Acute pancreatitis: from treatment to prevention

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CHAPTER 5

Splanchnic vein thrombosis in necrotizing pancreatitis: *a post-hoc analysis of a nationwide prospective cohort*

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ABSTRACT

Background: Treatment guidelines for splanchnic vein thrombosis in necrotizing pancreatitis are lacking due to a lack of data on the full clinical spectrum.

Methods: We performed a post-hoc analysis of a nationwide prospective necrotizing pancreatitis cohort. Multivariable analyses were used to identify risk factors and to compare the clinical course of patients with and without SVT.

Results: SVT was detected in 97 of the 432 included patients (22%) (median onset: 4 days). Risk factors were left, central, or subtotal necrosis (OR 28.49; 95% CI 20.09-40.40), right or diffuse necrosis (OR 5.75; 95% CI 3.89-8.50), and younger age (OR 0.99; 95% CI 0.98-1.00). Patients with SVT had higher rates of bleeding (n=10, 11%) and bowel ischemia (n=4, 4%) compared to patients without SVT (n=14, 4% and n=2, 0.6%; OR 3.24; 95% CI 1.27-8.23 and OR 7.29; 95% CI 1.31-40.40, respectively), and were independently associated with ICU admission (adjusted OR 2.53; 95% CI 1.37-4.68). Spontaneous recanalization occurred in 62% of patients (n=40/71). Radiological and clinical outcomes did not differ between patients treated with and without anticoagulants.

Discussion: SVT is a common and early complication of necrotizing pancreatitis, associated with parenchymal necrosis and younger age. SVT is associated with increased complications and a worse clinical course, whereas anticoagulation use does not appear to affect outcome.

INTRODUCTION

Splanchnic vein thrombosis (SVT) is a well-known complication of acute pancreatitis involving the splenic (SpIV), portal (PV) and/or superior mesenteric (SMV) vein (1-3). The exact incidence and pathophysiology remain unclear (4). Previous studies have demonstrated SVT in 2% to 51% of patients with acute pancreatitis, with the highest incidence in patients with necrotizing pancreatitis (1-3). Several mechanisms of SVT have been proposed in necrotizing pancreatitis, including local inflammatory infiltration, systemic inflammatory response, release of activated pancreatic enzymes, and extrinsic compression (5-7). Only a few studies have investigated the relationship between SVT and inflammatory markers, the location and extent of pancreatic parenchymal necrosis, the co-localization of such collections, and the presence of increased intra-abdominal pressure (8-13). These studies were mostly small (20 to 45 patients) and lacked a control group without SVT. In addition, there is a lack of data on the natural course of SVT following necrotizing pancreatitis, which may be due to imaging studies being guided by disease severity rather than systematical detection and evaluation of SVT. The timing of SVT onset and its evolution over time (i.e., resolution or progression) are particularly relevant, as these may have implications for (preventive) treatment, such as drainage of collections and therapeutic anticoagulation. Finally, it remains unclear whether SVT leads to worse clinical outcomes or whether the clinical course of patients with necrotizing pancreatitis depends mainly on the severity of the underlying disease. This uncertainty is driven by a serious risk of confounding in the currently available literature (8, 14-17).

We therefore performed the present study with the aim to determine the incidence, risk factors, natural course, and clinical outcomes of SVT in a large nationwide prospective cohort of patients with necrotizing pancreatitis. We also evaluated clinical and radiological outcomes associated with the use of therapeutic anticoagulation.

METHODS

Study design and population

This study was a post-hoc analysis of 639 patients with necrotizing pancreatitis included in the prospective nationwide registry of the Dutch Pancreatitis Study Group (DPSG). These patients were enrolled at 21 hospitals between 2004 and 2008 if they met the inclusion criteria of necrotizing pancreatitis, defined as a computed tomography severity index (CTSI) score of three or more, as assessed by a single expert pancreatic radiologist (TLB). For this study, patients were excluded if they had incomplete (follow-up) data or were lost to follow-up. All patients provided written

informed consent for the initial registration. Ethical approval by the medical ethical committee was waived for the current post-hoc analyses. This study was conducted according to the Strengthening the Reporting of Observational studies in Epidemiology (STROBE) guidelines (18).

Data collection

Clinical data from the index admission for acute pancreatitis were collected prospectively using a predefined, standardized case record form. This included age, sex, etiology, American Society of Anesthesiologist (ASA) classification, medical history (including venous thromboembolism), previous use of therapeutic anticoagulants, body mass index (BMI), smoking status, and peak laboratory values (CRP and leukocytes) in the first 48 h. Computed tomography (CT) scans were collected from all participating hospitals and were re-evaluated by a single radiologist (TLB). If patients were transferred, CT scans were obtained from both hospitals. Due to the multicenter design, a variety of CT scanners were used, but all were 16-slice or higher multidetector scanners with slice thicknesses ranging from 1.5 to 3 mm. The CTSI score, the presence, extent and location of (peri)pancreatic necrosis and collections were assessed on the first CT performed 72 h after the onset of acute pancreatitis. Left-sided necrosis referred to pancreatic tail necrosis, right-sided necrosis referred to pancreatic head necrosis, central necrosis to pancreatic neck and/or body necrosis, subtotal necrosis to pancreatic neck, body, and most of head and tail necrosis, and diffuse necrosis to uni- or multifocal areas of necrosis throughout the pancreas. The extent of pancreatic parenchymal necrosis was visually estimated as less than 30%, between 30% and 50%, and greater than 50%. All contrast-enhanced CTs were reviewed for the presence, location, and extent of SVT were also assessed on each CT scan. Long-term follow-up data, and collection of data on several factors related to SVT and the use of therapeutic anticoagulation, were collected retrospectively until January 2020.

Outcome measures and definitions

The primary outcome was the occurrence of SVT, defined as an intraluminal filling defect in one or more of the splanchnic veins. Vein compression or stenosis without an actual thrombus and the presence of collaterals without a visible vein were not sufficient for the diagnosis of SVT. Thrombus location was divided into SpIV, PV, SMV, or a combination. The degree of thrombus was classified as occlusive (absence of flow) or non-occlusive (presence of flow). In the case of multiple affected vessels, scoring was pragmatically considered occlusive if one thrombus was occlusive and another was non-occlusive. Collateral circulation was defined radiologically as the presence of varices, collaterals, or cavernomas. Co-localized compression (i.e., due to (peri) pancreatic fluid collections or edema) was also assessed on the initial CT scan of SVT diagnosis. Other radiological outcomes included recanalization, time to recanaliza-

tion, thrombus progression, and SVT recurrence. Recanalization was defined as the absence of a thrombus in a previously thrombosed splanchnic vein(s), except for an obliterated vein as a result of persistent thrombotic occlusion. Progression to other splanchnic vein(s), to total occlusion, or both, was defined as thrombus progression. Clinical outcomes included pancreatitis-related mortality, (multiple) organ failure, intensive care unit (ICU) admission, and SVT-related complications such as bleeding and bowel ischemia. Therapeutic anticoagulants referred to any agent prescribed at a therapeutic dose, such as low-molecular-weight heparin, unfractionated heparin, and vitamin K antagonist. A summary of all definitions is provided in Table S1.

Statistical analysis

Statistical analysis was performed with SPSS for Windows (version 26.0) (19). Continuous variables were expressed as mean (standard deviation [SD]) or median (interquartile range [IQR]), whereas categorical variables were expressed as absolute numbers and percentages. The Student's T test or Mann-Whitney U test was used to compare continuous variables, and chi-square test, or in the case of small groups, Fisher's exact test was used for categorical data. Multivariable logistic regression analyses were used to assess independent predictive factors for the development of SVT. The pattern of pancreatic parenchymal necrosis was reduced to (1) no necrosis (reference), (2) left, central, or subtotal necrosis, and (3) right or diffuse necrosis because of the limited number of cases. The percentage of necrotic tissue was not included to avoid multicollinearity. Subgroup analyses were performed to compare clinical outcomes between patients with and without SVT. Multivariable analyses adjusted for potential confounders with the presence of SVT as the dependent variable were used to assess the independent effect of SVT on these clinical outcomes. Covariates were added on the basis of clinical reasoning. Subgroup analyses were also performed to compare the radiological and clinical outcomes of patients with SVT treated with and without therapeutic anticoagulants. Multiple imputation was used for missing data for variables with less than 20% missing values. Results are reported as (adjusted) odds ratios (OR) with 95% confidence intervals (CI). A p-value less than 0.05 was considered statistically significant.

RESULTS

Between 2004 and 2008, 639 patients were enrolled in the prospective cohort of necrotizing pancreatitis. Of this cohort, 432 patients were eligible for this study; 203 patients had incomplete data, 4 patients were lost to follow-up, and 1 patient had pancreatic cancer in the retrospective evaluation. Baseline characteristics are summarized in Table 1. The median age was 58 years (IQR 45-70), and 273 patients (63%) were male. The most common etiologies were biliary (n=205, 47%), alcoholic (n=96,

22%), and idiopathic (n=92, 21%). Nine patients (2%) had a previous history of venous thromboembolism, and 23 patients (5%) were on therapeutic anticoagulants. Pancreatic parenchymal necrosis, with or without extrapancreatic necrosis, was present in of 235 patients (54%), while 197 patients (46%) had extrapancreatic necrosis only.

Diagnosis

Of the 432 patients included, 97 patients (22%) developed SVT. The median time to diagnosis of SVT after admission for acute pancreatitis was 4 days (IQR 2-7; Table 2). SVT was detected on the first CT scan in 76 patients (78%), on the second CT scan in 17 patients (18%), and on the third or subsequent CT scan in 4 patients (4%). At diagnosis, isolated SpIV was the most commonly involved vessel (n=32, 33%), followed by the isolated PV (n=20, 21%) and the isolated SMV (n=15, 16%). Seven patients (7%) had triple vessel thrombosis. Non-occlusive thrombosis was observed in 73 patients (75%) and occlusive thrombosis in 24 patients (25%). Collateral circulation was present in 7 patients (7%), and co-localized venous compression in 6 patients (6%). Figure 1 shows the pattern of pancreatic parenchymal necrosis per affected vessel at the time of diagnosis.

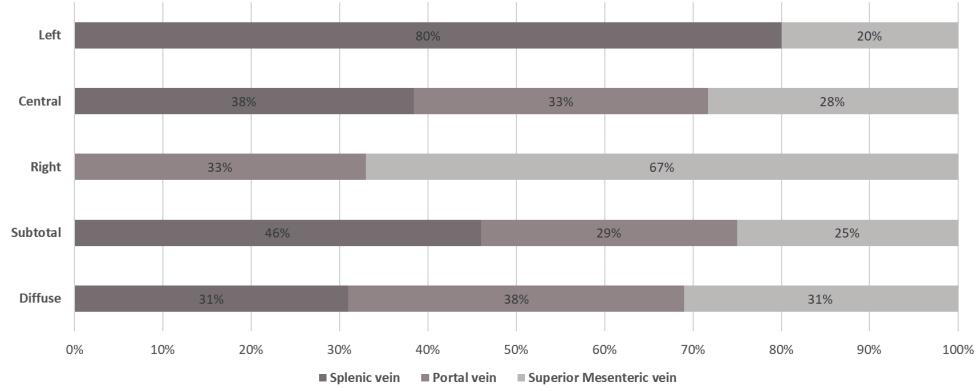

Figure 1. Pattern of pancreatic parenchymal necrosis per affected vessel

Risk factors

Univariable and multivariable analyses of risk factors for the development of SVT are shown in Table 3. Univariable analyses identified younger age, use of therapeutic anticoagulants on admission, a higher CRP level, left, central, or subtotal parenchymal necrosis, and right or diffuse parenchymal necrosis as risk factors. In multivariable analysis, left, central, or subtotal parenchymal necrosis (OR 28.49; 95% CI 20.09-40.40) and right or diffuse parenchymal necrosis (OR 5.75; 95% CI 3.89-8.50) were independently associated with the development of SVT, whereas higher age was a protective factor (OR 0.99 (95% CI 0.98-1.00).

Table 1. Patients and disease characteristics in 432 patients with necrotizing pancreatitis

	Overall (N = 432)	**No SVT (N = 335)**	**SVT (N = 97)**	**P-value**
Age (years)	58 (45-70)	59 (45-71)	56 (45-67)	0.072
Men	273 (63%)	215 (64%)	58 (60%)	0.430
Etiology				
Biliary	205 (47%)	164 (49%)	41 (42%)	0.245
Alcohol	96 (22%)	73 (22%)	23 (24%)	0.689
Idiopathic	92 (21%)	71 (21%)	21 (22%)	0.923
Other	39 (9%)	27 (8%)	12 (12%)	0.192
Medical history				
Cardiovascular (n=431)	165 (38%)	133 (40%)[a]	32 (33%)	0.223
VTE	9 (2%)	8 (2%)	1 (1%)	0.691
Pulmonary (n=430)	42 (10%)	35 (11%)[b]	7 (7%)	0.336
Chronic renal (n=430)	14 (3%)	12 (4%)[a]	2 (2%)[a]	0.745
Diabetes mellitus (n=431)	54 (13%)	47 (14%)	7 (7%)[a]	0.200
AC use at admission (n=425)	23 (5%)	21 (6%)[c]	2 (2%)[b]	0.127
ASA				
1	124 (29%)	90 (27%)	34 (35%)	0.117
2	246 (57%)	197 (59%)	49 (51%)	0.146
3	62 (14%)	48 (14%)	14 (14%)	0.979
4	0	0	0	-
BMI (n=214)	27 (25-31)	27 (25-31)[d]	26 (24-30)[e]	0.310
Smoking (n=123)	42 (34%)	32 (34%)[f]	10 (36%)[g]	0.842
Laboratory values[*]				
Leukocytes (n=395)	19 (15-23)	19 (15-22)[h]	19 (16-23)[i]	0.276
CRP (n=347)	301 (226-389)	293 (220-377)[j]	341 (223-437)[k]	0.012
Imaging severity				
CTSI	6 (4-8)	4 (4-6)	8 (6-10)	<0.001
Parenchymal necrosis	235 (54%)	145 (43%)	90 (93%)	<0.001
Right	9 (4%)	6 (4%)	3 (3%)	0.427
Left	26 (11%)	12 (8%)	14 (16%)	<0.001
Central	97 (41%)	54 (37%)	43 (48%)	<0.001
Subtotal	25 (11%)	7 (5%)	18 (20%)	<0.001
Diffuse	78 (33%)	66 (46%)	12 (13%)	0.098
Extent of necrosis				
<30%	96 (22%)	73 (22%)	23 (24%)	0.689
30-50%	67 (16%)	43 (13%)	24 (25%)	0.004
>50%	72 (17%)	29 (9%)	43 (44%)	<0.001
EXPN only	197 (46%)	190 (57%)	7 (7%)	<0.001

Data are presented as n (%) or median (IQR). Percentages may not total 100 because of rounding. Missing patients: a=1, b=2, c=5, d=171, e=47, f=240, g=69, h=31, i=6, k=11. [*]Highest value in the first 48 hours after admission. Abbreviations: AC anticoagulation, ASA American Society of Anesthesiologists, BMI body mass index, CRP c-reactive protein, CTSI computed tomography severity index, EXPN extrapancreatic necrosis, VTE venous thromboembolism.

Table 2. Radiological characteristics in 97 patients with splanchnic vein thrombosis

At the time of diagnosis	**Total (n=97)**
Time to diagnosis (days)	4 (2-7)
Number of CT scan with diagnosis	
First CT	76 (78%)
Second CT	17 (18%)
≥Third CT	4 (4%)
Anatomical location	
SpIV	32 (33%)
PV	20 (21%)
SMV	15 (16%)
SpIV + PV	11 (11%)
SpIV + SMV	5 (5%)
PV + SMV	7 (7%)
SpIV + PV + SMV	7 (7%)
Extent thrombosis	
Occlusive thrombosis	24 (25%)
Non-occlusive thrombosis	73 (75%)
Collateral circulation	9 (9%)
Co-localized compression	6 (6%)
At last imaging	**Total (n=88)***
Recanalization	50 (57%)
Time to recanalization (weeks)	4 (2-11)
Persistent thrombosis	38 (43%)
Anatomical location	
SpIV	23 (59%)
PV	7 (18%)
SMV	2 (5%)
SpIV + PV	5 (13%)
SpIV + SMV	0
PV + SMV	0
SpIV + PV + SMV	2 (5%)
Extent thrombosis	
Occlusive thrombosis	18 (46%)
Non-occlusive thrombosis	9 (23%)
Thrombotic obliteration	12 (31%)
Collateral circulation	25 (64%)
Radiologic follow-up (months)	10 (3-24)
CT scans per patients	7 (4-10)

*Data are presented as n (%) or median (interquartile range). Percentages may not total 100 because of rounding. *Follow-up imaging was missing in 9 out of 97 patients with splanchnic vein thrombosis. Abbreviations: CT computed tomography, PV portal vein, SMV superior mesenteric vein, SpIV splenic vein, SVT Splanchnic vein thrombosis.*

Table 3. Univariable and multivariable analyses: risk factors for developing splanchnic vein thrombosis (n=97)

	Univariable		Multivariable	
	OR (95% CI)	**P-value**	**OR (95% CI)**	**P-value**
Age	0.99 (0.98-0.99)	<0.001	0.99 (0.98-1.00)	<0.001
Male	0.83 (0.52-1.32)	0.431		
ASA ≥III	1.01 (0.53-1.92)	0.979		
AC use at admission[#]	0.39 (0.23-0.67)	0.001	0.63 (0.35-1.14)	0.124
Alcoholic etiology	1.11 (0.65-1.91)	0.689		
CRP[*,#]	1.00 (1.00-1.00)	<0.001	1.00 (1.00-1.00)	0.946
Leukocytes[¨,#]	1.01 (1.00-1.02)	0.208		
Pattern parenchymal necrosis				
Left, central, or subtotal	27.89 (19.95-38.98)	<0.001	28.49 (20.09-40.40)	<0.001
Right of diffuse	5.66 (3.86-8.29)	<0.001	5.75 (3.89-8.50)	<0.001

[*]Highest CRP in the first 48 hours after admission. [¨]Highest leucocytes in the first 48 hours after admission. [#]Missing data were imputed. Abbreviations: AC anticoagulation, ASA American Society of Anesthesiologists, CRP c-reactive protein, CTSI computed tomography severity index.

Clinical outcomes

Based on the cut-off between the 3rd and 4th quartile of the time to diagnosis of SVT, which is 7 days, we decided to report clinical outcomes that occurred beyond the first week after admission. During this first week, 7 patients (2%) died (n=5 patients without SVT and n=2 patients with SVT) and were therefore excluded from further analysis. The clinical outcomes of the remaining 425 patients are shown in Table 4. Of these, 55 patients (13%) died from pancreatitis-related causes. Persistent or new organ failure occurred in 154 patients (36%) and persistent or new multiple organ failure in 65 patients (15%). A total of 174 patients (41%) were hospitalized in the ICU after the first week. The median total hospital stay was 45 days (IQR 22-97). Bleeding occurred in 24 patients (6%), and bowel ischemia in 6 patients (1%). The median clinical follow-up period was 152 months (IQR 85-167). Univariable analysis showed a significant association between SVT and bleeding, with bleeding occurring more frequently in 10 patients with SVT (11%) compared to 14 patients without SVT (4%; OR 3.24; 95% CI 1.27-8.23; p=0.014) (Table S2). Spontaneous bleeding occurred in 5 patients with SVT versus 7 patients without SVT, and iatrogenic bleeding during or after invasive procedures (e.g., drainage, necrosectomy or other surgery) occurred in 5 patients with SVT versus 7 patients without SVT. The reported symptoms were gastrointestinal bleeding in 3 patients (melena in 1, hematemesis in 1, hematochezia in 1), intra-abdominal bleeding in 16 patients, combined gastrointestinal and intra-abdominal bleeding in 1 patients, clinical manifestations of bleeding in 2 patients, and unknown in 2 patients. None of the bleedings were related to gastroesophageal varices.

Bowel ischemia occurred in 4 patients with SVT (4%) compared to 2 patients without SVT (0.6%; OR 7.29; 95% CI 1.31-40.4; p=0.023). Three of these 4 patients had PV and/or SMV involvement, while the remaining patient developed abdominal compartment syndrome. Further details on bowel ischemia are provided in Table S3. Note that all patients with bowel ischemia in the SVT group died as a result of the ischemia. The limited number of events (n=24 for bleeding, n=6 for bowel ischemia) prevented multivariable analysis. Multivariable analysis adjusting for potential confounders on the clinical course showed no association between the presence of SVT and pancreatitis-related death and (multiple) organ failure (Table 4), but did show an association with a higher rate of ICU admission (OR 2.53; 95% CI 1.37-4.68; p=0.003).

Table 4. Multivariable comparison of clinical outcomes in patients with and without splanchnic vein thrombosis[*]

Outcome	Overall N = 425[^]	No SVT N = 330[a]	SVT N = 95[b]	Adjusted OR (95% CI)[#]	P-value
Pancreatitis-related death	55 (13%)	38 (12%)	17 (18%)	1.44 (0.64-3.26)	0.378
Organ failure	154 (36%)[c]	104 (32%)[c]	50 (53%)	0.88 (0.51-1.50)	0.636
Multiple organ failure	65 (15%)[c]	41 (12%)[c]	24 (25%)	1.17 (0.73-1.77)	0.584
ICU admission	174 (41%)	119 (36%)	57 (60%)	2.53 (1.37-4.68)	0.003
Total admission days	45 (22-97)	43 (22-96)	49 (30-100)	-	0.115

Data are presented as n (%) or median (IQR). [*]Clinical outcomes occurring 7 days after admission. [^]7 patients died in the first week ([a]=5 in no SVT group, [b]=2 in SVT group) and were therefore excluded for this analysis. Missing patients: c=1. [#]The covariates included per outcome are listed in the supplementary appendix (table S4). ~Assessed in univariable analysis. Abbreviations: ICU intensive care unit, SVT splanchnic vein thrombosis.

Therapeutic anticoagulation

Data on therapeutic anticoagulant treatment were available for 88 of the 97 patients with SVT (91%). Of these, 17 patients (19%) received therapeutic anticoagulation during their initial hospitalization, with two patients receiving anticoagulants prior to hospitalization (Table S5). In addition, therapeutic anticoagulation was initiated in six patients for indications other than SVT (n=3 pulmonary embolism, n=2 deep vein thrombosis, n=1 *de novo* atrial fibrillation). The initial anticoagulation regimen included therapeutic doses of low-molecular-weight heparin in 12 patients, a vitamin K antagonist in four patients, and unfractionated heparin in one patient. The duration of treatment varied from 1 to 12 months or more (n=12), to indefinite/end of follow-up (n=3). The duration of treatment was unclear in two patients. No significant differences were found between anatomical location, extent or progression of SVT, presence of collateral circulation, and whether patients were treated with therapeutic anticoagulants (Table S6). There was a trend towards a higher incidence of recanalization in patients who did not receive therapeutic anticoagulation (n=40/71,

62%) compared to those who did (n=6/17, 35%), although this was not statistically significant in univariable analyses (OR 0.34; 95% CI 0.11-1.04; p=0.052; Table S7). The median time to recanalization was similar between the groups (4 weeks (IQR 1-19) versus 3 weeks (IQR 3-9); p=0.728). The incidence of bleeding and bowel ischemia was also similar. Among patients on anticoagulants, 2 experienced bleeding (12%) and none experienced bowel ischemia. Among patients not on anticoagulants, 8 experienced bleeding (12%) and 4 experienced bowel ischemia (6%).

Radiologic follow-up

Follow-up imaging was available for 88 out of 97 patients (91%), with a median follow-up period of 10 months (IQR 3-24) and a median of 7 CT scans (IQR 4-10; Table S8). Recanalization was observed in 49 patients (56%) after a median of 4 weeks (IQR 2-11) (Table 2). In the 39 patients with persistent SVT, SpIV remained the most frequently involved vessel (n=23, 59%). The prevalence of thrombosis decreased by 90% and 66% for the SMV and PV, respectively, while the decrease for the SpIV was 42% (Figure S1). Compared to the first CT scan, more patients with persistent SVT had occlusive thrombosis (n=18, 46%) or vein obliteration (n=12, 31%) with collateral circulation (n=25, 64%) at the last scan. Thrombus progression was observed in 13 patients (14%), and one patient (1%) developed recurrent SVT. In univariable analysis (Table 5), SpIV thrombosis (OR 4.77 ;95% CI 1.83-12.46), occlusive thrombosis at diagnosis (OR 11.50; 95% CI 3.34-38.31), and thrombus progression (OR 22.62; 95% CI 2.78-183.70) were significantly risk factors for recanalization failure, whereas SMV thrombosis (OR 0.31; 95% CI 0.12-0.82) was a protective factor.

Table 5. Univariable analysis: risk factors for failure of recanalization (n=38)

	Univariable	
	OR (95% CI)	**P-value**
Age	1.00 (0.97-1.03)	0.961
Male sex	1.14 (0.48-2.72)	0.763
AC use[#]	2.93 (0.96-8.93)	0.058
SpIV thrombosis	4.77 (1.83-12.46)	<0.001
PV thrombosis	0.88 (0.38-2.05)	0.761
SMV thrombosis	0.31 (0.12-0.82)	0.017
Triple vessel thrombosis	1.84 (0.39-8.78)	0.443
Occlusive thrombosis	11.50 (3.45-38.31)	<0.001
Thrombus progression	22.62 (2.78-183.70)	<0.001
Timing of SVT (days)	0.99 (0.95-1.02)	0.424

[#]Missing data were not imputed. Abbreviations: AC anticoagulation, PV portal vein, SMV superior mesenteric vein, SpIV splenic vein.

DISCUSSION

This study represents one of the largest multicenter prospective cohorts of patients with necrotizing pancreatitis with long-term follow-up and showed an overall incidence of splanchnic vein thrombosis (SVT) of 22%. Pancreatic parenchymal necrosis, with a higher risk for left, central, or subtotal necrosis than for right or diffuse necrosis, and younger age were identified as independent risk factors for SVT. SVT is associated with higher rates of bleeding and bowel ischemia, and has an impact on ICU admission. Spontaneous recanalization was observed in more than 60% of patients. Therapeutic anticoagulation was infrequently administered and did not appear to affect radiological and clinical outcomes.

To our knowledge, the only other high-volume study reported a 50% incidence of SVT in patients with necrotizing pancreatitis (20). This higher rate may be due to a different definition combining intraluminal filling defect, presence of collaterals, and non-visualization of the vein. Furthermore, this cohort from a single tertiary center probably included more severely ill patients, leading to a possible overestimation. The median time to diagnosis found in our study was as early as 4 days, which could be even earlier depending on the timing of the first CT scan. This timing differed from previous reports, which reported a median of up to 17 days or several weeks (8, 21-23). The design of these studies may have resulted in delayed diagnosis due to the lack of early imaging studies performed at the referring hospitals. This is supported by the presence of collaterals at the time of diagnosis in more than one third of patients (23), compared to 7% in our study.

Factors contributing to the development of venous thrombosis are described in the Virchow's triad: stasis, endothelial injury, and hypercoagulability (24). Previous studies in necrotizing pancreatitis have suggested that stasis due to mechanical compression, as indicated by co-localized collections, is an important mechanism (9, 11). However, in our study, co-localized compression was often not seen at the time of diagnosis. This is consistent with a previous study showing that the organization of fluid collections typically takes several weeks (25). As secondary infection of (peri)pancreatic necrosis is also a relatively late manifestation of necrotizing pancreatitis (25, 26), we did not include both variables in the multivariable regression model. Nevertheless, we found that pancreatic parenchymal necrosis, as opposed to extrapancreatic necrosis, was the most significant independent risk factor for the development of SVT, with an OR of 28.49 for left, central, or subtotal necrosis and an OR of 5.75 for right or diffuse necrosis. Systemic inflammation markers such as CRP and leukocytes were not identified as risk factors. This suggests that local inflammatory infiltration, subsequently leading to direct endothelial injury, may play a primary role in the pathophysiology,

rather than systemic inflammation. This hypothesis is supported by the predominant involvement of the splenic vein that we and others have observed (8-10, 16, 22, 23, 27). The course of the SpIV along the pancreatic tail and body may explain why left-sided and centrally located parenchymal necrosis was found to be an independent risk factor. In addition, a previous study reported an almost threefold and eightfold higher incidence of SVT in patients with necrotizing pancreatitis, as compared to deep venous thromboembolism and pulmonary embolism (20). However, an unexpected finding was the significant association between SVT and a younger age. This may have been influenced by differences between the younger and older populations, such as BMI, nicotine use and etiology, whereas (time to) mortality did not show any differences (data not shown).

Previous research has suggested that timely drainage of (infected) necrotic collections may prevent the development of SVT (9, 11, 16), although this has not been extensively studied. Based on our observations that SVT is a very early complication and that no modifiable risk factors have been identified, we would not recommend a proactive drainage strategy to prevent of SVT. Another argument supporting this notion is that collections at this early stage are often not yet ''drainable". The question is whether drainage could improve the prognosis of SVT by reducing the exposure of the splanchnic vein to local inflammation. Our study shows that spontaneous recanalization occurs in over 60% of patients within a median of 3 weeks, probably with prophylactic dose anticoagulation.

A rational treatment for SVT when extrapolating from other venous thromboses is the administration of therapeutic anticoagulants. However, the current evidence-based guideline for the management of acute pancreatitis (28) withholds on recommendations due to a lack of high-quality studies (29-32). Therapeutic anticoagulants aim to prevent thrombus progression and recurrence to avoid complications such as portal hypertension and bowel ischemia, but carry an inherent risk of bleeding (33-36). While a recent survey by our group showed that the majority of pancreatologists prescribe therapeutic anticoagulants for SVT (37), our cohort had a low treatment rate (19%), which may be related to the fact that we included only patients with necrotizing pancreatitis. We found similar, albeit significant, rates of bleeding and bowel ischemia in patients treated with and without therapeutic anticoagulants. In order to avoid unnecessary treatment, it seems essential to identify those patients who are at higher risk of insufficient recanalization and thus more susceptible to potential complications. A previous study found that a higher CTSI, increased abdominal pressure, and SMV involvement were significant risk factors for the development of symptomatic SVT (38). In this study, thrombus progression, occlusive thrombosis, and SpIV thrombosis were found to be significant risk factors for insufficient recanalization in univariable

analysis. Although limited by the small number of patients with failed recanalization (n=38), this supports the idea of a targeted symptom-driven anticoagulation strategy rather than a universal approach (39).

A recent study proposed a selective regimen for patients with acute pancreatitis, reserving therapeutic anticoagulation for those with PV and SMV thrombosis, and progressive SpIV thrombosis (40). This study found a significantly higher recanalization rate in the former group (67%) compared to the latter group (18%), which is consistent with our findings. Of note, the number of patients with progressive SpIV thrombosis in this study was limited (n=11). Nevertheless, the reported recanalization rate in 63 patients with PV or SMV thrombosis after a median of 30 days was substantially higher than previously reported for the total population (29). These findings highlight the importance of further investigation of a targeted anticoagulation strategy, ideally in a prospective study with a control group not receiving anticoagulants. Based on our findings, we recommend that the site and extent of thrombosis be considered in future anticoagulation strategies.

When deciding on anticoagulant therapy, it is important to consider the patient's overall prognosis. Several studies have reported an association between acute pancreatitis patients diagnosed with SVT and worse clinical outcomes, including mortality (14, 15, 17), organ failure (8, 16), ICU admission (8, 17), admission days (8, 14, 15), discharge location (15), and readmissions (15). However, these studies did not adequately adjust for potential confounders, such as disease severity, or differentiate between baseline characteristics and actual outcomes. In our study, we performed multivariable analyses specifically focusing on the independent effect of SVT on mortality, organ failure, and ICU admission occurring after SVT diagnosis. We observed an independent association with new or continued ICU admission beyond one week after admission. We also observed higher rates of bleeding and bowel ischemia in patients with SVT compared with those without. However, due to the limited number of events, we were unable to adjust for covariates related to disease severity and therapeutic anticoagulation, and caution should be exercised in interpreting these results. We hypothesize that bleeding in the SVT group may be due to a more severe disease course (e.g., bleeding from pseudoaneurysm or iatrogenic bleeding resulting from more frequently performed interventions) rather than being directly caused by SVT itself. Notably, none of the bleeding events were associated with portal hypertension, even in the long term, and there were no differences in bleeding rates based on the use of therapeutic anticoagulation. Careful attention to collaterals, especially in the retroperitoneum or along the gastric wall, seems to be important in pre- and perioperative management. Bowel ischemia proved to be a major complication, leading

to death in all but one patient. Of the patients with SVT, 75% had portal or superior mesenteric vein involvement.

This study has several limitations. First, a substantial proportion of patients were excluded from the study because of incomplete follow-up data. This was mostly due to the transition from paper-based to electronic medical records. Second, there were missing data on some baseline characteristics, such as BMI and smoking, and on outcomes. Data on the in-hospital prescription of therapeutic anticoagulants were collected post hoc and only for patients with SVT. Third, the small number of patients receiving therapeutic anticoagulation limited a thorough assessment of its efficacy and safety. Moreover, it is likely that confounding by indication may have occurred because our study did not have a randomized design. Therefore, the data on anticoagulation are not robust enough to make recommendations. Fourth, we mainly analyzed SVT as one and the same entity (regardless of size, extent, and location). This may have influenced clinical outcomes and the effect of anticoagulation. The exclusion of luminal narrowing without a filling defect as a diagnostic criterion for splanchnic vein thrombosis may also have influenced clinical outcomes. Another factor influencing clinical outcomes is that our cohort consists of patients from the era of open surgical necrosectomy (2004-2008). After the publication of the PANTER trial in 2010 (41), which demonstrated the superiority of the minimally invasive step-up approach, the latter has become the standard of care. However, in the absence of (pharmacological) strategies to reduce disease severity, we believe that our data on the incidence, risk factors, and natural course of SVT are generalizable to the current necrotizing pancreatitis population. In fact, this relatively old cohort offers a complete radiologic evaluation of necrotizing pancreatitis (e.g., all CTs, including CTs performed at referring centers, were obtained and re-evaluated from each patient, even during long-term follow-up).

CONCLUSION

SVT occurs within the first 4 days of diagnosis, affecting nearly one in four patients with necrotizing pancreatitis, and resolves spontaneously in more than half of the patients. Independent risk factors for SVT include pancreatic parenchymal necrosis, with left, central, or subtotal necrosis being the most at-risk pattern, and younger age. SVT is associated with higher complication rates and shows an independent association with ICU admission. To optimize treatment strategies, future research should focus on identifying patients with SVT who remain free of complications and achieve recanalization without the use of therapeutic anticoagulation, and vice versa.

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Supplementary table S1. Definitions

Baseline	
Acute pancreatitis	When two of the following criteria were met: upper abdominal pain, serum lipase concentration (or amylase) ≥ 3 times higher than the upper limit of normal or features of acute pancreatitis on imaging
Pancreatic parenchymal necrosis	Diffuse or focal area(s) of non-enhancing pancreatic parenchyma as detected on contrast enhanced CT (CECT)
Right-sided necrosis	Lack of enhancement primarily in the pancreatic head
Left-sided necrosis	Lack of enhancement primarily in the pancreatic tail
Central gland necrosis	Lack of enhancement primarily in the pancreatic neck and/or body
Subtotal necrosis	Lack of enhancement in pancreatic neck, body and greater part of pancreatic head and tail
Diffuse necrosis	Lack of enhancement in uni- or multifocal area(s) throughout the pancreas
Extrapancreatic necrosis	Persistent peripancreatic fluid collections on contrast enhanced computed tomography (CECT) in the absence of pancreatic parenchymal non-enhancement
Splanchnic vein thrombosis	Intraluminal filling defect of the splenic, portal and/or superior mesenteric vein on CECT
Collateral circulation	One of the following: a) varices or b) collaterals or c) cavernoma
Obliteration	Non-visualization of an initially thrombosed splanchnic vein(s), with previous CECTs showing a persistent thrombosis
Progression	Progression into other splanchnic vein(s), into total occlusion, or both
Recanalization	Absence of thrombosis in an initially thrombosed splanchnic vein(s), except for an obliterated vein as a result of a persistent thrombosis
Clinical outcomes	
Bleeding	Bleeding requiring surgical, radiologic or endoscopic intervention
Bowel ischemia	Bowel ischemia requiring a surgical intervention
Organ failure	No organ failure is assumed in the absence of lab and/or information in the discharge letter and/or notes. Definitions are adapted from the Atlanta classification and the same as previously used in the PANTER trial
Cardiovascular	Systolic blood pressure < 90 mmHg despite adequate fluid resuscitation or need for vasopressor support
Pulmonary	PaO2 < 60 mmHg despite FiO2 30%, or the need for mechanical ventilation
Renal	Serum creatinine > 177 mmol/L after rehydration or need for hemofiltration or haemodialysis
Multiple organ failure	Failure of 2 or more organ systems on the same day

Supplementary table S2. Univariate comparison of clinical outcomes in patients with and without splanchnic vein thrombosis[*]

Outcome	Overall N = 425[^]	No SVT N = 330[a]	SVT N = 95[b]	OR (95% CI)	P-value
Pancreatitis related death	55 (13%)	38 (12%)	17 (18%)	1.68 (0.90-3.13)	0.103
Organ failure	154 (36%)[c]	104 (32%)[c]	50 (53%)	2.38 (1.50-3.79)	<0.001
Multiple organ failure	65 (15%)[c]	41 (12%)[c]	24 (25%)	2.35 (1.35-4.19)	0.003
Bleeding	24 (6%)[c]	14 (4%)	10 (11%)[c]	3.24 (1.27-8.23)	0.014
Bowel ischemia	6 (1%)[c]	2 (0.6%)	4 (4%)[c]	7.29 (1.31-40.4)	0.023
ICU admission	174 (41%)	119 (36%)	57 (60%)	2.71 (1.69-4.32)	<0.001
Total admission days	45 (22-97)	43 (22-96)	49 (30-100)	-	0.115

Data are presented as n (%) or median (IQR). [*]Clinical outcomes occurring 7 days after admission. [^]7 patients died in the first week ([a]=5 in no SVT group, [b]=2 in SVT group) and were therefore excluded for this analysis. Missing patients: c=1. Abbreviations: ICU intensive care unit, SVT splanchnic vein thrombosis.

Supplementary table S3. Bowel ischemia per individual patient

	Time diagnosis (days)[a]	SVT Location	SVT extent	Time most recent CT scan (days)[b]	Surgical operation	Mortality
Patient with splanchnic vein thrombosis						
1	16	Splenic vein	Occlusive	1	Non-operable. Autopsy: colon ischemia	Yes
2	41	Splenic vein Portal vein	Occlusive Non-occlusive	2	Non-operable. Autopsy: small bowel ischemia with pneumatosis	Yes
3	10	Sup. mesenteric vein	Non-occlusive	1	Ischemic colon requiring subtotal colectomy with end ileostomy	Yes
4	3	Sup. mesenteric vein	Non-occlusive	3	Small bowel ischemia requiring ileum resection with end ileostomy	Yes
Patients without splanchnic vein thrombosis						
1	N/A	N/A	N/A	N/A	Ischemic colon requiring transverse colectomy	No
2	N/A	N/A	N/A	N/A	Ischemic cecum requiring cecum resection with end ileostomy	Yes

[a]Time between diagnosis of splanchnic vein thrombosis and occurrence of bowel ischemia. [b]Time between occurrence of bowel ischemia and most recent CT scan. Abbreviations: CT Computed tomography, SVT Splanchnic vein thrombosis.

Supplementary table S4. Confounders per variable in the multivariate logistic regression model of clinical outcomes

Pancreatitis-related death *After 7 days*	Presence of splanchnic vein thrombosis, age, male sex, ASA classification ≥3, presence of pancreatic parenchymal necrosis >50%, occurrence of infected necrosis before 7 days, occurrence of organ failure before 7 days, occurrence of abdominal compartment syndrome before 7 days
(Multiple) organ failure *Either new-onset (multiple) organ failure after 7 days or ongoing (multiple) organ failure*	Presence of splanchnic vein thrombosis, age, male sex, ASA classification ≥3, presence of pancreatic parenchymal necrosis >50%, occurrence of infected necrosis before 7 days, occurrence of abdominal compartment syndrome before 7 days
ICU-admission *Either new ICU-admission after 7 days or ongoing ICU-admission*	Presence of splanchnic vein thrombosis, age, male sex, ASA classification ≥3, presence of pancreatic parenchymal necrosis >50%, occurrence of infected necrosis before 7 days, occurrence of organ failure before 7 days, occurrence of abdominal compartment syndrome before 7 days

Abbreviations: ASA American Society of Anaesthesiologists, ICU intensive care unit.

Supplementary table S5. Details on treatment with therapeutic anticoagulation

Patient	Indication	Agent	Duration
1	splanchnic vein thrombosis	LMWH à VKA	≥12 months
2	splanchnic vein thrombosis	LMWH	~1 month (until death)
3	splanchnic vein thrombosis	LMWH	unknown
4	de novo atrial fibrillation	LMWH à VKA	indefinite
5	splanchnic vein thrombosis	heparin	~2 months
6	splanchnic vein thrombosis	LMWH à VKA	~4 months
7	pulmonary embolism	LMWH à VKA	~5 months
8	pulmonary embolism	LWMH	unknown
9	splanchnic vein thrombosis	LMWH à VKA	~6 months
10	splanchnic vein thrombosis	VKA	~6 months
11	prior outpatient use (atrial fibrillation)	VKA	indefinite
12	deep vein thrombosis	LMWH à VKA	≥5 months
13	prior outpatient use (atrial fibrillation)	VKA	indefinite
14	splanchnic vein thrombosis	VKA	~3 months
15	pulmonary embolism	LWMH à VKA	~5 months
16	splanchnic vein thrombosis	LMWH	~1 month (until death)
17	deep vein thrombosis	LMWH à heparin	~1 month (until death)

≥*Greater than or equal to. ~More or less. Abbreviations: LMWH low molecular weight heparin, VKA vitamin K antagonist.*

Supplementary table S6. Characteristics of splanchnic vein thrombosis in 88 patients treated with or without therapeutic anticoagulation*

6a. Anatomical location

	SpIV (n=30)	**PV (n=15)**	**SMV (n=13)**	**SpIV+PV (n=11)**	**SpIV+SMV (n=5)**	**PV+SMV (n=7)**	**SpIV+PV+SMV (n=7)**
AC (n=17)	6 (20%)	3 (20%)	3 (23%)	1 (9%)	1 (20%)	1 (14%)	2 (29%)
No AC (n=71)	24 (80%)	12 (80%)	10 (77%)	10 (91%)	4 (80%)	6 (86%)	5 (71%)
P-value	0.907	0.941	0.710	0.684	1.000	1.000	0.616

6b. Extent thrombosis and collateral circulation at diagnosis, and thrombus progression over time

	Occlusive thrombosis (n=25)	**Non-occlusive thrombosis (n=63)**	**Collateral circulation (n=7)**	**Thrombus progression (n=12)**
AC (n=17)	7 (28%)	10 (16%)	1 (14%)	5 (42%)
No AC (n=71)	18 (72%)	53 (84%)	6 (86%)	7 (58%)
P-value	0.235	0.235	1.000	0.115

*Data are presented as n (%). *Anticoagulation status was missing in 9 out of 97 patients with splanchnic vein thrombosis. Abbreviations: AC anticoagulation, PV portal vein, SMV superior mesenteric vein, SpIV splenic vein.*

Supplementary table S7. Outcomes in 88 patients with splanchnic vein thrombosis treated with or without anticoagulation[*]

Outcome	AC (n=17)	No AC (n=71)	OR (95% CI)	P-value
Recanalization	6 (35%)	40 (62%)[a]	0.34 (011-1.04)	0.052
Time to recanalization (weeks)	4 (1-19)	3 (3-9)[a]	-	0.728
Bleeding	2 (12%)	8 (12%)[b,c]	1.00 (0.19-5.21)	1.000
Bowel ischemia	0	4 (6%)[b, c]	-	0.579

Data are presented as n (%) or median (IQR). [*]Anticoagulation status was missing in 9 out of 97 patients with splanchnic vein thrombosis. [a]Follow-up imaging was missing in 6 patients. [b]2 patients died in the first week and were therefore excluded for this analysis. [c]1 patient had missing data. Abbreviations: AC anticoagulation.

Supplementary table S8. Natural* course of splanchnic vein thrombosis in 97 patients

Pt	CT 1ˇ	CT 2	CT 3	CT 4	CT 5	CT 6	CT 7	CT 8
1^	total SpIV partial SMV	total SpIV partial SMV	total SpIV	total SpIV	total SpIV			
2	partial PV	partial PV	-	-	-			
3	partial SpIV partial PV partial SMV	partial SpIV partial PV	-	-	-	-	-	
4	partial SpIV partial PV	partial SpIV partial PV	partial SpIV	total SpIV#	total SpIV	total SpIV	total SpIV	total SpIV
15	total SpIV	total SpIV	total SpIV	total SpIV	total SpIV#			
25	partial PV	-	-	-	-	-	-	
32	partial SMV	partial SMV	-	-				
39	partial PV	-	-					
57^	total SpIV	total SpIV partial PV	total SpIV partial PV	total SpIV	total SpIV			
58	partial SpIV	total SpIV	total SpIV	total SpIV#	total SpIV	total SpIV		
66	partial SpIV	partial SpIV	total SpIV	total SpIV#	total SpIV			
69^	partial PV	partial PV	total SpIV total PV	total SpIV total PV	total SpIV total PV	total SpIV total PV	total SpIV total PV	total SpIV total PV
74	partial SMV	partial SMV	partial SMV	partial SMV	-	-		
87	total SpIV partial PV	total SpIV partial PV	total SpIV partial PV					
92	partial SpIV	partial SpIV	partial SpIV	-	-	-	-	
96^	partial SpIV	-	-	-	-			
97	partial PV	partial PV	partial PV	-	-	-	-	
98	partial PV	partial PV	partial PV	partial PV	partial PV	partial PV	partial PV	partial PV
100	partial SpIV partial PV	partial PV	total SpIV partial PV	total SpIV# partial PV	total SpIV	total SpIV	total SpIV	total SpIV
105	total SpIV	total SpIV	total SpIV					
118	total SpIV	total SpIV	total SpIV	total SpIV	total SpIV	total SpIV		
123	partial SpIV	partial SpIV	-	-	-			
125	partial SpIV partial SMV	partial SpIV partial SMV	partial SpIV partial SMV	partial SMV	-	-	-	-
131	total SpIV partial SMV	total SpIV partial SMV	-	-	-	-	-	-
144^	partial PV partial SMV	partial PV partial SMV	-	-	-	-	-	-
149^	partial SpIV	partial SpIV	total SpIV partial PV	total SpIV partial PV	-	-		

CT 9	CT 10	CT 11	CT 12	CT 13	CT 14	CT 15	CT 16	CT 17
total SpIV	total SpIV	total SpIV	total SpIV					
total SpIV total PV								
partial PV total SpIV	partial PV total SpIV	partial PV total SpIV	partial PV total SpIV	total SpIV	total SpIV			
-	-							
-	-	-						
-	-	-	-	-	-	-		

Supplementary table S8. Natural* course of splanchnic vein thrombosis in 97 patients (*continued*)

150	total SpIV	total SpIV partial PV	total SpIV partial PV	total SpIV# partial PV	total SpIV totial PV	total SpIV totial PV	total SpIV totial PV	total SpIV totial PV
154	partial SpIV partial PV	partial PV						
156	total SpIV	total SpIV	total SpIV					
185	partial PV	partial PV	partial PV	partial PV	partial PV			
198	partial PV	-						
199^	total SpIV partial PV partial SMV	total SpIV partial PV partial SMV	total SpIV partial PV partial SMV	total SpIV	total SpIV#	total SpIV	total SpIV	total SpIV
201^	partial SMV	-	-	-				
221	total SpIV partial PV partial SMV	total SpIV partial PV partial SMV	total SpIV partial PV partial SMV	total SpIV partial PV partial SMV	total SpIV partial PV partial SMV	total SpIV partial PV partial SMV	total SpIV partial PV partial SMV	
228	partial SpIV	partial SpIV	total SpIV	total SpIV	total SpIV	total SpIV#	total SpIV	total SpIV
261	partial PV partial SMV	partial PV partial SMV	-	-				
262	partial SpIV partial PV	-	-	-				
269	partial PV	-						
277	partial SMV	partial SMV	-	-	-	-	-	-
285^	partial PV	partial PV	partial PV	partial PV	total PV	total PV	total PV	
289	partial PV							
296	partial PV	partial PV	partial PV	partial PV	partial PV	partial PV	partial PV	partial PV
303^	partial PV	partial PV	partial PV	partial PV	partial PV	partial PV	partial PV	partial PV
305	partial PV	partial PV	partial PV	partial PV	partial PV	partial PV	-	-
317	partial PV partial SMV	partial PV	-	-	-	-	-	-
331	partial SpIV partial PV partial SMV	partial SpIV partial PV partial SMV	-	-	-	-	-	partial PV
335	total SpIV partial PV	total SpIV partial PV						
340	partial PV							
342	total SpIV	total SpIV	total SpIV	total SpIV	total SpIV	total SpIV	total SpIV#	
344	partial PV partial SMV	partial PV partial SMV	partial PV	partial PV	-	-	-	-
346	partial SMV	partial SMV	partial SMV	partial SMV	partial SMV	partial SMV		
354	partial SpIV	partial SpIV	-	-	-	-	-	-
355	partial SMV	partial SMV	-	-	-	-	-	-

total SpIV totial PV	total SpIV totial PV	total SpIV totial PV	total SpIV totial PV
total SpIV	total SpIV	total SpIV	
-	-	-	
partial PV partial PV	partial PV	-	-
-	-	-	-
-	-		
-			
-	-	-	-
-	-	-	-

Supplementary table S8. Natural* course of splanchnic vein thrombosis in 97 patients (*continued*)

359	partial SpIV	-	-	-				
374^	total SpIV	total SpIV	total SpIV	total SpIV	total SpIV	total SpIV	total SpIV	total SpIV
376	total SpIV	-	-	-	-	-		
380	partial SMV	partial SMV	-	-	-			
384	partial PV	partial PV	-	-	-	-	-	-
385^	total SpIV partial PV partial SMV	total SpIV partial PV partial SMV	total SpIV partial PV partial SMV	total SpIV partial PV partial SMV	total SpIV partial PV partial SMV	total SpIV partial PV	total SpIV partial PV	total SpIV partial PV
394	total SpIV	total SpIV#	total SpIV	total SpIV	total SpIV			
395	partial SpIV partial SMV	partial SpIV partial SMV	partial SpIV partial SMV	-	-	-	-	-
420	partial SMV	-	-	-	-	-	-	-
434^	total SpIV	total SpIV	total SpIV	total SpIV				
448	partial SpIV	partial SpIV	partial SpIV	-	-	-	-	-
449	partial PV							
450	partial SpIV partial PV partial SMV	partial SpIV partial PV	partial PV	partial PV	partial PV	partial PV	partial PV	partial PV
457	partial SpIV	-	-	-	-			
459	partial PV partial SMV	partial PV partial SMV	partial PV partial SMV	partial PV partial SMV	partial PV partial SMV	partial SMV	partial SMV	-
467	partial SpIV partial SMV	-	-	-	-	-	-	-
473	partial SpIV partial PV	partial SpIV partial PV	-	-	-	-	-	-
478^	partial SMV	partial PV partial SMV	partial PV partial SMV	partial PV partial SMV	partial PV partial SMV	partial PV	partial PV#	
485	partial PV	partial PV	partial PV	-	-			
488	partial SpIV partial PV	partial SpIV partial PV	-	-				
490	partial SMV	-	-	-	-	-	-	
496	partial SpIV							
506	partial PV partial SMV	partial PV partial SMV	partial PV partial SMV	partial PV partial SMV	partial PV partial SMV	partial PV	partial PV	partial PV
509	total SpIV total PV	total SpIV total PV	total SpIV total PV					
512	partial SpIV							
514^	partial SpIV	-	-	-	-	-	-	-

total SpIV

-

- - -

-

- -

partial PV partial PV partial PV partial PV partial PV partial PV partial PV partial PV

- - - - - - - - -

- -

- -

partial PV partial PV partial PV - - -

Supplementary table S8. Natural* course of splanchnic vein thrombosis in 97 patients (*continued*)

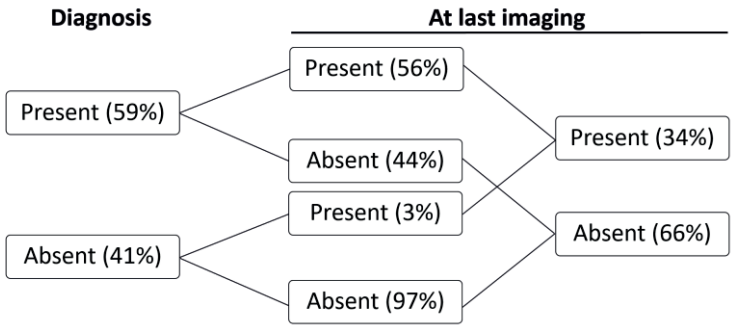
521	partial SMV	-	-	-	-	-	-	-
529	partial SpIV	-	-	-	-	-	-	
532	partial SpIV partial PV partial SMV	partial SpIV partial PV partial SMV						
535	partial PV	partial PV	-	-	-	-	-	-
538	partial PV	partial PV	partial PV	-	-	-	-	
539	total SpIV							
574	partial SpIV	partial SpIV						
583	partial SMV							
584	partial SpIV	total SpIV	total SpIV#	total SpIV	total SpIV	total SpIV	total SpIV	
592	total PV total SMV							
599	partial SMV	-						
600	partial SpIV	partial SpIV	partial SpIV	partial SpIV	partial SpIV	partial SpIV	partial SpIV	partial SpIV
603	partial SpIV	partial SpIV	-	-				
619	total SpIV partial PV	total SpIV	total SpIV	total SpIV	total SpIV	total SpIV	total SpIV	total SpIV
620^	partial SMV	partial SMV	partial SMV	partial SMV	partial SMV			
625	partial SMV							
627^	total SpIV partial PV	total SpIV partial PV	total SpIV partial PV	total SpIV	total SpIV			
638	total SpIV	total SpIV	total SpIV	total SpIV	total SpIV	total SpIV		

**17 out of 88 patients with a known anticoagulation status used anticoagulants. ˜CT 1= the first contrast-enhanced computed tomography that confirmed splanchnic vein thrombosis. #Obliterative vein from this CT onward. ^Patients on anticoagulation. Abbreviations: partial non-occlusive thrombosis, PV portal vein, SMV superior mesenteric vein, SpIV splenic vein, SVT Splanchnic vein thrombosis, total occlusive thrombosis.*

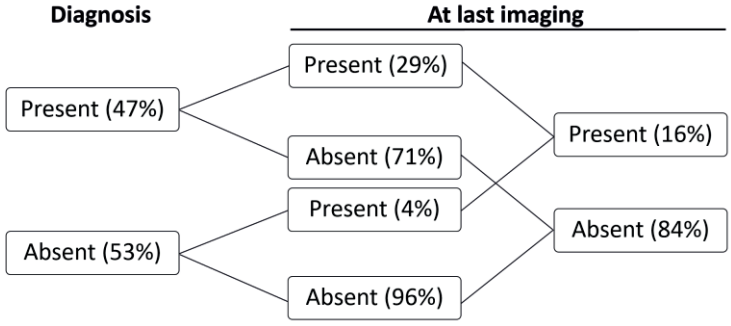
- - - -

total SpIV total SpIV total SpIV total SpIV total SpIV#

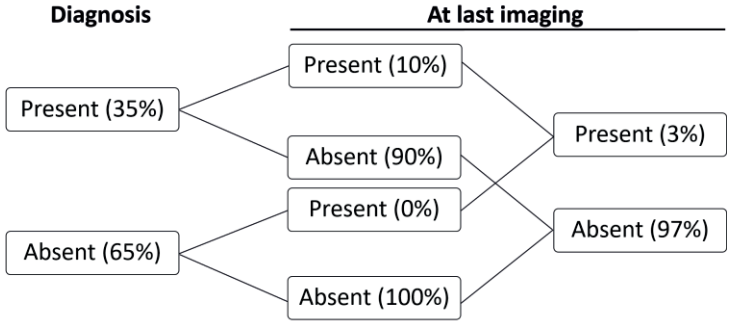
a) Splenic vein



b) Portal vein



c) Superior mesenteric vein



Supplementary figure S1. Outcome of obstruction per affected vessel compared to the initial diagnosis
Undertext: The decrease in prevalence of splanchnic vein thrombosis corresponds to the difference in obstructed venous segments between diagnosis and last imaging.