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## A Higher Altitude Is an Independent Risk Factor for Venous Thromboembolisms After Total Hip Arthroplasty

Dhanur Damodar, MD<sup>a</sup>, Chester J. Donnally III, MD<sup>a</sup>, Jonathan I. Sheu, MD<sup>c</sup>, Tsun Y. Law, MBA, MD<sup>b</sup>, Martin W. Roche, MD<sup>b</sup>, Victor H. Hernandez, MD<sup>a,\*</sup>

<sup>a</sup> Department of Orthopedic Surgery, University of Miami Hospital, Miami, Florida

<sup>b</sup> Department of Orthopedic Surgery, Holy Cross Hospital, Orthopedic Research Institute, Fort Lauderdale, Florida

<sup>c</sup> Department of Education, University of Miami Leonard M. Miller School of Medicine, Miami, Florida

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## ABSTRACT

*Background:* High altitudes lead to physiological changes that may predispose to venous thromboembolisms (VTEs) including deep vein thrombosis and pulmonary embolism (PE). No prior study has evaluated if there is also a higher risk of VTEs for total hip arthroplasties (THAs) performed at higher elevations. The purpose of this retrospective study was to identify if undergoing THA at a higher altitude center (>4000 feet above sea level) is an independent risk factor for a postoperative VTE.

*Methods:* A thorough evaluation of the Pearl Diver Database was performed for patients undergoing THAs from 2005 to 2014. Using International Classification of Diseases Ninth Edition facilitated in ascertaining patients who underwent THA. Using the ZIP codes of the hospitals where the procedure occurred, we separated our groups into high-altitude (>4000 ft) and low-altitude (<100 ft) groups. *Results:* In the first 30 postoperative days, patients undergoing THA at a higher altitude experienced a significantly higher rate of PEs (odds ratio, 1.74; P = .003) when compared to similar patients at lower altitudes. This trend was also present for PE (odds ratio, 1.59; P < .001) at 90 days postoperatively. *Conclusion:* THAs performed at higher altitudes (>4000 feet) have a higher rate of acute postoperative PEs in the first 30 days and also 90 days postoperatively when compared to matched patients receiving the same surgery at a lower altitude (<100 feet). THA patients at high altitude should be counseled on these increased risks; however, owing to retrospective nature and confounders, prospective studies are necessary to explore this outcome in more detail.

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\* Reprint requests: Victor H. Hernandez, MD, Department of Orthopedics, University of Miami Hospital, 1400 NW 12th Avenue, Miami, FL 33136.

After most orthopedic surgery, chemical prophylaxis is a mainstay of the anticoagulation protocol. For patients undergoing total hip arthroplasty (THA) and total knee arthroplasty (TKA), postoperative venous thromboembolism (VTE) is associated with high morbidity and mortality. In total joint arthroplasty (TJA), VTE is a comprehensively studied postoperative complication [1]. Studies have shown 3%-4% readmission rates after THA and TKA due to VTE [2]. Based on revised guidelines in 2011, the American Academy of Orthopedic Surgeons recommends that all patients undergoing elective THA and TKA receive deep vein thrombosis (DVT) prophylaxis postoperatively [3]. In 2012, the American College of Chest Physicians published new guidelines recommending that THA and TKA patients receive VTE prophylaxis for at least 10-14 days. The guidelines also state that prophylaxis may be extended for up to 35 days [4]. The type of VTE prophylaxis and duration of treatment, however, appear to be more surgeon dependent.

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An additional practice of most TJA surgeons is to try and limit the modifiable risk factors for VTE, such as smoking, elevated body mass index (BMI >30), as well as to encourage early ambulation. One risk factor for postoperative VTEs that has been demonstrated in other orthopedic procedures is altitude, with the thought process that higher altitudes may predispose patients to an increased risk of VTEs. While this has been evaluated for postoperative orthopedic patients undergoing acute air travel, the influence of altitude has never been explored in TJA patients [5].

Higher altitudes lead to physiologic changes that may predispose to VTE including DVT and pulmonary embolism (PE). Several studies have demonstrated an increase in factors contributing to Virchow's triad (hypercoagulability, venous stasis, and vessel wall injury) at high altitudes [6–8]. Prior studies have noted increased rates of VTE in patients undergoing arthroscopic knee and shoulder surgery at high elevation centers (>4000 feet) compared with low elevation centers (<100 feet) [9–11]. No study has evaluated if there is also a higher risk of VTEs for THA procedures performed at higher elevations compared to lower elevations.

The purpose of this study was to compare the rates of DVT and PEs in patients undergoing THA at low-altitude centers compared to those at higher altitude centers. Through this, we are able to determine if altitude is a potentially modifiable risk factor for VTEs following these procedures. Our hypothesis is that patients undergoing THA at higher altitudes will have higher incidence of VTEs than patients at lower altitudes.

#### **Materials and Methods**

A retrospective study was done using the national provider database by the name of Pearl Diver (Pearl Diver Technologies, Inc., Fort Wayne, IN) which is compliant with the Health Insurance Portability and Accountability Act. Pearl Diver is a publicly available database which holds the records of over 23 million patients. Our study looked at the Medicare provider for our population, from the years of 2005 to 2014. Using the International Classification of Diseases, Ninth Edition (ICD-9) codes facilitated in ascertaining our population.

Patients who underwent primary THA from the years of 2005 to 2014 were identified using the ICD-9 procedure code ICD-9-P-81.51. Patients were stratified into 2 groups. Those who had the procedure in areas with an altitude >4000 feet were defined as the "high-altitude group," and the control group which had the procedure at <100 feet were defined as the "low-altitude group". Five-digit zip codes provided through the Zip Code Database (Datasheet LLC, Hopewell Junction, NY) provided the geographic locations of the US mainland with respect to altitude (Fig. 1). An assumption was made that zip code of procedure was the same as zip code of recuperation

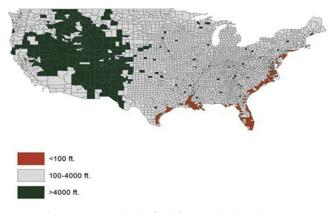


Fig. 1. Geographic altitude (feet) of the mainland United States.

for these patients. After our inclusion criteria were defined, our exclusion criteria included those patients with a prior history of DVT and/or PE. Additional exclusion criteria excluded those patients with a prior history of hypercoagulable state and patients with any unspecified coagulation defect. There is no evidence in the literature to suggest that surgeons at high altitudes use more frequent Doppler screening or more rigorous prophylaxis; however, this possibility cannot be excluded.

Using Boolean operations, the patients in the high-altitude group were match controlled with the patients in the lowaltitude group. Patients were also matched based on comorbidities, which are known to lead to thromboembolic events, including BMI >30, tobacco use, hypertension, diabetes, and hyperlipidemia.

The matching process is done 1:1 based on age, sex, and 5 comorbidities known to be associated with increased risk of postoperative VTE: obesity (BMI 30), tobacco use, hypertension, diabetes mellitus, and hyperlipidemia. Rates of DVT and PE were assessed in both groups within 30 days and 90 days of the aforementioned procedures. Descriptive and statistical analysis was performed using the programming language R (University of Auckland, New Zealand). Statistical analysis included calculating odds ratios (ORs) and 95% confidence intervals via binary logistic regression. Risk ratios (RRs) were calculated from odds ratios and event prevalence in the low-altitude group. Number needed to harm (NNH) was calculated from event incidence in both groups. Statistical significance was defined as P < .05.

## Results

A total of 206,115 THA patients met all inclusion criteria before breakdown by zip code. A total of 42,780 THA patients had their procedures performed at an altitude of greater than or equal to 4000 feet and formed the high-altitude study group, and 163,335 THA patients had their procedures performed at an altitude of less than or equal to 100 feet and formed the low-altitude study group. Of these, 87,033 THA age- and gender-matched patients (Table 1) were identified for inclusion in this study.

For patients undergoing THA, the overall VTE rate within 30 days was 0.28%; the overall DVT rate within 30 days was 0.28%, and the overall PE rate within the same time frame was 0.15%. Within 90 days, the overall VTE rate rose to 0.60%; the overall DVT rate within 90 days rose to 0.60% and the overall PE rate within the same time frame rose to 0.41%.

Within the first 30 days, the PE rate in patients undergoing THA at higher altitudes was significantly higher (OR 1.74; P = .003) when compared to similar patients at lower altitudes. This was also true for the PE rate (OR 1.60; P < .001) at 90 days postoperatively (Figs. 2 and 3, Table 2). The risk of PEs was elevated at both 30 (RR 1.74) and 90 days (RR 1.59) postoperatively. The NNH for a PE at 30 days was 1250; the NNH for a PE at 90 days was 526.3. The incidence of DVT and overall VTE did not increase significantly from low to high altitude for either 30 or 90 days after primary surgery.

#### Discussion

In this study, we found Medicare patients undergoing THA were 1.74 and 1.60 times more likely to have postoperative PEs at higher elevations compared to centers at sea level within 30 and 90 days of their procedures, respectively.

It is thought that physiological effects on the body at higher altitudes is one of the contributing factors that may predispose patients to higher VTE rates [6-8,12-14]. As one would expect, the body undergoes a host of physiologic changes as it enters a high-altitude environment. First, it compensates by changing its ventilation rate. As the body adjusts, changes then occur to the oxygen-

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