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Risk of venous thromboembolism occurrence among adults with selected autoimmune diseases: A study among a U.S. cohort of commercial insurance enrollees☆

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ABSTRACT

Objective: This study assessed the risk of venous thromboembolism (VTE) among privately insured adults in the U.S. with one or more of the following autoimmune diseases: autoimmune hemolytic anemia (AIHA), immune thrombocytopenic purpura (ITP), rheumatoid arthritis (RA), and systemic lupus erythematosus (SLE).
Materials and Methods: Using the Truven Health MarketScan® Databases, patients 18–64 years of age with a diagnosis of AIHA, ITP, RA, or SLE in 2007 and a sex and age-group matched comparison group of enrollees were followed up through 2010 to identify VTE events. Survival curve and Cox proportional hazards analyses were conducted to assess differences between groups.
Results: Among patients with AIHA, ITP, RA, or SLE, or >1 of these diseases, the risk of at least one VTE event was 19.74, 7.72, 4.90, 9.89, and 13.35 per 1,000 person-years, respectively; among the comparison group, the risk was 1.91 per 1,000 person-years. The adjusted hazard ratios (aHRs) for VTE among patients with AIHA, ITP, RA, or SLE, or >1 of these diseases (when compared with the comparison group) tended to decline over follow-up time; at 1 year, the aHRs were 6.30 (95% confidence interval [CI]: 4.44–8.94), 2.95 (95% CI: 2.18–4.00), 2.13 (95% CI: 1.89–2.40), 4.68 (95% CI: 4.10–5.33), and 5.11 (95% CI: 4.26–6.14), respectively.
Conclusion: Having AIHA, ITP, RA, or SLE, or >1 of these diseases was associated with an increased likelihood of a VTE event. More research is necessary to develop better understanding of VTE occurrence among people with autoimmune diseases.

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Introduction

Venous thromboembolism (VTE), which consists of deep vein thrombosis (DVT) or pulmonary embolism (PE), or both, is an important public health concern [1–3]. It has been estimated that 350,000–900,000 people in the United States might suffer a VTE each year [4–7]. Research increasingly has indicated that many autoimmune diseases might be associated with an increased risk of VTE occurrence [8–16]. For example, the increased risk of VTE associated with systemic lupus erythematosus (SLE) has been reported previously by a number of studies [12,15,17–19]. Investigators in the United Kingdom identified hospitalizations of people for one or more of several autoimmune diseases using three different hospitalization information datasets and then followed up available information in order to identify subsequent hospitalizations of these individuals for VTE; in the largest of these datasets, a statistically significant increased rate ratio for VTE was found for SLE, rheumatoid arthritis (RA), idiopathic thrombocytopenic purpura (ITP), and autoimmune hemolytic anemia (AIHA), as well as the other autoimmune diseases assessed [13].

The deleterious effects that VTE can have on life and health can be minimized through the prevention of VTE occurrence and through appropriate diagnosis and treatment. In this context, better understanding of the epidemiology of VTE – including risk factors for VTE

Abbreviations: aHR, adjusted hazards ratio; AIHA, autoimmune hemolytic anemia; CI, confidence interval; CPT, Current Procedural Terminology; DVT, deep vein thrombosis; ICD-9-CM, International Classification of Diseases, 9th Revision, Clinical Modification; ITP, immune thrombocytopenic purpura; PE, pulmonary embolism; RA, rheumatoid arthritis; SLE, systemic lupus erythematosus; VTE, venous thromboembolism.

☆ Authors' note: The findings and conclusions in this report are those of the authors and do not necessarily represent the official policy of the Centers for Disease Control and Prevention.

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occurrence – can be helpful in achieving greater awareness and vigilance among providers and others with regard to people who might be at increased risk of VTE, patient assessment and screening, implementation of appropriate prevention strategies, diagnosis of VTE events, and patient management. Using a large, claims-based data source that included individuals enrolled in employer-sponsored commercial health plans, this study assessed VTE occurrence among 18–64-year-old adults diagnosed with four selected autoimmune diseases: AIHA, ITP, RA, and SLE. Our aim was to add to the growing evidence of the association between autoimmune diseases and VTE and epidemiologic understanding in this regard [8–16]. We previously reported findings of a cross-sectional study using U.S. hospitalization data that indicated an increased likelihood of VTE diagnosis associated with a diagnosis of these autoimmune diseases [20]. The objectives of this study were to assess the risk of VTE among commercial health insurance enrollees who had a diagnosis of one or more of the same four autoimmune diseases using a longitudinal approach.

Materials and Methods

A retrospective cohort approach was used to identify individuals with and those without a diagnosis of any of the autoimmune diseases of interest and follow up these individuals to identify VTE occurrence.

Data Source

We used data from the Truven Health MarketScan® Commercial Claims and Encounters Databases [MarketScan is a registered trademark of Truven Health Analytics Inc] for the years 2007–2010. These databases contained health care claims-based information for enrollees in large employer-sponsored health insurance plans across the United States. The 2007–2010 Commercial Claims databases contained information for approximately 28,762,000–45,240,000 enrollees during each of these years. The data included inpatient claims, outpatient claims, outpatient pharmacy claims, and plan enrollment information.

Information available for enrollees included sex, age, and the starting and ending dates of enrollment. Inpatient and outpatient databases included information on diagnoses and performed procedures; diagnoses information was indicated using *International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM)* codes and, in the inpatient data, procedures performed were indicated using *ICD-9-CM* codes and the American Medical Association's *Current Procedural Terminology (CPT®)* code sets. Each individual in the MarketScan data had a unique encrypted enrollee identification number that could not be used to identify the individual, but could be used to link information for the individual within and across the various datasets and across years as long as they remained employed by the same employer.

Study Population

The *study group* consisted of all adults 18–64 years of age who were enrolled in the health insurance plans included in the MarketScan Commercial Claims databases during any time in 2007 and remained continuously enrolled for any length of time (with the cutoff for assessing continuity occurring at December 31, 2010), and who also had diagnoses of one or more of the four autoimmune diseases of interest (AIHA, ITP, RA, and SLE) during 2007. For the purposes of this study, continuous enrollment was defined as there being no more than 1 day of gap in enrollment in the health plan during each enrollee's enrollment period. Identification of a diagnosis of any of the autoimmune diseases of interest was based on the presence of the respective *ICD-9-CM* diagnosis codes (see Appendix A for codes used in this study) in the diagnosis information provided in the outpatient and inpatient health care encounter information. Specifically, an enrollee was defined as having a diagnosis of an autoimmune disease of interest if the person had an inpatient diagnosis of the disease or if the person had at least two outpatient diagnoses of the disease at least 30 days apart during the study period (with the first diagnosis occurring during 2007).

A *comparison group* was identified by first identifying all adults 18–64 years of age who were enrolled at any time during 2007 and who did not have a diagnosis of any of the four autoimmune diseases of interest during the study period (January1, 2007–December 31, 2010). From this group of enrollees, a random sample (without replacement) was selected in an approximately 2-to-1 ratio to the number of individuals in the study cohort. The random sample was selected so that the sex and age group (18–34, 35–44, 45–54, and 55–64 years) proportions were approximately equivalent to those of the study group. Individuals who were not enrolled continuously were excluded from the comparison group. Continuous enrollment for this group was defined in the same way as for the study group.

Definition of Outcomes

The outcome of interest for this study was the first occurrence of a VTE event during the follow-up period (follow-up period start- and end-points are described in the following section). *ICD-9-CM* diagnosis codes related to DVT or PE, or both (see Appendix A for codes used in this study), were used to identify any VTE diagnosis recorded in inpatient and outpatient claims. A participant in this study was identified as having had a VTE event if at any time during the follow-up period there was an inpatient diagnosis of VTE or an outpatient diagnosis of VTE combined with an outpatient drug claim for anticoagulant medication within 14 days following the outpatient VTE diagnosis. This included diagnosis of any VTE event during the same hospitalization as a diagnosis of any of the selected autoimmune diseases; when such occurred, the date of hospital admission was inferred as the date of diagnosis for both events.

Follow-up Start and Endpoint

Information for all inpatient admissions and outpatient services during the period 2007–2010 for the study and comparison groups was linked with respect to each study participant. For the study group, the start of follow-up was the earliest identified date of diagnosis of any of the four autoimmune diseases of interest during the study period. For the comparison group, the start of follow-up was either January 1, 2007, or their first date of enrollment (i.e., when that was after January 1, 2007). For both the study and comparison groups, the follow-up endpoint was the date of the first VTE event identified (for those with a VTE event) or the earlier of either the last date of enrollment (as indicated in the MarketScan data used) or December 31, 2010.

Other Medical Characteristics of Study Participants

The diagnosis of selected medical conditions among study participants and whether they had venous catheterization or other surgery related procedures during the follow-up period were identified as these might affect the likelihood of a VTE event. *ICD-9-CM* diagnosis codes were used to identify diagnoses of selected medical conditions: cancer; heart failure; stroke; chronic obstructive pulmonary disease; injury; infection; kidney disease (chronic kidney disease, chronic glomerulonephritis, or nephrotic syndrome); varicose veins; paralysis of limb; diabetes; Crohn's disease or ulcerative colitis, or both; and pregnancy or delivery-related hospitalizations, or both (see Appendix A for codes used in this study). For each medical condition, an enrollee was defined as having a diagnosis of the condition if, during the follow-up period, there was an inpatient diagnosis of the disease or if there were at least two outpatient diagnoses of the disease at least 30 days apart. *ICD-9-CM* procedure codes and *CPT* codes were used to identify venous catheterization and other surgery-related procedures (broadly defined as having any surgery-related procedure) (see Appendix A for the codes used in this study).