Original Study

Venous Thromboembolism in Female Adolescents: Patient Characteristics

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A B S T R A C T

Study Objective: Our goal was to describe the period prevalence of venous thromboembolism (VTE) and characterize adolescent female patients diagnosed with VTE by describing their age, race, and number of comorbidities. Female adolescents with estrogen exposure were of particular interest because estrogen-containing contraceptives increase the risk of VTE.
Design, Setting, Participants, and Interventions: We queried the Pediatric Health Information System database for International Classification of Diseases, Ninth/Tenth Revision, Clinical Modification codes to identify female patients aged 12-18 years diagnosed with a VTE or pulmonary embolism from April 2006 to March 2016 in the United States. Patient demographic characteristics and comorbidities were also analyzed. We divided our study population into two five-year groups and calculated the change in period prevalence of VTE between those groups.
Main Outcome Measures: Primary diagnosis of VTE in the extremities, or pulmonary embolism.
Results: The period prevalence of VTE increased from 2.3 female adolescents per 10,000 hospitalized children (group 1) to 3.3 per 10,000 (group 2), representing a statistically significant increase of 0.010% ($P < .001$). Caucasian and black individuals were most commonly affected. The number of girls affected increased steadily from ages 12 to 16 years and a large percentage (59.6%) had four or more comorbidities. In patients (n = 32) with estrogen exposure, more than 96% had one or more comorbidity in addition to estrogen exposure.
Conclusion: Pediatric health care providers should be aware that the period prevalence of VTEs in female adolescents is increasing. Those with a history of estrogen exposure rarely develop VTEs from estrogen alone and they typically have multiple comorbidities.
Key Words: Adolescent, Pediatric, Venous thromboembolism, Pulmonary embolism, Estrogen

Introduction

Venous thromboembolism (VTE) and pulmonary embolism (PE) in the adult population are well understood, however fewer studies have examined these conditions in the pediatric population.[1] The incidence of VTEs in the general pediatric population is reported to be 0.07-0.49 cases per 10,000 children.[1,2] In hospitalized children, the incidence is higher and appears to be increasing; one study from 1992-2005 cited the incidence to be 0.3-28.8 cases per 10,000, whereas another from 2001-2007 reported an increase from 34 to 58 cases per 10,000 hospital admissions.[3,4]

Children younger than one year old and adolescents are at the highest risk of developing a VTE in the pediatric population.[1–5] The mortality rate for children diagnosed with VTE or PE is 2.2% and recurrence and post phlebitic syndrome are common complications.[1] Risk factors in this population include obesity, recent surgery, malignancy, family history of VTE or inherited thrombophilia, tobacco use, combination oral contraceptive pills (COCPs), pregnancy, immobility, congenital venous anomalies, and presence of a central venous catheter.[4–7] Pediatric patients with comorbidities such as cancer, nephrotic syndrome, inflammatory bowel disease, and congenital heart disease are also more likely to develop a VTE.[6]

Female adolescents are often prescribed COCPs for birth control, acne, abnormal uterine bleeding, and dysmenorrhea.[7,8] However, exposure to estrogen promotes a procoagulant state that can increase the risk of VTEs particularly in patients with additional risk factors.[9] The primary goal of this study was to characterize female adolescents diagnosed with VTE by describing their age, race, and number of comorbidities in order to recognize which female adolescents develop VTE; there is a paucity of literature focusing on this unique population. Understanding which female adolescents are at high risk of developing a VTE can assist physicians in counseling patients regarding risks and benefits of COCP use.

The secondary objective of this study was to investigate the period prevalence of VTEs in female adolescents over a recent 10-year period at children's hospitals across the country. We hypothesized that the period prevalence of VTE would decrease over the 10-year study period because of the increased use of progestin-only long-acting reversible contraception (LARC) in adolescents aged 15-19 years in recent years and decreasing teen pregnancy rates.[10,11] Previously, 0.4% of adolescents used LARC from 2006 to 2008 and this number increased to 1.5% from 2008 to 2010.[11]

The authors indicate no conflicts of interest.

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Materials and Methods

Data Source

The Pediatric Health Information System (PHIS) database is an administrative database comprised of deidentified billing data detailing patient demographic information and diagnoses. Up to 49 hospitals located in large urban centers in the United States contributed to the database from April 2006 to March 2016.

Population

Female patients aged 12-18 years diagnosed with a VTE or PE were identified over a 10-year period of time (April 2006 to March 2016). To detect a change in the period prevalence of VTEs over the 10-year study period, the population was divided into two five-year time periods using the most recent PHIS data available: Group 1 (April 2006 to March 2011), and Group 2 (April 2011 to March 2016).

The term "venous thromboembolism" includes a primary diagnosis of VTE in the extremities or a PE. Female adolescents diagnosed with VTE in nonextremity venous systems were excluded from our study. Primary discharge diagnosis of VTE in the extremity or PE was established using International Classification of Diseases, Ninth/Tenth Revision, Clinical Modification (ICD-9/10-CM) coding; a list of these codes are shown in Tables 1 and 2. In this study we intentionally excluded patients with a secondary diagnosis of VTE to focus on patients that were less likely to have been exposed to iatrogenic risk factors such as central venous catheter insertion.

Demographic Characteristics

We queried the PHIS database for girls aged 12-18 years with the primary diagnosis codes listed in Tables 1 and 2 and analyzed age and race data for each patient. These data were compared with the hospitalized population of female adolescents aged 12-18 years in the PHIS database who were discharged during our study period.

Table 1
ICD-9 Codes Queried for in the PHIS Database

415.19	Other Pulmonary Embolism and Infarction
453.40	Venous embolism and thrombosis of unspecified deep vessels of lower extremity
453.41	Acute venous embolism and thrombosis of deep vessels of proximal lower extremity
453.42	Acute venous embolism and thrombosis of deep vessels of distal lower extremity
453.82	Acute venous embolism and thrombosis of deep veins of upper extremity
453.83	Acute venous embolism and thrombosis of upper extremity, unspecified
453.84	Acute venous embolism and thrombosis of axillary veins
453.89	Acute venous embolism and thrombosis of other specified veins

ICD, International Classification of Diseases; PHIS, Pediatric Health Information System.

Table 2
ICD-10 Codes Queried for in the PHIS Database

I26.99	Other Pulmonary Embolism without Acute Cor Pulmonale
I82.40	Acute embolism and thrombosis of unspecified deep veins of lower extremity
I82.401	Acute embolism and thrombosis of unspecified deep veins of right lower extremity
I82.402	Acute embolism and thrombosis of unspecified deep veins of left lower extremity
I82.403	Acute embolism and thrombosis of unspecified deep veins of bilateral lower extremity
I82.409	Acute embolism and thrombosis of unspecified deep veins of unspecified lower extremity
I82.41	Acute embolism and thrombosis of femoral vein
I82.411	Acute embolism and thrombosis of right femoral vein
I82.412	Acute embolism and thrombosis of left femoral vein
I82.413	Acute embolism and thrombosis of femoral vein, bilateral
I82.419	Acute embolism and thrombosis of unspecified femoral vein
I82.42	Acute embolism and thrombosis of iliac vein
I82.421	Acute embolism and thrombosis of right iliac vein
I82.422	Acute embolism and thrombosis of left iliac vein
I82.423	Acute embolism and thrombosis of bilateral iliac vein
I82.429	Acute embolism and thrombosis of unspecified iliac vein
I82.43	Acute embolism and thrombosis of popliteal vein
I82.431	Acute embolism and thrombosis of right popliteal vein
I82.432	Acute embolism and thrombosis of left popliteal vein
I82.433	Acute embolism and thrombosis of bilateral popliteal veins
I82.439	Acute embolism and thrombosis of unspecified popliteal veins
I82.44	Acute embolism and thrombosis of tibial vein
I82.441	Acute embolism and thrombosis of right tibial vein
I82.442	Acute embolism and thrombosis of left tibial vein
I82.443	Acute embolism and thrombosis of unspecified tibial vein
I82.449	Acute embolism and thrombosis of unspecified tibial vein
I82.49	Acute embolism and thrombosis of other specified deep vein of lower extremity
I82.491	Acute embolism and thrombosis of other specified deep vein of right lower extremity
I82.492	Acute embolism and thrombosis of other specified deep vein of left lower extremity
I82.493	Acute embolism and thrombosis of other specified deep veins of bilateral lower extremity
I82.499	Acute embolism and thrombosis of other specified deep vein of unspecified lower extremity
I82.4Y	Acute embolism and thrombosis of unspecified deep veins of proximal lower extremity
I82.4Y1	Acute embolism and thrombosis of unspecified deep veins of right proximal lower extremity
I82.4Y2	Acute embolism and thrombosis of unspecified deep veins of left proximal lower extremity
I824Y3	Acute embolism and thrombosis of unspecified deep veins of bilateral proximal lower extremity
I82.4Y9	Acute embolism and thrombosis of unspecified deep veins of unspecified proximal lower extremity
I82.4Z	Acute embolism and thrombosis of unspecified deep veins of distal lower extremity
I82.4Z1	Acute embolism and thrombosis of unspecified deep veins of right distal lower extremity
I82.4Z2	Acute embolism and thrombosis of unspecified deep veins of left distal lower extremity
I82.4Z3	Acute embolism and thrombosis of unspecified deep veins of bilateral distal lower extremity
I824Z9	Acute embolism and thrombosis of unspecified deep veins of unspecified distal lower extremity
I82.62	Acute embolism and thrombosis of deep veins of upper extremity
I82.621	Acute embolism and thrombosis of deep veins of right upper extremity
I82.622	Acute embolism and thrombosis of deep veins of left upper extremity
I82.623	Acute embolism and thrombosis of deep veins of bilateral upper extremity
I82.629	Acute embolism and thrombosis of deep veins of unspecified upper extremity
I82.A1	Acute embolism and thrombosis of axillary vein
I82.A11	Acute embolism and thrombosis of right axillary vein
I82.A12	Acute embolism and thrombosis of left axillary vein
I82.A13	Acute embolism and thrombosis of bilateral axillary vein
I82.A19	Acute embolism and thrombosis of unspecified axillary vein

ICD, International Classification of Diseases; PHIS, Pediatric Health Information System.