Risk of Venous Thromboembolism in Hospitalized Psoriasis Patients

Christopher G. Gibson[1,*], Bhakti B. Chavan[2], Ruby S. Gibson[3], Francis Essien[4], Melissa J. Newman[1], Robert L. Zee[1], Stephanie J. Ott[5] and Irving L. Rosenberg[5]

[1]*Department of Internal Medicine, Fairfield Medical Center, Lancaster, Ohio, USA*

[2]*Ohio University Heritage College of Osteopathic Medicine, Dublin, OH, USA*

[3]*Long School of Medicine, University of Texas Health San Antonio, San Antonio, TX, USA*

[4]*Department of Internal Medicine, Keesler Air Force Base, Biloxi, MS, USA*

[5]*Department of Rheumatology at the Fairfield Medical Center, Lancaster, OH, USA*

Abstract: *Background*: Psoriasis is associated with increased mortality but the underlying pathophysiology has yet to be copiously recognized. There are several models that demonstrate that psoriasis is not only a disease of the skin, but also has major systemic involvement of the internal organs. Psoriasis is a chronic inflammatory skin disease with a wide range of clinical manifestations. The purpose of this article is to evaluate a nationwide database to compare the incidence, prevalence, and inpatient burden of venous thromboembolism in patients with and without psoriasis.

Methods and Results: A cross-sectional study to examine the risk of incidence of VTE among patients with PsO. A total of 31,268 patients (0.4%) were diagnosed with PsO in a sample size of 7,103,377 (99.6%). A greater proportion of patients with PsO experienced either a DVT or PE compared to those who did not have PsO (1.4% vs. 1.2%). 445 patients (1.4%) were diagnosed with a DVT or PE with a p-value of < 0.001 compared to those who did not have psoriasis 85,135 (1.2%). An association with patients who died while in the hospital was found with 1.9% of patients with PsO died when compared with those without PsO.

Conclusion: Psoriasis patients were also noted to have an increased length of hospitalization than the control group. Other factors such as race and socioeconomic factors were also found to have an association with the development with VTEs.

Keywords: Psoriasis, Epidemiology, Inflammation, Embolism, Thrombosis, Venous Thromboembolism.

INTRODUCTION

Psoriasis (PsO) is a chronic inflammatory disease of the skin that affects approximately 2% of the American population [1]. This skin condition is characterized by well-demarcated plaques with silvery scales and clinical manifestations that vary, ranging from a localized to an extensive disease burden [2]. Deep vein thrombosis (DVT) and pulmonary embolism (PE) are clinical manifestations of venous thromboembolism (VTE) with potentially fatal consequences. The triad of Virchow describes three broad categories of factors that are thought to contribute to thrombosis [3]:

1. Hypercoagulability
2. Hemodynamic changes to include stasis, turbulence
3. Endothelial injury or dysfunction

Several other studies have demonstrated that joint replacement, cancer, smoking, age, immobilization, and diabetes are acquired risk factors for VTE [4]. In addition, the systemic inflammation in autoimmune diseases such as rheumatoid arthritis and systemic lupus erythematosus increases the risk of VTE [5-7]. The objective of this article is to use a nationwide database to compare the incidence, prevalence, and inpatient economic burden of venous thromboembolism in patients with and without psoriasis.

METHODS

Study Design

We designed a cross-sectional study to examine the risk of incidence of VTE among patients with PsO utilizing the Healthcare Cost and Utilization Project's National Inpatient Sample (NIS) database. The NIS is the largest inpatient care database in the United States, containing demographic and clinical information from approximately 8 million hospital stays from about 1000 hospitals sampled to approximate a 20% stratified sample of U.S. community hospitals [8]. We queried the NIS database and identified hospitalized adults ≥ 18 and < 100 years. Patients hospitalized with PsO were identified when assigned with an International Classification of Diseases, Tenth Revision (ICD-10) system [9].

*Address correspondence to this author at the Office of Graduate Medical Education, 401 N Ewing St, Lancaster, OH 43130, USA; Tel: (740) 652-4779; E-mail: drcgibson@fmchealth.org

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Study Participants

Patients with PsO were identified by hospitalizations with the primary endpoint as an in-hospital diagnosis of DVT, PE, or VTE. We used ICD-10 codes to identify hospitalizations of patients aged 18 years or older for which VTE, DVT, or PE was the primary discharge diagnosis. For DVT, PE, and VTE we used the following ICD 10 codes I82.409, I26.9, and I82.40 respectively. In this large database, we identified risk factors for VTE, including history of tobacco use, obesity, and diabetes mellitus as defined by their appropriate ICD-10 codes.

Statistical Analysis

Descriptive statistics was performed to summarize and describe the distribution of study variables. Bivariate analysis was performed using chi-square (χ^2) statistics to evaluate the association between diagnosis of DVT/PE and study characteristics. Alpha was set at 0.05. All analyses were performed using SAS version 9.4 [10]. Psoriasis status was included as a time dependent variable, age, gender, smoking status, insurance status, household income, BMI, race, were included as fixed variables. A two-sided p-value < 0.05 was considered statistically significant.

RESULTS

A total of 31,268 patients (0.4%) were diagnosed with PsO in a sample size of 7,103,377 (99.6%) (Table **1**). A greater proportion of patients with PsO experienced either a DVT or PE compared to those who did not have PsO (1.4% vs. 1.2%) and this association was statistically significant (p<0.001). 445 patients (1.4%) were diagnosed with a DVT or PE with a p-value of < 0.001 (Table **2**) compared to those who did not have psoriasis 85,135 (1.2%). We also found an association with patients who died while in the hospital. 2,603 (1.9%) patients with PsO died when compared with those without PsO (Table **2**). An association with income was also found. There were a greater number of patients in the 0-25th percentile and 26th-50th percentile who were found to have a VTE; 24,842 and 21,483 respectively. Only 17,174 patients in the 76th-100th percentile for income were found to have a VTE. This also was statistically significant with a p-value of <0.001.

Body mass index (BMI) was associated with an increased risk of VTE. In the obese population 13,600 (1.8%) experienced a VTE with a p-value of < 0.001.

Table 1: Overall Characteristics of Patients

Characteristic	Overall N (wt%)
Age	
18-24 years	372560 (5.2)
25-34 years	796843 11.2)
35-49 years	882041 (12.4)
50-64 years	1446936 (20.3)
≥65 years	2539347 (35.6)
Gender	
Male	3086070 (43.3)
Female	4044830 (56.7)
Race	
White	4425832 (65.4)
Black	1029307 (15.2)
Hispanic	830225 (12.3)
Other	482615 (7.1)
Income	
0-25th percentile	2152900 (30.7)
26th to 50th percentile	1783192 (25.4)
51st to 75th percentile	1677599 (23.9)
76th to 100th percentile	1399948 (20.0)
Length of stay	
≤3 days	4325540 (60.6)
4-7 days	1827537 (25.6)
8-14 days	672194 (9.4)
15-30 days	245501 (3.4)
≥31 days	63961 (0.9)
Died	
No	6992652 (98.1)
Yes	136118 (1.9)
Psoriasis	
No	7103377 (99.6)
Yes	31713 (0.4)
DVT/PE	
No	7049510 (98.8)
Yes	85580(1.2)

Abbreviation: N Frequency; wt.% weighted percentage.

Black and Caucasian groups were more likely to develop VTE than the other races 1.4% to 1.3% respectively.

DISCUSSION

The diagnosis of PsO is primarily clinical with different types of psoriasis. The most common variant

Table 2: Bivariate Association between VTE and the Study Variables

	Deep vein thrombosis/Pulmonary embolism		*p* value
	No	Yes	
	N(wt.%)	N(wt.%)	
Age			<0.001***
18-24 years	371265 (99.7)	1295 (0.3)	
25-34 years	793019 (99.5)	3824 (0.5)	
35-49 years	870649 (98.7)	11392 (1.3)	
50-64 years	1423560 (98.4)	23376 (1.6)	
≥65 years	2494086 (98.2)	45261 (1.8)	
Gender			<0.001***
Male	3044630 (98.7)	41440 (1.3)	
Female	4000770 (98.9)	44060 (1.1)	
Race			<0.001***
White	4367077 (98.7)	58755 (1.3)	
Black	1015194 (98.6)	14113 (1.4)	
Hispanic	824537 (99.3)	5688 (0.7)	
Other	479162 (99.3)	3453 (0.7)	
Income			<0.001***
0-25th percentile	2128058 (98.8)	24842 (1.2)	
26th to 50th percentile (median)	1761709 (98.8)	21483 (1.2)	
51st to 75th percentile	1657054 (98.8)	20545 (1.2)	
76th to 100th percentile	1382774 (98.8)	17174 (1.2)	
Body mass index			<0.001***
Underweight	112536 (98.9)	1287 (1.1)	
Normal	68076 (98.7)	881 (1.3)	
Overweight	77958 (98.5)	1178 (1.5)	
Obese	749411 (98.2)	13600 (1.8)	
Hospital region			<0.001***
Northeast	1303550 (98.8)	16321 (1.2)	
Midwest or North Central	1566491 (98.7)	20308 (1.3)	
South	2769993 (98.8)	33822 (1.2)	
West	1409476 (98.9)	15129 (1.1)	
Hospital bedsize			<0.001***
Rural	1320161 (98.9)	14825 (1.1)	
Urban, non teaching	2046749 (98.8)	24541 (1.2)	
Urban, teaching	3682600 (98.8)	46214 (1.2)	
Length of stay			<0.001***
≤3 days	4283015 (99.0)	42525 (1.0)	
4-7 days	1798531 (98.4)	29006 (1.6)	
8-14 days	661503 (98.4)	10691 (1.6)	
15-30 days	242616 (98.8)	2885 (1.2)	
≥31 days	63491 (99.3)	470 (0.7)	

(Table 2). Continued.

	Deep vein thrombosis/Pulmonary embolism		*p* value
	No	Yes	
	N(wt.%)	N(wt.%)	
Tobacco			<0.001***
No	6960944 (98.8)	84270 (1.2)	
Yes	88566 (98.5)	1310 (1.5)	
Diabetes mellitus			<0.001***
No	5489005 (98.9)	63117 (1.1)	
Yes	1560505 (98.6)	22463 (1.4)	
Hypertension			<0.001***
No	4769997 (99.1)	42627 (0.9)	
Yes	2279513 (98.2)	42953 (1.8)	
Hyperlipidemia			<0.001***
No	5255196 (99.0)	52126 (1.0)	
Yes	1794314 (98.2)	33454 (1.8)	
Died			<0.001***
No	6909757 (98.8)	82895 (1.2)	
Yes	133515 (98.1)	2603 (1.9)	
Psoriasis			<0.001***
No	7018242 (98.8)	85135 (1.2)	
Yes	31268 (98.6)	445 (1.4)	

Abbreviation: N Frequency; wt.% weighted percentage; ***p<0.001.

of psoriasis is plaque psoriasis, affecting 80% to 90% of patients with psoriasis [2]. The hallmark of classic plaque psoriasis is well-demarcated, symmetric, and erythematous plaques with overlying silvery scales. Plaques are typically located on the scalp, trunk, buttocks, and extremities but can occur anywhere on the body. Patients can also have nail involvement, which can present without concomitant plaques.

Psoriasis is a chronic inflammatory condition known to increase the risk of atherosclerosis, cardiovascular events and metabolic syndrome [11]. The pathophysiology of psoriasis is characterized by T-cell activation and T-helper cell type 1 (Th1) cytokines with other studies showing an increase of markers of systemic inflammation such as serum c-reactive protein (CRP), interleukin (IL)-6, IL-8, and tumor necrosis factor (TNF) [12-20]. Psoriasis is characterized by (Th1) and (Th17) driven inflammation. These have also been found to play a significant role in adverse cardiovascular events. In addition, psoriasis has been shown to increase platelet activation [7] and platelet hypercoagulability. Our data uses a large national sample to illustrate an increased risk for VTE in hospitalized patients with psoriasis than with those without the skin condition. Psoriasis patients were also noted to have an increased length of hospitalization than the control group. Other factors such as race and socioeconomic factors were also found to have an association with the development with VTEs. Males with psoriasis were found to have an increased risk of DVT which corresponds to the literature [21].

LIMITATIONS AND STRENGTHS

One of the major strengths of our study is that the data was derived from the large nationwide registry. To our knowledge this analysis is one of the largest studies that focuses on VTE risk factors. Selection bias was able to be avoided because of the unique nature of the database. We were able to attain information regarding gender, age, socioeconomic status, health insurance coverage. This is the first large scale population investigation of a critically important outcome in a relatively common disease. The diversity of the data from large and small hospital systems, as well as from both rural and urban areas allows for adequate generalization of the findings. Some limitations to our paper include the potential of having miscoding diagnoses which would then subsequently lead to an error in our analysis. Other limitations include disease severity, duration, treatments or antiplatelet/anticoagulation which were not available in the NIS database.

CONFIDENTIALITY AND RECORDS

Any identifying information was removed, the Office of Human Research Protections for Mount Carmel Health System and the Institutional Review Board approved of this paper.

DECLARATION OF CONFLICTING INTERESTS

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