



# A Higher Altitude Is Associated with Increased Incidence of Infections following Primary Total Hip Arthroplasty

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**Purpose:** The purpose of this study was to evaluate whether patients undergoing primary total hip arthroplasty (THA) at a higher elevation have higher rates of: 1) in-hospital length of stay (LOS); 2) surgical site infections (SSIs); 3) periprosthetic joint infections (PJIs); and 4) costs.

**Materials and Methods:** The Medicare claims database was used to identify patients who underwent primary THA at an altitude higher than 4,000 feet (ft). High-altitude patients were matched to patients who underwent primary THA at an altitude less than 100 ft, yielding 24,958 and 124,765 patients respectively. Outcomes that were assessed included in-hospital LOS, SSIs, PJIs, and costs of care. A *P*-value less than 0.001 was considered statistically significant.

**Results:** Patients in the study group had significantly longer in-hospital LOS (4 days vs 3 days,  $P < 0.0001$ ). In addition, patients in the study group had a significantly higher incidence and odds of developing SSIs (1.16% vs 0.86%; odds ratio [OR], 1.34;  $P < 0.0001$ ) and PJIs (0.91% vs 0.58%; OR, 1.56;  $P < 0.0001$ ) within 90-days following the index procedure, compared to matched controls. Higher altitude patients incurred higher day of surgery (\$16,139.76 vs \$15,279.42;  $P < 0.0001$ ) and 90-day costs (\$18,647.51 vs \$16,401.62;  $P < 0.0001$ ).

**Conclusion:** This study demonstrated that primary THA procedures performed at an elevation higher than 4,000 ft are associated with longer in-hospital LOS, higher rates of SSIs, PJIs, and costs of care. Orthopedists and other healthcare professionals can use this information to provide adequate education for these patients regarding the potential complications that may occur following their procedure.

**Key Words:** Total hip arthroplasty, Altitude, Costs, Medicare, Database

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## INTRODUCTION

It has been postulated that in higher altitude environments, the decrease in the partial pressure of oxygen can have an effect on postoperative outcomes<sup>1</sup>. With a decrease in the partial pressure of oxygen at higher altitudes, systemic variations in the oxygen-hemoglobin curve and oxygen saturation percentages can lead to a state of constant endothelial cell damage and repair<sup>2-5</sup>. Higher altitudes also alter immune responses, therefore potentially creating an immunosuppressive environment for patients<sup>6</sup>. The hypox-

ic environment, paired with the various systemic physiological changes associated with higher altitudes, can lead to an increased susceptibility to infectious pathogens postoperatively<sup>6-8</sup>). Further exploration of the relationship between higher altitude and postoperative infections in primary total hip arthroplasties (THA) is important given that the hypoxic conditions and systemic stress on the body could potentiate such complications.

While studies focused on high altitude and the increased potential for venous thromboembolism in THAs and other orthopedic procedures have been reported, research regarding the effect of altitude on other potentially devastating postoperative complications, namely, postoperative infections is lacking<sup>7-10</sup>). Adequately powered retrospective studies with well-defined inclusion and exclusion criteria investigating the effects of altitude on infectious outcomes following a primary THA are limited. Thus, there is a need for large-scale retrospective queries investigating the relationship between primary total hip arthroplasties and the effect of altitude on postoperative infections. Understanding this relationship is a vital step towards improving patient education and postsurgical patient care. Improved knowledge of the increased risk of postoperative complications at higher altitudes can enable orthopedists to mitigate these risks.

The current study utilized a United States (U.S.)-based nationwide administrative claims database to identify patients who had a primary THA at an altitude above 4,000 (ft). The purpose of this study was to evaluate whether patients undergoing primary THA at an elevation higher than 4,000 ft have worse outcomes compared to patients undergoing primary THA at an elevation less than 100 ft. Specifically, this study compared rates of: 1) in-hospital length of stay (LOS); 2) surgical site infections (SSIs); 3) periprosthetic joint infections (PJIs); and 4) costs.

## MATERIALS AND METHODS

### 1. Registry

A retrospective level III case-control study using the 100% Medicare Standard Analytical Files (SAF) from the PearlDiver (PearlDiver Technologies, Fort Wayne, IN, USA) database was conducted. A query from January 1, 2005 to March 31, 2014 was performed using International Classification of Disease, ninth revision (ICD-9), and Current Procedural Terminology (CPT) codes. Because the database contains deidentified patient information, our institution deemed the study exempt from Institutional Review

Board (IRB) approvals.

### 2. Cohorts

Using Boolean command operations, the inclusion criteria for the study group consisted of patients undergoing primary THA at an altitude higher than 4,000 ft; patients undergoing primary THA at less than 100 ft were included in the control group. These altitudes were chosen because they had been used in a previous publication which found that arthroscopic surgery performed at an altitude higher than 4,000 ft was a significant risk factor for the development of postoperative venous thromboembolism when compared with matched patients undergoing the same procedure at an altitude less than or equal to 100 ft<sup>10</sup>). Information from Zip-Code database (Datashet, LLC, Hopewell Junction, NY, USA) was used to filter all primary THAs at an altitude less than 100 ft and altitude greater than 4,000 ft. Patients undergoing primary THA were queried using ICD-9 and CPT codes 81.51 and 27130, respectively. Patients who developed SSIs were identified using the following ICD-9 and CPT codes: 998.59, 998.51, 86.04, 20005, and 11981. Patients who developed PJIs were identified using ICD-9 diagnostic code 996.66. To control for confounding, study group patients were randomly matched to controls in a 1:5 ratio according to age, sex, and the following medical comorbidities: chronic obstructive pulmonary disease, depression, diabetes mellitus, hyperlipidemia, hypertension, and tobacco. The query yielded 149,719 patients in the study (n=24,958) and control (n=124,765) cohort (Table 1). Pearson's chi-square analysis showed that matching was successful as no statistical differences were observed between the matched cohorts (Table 1).

### 3. Endpoints

The primary outcomes analyzed included comparing in-hospital LOS, rates of SSIs and PJIs within 90-days following the index procedure, and 90-day episode of care (EOC) costs. The 90-day cutoff was chosen in order to be compliant with the bundled payment care initiative (BPCI) set in place by the Centers for Medicare and Medicaid Services (CMS). CMS initiated the BPCI program in 2013 to improve outcomes and reduce costs in numerous clinical settings, including THA<sup>11</sup>). The BPCI program through Model 2 bundles payment for acute hospitalization and up to 90 days of post-acute care<sup>12</sup>).

**Table 1.** Demographics of Patients Undergoing Primary Total Hip Arthroplasty at an Altitude Higher than 4,000 ft and Matched Controls

Demographic	>4,000 ft (n=24,958)	<100 ft (n=124,765)	P-value*
Age (yr)			0.99
<64	2,230 (8.9)	11,144 (8.9)	
65-69	6,758 (27.1)	33,782 (27.1)	
70-74	5,599 (22.4)	27,994 (22.4)	
75-79	4,804 (19.2)	24,017 (19.2)	
80-84	3,336 (13.4)	16,678 (13.4)	
>85	2,231 (8.9)	11,150 (8.9)	
Sex			0.99
Female	14,992 (60.1)	74,961 (60.1)	
Male	9,966 (39.9)	49,804 (39.9)	
Comorbidity			
COPD	260 (1.0)	1,281 (1.0)	0.99
Depression	6,881 (27.6)	34,393 (27.6)	0.99
Diabetes mellitus	6,593 (26.4)	32,949 (26.4)	0.99
Hyperlipidemia	15,241 (61.1)	76,198 (61.1)	0.99
Hypertension	20,380 (81.7)	101,881 (81.7)	0.99
Tobacco	3,356 (13.4)	16,762 (13.4)	0.99

Values are presented as number (%).

ft: feet, COPD: chronic obstructive pulmonary disease.

\* By Pearson’s chi-square analysis.

#### 4. Data Analyses

Statistical analyses were performed using the R statistical software integrated into the PearlDiver supercomputer. Significance between the continuous variables (i.e., LOS and episode of care costs) between the two cohorts was tested using Welch’s *t*-tests. Logistic regression analyses were performed to calculate odds ratio (OR), 95% confidence intervals (95% CI), and *P*-values on the effects of elevation rates on SSIs and PJIs within 90-days following the index procedure. Due to the ease of finding statistical differences with large administrative databases, a *P*-value less than 0.001 was considered statistically significant.

### RESULTS

#### 1. In-Hospital LOS and Costs of Care

Patients in the study group had significantly longer in-hospital LOS compared to matched controls (4 days vs 3 days; *P*<0.0001). In addition, patients in the study group incurred significantly higher day of surgery (\$16,139.76 vs \$15,279.42; *P*<0.0001) and total global 90-day EOC costs (\$18,647.51 vs \$16,401.62; *P*<0.0001) compared to patients undergoing primary THA at less than 100 ft ele-

vation.

#### 2. Surgical Site and Peri-Prosthetic Joint Infections

The results of the study demonstrated that patients undergoing primary THA at an elevation higher than 4,000 ft had a significantly higher incidence and odds of developing SSIs (1.16% vs 0.86%; OR, 1.34; 95% CI, 1.17-1.53; *P*<0.0001) and PJIs (0.91% vs 0.58%; OR, 1.56; 95% CI, 1.34-1.81; *P*<0.0001) within 90-days following the index procedure, compared to matched controls undergoing the procedure at an elevation of less than 100 ft (Table 2).

### DISCUSSION

High altitude surgical procedures constitute a unique challenge due to the hypoxic environment in which they are performed, which may lead to several postoperative consequences. Within this oxygen-depleted environment, a patient’s oxygen-saturation curve is altered, and saturation percentages are decreased rendering patients more susceptible to systemic infection<sup>6-8</sup>. A literature review found little detail regarding the effect of high altitudes on postoperative infections in primary THA. This study focused on primary THAs performed in a high altitude (>4,000 ft) environment and

**Table 2.** Frequency of Surgical Site Infections and Peri-Prosthetic Joint Infections within 90-Days following Primary Total Hip Arthroplasty at an Altitude Higher than 4,000 ft and Less than 100 ft

Ninety-day infections assessed	>4,000 ft	<100 ft	OR	95% CI	P-value
Surgical site infections	1.16%	0.86%	1.34	1.17-1.53	<0.0001
Peri-prosthetic joint infections	0.91%	0.58%	1.56	1.34-1.81	<0.0001

OR: odds ratio, 95% CI: 95% confidence interval, ft: feet.

subsequently analyzed postoperative outcomes including in-hospital LOS, surgical site infections (SSIs), periprosthetic joint infections (PJIs), and costs. Results of our study indicated that patients in the study group had a significantly longer in-hospital LOS, increased incidence and odds of developing SSIs and PJIs, and increased day of surgery costs and total global 90-day EOC costs compared with matched controls. With these results, orthopedic surgeons at high altitude are afforded increased knowledge of the unique complication rates they can expect in primary THA, and can therefore take steps to mitigate these complications and educate their patients.

Our study found that high altitude primary THA patients who had a higher rate of SSI and PJI also had a longer LOS, which is in agreement with other studies that focused on hospital acquired infections and the effect on LOS. One study by Horn et al.<sup>13)</sup>, focused on spine surgery and hospital-acquired conditions (HACs), found an association of HACs with a significantly increased LOS and burden of cost compared to controls. On average, patients who experienced at least one HAC had a 1.48 days longer LOS and episode payments of at least \$8,893 greater than matched controls<sup>13)</sup>. A separate study by Arefian et al.<sup>14)</sup>, which conducted an analysis of patients in a German university hospital, further statistically established that the estimated mean additional LOS due to hospital-acquired infections was 8.45 days per case and additional costs incurred were between \$7,453-\$15,155 per infected patient. Finally, an interesting study by Whitehouse et al.<sup>15)</sup>, which explored the impact of SSIs following orthopedic surgeries, established that identification of an SSI extended postoperative LOS by a median of 14 days and that the median total cost for infected patients (\$24,344) was statistically significantly higher than that of controls (\$6,636).

The current study demonstrated a significantly increased incidence of SSIs (1.16% vs 0.86%; OR, 1.34; 95% CI, 1.17-1.53;  $P<0.0001$ ) and PJIs (0.91% vs 0.58%; OR, 1.56; 95% CI, 1.34-1.81;  $P<0.0001$ ) at high altitude. A recent study by Aasen et al.<sup>1)</sup> focused on the association of hospital altitude and postoperative infectious complications after major operations. This study included various types of procedures

including urological, vascular, plastic-reconstructive, and orthopedic and compared the rates of SSIs and urinary tract infections (UTIs) at varying levels of altitudes<sup>1)</sup>. Their results, when stratifying by 1,000-ft increments, showed no statistically significant difference in SSI or UTIs and even demonstrated decreased pneumonia incidence at higher altitudes<sup>1)</sup>. The difference in the results by Aasen et al.<sup>1)</sup> versus those of this study may be largely attributed to the difference in surgery types. While the study by Aasen et al.<sup>1)</sup> focused on all types of surgeries, our study focused solely on primary THAs. In addition, the study by Aasen et al.<sup>1)</sup> compared varying levels of altitude while our study compared altitudes higher than 4,000 ft to altitudes 100 ft and less. In addition, our study used age and demographically matched controls in a 1:5 ratio to help mitigate confounding factors while the study by Aasen et al.<sup>1)</sup> did not use matched control groups, which could potentially explain the discrepancies in results. Based on previous literature investigating the effects of high altitude, we postulate that the results of the current study are most likely attributed to alterations in oxygen partial pressures and oxygen saturation curves, along with the immunosuppressive effects of high altitude<sup>2-8)</sup>. A combination of these effects can lead to increased susceptibility to infectious pathogens and thus postoperative infections. A study by Singh et al.<sup>16)</sup> investigated the effect of high altitude and the incidence of herpes zoster. This study specifically states that the decrease in cell-mediated immunity from the high stress environment of high altitudes can lead to reactivation of herpes zoster. While this is specifically for herpes zoster, the concept of immunosuppression leading to a favorable environment for certain pathogens can provide a possible explanation for the increased incidence of infections seen in our study population. However, further analysis and characterization of these immunosuppressive and hematological consequences at high altitude would be important in order to determine the true influence of altitude on postoperative infection rates. Further research is needed to determine differences between pathogens in high versus low altitude, which would afford orthopedists greater knowledge of potential postoperative complications in a higher altitude environment. Additionally, rates of infections differ widely with

different surgical procedures. According to a study conducted by Saeed et al.<sup>17)</sup>, incidence of procedure-specific surgical site infection varies widely among types of procedures. Future studies are needed to explore and expand upon factors that may influence these varied procedure-specific infection rates.

Our study established an association of higher altitude with a statistically significant increase in costs of care, which likely result from the increased LOS and increased infection rates. There is a well-established, important consequential relationship between infections, LOS, and cost of care. Studies by Horn et al.<sup>13)</sup>, Arefian et al.<sup>14)</sup>, and Whitehouse et al.<sup>15)</sup> reported statistically significant findings of increased LOS leading to significantly increased costs of care. Results of a study by Blumberg et al.<sup>18)</sup>, focused on the relationship between healthcare costs and SSIs in spinal surgery patients, indicated that the mean direct cost of treating an SSI was \$16,242 and various other factors including LOS and number of SSIs showed significant positive association with increased treatment costs. In a study by Molloy et al.<sup>19)</sup>, focused on LOS and its relationship to hospital costs specifically in total knee and hip arthroplasties, the authors stated that the burden of cost is impacted by the LOS postoperatively, and that from 2002 to 2013, overall hospital costs also increased. These studies further reinforce the idea that the LOS, SSIs, and PJIs directly impact the costs of care for primary THA patients.

There are limitations associated with this retrospective database study. Database studies are naturally susceptible to human miscoding errors, which can correlate to underreporting or overreporting<sup>7)</sup>. While it is clear that there is a statistically significant difference between controls and study group patients with respect to various postoperative outcomes, this correlation does not conclude causation. We were also unable to control for operative timings, length of operations, and were unable to ensure that discharged patients were at the same elevations for 90 days postoperatively<sup>7)</sup>. In addition, the etiology or mechanism behind the significant differences in postoperative outcomes cannot be determined without a randomized controlled trial. Furthermore, determination of PJIs requires values of C-reactive protein, erythrocyte sedimentation rate, cultures, and other laboratory markers to make the diagnosis of PJI. Due to restrictions of the PearlDiver database, we were unable to ascertain these markers; however, this could certainly serve as the basis for future prospective studies. Despite these limitations, there is value in this study. This study provides a thorough multivariate statistical analysis of a possible link between altitude and major

postoperative outcomes, which can be used to help guide orthopedic patient care, and promote future research and exploration of these variables.

## CONCLUSION

In our study, we found that higher altitudes had a significant impact on infection rates in patients undergoing a primary THA. With our results, we recognize the importance of further studies to complement and expand our understanding of the relationship between altitude and postoperative infections. Future studies should focus on establishing a causal relationship between which measured variables or comorbidities are most likely to cause various infectious and systemic complications seen in primary THAs at high altitudes. Randomized controlled trials examining primary THA patients at varying altitudes and subsequent complications that occur can provide further insight on this relationship. This study provided a strong foundational understanding on the relationship between postoperative outcomes and primary THAs at high versus low altitude, which will provide orthopedists awareness and guidance on management of postoperative care on patients in high altitudes.

## CONFLICT OF INTEREST

The authors declare that there is no potential conflict of interest relevant to this article.

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