Chronic Mesenteric Venous Thrombosis: Evaluation and Determinants of Survival During Long-Term Follow-up

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Background & Aims: **The natural history of chronic portomesenteric (PM) and portosplenomesenteric (PSM) venous thrombosis is defined poorly. Therapeutic options are limited, and are directed at the prevention of variceal bleeding and the control of abdominal pain related to gastrointestinal hyperemia.** ***Methods:*** **Patients with extensive PM and PSM thrombosis were reviewed retrospectively to evaluate the efficacy of medical therapy and to determine which clinical variables had prognostic significance regarding long-term survival.** ***Results:*** **Sixty patients, with a median age at diagnosis of 44 years (range, 18–68 y), were assessed. The median follow-up period was 3.5 years (range, 0.2–32.0 y). The overall survival rate was 73.3%, with 1- and 5-year survival rates of 81.6%, and 78.3%, respectively. One- and 5-year survival rates, excluding patients who died from malignancy-related causes, were 85.7% and 82.1%, respectively. Factors associated with improved survival included treatment with β-blockers (P = .02; odds ratio [OR], .09; 95% confidence interval [CI], 0.01–0.70) and anticoagulation (P = .005; OR, 0.01; 95% CI, <0.01 to 0.26). Eighteen patients in total were anticoagulated, including 8 patients who had variceal bleeding, all of whom underwent endoscopic band ligation of esophageal varices before anticoagulation. By using Cox regression analysis, variables associated with reduced survival were the presence of ascites (P = .001; OR, 42.6; 95% CI, 5.03–360), and hyperbilirubinemia (P = .01; OR, 13.8; 95% CI, 1.9–100) at presentation. Six patients died of variceal hemorrhage.** ***Conclusions:*** **Patients with chronic PM and PSM venous thrombosis without underlying malignancy have an acceptable long-term survival. Treatment with β-blockers and anticoagulation appears to improve outcome.**

Chronic portomesenteric (PM) and portosplenomesenteric (PSM) venous thrombosis are rare conditions that usually are related to thrombophilia, intra-abdominal inflammatory disease, and, less commonly, owing to cirrhosis and malignancy. The clinical presentation varies according to the temporal relationship to thrombosis. Patients with acute mesenteric and portal vein (PV) thrombosis present with sudden onset of abdominal pain as a result of bowel ischemia and infarction. For such patients, the mortality of acute thrombosis is high, with reported 30-day and 3-year mortality rates of 23%–27% and 64%–67%, respectively.[1,2] In contrast, the presenting symptoms and signs of chronic PM and PSM venous thrombosis are frequently nonspecific with abdominal symptoms or variceal bleeding.

The natural history of chronic PM and PSM venous thrombosis is unknown, with current therapeutic measures directed at prevention of variceal bleeding and symptom control. Because conventional portosystemic surgical and radiologic shunts are not possible, medical management is the mainstay of treatment. Evidence from retrospective case series, of patients with cirrhotic and noncirrhotic extrahepatic portal vein thrombosis (EHPVT), suggests that death from variceal bleeding occurs infrequently, with mortality owing to the underlying disease process or bowel infarction.[3,4] Case series of patients with acute noncirrhotic PV and superior mesenteric vein (SMV) thrombosis managed with early initiation of anticoagulation have shown benefit by reducing complications of bowel necrosis owing to recanalization of thrombosed vessels.[3,5–7] However, none have shown improved survival with medical management.

Because the risk-benefit analysis of anticoagulation in patients with chronic thrombosis is unknown, initiation of treatment is tempered by the theoretic increased risk of life-threatening hemorrhage. For that reason, we have undertaken a review of patients with PM and PSM thrombosis to examine the causative risk factors, clinical determinants of long-term survival, and the efficacy of anticoagulation and β-blockers in this patient group.

Patients and Methods

All patients with chronic PM and PSM venous thrombosis diagnosed at King's College Hospital in London between January 1973 and June 2005 were reviewed. The diagnosis of chronic PM and PSM venous thrombosis was made on the basis of computerized tomography (CT), magnetic resonance imaging, and/or aortoportography. The chronicity of thrombosis was established by a follow-up period of more than 3 months, with evidence of persistent splanchnic venous occlusion on radiologic examination. Supportive evidence of chronic thrombosis was suggested by the presence of extensive intra-abdominal venous collaterals, cavernous transformation of the portal vein, and splenomegaly.

Patient demographics including clinical presentation, laboratory data, hematologic investigations for procoagulant conditions, medical treatment, and endoscopic data were collated from the medical record. The assessment for hematologic procoagulant conditions was in accordance with medical practice of the day. Liver biopsy examinations were performed as deemed clinically appropriate. The presence of esophageal and gastric varices and variceal bleeding was assessed by esophagogastroduodenoscopy.

Abbreviations used in this paper: CI, confidence interval; CT, computerized tomography; EHPVT, extrahepatic portal vein thrombosis; EV, esophageal varices; EVBL, endoscopic variceal band ligation; MPD, myeloproliferative; MRV, magnetic resonance venography; OR, odds ratio; PM, portomesenteric; PSM, portosplenomesenteric; PV, portal vein; SMV, superior mesenteric vein.

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The primary outcome measure was survival. Secondary outcomes included prevention of primary or recurrent variceal bleeding.

The management of portal hypertension at King's College Hospital is aimed at the prevention of first variceal bleeding episode with nonselective β-blockers (propranolol). Treatment was considered adequate if there was a 25% reduction in the resting heart rate or reduction of the resting heart rate to 60 or less per minute. Secondary prophylaxis was with β-blockade, as described previously, and endoscopic injection sclerotherapy or endoscopic variceal band ligation (EVBL) with eradication of esophageal varices. Gastric varices, which had bled or showed high-risk stigmata of bleeding, were injected with Histoacryl glue (Braun Medical Ltd, Melsungen, Germany). Coumadin was commenced in patients with a recognized procoagulant condition, in whom no contraindication to treatment existed, aiming for a therapeutic international normalized ratio of 2.0–3.0. Anticoagulation was commenced only in patients with previous variceal bleeding after eradication of varices.

Statistical Analysis

For quantitative data, analysis was performed using the Mann–Whitney and Kruskal–Wallis tests for comparisons of 2 or more independent groups. The difference in proportions of categoric data was ascertained by the Fisher exact test when the number of subjects was less than 5, and by the χ^2 test for 2×2 tables when the number of subjects in each cell was 5 or more. Continuous data were categorized into normal and abnormal values for multivariate analysis. Multivariate Cox regression analysis was conducted to analyze clinical variables and treatment outcome. Survival plots were generated according to the Kaplan–Meier method and were compared using the log-rank test. Data are expressed as means or median, range and interquartile range when appropriate. *P* values less than .05 were considered significant. All analysis was performed using SPSS 13.0 (SPSS Inc., Chicago, IL).

Results

The study group was composed of 60 patients (31 women, 29 men). The median age at the time of diagnosis of PM or PSM venous thrombosis was 44 years (range, 18–68 y). Forty-eight of 60 (80%) patients were of European ethnicity, 8 (13.3%) from the Indian subcontinent, and 4 (6.7%) were of African ethnicity. The median follow-up period was 3.5 years (range, 0.3–32.0 y).

All patients underwent abdominal ultrasound scan with Doppler assessment of the portal vein, confirming extrahepatic PV occlusion. Occlusion of the PM or PSM veins was confirmed by a combination of CT, magnetic resonance venography (MRV), and/or aortoportography. Fifty patients underwent CT scan, 23 patients MRV, and 29 patients aortoportography. The pattern of splanchnic venous thrombosis was PSM thrombosis in 54 patients and PM thrombosis in 6 patients. These 6 patients had evidence of proximal splenic vein patency. The presenting features were variceal bleeding in 31 of 60 (51.7%) patients, abdominal pain in 18 of 60 (30.0%) patients, abdominal pain and ascites in 4 of 60 (6.7%) patients, ascites in 2 of 60 (3.3%) patients, and 5 of 60 (8.3%) cases were discovered incidentally during investigation of thrombocytopenia, anemia, splenomegaly, or increased liver enzyme levels.

Table 1. Cause of Chronic PM and PSM Venous Thrombosis

Risk factor (n)	n	(%)
Acquired disorder	17/60	(28.3)
Myeloproliferative disorder		
Polycythemia rubra vera	4/60	(6.7)
Essential thrombocythemia	3/60	(5.0)
Myelofibrosis	1/60	(1.7)
Unclassified	3/60	(5.0)
Antiphospholipid syndrome	5/51	(9.8)
Monoclonal gammopathy	1/49	(2.0)
Heritable disorder	9/60	(15.0)
Factor V Leiden mutation	3/49	(6.1)
Paroxysmal nocturnal hemoglobinuria	2/34	(5.9)
Sickle cell disease	1/9	(11.1)
Antithrombin III deficiency	1/49	(2.0)
Protein S deficiency	1/49	(2.0)
Plasminogen deficiency	1/36	(2.8)
Cirrhosis (ALD = 2, HBV = 2, AIH = 1, cryptogenic = 1)	6/60	(10.0)
Intra-abdominal infection (4 umbilical vein sepsis, 1 liver abscess)	5/60	(8.3)
Cancer (HCC = 3, TCC = 1)	4/60	(6.7)
Oral contraceptive pill	4/60	(6.7)
Postoperative	3/60	(5.0)
Pancreatitis	2/60	(3.3)
Congenital venous anomaly	2/60	(3.3)
Intestinal volvulus	1/60	(1.7)
Idiopathic (unknown)	17/60	(28.3)

NOTE. Seventy risk factors were identified in 60 patients.
ALD, alcoholic liver disease; HBV, hepatitis B virus; AIH, autoimmune hepatitis; HCC, hepatocellular carcinoma; TCC, transitional cell carcinoma.

Etiology of Portomesenteric and Portosplenomesenteric Thrombosis

The causes of PM and PSM venous thrombosis are shown in Table 1. Ten (16.7%) patients had more than 1 procoagulant risk factor identified. Acquired procoagulant conditions, predominantly myeloproliferative disorders, accounted for thrombosis in 17 of 60 (28.3%) patients. Seventeen (28.3%) patients had no identifiable procoagulant condition. Six (10%) patients had cirrhosis, 2 of these patients had additional procoagulant risk factors of factor V Leiden mutation and hepatocellular carcinoma. Thirty patients (50%) underwent liver biopsy examination, including the aforementioned 6 patients with cirrhosis. Of the remaining patients, 19 of 30 (63.3%) had normal biopsy specimens or mild fibrosis, and 5 of 30 (16.7%) had nodular regenerative hyperplasia.

Of those patients with malignancy, 3 patients with hepatocellular carcinoma died from metastatic cancer at a median of 4 months after the diagnosis of venous thrombosis. The fourth patient with transitional cell carcinoma presented with variceal bleeding and died 2 years later of metastatic disease. Three patients developed PSM thrombosis after abdominal surgery, presenting a median of 5 years after intervention.

Outcome and Variables Associated With Outcome

During the follow-up period, 16 patients died, with an overall survival rate of 73.3%. The causes of death are shown in Table 2. The overall survival at 1- and 5-years was 81.6%, and