Upper extremity deep venous thrombosis after port insertion: What are the risk factors?

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Background. *Totally implantable venous access devices (ports) are widely used, especially for cancer chemotherapy. Although their use has been associated with upper extremity deep venous thrombosis, the risk factors of upper extremity deep venous thrombosis in patients with a port are not studied adequately.*
Methods. *The Healthcare Cost and Utilization Project's Florida State Ambulatory Surgery and Services Database was queried between 2007 and 2011 for patients who underwent outpatient port insertion, identified by Current Procedural Terminology code. Patients were followed in the State Ambulatory Surgery and Services Database, State Inpatient Database, and State Emergency Department Database for upper extremity deep venous thrombosis occurrence. The cohort was divided into a test cohort and a validation cohort based on the year of port placement. A multivariable logistic regression model was developed to identify risk factors for upper extremity deep venous thrombosis in patients with a port. The model then was tested on the validation cohort.*
Results. *Of the 51,049 patients in the derivation cohort, 926 (1.81%) developed an upper extremity deep venous thrombosis. On multivariate analysis, independently significant predictors of upper extremity deep venous thrombosis included age <65 years (odds ratio = 1.22), Elixhauser score of 1 to 2 compared with zero (odds ratio = 1.17), end-stage renal disease (versus no kidney disease; odds ratio = 2.63), history of any deep venous thrombosis (odds ratio = 1.77), all-cause 30-day revisit (odds ratio = 2.36), African American race (versus white; odds ratio = 1.86), and other nonwhite races (odds ratio = 1.35). Additionally, compared with genitourinary malignancies, patients with gastrointestinal (odds ratio = 1.55), metastatic (odds ratio = 1.76), and lung cancers (odds ratio = 1.68) had greater risks of developing an upper extremity deep venous thrombosis.*
Conclusion. *This study identified major risk factors of upper extremity deep venous thrombosis. Further studies are needed to evaluate the appropriateness of thromboprophylaxis in patients at greater risk of upper extremity deep venous thrombosis. (Surgery 2017;■:■-■.)*

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TOTALLY IMPLANTABLE VENOUS ACCESS DEVICES (portacaths or ports) are used widely for long-term access to central veins, especially for cancer chemotherapy.[1] Ports are covered by patients' skin; therefore, they are less prone to infection, do not restrict motion, and are visually more appealing.[1] However, the indwelling catheter of ports, coupled with a hypercoagulable state that is associated with some cancers, puts patients at great risk for the development of an upper extremity deep venous thrombosis (U-DVT).[2,3]

U-DVT can lead to further complications, including port failure, pulmonary thromboembolism, venous insufficiency, and post-thrombotic syndrome.[3] However, due to the low event rate of U-DVT after port insertion, as well as the adverse events associated with anticoagulant use, current consensus does not support routine thromboprophylaxis after port insertion.[4] Nevertheless, the topic remains controversial, with a recent Cochrane review concluding that a benefit exists for thromboprophylaxis for indwelling

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ports, especially with low-molecular-weight heparin.[5] The risk factors of U-DVT often are assumed to be the same as those of lower extremity DVT[6]; however, previous studies have shown that the risk factors for lower extremity DVT and U-DVT are considerably different.[2,7]

The aim of the present study is to determine the predisposing factors of U-DVT in patients with an indwelling port in order to identify patients at greater risk of U-DVT development who would potentially benefit from thromboprophylaxis.

METHODS

Study populations. Discharge data were reviewed retrospectively from the Agency for Healthcare Research and Quality Healthcare Cost and Utilization Project's (HCUP) Florida State Ambulatory Surgery Database (SASD) for patients aged 18 to 95 years who had undergone an outpatient port insertion as defined by Current Procedural Terminology (CPT) code (36561) between 2007 and 2011. The CPT code was chosen to maximize the specificity of the index procedure. The index procedure was the first instance of port implantation during the study period. The cohort was then divided into a derivation cohort and a validation cohort based on the year of port insertion. Patients who had their first index procedure from 2009 to 2011 were included in the derivation cohort, whereas the validation cohort comprised those who had a port inserted during 2007 and 2008. Patients were followed for revisit data captured in the Florida SASD, in addition to the Florida State Emergency Department Database and the Florida State Inpatient Database. CPT coding is maintained by the American Medical Association.[8]

Primary outcome. Occurrence of an acute U-DVT at a revisit after the index procedure, as determined by the *International Classification of Diseases* (ICD-9) code (453.8) recorded in Florida State Emergency Department Database, SASD, or State Inpatient Database, was defined as the primary outcome. Those patients identified by codes relating to superficial or distal deep veins of the upper extremities were not considered as having a U-DVT (ICD-9 codes: 453.81, 453.82). Patients whose DVTs were not related to upper extremities also were excluded (453.89). ICD coding is developed and maintained by the World Health Organization.[9]

Site-specific 5-digit ICD-9 codes for U-DVT have been available since 2009 and were used for the derivation cohort. For patients diagnosed prior to 2009 (the validation cohort), the available 4-digit ICD-9 code (453.8) was used to capture early and late onset U-DVTs.

Covariates. All covariates were recorded at the first index visit. These included demographic data (sex, age, and race), as well as baseline comorbidities such as diabetes mellitus, hypertension, hyperlipidemia, chronic obstructive pulmonary disease, history of DVT, smoking, autoimmune diseases, and renal failure. Additional covariates that were recorded at the index visit included long-term use of anticoagulants and antiplatelet drugs, insurance type, and Elixhauser comorbidity index.[10] Elixhauser score is an aggregate measure of patients' comorbidities based on ICD-9 codes and is derived from 30 comorbidity categories via weighing algorithms.[10,11] For this study, the Elixhauser score was calculated using Elixhauser Comorbidity Software, version 3.7, which is provided by HCUP and creates 29 Elixhauser comorbidity measures.[12]

Indications for port placement were deduced similarly from the diagnosis codes at the index visit. Cancer diagnoses were defined and examined separately but were later grouped based on their anatomic locations. However, metastatic diseases were grouped together regardless of their primary site or the site to which they had metastasized. Hematologic malignancies also were grouped separately. Noncancer indications of port implantation were treated as one category if no cancer diagnosis was coded at the index visit. The full list of covariates and their corresponding ICD-9 codes are provided in Appendix 1.

Statistical analysis. SAS version 9.4 (SAS Institute, Cary, NC) was used for data preparation and analyses. χ^2 tests were used for univariate analyses, as appropriate. Variables that were deemed clinically relevant and had a P value $< .1$ on univariate screen were included in the multivariate logistic regression model. The Firth penalized likelihood ratio was used to minimize the bias associated with small event rates.[13-15] C-statistics were used to gauge the discriminatory power of the final model on the derivation and validation cohorts.

Risk scores were derived from the final model, which was bootstrapped for 500 estimations. The scores were calculated by dividing the median of the coefficient estimates for each risk factor by that of sex as the baseline.

RESULTS

The derivation cohort included 51,049 patients, of whom 926 (1.81%) developed a U-DVT. The mean age of the derivation cohort was 62.62 years (SD = 13.19), and 61.92% were female. Breast