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Management of Acute Non-cirrhotic and Non-malignant Portal Vein Thrombosis: A Systematic Review

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Abstract
Background No definitive evidence exists regarding the treatment of acute portal vein thrombosis (PVT). Treatment modalities described include conservative management, anticoagulation, thrombolysis, and thrombectomy. This review examines the impact of such treatment, its outcomes, and the complications resulting from the resultant portal hypertension.
Methods A Medline literature search was undertaken using the keywords *portal vein thrombosis*, *anticoagulation*, *thrombolysis*, and *thrombectomy*. The primary end point was portal vein recanalization. Secondary outcome measures were morbidity and the development of portal hypertension and its sequelae, including variceal bleeding. Data from articles relating to PVT in the context of cirrhosis, malignancy, or liver transplant were excluded.
Results Early systemic anticoagulation results in complete portal vein recanalization in 38.3% of cases and partial recanalization in 14.0% of cases. Spontaneous recanalization without treatment can only be expected in up to 16.7% of patients. Frequently this is only when associated with self-limiting underlying pathology and/or minimal thrombus extension. Thrombolysis can be associated with major complications in up to 60% of patients.
Conclusions The natural history of acute PVT is poorly described. Spontaneous resolution of acute portal vein thrombosis is uncommon. Early anticoagulation results in a satisfactory rate of recanalization with minimal procedure-associated morbidity. Thrombolysis should be used with caution and only considered if the disease is progressive and signs of mesenteric ischemia are present. Further well-designed trials with precise outcome reporting are needed to improve our understanding of the disease.

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Introduction

Thrombosis of the portal vein relates to thrombosis that develops within the trunk of the portal vein including its right and left intrahepatic branches. Although it may present in isolation, the thrombosis may extend to the superior mesenteric vein and/or splenic vein. It remains an important cause of prehepatic portal hypertension [1]. If the thrombosis involves the mesenteric venous arches and superior mesenteric vein, intestinal ischemia necessitating extensive bowel resection may ensue.

The natural history of acute portal vein thrombosis (PVT) is poorly understood. Clinical manifestations are frequently nonspecific, allowing subclinical acute PVT to progress to chronicity with associated portal hypertensive complications. The etiology of non-cirrhotic, non-malignant, and non-transplant acute PVT is related to a prothrombotic state. This may be due to hypercoagulability or a hypofibrinolytic state. A prothrombotic state can result from a thrombophilia, such as protein C deficiency or antiphospholipid syndrome, or a myeloproliferative disorder (MPD). Abdominal trauma (including surgical intervention, particularly splenectomy for MPD) and abdominal sepsis may also lead to acute PVT due to the increased thrombotic risk and/or pylephlebitis.

Acute PVT must be distinguished from chronic PVT, which is managed differently [2, 3]. Acute PVT can be distinguished radiologically by the absence of venous collaterals and portal cavernoma bypassing the obstructed

segment [1]. At present, there is little consensus regarding the most appropriate management and follow-up of patients with acute PVT. Treatment aims to prevent thrombus extension, produce recanalization of the portal vein, and prevent the complications of chronic PVT.

A number of authors have reported differing degrees of success following management by anticoagulation, thrombolysis, thrombectomy, or a combination of these treatments. Genuine equipoise exists as to the optimal management of acute PVT. Etiologies, including predisposing factors and optimal imaging modalities for the diagnosis of PVT, have been extensively described elsewhere and will not be covered any further in this review. This systematic review aims to appraise the current evidence for the management of non-cirrhotic and non-malignant acute PVT.

Methods

A Medline literature search was undertaken using keywords *portal vein thrombosis*, *anticoagulation*, *thrombolysis*, and *thrombectomy*. The inclusion criteria were studies examining the impact of treatment, or non-treatment, in the management of acute portal vein thrombosis. Search limits were 1950 to December 2010 and English language manuscripts only. Articles relating to PVT in the context of cirrhosis, malignancy, or liver transplant were excluded unless data could be extracted for the non-cirrhotic, malignant, or non-transplant cases. This is because the prognosis in these pathologies is affected by factors not relevant to PVT per se.

Only acute PVT was included, and data relating to patients with the presence of a portal cavernoma or collateralization at diagnosis were excluded. All articles retrieved had the references cross-checked to ensure capture of cited pertinent articles. The primary end point was recanalization of the portal vein. Secondary end points were morbidity, either from PVT management or PVT itself, the development of portal hypertension in follow-up, and its sequelae, including variceal bleeding.

Results

A total of 406 articles were retrieved, and 29 articles that met the inclusion criteria were identified [4–32]. These included a total data set of 315 patients (range: 1–95 patients). Only one study was not a retrospective case series or case study [32]. There were 12 case series [4–15] and 16 case reports [16–31]. There were no randomized controlled trials, and just a single prospective multi-center follow-up study was cited [32]. The period of follow-up varied considerably between 0 and 6 years from diagnosis and was 12 months or more in 15 articles [4–10, 12, 14, 15, 20, 24, 27, 31, 32] and less than 12 months in 7 articles [17, 18, 22, 25, 26, 28, 30]. There was no follow-up stated in 5 articles [16, 19, 21, 23, 29]. Follow-up was mentioned in one article but the duration was not stated [10].

The methods of treating acute PVT described in the literature comprised conservative management, anticoagulation, thrombolysis, and thrombectomy.

Conservative management

Four articles were identified describing patients in whom no anticoagulation was given [5, 9, 22, 32]. This included a total of 12 cases (Table 1), 11 of which were from articles also reporting the outcomes from anticoagulation [5, 9, 22]. The reasons for withholding anticoagulation were unknown in 9/12 patients. Eight additional cases were described when anticoagulation was only started after a significant delay following the onset of symptoms (34–89 days) [5, 22]. Only one case of a patient given antiplatelet medication was included [22].

Of the 12 cases where no treatment was given, 10 (83.3%) remained occluded and recanalization occurred spontaneously in just 2 (16.7%). The two cases where recanalization occurred followed insults that were self-limiting or that resolved. One occurred after a laparoscopic Nissen's fundoplication [22], and the other after an episode of acute pancreatitis [32]. No other prothrombotic conditions were identified in either of these patients. One of these patients had

Table 1 Outcomes of conservative management

Author	Year	Number of patients	Site of thrombus	Outcomes
Davies et al. [22]	2002	1	PV and partial SMV	Recanalization at 3 weeks
Plessier et al. [32]	2010	7[a]	PV ± SV, SMV	1 partial recanalization[b]
Turnes et al. [5]	2008	11	PV ± SV, SMV	No recanalization
Condat et al. [9]	2000	2	PV ± SV, SMV	No recanalization

PV portal vein, *SV* splenic vein, *SMV* superior mesenteric vein

[a] This comprised 2 patients given no anticoagulation, 1 patient given antiplatelet therapy only, and 4 patients to whom anticoagulation was given 34–76 days from diagnosis

[b] In one of the patients given delayed anticoagulation

thrombosis confined to the portal vein [32] and the other had thrombosis of the portal vein and a partial SMV occlusion [22].

Long-term outcomes specific to patients treated conservatively could not be discerned from three articles, as they were combined with patients given anticoagulation or thrombolysis where recanalization did not occur [5, 9, 32].

An article by Baril and colleagues (not included in Table 1, as data for non-malignant pathology could not be extracted) reported a cohort of 44 patients, of which 32 were not anticoagulated for reasons that are not discussed (although 8 had underlying malignancy) [33]. Two patients developed necrotic bowel and a further two died with bowel ischemia. None of the 12 patients who were anticoagulated died or developed ischemic bowel.

Anticoagulation

Fifteen articles were identified relating to anticoagulation used in the management of acute PVT [4–11, 16–21, 31] and included a total of 228 patients (Table 2). Nine of these articles had follow-up of at least 12 months [4–9, 11, 20, 31]. The location and extent of thrombus was variable and in some cases included the splenic and/or superior mesenteric veins. The method of initial anticoagulation differed with both intravenous and subcutaneous administration of heparin being employed. The initiation and duration of oral anticoagulation also varied, and 10 articles described the timing of the initiation of anticoagulation following the onset of symptoms [4, 5, 9, 16–21, 31]. This was within 7 days in five articles [4, 17–20] and between 7 and 30 days in the other five articles [5, 9, 16, 21, 31].

Minor short-term complications directly relating to anticoagulation were described in 3 cases, consisting of a retroperitoneal hemorrhage in 1 patient and 2 gum hemorrhages and/or epistaxis [5, 8], but all responded to non-operative management. In total, 116 (52.3%) patients had a complete ($n = 85$) or partial ($n = 31$) recanalization of the portal vein, equating to 38.3% and 14.0% of patients, respectively.

Recanalization on repeat imaging was observed between 1 week and 197 days following the initial diagnosis. Sheen et al. reported the longest time following diagnosis before resolution of the thrombus, with a median of 197 days [11]. Their article does not state the upper limit and patients were only anticoagulated for 3 months. Anticoagulation was only continued if a prothrombotic disorder was identified. There is, however, a potential time lag following diagnosis when repeat imaging is performed (imaging may be performed some time after recanalization has occurred), which may result in an overestimation of the time taken for resolution of the thrombus. Despite this, as recanalization has been reported up to 197 days from diagnosis, anticoagulation would appear to be indicated for at least 6 months.

Discharging patients on oral anticoagulation was specifically described in nine articles [4–6, 8, 11, 16, 18–20]. Two authors stated that they recommended lifelong anticoagulation if the PVT were associated with a prothrombotic disorder [4, 8]. Oral anticoagulation was lifelong regardless of underlying pathology in two series [5, 20].

The nine articles with at least 12 months of follow-up included 211 patients, and in 42 (19.9%) of these a portal cavernoma developed. Seven articles described the repeat imaging of the portal vein after discharge and therefore this complication may be underestimated [4–6, 10, 17, 18, 31]. One of these articles stated that no patient developed portal hypertension in follow-up, but it failed to state how and at what stage this was assessed [10].

Four authors described the use of endoscopy in patients with persistent portal vein occlusion [5–7, 9]. Varices were observed in 47 patients and an additional 5 patients had developed dilated esophagogastric veins. Upper gastrointestinal bleeds attributable to varices was described in five patients, all of whom had failed to completely recanalize the portal vein. It was not stated if these represent the same cohort of patients in whom a portal cavernoma had developed.

There were 13 cases of ascites [5, 7] and two small bowel resections for structuring [6]. There was also one case of hemorrhage into an ovarian cyst, which occurred 15 months after the initiation of oral anticoagulation and required operative intervention [9]. Oral anticoagulation was substituted for antiplatelet therapy at this point. Of the remaining six articles with no long-term follow-up, cavernous transformation was described in one case. This was in a patient with partial recanalization of the portal vein on repeat imaging 6 weeks from diagnosis [18].

Thrombolysis/thrombectomy

Thirteen articles were identified describing thrombolysis [12–15, 23–31]. Four included thrombectomy in addition to thrombolysis [14, 24, 30, 31] and the total study group was 71 patients (Table 3). In addition all patients received anticoagulation with heparin during treatment and 12 authors described long-term warfarin use on discharge. Thrombolysis was initiated in 34 patients after a failed trial of anticoagulation [12, 14, 15]. Increasing pain or thrombus extension was described as the reason for initiating thrombolytic therapy in these patients. The thrombolytic agent and dose varied as did the mode of administration and the delay in treatment from onset of symptoms, which was between 4 and 60 days.

Recanalization of the portal vein was complete in 29 patients (40.8%), partial in 32 (45.1%), and remained

Table 2 Outcomes of anticoagulation

Author	Year	Number of patients	Site of thrombus	Intervention	Time[a]	Duration of treatment	Days inpatient	Symptomatic improvement
Squizzato et al. [16]	2006	1	Left branch PV	LMWH 8000 IU bd, OA INR 2.5	<1 month	A few days LMWH, 6 months OA	10	N/a. no abdominal symptoms initially
Rahmouni et al. [4]	1992	3	PV ± SV	IV heparin 25–35,000 IU/day, OA	<1 week	OA 5–6 months	–	–
Plessier et al. [32]	2010	95	PV ± SV, SMV	61 had LMWH. 23 had UFH, 11 had OA	<23 days	–	–	–
Louvet et al. [17]	2006	1	Left PV branch and partial R	Tinzaparin 10,000 IU/day for 3 days, fluindione 20 mg/day	<1 week	–	–	1 month
Turnes et al. [5]	2008	27	PV ± SV, SMV	IV or LMWH, OA	<30 days	OA 6 months or lifelong if prothrombotic condition	–	–
Joh and Kim [6]	2005	5	PV ± SMV	Nadroparine Ca 2,850 IU bd in 2 patients, UFH in 1 patient, enoxaparin 40 mg bd in 2 patients	–	OA lifelong	Mean 31 (13–63)	–
Miniati et al. [18]	2005	1	PV, SV and SMV	IV heparin, OA	5 days	6 months OA, few days LMWH	10	5 days
Crowe et al. [19]	1992	1	PV, SV and SMV	IV heparin, OA	4 days	3 months OA	–	Yes but time not specified
Sogaard et al. [7]	2007	17	PV ± SV ± SMV	Not specified, 16/17 "anticoagulated"	–	–	–	–
Amitrano et al. [8]	2007	21	PV ± SV ± SMV	LMWH 200 IU/kg/day, OA	–	6 months OA (lifelong if bowel resection, incomplete recanalization, thrombophilia)	–	–
Condat et al. [9]	2000		PV ± SV ± SMV	IV heparin, OA	Median 14 days (1–30)	28 days–4 months	–	Yes but time not specified
Hegenbarth et al. [20]	2002	1	PV and SMV	Dalteparin 15,000 IU/day, OA	<1 week	Lifelong OA	–	Yes but time not specified
Romano et al. [10]	2006	12	PV ± SV ± SMV	IV heparin, OA	–	–	–	–
Gopal et al. [21]	2009	1	Right branch PV, PV trunk and SMV	5,000 IU heparin tds	7 days	6 weeks 40 mg LMWH, 100 mg aspirin 3 months	20	–
Sheen et al. [11]	2000	9	PV ± unknown	IV hep, OA	–	3 m OA, IV heparin stopped once therapeutic	–	–

Author	Recanalization	Follow-up	Re-imaging for complications	Discharge medication	Authors' recommendation	Complications	
						Short term	Long term
Squizzato et al.	Yes, 7 days on CT	No	No	OA 6 months	–	–	–
Rahmouni et al.	Yes, 2–3 weeks on CT	Yes, 1 year	Yes	OA 6 months	Lifelong OA for PT disorder	–	–
Plessier et al.	Yes, 39% recanalized (38% in the 83 patients with thrombus confined to the portal vein only)	Yes, 1 year	Yes	–	Thrombolysis for those unlikely to recanalize (i.e. with SV thrombus and/or ascites)	–	Portal cavernoma in 40%

Table 2 continued

Author	Recanalization	Follow-up	Re-imaging for complications	Discharge medication	Authors' recommendation	Complications	
						Short term	Long term
Louvet et al.	2 months	2 months MRA no thrombus	Yes, no mention of portal cavernoma specifically	–	–	–	–
Turnes et al.	Yes, in 12/27[b] (6 complete/ 6 partial)	Mean 43 months (6–112)	Yes	OA 6 months	Lifelong OA if PT disorder	1 retroperitoneal haematoma	29/38 had OGD. 55% had varices after 7 months (1–40 months). 4 variceal bleeds in partial recanalization group. Ascites in 5 cases (6–102 months) in non-complete recanalization group
Joh and Kim	All had >50% lysis (time and amount not specified)	Mean 32 months	Yes	OA lifelong	All lifelong OA	–	2/5 developed small bowel stricture; varices developed in 2/5; cavernoma in 4/5
Miniati et al.	6 weeks CT showed cavernoma and persistent thrombus; 6 months CT showed flow in PV but extensive collateralization	6 months	Yes, 6 months	OA 6 months	–	–	–
Crowe et al.	Not stated	Not stated when	no	OA 3 months	–	–	–
Sogaard et al.	10 had "improved portal flow", unknown when checked	39 +/−41 months	No mention of portal cavernoma but had OGD	–	–		29% gastropathy, 24% gastric varices, 47% varices (6% large), 0 variceal bleeds, 47% ascites
Amitrano et al.	45.5% had complete recanalization, unknown when checked	41 months median (3–500)	No mention of portal cavernoma but had OGD	OA for at least 6 months	OA lifelong if PT disorder, bowel resection or incomplete recanalization	Minor bleed in 2 (epistaxis, gum)	Rethrombosis at 22 months
Condat et al.	27 followed up (10 complete/ 15 partial/2 none). 2 with no treatment had no recanalization at mean 4.9 months (range: 0.25–36 months) from diagnosis	30 months mean (0.3–105)	No mention portal cavernoma but had OGD	-	Anticoagulation most beneficial in those with PT disorder as prevents thrombus extension	-	OGD in 23/33, 5 had dilated gastro-esophageal veins. 1 had × 2 variceal bleeds at 2 years;1 hemorrhage into an ovarian cyst
Hegenbarth et al.	2 months MRA showed free PV flow	2.5 years, unknown if imaged	2 months MRA only	OA	Lifelong OA	–	Not stated
Romano et al.	At follow-up 7 patients had recanalization (all started anticoagulation within 15 days from diagnosis)	Yes unknown when	"No portal hypertension" unknown how checked (not stated)	–	–	–	–
Gopal et al.	Day 16 CT greatly resolved	No	No	–	–	–	Not stated
Sheen et al	Median 197 days from diagnosis; resolved in 5/9 patients	49–532 days	No	OA	–	–	Not stated

PV portal vein, *SV* splenic vein, *SMV* superior mesenteric vein, *LMWH* low molecular weight heparin, *OA* oral anticoagulant, *UFH* unfractionated heparin, *IV* intravenous, *PT* prothrombotic, *MRA* magnetic resonance angiography, *CT* computed tomography, *OGD* esosophogastric and duodenoscopy

[a] Time anticoagulation was initiated from diagnosis of acute portal vein thrombosis (PVT)

[b] This was in 10/16 of patients in whom heparin was initiated in the first week and in 2/11 of patients in whom it was initiated after 1 week

Table 3 Outcomes of thrombolysis/thrombectomy

Author	Year	Number of patients	Site of occlusion	Method^	After failed trial of anticoagulation	Intervention	Duration treatment	How soon lysis initiated from diagnosis
Henao et al. [23]	2003	1	SMV and PV	Via SMA	No	Rt-PA 2 mg bolus, 2 mg/h	2 days	Exact unknown, <3 weeks
Wang et al. [12]	2010	16	SMV and PV	Via radial artery	Yes, worsening symptoms	50,000 IU UK continuous, mean total 8.6 million IU	7.1 ± 2.5 days	Mean 9.7 days
Kercher et al. [24]	2002	1	SMV and PV	Transhepatic	No	UK, suction embolectomy and angioplasty	45 h	<6 days
Nakai et al. [25]	2006	1	PV	Transhepatic	No	UK and balloon-occluded retrograde trans-venous obliteration (BRTO) technique.	2 days	–
Tsujikawa et al. [26]	1996	1	SMV and PV	Via SMA	No	Rt-PA 1.6 mil IU/h, then UK 1.2 10*5 IU 14/7	14 days	Unknown <3 weeks
Malkowski et al. [13]	2003	33 (5 had no treatment)	PV	Systemic	No	Rt-PA (5 treated symptomatically only—all died)	1 day	8–60 days
Tateishi et al. [27]	2001	1	PV, mesenteric vein and SV	Systemic and via SMA	No	60,000 U UK/day systemic and 240,000 U UK/day via SMA	–	12 days
Al Haq et al. [28]	1996	1	PV	Systemic	No	250,000 U bolus streptokinase then 100,000/h 3 days	3 days	4 days
Poplausky et al. [29]	1996	1	SMV and PV	Via SMA	No	100,000 U UK/h	2 days	Unknown <3 weeks
Wang et al. [14]	2009	6 (only 2 non-cirrhotic)	SMV and PV	Transjugular intrahepatic	Yes, worsening symptoms	200–300,000 U UK spray and suction embolectomy, 50,000 U/h UK	3–6 days	11–28 days
Rosen and Sheiman [30]	2000	1	SMV and PV	Mechanical thrombectomy and rt-PA via SMA	No	TPA after mechanical thrombectomy	14 h	5 days
Preventza et al. [31]	2005	1	SMV and PV	Thrombectomy	No	Percutaneous transcutaneous PV thrombectomy	–	<1 week
Hollingshead et al. [15]	2005	16	13 had SMV + main PV + intrahepatic PV, 2 SMV only, 1 SMV and PV	Via SMA in 10, via PV in 6	Yes, worsening pain or extension thrombus	Various: UK in 12, rt-PA in 4	2.3–72 h	Mean 14.3 days (range 2–39 days)

Author	Days inpatient	Follow-up	Imaging at follow-up	Clinical improvement	Recanalization	Discharge medication	Complications	
							Long term	Short term
Henao et al.	Not specified	None, 2 days angiogram only	No	After 24 h	Yes, 2 days	OA unknown how long	–	–
Wang et al.	12 ± 6.0	44 ± 18.5 months, no recurrence	Yes	24–36 h	9 complete, 7 partial	Lifelong OA	5 had cavernous transformation PV, 3 mild varices/no bleed	Minor puncture site bleed
Kercher et al.	>6 unknown exact	15 months	Yes 15 months	Not specified	Right PV remained thrombosed	OA unknown how long	None, R PV remained thrombosed at 15/12 follow-up, no portal hypertension	Hematuria/ epistaxis

Table 3 continued

Author	Days inpatient	Follow-up	Imaging at follow-up	Clinical improvement	Recanalization	Discharge medication	Complications	
							Long term	Short term
Nakai et al.	Not specified	6 months CT patent PV	Yes 6 months CT	N/a (asymptomatic)	Yes, 2 days	Not stated	none at 15 months	–
Tsujikawa et al.	Not specified	2 months, CT no thrombus	No	Not specified	Yes, 7 days	OA unknown how long		–
Malkowski et al.	Not specified	9 months to 6 years	Yes	10 patients: 2–5 days in those with symptoms <14 days	Yes in 10. 3 with symptoms of <30 days partial PVT persisted. All patients with >30 days symptoms remained occluded.	OA 12 months	4 deaths (rethrombosis, liver failure, stroke). 8 needed sclerotherapy for varices	–
Tateishi et al.	>46, unknown exactly when	12 months	No	<3 days but thrombus remained therefore via SMA	Thrombosis remained in PV trunk and proximal SMA	Not stated	–	Central line thrombosis, cavernous transformation, laparotomy for partial small bowel stenosis
Al Haq et al.	Not specified	8 months	8 months yes	1 day	Yes, 6 weeks. USS no thrombus	OA 8 months	–	–
Poplausky et al.	Not specified	None	3 weeks only	1 day	Yes, 3 weeks CT showed resolution	OA unknown how long	–	–
Wang et al.	6–14	40 ± 16.5 months (no cavernous transformation)	Yes	12–24 h	Yes, <6 days	Lifelong OA	–	–
Rosen et al.	Not specified	6 months	No	14 h	Yes, 3 days CT	OA unknown how long	–	–
Preventza et al.	Not specified	2 years, unknown if imaging done	No	Not specified	Yes, immediately on USS	OA unknown how long	–	–
Hollingshead et al.	Not specified	Mean 2.3 years (range 0.04–8.5 years)	Yes in some	85% had symptom relief before discharge unknown when	×1 complete, × 4 none, 11 partial (<90%)	OA, heparin, aspirin in × 4	13 had imaging. 11 had cavernoma (all had partial or no lysis) a mean 3.3 months from treatment (range: 0–9 months)	×1 death. × 7 blood transfusion, × 2 intra-abdominal bleed, × 1 perihepatic bleed, × 2 required thrombolysis to stop prematurely. 60% had major and 15% minor complications

PV portal vein, *SV* splenic vein, *SMV* superior mesenteric vein, *SMA* superior mesenteric artery, *rt-PA* tissue plasminogen activator, *UK* urokinase, *CT* computed tomography, *USS* ultrasound, *OA* oral anticoagulant

occluded in 10 patients (14.1%). Procedure related morbidity was described in 15 patients with two reports of a minor puncture site bleed or epistaxis [12, 24]. One patient had a central line thrombosis and also required a laparotomy for partial small bowel stenosis. At laparotomy a membranous covering of the small intestine was found and ablated and no small bowel resection was required [27].

In the study of 16 patients by Hollingshead et al. there were two intra-abdominal hemorrhages, one perihepatic bleed, and two patients had to have their thrombolysis stopped prematurely [15]. This was due to gross hematuria in one case and a falling hematocrit and headaches in the other. Furthermore there was one fatality resulting from sepsis, gastrointestinal hemorrhage and necrotic bowel 2 weeks after thrombolytic therapy. The authors stated that combining thrombolytic therapy with anticoagulation increased the risk of bleeding.

Seven articles had follow-up periods exceeding 12 months in a patient population (across studies) of [12–15, 24, 27, 31]. In these patients cavernous transformation was reported specifically in 16, non-bleeding varices in 11, and re-thrombosis in 1 patient. The monitoring for portal hypertension was described in 50% (7) of articles [12–15, 24, 25, 28]. In an additional article repeat imaging in the follow-up period was only reported at 3 weeks [29]. The lack of specific monitoring is likely to underestimate the frequency of portal hypertension and its associated complications. Of the six articles that did not describe re-imaging for portal hypertension one article comprised a case study where the portal vein remained occluded following intervention [27].

Clinical outcomes according to portal vein recanalization

Five articles were identified that described subgroup data for long-term outcomes of patients with respect to the response to therapy for PVT [5, 6, 9, 13, 18]. Follow-up ranged from 6 months to 6 years, and a total of 111 patients were included. Outcomes are shown in Table 4.

Despite the heterogeneity of the underlying pathology and extent of the thrombus, the results show improved outcomes in patients where complete recanalization of the portal vein occurs compared to those in which it remains occluded. Even a partial recanalization confers some benefits. In the 26 patients with complete recanalization, there were no complications of portal hypertension reported. Partial recanalization was described in 50 patients and in 5 of these, in the article by Joh and Kim, lysis was described as being at least 50% and it is not clear whether some of these may represent complete recanalizations [6]. Varices were encountered in four patients, ascites in two and a small bowel stricture requiring

Table 4 Outcomes as per portal vein recanalization

Author	Year	Follow-up	Management	PV recanalized		PV partially recanalized		PV remained occluded	
				No.	Outcomes	No.	Outcomes	No.	Outcomes
Condat et al. [9]	2000	30 months (0.3–105)	Anticoagulation	10	–	15	×1 developed esophageal varices	4	×1 bleed from esophageal varices 2 years later
Miniati et al. [18]	2005	6 months	Anticoagulation	1	2 months imaging demonstrated thrombus in mesenteric venous plexus At 6 months there was portal flow but extensive collateralization and cavernous transformation.			–	
Joh and Kim [6]	2005	32 months (1–79)	Anticoagulation	6 (1 cirrhotic)	Cavernous transformation in 4 patients, 1 patient had a small bowel stricture requiring resection, esophageal varices in 2. All had >50% thrombus lysis; exact amount unspecified			–	
Malkowski et al. [13]	2003	9 months to 6 years	Thrombolysis	10	–	13	In 8 cases 5 years after recanalization symptoms of portal hypertension occurred. Entered program of prophylactic sclerotherapy	5	Required repetitive endoscopic sclerotherapy of esophageal varices
Turnes et al. [5]	2008	43 months (range: 6–112)	Anticoagulation	6	No varices present	6	Varices present in 1, ascites in 2	26	16 out of 25 had esophageal varices, 3 had ascites

resection in one patient. Eight patients entered a program of sclerotherapy after developing undefined symptoms of portal hypertension [13].

Discussion

The aim of this systematic review was to re-examine the evidence relating to the management of acute PVT in the context of non-cirrhotic, non-malignant, and non-transplant liver pathologies. Four methods of managing acute PVT were identified comprising conservative, thrombolysis, anticoagulation, and thrombectomy.

It is clear that the natural history of acute PVT has not been studied in any detail. Due to the relative rarity of the condition and its unpredictable presentation there are no randomized control trials and therefore no control groups. There is considerable variation in the investigation and diagnosis of acute PVT and in some reports the presence or absence of portal cavernoma at initial diagnostic imaging is not discussed. This is important when portal hypertensive and complications are described at follow-up and interpreting the success of management requires knowledge of any pre-existing pathology. Many studies report outcomes in combination with cirrhotic or malignant causes and data cannot be extracted for other pathologies.

The majority of articles are retrospective case series or case studies and there is no description of a standardized monitoring protocol for complications of acute PVT (frequently no monitoring was reported at all). The studies evaluating thrombolysis often used thrombolytic therapy after failed anticoagulation or worsening symptoms, and therefore comparisons are prone to selection bias. In addition, the time lag from diagnosis to initiating thrombolysis may allow the thrombus to become organized and therefore reduce the therapeutic potential of lytic therapies. This time lag before intervention may allow some acute PVTs to become chronic which cannot be quantified if imaging was not repeated. Although the studies evaluating anticoagulation concluded relatively consistently that they were successful, there are a number of issues which raise questions about the validity of these claims. The numbers of patients given anticoagulation in the reported series is low and due to rarity of acute PVT the time period for patient accrual spans a minimum of 7 and maximum of 17 years [31]. In addition the extent of thrombosis and initiation of treatment from diagnosis varies considerably [34].

The clinical course of acute PVT depends on its evolution, thrombotic extent, and nature of underlying disease processes [5, 8, 9, 13, 34, 35]. Patients with prothrombotic pathologies have increased rates of recurrent thrombosis. Some studies report lower or failed rates of recanalization in patients with two or more etiological factors predisposing to thrombus formation [5]. In addition, the extent of thrombus extension may affect the results and therefore it is difficult to be dogmatic about the prognosis.

Frequently articles report outcomes in combination with cirrhotic or malignant causes and identifying the contribution of other pathologies is impossible. In addition long-term morbidity is not always correlated with the occurrence or extent of recanalization and firm conclusions regarding the effect of early recanalization are therefore difficult to make. Management decisions are frequently individualized depending on the level of local expertise and are not evidence based. In addition, as many reports are case studies or small case series, novel treatment strategies are prone to publication bias.

With conservative management spontaneous recanalization of the portal vein although reported is extremely uncommon [34], and the risk of developing chronic portal hypertension and its associated complications appear to be high. Where spontaneous recanalization has been described, the underlying cause of the PVT was generally a self-limiting condition, with no underlying prothrombotic disease, less extensive thrombus and no permanent anatomical consequences [22, 32]. Spontaneous recanalization is more likely in these patients, which again highlights the difficulties associated with the heterogeneity of articles reporting outcomes of acute PVT. This heterogeneity of patients combined with the lack of standardized monitoring means that guidelines for management can only be grade C or D recommendations.

Anticoagulation following acute PVT results in complete and partial recanalization of the portal vein in 38.3% and 14.0%, respectively, and no mortality has been reported associated with the procedure. The only morbidity described was minor hemorrhage which required only conservative management and one ovarian cyst hemorrhage which although requiring operative management had a favorable outcome. The timing of the initial anticoagulant therapy following diagnosis varied between 1 and 30 days and was not stated in five articles. Delay appears to be significant as several authors describe reduced efficacy of the anticoagulation as a direct consequence [5, 31, 34]. The outcome of treatment, specifically in respect of achieving recanalization, is not always reported relative to the time from diagnosis to the beginning of treatment.

Although the methods of anticoagulation vary and included intravenous and subcutaneous administration of heparin and oral anticoagulation, Plessier et al. concluded that the type of anticoagulation used was not important [31]. Subcutaneous low molecular weight heparin (LMWH) has a more predictable dose response, a lower risk of bleeding and is as effective and safe as intravenous heparin [34] and it is appropriate to initiate such therapy early in the majority of cases. There are, however, exceptions and

clinical judgment is required. If the thrombosis occurs in the immediate postoperative period or follows an episode of hemorrhagic pancreatitis then the risk of hemorrhagic complications are significantly increased and a careful, balanced assessment of relative risk (which will reduce with time) is required.

Studies which have examined thrombolytic therapy for PVT are prone to publication bias and major complications are reported in up to 60% of cases [15]. There was however consensus among several authors that such therapy should only be considered if there were no improvement in symptoms or there was extensive disease with propagation of the thrombus [12, 15]. Although exact figures are not available the mortality rate from acute PVT, is not high enough to justify this high-risk treatment in the initial management of the disease. Authors report mortality from acute PVT as a consequence of the underlying disease as opposed to the PVT itself [5–7, 9, 31].

There is also little data regarding the monitoring of patients with acute PVT. The frequency of portal hypertension-related complications is higher in those with incomplete or no recanalization. Early recanalization is therefore important to reduce the risk of subsequent variceal bleeding [34]. Varices may develop as early as one month after acute PVT and therefore surveillance from this point onward is appropriate [34]. In patients with chronic PVT or portal cavernoma formation, upper gastrointestinal endoscopy demonstrates varices in 20%–55% of cases [34]. We believe that all patients require follow up after acute PVT irrespective of the outcome of the treatment. The most appropriate method of surveillance for these patients at risk of complications from portal hypertensive is unknown but should probably be more rigorous in those who fail to recanalize the portal vein.

From the data presented in this systematic review it is possible to conclude that spontaneous resolution of acute PVT is uncommon. Acute PVT can be recanalized completely in 38.3% and partially in 14.0% of patients with early administration of systemic anticoagulants. Subcutaneous heparin appears to be as effective as intravenous heparin (until oral anticoagulation is initiated) and has the added advantage of a safer side effect profile and requires no monitoring. Treatment is recommended for at least 6 months and oral anticoagulants should be administered for life in patients with prothrombotic disease. Percutaneous thrombolysis of the portal vein can be considered with caution if recent acute PVT is progressive and signs of ischemia are present. Such intervention has been associated with major complications in up to 60% and when used with anticoagulation the risk of hemorrhage is increased. Patients with PVT should be followed up after the acute event for signs of portal hypertension even if the outcome of treatment was complete recanalization.

The reporting of future studies describing the management of acute PVT could be improved in order to improve study homogeneity. Attempts must be made to control for the underlying pathology and thrombus extension and follow-up must be reported in relation to treatment outcome so that the natural history of acute PVT may be understood more clearly. Currently the proportion of patients who progress to chronic PVT following an acute episode is unknown. The results of the treatment of acute PVT depend on a number of variables that influence the outcome including thrombus extension, underlying pathology and delays in initiating anticoagulation following diagnosis. Further well-designed studies, where outcomes are clearly reported and treatments are protocol driven rather than on an individual basis, are needed to improve our understanding of the disease process and allow us to be dogmatic about the best method of treatment.

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