META ANALYSIS AND SYSTEMATIC REVIEW

Incidence and treatment of splanchnic vein thrombosis in patients with acute pancreatitis: A systematic review and meta-analysis

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Abstract

Background and Aim: This meta-analysis aimed to estimate the incidence of splanchnic vein thrombosis (SVT) in patients with acute pancreatitis and assess the effects of therapeutic anticoagulation.

Methods: Systematic searches of the Medline, Embase, and Cochrane databases were undertaken to identify studies reporting the incidence and outcomes associated with SVT in patients with acute pancreatitis. The pooled incidence, odds ratios (ORs) and 95% confidence intervals (CIs) were calculated using a random effects model. PROSPERO database registration no. CRD 42021230912.

Results: Only 18 of the 238 studies identified met the inclusion criteria. Of the 943 patients who had SVT, 264 (28.0%) received anticoagulation. The pooled incidence of SVT at first presentation of acute pancreatitis was 15% (95% CI 5 to 26%), but was 17% (95% CI 14 to 20%) in all studies. Recanalization was more likely to occur in the anticoagulation-treated than in the untreated group (OR 0.51, 95% CI 0.31 to 0.83, P = 0.007). There were no differences in hemorrhagic complications (OR 2.27, 95% CI 0.81 to 6.37, P = 0.12) or overall mortality (OR 2.37, 95% CI 0.86 to 6.52, P = 0.10) in relation to the use of anticoagulation. The overall incidence of portal hypertension in patients was 60% (95% CI 55 to 65%). However, it was not possible to determine the incidence in each group.

Conclusions: The incidence of SVT in patients with acute pancreatitis is significant. Treatment with anticoagulants improved the odds of recanalization but did not increase the risk of hemorrhagic complications or overall mortality.

Introduction

Vascular complications associated with acute pancreatitis are common and are a major cause of morbidity and mortality. Splanchnic vein thrombosis (SVT) is a recognized venous complication of acute pancreatitis resulting from a combination of both local and systemic prothrombotic factors that are not completely understood. The term SVT encompasses the three sites of portomesenteric thrombosis: splenic vein thrombosis (SpVT), portal vein thrombosis (PVT), and superior mesenteric vein thrombosis (SMVT), with SpVT being the commonest in patients with acute pancreatitis.1,2,3

More severe presentations of acute pancreatitis, necrotizing acute pancreatitis and recurrent presentations have been shown to have a higher occurrence of SVT.1,4,5 However, other studies have suggested that SVT may occur on index presentations and in more moderate cases of acute pancreatitis.4-6 SVT is often asymptomatic and identified incidentally on imaging, although in some instances it can present with symptoms associated with life-threatening ischemia.7-9 If left untreated, SVT can lead to complications such as portal hypertension, mesenteric ischemia and infarction.10 The use of unfractionated heparin or low molecular weight heparin followed by transition to an oral vitamin K antagonist is the most common approach to attempt to recanalize the vein and avoid further complications following SVT. There is, however, a paucity of studies assessing the efficacy and risks of anticoagulation.11,12 It is possible that the sooner anticoagulation is initiated, the more likely is successful recanalization to occur.7,11 However, the decision to treat SVT actively must be balanced with the risk of bleeding secondary to other vascular complications associated with acute pancreatitis, such as a bleed into a pseudocyst, erosion of branches of the coeliac axis and superior mesenteric artery, and development of pseudoaneurysms.13,14
Due to the heterogenous presentation of SVT, it is likely to be underdiagnosed and, therefore, the exact incidence in the setting of acute pancreatitis is not known. Moreover, there is also a paucity of high-quality evidence evaluating use of anticoagulation regimens and the overall outcomes of patients who develop SVT associated with acute pancreatitis. The aim of this systematic review and meta-analysis was to determine the incidence and outcomes of SVT in patients with acute pancreatitis managed with and without anticoagulation.

Methods

The systematic review was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement. The protocol was registered with the PROSPERO database (https://www.crd.york.ac.uk/prospero/Registration No. CRD 42021230912).

Literature search. A comprehensive and systematic search of the Medline, EMBASE, Cochrane Library and Clinicaltrials.org databases from January 1947 to February 2021 was performed to identify studies reporting the incidence and outcomes of SVT in acute pancreatitis.

The search terms included: [“acute pancreatitis”] AND [“portal vein thrombosis”] or [“venous thromboembolism”] or [“venous thrombosis”] or [“VTE”] or [“liver vein thrombosis”] AND [“anticoagulation”] or [“thromboembolism treatment”] or [“heparin”] or [“anticoagulant agent”] or [“enoxaparin”] or [“treatment dose enoxaparin”] or [“low molecular weight heparin”] mapped to corresponding Medline Subject Headings (MeSH). Hand searches of thesis repositories, relevant conference abstracts and bibliographies of relevant studies were undertaken to ensure comprehensive study inclusion. Previously conducted systematic reviews on this subject were also identified during this process. No language or geographical limitations were applied.

Article selection. The titles and abstracts of studies identified from the searches were screened for suitability, against the inclusion criteria independently by two study authors (F. S. A, A. A.). The remaining full-text articles were screened in detail independently and all discordance adjudicated by a third reviewer (S. S.).

Inclusion and exclusion criteria. Studies were included if they were performed on adult human subjects with a primary diagnosis of acute pancreatitis and reported on SVT in all or some of their cohort. They also had to report at least one relevant clinical outcome. Abstracts were only included if they were not published as full papers.

Studies in children, or those in adults but not reporting SVT, or any relevant clinical outcome were excluded. Animal studies were not considered, as were case reports, correspondence, comments and editorials.

Outcomes. The primary outcome was the incidence of SVT in patients with acute pancreatitis overall and then incidence of SVT at first presentation of acute pancreatitis separately.

Secondary outcomes included recanalization in anticoagulation-treated versus untreated patients, hemorrhagic complications, incidence of portal hypertension and mortality.

Data extraction. Studies identified from the database search were screened based on titles and abstracts and independently assessed by two reviewers. Three reviewers then independently assessed the full text of the retrieved studies to ensure they met the inclusion criteria, with any dissenting opinions resolved by a consensus decision. A standardized data collection form was used to collate information on incidence and outcomes from the included articles. Data on individual study characteristics included: first author, publication year, country, number of patients with acute pancreatitis, number of patients who developed SVT, number treated with anticoagulation, type, dose and route of anticoagulant therapy, and underlying etiology of acute pancreatitis. Demographic characteristics, such as age and sex in each study were extracted if reported.

Statistical analysis. Meta-analyses of pooled data were performed using Review Manager (RevMan) version 5.3. Statistical analysis was performed using STATA version 15 (StataCorp, College Station, TX, USA). For dichotomous outcomes, the odds ratios (ORs) were calculated with their respective 95% confidence intervals (95% CI) using the Mantel–Haenszel random-effects model. To quantify the incidence of SVT as a proportion of total number of patients, a meta-analysis of proportions based on the number of SVT in acute pancreatitis as reported in each study was undertaken. To achieve this, a Freeman–Tukey transformation was used to establish a variance of the raw proportions of each study and then pooled using a random effects model. The quantity of heterogeneity was measured using the $I^2$ statistic with $I^2 \geq 75\%$ considered to represent high heterogeneity.

Risk of bias. The risk of bias of the included studies was assessed using the Newcastle–Ottawa Scale for non-randomized studies and studies were reported as having low, moderate, or high risk of bias.

Publication bias. Publication bias was assessed by visual inspection of asymmetry in the funnel plot based on the outcome of failure of recanalization.

Results

Description of the included studies. A total of 236 studies were identified from the combined electronic database searches with an additional 19 references identified from hand searches (Fig. 1). After critical review, 18 observational (15 retrospective and 3 prospective) studies published between 2008 and 2020 met the inclusion criteria. Seven of these studies were published only in abstract form. The studies originated from North America ($n = 9$), Europe ($n = 6$), and Asia ($n = 3$) (Table 1).

Nine studies specified the protocol for anticoagulation (Table 1) and indications included triple vessel involvement, SVT in the absence of varices or collaterals,
presence of pulmonary emboli,4,8,31 presence of deep vein thrombosis,3,4,31 stroke during admission,9 and presence of complications as a result of SVT.8 Inter-study and intra-study variability was observed in relation to the therapeutic anticoagulation regimens and duration of treatment (Table 1).

**Patient characteristics.** A total of 943 patients with acute pancreatitis developed SVT across the 18 included studies. Fourteen studies specified the age of patients with the median age of patients who developed SVT being 53 years (interquartile range 50.6–56.3 years). There was a male preponderance (67.3%) among patients who developed SVT in the nine studies that reported the sex. Overall, 264 of the 943 (28.0%) patients diagnosed with SVT received therapeutic anticoagulation (Table 2).

**Incidence of splanchnic vein thrombosis in patients with acute pancreatitis.** A total of 16 studies reported incidence rates of SVT in acute pancreatitis. Three studies recruited only patients with a first presentation of acute pancreatitis.3,8,22 The total number of patients with a first presentation of acute pancreatitis patients was 335, of whom 53 developed SVT. The incidence quoted from the individual studies ranged from 6% to 23%. The pooled incidence was 15% (95% CI 5% to 26%).

Another 13 studies reported on all presentations of acute pancreatitis without distinguishing between first or subsequent presentations, with 816 patients found to have SVT with incidence rates ranging between 2% and 51%.1,4,20,21,23,24,26–32

The overall incidence of SVT across the 16 studies was 17% (95% CI 14% to 20%). Significant heterogeneity was observed among studies ($I^2 = 98.2\%$) despite stratification for incidence at first presentation, and for all presentations of acute pancreatitis.

**Distribution of splanchnic vein thrombosis.** Fourteen studies, including 741 patients reported on the extent and distribution of thrombosis across the splanchnic vessels. These results are summarized in Table 3. Isolated SpVT was the most commonly identified form of SVT in 47.6% of patients, followed by isolated PVT in 15.5%. Thrombotic involvement of all the three splanchnic vessels was observed in only 7.6% of patients.

**Etiology of acute pancreatitis associated with splanchnic vein thrombosis.** Seven studies reported the etiology of acute pancreatitis in 328 patients. The most common cause of pancreatitis in patients also identified to have SVT was gallstones in 97 patients (29.6%), closely followed by alcohol consumption in 92 patients (28.0%). Idiopathic causes and hypertriglyceridemia were responsible in 68 (20.7%) and 16 patients (4.9%), respectively. The least common etiologies were iatrogenic and drug-induced pancreatitis in 7 patients each (2.1%). The remaining 48 patients (14.6%) were reported to have developed acute pancreatitis due to “other” or unspecified reasons.

**Secondary outcomes.** Although no distinction was made between the anticoagulated and control groups, four studies
reported the overall presence of portal hypertension in the patients who developed SVT, with a pooled incidence of 60% (95% CI 55% to 65% \( I^2 = 0\% \)). Outcomes of the patients in the treatment and control groups are summarized in Figure 2. The results show that recanalization of the thrombosed veins was more likely to occur in patients who received anticoagulation (Fig. 2a). There were no statistically significant differences between the groups when hemorrhagic complications (Fig. 2b), and overall mortality (Fig. 2c) were considered. However, mortality rates in the anticoagulated and untreated groups were 23.4% and 18.3%, respectively. Subgroup analysis of full-text articles only (Fig. 3) demonstrated that recanalization was more likely to occur in the anticoagulated group. The differences in hemorrhagic complications and mortality between the two groups were also not statistically significant.

Five studies reported both the overall mortality in the acute pancreatitis cohort without SVT and the mortality in those that developed an SVT. We found no difference in the risk of mortality between the two groups; 5% (95% CI 0% to 10%) in the former group and 7% (95% CI 2% to 12%) in the latter.

**Risk of bias and publication bias.** The majority of studies (77.8% [14/18]) were rated as having a moderate risk of bias, due to their retrospective nature, low number of patients and no detailed description of how patients were allocated to receive anticoagulation treatment or no treatment (Table 1). Other studies (22.2% [4/18]) reported little or no information on cohort identification and were noted to give anticoagulation to less than 10% of their population. There was, however, no significant asymmetry in the plot for publication bias (Fig. 4).

**Table 1** Study characteristics

| Reference          | Country | Study design | No. of patients with acute pancreatitis | Incidence of SVT n (%) | Anticoagulation regimen | Risk of bias |
|--------------------|---------|--------------|----------------------------------------|------------------------|-------------------------|--------------|
| Harris 2008^25     | USA     | Retrospective | —                                      | 63                     | Unspecified             | High         |
| Pribramskas 2009^32| USA     | Retrospective | 1155                                   | 50 (4.3%)              | Unspecified             | Moderate     |
| Vyas 2009^24       | UK      | Retrospective | 87                                     | 22 (25.3%)             | Unspecified             | High         |
| Gonzalez 2011^1    | UK      | Prospective   | 127                                    | 20 (15.7%)             | A) LMWH (1 mg/kg/B) Warfarin (INR 1.8–2.0)(TD: Unspecified) | Moderate     |
| Muddana 2012^21    | USA     | Prospective   | 193                                    | 41 (21.2%)             | Unspecified             | High         |
| Hall 2013^19       | UK      | Retrospective | —                                      | 11                     | LMWH (not adjusted for weight) + Warfarin/UH + Warfarin/Warfarin alone (TD: 2 months – lifelong) | High         |
| Harris 2013^4      | USA     | Retrospective | 2454                                   | 45 (1.8%)              | (A) MWH: 1 mg/kg BD, UH: initial bolus 80 U/kg + initial infusion of 18 U/kg/h Warfarin (INR 2–3) (TD: 3–12 months) | Moderate     |
| Easler 2014^5      | USA     | Retrospective | 122                                    | 22 (18.0%)             | Unspecified             | Moderate     |
| Toqué 2015^78      | France  | Retrospective | 318                                    | 19 (6.0%)              | (B) Unspecified         | Moderate     |
| Yang 2015^23       | USA     | Retrospective | 967                                    | 21 (2.2%)              | (A) UH, direct thrombin inhibitor (B) Warfarin (TD: unspecified) | Moderate     |
| Anderson 2017^21   | USA     | Retrospective | 4980                                   | 128 (2.6%)             | Unspecified             | Moderate     |
| Wang 2017^22       | USA     | Retrospective | 108                                    | 7 (6.5%)               | Unspecified             | High         |
| Ahmed 2018^29      | India   | Retrospective | 96                                     | 26 (27.1%)             | —                       | Moderate     |
| Garret 2018^30     | UK      | Retrospective | 148                                    | 76 (51.4%)             | Unspecified             | Moderate     |
| Junare 2020^8      | India   | Prospective   | 105                                    | 24 (22.9%)             | (A) UH                  | Moderate     |
| Maatman 2020^26    | USA     | Retrospective | 570                                    | 257 (45.1%)            | (B) Warfarin (INR 2–3) (TD: unspecified) | Moderate     |
| Pagliari 2020^20   | Italy   | Retrospective | 221                                    | 27 (12.2%)             | (A) LMWH 100U/kg BD (B) Warfarin (INR 2–3), Fondaparinux (7.5 g OD), apixaban (5 mg BD) (TD: 1.5–9 months) | Moderate     |
| Zhou 2020^27       | China   | Retrospective | 273                                    | 84 (30.8)              | LMWH TD: BD            | Moderate     |

(A) Initial management, (B) subsequent management/management on discharge.
INR, international normalized ratio; LMWH, low molecular weight heparin; TD, treatment duration; UH, unfractioned heparin.

Discussion

This systematic review found a contemporary data set of studies published between 2008 and 2020 to define the incidence of SVT in patients with acute pancreatitis. The pooled incidence from the three studies reporting SVT at first presentation of acute pancreatitis was 15%, as compared with the overall pooled incidence of SVT which was 17%, albeit with clinical and statistical heterogeneity among studies. Treatment with anticoagulation led to significant improvements in the rate of recanalization. There was no statistically significant increase in hemorrhagic complications or overall mortality. However, mortality in the anticoagulated group was 23.4% compared with 18.3% in the untreated group. Absence of a statistically significant difference in mortality could possibly be because of a type II error.
The overall incidence of SVT in patients with acute pancreatitis in the literature is probably underestimated, as most cases reported on cross-sectional imaging are found incidentally, and the absence of imaging in mild to moderate cases of pancreatitis could lead to co-existing SVT being missed. A previous systematic review reported a pooled incidence of SVT in acute pancreatitis of 16.6% (95% CI 10.0% to 24.5%, I² = 98%, P < 0.001), ranging between 0.3% and 62.1%, similar to our study. Further epidemiological studies would be necessary to define the true incidence within different populations. Our study has also confirmed that SpVT is the most common subtype of SVT observed in patients with acute pancreatitis.

The rate of spontaneous recanalization in patients with SVT is reported to be approximately 30%, suggesting that not all patients require therapeutic anticoagulation to aid recovery. It has been suggested that treatment should be reserved for those who develop...
In our meta-analysis of all studies, 26.8% of patients showed spontaneous recanalization without treatment, while recanalization occurred in 50.4% of patients with SVT who received anticoagulation treatment. The impact of the severity of acute pancreatitis on the likelihood of spontaneous recanalization could not be inferred from the individual studies. Overall, in the present meta-analysis, the use of therapeutic anticoagulation resulted in a statistically significant increase in rate of recanalization ($P = 0.007$) but there was no increase in hemorrhagic complications ($P = 0.12$) or mortality ($P = 0.10$). This contrasts significantly with an earlier meta-analysis that included only 5 studies, that suggested that there was no difference in either recanalization rates (OR 1.02, 95% CI 0.59 to 2.77), or mortality (OR 2.30, 95% CI 0.87 to 6.08) between treated and untreated groups.

Figure 2 Forest plots comparing (a) recanalization rates, (b) hemorrhagic complications and (c) mortality in patients with splanchnic vein thrombosis who received and did not receive anticoagulation—full-text studies and abstracts.

complications.\textsuperscript{1} In our meta-analysis of all studies, 26.8% of patients showed spontaneous recanalization without treatment, while recanalization occurred in 50.4% of patients with SVT who received anticoagulation treatment. The impact of the severity of acute pancreatitis on the likelihood of spontaneous recanalization could not be inferred from the individual studies. Overall, in the present meta-analysis, the use of therapeutic anticoagulation resulted in a statistically significant increase in rate of recanalization ($P = 0.007$) but there was no increase in hemorrhagic complications ($P = 0.12$) or mortality ($P = 0.10$). This contrasts significantly with an earlier meta-analysis that included only 5 studies, that suggested that there was no difference in either recanalization rates (OR 1.02, 95% CI 0.59 to 2.77), or mortality (OR 2.30, 95% CI 0.87 to 6.08) between treated and untreated groups.\textsuperscript{34} The difference in outcomes between the two meta-analyses can be accounted for by the larger number of patients with SVT included in our analysis.

The overall prognosis, in terms of portal hypertension, ischemia and infarction, is similar in patients with incidental SVT or symptomatic SVT.\textsuperscript{35} Given that therapeutic anticoagulation results in an increased rate of splanchnic vein recanalization in acute pancreatitis it would suggest that therapeutic anticoagulation would be of use in both incidental and symptomatic SVT groups.\textsuperscript{35-37} Patients with PVT and SMVT subtypes may have a reduced rate of spontaneous recanalization and a higher mortality rate; potentially implying that this specific cohort of patients with SVT could benefit more from therapeutic anticoagulation.\textsuperscript{1} However, we did not observe a difference in overall mortality between the treated and control groups to justify anticoagulation therapy. It is difficult to distinguish between mortality related to progression of acute pancreatitis and due to complications from SVT associated with pancreatitis alone. Our analysis of mortality risk in patients with pancreatitis with and without SVT, found no difference in risk (pancreatitis without SVT group mortality of 5% [95% CI 1% to 10%] and pancreatitis with SVT mortality of 7% [95% CI 2% to 12%]). If the mortality risk was related to severe acute pancreatitis alone and not the complications of SVT, then it could possibly explain the lack of difference seen in mortality, in spite of higher rates of recanalization in the treated group. Furthermore, the lack of long-term follow-up in the included studies makes it difficult to assess the long-term clinical impact of recanalization on morbidity and SVT-specific mortality beyond...
Further prospective studies are required to assess the impact of anticoagulation on patients with SVT with regard to the development of portal hypertension in the long term. There are some limitations of this review. The studies included have a moderate risk of bias, due to the risk of a selection bias, lack of randomization or standardized treatment protocols. Studies reporting on the same patient population were excluded, however, in some instances we were unable to discern whether the same group of authors utilized the same patient data across different studies, and therefore, the studies were included.4,23,25,32 It was not possible to reach a conclusion as to the anticoagulant of choice or the duration of treatment due to the variability observed in these variables, between, and within studies. Seven studies were published in abstract form only and it was not possible to get the complete data set from these.21–25,31,32

### Figure 3

Forest plots comparing (a) recanalization rates, (b) hemorrhagic complications and (c) mortality in patients with splanchnic vein thrombosis who received and did not receive anticoagulation—full-text studies only.

### Figure 4

Funnel plot demonstrating lack of publication bias based on the outcome of failure of recanalization.

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| Study or Subgroup | Anticoagulation | Control | Odds Ratio | Odds Ratio |
|------------------|-----------------|---------|------------|------------|
|                  | Events          | Total   | Weight     | M-H, Random, 95% CI | M-H, Random, 95% CI |
| González 2011    | 2               | 14      | 16         | 15.0%       | 0.33 [0.03, 3.20]   |
| Hall 2013        | 2               | 7       | 4          | 7.2%        | 0.05 [0.00, 1.34]   |
| Harris 2013      | 15              | 17      | 25         | 21.3%       | 0.90 [0.13, 6.02]   |
| Junare 2020      | 6               | 12      | 7          | 29.7%       | 0.71 [0.14, 3.58]   |
| Pagliari 2020    | 5               | 16      | 8          | 26.8%       | 0.17 [0.03, 0.93]   |
| Total (95% CI)   | 56              | 71      | 100.0%     | 0.38 [0.16, 0.91] |
| Total events     | 30              | 56      |            |             |

Heterogeneity: $I^2 = 0.00, \chi^2 = 3.72, df = 4 (P = 0.45); I^2 = 0$

Test for overall effect: $Z = 2.18 (P = 0.03)$

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| Study or Subgroup | Anticoagulation | Control | Odds Ratio | Odds Ratio |
|------------------|-----------------|---------|------------|------------|
|                  | Events          | Total   | Weight     | M-H, Random, 95% CI | M-H, Random, 95% CI |
| Easley 2014      | 2               | 6       | 0          | 9.2%        | 18.33 [0.74, 454.42] |
| Garret 2018      | 10              | 39      | 3          | 33.3%       | 3.91 [0.98, 15.57]   |
| Hall 2013        | 2               | 7       | 0          | 8.8%        | 4.09 [0.15, 108.94]  |
| Harris 2013      | 2               | 17      | 5          | 24.2%       | 0.01 [0.11, 3.58]    |
| Junare 2020      | 3               | 12      | 0          | 9.9%        | 9.21 [0.42, 200.59]  |
| Pagliari 2020    | 0               | 16      | 11         | Not estimable |                     |
| Zhou 2020        | 1               | 36      | 2          | 14.7%       | 0.66 [0.06, 7.54]    |
| Total (95% CI)   | 133             | 156     | 100.0%     | 2.42 [0.86, 6.78] |
| Total events     | 20              | 30      |            |             |

Heterogeneity: $I^2 = 0.33, \chi^2 = 6.24, df = 5 (P = 0.28); I^2 = 20$

Test for overall effect: $Z = 1.68 (P = 0.09)$

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| Study or Subgroup | Anticoagulation | Control | Odds Ratio | Odds Ratio |
|------------------|-----------------|---------|------------|------------|
|                  | Events          | Total   | Weight     | M-H, Random, 95% CI | M-H, Random, 95% CI |
| Harris 2013      | 2               | 17      | 1          | 51.0%       | 3.60 [0.30, 43.08]   |
| Junare 2020      | 1               | 12      | 2          | 49.0%       | 0.45 [0.04, 5.81]    |
| Pagliari 2020    | 0               | 16      | 0          | Not estimable |                     |
| Total (95% CI)   | 45              | 51      | 100.0%     | 1.31 [0.17, 9.93] |
| Total events     | 3               | 3       |            |             |

Heterogeneity: $I^2 = 0.49, \chi^2 = 1.30, df = 1 (P = 0.25); I^2 = 23$

Test for overall effect: $Z = 0.26 (P = 0.80)$
Not all studies stratified the severity of pancreatitis, thereby preventing a comparison between the severity of pancreatitis and the incidence of SVT. We were limited in our ability to compare the risk of hemorrhagic complications and mortality in the studies reporting recanalization rates due to the variability in reporting these outcomes among them. While some studies suggest that different subtypes of SVT may vary prognostically, we are unable to compare them fully and recognize the need for further studies to directly compare the outcomes associated with the different subtypes. In addition, there were insufficient data to assess longer term outcomes following anticoagulation.32

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