Original Article

Prevalence of splenic vein thrombosis and risk of gastrointestinal bleeding in chronic pancreatitis patients attending a tertiary hospital in western India

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Abstract

Background: Splenic vein thrombosis (SVT) is most commonly caused by acute and chronic pancreatitis (CP). Variceal gastrointestinal (GI) bleeding is a potentially life-threatening event in such patients. The aim of this study was to determine the prevalence of SVT in CP patients and the risk of variceal GI bleeding. **Materials and Methods:** A total of 187 consecutive patients with a diagnosis of CP were assessed for the presence of SVT at the gastroenterology department of a tertiary care hospital. Thirty seven patients had evidence of SVT. Patients with portal vein thrombosis or cirrhosis were excluded. Potential factors associated with SVT were assessed. **Results:** Of the 187 CP patients assessed, 37 patients (19.8%) (male 33; female 4; mean age 41.9 years) had evidence of SVT. Among patients with SVT, most common etiology of CP was alcohol abuse (70.3%). Seven patients (18.9%) with SVT presented with clinically significant upper GI bleeding. The source of GI bleeding was gastric varices in three patients (8.1%) and non-variceal source in four patients (10.8%). All three patients with gastric varices were managed by splenectomy. There were no new variceal bleeding episodes in other 33 patients (89.2%) during mean follow-up of 16.4 months. On comparison of patients with and without SVT, the factors associated with significantly higher incidence of SVT were smoking ($P = 0.019$, odds ratio 3.021, 95% confidence interval 1.195–7.633) and presence of pseudocyst ($P = 0.008$, odds ratio 3.743, 95% confidence interval 1.403–9.983). Complete resolution of SVT was seen in three patients (8.1%) after resolution of underlying pseudocyst. **Conclusion:** SVT is a common complication of CP, particularly in patients with pseudocysts and history of smoking. Most patients remain asymptomatic and the risk of variceal bleeding is low. Splenectomy is the treatment of choice in patients with variceal bleeding. Conservative approach is preferred in other patients. Resolution of pseudocysts may lead to resolution of SVT in some patients.

Keywords: Chronic pancreatitis, gastrointestinal bleeding, pseudocysts, splenic vein thrombosis

Introduction

Splenic vein thrombosis (SVT) is caused by diverse etiologies, the most common etiology being acute or chronic pancreatitis (CP).[1-4] Pancreatic tumors, both benign and malignant, account for less number of cases of SVT. SVT has been reported in 5–22% of CP patients.[5-8] SVT may result in a localized form of portal hypertension called sinistral portal hypertension (SPH) or left-sided portal hypertension with the formation of isolated gastric or gastroesophageal varices. Bleeding from gastric varices is a potentially life-threatening condition.[7,9] Earlier reports indicated a high risk of variceal bleeding in SPH induced by pancreatitis.[10,11] However, in recent literature most patients with SVT were asymptomatic and the risk of variceal bleeding was very low.[6,12] Patients who present with variceal bleeding are treated by splenectomy after initial control of acute bleeding by endoscopic measures. For

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patients with no history of variceal bleeding, conservative management is the preferred approach. When CP patients with SVT undergo pancreatic surgery, addition of prophylactic splenectomy is recommended by some authors when there is evidence of portal hypertension on imaging or upper gastrointestinal (GI) endoscopy.[5,6,13] The aim of this study was to assess the prevalence of SVT and the risk of variceal bleeding in patients with CP.

Subjects and Methods

Study design

This study was conducted at a tertiary care public hospital between October 2015 to October 2017. The study was approved by the institutional ethics committee. All patients gave written informed consent for the study. A consecutive series of 187 patients with a diagnosis of CP attending gastroenterology OPD or admitted as inpatients were assessed for evidence SVT on contrast-enhanced computed tomography (CT) of abdomen. Thrombus was defined as filling defect within the lumen of the splenic vein on CT. Thirty seven patients with evidence of SVT on CT constituted the study group. Patients with concomitant portal vein obstruction or clinical, biochemical, imaging, or histological evidence of liver cirrhosis were excluded from the study. Diagnostic tools

The diagnosis of CP was based on clinical features and imaging evidence of pancreatic calcification, parenchymal atrophy, or characteristic ductal abnormalities. Patient demographics, signs and symptoms, detailed history of alcohol consumption and smoking habits, laboratory parameters, details of endoscopic and surgical interventions performed were recorded. Alcoholic CP was diagnosed if patients consumed >80 g alcohol per day for at least 5 years.[14] Tropical pancreatitis was diagnosed in patients with onset of symptoms before 30 years of age, low body mass index (<18.0 kg/m^2), and absence of other etiologies like alcoholism.[14] Pancreas divisum was diagnosed by magnetic resonance cholangiopancreatography (MRCP). Other patients were considered to have idiopathic pancreatitis after excluding known etiologies like hypertriglyceridemia and hypercalcemia. Upper GI endoscopy was performed in all 37 patients with SVT to assess the variceal status and to diagnose the etiology of GI bleeding. Seven patients with history of clinically significant upper GI bleeding underwent digital subtraction angiography also. Clinically significant upper GI bleeding was defined by any of the following: presence of melena, hemoglobin drop > 2 g/dL, requirement of blood transfusion, emergent endoscopy, or surgical procedure. Gastroesophageal variceal bleeding was defined as bleeding from varices diagnosed on upper GI endoscopy after excluding all other causes of upper GI bleeding. All patients were followed-up by three monthly visits in outpatient department. Color Doppler ultrasonography was performed at 3 months of follow-up in 29 patients with SVT. Upper GI endoscopy was repeated whenever deemed appropriate by clinical indications.

Data analysis and ethical approval

Statistical analysis was performed using the statistical software SPSS 20.0 (IBM, Armonk, NY, USA). Baseline data were presented as mean ± SD for continuous variables and as proportions for categorical variables. For comparison between two groups, the Chi-square test or Fisher's exact test was used for discrete variables and the Mann–Whitney test for continuous variables. Binary logistic regression analysis was performed to determine the odds ratio (OR) of independent factors in patients with CP and SVT. A two-tailed *P* value of <0.05 was considered statistically significant. Ethical approval was obtained from the institutional ethics committee.

Results

Of the 187 CP patients assessed, 37 patients (19.8%) (male 33; female 4; mean age 41.9 years) had evidence of SVT on CT abdomen. Among these 37 patients, 16 patients (43.2%) were smokers, 6 patients (16.2%) had diabetes mellitus, 5 patients (13.5%) had a history of steatorrhea, and most common etiology for CP was alcohol abuse (70.3%). Comparison of demographic and clinicopathological features in patients with or without SVT are shown in Table 1. On comparison of demographic feature between patients with and without SVT, smoking was associated with significantly higher incidence of SVT on both univariate (P = 0.001) and logistic regression analysis (P = 0.019, OR 3.021, 95% confidence interval 1.195–7.633).

Upper GI endoscopic evaluation revealed isolated gastric varices in seven patients (18.9%) and one patient (2.7%) had both esophageal and gastric varices. Seven patients (18.9%) had a history of clinically significant upper GI bleeding. The source of GI bleeding was gastric varices in three patients, splenic artery pseudoaneurysm in two patients, and one each from gastric ulcer and Mallory–Weiss tear.

All three patients with gastric variceal bleeding underwent endoscopic cyanoacrylate glue injection for control of acute bleeding. Subsequently two of these patients were managed by splenectomy and one patient refused splenectomy. Both patients with splenic artery pseudoaneurysm were managed by coil embolization initially followed by distal pancreatectomy with splenectomy. Splenomegaly was present in 13 patients (35.1%) with SVT. All eight patients with gastroesophageal varices had splenomegaly with one patient having features of hypersplenism.

Twenty seven patients (73%) with SVT had imaging evidence of pseudocysts. Four of these patients underwent endoscopic cystogastrostomy and one patient was treated by both endoscopic cystogastrostomy and main pancreatic duct stenting. One patient developed severe bleeding from cystogastrostomy site during the procedure, which was managed conservatively. Nine patients (24.3%) had evidence of pancreatic ascites. Five of these patients underwent main pancreatic duct stenting for the treatment of pancreatic ascites and one patient was treated

Table 1: Demographic and clinicopathological characteristics of subjects

Feature	Patients without splenic vein thrombosis (*n*=150)	Patients with splenic vein thrombosis (*n*=37)	*P*
Age (years, mean±SD)	40.0±8.5	41.9±9.7	0.310
Male	141 (94%)	33 (89.2%)	0.292
Etiology			0.143
Alcoholic	110 (73.3%)	26 (70.3%)	
Tropical	12 (8%)	2 (5.4%)	
Idiopathic	26 (17.3%)	6 (16.2%)	
Pancreas divisum	2 (1.3%)	3 (8.1%)	
Duration of symptoms (years, mean±SD)	3.8±5.0	3.2±2.5	0.680
Smoking	27 (18%)	16 (43.2%)	0.001
Diabetes mellitus	21 (14%)	8 (21.6%)	0.251
Steatorrhea	15 (10%)	6 (16.2%)	0.283
BMI (kg/m^2, mean±SD)	18.2±3.5	18.12±3.1	0.682
Splenomegaly	9 (6%)	13 (35.1%)	0.001
Pancreatic ascites	22 (14.7%)	6 (16.2%)	0.813
Parenchymal atrophy	105 (70%)	22 (59.5%)	0.219
Parenchymal calcification	71 (47.3%)	15 (40.5%)	0.458
Pseudocyst	65 (43.3%)	27 (73%)	0.001
Pseudoaneurysm	6 (4%)	4 (10.8%)	0.111
Platelet count (mean±SD) × 10^9/L	264.6±96.3	278.8±88.4	0.415
Hemoglobin (g/dL, mean±SD)	11.6±2.4	11.8±2.8	0.404

Table 2: Surgical and endoscopic interventions in patient with chronic pancreatitis and splenic vein thrombosis

Intervention	*n* (%) (*n*=37)
No intervention	18 (48.6%)
Endoscopic cystogastrostomy	5 (13.5%)
Main pancreatic duct stenting	6 (16.2%)
Dorsal pancreatic duct stenting	2 (5.4%)
Distal pancreatectomy with splenectomy	3 (8.1%)
Lateral pancreatic jejunostomy	1 (2.7%)
Splenectomy	3 (8.1%)

*One patient underwent both cystogastrostomy and main pancreatic duct stenting

by distal pancreatectomy with splenectomy. Two patients with pancreas divisum underwent minor papilla sphincterotomy and dorsal duct stenting. On comparison of clinicopathological features between patients with and without SVT, presence of pseudocyst was associated with significantly higher incidence of SVT on both univariate (P = 0.001) and logistic regression analysis (P = 0.008, OR 3.743, 95% confidence interval 1.403–9.983). Etiology of CP (P = 0.143), presence of calcification (P = 0.458), parenchymal atrophy (P = 0.219), and pancreatic ascites (P = 0.813) did not vary significantly between patients with and without SVT [Table 2].

The mean length of follow-up was 16.4 ± 7.3 months. One patient with gastric variceal bleeding, who was managed only with endoscopic cyanoacrylate injection therapy without splenectomy, developed recurrence of variceal bleeding after 1 month of discharge from the hospital. Subsequently this patient was treated with splenectomy after control of acute bleeding by endoscopic measures. There were no new or recurrent variceal bleeding episodes in other patients during follow-up. Complete resolution of SVT on follow-up color Doppler ultrasonography was observed in three patients (8.1%). Two of these patients had undergone pseudocyst drainage by endoscopic cystogastrostomy and in the other patient there was spontaneous resolution of pseudocyst. One patient died at 6 months of follow-up which was unrelated to pancreatic pathology.

Discussion

The splenic vein traverses the superior pancreatic surface. This anatomical proximity makes splenic vein susceptible to involvement by nearby inflammatory pancreatic process or compression by pseudocyst, mass-forming pancreatitis, or pancreatic neoplasm.[4,15,16] Occlusion of the splenic vein with concomitant uninterrupted blood flow through the splenic artery leads to increased pressure in the splenic venous system. The increased pressure gets transmitted through anastomosis between splenic vein and gastric or gastroepiploic veins. The result is the formation of gastric or gastroesophageal varices.[3,4] The resulting condition is called sinistral or left-sided or segmental portal hypertension. In most studies of SPH, isolated gastric varices are commonly found. However, combined gastroesophageal or rarely isolated esophageal varices can occur.[4,6]

Occurrence of variceal bleeding secondary to SVT is a potentially life-threatening event. The reported frequency of this complication varies considerably between the older and recent studies. In the study reported by Loftus *et al.* 24 of 37 (65%) patients with SPH presented with GI bleeding.[14] Similarly, Madsen *et al.* reported bleeding as the most common symptom (72%) in patients with SPH.[1] In recent studies of SVT in CP, the reported rates of variceal bleeding are much lower (4–17%).[5,6,12] The reason for this might be the increased availability of sensitive cross-sectional imaging modalities like CT/MRI, which can detect SVT in patients

who are mostly asymptomatic.[12] In our study the frequency of variceal bleeding was 8.3%, which is in accordance with the results of recent studies.

Splenomegaly is a common feature in patients with CP and SVT. Some studies report splenomegaly as universal feature.[3,17] In our study 13 patients (36%) had splenomegaly. Similar to this finding, others studies have reported splenomegaly in <50% of patients.[4,6,18] Hypersplenism is a variable feature among different studies.[3,4,6] In our study only one patient had features of hypersplenism.

The severity and duration of underlying CP does not correlate with the presence of SVT.[5,11] Presence of pseudocyst has been reported as a common finding in patients with pancreatitis and SVT. In a study by Agarwal *et al.*, among the various factors only the presence of pseudocyst was associated with significantly higher incidence of SVT in patients with CP.[5] Similar to this finding Heider *et al.* also reported presence of pseudocyst in 90% of patients with pancreatitis-induced SVT.[9] In our study the presence of pseudocyst ($P = 0.008$, OR 3.743, 95% confidence interval 1.403–9.983) and smoking ($P = 0.019$, OR 3.021, 95% confidence interval 1.195–7.633) were associated with significantly higher incidence of SVT.

Both surgical and non-surgical approaches have been proposed for the treatment of SVT associated with CP. For control of acute gastric variceal bleeding, endoscopic cyanoacrylate glue injection is a very effective treatment modality.[19,20] For patients presenting with significant or recurrent variceal bleeding splenectomy is the treatment of choice.[2,3,5,9] Recent reports have also suggested other modalities like splenic artery embolization (SAE) as an effective alternative, particularly in high surgical risk patients.[2,9,21,22] SAE can also be performed prior to splenectomy to decrease arterial flow into the left portal system.[4,23,24] Splenectomy and SAE interrupt the arterial supply to the feeding collateral veins and thus decompressing gastric varices and consequently reduced risk of variceal re-bleeding.[3,15,25]

What remains controversial is the management of patients with no history of variceal bleeding. Routine splenectomy was advocated by several authors in the past considering the high frequency of GI bleeding reported in patients with SVT in older literature.[10,11] However, several recent reports advice against routine splenectomy in patients with no history of variceal bleeding.[6,12,15,25,26] The factors favoring conservative approach in such patients are low frequency of variceal bleeding with no mortality related to GI bleeding, resolution of SVT after drainage, or spontaneous resolution of underlying pseudocyst. Some authors recommend prophylactic splenectomy in asymptomatic SVT patients during surgical treatment of underlying CP to facilitate surgery and to avoid future variceal bleeding.[5]

In our study three patients (8.1%) had complete resolution of SVT on follow-up. Two of these patients were treated by endoscopic pseudocyst drainage. Contrary to this finding, a study of 34 patients of CP with SVT did not find resolution of SVT in any patients after pancreatic ductal decompression or pseudocyst drainage.[6]

In patients of CP with SVT who present with GI bleeding, it is important to look for sources of non-variceal bleeding like pseudoaneurysm as the treatment of these conditions is totally different.[12] In our study four patients (10.8%) had non-variceal upper GI bleeding. This study is particularly useful for practicing physicians as it helps in prognosticating the disease and helps in early identification of impending complications, thus allowing necessary steps in preventing them. It also guides us in stratifying patients who require endoscopic surveillance for development of varices. Our study has several limitations. The duration of follow up was shorter. Thrombophilia work up and test for pancreatic exocrine insufficiency were not done. Many patients in our study were referred from other hospitals for endoscopic intervention, so the clinical profile of these patients might be different from those patients seen at general hospitals.

In conclusion, SVT is a common complication of CP, particularly in patients with pseudocysts and history of smoking. Most patients remain asymptomatic and the risk of variceal bleeding is low (8%). Splenectomy is the definitive treatment in patients with variceal bleeding. For patients with no history of variceal bleeding a conservative approach is preferred. Resolution of pseudocyst, either spontaneously or after surgical drainage may lead to resolution of SVT in some patients. In patients with CP and SVT, non-variceal upper GI bleeding is as common as variceal bleeding. So it is important to look for non-variceal bleeding sources in such patients.

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Conflicts of interest

There are no conflicts of interest.

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