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# In-Hospital Morbidity and Mortality Following Total Joint Arthroplasty in Patients with Hemoglobinopathies

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ABSTRACT

Given the growing patient population with hemoglobinopathies needing total joint arthroplasty (TJA) and paucity of literature addressing this cohort, we examined the in-hospital complications in patients with hemoglobinopathies undergoing TJA. International Classification of Diseases, Ninth Revision codes were used to search the Nationwide Inpatient Sample database for hemoglobinopathy patients undergoing primary or revision TJA. Hemoglobinopathy patients had a significant increase in cardiac, respiratory, and wound complications; blood product transfusion; pulmonary embolism; surgical site infection; and systemic infection events, while there was no significant effect on deaths, deep vein thrombosis, and renal complications. It may be prudent to implement blood conservation strategies as well as diligent postoperative protocols to minimize the need for transfusion and related complications in this patient population.



The prevalence of hemoglobinopathy is estimated to be 3% in North America and 5.2% worldwide [1], and these rates are expected to rise by 2050 [2]. Sickle cell is the most common form of hemoglobinopathy that is found in 83% of patients with the diagnosis of hemoglobinopathy [1]. Hemoglobinopathies are associated with many medical [3] and surgical [4] complications, and patients are more likely to need surgical procedures [5]. With such a dramatic predicted increase in a problem that already has known consequences, it is important to understand the nature of these consequences and their relevance in a clinical setting. Joint osteonecrosis is a common condition in hemoglobinopathy patients that may result in a need for total joint arthroplasty (TJA) [3]. It is estimated that up to 50% of people with sickle cell disease develop hip osteonecrosis in their lifetime [6,7]. Total joint arthroplasty in patients with hemoglobinopathy and osteonecrosis of the femoral head has been associated with many complications and mixed outcomes [8–11]. There is little in the literature regarding the outcome of TJA in patients with other types of hemoglobinopathy. One review article examined the perioperative complications in all hemoglobinopathy patients undergoing total hip arthroplasty (THA) and found an array of outcomes [12]. Only one study in the literature examines the outcome of total knee arthroplasty (TKA) in patients with hemoglobinopathy [13]. Prior reports have also shown a higher incidence of revision arthroplasty in patients with hemoglobinopathy [14–16]. However, no study has directly examined the in-hospital complications in a large population of hemoglobinopathy patients undergoing primary and revision TJA. Thus, the purpose of this study was to examine the in-hospital complications and mortality in patients with all types of hemoglobinopathy undergoing TJA.

## Materials and Methods

Nationwide Inpatient Sample (NIS) data from 1993 to 2011 were utilized for this study. Since the NIS database has been sufficiently de-identified, this study was exempt from institutional review board review. Patients with a history of hemoglobinopathy who underwent THA or TKA (primary or revision) were identified using International Classification of Diseases, Ninth Revision (ICD-9) codes (Table 1).

For all patients, data on demographics (age, gender, and race), insurance type, hospital type (urban academic, urban private, or rural), hospital size (small, medium, or large), region (Northeast, Midwest, West, and South), underlying joint disorder (osteoarthritis or osteonecrosis), and in-hospital mortality were obtained. ICD-9 codes were used to identify postoperative cardiac, respiratory, pulmonary embolism (PE), deep venous thrombosis (DVT), surgical site infection (SSI), systemic infection, acute renal failure (ARF), and wound-related complications (disruption of the wound, hemorrhage, hematoma, seroma and non-healing wound) (Table 2).

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**Table 1**
ICD-9 Condition Codes Used.

| Condition | ICD-9 Code |
|---|---|
| Primary THA | 81.51 |
| Revision THA | 81.53 or 00.70–00.73 |
| Primary TKA | 81.54 |
| Revision TKA | 81.55 or 00.80–00.84 |
| Thalassemia | 282.4 excluded 282.41–282.42 |
| Sickle cell trait | 282.5 |
| Sickle cell disease | 282.6 |
| Sickle cell thalassemia | 282.41–282.42 |
| Other hemoglobinopathies | 282.7 |

## Statistical Analysis

Multivariate logistic regressions were used to determine if having a history of hemoglobinopathy was an independent predictor for cardiac and respiratory complications, PE, DVT, SSI, wound complications, systemic infection, ARF, and in-hospital mortality. A full regression model was created for each complication, transfusion, and mortality, incorporating all possible factors, including demographics; hospital region, setting, and size; primary payer; year of surgery; underlying joint disorder; type of TJA (revision versus primary); and type of joint (knee versus hip). The type of TJA (revision versus primary) and hip or knee joint was compared separately from complications. The reported odds ratios (ORs) and confidence intervals (CIs) were based on the multivariate analyses. For each group, the adjusted OR of each complication is presented in a forest plot with their 95% CI. CIs that were above 1.0 were considered statistically significant at $P < 0.05$. All analyses were performed using R 3.1.1 (R Foundation for Statistical Computing, Vienna, Austria) using the 'rms' package to perform the logistic regression. *P*-values less than 0.05 were considered statistically significant.

## Results

A total of 4919 patients (0.2%) with hemoglobinopathy undergoing TJA were included. The proportion of patients undergoing TJA who had a hemoglobinopathy increased during the study period (Fig. 1A). Hemoglobinopathy was more prevalent in patients undergoing THA (n = 2667) compared to TKA (n = 2552) (Fig. 1B), but there was no difference in the rate of increase over time. There was also no difference in the growth rates between revision (n = 779) and primary (n = 4140) TJA (Fig. 2).

Table 3 shows prevalence of different types of hemoglobinopathies in the TJA patients in this cohort. More than half of joint arthroplasty patients with a hemoglobinopathy had a diagnosis of sickle cell disease or trait (59.9%). Thalassemia, however, accounted for more than a third (38.5%) of patients in the cohort. Patients with a hemoglobinopathy were more likely to be: younger, female, African-American and on Medicaid. They were also less likely to live in rural areas than in urban areas. Fewer hemoglobinopathy patients had concurrent osteoarthritis and were more likely to have osteonecrosis of the femoral head. A higher proportion of hemoglobinopathy patients underwent primary THA compared with patients without diagnosis of hemoglobinopathy (42.5% in hemoglobinopathy group vs 30.5% in the non-hemoglobinopathy group; $P < 0.0001$), and a lower proportion of hemoglobinopathy patients received primary TKA compared with non-hemoglobinopathy patients (41.6% in the hemoglobinopathy group vs 59.0% in the non-hemoglobinopathy group; $P < 0.0001$). Furthermore, a higher proportion of hemoglobinopathy patients received revision THA compared to non-hemoglobinopathy patients (11.7% in the hemoglobinopathy group vs 5.3% in the non-hemoglobinopathy group; $P < 0.0001$), whereas there was a similar proportion of hemoglobinopathy patients who received revision TKA compared to non-hemoglobinopathy patients (4.2% vs 5.1%, respectively; $P = 0.055$). The demographic of the patients in this study is demonstrated in Table 4.

### *In-Hospital Outcomes*

Cardiac events (29.0% in the hemoglobinopathy group versus 27.6% in the non-hemoglobinopathy group) and transfusion events (40.5% in the hemoglobinopathy group versus 20.4% in the non-hemoglobinopathy group) were significantly higher in the hemoglobinopathy patients. Transfusions (OR = 2.3, 95% CI 2.13–2.43, $P < 0.0001$) and cardiac events (OR = 1.3, 95% CI 1.20–1.38, $P < 0.0001$) were significantly different between the two groups (Fig. 3). After transfusion and cardiac events, the most frequent complication was respiratory events (4.4% in the hemoglobinopathy group versus 3.2% without a hemoglobinopathy), which had an OR of 1.5 (95% CI 1.31–1.79; $P < 0.0001$). SSIs were more commonly seen in hemoglobinopathy patients (2.6%) versus non-hemoglobinopathy patients (1.3%), with an OR of 1.4 (95% CI 1.19–1.83, $P = 0.003$). Hemoglobinopathy patients also had more wound related complications (2.3% vs 1.3%, OR = 1.4, 95% CI 1.11–1.72, $P = 0.003$) and systemic infection events (0.3% vs 0.1%, OR = 1.9, 95% CI 1.12–3.18, $P = 0.02$) in comparison to non-hemoglobinopathy patients (Fig. 3). The diagnosis of hemoglobinopathy had no effect on overall mortality (0.3% hemoglobinopathy vs 0.2% non-hemoglobinopathy; OR = 1.4, 95% CI 0.70–2.83, $P = 0.34$). The percentage of in-hospital complications for DVT (0.9% vs 0.6%) and renal complications (1.7% vs 1.1%) was also higher in patients with hemoglobinopathies, but the difference was not statistically significant ($P = 0.12$). (See Figs. 4 and 5.)

## Discussion

The prevalence of patients with hemoglobinopathies is expected to rise over the next 35 years [1,2]. In addition, recent treatment advances have changed the nature of the illness from a fatal condition in childhood into a chronic disease in adults [17]. Given that many of these patients undergo a TJA during their lifetime, a large part of management is understanding the effect that hemoglobinopathies have on in-hospital complications. However, the literature on this topic reports varying outcomes [7,18–20]. Some reviews have examined perioperative

**Table 2**
ICD-9 Diagnosis Codes Used.

| Complications | ICD-9 Diagnosis Codes for Major Complications |
|---|---|
| Transfusion | 99.0, 99.02, 99.04 |
| Cardiac | 285.1, 426.0, 426.6, 427.1, 427.31, 427.32, 427.5, 427.69, 427.89, 428.21, 428.31,428.33, 428.9, 444.89, 458.29, 785.51, 997.1, 998.0, 410.0, 410.01, 410.02, 410.1, 410.10, 410.11, 410.12, 410.20, 410.21, 410.22, 410.30, 410.31, 410.32, 410.40, 410.41, 410.42, 410.50, 410.52, 410.60, 410.61, 410.62, 410.70, 410.71, 410.72, 410.80, 410.82, 410.90, 410.91, 410.92 |
| Respiratory | 041.3, 486.0, 511.9, 512.1, 514.0, 518.0, 518.4, 518.5, 518.81, 997.3 |
| Pulmonary embolism | 415.11, 415.19 |
| Deep venous thrombosis | 451.1, 451.2, 451.2, 451.8, 451.9, 453.2, 453.4, 453.8, 453.9 |
| Surgical site infection | 996.6 |
| Systemic infection | 995.90, 995.91, 995.92, 995.93, 995.94, 785.52 |
| Acute renal failure | 584.5–584.9 |
| Wound-related complication | 998.30, 998.31, 998. 32, 998.33, 998.10, 998.11, 998.12, 998.13, 998.83 |