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Prognostic Factors and Treatment Outcome in Mesenteric Vein Thrombosis

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Background Mesenteric vein thrombosis (MVT) can result in intestinal ischemia and is associated with high morbidity and mortality due in part to its frequent delay in diagnosis. The purpose of this study was to evaluate clinical presentation, diagnostic evaluation, and treatment outcome of MVT.

Methods Hospital records and clinical data of all patients treated for MVT were reviewed during a recent 14-year period. Clinical outcome and factors affecting survival were analyzed.

Results A total of 68 patients were included in the study. Abdominal exploration was performed in 23 patients (34%), and second-look operation was necessary in 18 patients (26%). Three patients (4%) underwent unsuccessful operative mesenteric vein thrombectomy, whereas percutaneous transhepatic mesenteric thrombectomy was performed successfully in 3 patients (4%). The 30-day mortality rate was 20%. Forty-six of the 54 survivors were treated with long-term oral anticoagulation therapy. Actuarial survival at 2, 4, 6, and 10 years was 68%, 57%, 43%, and 22%, respectively. Risk factor analysis showed malignancy ($P < .002$), age >60 years ($P < .005$), cirrhosis ($P < .02$), symptom duration ($P < .005$), and bowel resection ($P < .03$) were associated with mortality. Logistic regression analysis showed age >60 years (odds ratio [OR], 3.64; $P = .03$), malignancy (OR, 3.88; $P = .02$), and prolonged symptom duration (OR, 5.62; $P = .01$) were independent predictors of mortality.

Conclusions MVT is associated with significant mortality. Prompt diagnostic evaluation with computed tomography may reduce potential treatment delay. Underlying malignancy, advanced age, and prolonged symptom duration are predictive of poor outcome.

Keywords: mesenteric vein thrombosis; intestinal ischemia; clinical outcome

Introduction

Mesenteric vein thrombosis (MVT) is a severe disease process that can result in intestinal ischemia and, ultimately, intestinal infarction requiring surgical intervention. Although MVT accounts for only 5% to 15% of all episodes of mesenteric ischemia,[1-3] the morbidity and mortality surrounding this condition has distinguished this disorder since its first true separate clinical characterization by Warren and Eberhard in 1935.[4]

Over the past decade, several studies demonstrated the importance of systemic anticoagulation in early treatment of patients with MVT.[5,6] The improvement in treatment outcome has been aided by advances in modern imaging technique such as computed tomography (CT), which has consistently demonstrated a diagnostic accuracy of more than 90% in MVT.[2,7,8] Although several recent studies

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have conveyed an improving mortality rate ranging from 13% to 38%,[2,9-11] in contrast to a much higher fatality rate of more than 50% in earlier studies,[12,13] MVT remained a formidable and challenging disease due in part to the nonspecific clinical abdominal signs at presentation, frequent delay in diagnosis, and association with risk factors unknown to the patient, such as a hypercoagulable disorder or underlying malignancy.

As a result of the therapeutic challenge of this condition, a better understanding of MVT is warranted to optimize both medical and surgical management and improve treatment outcome. This study was undertaken not only to review the treatment strategy and clinical outcome in patients with MVT at our institution but also to evaluate clinical variables associated with mortality in patients with MVT.

Patients and Methods

From May 1991 to August 2005, the hospital records and clinic charts of all patients who were diagnosed with MVT were analyzed. Patients whose diagnosis of MVT based on postmortem autopsy were excluded from the study. Moreover, patients who were asymptomatic and had an incidental finding of MVT based on abdominal CT scan, which was obtained for other diagnostic evaluation, were similarly excluded from the analysis. Clinical data including demographic information, presenting symptoms, comorbid medical conditions, laboratory and radiographic examinations, treatment approach and outcome, as well as follow-up visit records were analyzed. Primary MVT was defined as idiopathic or spontaneous MVT without associated predisposing or etiologic condition. In contrast, those with preexisting conditions that may predispose to MVT, such as trauma, infection, or hypercoagulable disorder, were regarded as secondary MVT. Intravenous heparin was the mainstay of treatment modality once a patient was diagnosed with MVT. Treatment outcome, with a particular emphasis on surgical intervention for complications related to MVT, was examined.

Radiographic criteria for the diagnosis of MVT were made based on the presence of the following conditions. Ultrasonographic diagnosis of MVT was based on the presence of thrombus or lack of flow in the superior mesenteric–portal venous circulation. Computed tomographic diagnosis of MVT was based on the presence of superior mesenteric venous (SMV) thrombosis, venous collaterals surrounding the occluded superior mesenteric vein, and/or thickening of ischemic bowel wall. Mesenteric angiographic diagnosis of MVT was based on the presence of SMV thrombus as demonstrated on the venous phase or failure to visualize the SMV with an adequate arterial inflow study.

Statistical analysis was performed to determine the association between relevant risk factors and treatment mortality with Fisher's exact test or Pearson's χ^2 test in categorical variables. Wilcoxon rank–sum test was used to test for differences in continuous variables. Risk factors affecting mortality were analyzed by univariate analysis, which was followed by multivariate stepwise logistic regression analyses. Only variables with at least 70% of the data present or recorded were used in all analyses. Kaplan–Meier method was used to assess survival rate. All statistical analyses were performed using a statistical software program (SAS Institute, Cary, NC). All values were expressed as mean ± standard error mean. Statistical significance was accepted with a *P* value of less than .05.

Results

Patient Information and Clinical Presentation

A total of 68 patients (36 females) were diagnosed with MVT during the study period. Among them, the median age was 48.5 years (range 21 to 83). Relevant demographic information as well as predisposing or etiologic conditions of MVT are listed in Table 1. Primary and secondary MVT occurred in 21 patients (31%) and 47 patients (69%), respectively. Importantly, the most common etiological factor in secondary MVT was previous abdominal operation (32%) followed by hypercoagulable disorder (29%) and deep vein thrombosis (26%). With regard to presenting symptoms, abdominal pain was the most common presenting symptom, which was present in 66 patients (97%, Table 2). Among them, 13% were felt to have signs of peritonitis at the time of physical examination on presentation, and they were taken to the operation room for immediate exploration, whereas 26% had abdominal voluntary guarding. Other common signs or symptoms on presentation included nausea and vomiting (n = 35, 51%), tachycardia (n = 32, 47%), abdominal distention (n = 21, 31%), and diarrhea (n = 21, 31%). Among the 66 patients who presented with abdominal pain, the mean duration of symptoms was 2.3 ± 1.6 days.

Table 1. Predisposing Conditions Associated With MVT

Condition	Number of Patients
Primary MVT	21 (31%)
Secondary MVT	47 (69%)
Previous abdominal operation	22 (32%)
Hypercoagulable condition	20 (29%)
Factor V Leiden deficiency	9 (13%)
Protein C deficiency	5 (7%)
Protein S deficiency	4 (6%)
Antiphospholipid antibody syndrome	2 (3%)
Deep vein thrombosis	18 (26%)
Malignancy	14 (21%)
Smoking	14 (21%)
Previous MVT	13 (19%)
Cirrhosis/portal hypertension	13 (19%)
Pancreatitis	12 (17%)
Alcohol abuse	10 (15%)
Oral contraceptive usage	5 (7%)

Abbreviation: MVT, mesenteric vein thrombosis.

Table 2. Presenting Signs or Symptoms in Patients With Mesenteric Venous Thrombosis

Presenting Sign or Symptom	No. of Patients	Percentage
Abdominal pain	66	97
Peritonitis	9	13
Abdominal voluntary guarding	18	26
Nausea/vomiting	35	51
Tachycardia (HR > 100 bpm)	32	47
Abdominal distension	21	31
Diarrhea	21	31
Upper GI bleeding	18	26
Lower GI bleeding	15	22
Constipation	10	15
Fever	5	7

Abbreviations: HR, heart rate; bpm, beats per minute; GI, gastrointestinal.

Laboratory and Radiographic Evaluation

Relevant laboratory findings are listed in Table 3, which also included proportions of patients with abnormal laboratory results. Leukocytosis, with a mean value of 17.8×10^9/mL, was present in more than 88% of patients. Other commonly encountered abnormal laboratory results included elevated amylase level (n = 35, 51%), elevated aspartate aminotransferase level (n = 32, 47%), and acidosis (n = 30, 44%).

Plain abdominal radiograph was performed in all patients, and it was considered normal in 23 patients (34%). However, evidence of bowel distention and signs suggestive of an ileus were noted in 43 patients (63%) and 35 patients (51%), respectively. Abdominal CT scan with intravenous contrast was performed in 50 patients (74%). Presence of thrombus in the superior mesenteric vein was noted in 46 patients (68%). Abnormal findings suggestive of intestinal ischemia associated with MVT, such as thickened bowel wall, pneumatosis intestinalis, free peritoneal fluid, and severe bowel dilatation, were noted in 49 patients (72%). Overall, 47 patients (94%) who underwent CT scan showed abnormal findings associated with MVT. Mesenteric arteriography with delayed contrast venography was performed in 10 patients (15%). Evidence of filling defect or thrombus in the SMV was noted only in 6 of them (sensitivity 70%). Other diagnostic evaluations included magnetic resonance angiography (n = 7) and mesenteric color duplex ultrasonography (n = 8). These 2 diagnostic modalities showed SMV thrombus or filling defect in 5 and 6 patients, respectively. As a result, the sensitivity of magnetic resonance angiography and duplex ultrasound in the diagnosis of MVT based on our series was 71% and 75%, respectively. In 16 patients, the diagnosis of MVT was made based on intraoperative findings.

Treatment

Forty-six patients (68%) had symptoms lasting more than 2 days before therapy was initiated. Systemic anticoagulation with intravenous heparin was the mainstay of therapy, which was initiated in 58 patients (85%) once the diagnosis of MVT was made. Exploratory laparotomy was performed in 23 patients (34%) due in part to either the presence of peritoneal signs (n = 9) or progressive worsening of abdominal symptoms despite anticoagulation therapy (n = 14). Among patients who underwent surgical exploration, 15 patients (65%) had abdominal symptoms for more than 48 hours, and only 5 patients (22%) underwent operation with symptoms for less than 24 hours. Preoperative systemic anticoagulation was administered in 16 patients prior to their laparotomy. The diagnosis of MVT was established in 3 patients based on intraoperative finding, and systemic anticoagulation was commenced intraoperatively. Four patients received anticoagulation following the abdominal operation. No hemorrhagic complications occurred in our series in those who underwent abdominal exploration while concurrently receiving systemic anticoagulation.

Table 3. Summary of Laboratory Findings at Admission

Serum Laboratory Parameter (Normal Value Range)	Number of Patients Who Had the Serum Test	Mean Value	Proportion of Patients With Abnormal Lab Findings (n and %)
Leukocyte count (<11 × 10^9/mL)	68 (100%)	17.8 × 10^9/mL	60 (88%)
Amylase (<123 U/L)	58 (85%)	86 U/L	35 (51%)
AST (7-28 U/L)	62 (91%)	43 U/L	32 (47%)
Base deficit (<–2)	63 (93%)	–3.8	30 (44%)
Lactate level (<2.0 mmol/L)	52 (76%)	2.5 mmol/L	28 (41%)
Creatine kinase (<328 U/L)	49 (72%)	335 U/L	23 (34%)
Urea nitrogen (BUN) (7-18 mg/dL)	68 (100%)	18 mg/dL	19 (28%)
Creatinine (0.8-1.4 mg/dL)	68 (100%)	1.6 mg/dL	17 (25%)
Hemoglobin (13.5-17 g/dL)	68 (100%)	12.3 g/dL	11 (16%)

Abbreviations: AST, aspartate aminotransferase; BUN, blood urea nitrogen.

A staged second-look operation was necessary in 18 out of 23 patients who underwent exploration (78%). Among those 23 patients, 17 (74%) required bowel resection due to either clinically suspected and intraoperatively confirmed transmural bowel necrosis (n = 15) or intestinal perforation (n = 2). Thirteen patients (56%) had bowel resection at the initial laparotomy, whereas 4 patients had bowel resection during the second-look operation. Whereas bowel resection with primary intestinal anastomosis was performed in 12 patients, a temporary ileostomy or colostomy was created in the remaining 5 patients. The extent of bowel resection ranged from 20 to 150 cm, with a mean length of 85.2 ± 16cm at the initial laparotomy. Among patients who required bowel resection during the second-look operation, the mean length of bowel resection was 40.6 ± 12cm.

Operative mesenteric vein thrombectomy was performed in 3 patients (4%) at the time of abdominal exploration. In all these cases, SMV was isolated once the transverse colon was elevated and the ligament of Treitz was released. A 3-F Fogarty embolectomy catheter was passed in a retrograde fashion to achieve SMV thrombectomy. Percutaneous transhepatic mesenteric thrombectomy plus thrombolysis using recombinant tissue plasminogen activator (Genentech; San Francisco, CA) was performed in 3 patients (4%) with SMV thrombosis. In these cases, percutanous access of the portal vein was established under ultrasound guidance. A transhepatic access to the portal vein was established with a 7-F introducer sheath. Rheolytic thrombectomy using the AngioJet thrombectomy system (Possis Medical Inc, Minneapolis, MN) was performed. Detailed description of this treatment strategy has been previously described by our group.[14]

Clinical Outcome

Among patients who underwent abdominal operation, operative morbidity rate was 49% (n = 11). Perioperative complications included pneumonia (n = 2), prolonged intubation (n = 1), renal insufficiency (creatinine > 2.0 mg/dL; n = 2), wound dehiscence (n = 1), lower gastrointestinal bleeding (n = 1), prolonged ileus (>10 days; n = 2), and urinary tract infection (n = 2). Transient hemodialysis was required in 1 patient due to renal failure. Two patients developed short-gut syndrome due in part to the extensive bowel resection and required long-term intravenous hyperalimentation. Despite postoperative anticoagulation therapy, 3 patients who underwent surgical mesenteric venous thrombectomy developed recurrent thrombosis as documented by CT scan all within 7 days of the postoperative period. In contrast, 3 patients who underwent catheter-based transhepatic mesenteric vein thrombectomy and thrombolysis showed patent SMV at the time of discharge, as documented by CT (n = 2) and magnetic resonance venogram (n = 1). All 3 patients remained free of symptoms during the follow-up period at 9 months. The 30-day operative mortality rate in our series was 26% (n = 6), which occurred in 2 patients whose MVT was attributed to metastatic ovarian cancer and colon cancer. Three patients died during the immediate postoperative period because of multiorgan failure whereas pulmonary embolism was responsible for the remaining postoperative death.

The overall 30-day mortality rate in our series was 21%. The cause of death of these patients included underlying malignancy (n = 4), cardiac arrest (n = 1), stroke (n = 1), cirrhosis/liver failure (n = 3), and multiorgan failure (n = 5). Late follow-up clinic

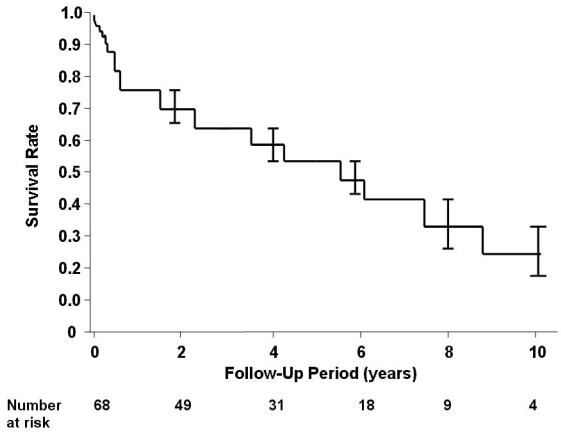

Figure 1. Survival rate in patients with mesenteric vein thrombosis.

records were available on 46 patients (90%) of the MVT survivors following the initial hospitalization. The mean follow-up period was 46.9 months. Late death occurred in 7 patients, and the causes of late death included recurrent malignancy (n = 2), cirrhosis (n = 3), traumatic injury (n = 1), and unknown cause (n = 1). Among the 31 long-term survivors, all but 4 patients were on chronic oral anticoagulation therapy, and they remain free of symptoms. Using Kaplan–Meier analysis, actuarial survival at 2, 4, 6, and 10 years were 68% (95% confidence interval [CI] = 87% to 98%), 57% (95% CI = 83% to 90%), 43% (95% CI = 69% to 82%), and 22% (95% CI = 57% to 75%), respectively (Figure 1).

Risk Factor Analysis of Mortality

Univariate analysis of relevant demographic, comorbid conditions and treatment strategies in relation to mortality was performed. No significant differences were found with regard to etiology, physical examination, laboratory tests, or diagnostic results. Univariate analysis showed malignancy ($P < .01$), renal insufficiency ($P < .04$), age >60 years ($P < .001$), cirrhosis ($P < .02$), prolonged symptom duration (>48 hours of abdominal pain; $P < .02$), and bowel resection ($P < .01$) were associated with decreased survival. Multivariate analysis revealed that increased age >60 years, malignancy, and prolonged symptom duration were independent predictors of mortality (Table 4).

Table 4. Multivariate Analysis of Risk Factors Predictive of Mortality in Patients With MVT

Variable	*P* Value	Odds Ratio (95% CI)
Increased age (>60 years)	.03	3.64 (1.2-4.89)
Malignancy	.02	3.88 (1.1-5.3)
Prolonged symptom duration	.01	5.62 (0.5-6.4)

Abbreviations: MTV, mesenteric vein thrombosis; CI, confidence interval.

Discussion

Mesenteric venous thrombosis is a rare but formidable condition that is associated with high morbidity and mortality. This condition is responsible for 5.2% of all causes of mesenteric ischemia at our institution. This uncommon incidence is consistent with findings from other series, which reported MVT to be the cause of intestinal infarction in 5% to 25% of the patients with mesenteric ischemia.[15,16] Our study is notable because it demonstrated that despite modern imaging evaluation coupled with aggressive medical and surgical interventions, the 30-day mortality of this condition remained significant at 20%. Moreover, risk factor analysis revealed that increased age and prolonged abdominal symptoms prior to initiation of therapy are predictive of fatal outcome.

In our study, predisposing conditions that might lead to the development of MVT were identified in 69% of patients, whereas the remaining patients were considered to have a primary MVT. This finding is similar to other series, which showed that secondary MVT with identifiable risk factors can occur in 55% to 79% of patients with MVT.[3,5,16,17] Although it is noteworthy that more than 1 predisposing condition may be present in a patient with MVT, our study showed that nearly one third of patients with secondary MVT had either previous abdominal operation or hypercoagulable disorder. Several of other predisposing conditions may have an indirect and confounding effect contributing to a hypercoagulable milieu, which included the use of oral contraceptive drugs, malignancy, and cirrhosis. Our study showed that alcohol abuse and pancreatitis occurred in 15% and 17% of patients, respectively. The incidences of these 2 variables were higher compared with many earlier series.[5,11,13,18,19]

Systemic anticoagulation is the mainstay of therapy in patients with MVT. Only patients who developed catastrophic abdominal symptoms such as peritoneal signs should undergo abdominal exploration and possible

bowel resection for transmural intestinal infarction. The importance of anticoagulation therapy in the management of MVT was highlighted in a report by Abdu et al,[20] who reviewed the literature from 1911 to 1984 and reported that the use of anticoagulants as an adjunct to bowel resection significantly increased the patient survival rate. Several studies have similarly showed that anticoagulation significantly improved patient survival in contrast to patients who did not receive anticoagulation therapy.[2,21] A recent report by Brunaud et al[5] underscored a similar principle of nonoperative therapy of MVT. These authors showed that nonoperative therapy can result in a favorable treatment outcome. However, in the situation of bowel perforation or intestinal infarction with transmural necrosis, the consensus of treatment remained abdominal exploration with bowel resection.[11,18,19]

In our study, abdominal exploration was performed in 34% of patients whose surgical indication included peritoneal signs or worsening abdominal symptoms despite medical management. We did not believe that a second-look operation is uniformly indicated in patients who underwent bowel resection. However, we routinely checked for intraoperative mesenteric Doppler signals to assess the intestinal viability following bowel resection. Only in situations in which the bowel viability following resection remained questionable was a second-look operation performed, typically within 24 or 36 hours. This treatment strategy is similar to several clinical series that highlighted the importance of a second-look operation in the surgical management of MVT.[9,22,23] Among the 18 patients who underwent a second-look operation in our study, 4 patients (22%) required bowel resection. In patients who were critically ill or had questionable bowel margins following bowel resection, we preferred to create a temporary ileostomy or colostomy, which was necessary in 5 patients. This technique enabled us to carefully monitor the bowel viability by assessing the ileostomy site while the patients recovered postoperatively. A staged ileostomy or colostomy takedown operation was scheduled once patients were fully recovered from their initial abdominal operation, which was performed in all 5 patients in our series.

The role of operative mesenteric vein thrombectomy remained a subject of controversy, as studies describing this technique remained limited without long-term follow-up.[24-26] We performed operative SMV thrombectomy using a Fogarty embolectomy balloon catheter in 3 patients because of extensive thrombosis involving the portal–mesenteric venous system. In all cases, large amounts of venous thrombus were extracted, and the SMV remained patent immediately following the operation. However, we were unable to maintain significant patency in the mesenteric venous circulation in these patients.

Because of the advent of a catheter-directed thrombectomy system, we have previously reported our experience in using a rheolytic thrombectomy catheter system in patients with both acute arterial and deep venous thrombosis.[27-29] We applied this catheter-directed thrombectomy system in 3 patients via a transhepatic access under ultrasound guidance. All 3 patients remained symptom free during the follow-up period. Although the small number of patients does not allow generalizations, the favorable outcome of this small subgroup indicates that percutaneous intervention should be given a serious consideration in selected patients who do not have peritoneal signs and can be closely followed for evidence of serious bleeding.

Our study showed a 30-day mortality rate of 20%, which compared favorably to several other contemporary series that ranged from 21% to 27%.[11,19,30] Risk factor analysis showed that malignancy, increased age, prolonged symptom duration, and bowel resection were associated with increased mortality. Further assessment using the multivariate analysis revealed that age greater than 60 years and prolonged symptom duration were independent predictors of fatality. Berney et al[31] reported their findings of risk factor analysis in patients with portomesenteric venous thrombosis. Similar to our findings, these researchers reported that malignancy was associated with poor prognosis. In contrast to our report, their study revealed that patients with cirrhosis and gastrointestinal bleeding were more likely to experience a detrimental outcome when diagnosed with MVT.[31] Several other studies have noted the critical role of prompt diagnosis in patients with MVT, further highlighting the notion that delayed diagnosis, which invariably leads to prolonged symptom duration, could lead to poor treatment outcome.[3,7,18,32]

There are undoubtedly several limitations in our study, which included the retrospective study design that may result in possible patient selection and treatment bias. Because only patients with a primary diagnosis of MVT were included in the analysis, we may potentially underestimate the true mortality rate of this condition in our series. Furthermore, although systemic anticoagulation was the main

therapeutic strategy of this condition, the timing of this treatment initiation was not uniform as many patients had a delayed diagnosis because of nonspecific disease symptoms. Finally, the surgical treatment, particularly related to the thrombectomy strategy, was largely based on the preference of the individual physician. Keeping these study limitations in mind, nonetheless, we believe our findings remain notable as it underscores the frailty of elderly patients suffering from this condition.

In summary, the modern therapeutic approach of MVT requires a high index of clinical suspicion with prompt imaging evaluation to first establish the diagnosis. At the present time, abdominal CT scan provides the greatest diagnostic accuracy for this condition. Once the diagnosis of MVT is made, the primary therapeutic modality is systemic anticoagulation, whereas abdominal exploration with bowel resection is reserved for patients with catastrophic sequelae of MVT. Our study suggested that surgical mesenteric thrombectomy is ineffective in restoring mesenteric venous patency. Although our experience remained limited, percutaneous transhepatic mesenteric venous thrombectomy may hold promise as a treatment strategy in patients with symptomatic MVT. Only timely diagnosis and prompt appropriate therapy would ensure satisfactory treatment outcomes in patients with MVT.

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