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Survival after splanchnic vein thrombosis: A 20-year nationwide cohort study

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ABSTRACT

Introduction: Splanchnic vein thrombosis (SVT) is a rare condition with a poorly understood prognosis.
Materials and methods: We conducted a population-based cohort study (1994–2013), using data from Danish nationwide medical registries, to examine the short- and long-term prognosis of SVT. We identified 1915 incident cases of SVT and a matched comparison cohort of 18,267 persons without SVT (matched by cancer, cirrhosis, pancreatitis, alcohol-related disease, atrial fibrillation/flutter, venous thromboembolism, heart failure, and inflammatory bowel disease). We used the Kaplan-Meier method to calculate absolute risk of death. Using stratified Cox regression, we computed mortality rate ratios (MRRs) with 95% confidence intervals (CIs), comparing SVT patients with the comparison cohort.
Results: We identified 1,500 (78%) patients with portal vein thrombosis, 204 (11%) with hepatic vein thrombosis, and 211 (11%) with mesenteric vein thrombosis. The mortality risks were markedly higher for SVT patients than for the comparison cohort during the first 5 years of follow-up (30-day risk: 20.6% vs. 0.7%; 31–364-day risk: 21.7% vs. 4.7%; and 1–5-year risk: 25.4% vs. 17.7%). The corresponding MRRs were 40.7 (95% CI: 32.4–51.1), 7.4 (95% CI: 6.4–8.6), and 2.4 (95% CI: 2.1–2.8), respectively. The 30-day mortality was higher after mesenteric vein thrombosis than portal and hepatic vein thrombosis, whereas portal vein thrombosis had a stronger impact on mortality after 30 days than hepatic and mesenteric vein thrombosis.
Conclusions: Splanchnic vein thrombosis has a poor short- and long-term prognosis that varies according to subtype of thrombosis. Reasons for the increased mortality in patients with SVT need further clarification.

1. Introduction

Splanchnic vein thrombosis (SVT) — thrombosis of portal, hepatic, or mesenteric veins is a rare presentation of venous thrombosis [1]. The limited data available on incidence of SVT show a large range, i.e., between 1 per million [2] and 1 per 100.000 [3] persons per year. A Swedish autopsy study found a prevalence of portal vein thrombosis of 1 per 100 persons [4], suggesting that this type of thrombosis is much more common than perceived. The elements of Virchow's triad, including hypercoagulability, endothelial injury (e.g., tumor invasion, surgical trauma, infection, or inflammation), and venous stasis (e.g., compression caused by a solid tumor, abscess, hepato- or splenomegaly, or depressed cardiac output) are also applicable in the pathogenesis of SVT [1,5].

Cirrhosis, hepato-biliary cancers, and intra-abdominal infection or inflammation are among the most important local precipitating factors for SVT [1]. Congestive heart failure and atrial fibrillation increase the risk of venous thromboembolism [6] and may also increase risk of SVT. The most common systemic risk factors are myeloproliferative neoplasms and prothrombotic genetic conditions (e.g., mutation in Factor V Leiden or prothrombin) [7]. Finally, pregnancy and oral contraceptives also may cause SVT [1], although young women likely represent only a small number of SVT patients. Patients presenting with SVT are mainly diagnosed and treated in hematological and gastroenterological departments, depending on their underlying disease. Some also are diagnosed accidentally when undergoing an abdominal ultrasound or computerized tomography (CT) scan for another indication [8]. In some cases, SVTs are found only at autopsy [4].

The prognosis after SVT is poorly understood. Underlying comorbidities [9] and location of thrombosis likely impact prognosis [10]. The aim of our study was to examine survival in a nationwide population-based cohort of patients with incident SVT and to explore whether specific prevalent diseases modify this outcome.

2. Patients and methods

2.1. Setting and data sources

We conducted a population-based nationwide Danish cohort study of incident cases of SVT diagnosed between 1994 and 2013 (the

Abbreviations: SVT, Splanchnic vein thrombosis; DNPR, Danish National Patient Registry; ICD, International Classification of Diseases; IQR, Interquartile range; MRR, Mortality rate ratio; CI, Confidence interval.

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cumulative Danish population in this period was 7.3 million persons), using data from the Danish National Patient Registry (DNPR) [11], and the Danish Civil Registration System [12]. The Danish National Health Service provides tax-funded medical care to all Danish residents and guarantees free-of-charge access to hospitals and outpatient clinics [13].

2.2. Study population

The DNPR contains data on all hospital inpatient contacts since 1977, registered according to the International Classification of Diseases (ICD) 8th and 10th version [11]. The ICD-10 was introduced in Denmark in 1994. The DNPR also covers data from outpatient clinic visits since 1994. We therefore started our study in 1994. For each hospital contact, the treating physician assigns a primary discharge diagnosis and may also assign up to 19 secondary diagnoses. Surgical procedures have been coded in the DNPR using the Nordic Medico Statistical Committee Classification system since 1996 [14].

We identified all hospital inpatients and outpatients diagnosed with a first-time SVT during 1994 through 2013, including both primary and secondary diagnoses. Patients with only an emergency room SVT diagnosis were excluded from the analysis because of concerns about a possible lower diagnostic predictive value in this setting [15]. We also did not include patients who were diagnosed with SVT before 1994, to avoid capturing recurrent thrombosis. All diagnosis codes used are provided in the Supplemental Appendix, for online only.

Table 1
Characteristics for patients with SVT and for the general population comparison cohort.

	SVT cohort $n = 1915$, n (%)	Comparison cohort $n = 18.267$, n (%)
Age categories (y)		
<40	271 (14.1)	2633 (14.4)
40–64	777 (40.6)	7345 (40.2)
65+	867 (45.3)	8289 (45.4)
Calendar period		
1994–1999	270 (14.1)	2605 (14.3)
2000–2005	445 (23.2)	4297 (23.5)
2006–2013	1200 (62.7)	11,365 (62.2)
Matching factors		
Liver cirrhosis	216 (11.3)	1671 (9.2)
Pancreatitis	206 (10.8)	1821 (10.0)
Liver cancer	32 (1.7)	107 (0.6)
Pancreatic cancer	41 (2.1)	270 (1.5)
Other gastrointestinal cancer	104 (5.4)	970 (5.3)
Myeloproliferative neoplasm	23 (1.2)	179 (1.0)
Extra-intestinal cancer	200 (10.4)	1818 (10.0)
Atrial fibrillation or flutter	173 (9.0)	1545 (8.5)
Venous thromboembolism	132 (6.9)	1069 (5.9)
Congestive heart failure	169 (8.8)	1479 (8.1)
Other alcohol-related disease	194 (10.1)	1667 (9.1)
Inflammatory bowel disease	69 (3.6)	588 (3.2)
Comorbid conditions		
Myocardial infarction	140 (7.3)	982 (5.4)
Peripheral vascular disease	173 (9.0)	809 (4.4)
Cerebrovascular disease	200 (10.4)	1451 (7.9)
Dementia	33 (1.7)	239 (1.3)
Chronic pulmonary disease	208 (10.9)	1479 (8.1)
Connective tissue disease	90 (4.7)	545 (3.0)
Ulcer disease	220 (11.5)	1074 (5.9)
Mild liver disease	266 (13.9)	1909 (10.5)
Diabetes	278 (14.5)	1314 (7.2)
Diabetes with end-organ failure	129 (6.7)	628 (3.4)
Hemiplegia	8 (0.4)	54 (0.3)
Moderate to severe renal disease	86 (4.5)	391 (2.1)
AIDS	6 (0.3)	19 (0.1)
Other covariates		
Pregnancy or childbirth within 90 days	6 (0.3)	37 (0.2)
Surgical procedures within 90 days	763 (39.8)	1668 (9.1)

2.3. Comparison cohort

We used the Danish Civil Registration System and DNPR to create a population-based comparison cohort. For each patient with SVT we randomly matched 10 persons from the Danish general population on sex, year of birth (5-year intervals), date of SVT diagnosis, and several comorbidities. The underlying comorbidities used for the matching included cirrhosis, pancreatitis, liver cancer, pancreatic cancer, other gastrointestinal cancer, myeloproliferative neoplasms, extra-intestinal cancer, atrial fibrillation or flutter, venous thromboembolism, congestive heart failure, other alcohol-related disease (not cirrhosis and pancreatitis), and inflammatory bowel disease diagnosed any time before the index date. The index date for each member of the comparison cohort corresponded to the hospital admission date or hospital outpatient contact date for the matched incident SVT case.

2.4. Patient characteristics

In addition to the matching factors, we obtained information on diseases (diagnosed prior to SVT/index date) included in the Charlson Comorbidity Index [16,17]: myocardial infarction, peripheral vascular disease, cerebrovascular disease, dementia, chronic pulmonary disease, connective tissue disease, ulcer disease, mild liver disease, diabetes, hemiplegia, moderate to severe renal disease, and AIDS. In addition, we included information on pregnancy or childbirth within 90 days before index date. We also obtained information on surgical procedures performed within 90 days before the index date. Finally, we calculated the frequency of patients that were diagnosed with ischemic colitis or intestinal infarction during same admission or subsequently.

2.5. Statistical analysis

We characterized SVT patients and the comparison cohort members by sex, age category, calendar period of diagnosis, and covariates. We calculated median age at the index date and median follow-up period (interquartile range (IQR)) for all patients and for 30-day survivors. We followed both cohorts from SVT/index date until death from any cause, emigration, 30 November 2013, or 20 years of follow-up, whichever came first. Using the Kaplan-Meier method [18], we computed mortality risks for several subcohorts (e.g. cancer and cirrhosis patients), and for several follow-up periods (30 days, 31–364 days, 1–5 years, >5–20 years). In addition, we illustrated graphically the mortality (absolute risk) observed in the SVT and comparison cohorts.

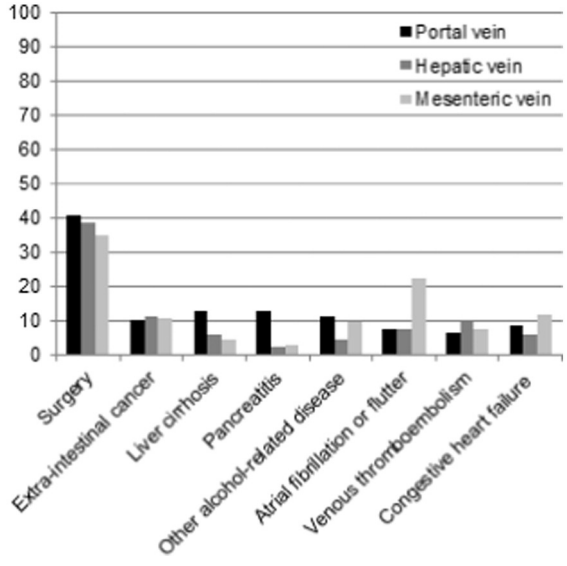

Fig. 1. Frequencies (%) of selected comorbidities and conditions by type of thrombosis.