

# Venous thromboembolism: Risk factors, comorbidities, and treatment-associated risk of bleeding.

## Akademisk avhandling

Som för avläggande av medicine doktorsexamen vid Sahlgrenska akademien,  
Göteborgs universitet kommer att offentligen försvaras i Järneken aula,  
Kvinnokliniken, Diagnosvägen 15, plan 0, Sahlgrenska Universitetssjukhuset/Östra  
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av

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Anders Gottsäter, Professor  
Lunds universitet, Sverige

## Avhandlingen baseras på följande delarbeten

- I. Glise Sandblad K, Jern S, Åberg M, Robertson J, Torén K, Lindgren M, Adiels M, Hansson PO, Rosengren A. Obesity in adolescent men increases the risk of venous thromboembolism in adult life. *J Intern Med.* 2020;287:734–745.
- II. Glise Sandblad K, Rosengren A, Sörbo J, Jern S, Hansson PO. Pulmonary embolism and deep vein thrombosis—comorbidities and temporary provoking factors in a register-based study of 1.48 million people. *Res Pract Thromb Haemost.* 2022;6:e12714.
- III. Glise Sandblad K, Hansson PO, Philipson J, Mahmoud A, Karlsson P, Rosengren A, Sörbo J. Prevalence of Cancer in Patients with Venous Thromboembolism: A Retrospective Nationwide Case-Control Study in Sweden. *Clinical and Applied Thrombosis/Hemostasis.* 2023;29:1–10.
- IV. Glise Sandblad K, Schulman S, Rosengren A, Sörbo J, Philipson J, Hansson PO. Association of type of oral anticoagulation with risk of bleeding in 45,114 patients with venous thromboembolism during initial and extended treatment- A nationwide register-based study. *J Intern Med.* 2023;00:1–18.

# Venous thromboembolism: Risk factors, comorbidities, and treatment-associated risk of bleeding.

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## ABSTRACT

**Background:** Venous thromboembolism (VTE) is the third most common cardiovascular disease, consisting mainly of deep vein thrombosis (DVT) and pulmonary embolism (PE). Since VTE often is a preventable disease, knowledge of risk factors is critical. Following a VTE, many patients are subjected to extended anticoagulant treatment. However, the bleeding risk during extended treatment is largely unknown.

**Aim:** To study risk factors in patients with VTE and to determine the occurrence of major bleeding during VTE treatment.

**Methods:** Paper *I*: 1.6 million men from The Swedish Military Service Conscription Register were grouped based on BMI and followed through nationwide registries to determine the risk of a first-time VTE. Papers *II-IV*: The National Patient Register, the National Cause of Death Register, the National Prescribed Drug Register, and the Total Population Register were used to identify almost 300,000 patients with first-time PE or DVT and 1,200,000 matched controls. PE and DVT patients and their respective controls were compared regarding comorbidities and temporary provoking factors (*II*), the prevalence of different cancers (*III*), and, between 2014–2020, the risk of bleeding during anticoagulant treatment (*IV*).

**Results:** Paper *I*: Men who were overweight or obese at enlistment had a high risk of VTE later in life. Paper *II*: Patients with PE more often had underlying cardiovascular disease, while patients with DVT were more likely to have recent musculoskeletal surgery or fracture. Paper *III*: VTE had a strong association with pancreatic, brain, or liver cancer, while the association was weak with recent diagnoses of bladder/urinary tract cancer, kidney cancer, or uterine cancer. Paper *IV*: During initial treatment (0–6 months), patients treated with apixaban had a lower bleeding risk than patients treated with warfarin or rivaroxaban. During extended treatment (6 months–5 years), both apixaban and rivaroxaban had a low bleeding risk, lower than warfarin.

**Conclusion:** The increasing prevalence of obesity might imply an increase in VTE in the coming decades. Patients with cardiopulmonary disease had a higher risk of PE than DVT. Risks of VTE differ widely for various cancers. Apixaban carried a lower risk of bleeding than rivaroxaban and warfarin in the initial treatment, while both apixaban and rivaroxaban had a low risk of bleeding, and lower than warfarin, in extended treatment. These findings are important for VTE prophylaxis and treatment in clinical praxis.

**Keywords:** Venous thromboembolism, registries, overweight, body mass index, incidence, cardiovascular disease, anticoagulants, apixaban, rivaroxaban, warfarin, hemorrhage.