

Patients with Multiple Myeloma Have Increased Risks of Medical, but Not Surgical, Complications Following Total Shoulder Arthroplasty

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Background: Multiple myeloma (MM) is a hematologic malignancy associated with characteristic lytic bone lesions. Due to weakened bone quality from these lesions, MM has been previously associated with poor orthopaedic surgery outcomes, but this is understudied in the setting of total shoulder arthroplasty (TSA).

Purpose: The purpose of this study was to investigate if patients with MM have increased risks of requiring revision after TSA.

Methods: This was a retrospective review of a national insurance database. Patients who underwent TSA were identified and stratified by previous diagnoses of MM. The primary outcome was the incidence of TSA revision. Patients with and without MM were matched at a 1:4 ratio on the basis of age, biological sex, and CCI. Chi square analyses of the matched cohorts were performed to evaluate outcomes of interest.

Results: Of 286,552 patients who underwent TSA, 1,949 (0.7%) patients had previous MM diagnoses. There was not a significant difference in the incidence of revision TSA between cohorts (3.7% vs 3.8%, $p>0.99$). Patients with MM were found to have significantly higher rates of fragility fracture (27.5% vs 16.9%, $p<0.001$), incision and drainage (0.6% vs 0.3%, $p=0.015$), acute kidney injury (3.4% vs 1.4%, $p<0.001$), pneumonia (2.6% vs 1.5%, $p<0.001$), stroke (1.7% vs 1.0%, $p=0.0019$), and blood transfusion (1.0% vs 0.6%, $p=0.049$).

Conclusion: Patients with MM do not have an increased risk of TSA revision but are at increased risk for several medical complications. These results should inform shared decision-making for physicians and MM patients with end-stage shoulder osteoarthritis.

What this study adds: This is a large-scale study demonstrating that while patients with MM undergoing TSA do not have an increased risk of revision surgery; however, they are at significantly higher risk for several medical complications.

Potential impacts on research, practice or policy: This study provides reassuring findings can guide clinical practice by informing shared decision-making and treatment planning for patients with multiple myeloma and shoulder osteoarthritis, while helping to guide future research and policy aimed at optimizing perioperative care for this growing patient population.

Study Design: Retrospective Cohort Study

Level of Evidence: Level III

Keywords: Arthroplasty, Complications, Fragility fractures, Hematologic malignancy, Multiple myeloma, Orthopedics, Osteoarthritis, Shoulder prosthesis.

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INTRODUCTION

Multiple myeloma (MM) is a hematologic malignancy characterized by the uncontrolled clonal proliferation of plasma cells, leading to an overproduction of monoclonal immunoglobulins and resultant end-organ damage [1]. MM is most often described clinically as a distinct and advanced stage of the spectrum of proliferative plasma cell disorders,

which also includes monoclonal gammopathy of undetermined significance (MGUS) and smoldering multiple myeloma (SMM) [2]. Diagnostic criteria for MM consist of greater than 10% bone marrow infiltration of myeloma cells, with at least one symptom that is part of the classic "CRAB" criteria, an acronym that includes hypercalcemia, renal dysfunction, anemia, and lytic bone disease [3].

A number of skeletal derangements occur within the multiple myeloma pathogenesis cascade. MM contributes to

enhanced activity of osteoclasts, which concurrently causes osteoblast dysfunction [4]. Bone quality is further weakened by the interaction between myeloma cells and osteocytes, resulting in sustained bone loss through osteocyte apoptosis and release of RANKL and sclerostin [4][5]. Bone pain from lytic lesions is one of the characteristic presenting symptoms of MM [11]. Ameliorating these symptoms is a major focus of treatment strategies, however, MM treatment itself can also harm bone health [5][6][7]. Both myeloma-induced osteoporosis and radiation-induced osteoporosis have been associated with increased risks of fractures [7]. Further, corticosteroid use among MM patients was found to be the greatest predictive factor for fragility fracture and aseptic loosening for those with joint arthroplasty implants, due to irradiation-induced osteoporosis [5][6]. These detrimental effects on bone health have dire implications, as MM patients who experience fractures are at a significantly increased risk of mortality [8].

For patients with end-stage shoulder osteoarthritis or inflammatory arthropathy, total shoulder arthroplasty (TSA) is a common and widely successful surgical intervention [9]. To our knowledge, the outcomes of TSA in MM patients are yet to be investigated. In the literature for total knee arthroplasty (TKA) and total hip arthroplasty (THA), prior studies have shown that MM patients were at increased risk of revision and early postoperative complications, especially surgical site infection and thromboembolic events [10][11]. Therefore, the aim of this study was to evaluate the medical and surgical outcomes of TSA in patients with MM, compared to the outcomes of those without MM. We hypothesized that MM patients would experience a higher incidence of complications and revision rates.

METHODS

Data Source

This was a retrospective cohort analysis of the PearlDiver Database (Colorado Springs, CO), an all-payer claims record of over 165 million patients from 2010 through the last quarter of 2022. This database allows patients to be tracked regardless of changes in insurance status or facility usage, allowing longitudinal follow-up and minimizing attrition bias. Because the database only contains deidentified patient information, the Institutional Review Board at our Institution deemed this study as exempt (IRB00387181).

Patient Population

Patients with MM who underwent TSA due to osteoarthritis were identified using International Classification of Diseases 9th Edition (ICD-9) and 10th Edition (ICD-10) codes, and Current Procedural Terminology (CPT) codes (**Appendix 1**). Only patients with at least two-year follow-up were included

in the study. These criteria facilitated the creation of two cohorts of TSA patients, one consisting of patients with MM diagnoses ("MM cohort") and one of patients without a history of MM ("control cohort").

Demographic Variables and Outcome Measures

Patients in the MM and control cohorts were assessed for differences in age, biological sex, and Charlson comorbidity index (CCI) scores. CCI represents a composite of many common comorbidities, assigning a numeric value to represent comorbidity burden [12]. A variety of common comorbid conditions were assessed between the two cohorts to characterize specific differences in disease burden.

The primary outcome of interest was incidence of TSA revision. Specific revision etiologies were also investigated, including aseptic revision, revision due to instability, revision due to periprosthetic fracture (PPF), revision due to periprosthetic joint infection (PJI), and revision due to rotator cuff tear (RCT). Other surgical complications assessed included the incidence of fragility fracture and the incidence of incision and drainage within 2 years, and surgical site infection (SSI) and wound dehiscence within 90 days. The secondary outcome of interest was the incidence of medical complications within 90 days of the index TSA procedure. The medical complications included were acute kidney injury (AKI), cardiac arrest, deep venous thrombosis (DVT), pneumonia, pulmonary embolism (PE), stroke, transfusion, and urinary tract infection (UTI).

Statistical Analysis

Patients in the MM and control cohorts were matched at a 1:4 ratio on the basis of age, biological sex, and CCI. For demographic analyses, Student's T-tests and Chi square tests were used to compare continuous and categorical variables, respectively. For outcomes, Chi square analyses of the matched cohorts were performed. Significance was set at $p < 0.05$.

RESULTS

Patient Demographics

Among 286,552 TSA patients included, 1,949 (0.7 %) had multiple myeloma (MM); 7,731 matched controls were identified. Before matching, MM patients were older (68.6 vs 68.1 years, $p = 0.002$), had higher CCI scores (2.8 vs 1.9, $p < 0.001$), and were more often male (51.4 % vs 44.1 %, $p < 0.001$; **Table 1**). After matching, no differences remained in age, sex, or CCI (all $p > 0.99$). Comorbidity frequencies before and after matching are summarized in **Table 2**.

Table 1. Patient Cohort Demographics

Demographic	Multiple Myeloma Patients	Control Patients	P Value
Age (Mean [SD])	68.6 (7.8)	68.1 (8.8)	0.0020
CCI (Mean [SD])	2.8 (2.7)	1.9 (2.2)	<0.001
Biological Sex			<0.001
% Female	48.6%	55.9%	
% Male	51.4%	44.1%	

Table 2. Comorbidity Profile of Patients in the Multiple Myeloma and Control Cohorts

Comorbidities	Unmatched Comparison			Matched Comparison		
	MM N (%)	Control N (%)	P Value	MM N (%)	Control N (%)	P Value
Acute Blood Loss Anemia	113 (5.8)	7,953 (2.8)	<0.001	109 (5.6)	239 (3.1)	<0.001
Alcohol Use Disorder	80 (4.1)	11,764 (4.1)	0.99	77 (4.0)	368 (4.8)	0.16
Arrhythmia	479 (24.6)	54,626 (19.2)	<0.001	473 (24.4)	1,730 (22.4)	0.058
Chronic Kidney Disease	477 (24.5)	33,991 (11.9)	<0.001	471 (24.3)	1,358 (17.4)	<0.001
Coagulopathy	286 (14.7)	16,745 (5.9)	<0.001	282 (14.6)	570 (7.4)	<0.001
Collagen Vascular Disease	163 (8.4)	18,871 (6.6)	0.0026	161 (8.3)	595 (7.7)	0.39
Congestive Heart Failure	224 (11.5)	22,252 (7.8)	<0.001	219 (11.3)	824 (10.7)	0.43
Dementia	45 (2.3)	4,568 (1.6)	0.018	45 (2.3)	153 (2.0)	0.38
Depression	581 (29.8)	86,653 (30.4)	0.56	577 (29.8)	2,637 (34.1)	<0.001
Diabetes Mellitus	813 (41.7)	101,729 (35.7)	<0.001	804 (41.5)	3,494 (45.2)	0.0040
Electrolyte Disorders	608 (31.2)	62,695 (22.0)	<0.001	598 (30.9)	1,996 (25.8)	<0.001
Hypertension	1,543 (79.2)	210,963 (74.1)	<0.001	1,532 (79.1)	6,272 (81.1)	0.050
Hypotension	520 (26.7)	66,906 (23.5)	0.0011	516 (26.7)	1,886 (24.4)	0.043
Iron Deficiency Anemia	440 (22.6)	33,477 (11.8)	<0.001	434 (22.4)	1,044 (13.5)	<0.001
Liver Disease	280 (14.4)	29,845 (10.5)	<0.001	276 (14.3)	981 (12.7)	0.073
Neurologic Disorders	125 (6.4)	17,014 (6.0)	0.45	122 (6.3)	498 (6.4)	0.86
Obesity	570 (29.2)	80,810 (28.4)	0.42	565 (29.2)	2,501 (32.4)	0.0081
Osteoporosis	385 (19.8)	41,894 (14.7)	<0.001	381 (19.7)	1,126 (14.6)	<0.001
Paralysis	42 (2.2)	4,861 (1.7)	0.15	41 (2.1)	199 (2.6)	0.28
Peptic Ulcer Disease	123 (6.3)	12,503 (4.4)	<0.001	122 (6.3)	433 (5.6)	0.26
Peripheral Vascular Disease	485 (24.9)	49,457 (17.4)	<0.001	479 (24.7)	1,722 (22.3)	0.022
Psychosis	45 (2.3)	7,557 (2.7)	0.38	43 (2.2)	215 (2.8)	0.20
Pulmonary Circulatory Disease	185 (9.5)	16,764 (5.9)	<0.001	180 (9.3)	556 (7.2)	0.0021
Pulmonary Disorders	654 (33.6)	85,079 (29.9)	<0.001	647 (33.4)	2,776 (35.9)	0.043
Rheumatoid Arthritis	182 (9.3)	20,433 (7.2)	<0.001	180 (9.3)	645 (8.3)	0.19

Substance Use Disorder	111 (5.7)	16,891 (5.9)	0.69	108 (5.6)	582 (7.5)	0.0034
Tobacco Use	518 (26.6)	74,822 (26.3)	0.79	512 (26.4)	2,283 (29.5)	0.0081
Valvular Disease	424 (21.8)	47,078 (16.5)	<0.001	419 (21.6)	1,490 (19.3)	0.021
Vitamin D Deficiency	411 (21.1)	52,388 (18.4)	0.0026	406 (21.0)	1,561 (20.2)	0.47

Total Shoulder Arthroplasty Outcomes

Overall revision rates were similar between MM and control patients (3.7 % vs 3.8 %, $p > 0.99$), and there were no differences in specific revision etiologies, surgical-site infection, or wound dehiscence. MM patients, however, demonstrated higher rates of fragility fracture (27.5 % vs 16.9 %, $p < 0.001$) and incision & drainage (0.6 % vs 0.3 %, $p = 0.015$).

Within 90 days post-TSA, MM patients experienced more medical complications (Table 3): acute kidney injury 3.4 % vs 1.4 % ($p < 0.001$), pneumonia 2.6 % vs 1.5 % ($p < 0.001$), strokes 1.7 % vs 1.0 % ($p = 0.002$), and transfusion 1.0 % vs 0.6 % ($p = 0.049$). No differences were observed for cardiac arrest, deep venous thrombosis, pulmonary embolism, or urinary tract infection (Table 3).

DISCUSSION

The aim of this study was to evaluate the short-term outcomes of total shoulder arthroplasty (TSA) in patients with multiple myeloma (MM). Our most important finding was that there was no significant difference in TSA revision rates between patients with and without MM, contrasting with prior research indicating higher revision risks for MM patients undergoing hip and knee arthroplasties [11]. The absence of increased revision risk in TSA likely reflects the shoulder's lower biomechanical demand compared with weight-bearing joints. Ultimately, the similar revision rates for TSA in MM patients is reassuring for surgeons and patients alike. This data is helpful for pre-operative counseling on anticipated outcomes.

MM patients demonstrated a significantly higher incidence of fragility fractures. This result is consistent with previous studies that have also shown an association between MM and fragility fractures, with notable predictors including age, increased weight at diagnosis, oral corticosteroid use, and chemotherapy [6]. The presence of lytic bone lesions, considered a defining MM criterion per the International Myeloma Working Group (IWIG) guidelines [13]. Lytic lesions directly impact bone strength, yet not all fractures in MM patients are attributable to such lesions [14]. Approximately one-third occur as fragility fractures in tumor-free sites and may occur independent of MM activity. Further, oral corticosteroids are a mainstay of MM treatment, but are also a significant risk factor for fragility fracture outside of MM involvement [6]. This aligns with recommendations that advise against corticosteroid-based MM treatment in cases of fragility fractures without CRAB criteria, and also suggests that not all fragility fractures are signs of MM progression [15]. We recommend that all TSA patients with MM are counseled postoperatively about the elevated risk of fractures and falls.

Notably, MM patients had an elevated rate of undergoing incision and debridement (I&D) after TSA compared to controls. Studies from the THA and TKA literature have not previously reported this finding, as these studies did not report on I&D rates specifically [10][11]. The elevated risk of I&D after TSA in MM patients is most likely attributable to chronic immunosuppression. Previous studies have demonstrated increased risks of infections and renal failure in MM patients, which may occur as a result of immunosuppression [4][9][11]. Interestingly, MM patients did not have an elevated risk of implant revision secondary to periprosthetic joint infection, thus, this 90-day elevated risk of incision and drainage may represent an increased risk of extraarticular surgical site infection as opposed to that of intraarticular infection.

MM patients exhibited higher rates of acute kidney injury, pneumonia, stroke, and transfusion. Renal dysfunction, present in nearly one-quarter of MM patients at baseline, predisposes to postoperative AKI and anemia, contributing to transfusion requirements [16]. Iron overload secondary to repeated transfusions may further increase infection susceptibility [2][7][10]. Increased pneumonia incidence likely reflects immunosuppression related to disease and therapy. No significant difference was seen in thromboembolic events (Deep Vein Thrombosis or Pulmonary Embolism). Prior studies described elevated risk in cancer arthroplasty cohorts [17][18], but the lack of difference here may reflect heightened awareness and adherence to VTE prophylaxis protocols in MM patients, including perioperative heparin or Low Molecular Weight Heparin use [17].

This study has limitations inherent to its observational and retrospective design. As a retrospective study, we cannot infer causation from our results, only correlation. This study used administrative data that does not capture specific treatment regimens or disease stages in MM patients, which may have impacted the results. While PearlDiver is an extensive database with over 140 million patient records, it only includes information from insured patients, which may have limited generalizability. We could not differentiate anatomic and reverse TSA in this study because they share a common CPT code. The use of this national database may have restricted the granularity of some clinical details, such as functional outcomes, intraoperative variables, and quality of life post-TSA. Additionally, regression modeling to allow for patient specific risk calculation could not be performed due to the unavailability of clinical variables within the database. We were also unable to control differences in MM treatment between patients, which may have impacted on the results. However, our large sample size and matched control cohort provides strength to our findings, allowing for an adequate comparison of TSA outcomes between MM and non-MM populations. Further research should focus on refining perioperative protocols to mitigate postoperative risks in this growing patient population.

Table 3. Matched Incidence of Surgical and Medical Postoperative Complications among TSA Patients with and Without Multiple Myeloma

Complication	Percentage of Multiple Myeloma Patients	Percentage of Control Patients	P Value
Surgical Complications			
Revision	73 (3.7)	10,713 (3.8)	>0.99
Aseptic Revision	54 (2.8)	8,830 (3.1)	0.44
Fragility Fracture	536 (27.5)	48,076 (16.9)	<0.001
Incision & Drainage	11 (0.6)	731 (0.3)	0.015
Revision Due to Dislocation or Subluxation	7 (0.4)	1,175 (0.4)	0.85
Revision Due to Periprosthetic Fracture	3 (0.2)	401 (0.1)	>0.99
Revision Due to Prosthetic Joint Infection	16 (0.8)	1,736 (0.6)	0.30
Revision Due to Rotator Cuff Tear	19 (1.0)	3,565 (1.3)	0.32
Surgical Site Infection	1 (0.1)	177 (0.1)	>0.99
Wound Dehiscence	6 (0.3)	692 (0.2)	0.73
Medical Complications			
Acute Kidney Injury	66 (3.4)	4,001 (1.4)	<0.001
Cardiac Arrest	0 (0.0)	135 (0.1)	0.66
Deep Venous Thrombosis	12 (0.6)	1,348 (0.5)	0.46
Pneumonia	50 (2.6)	4,231 (1.5)	<0.001
Pulmonary Embolism	7 (0.4)	928 (0.3)	0.96
Stroke	33 (1.7)	2,771 (1.0)	0.0019
Transfusion	19 (1.0)	1,716 (0.6)	0.049
Urinary Tract Infection	73 (3.7)	8,561 (3.0)	0.067

CONCLUSION

Our study demonstrates that MM patients undergoing TSA had no difference in revision rates, as compared to healthy controls. However, MM patients do have elevated risks for several medical and surgical complications such as an increased rate of incision and drainage, fragility fractures, acute kidney injury, pneumonia, and postoperative blood transfusion. These findings highlight the need for specialized perioperative care for MM patients undergoing TSA, given their complex health profiles and the risks associated with their disease and treatments.

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Ethical Approval: Study deemed as exempt (IRB00387181).

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