Acute Portal Vein Thrombosis Unrelated to Cirrhosis: A Prospective Multicenter Follow-up Study

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Current recommendations for early anticoagulation in acute portal vein thrombosis unrelated to cirrhosis or malignancy are based on limited evidence. The aim of this study was to prospectively assess the risk factors, outcome, and prognosis in patients managed according to these recommendations. We enrolled 102 patients with acute thrombosis of the portal vein, or its left or right branch. Laboratory investigations for prothrombotic factors were centralized. Thrombus extension and recanalization were assessed by expert radiologists. A local risk factor was identified in 21% of patients, and one or several general prothrombotic conditions in 52%. Anticoagulation was given to 95 patients. After a median of 234 days, the portal vein and its left or right branch were patent in 39% of anticoagulated patients (versus 13% initially), the splenic vein in 80% (versus 57% initially), and the superior mesenteric vein in 73% (versus 42% initially). Failure to recanalize the portal vein was independently related to the presence of ascites (hazard ratio 3.8, 95% confidence interval 1.3-11.1) and an occluded splenic vein (hazard ratio 3.5, 95% confidence interval 1.4-8.9). Gastrointestinal bleeding and intestinal infarction occurred in nine and two patients, respectively. Two patients died from causes unrelated to thrombosis or anticoagulation therapy. *Conclusion:* Recanalization occurs in one-third of patients receiving early anticoagulation for acute portal vein thrombosis, whereas thrombus extension, intestinal infarction, severe bleeding, and death are rare. Alternative therapy should be considered when ascites and splenic vein obstruction are present. (HEPATOLOGY **2010;51:210-218.**)

Acute portal vein thrombosis (PVT) is characterized by the recent development of a thrombus in the portal vein or its left or right branches.[1,2] Extension to mesenteric venous arches causes intestinal infarction, with a reported mortality of up to 50%.[3,4] Without recanalization, a cavernoma develops, associated with a permanent risk of potentially fatal gastrointestinal bleeding, recurrent thrombosis, or biliary obstruction.[1,5,7] Recanalization is therefore a major goal for the treatment of acute PVT and is often a pressing challenge, because most PVT cases are recognized at the acute stage.[8] Expert panels have recommended early anticoagulation therapy for acute PVT.[2] However, these recommendations are based on small retrospective cohort studies performed over several decades.[9-11]

The aim of this study was to prospectively assess (1) patient characteristics of those presenting with acute PVT unrelated to cirrhosis or malignancy; (2) the incidence and predictive factors of recanalization in patients managed according to recent recommendations; and (3) the incidence of disease- and treatment-related complications.

Patients and Methods

Between October 2003 and October 2005, incident cases of acute PVT were enrolled in seven European coun-

Abbreviations: CI, confidence interval; HR, hazard ratio; PVT, portal vein thrombosis, MPD, myeloproliferative disorder.

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tries (Belgium, France, Germany, Italy, The Netherlands, Spain, and Switzerland). Diagnostic criteria were imaging evidence of solid material in the portal vein lumen or in its left or right branch, and the absence of porto-portal collaterals. Thus, all patients with portal vein cavernoma were excluded. In case of disagreement, diagnostic procedures were ranked in the following order of decreasing accuracy: computerized tomography, magnetic resonance imaging, and Doppler ultrasound. Patients with cirrhosis, variceal bleeding, or abdominal malignancies were excluded on the basis of history, clinical and laboratory findings, and imaging of the liver, bile ducts, pancreas, and other abdominal organs based on a central review of imaging studies. Specifically, we excluded patients with biopsy-proven cirrhosis or with clinical, laboratory, or imaging evidence of chronic liver disease, within a context of chronic alcoholism, viral hepatitis, autoimmunity, Wilson's disease, iron overload, or Budd-Chiari syndrome. The following features were considered suggestive for cirrhosis unless liver biopsy proved it to be absent: past history of ascites or encephalopathy, presence of spider angiomata, jaundice, encephalopathy, nodular surface of the liver, portosystemic collaterals (including gastroesophageal varices), decreased prothrombin or serum albumin levels, and increased serum bilirubin level. Patients with unexplained clinical features of chronic liver disease or alterations of liver tests or liver imaging were included only when cirrhosis was ruled out by liver biopsy.

Patients were managed by their referring specialists in contact with national coordinating centers. Protocol recommendations included (1) a comprehensive evaluation of local and general risk factors for thrombosis; (2) blood sampling for centralized plasma and DNA storage; (3) early initiation of heparin therapy followed by oral anticoagulation targeting an international normalized ratio of 2 to 3, according to current recommendations for deep vein thrombosis (5th American College of Chest Physicians Guidelines for Deep Vein Thrombosis)[12]; (4) 6 months of anticoagulation therapy, prolonged to long-term if a permanent prothrombotic disorder was found and/or the mesenteric vein was obstructed; and (5) clinical, laboratory, and radiological follow-up examinations. However, the final choice of the type and duration of anticoagulation treatment was left to the judgment of the referring specialist according to the risk of bleeding based on past and recent history; the possible need for urgent invasive therapy for local factors; and a history of intolerance to heparin. Therefore, patients were included in the descriptive analyses but excluded from the therapeutic and prognostic analyses if they received only antiplatelet agents, were not given anticoagulation, or were given anticoagulation beyond 30 days after the retrospectively defined date of diagnosis (as defined below).

Definitions. Date of diagnosis corresponded to the date of the imaging study where diagnostic criteria were met after centralized review. As a result, in some patients, the date of diagnosis could precede or follow by a few days the date when the clinical diagnosis was actually made. Radiological images were collected and reviewed by expert radiologists during a centralized national review. The following segments were examined: portal vein, right and left portal vein branches, and terminal segment of the superior mesenteric and splenic veins. Patency was defined as visualization of a completely normal venous segment; obstruction as the presence of solid material in the vascular lumen or obliteration of the normal lumen; and recanalization as the normal appearance of a previously obstructed segment. Cavernoma was defined as the presence of clear porto-portal collaterals. A diagnosis of mesenteric infarction was based on evidence in a pathology specimen.

Follow-up and Data Collection. Patients were followed from the date of diagnosis until death, study closure (May 1, 2006), or the date of the last visit. Clinical, laboratory and radiological data were collected at diagnosis, at predefined intervals (1, 3, 6, 12, 18, 24 months), and during significant clinical events. Blood samples were obtained for centralized etiological workup. Risk factors for thrombosis were investigated as described.[13,14] All collected data were confirmed by national and international experts before freezing for analyses.

Endpoints. Endpoints included: (1) patency of the portal vein trunk and at least one of its main right or left branches as a result of recanalization or lack of extension; (2) patency of the superior mesenteric and splenic veins; and (3) bleeding, intestinal infarction, or death. For any venous segment, patency may thus correspond to the absence of extension of thrombosis to this segment if initially patent, or to recanalization if initially obstructed.

Statistical Analyses. Quantitative variables are expressed as the mean ($\pm$ standard error), or median and range, and qualitative variables as absolute and relative frequencies. Comparisons between groups of quantitative and qualitative variables were made by the Wilcoxon and chi square tests, respectively. Recanalization rates were assessed using Cox models. Independent predictive factors for lack of recanalization were assessed with Cox model regression. Overall survival rates were assessed by the Kaplan-Meier method. Comparisons of recanalization rates with risk factors were made by the log rank test. All tests were two-sided, and $P < 0.05$ was considered significant. Data handling and analysis were performed with SPSS version 12.0 software (SPSS Inc., Chicago, IL).

Table 1. Clinical and Radiological Characteristics at Diagnosis in 102 Patients with Acute PVT

Sex, female/male	50/52
Age, median (range)	48 (16–84)
Abdominal pain, n (%)	93 (91)
Fever, n (%)	54 (53)
Ascites, n (%)	39 (38)
Small volume ascites,* n (%)	34 (33)**
Clinical ascites, n (%)	5 (5)
Splenomegaly at imaging, n (%)	38 (37)
Hepatomegaly at imaging, n (%)	25 (25)
Prothrombin ratio, %, median (range)	84 (27–114)
Serum bilirubin, μmol/L, median (range)	15 (2–207)
Alanine aminotransferase, median (range)	46 (13–1,484)
Serum creatinine, μmol/L, median (range)	76 (28–163)
Hemoglobin, mmol/L, median (range)	8 (3–12.5)
Leukocytes, 10^9/L, median (range)	9.3 (1–34)
Platelets, 10^9/L, median (range)	274 (55–949)
C-reactive protein, UI, median (range)	52 (1–529)
Elevated C-reactive protein or fever, n (%)	86 (84)

*Only visible at imaging.
**86% of total ascites.

The study was approved by all national and, if necessary, local ethics committees. All enrolled patients agreed to participate by completing a written informed consent form after receiving complete oral and written information.

Results

One patient refused to be included in the study. Out of 138 consecutive consenting patients with noncirrhotic portal vein thrombosis, 36 were excluded for the following reasons: presentation with a portal cavernoma (n = 33), or with ruptured esophageal varices (n = 3). Seven patients were included in the descriptive analysis, but were excluded from the therapeutic and prognostic analyses: one received low-dose aspirin, four patients had anticoagulation introduced more than 30 days after diagnosis (at day 35, 55, 65, and 76, respectively), and two have not received anticoagulation. Therefore, 102 patients were included in the descriptive analysis and 95 patients in the therapeutic and prognostic analysis.

Patient Characteristics at Diagnosis

One hundred two patients were enrolled and followed-up for a median of 242 days (range, 0-904 days): eight in Belgium, four in Germany, 16 in Italy, 42 in France, 19 in The Netherlands, eight in Spain, and five in Switzerland. Three patients were lost to follow-up before the protocol 1-month evaluation.

The main features at diagnosis are presented in Table 1. Most patients had fever or elevated C-reactive protein levels, with or without an inflammatory focus. Moderate yet clinically detectable ascites was observed in only five patients, two of whom developed intestinal infarction. However, clinically undetectable ascites was detected at imaging in 34 patients. The presence of ascites was not associated to atrophy–hypertrophy complex, jaundice, splenomegaly, time to diagnosis, or time to treatment. Splenomegaly was present in 38 (37%) patients, 15 of whom (40%) had a myeloproliferative disorder (MPD), whereas among the 64 patients without splenomegaly, only five (8%) had an MPD ($P = 0.001$, chi square test). Splenomegaly was not associated with atrophy–hypertrophy complex, jaundice, ascites, splenic vein thrombosis, time to diagnosis, or time to initiation of therapy.

As shown in Table 2, at least one general risk factor for venous thrombosis (excluding exogenous oestrogens or progestatives and systemic inflammation) and local factors were found in 52% and 21% of patients, respectively. Obliterative portal venopathy as characterized by Ludwig et al.[15] was found in three of the 16 patients who underwent liver biopsy, and pure nodular regenerative hyperplasia, small duct sclerosing cholangitis without fibrosis, and bacterial cholangitis was found in one patient each. The remaining 10 patients had histologically normal liver and bile ducts.

Treatment

Anticoagulation was administered to 95 patients (93%) for a median duration of 234 days (range, 7-937 days). Median interval from first symptoms to start of treatment was 13 days (range, 0-140 days), and from diagnosis to treatment was 0 days (range, −7 to 21 days) (Fig. 1). Three patients, for whom portal vein thrombosis was suspected on clinical and ultrasound data, had had anticoagulation initiation 7, 5, and 3 days respectively prior to diagnosis confirmation with computed tomography.

Initial treatment was heparin in 84 patients (unfractionated heparin in 23 patients, low molecular weight heparin in 61 patients), and vitamin K antagonists in 11. A transjugular intrahepatic portosystemic shunt was inserted in one patient who also received anticoagulation treatment and thrombolysis.

Portal Venous Obstruction at Diagnosis in the 95 Patients Receiving Anticoagulation

Obstruction of the portal vein or of its two branches was found in 83 patients (87%). The 12 remaining patients had only a single obstructed portal vein branch (with or without splenic or superior mesenteric vein obstruction) were all symptomatic. Seven patients had only left or right portal vein thrombosis. All had clinical symptoms. The splenic vein or the superior mesenteric vein

Table 2. Risk Factors Identified at Diagnosis in 102 Patients with Acute PVT

	Number Tested	Number Positive	Number Positive/Number Tested (%)
Myeloproliferative disease	102	21	21
JAK 2–positive	82	14	16
Antiphospholipid syndrome	90	8	8
Protein C deficiency	86	1	1
Protein S deficiency	85	5	5
Antithrombin deficiency	89	2	2
Prothrombine gene mutation	98	14	14
Factor V Leiden	94	3	3
Homozygous MTHFR mutation	78	9	11
Hyperhomocysteinemia	69	8	11
Number of prothrombotic disorders, 0/1/2		49/43/10	48/42/10
Connective tissue disease	101	4	4
Hormonal contraception or replacement therapy, n (%)	50	22	44
Personal history of deep vein thrombosis	100	14	14
Family history of deep vein thrombosis	96	23	24
Local factor*	102	22	21
Acute Pancreatitis		8	8
Cholecystis or cholangitis		6	6
Liver abscess		5	5
Gastritis		2	2
Inflammatory bowel disease		1	1
Diverticulitis		1	1
Cytomegalovirus hepatitis		1	1
Abdominal trauma		1	1
General prothrombotic disorder in patients with a local factor		8	36
No causal factor		25	25

*Patients may have two local factors.

were obstructed in 41 (43%) and 55 (58%) patients, respectively. Extensive obstruction of the portal vein and its right and left branches, superior mesenteric vein, and splenic vein was found in 28 patients (29%).

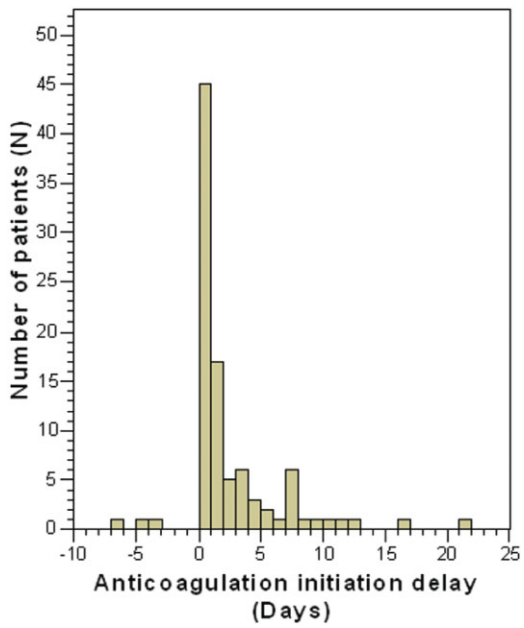

Fig. 1. Distribution of time from diagnosis to initiation of anticoagulation therapy. Date of diagnosis was the date when imaging diagnostic criteria were fulfilled at central retrospective review.

Outcome in the 95 Patients Receiving Anticoagulation

Patency of Portal Venous Segments at the End of Follow-up. Figure 2 shows the outcome of venous obstruction compared with initial findings. Compared with baseline, the prevalence of obstruction decreased by 30% for the portal vein or its two main branches, 54% for the splenic vein, 53% for the superior mesenteric vein, and 54% for simultaneous obstruction of all above veins. The portal venous system was completely patent in 19 patients. A portal cavernoma developed in 38 patients.

None of the 12 patients with obstruction of a single portal vein branch developed obstruction of the portal vein or both branches. There was no extension to the mesenteric or splenic vein during follow up.

Recanalization of the Portal Vein Trunk and/or Main Branches. Figure 3 shows that the 1-year recanalization rate was 38% in the 83 patients with initial obstruction of the portal vein or both branches. Recanalization did not occur in any of the patients beyond the sixth month after anticoagulation treatment was initiated. Univariate analysis revealed that factors predicting failure of recanalization were ascites detected clinically or at imaging (hazard ratio [HR] 4.4, 95% confidence interval [CI] 1.5-12.8); the presence of the V617F-JAK2 mutation (HR 2.4, 95% CI 1.3-4.7); duration of antico-

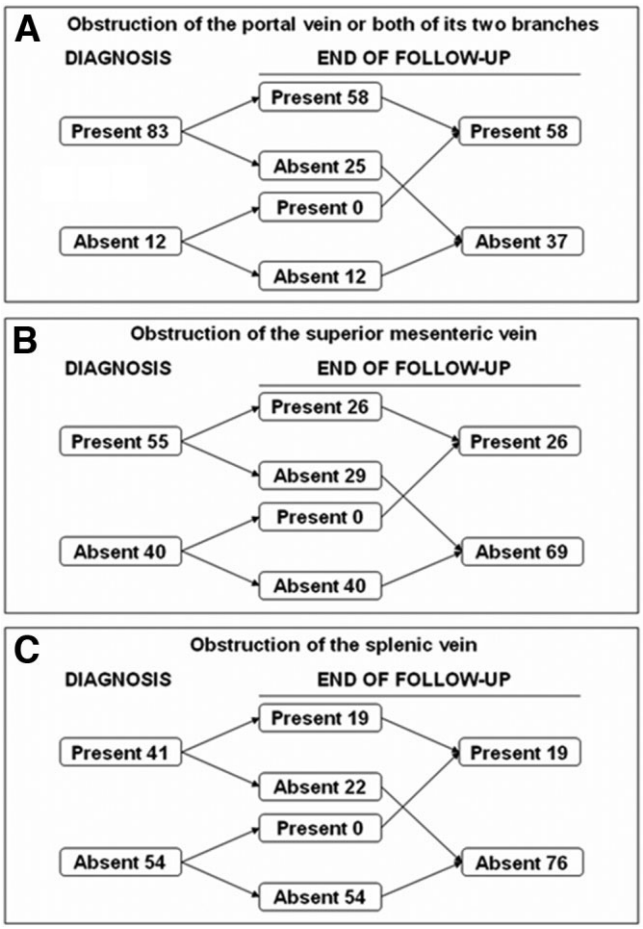

Fig. 2. Distribution of obstructed venous segments at diagnosis and at the end of follow-up in 95 patients receiving anticoagulation therapy. (A) Portal vein or both its branches. (B) Superior mesenteric vein. (C) Splenic vein. Recanalization corresponds to present at diagnosis and absent at the end of follow-up. Nonprogression corresponds to absent at diagnosis and at the end of follow-up.

agulation therapy (HR 1.01, 95% CI 1.001-1.007); splenic vein obstruction (HR 4, 95% CI 1.6-10.1); and superior mesenteric vein obstruction (HR 3, 95% CI 1.3-6). Factors predicting recanalization were familial history of venous thrombosis (HR 2.3, 95% CI 1.1-5). The outcome did not differ according to the type or number of thrombotic risk factors or the timing of anticoagulation treatment from first symptoms (heparin-based treatment initiated within 7 days in 26 patients, or between 7 and 30 days in 58 patients). The only independent factors found at multivariate analysis were ascites (assessed clinically or at imaging) (HR 3.8, 95% CI 1.3-11.1) and splenic vein obstruction (HR 3.5, 95% CI 1.4-8.9). Figure 4 shows that recanalization did not occur in any of the 19 patients with both splenic vein obstruction and ascites.

Recanalization of Splenic Vein or Mesenteric Veins. Figure 3 shows that the 1-year recanalization rate was 61% for the superior mesenteric vein, and 54% for the splenic vein. There was no apparent plateau in recanalization over time for these two veins. Patient characteristics were not significantly different in those with recanalization and those without (data not shown). Among the 13 patients in whom recanalization of the mesenteric vein was documented to occur after 6 months, nine were still on anticoagulation. Among the eight patients who had recanalization of the splenic vein documented after 6 months, five were still on anticoagulation.

Outcome in Patients Not Receiving Early Anticoagulation Therapy

Two patients did not receive anticoagulation therapy. One of these patients had acute pancreatitis as the only cause of portal vein obstruction; he fully recovered with a patent portal venous system. The other patient had the lupus anticoagulant and had persisting occlusion of the left portal vein at the end of follow-up. One patient receiving only antiplatelet therapy did not recanalize. Among the four patients who had anticoagulation initiated 34 to 76 days after diagnosis; none recanalized the portal vein. Partial recanalization was observed in only one of these four patients: he had portal, mesenteric and right portal branch obstruction, was treated 65 days after diagnosis, and recanalized the mesenteric vein and the right portal branch.

Bleeding, Intestinal Infarction, and Death in Patients Receiving Anticoagulation Therapy

Bleeding occurred in nine of the 95 patients (gastrointestinal or nasal in seven, intra-abdominal in one, bone marrow biopsy-related hematoma in one). Bleeding required transfusion or a prolonged hospital stay in five patients. There were no bleeding-related mortalities. Two patients who developed mesenteric infarction 6 and 12 days after beginning anticoagulation underwent 140-cm-long and 40-cm-long intestinal resection, respectively. Both patients survived with good clinical outcome. Two patients died: one from sepsis 14 months after diagnosis, and one from cholangiocarcinoma that was undetectable upon review of an initial computed tomography scan but was diagnosed 6 months after PVT.

Discussion

This study in 102 patients with acute PVT prospectively enrolled over a period of 2 years clarifies manifestations, etiology, and outcome of anticoagulation therapy in this disease. Previously reported studies on acute PVT (most of them coming from centers participating to this consortium)[8,10,11] yielded relatively consistent results which have based the current recommendation for man-

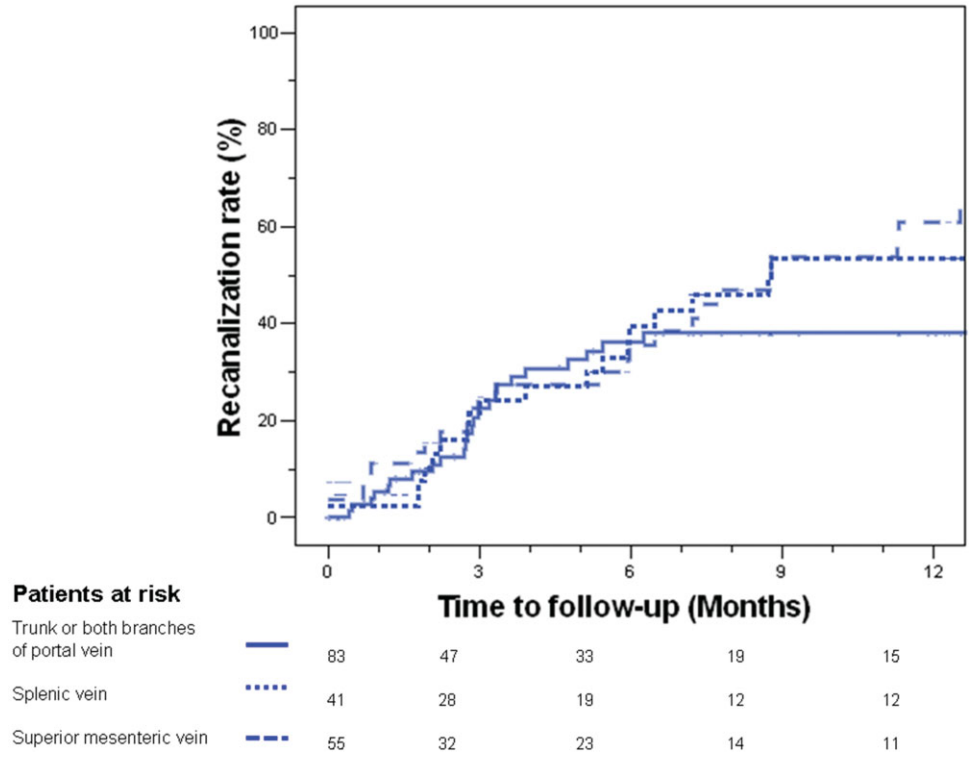

Fig. 3. Recanalization rate in anticoagulated patients with initial obstruction of portal vein or both its main branches (n = 83), superior mesenteric vein (n = 55), or splenic vein (n = 41).

agement.[2] However, these and subsequent studies[7,9,16] all suffered from limitations that questioned the validity of their interpretation, and inspired the design of the present collaborative study. First, the number of patients given anticoagulation therapy was low (27 in the largest of these former studies).[11] Second, the time period for patients' accrual spanned 7 to 17 years. Third, a formal evaluation of the initial aspect of acute thrombosis and of the extent of the obstructed segments was not based on predefined standardized criteria and expert review. Fourth, investigations for causes were neither comprehensive, nor did they always use the most accurate tests (such as the assessment of V617F JAK2 mutation). Finally, a referral bias in tertiary centers could not be ruled out, whereas the present study was based on patients' identification through nationwide networks.

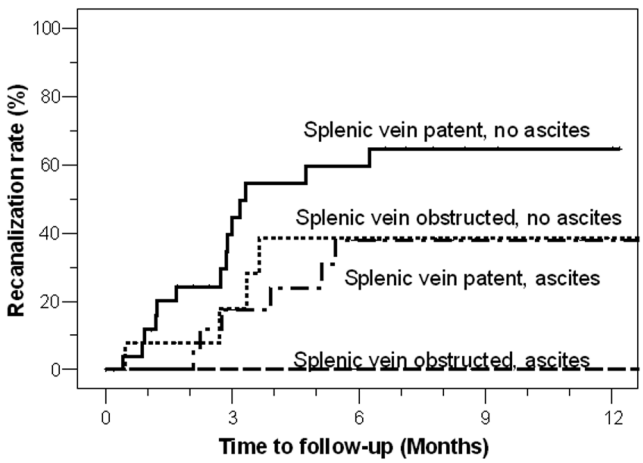

Fig. 4. Cumulative rates of recanalization on anticoagulation therapy in patients according to whether splenic vein was obstructed or permeable, and whether ascites was present or absent at imaging. All patients had initial obstruction of the portal vein or both its branches. Recanalization corresponds to full patency of the portal vein and at least one main branch at the end of follow-up.

Our study is a prospective, multicenter European study including 4 times as many patients as any of the previous studies, in a defined period of 2 years. All patients had a clearly visible thrombus in the absence of cavernoma (which usually develops in a few weeks in the absence of recanalization) and most had symptoms of an acute illness. Although extension of the thrombus was not a criterion for inclusion, enrolled patients suffered from a severe form of the disease. Indeed, the extrahepatic portal vein was completely blocked in approximately 90% of patients who were thus at risk of permanent portal hypertension. Furthermore, two-thirds of the patients had superior mesenteric vein involvement and were thus at of risk intestinal infarction.

The present cohort differs from previous reports by a yet unnoticed, high prevalence of ascites and spleen enlargement. This finding is probably related in a large part to a systematic central review of images. Ascitic fluid was frequently detected at early imaging, although clinically detectable ascites was rare. Ascites has been reported to

herald intestinal infarction in patients with mesenteric vein thrombosis,[17] which was confirmed in the present study with respect to clinically detectable ascites, although not with ascites that could be detected only at imaging. Spleen enlargement was shown here to be related in part to an underlying MPD, and possibly to acute congestion. Liver biopsy was not routinely performed for obvious ethical reasons in candidates for early anticoagulation. However, underlying cirrhosis was ruled out as an explanation for ascites and spleen enlargement. Indeed, we excluded patients with known causal factors for cirrhosis, or a portosystemic collateral circulation (including esophageal varices), or laboratory evidence of liver insufficiency, or a nodular liver at imaging, all features with a high negative predictive value.[18] Actually, none of the patients who eventually had a liver biopsy were found to have cirrhosis. However, we cannot fully exclude that a proportion of the patients had a certain degree of intrahepatic portal venous obstruction preceding the development of acute extrahepatic PVT.

Previous retrospective studies have identified local factors in 25% of acute PVT patients. The results in this prospective study were similar (21%), meaning that the reason why thrombosis develops in this particular vein remains unanswered in most patients**.** However, this study suggests that intrahepatic vascular disease is an underestimated risk factor for acute PVT.[19] Obliterative portal venopathy or nodular regenerative hyperplasia was documented in only 3% of patients. However, intrahepatic vascular disease accounted for 25% of those who underwent liver biopsy, because there were some anomalies in liver tests or imaging. Using comprehensive investigations with updated tools, a general risk factor for venous thrombosis was identified in 52% of patients. There was a predominance of MPD (21% of patients), G20210A prothrombin gene mutation (14%), and antiphospholipid syndrome (9%). Thirty-six percent of patients had a local factor with a general risk factor, and 25% had no identified factor. These results support the recommendation that all acute PVT patients—with or without local factors—should be investigated for prothrombotic disorders and considered for early anticoagulation without waiting for test results.

A randomized controlled trial of anticoagulation for acute PVT is not realistic due to the rarity and heterogeneity of this disorder. This study has clarified the overall outcome of early anticoagulation therapy using homogeneous inclusion criteria and endpoints. Treatment recommendations were closely followed so that only seven patients could not receive early anticoagulation therapy. Eighty-nine percent of the anticoagulated patients received heparin-based therapy, and 83% had anticoagulation initiated within 5 days of diagnosis. The main outcomes were an absence of thrombus extension, and a high rate of recanalization. Furthermore, the incidence of intestinal infarction was only 3% in patients with superior mesenteric vein obstruction. This is similar to results in a medical series of 33 patients treated with early anticoagulation,[11] but much lower than in unselected or surgical patients (20%-50%) who did not all receive anticoagulation.[4] Analyses of suboptimal power failed to disclose any differences according to the type of anticoagulation agents or the delay in initiating anticoagulation. However, according to the current data on treatment of deep vein thrombosis,[20] somewhat higher rates of recanalization without increased risk of bleeding could be expected from even earlier initiation of heparin-based therapy in all patients. If this proved true for portal vein thrombosis, hasting recognition and therapy of this rare condition, would be crucial for improving results on a population basis.

Although a recovered patency of the portal vein and at least one main branch was reached in one-third of patients receiving anticoagulation therapy, obstruction of the portal vein or both of its two main branches persisted until the end of follow-up in the rest. The latter patients will probably develop permanent portal hypertension because no recanalization occurred between 6 and 12 months after anticoagulation began. Indeed, a portal cavernoma had already developed in 40% of patients by the end of follow-up. Thus, early anticoagulation is less effective in inducing recanalization of complete extrahepatic portal vein obstruction than in preventing extension to or from the portal vein. Nevertheless, recanalization rates approached 60% in superior mesenteric and splenic veins. This outcome is clinically significant, because a preserved mesenteric vein is a major predictor of long-term survival.[21] Moreover, recanalization of these veins steadily increased during follow-up. Further studies are needed to assess whether anticoagulation should be maintained until recanalization of these veins. Finally, the absence of PVT-related deaths in this cohort is remarkable, especially because most of these patients had extensive thrombosis of the portal venous system at inclusion.[21]

In patients with acute PVT, the baseline risk of bleeding can be increased by portal hypertension and intestinal ischemia. Although 5% of our patients experienced major bleeding, there were no bleeding-related deaths. It should be noted that this rate of severe bleeding is similar to that observed with anticoagulation for deep vein thrombosis at other sites.[22]

Multivariate analyses disclosed that patients with a combination of splenic vein obstruction and ascites have very little chance of recanalization during antico-

agulation. It is noteworthy that underlying risk factors for venous thrombosis did not bring additional independent information. Furthermore, the type of anticoagulation initially given (unfractionated heparin, low-molecular-weight heparin, or oral vitamin K antagonists) did not appear to impact on recanalization. Additional or alternative therapeutic options should be considered to increase the recanalization rate, but current options include high-risk procedures. Pharmacological or instrumental thrombolysis have recently been proposed by a direct, percutaneous transhepatic approach to the portal vein, or by superior mesenteric artery catherization.[4,23-25] These invasive, poorly evaluated procedures should only be considered for patients with the least chance of recanalization during anticoagulation therapy. Hence, the simple and powerful independent predictors of recanalization identified in this study are an important clinical tool. Patients with a combination of splenic vein obstruction and ascites could be candidates for alternative treatment. However, the low mortality rate of chronic PVT should also be considered when deciding on invasive therapy during acute stage PVT.[1] In these patients, new anticoagulant agents may be worth testing in controlled trials. Furthermore, an interaction between the type of underlying risk factor for thrombosis and the type of anticoagulant agent to be given should be investigated.

In conclusion, this study supports early anticoagulation of patients with acute PVT because of the high prevalence of permanent risk factors for venous thrombosis; the absence of thrombus extension, the limited number of cases with intestinal infarction; the high rate of splanchnic vein recanalization; and the low rate of severe bleeding. However, in patients with splenic vein thrombosis and ascites detected at imaging, recanalization on anticoagulation is unlikely, and thus other treatment options should be considered.

APPENDIX

The following investigators comprised the European Network for Vascular Disorders of the Liver (EN-Vie) Scientific Board: Mathias Bahr (Hannover, Germany), Elwyn Elias (Birmingham, United Kingdom), Joan-Carlos Garcia-Pagan (Barcelona, Spain), Antoine Hadengue (Geneva, Switzerland), Harry L.A. Janssen (Rotterdam, The Netherlands), Philippe Langlet (Brussels, Belgium), Helena Miranda (Porto, Portugal), Massimo Primignani (Milan, Italy), and Dominique Valla (Clichy, France).

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