also a statistically significant difference at the 1-90 day interval with 20 (4%) females and 2 (1%) males readmitted for mechanical complications (p<0.05). It was found that there were no differences at 31-60 and 61-90 days. Additionally, there were no statistically significant differences in non-mechanical readmission rates analyzed by gender at the 1-30, 31-60, 1-60, 61-90 or 1-90 days as shown in table 2.

Analysis then compared readmission rate by antidepressant class. There were 453 (65%) patients that were taking selective serotonin reuptake inhibitors (SSRIs) and 696 patients using other antidepressant classes which include

Table 1: Readmission rates by Antidepressant use

	No Antidepressant n=4239	Any Antidepressant n=696	p-value
Age, n, mean (SD)	66.562 (10.436)	66.235 (10.022)	0.428
Gender=F, n (%)	2217 (52.30%)	497 (71.41%)	**<0.001**
Readmission Rates			
1-30 days	110 (2.6%)	37 (5.3%)	**<0.001**
31-60 days	31 (0.7%)	10 (1.4%)	0.057
60 day	131 (3%)	47 (6.8)	**<0.05**
61-90 days	39 (0.9%)	9 (1.3%)	0.353
90 day	180 (4.2%)	56 (8%)	**<0.05**
Mechanical Readmission Rates			
1-30 days	49 (1.2%)	16 (2.3%)	**0.014**
31-60 days	7 (0.2%)	4 (0.6%)	0.066
60 day	56 (1.3%)	20 (2.9%)	**<0.05**
61-90 days	3 (0.1%)	2 (0.3%)	0.148
90 day	59 (1.4%)	22 (3.2%)	**<0.05**
Non Mechanical Readmission Rates			
1-30 days	24 (0.6%)	7 (1%)	0.174
31-60 days	31 (0.7%)	11 (1.6%)	**0.024**
60 day	55 (1.3%)	18 (2.6%)	>0.05
61-90 days	33 (0.8%)	6 (0.9%)	>0.05
90 day	88 (2.1%)	24 (3.5%)	>0.05
Comorbidities			
Lung Disease	129 (3%)	56 (8%)	**<0.001**
Cardiac	719 (17%)	130 (18.7%)	0.266
DM	399 (9.4%)	95 (13.6%)	**0.001**
Smoking History	246 (5.8%)	66 (9.5%)	**<0.001**
Renal	141 (3.3%)	25 (3.6%)	0.719
ETOH	33 (0.8%)	13 (1.9%)	**0.006**
Depression	215 (5.1%)	393 (56.5%)	**<0.001**

Table 2: Subanalysis of readmission by gender

	Female + Any Antidepressant (n=497)	Male + Any Antidepressant (n=199)	p-value
Readmission Rates			
1-30 days	27/497 (5.4%)	10/199 (5%)	0.826
31-60 days	9/497 (1.8%)	1/199 (0.5%)	0.296
60 day	36 (7.3%)	11 (5.5%)	>0.05
61-90 days	6/497 (1.2%)	3/199 (1.5%)	0.72
90 day	42 (8.5%)	14 (7%)	>.05
Mechanical Readmission Rates			
1-30 days	16/497 (3.2%)	0/199 (0%)	**0.009**
31-60 days	3/497 (0.6%)	1/199 (0.5%)	>0.999
60 day	19 (3.8%)	1 (0.5%)	**<0.05**
61-90 days	1/497 (0.2%)	1/199 (0.5%)	0.49
90 day	20 (4%)	2 (1%)	**<0.05**
Non Mechanical Readmission Rates			

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1-30 days	3/497 (0.6%)	4/199 (2%)	0.107
31-60 days	10/497 (2%)	1/199 (0.5%)	0.193
60 day	13 (2.6%)	5 (2.5%)	>0.05
61-90 days	4/497 (0.8%)	2/199 (1%)	>0.999
90 day	17 (4.3%)	7 (3.5%)	>0.05
Comorbidities			
Lung Disease	40/497 (8%)	16/199 (8%)	0.997
Cardiac	73/497 (14.7%)	57/199 (28.6%)	**<0.001**
DM	57/497 (11.5%)	38/199 (19.1%)	**0.015**
Smoking History	45/497 (9.1%)	21/199 (10.6%)	0.554
Renal	12/497 (2.4%)	13/199 (6.5%)	0.029
ETOH	8/497 (1.6%)	5/199 (2.5%)	0.468
Depression	289/497 (58.1%)	104/199 (52.3%)	0.159

Table 3: Subanalysis of readmission by antidepressant class

	SSRI (n=453)	Any AD (n=696)	p-value
Readmission Rates			
1-30 days	24/453 (5.2%)	37/696 (5.3%)	0.998
31-60 days	5/453 (1.1%)	10/696 (1.4%)	0.621
60 day	29 (6.4%)	47 (6.8%)	>.05
61-90 days	4/453 (0.8%)	9/696 (1.2%)	0.583
90 day	33 (7.3%)	56 (8.0%)	>.05
Mechanical Readmission Rates			
1-30 days	10/453 (2.2%)	16/696 (2.2%)	0.924
31-60 days	2/453 (0.4%)	4/696 (0.5%)	>0.999
60 day	12 (2.6%)	20 (2.9%)	>.05
61-90 days	1/453 (0.2%)	2/696 (0.2%)	>0.999
90 day	13 (2.9%)	22 (3%)	>.05
Non Mechanical Readmission Rates			
1-30 days	6/453 (1.3%)	7/696 (1.0%)	0.624
31-60 days	6/453 (1.3%)	11/696 (1.5%)	0.725
60 day	12 (2.6%)	18 (2.6%)	>.05
61-90 days	2/453 (0.4%)	6/696 (0.8%)	0.491
90 day	14 (3.0%)	24 (3.4%)	>.05
Comorbidities			
Lung Disease	31/453 (6.8%)	56/696 (8.0%)	0.452
Cardiac	63/453 (13.9%)	130/696 (18.6%)	**0.032**
DM	61/453 (13.4%)	95/696 (13.6%)	0.944
Smoking History	43/453 (9.4%)	66/696 (9.4%)	0.983
Renal	20/453 (4.4%)	25/696 (3.5%)	0.485
ETOH	10/453 (2.2%)	13/696 (1.8%)	0.688
Depression	275/453 (60.7%)	393/696 (56.3%)	0.138

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tricylic antidepressants or monoamine reuptake inhibitors. The only statistically significant difference in comorbidity was that 63 (13.9%) patients on SSRIs had a history of cardiac disease compared to 130 (18.6%) that were on a different antidepressant (P=0.032.) This sub analysis showed no significant difference in overall readmission rate at 1-30, 31-60, 1-60, 61-90 or 1-90 days intervals. Additionally, there were no significant differences in mechanical complication rates between the two groups at 1-30, 31-60, 1-60. 61-90 or 1-90 day intervals. Further subgroup analysis revealed no significant difference in non mechanical complication rates at 1-30, 31-60, 1-60, 61-90 and 1-90 days intervals as shown in table 3.

Discussion

Patients taking any class of AD medication were readmitted at 30-days for all causes at a significantly greater rate than AD naïve patients (5.3% v. 2.6%, p<0.001) (Table 1). This group of patients also demonstrated a significantly greater risk for 30-day mechanical complications (2.3% v. 1.2%, p=0.014) and 60-day non-mechanical complications (1.6% vs 0.7%, p=0.024) as well. Within cohort analysis, individual medication classes did not reveal any significant influence on readmissions, regardless of readmission cause. Gender, however, was a significant factor regardless of AD class. Females taking any AD medication were readmitted significantly more often than males for mechanical complications within 30-days of their procedure (3.2% v. 0%, p=0.009). Readmissions after THA procedures are of importance to both the patient and hospital alike. Hospitals hope to produce efficient, quality care for their patients while patients look to achieve a speedy, uncomplicated recovery from their surgery. As the population continues to age, the number of total hip arthroplasty will continue to increase.3 Similarly, it has been found that between 2015-2018 13.2% of the adults aged 18 and over used antidepressant medications in the past 30 days, and that use was higher in women compared to men (17.7% vs 8.4%). Further, during the same period, antidepressant use increased with age, overall in both sexes and the use was highest among women aged 60 and over (24.3%.)12 As such, mental health needs need to be considered as a significant risk factor because mental illness and antidepressant use has significant impact on outcome of total joint arthroplasties [13-15].

Age accompanying psychiatric medications is a known important factor to consider in regard to surgical planning. The average age of the patients in our analysis was 66 years old, in line with the general age at which patients undergo arthroplasty procedures. Being of geriatric age and taking antidepressants pertains to increased risk as well. Pavon and colleagues looked at approximately 5,000 patients over the age of 60 admitted to their surgical service and demonstrated an increased risk for readmission for any cause within 90

days if taking antidepressants [16]. Similarly, Bovonratwet et al completed a study examining risk factors for 30-day readmission after outpatient total hip arthroplasty. In total, 5,245 patients were identified in the National Quality Improvement Program Database. The incidence of 30-day readmission after outpatient total hip arthroplasty was 1.6% with the primary risk factor being patient age (RR=2.3%, 95% CI=1.15-4.62.) [17]. Further, Cantrell et al. conducted a study reviewing the risk factors for readmission within thirty days following revision total hip arthroplasty. Utilizing the ACS-NSQIP database, 10,032 patients were identified that underwent a total hip arthroplasty between 2005 to 2018. Of those, 855 (8.5%) were readmitted within 30 days with increasing age being a significantly positive risk factor for 30 day readmission.18

Our results suggested that gender may also modulate a patient's risk of readmission, as female patients taking AD medication were readmitted significantly more often for mechanical complications than other females not taking AD medication, regardless of its class as shown in table 1. Inacio et. al reported on a similar phenomenon, demonstrating that females undergoing THA are at greater risk for implant failure and revision at 5 years post-op than men [19].

Overall, our study illustrated how patients taking any class of AD medication are at significantly greater risk for a short-term readmission, particularly from mechanical complications at 30-days, and non-mechanical complications at 60-days (Table 1). No specific class of AD medication was shown to pose a greater risk of readmission after THA (Table 3). This finding was similar to the findings of Jorgensen et al. They completed a multicenter study with prospective registration on preoperative comorbidity, 30 and 90 day followup, and information on dispensed prescriptions on psychopharmacological treatment. They identified 8,757 patients who underwent total hip or total knee arthroplasty and found 1,001 (11.4%) had a psychiatric disorder. Of those, 43.4% used SSRIs, and 31.6% used other antidepressants. Similar to the the results of our study (Table 1 and Table 3), patients with a history of psychiatric disorder as well as taking any form of antidepressant were at an increased risk of 30 and 90 day readmission [20]. Similarly, Knapp et al evaluated the readmission rates of patients undergoing total hip or knee arthroplasty with the diagnoses of anxiety or depression based on psychopharmacologic therapy prescription. A total of 4,107 cases were included, of which 4.28% had a readmission within 90 days [21]. The findings of our study as well as knapp et all are in line with several other studies that demonstrated patients with diagnoses of depression, anxiety have shown inferior outcomes and increased risk of readmission [10,22-26].

Ample literature implores physicians to consider educating their patients on how mental health and medication usage

may affect recovery from a THA procedure. Depression and baseline mental health, in general, has been shown to decrease patient outcomes across the board. Halawi et al. sought to clarify this effect and demonstrated how baseline mental health modulates the effect of depression on patient reported outcomes in TJA. Those exhibiting both poor baseline mental health and depression did not reach the threshold for good mental health at 1 year, despite having reported similar net gains in physical function to patients without depression [27]. Additionally, Greene et al. showed how AD use, regardless of class, was associated with more perceived pain and reduced measures of Health-Related Quality of Life following THA [28]. One could postulate that even with good physical results, if patients on ADs are still in pain and unhappy with their outcomes, complications naturally could arise.

Those involved with the orthopedic team should be diligent when gathering a past medical history of the patient, and should be attentive to the patient's mental health. Questionnaires, such as the patient health questionnaire 9, should be applied to screen for at risk patients. Pan et al demonstrated that mental health questionnaires may be applied as they may more accurately determine at-risk patients than either prior depression, anxiety or medication history due to undiagnosed or untreated disease [24]. Medical teams should implement targeted interventions to lower rates of readmission in at-risk patients through telephone calls to encourage medications compliance, and a more complex psychosocial intervention [29]. Gilbody et al. demonstrated this through a meta-analysis of 37 randomized studies which 12,355 patients with depression receiving primary care to quantify the short and long term effectiveness of collaborative care in patients with depression. They concluded that depression outcomes were improved at 6 months (standardized mean difference, .25; 95% confidence interval, .18-.32) and evidence of long-term benefit for up to 5 years (standardized mean difference, .15; .95% confidence interval, 0.001-0.31) [29]. The findings of Gilbody et al can be seen in a study by Kohring et al. They found that in patients with depression who underwent total joint arthroplasty who were "untreated" had a lower magnitude of change in physical function score [30].

We recognize there are several limitations to this study, the most obvious of which is its retrospective nature subjecting results to sampling bias and misclassification bias, the latter of which is important in establishing our study group of patients taking a form of antidepressant. We suggested the presence of an antidepressant medication in the encounters billing abstract, which could have potentially led to misclassification and provided no information regarding patient history with AD medications. Table 1, which demonstrates how patients taking any form of AD presented with significantly more comorbidities than the control group, should also be taken into consideration in the review of our results as it may lend itself to the significant difference in non-mechanical readmissions

at 60 days between the two groups. Another factor that may have affected the significance of readmission rates is the sample sizes between each group. There were far more female patients in this study than male patients. Depression is known to be more prevalent in women than in men, and this coupled with osteopenia's propensity to affect women, is a selection bias which could have skewed our results. Further research will need to be done to determine a more significant link between the use of AD medications, and TJA readmissions as well as the exact cause of such medications on readmissions. TJA patients should also be counseled on the potential risks of AD medications on readmission.

Conclusion

As the population continues to age, the number of total joint arthroplasties is expected to increase. Along similar lines, the prevalence of those with mental health disorders is expected to rise concurrently with an increase in antidepressant medication prescription. Our study demonstrates that patients that are female and taking antidepressants are at an increased risk of readmission following total hip arthroplasty. Medical teams need to be cognisant of patients taking antidepressants for mental health who are presenting for potential total hip arthroplasty.

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