

# **Abstract**

## **Introduction**

Severe acute pancreatitis (SAP) is a common diagnosis in emergency general surgery and can be a cause of significant morbidity and mortality. A consequence of SAP is thrombus in the splanchnic veins. These thrombi can potentially lead to bowel ischaemia or hepatic failure. However, another complication of SAP is retroperitoneal bleeding. At this time, it is thus unclear if treating patients with splanchnic vein thrombosis in the context of SAP is associated with any outcome benefit. A systematic review might clarify this question.

## **Methods**

A two fold search strategy (one broad and one precise) looked at all published literature. The review was registered on PROSPERO (ID: CRD42018102705). Medline, EMBASE, PubMed, Cochrane and Web of Science databases were searched and potentially relevant papers were reviewed independently by two researchers. Any disagreement was reviewed by a third independent researcher. Primary outcome was reestablishment of flow in the thrombosed vein versus bleeding complications

## **Results**

Of 1462 papers assessed, a total of 16 papers were eligible for inclusion. There were no randomised controlled trials, 2 were case series, 5 retrospective single centre reviews and 9 studies case reports. There were a total of 198 patients in these studies of whom 92 (46.6%) received anticoagulation therapy. The rates of recanalization of veins in the treated and non-treated groups was 14% and 11% and bleeding complications were 16% and 5%; respectively. However, the included studies were too heterogeneous to undertake a meta-analysis.

## **Conclusion**

The systematic review highlights the lack evidence addressing this clinical question. Therefore a randomised controlled trial would be appropriate to undertake.

## Introduction

Acute pancreatitis is a common cause of emergency admission to general surgical departments across the world. It has an incidence of between 13-45 per 100,000 of the UK population<sup>1</sup>. Pancreatitis has a spectrum of severities and related mortality. Accordingly, severe acute pancreatitis (SAP) is associated with mortality rates of greater than 40%<sup>2</sup>. Sequelae of this condition includes multi-organ failure, intra-abdominal collections, and thrombosis of the splanchnic veins including splenic, superior mesenteric and portal veins<sup>3</sup>.

Splanchnic vein thrombosis (SVT) has been shown to be a complication in more than a fifth of cases with severe acute pancreatitis<sup>4</sup>. The aetiology is postulated to be caused by the pro-thrombotic nature of the acute inflammatory condition, with contributions from the systemic response to the injury, hypovolaemia and fluid shifts<sup>5</sup>. Without treatment, the thrombus can go on precipitate bowel ischaemia, hepatic failure or chronic portal hypertension<sup>6</sup>. Accordingly, anticoagulation would seem a necessity in these cases. However, this could bring about significant risks associated with these treatments. Patients with acute severe pancreatitis are also at risk of bleeding. This can be into the retroperitoneum or from pseudo-aneurysms of major visceral arteries<sup>7</sup>. Such bleeding could be catastrophic in the context of an anticoagulated patient<sup>8</sup>.

Thus, the risks versus benefits of anticoagulation in the treatment of splanchnic venous thrombosis are unknown and is not well evaluated in the literature. Indeed, the answer to this question remains entirely in equipoise with no simple answer being able to be elucidated from basic surgical first principles or from the available literature. Although clearly reported as a complication of acute pancreatitis, there appears little direct studies or guidance on the preferential management of this condition.

The aims of this study are to undertake a systematic review to explore the current published literature on whether the data is sufficient to recommend anticoagulation in this setting or to advocate its avoidance. This subject has particular relevance to

emergency general surgery- a specialty with less supporting evidence than its more well established comparators<sup>9</sup>.

# Methods

## Study Methodology

This is a systematic review in which the PRISMA checklist was utilised and standard review techniques observed. The protocol has been registered prior to starting the systematic review process and can be found on the PROSPERO register (ID: CRD42018102705).

## Eligibility criteria

A focused review question was identified prior to searching using the population, intervention, comparison and outcomes (PICO) framework. Selected population was individuals with splanchnic vein thrombosis in acute pancreatitis (irrespective of cause of pancreatitis). The population was specifically that of adults (i.e. people aged over 18 years old) who had the above-defined disease. Intervention arm included therapeutic anticoagulation (including interventional techniques). Comparison with the control arm were those individuals within the population who were not treated with therapeutic anticoagulation (this included those with prophylactic doses of low molecular weight heparin). Primary outcomes were 1. Recanalization versus bleeding complication, 2. Mortality and 3. Length of hospital stay.

Relevant studies were included irrespective of the study type, publication year or language of publication. Translation facilities were utilised where appropriate.

## Databases and search strategies

Electronic searches were performed on Medline, EMBASE, PubMed, Cochrane and Web of Science databases. Searches were two-fold to allow identification of all currently available studies and ensure none were missed:

1. A broad search strategy for each of the above database, simply using terms 'pancreatitis' and 'anticoagulation' – this allowed identification of a broad number of studies.
2. A MeSH constructed search strategy which was similar for each of the databases. This allowed more relevant studies to be identified, however due to paucity of results available on the subject currently, strategy 1 was also utilised to ensure no relevant studies were missed out. Exact match of the

search strategies was not possible due to differences in interface between the search algorithms of the individual databases. All search strategies are listed in supplementary file 1.

Three authors performed the searches (GL, GR and WN) and any difference in opinion when including studies were resolved through team discussion. Authors of studies that appeared relevant, but were missing of essential information, were contacted via e-mail, with a two-week deadline for response given. A log of each search was kept by exporting them into the Rayyan platform ([www.rayyan.qcri.org](http://www.rayyan.qcri.org)).

### **Inclusion and exclusion criteria**

Studies were reviewed at title, abstract and full-text stage and were included or excluded accordingly depending on the following inclusion-exclusion criteria.

#### *Inclusion criteria:*

1. All other reports on the use of this intervention (anticoagulant) in the above-defined population
2. Studies on adults (age > 18 years) only

#### *Exclusion criteria:*

1. Studies looking at chronic pancreatitis
2. Studies looking at pancreatitis after pancreatic resections or transplant
3. Studies on patients less than 18 years of age
4. Animal studies

### **Study selection and data extraction**

A flowchart was created to display number of studies included and excluded at each review stage (see chart 1). Inclusion and exclusion criteria were utilised to aid this process. Three authors performed the process separately (GR, GL, WN) and any disagreements in the outcomes were resolved through team discussion.

A cloud based data extraction template was used by GR, GL and WN to facilitate data collection. The data extraction template was designed by input from all authors. During the data extraction process, quality of included studies was also assessed using the Downs and Black checklist<sup>10</sup> (outcomes of this for each study can be found in table 1).

The Downs & Blacks assessment tool was performed on each of the studies to give a quantitative assessment of the evidence available. The specific scores for each study are shown in the table above with the complete table in the appendices. The original criteria for the final question was modified to only give a response of “1” if a power calculation was used. The use of “0” in the chart was used for both a No response and unable to determine.

### **Ethics and support**

Given the nature of this systematic review, no ethical permissions were deemed necessary. This project was supported by the Royal College of Surgeons of England Systematic review team.

## Results

A total of 16 studies were included in the systematic review. Figure 1 shows the flowchart for these searches. None of the studies were randomised controlled trials. 9 studies were case reports, 2 were case series and the remainder were review studies.

### Single centre case series

There were 5 single centre studies included in the review, summarised in Table 1, with a total number of 182 patients. Due to the paucity of studies and their significant differences, meta-analysis and synthesis of results was not deemed possible.

Harris *et al.* (2013)<sup>11</sup> described their experience of splanchnic vein thrombosis in 45 patients with acute pancreatitis, the majority occurring solely in the splenic vein. Of 17 that were treated with anticoagulation, only 2 patients recanalised (12%). The timing of this recanalization was not mentioned in this paper. A similar rate for those that were not treated (11%). Bleeding complications were observed in 8 patients, with only 1 on anticoagulation at the time. Gonzelez *et al.* (2011)<sup>6</sup> reported 20 patients in which 4 were treated. No haemorrhagic complications due to anticoagulation and little difference between cavernoma formation (porto-portal shunts) rate were observed. However, those treated had a lower rate of developing other collateral vessels in this study.

Toqué *et al.* (2015)<sup>12</sup> performed a retrospective analysis of 19 patients. The majority (79%) received therapeutic anticoagulation with 26.3% achieving complete recanalisation. No significant bleeding complications were reported. Garret *et al.* (2018)<sup>13</sup> reviewed a cohort of 76 patients who had been admitted to an intensive care unit and had reports a 26% rate of a bleeding complication in those treated with systemic anticoagulation. Treatment did not prevent the formation of cavernoma in this group of patients.

In 2013, Easler *et al.*<sup>14</sup> analysed 22 patients who developed splanchnic vein thrombosis following acute pancreatitis, with the thrombosis again predominantly occurring in the splenic then portal veins. No patient had treatment specifically for the thrombosis but two had a bleeding complication, whilst one of these was on

anticoagulation (for another cause). No complication was attributable to the thrombosis.

### **Case Series**

There are two defined case series describing 7 patients (6 male:1 female) with a mean age of 48.5 years old. Crowe *et al.* (1995)<sup>15</sup> describe 4 case of superior mesenteric vein thrombus, which were not treated with any anticoagulation. On follow up imaging 3 had completely resolved. The patient who had not had resolution on 3 month CT imaging, remained well during study follow up of 5 years. Conversely, Li *et al.* (2016)<sup>16</sup> report 3 cases with both splenic and portal vein thrombosis, with resolution in all 3 cases following treatment with low molecular weight heparin and subsequent warfarin therapy. They were able to report no complications and describe this treatment as safe.

### **Case Reports**

Of the 9 case reports, the majority are male (8:1) with an average age of 52 (range 30-73). The location of thrombus in these reports is predominantly in the portal vein (66%), with both splenic and mesenteric occurring in 4 (44%).

Eight of the reports depict an intervention with the use of either unfractionated heparin or low molecular weight heparin (LMWH) and subsequent warfarin the most commonly used in 5 cases. The other three either used just LMWH, had the addition of urokinase or only defined their intervention as “anticoagulation”.

Three of those treated had favourable objective outcomes either with partial recanalisation or complete resolution, whilst two showed either no resolution or complete occlusion. Two had positive subjective reviews of recovery. One patient died of hepatic infarction and multi-organ failure. One of the patients treated with unfractionated heparin and warfarin developed bleeding into a pseudocyst. Although the majority of the case reports suggested treatment, Na *et al.* (2011)<sup>17</sup> indicated complete resolution of a mesenteric vein thrombus, with no surgical or medical intervention.

## **Quality control**

Table 4 lists the quality assessment of each of the papers included and demonstrate a paucity of quality studies available in the literature. The average score overall for all 16 studies was 7.4/28.

## Discussion

The aim of this systematic review was to address whether anticoagulation should be given to patients with mesenteric vein thrombosis in severe acute pancreatitis. It has been undertaken in a logical, meticulous fashion and only 16 papers of relevance were identified. If the epidemiological estimates of thrombosis in SAP are accurate<sup>4</sup>, this is a common sequelae of acute pancreatitis and it was unexpected that there was a lack of high quality studies addressing this issue. As a consequence, it is difficult to recommend one treatment over the other for splanchnic vein thrombosis in acute pancreatitis using a synthesis of the currently published literature as no meta-analysis was possible.

The findings of our analysis of relevant publications are that, in this population of patients, 46.6% received anticoagulation. Re-canalisation and bleeding complications were observed in a proportion of both comparison groups (treatment versus no treatment). Therefore, there is little trend towards the appropriate management strategy. Indeed, most authors of the included studies portrayed their own inferences from their study series and all acknowledge the lack of guidance from previous publications. There was also significant heterogeneity of the splanchnic vein thrombosis associated with patients who have developed pancreatic necrosis<sup>14</sup>.

The most common location is in splenic vein. However, the portal vein and superior mesenteric veins can also be involved. It is thus unclear as to whether the treatment strategy would alter given the anatomical location of the thrombus. The portal vein thrombus has been used as an indicator of severity due to the risk of impaired liver function, and has been shown to have a predominance for treatment with anticoagulants<sup>6</sup>. This is despite no difference in eventual recanalisation rates. Whilst these are, by definition, deep vein thromboses, the added complicating factor is the risk of significant retroperitoneal bleeding and potential exsanguination.

Another critical question is what defines a thrombosis. Again, there is heterology between the studies. Garret et al<sup>13</sup> and Harris et al<sup>11</sup> defined SVT as either visualising thrombus in the vein, if the vein was compressed or was not visualized

with the presence of collaterals. Easler et al<sup>14</sup> differentiated thrombosis from narrowing in their study. Others did not specify the diagnosis criteria for SVT. Such a definition would be required in any future prospective study as anticoagulation treatment efficacy could differ depending on the presence of thrombus within a vein and complete occlusion of the vessel.

Almost all of the anticoagulation used in this setting was either low molecular weight heparin or warfarin. Indeed, only one publication reported on a different agent-urokinase<sup>22</sup>. In other settings, such as patients who have atrial fibrillation and DVT, novel anticoagulants have become commonplace in clinical practice. There are advantages in the lack of requirement for therapeutic level testing<sup>26</sup>. However, given that there are few reversal agents<sup>27</sup>, and they rely upon regular oral absorption<sup>26</sup> which can be compromised in pancreatitis, they therefore cannot be recommended in this setting. Our search strategy encompassed any publication potentially using these agents and did not find any.

That this question has yet to be answered in any of the literature is perhaps intriguing. It is a common problem and one which treatment seems to be occurring on the basis of clinician opinion rather than with an evidence base. As such, the treatment remains entirely in equipoise and a randomised controlled trial may assist in establishing the correct management course. To our knowledge, no such trial is being undertaken or planned. However, any such RCT would need to be appropriately powered and likely to be multi centre in nature. As SAP patients are having their care more commonly undertaken in specialised centres, this is not unfeasible in modern surgical management.

The strengths of this work are the rigorous nature in which the systematic review was performed. We have been able to carefully dissect the literature and undertake, what we believe, to be a comprehensive search. Although the intention was also to attempt to perform a meta-analysis of the available results, we were aware of potential challenges from the start due to predicted paucity of studies on the subject which is an acknowledged limitation.

In conclusion, the available literature is of limited quality and it is not clear whether the therapeutic anticoagulation is necessary or required in cases with ASP

associated with splanchnic venous thrombosis. Given the potential morbidity and mortality concerns with either under-treatment or the consequence of bleeding whilst on treatment, this question is clinically relevant and one which will require randomised controlled studies to address.

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Figure 1:Flowchart diagram

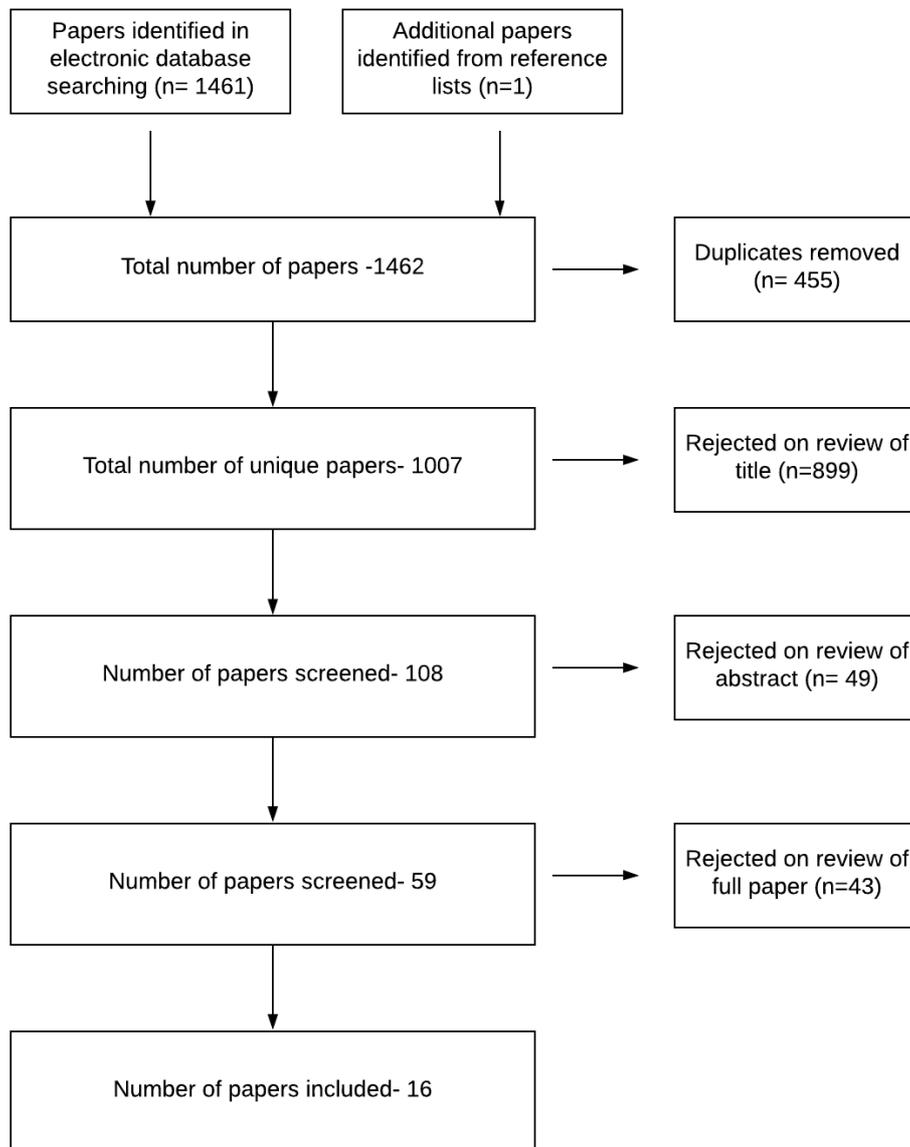


Table 1: Individual Centre studies

Reference	Number (M:F) Mean Age	Thrombus Location	Intervention	Comparison	Outcome (Measure)
Toqué L <i>et al.</i> (2015) <sup>12</sup>	19 (17:2) 57	Splenic, portal and superior mesenteric vein thrombus	Therapeutic Anticoagulation (n=15)	No treatment (n=4)	At 2 years, 26.3 % complete resolution in treatment group, with 31.6% suffering portal cavernoma.
Garret <i>et al.</i> (2018) <sup>13</sup>	76 (Not available) 54	Portal, splenic & mesenteric venous thrombosis	Effective Systemic anticoagulation (n=39)  10 receiving AC bled	No treatment (n=37)	Cavernoma developed in 25 of treatment group (68%) & in 9/18 no treatment group 50%
Harris <i>et al.</i> (2013) <sup>11</sup>	45 (31:14) 58	Splanchnic vein thrombosis (30 involving the splenic vein)	LWMH or Unfractionated Heparin then oral anti-coagulation (n=17) 12%(2) recanalised	No treatment (n=28) 11% (3/28) recanalised. 54% (15/28) developed collaterals compared to 35% (6/28) in treatment group	Bleeding complication in 5 (18% on no AC) compared to 2 (12%on AC).
Gonzalez <i>et al.</i> (2011) <sup>6</sup>	20 (9:11) 53.5 (Median )	Splanchnic vein thrombus	Enoxaparin (1mg/Kg BD) then warfarin. 4 treated with 50% recanalization rate	16 not treated with a 25% recanalization rate (4/16).	No haemorrhagic complications related to treatment.
Easler <i>et al.</i> (2014) <sup>14</sup>	22 (14:8) 54	Portal, splenic & mesenteric venous thrombosis	Anticoagulation for 26% 6/22 (Only given for other indication e.g. DVT)	No treatment n=16	2 treated developed bleeding complication (33%). Clot resolution seen in 2/22

Table 2: Case Series

<b>Reference</b>	<b>Number (M:F) Mean Age</b>	<b>Thrombus location</b>	<b>Intervention</b>	<b>Outcome (Measure)</b>
Crowe P M <i>et al.</i> (1995) <sup>15</sup>	4 (3:1) 48	Superior mesenteric vein	No intervention	75% resolution of thrombosis (CT Imaging/Doppler)
S Li <i>et al.</i> (2016) <sup>16</sup>	3 (3:0) 49	Portal and splenic veins	LMWN and then warfarin	At 6 months, 100% resolution following treatment (Doppler Ultrasound)

Table 3: Case Reports

<b>Study</b>	<b>Age/Sex</b>	<b>Case</b>	<b>Intervention</b>	<b>Outcome (Measure)</b>
Das S <i>et al.</i> (2017) <sup>18</sup>	38, M	Thrombus in splenic, portal vein and right portal vein bifurcation	LMWH	Death, resultant hepatic infarction and Multi-organ failure (Descriptive)
Krummen D M <i>et al.</i> (1996) <sup>19</sup>	61, F	Asymptomatic incomplete thrombus of superior mesenteric vein	Intravenous heparin and subsequent warfarin therapy (1 month)	Implied good recovery (No measure)
Ankouane F <i>et al.</i> (2015) <sup>20</sup>	46, M	Portal, splenic and mesenteric thrombus associated with Protein S & C deficiencies	Enoxaparin (1mg/kg twice daily) then warfarin	Partial recanalization at 10 days (Doppler Ultrasound) and Collateral vessels at 30 days (CT Imaging)
De Cicco I & Varon J (2009) <sup>21</sup>	30, M	Portal and splenic thrombus	Anticoagulation	Discharged home (No measure)
Na B S <i>et al.</i> (2011) <sup>17</sup>	45, M	Superior mesenteric vein thrombus	No Intervention	Complete resolution at 6 weeks (CT Imaging)
Cheung D Y <i>et al.</i> (2005) <sup>22</sup>	63, M	Portal vein thrombus	LMWH & Urokinase (inc. balloon dilatation then Warfarin)	No resolution but no progression on oral warfarin (CT Imaging)
Seong J S <i>et al.</i> (2014) <sup>23</sup>	43, M	Portal and splenic vein thrombus	LMWH and subsequent oral anticoagulants	Full dissolution of thrombus at 3 months (CT Imaging)
EI-Wahsh M (2006) <sup>24</sup>	58, M	Portal vein thrombus	Enoxaparin (100 IU/kg twice daily) then warfarin	At 10 weeks complete occlusion persisted, collaterals developed (Magnetic resonance venography)
Park W S <i>et al.</i> (2012) <sup>25</sup>	73, M	Portal vein trunk thrombosis with progression to right and left veins	Intravenous heparin then warfarin	Partial recanalization but complicated by bleeding pseudocyst rupturing duodenum (CT Imaging)

**Table 4- Downs and Black**

<b>Study</b>	<b>Score</b>	<b>Study</b>	<b>Score</b>
Das S <i>et al.</i> (2017) <sup>18</sup>	<b>4</b>	Park W S <i>et al.</i> (2012) <sup>25</sup>	<b>5</b>
Krummen D M <i>et al.</i> (1996) <sup>19</sup>	<b>5</b>	Crowe P M <i>et al.</i> (1995) <sup>15</sup>	<b>9</b>
Ankouane F <i>et al.</i> (2015) <sup>20</sup>	<b>5</b>	S Li <i>et al.</i> (2016) <sup>16</sup>	<b>9</b>
De Cicco I & Varon J (2009) <sup>21</sup>	<b>5</b>	Toqué L <i>et al.</i> (2015) <sup>12</sup>	<b>7</b>
Na B S <i>et al.</i> (2011) <sup>17</sup>	<b>5</b>	Garret <i>et al.</i> (2018) <sup>13</sup>	<b>13</b>
Cheung D Y <i>et al.</i> (2005) <sup>22</sup>	<b>5</b>	Harris <i>et al.</i> (2013) <sup>11</sup>	<b>10</b>
Seong J S <i>et al.</i> (2014) <sup>23</sup>	<b>5</b>	Gonzelez <i>et al.</i> (2011) <sup>6</sup>	<b>12</b>
El-Wahsh M (2006) <sup>24</sup>	<b>5</b>	Easler <i>et al.</i> (2014) <sup>14</sup>	<b>13</b>

## Supplementary figure 1

Broad search

### Pubmed Search terms used (18/3/2018) (524 papers)

1. pancreatitis AND anticoagulation (searched on Pubmed, 24/02/2018)

524 papers identified. Relevance searches by BN and GR on the Rayyan platform

### Medline search terms used so far (27 papers)

1. exp PANCREATITIS, ACUTE NECROTIZING/ or exp PANCREATITIS/ or exp PANCREATITIS, ALCOHOLIC/
2. exp Mesenteric Vascular Occlusion/ or exp Mesenteric Ischemia/ or mesenteric ischaemia.mp. or exp Mesenteric Arteries/
3. (mesenteric adj3 thrombosis).mp.
4. (splanchnic adj3 thromb\*).mp.
5. (splanchnic adj3 occlu\*).mp.
6. (splanchnic adj3 ischaemi\*).mp.
7. (mesenteric adj3 ischaem\*).mp.
8. (mesenteric adj2 clot\*).mp.
9. (splanchnic adj2 clot\*).mp.
10. exp Warfarin/ or exp Heparin/ or exp Anticoagulants/
11. (novel adj2 anticoag\*).mp.
12. (direct adj3 anticoag\*).mp.
13. (blood adj2 thin\*).mp.
14. Tissue Plasminogen Activator/ or Fibrinolytic Agents/ or Thrombolytic Therapy/
15. anticoag\*.mp.
16. (portal adj3 ischaem\*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
17. (portal adj3 clot\*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
18. (portal adj3 thromb\*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
19. (splenic adj3 ischaem\*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
20. (splenic adj3 thromb\*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

21. (splenic adj3 clot\*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
22. (visceral adj3 thromb\*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
23. (visceral adj3 clot\*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
24. (visceral adj3 ischaem\*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
25. (severe adj2 pancreatitis).mp.
26. exp DALTEPARIN/
27. exp COUMARINS/
28. exp PHENINDIONE/
29. exp ENOXAPARIN/
30. exp RIVAROXABAN/
31. APIXABAN.mp.
32. dabigatran.mp.
33. edoxaban.mp.
34. fondaparinux.mp.
35. (vitamin adj2 k adj2 antagonist).mp.
36. tinzaparin.mp.
37. exp Urokinase-Type Plasminogen Activator/
38. 1 or 25
39. 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24
40. 10 or 11 or 12 or 13 or 14 or 15 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37

41. 38 and 39 and 40

Searched on 19/03/2018 By GL

### **Embase search (157 papers)**

1. pancreatitis.mp. or exp acute pancreatitis/ or exp acute hemorrhagic pancreatitis/ or exp pancreatitis/ or exp alcoholic pancreatitis/
2. (severe adj2 pancreatitis).mp.
3. mesenteric ischaemia.mp. or exp mesenteric ischemia/
4. exp mesenteric blood vessel occlusion/ or exp mesenteric artery occlusion/ or exp mesenteric ischemia/
5. (mesenteric adj2 clot\*).mp.
6. (mesenteric adj3 ischaem\*).mp.
7. (mesenteric adj3 thrombosis).mp.
8. (splanchnic adj2 clot\*).mp.
9. (splanchnic adj3 ischaemi\*).mp.
10. (splanchnic adj3 occlu\*).mp.
11. (splanchnic adj3 thromb\*).mp.
12. (portal adj3 clot\*).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word]
13. (portal adj3 ischaem\*).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word]
14. (portal adj3 thromb\*).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word]
15. (splenic adj3 clot\*).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word]
16. (splenic adj3 ischaem\*).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word]
17. (splenic adj3 thromb\*).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word]
18. (visceral adj3 clot\*).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word]
19. (visceral adj3 ischaem\*).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word]
20. (visceral adj3 thromb\*).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word]
21. exp warfarin/
22. exp heparin/





#42	Search enoxaparin	4747
#41	Search PHENINDIONE	895
#40	Search coumarins	48316
#39	Search dalteparin	1239
#38	Search severe pancreatitis	9263
#37	Search visceral isch*	346
#36	Search visceral clot	42
#35	Search visceral thomb* Schema: all	0
#34	Search visceral thomb*	0
#33	Search visceral thromb	177
#32	Search visceral thomb	0
#31	Search splenic clot*	452
#30	Search splenic thromb*	25
#29	Search splenic ischaem*	163
#28	Search portal thromb*	562
#27	Search portal clot*	297
#26	Search portal isch*	11
#25	Search anticoag*	242584
#24	Search Thrombolytic Therap	153
#23	Search Fibrinolytic Agents	167522
#21	Search blood thin*	141
#20	Search direct anticoa*	119
#19	Search novel anticoa*	511
#18	Search anticoagulant	229959
#17	Search heparin [mh]	61608
#16	Search heparin (mh)	119
#15	Search heparin(MH)	119

#13	Search heparin	94444
#12	Search warfarin	27020
#11	Search splanchnic clot	9
#10	Search mesenteric clot	107
#9	Search mesenteric isch*	2809
#8	Search splanchnic ischaemia	1271
#7	Search splanchnic occlusion	727
#6	Search splanchnic thrombus	545
#5	Search mesenteric thrombus	6861
#4	Search mesenteric adj3 thrombus Schema: all	0
#3	Search mesenteric adj3 thrombus	0
#2	Search mesenteric vascular occlusion	5031
#1	Search pancreatitis	63764

Cochrane search- 1 result (excluded after review of title and abstract)

Search Name:

Date Run: 19/03/18 15:37:37.724

Description:

ID	Search Hits	
#1	MeSH descriptor: [Pancreatitis] explode all trees	1181
#2	severe adj2 pancreatitis	65
#3	acute adj2 pancreatitis	60
#4	alcoholic adj2 pancreatitis	16
#5	MeSH descriptor: [Mesenteric Ischemia] explode all trees	2
#6	mesenteric adj2 thromb*	5
#7	mesenteric adj2 clot	0
#8	splanchnic adj3 isch?em*	6
#9	splanchnic adj3 clot*	1
#10	splanchnic adj3 occlu*	1
#11	splanchnic adj3 thromb*	5
#12	portal adj3 isch?em*	98
#13	portal adj3 thromb*	131
#14	portal adj3 clot*	63
#15	portal adj3 occlu*	62
#16	splenic adj3 isch?em*	4
#17	splenic adj3 clot*	4
#18	splenic adj3 thromb*	13
#19	splenic adj3 occlu*	5

#20 visceral adj3 clot\* 15  
 #21 visceral adj3 isch?em\* 14  
 #22 visceral adj3 thromb\* 24  
 #23 visceral adj3 occlu\* 12  
 #24 MeSH descriptor: [Warfarin] explode all trees 1503  
 #25 MeSH descriptor: [Heparin] explode all trees 4519  
 #26 MeSH descriptor: [Anticoagulants] explode all trees 4876  
 #27 novel adj3 anticoag\* 32  
 #28 direct adj3 anticoag\* 146  
 #29 blood adj3 thin\* 342  
 #30 MeSH descriptor: [Thrombolytic Therapy] this term only 1779  
 #31 MeSH descriptor: [Fibrinolysis] explode all trees 963  
 #32 MeSH descriptor: [Tissue Plasminogen Activator] explode all trees 1543  
 #33 dalteparin 647  
 #34 coumarin\* 401  
 #35 enoxaparin 1888  
 #36 phenindione 64  
 #37 rivaroxaban 925  
 #38 apixaban 577  
 #39 dabigatran 736  
 #40 edoxaban 324  
 #41 fondaparinux 419  
 #42 vitamin adj2 k adj2 antagonist\* 35  
 #43 tinzaparin 269  
 #44 urokinase 966  
 #45 #1 or #2 or #3 or #4 1237  
 #46 #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17  
 or #18 or #19 or #20 or #21 or #22 or #23 273  
 #47 #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or  
 #36 or #37 or #38 or #39 or #40 or #41 or #42 or #43 or #44 14102  
 #48 #45 and #46 and #47 1

#### Web of Science - GL - 32 results

# 1 TS=pancreatitis  
 # 2 TS=(acute pancreatitis)  
 # 3 TS=(severe pancreatitis)  
 # 4 TS=(alcoholic pancreatitis)  
 # 5 TS=(necroti?ing pancreatitis)  
 # 6 TS=(mesenteric adj2 isch?em\* OR mesenteric adj2 occlusion OR mesenteric adj2  
 clot\* OR mesenteric thromb\*)  
 # 7 TS=(splanchnic adj2 isch?em\* OR splanchnic adj2 occlusion OR splanchnic adj2  
 clot\* OR splanchnic thromb\*)  
 # 8 TS=(splenic adj2 isch?em\* OR splenic adj2 occlusion OR splenic adj2 clot\* OR  
 splenic thromb\*)  
 # 9 . TS=(portal adj2 isch?em\* OR portal adj2 occlusion OR portal adj2 clot\* OR portal  
 thromb\*)  
 # 10 TS=(visceral adj2 isch?em\* OR visceral adj2 occlusion OR visceral adj2 clot\* OR  
 visceral thromb\*)  
 # 11 TS=(Warfarin OR heparin OR anticoagulant\* OR novel adj2 anticoag\* OR direct  
 adj2 anticoag\* OR blood thin\* OR fibrinoly\* OR thromboly\* OR tissue adj1 plasminogen OR  
 dalteparin OR enoxaparin OR rivaroxaban OR dabigatran OR apixaban OR coumarin\* OR

phenindione OR edoxaban OR fondaparinux OR tinzaparin OR urokinase OR vitamin adj2  
K adj2 antagonist\*)

# 12 #5 OR #4 OR #3 OR #2 OR #1

# 13 #10 OR #9 OR #8 OR #7 OR #6

# 14 #13 AND #12 AND #11

