Venous Thromboembolism in Special Populations

Preexisting Cardiopulmonary Disease, Cirrhosis, End-Stage Renal Disease, and Asplenia

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KEYWORDS

• Pulmonary embolism • Venous thromboembolism • Cardiopulmonary disease • Cirrhosis
• Renal failure • Asplenia • Splenectomy

KEY POINTS

- Preexisting cardiopulmonary disease, such as atrial fibrillation, heart failure, and chronic obstructive pulmonary disease, is associated with worse prognosis in venous thromboembolic disease.
- Chronic liver disease patients have substantially increased risk of venous thromboembolism (VTE), and the risk for deep vein thrombosis is higher than for PE.
- Patients with renal disease have increased risk for VTE, suffer worse outcomes, and have limitations to anticoagulation due to bleeding and drug clearance.
- Asplenia, in particular splenectomy for hematologic disease, is associated with increased risk for VTE.

INTRODUCTION

Venous thromboembolism (VTE) includes deep vein thrombosis (DVT) and pulmonary embolism (PE). There are approximately 900,000 cases of VTE per year in the United States, of which 150 to 250,000 are PE-related hospitalizations and 60 to 100,000 PE-related deaths, making it the third most common cause of cardiovascular death.[1]

VTE is associated with inherited (factor V Leiden, prothrombin mutation, antithrombin deficiency, protein C and S deficiency, and so forth) and acquired risk factors (immobilization, trauma, major surgery, malignancy, pregnancy, congestive heart failure, chronic obstructive pulmonary disease, nephrotic syndrome, liver disease, and so forth). Some of these risk factors, along with other clinical assessments, are included in the Wells rule and Geneva scores, to classify patients into pretest probability of PE diagnosis.[2–4]

Acute PE spans a wide spectrum of clinical outcomes mainly based on the right ventricle capacity to tolerate strain. The PE score index (PESI) is a validated clinical prediction rule that classifies patients with increasing risk of mortality and/or other adverse medical outcomes.[5,6] Heart failure (HF) and chronic lung disease are both included in the PESI calculation (**Table 1**).

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Table 1
Summary of characteristics of venous thromboembolism in special population

Special Population	Examples of Specific Conditions	Effect on Venous Thromboembolism Risk or Incidence	Effect on Venous Thromboembolism Outcomes	Therapeutic Considerations
Cardiopulmonary disease	AF	PE is a risk factor for AF.[14] May Increase VTE risk[18–20]	Higher mortality[17]	No specific recommendation
	Heart failure	N/A	Worse prognosis[5,6] Higher mortality[21]	
	AE-COPD	Increased VTE risk[28–31]	Worse prognosis[5,6]	
Cirrhosis		Increased VTE risk[41–44]	Increased length of stay and hospitalization cost[41]	LMWH is preferred over VKA[35]
Renal disease		Increased VTE risk[51–53]	Worse outcomes[47,48] Increased bleeding complications[48,57–60]	VKA is preferred anticoagulant[35] LMWH may increase bleeding.[63] DOACs not indicated in CrCl <30 mL/min or dialysis[67–70]
Asplenia	Surgical splenectomy Trauma Hematologic Thalassemia Hemolytic Anemia Sickle cell disease	Increased VTE risk[71,73–77]	Higher PE mortality[75]	Do not withhold thromboprophylaxis for patients undergoing splenectomy.[78]

Abbreviations: AE-COPD, acute exacerbation of chronic obstructive pulmonary disease; AF, atrial fibrillation; CrCl, creatinine clearance; DOAC, direct oral anticoagulant; LMWH, low molecular weight heparin; PE, pulmonary embolism; VKA, vitamin K antagonist; VTE, venous thromboembolism.

The goal of this review is to discuss the intrinsic details of patients with preexisting cardiopulmonary diseases, cirrhosis, renal dysfunction, and asplenia. Presence of these conditions not only increases the risk of VTE but also carries worse outcomes. The complexity of the use and choice of anticoagulation in these special populations are also reviewed.

CARDIOPULMONARY DISEASE

Cardiovascular Disease

Preexisting cardiovascular disease is common in VTE patients. Clinical characteristics of 1023 patients presenting with PE between 2000 and 2007 showed that 44% of patients had cardiovascular disease, including ischemic heart disease, stroke, heart failure, peripheral vascular disease, valvular heart disease (with or without prosthetic valve), and/or atrial fibrillation/flutter (AF).[7] These patients with underlying cardiovascular disease at baseline had a 2.2-fold (95% CI, 1.75–2.72; $P<.0001$) increased risk of death during long-term follow-up compared with those without baseline cardiovascular disease when presenting with acute PE.[7] In a Taiwanese population-based retrospective study, an increased risk of major adverse cardiovascular events (adjusted hazard ratio [HR] 1.86, 95% CI, 1.65–2.09; $P<.0001$) in patients with VTE, including acute coronary syndrome and stroke, was observed.[8] This risk increased with age and was up to 15-fold higher (95% CI, 8.14–28.95; $P<.0001$) in patients over 75 years old. Also comorbidities, such as diabetes mellitus, hypertension, and stroke, increased the risk of major adverse cardiovascular events, but hyperlipidemia reduced the risks of cardiovascular events.[8]

Atrial Fibrillation

AF is the most common sustained chronic cardiac arrhythmia, with a lifetime prevalence of up to