Hypercoagulability status, operative mortality, and long-term survival in patients operated on for mesenteric venous thrombosis

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ABSTRACT

Objective: Mesenteric venous thrombosis (MVT) is a rare cause of acute surgical abdomen, with high mortality. The aim of this study was to analyze long-term outcomes and possible factors influencing its prognosis.

Methods: All patients who underwent urgent surgery for MVT from 1990 to 2020 in our center were reviewed. Epidemiological, clinical, and surgical data; postoperative outcomes; origin of thrombosis; and long-term survival were analyzed. Patients were divided into two groups: primary MVT (hypercoagulability disorders or idiopathic MVT) and secondary MVT (underlying disease).

Results: Fifty-five patients, 36 (65.5%) men and 19 (34.5%) women, mean age 66.7 years (standard deviation: ±18.0 years), underwent surgery for MVT. Arterial hypertension (63.6%) was the most prevalent comorbidity. Regarding the possible origin of MVT, 41 (74.5%) patients had primary MVT and 14 (25.5%) patients had secondary MVT. From these, 11 (20%) patients had hypercoagulable states, 7 (12.7%) had neoplasia, 4 (7.3%) had abdominal infection, 3 (5.5%) had liver cirrhosis, 1 (1.8%) patient had recurrent pulmonary thromboembolism, and 1 (1.8%) had deep venous thrombosis. Computed tomography was diagnostic of MVT in 87.9% of the cases. Intestinal resection was performed in 45 patients due to ischemia. Only 6 patients (10.9%) had no complication, 17 patients (30.9%) presented minor complications, and 32 patients (58.2%) presented severe complications according to the Clavien-Dindo classification. Operative mortality was 23.6%. In univariate analysis, comorbidity measured by the Charlson index ($P = .019$) and massive ischemia ($P = .002$) were related to operative mortality. The probability of being alive at 1, 3, and 5 years was 66.4%, 57.9%, and 51.0%, respectively. In univariate analysis of survival, age ($P < .001$), comorbidity ($P < .001$), and type of MVT ($P = .003$) were associated with a good prognosis. Age ($P = .002$; hazard ratio: 1.05, 95% confidence interval: 1.02-1.09) and comorbidity ($P = .019$; hazard ratio: 1.28, 95% confidence interval: 1.04-1.57) behaved as independent prognostic factors for survival.

Conclusions: Surgical MVT continues to show high lethality. Age and comorbidity according to the Charlson index correlate well with mortality risk. Primary MVT tends to have a better prognosis than secondary MVT. (J Vasc Surg Venous Lymphat Disord 2023;■:1-10.)

Keywords: Mesenteric venous thrombosis; Hypercoagulability; Thrombophilia; Prognostic factors; Intestinal ischemia

Mesenteric venous thrombosis (MVT) is a rare disease with an estimated incidence of 1 to 4 cases per million people.[1,2] It is a form of acute mesenteric ischemia, representing 5% to 15%[3,4] due to thrombosis in the spleno-porto-mesenteric venous axis.[5] Initially, it was described in 1895 by Elliot[6] and was redefined in 1935 by Warren and Eberhardt.[7] Hypercoagulability states, intra-abdominal inflammatory processes, trauma, cancer, portal hypertension, and cirrhosis are some of the risk factors for MVT.[8-11] Early diagnosis is difficult due to nonspecific clinical features and biomarkers.[12] Immediate anticoagulation is the cornerstone of treatment,[12] which can achieve recanalization greater than 80% and reduce mortality,[13,14] which ranges between 12% and 50%.[15-17]

However, some patients presenting with intestinal necrosis and signs of septic shock may require surgery, including bowel resection.[18] Irreversible intestinal ischemia remains the main reason for poor prognosis.[12] Mortality rates associated with bowel resection for irreversible ischemia range from 20% to 60%.[19,20] These cases of MVT requiring urgent surgical intervention constitute a subgroup with a poorer prognosis and a management challenge. However, the factors that are associated with poor outcomes of this ischemic condition in surgical patients, especially in the long term, have not been well studied.

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The aim of this study was to analyze the clinical characteristics, risk factors, and long-term outcomes of a subgroup of patients undergoing emergency surgery for MVT.

MATERIALS AND METHODS

A retrospective observational study of 55 patients with a diagnosis of MVT who required surgical exploration to assess bowel viability at our institution between 1990 and 2020 was performed. Patients with MVT treated conservatively and without sufficient data in the history for the study were excluded. All study participants provided informed consent, and the study was approved by the hospital's research ethics committee (code 160079/730).

The patients were evaluated by the surgeon after being notified by the emergency physician, when abdominal pain with peritonitis, septic shock, or radiological signs of intestinal ischemia were confirmed. Exploratory laparotomy and bowel resection were performed in case of transmural necrosis. The transit was reconstructed by anastomosis between the necrosis-free ends, or stomas were left, depending on the state of the rest of the intestine and the hemodynamic situation of the patient. In cases with nontransmural, reversible, or doubtful ischemia, the bowel was left in situ for further assessment by second-look laparotomy. The definitive diagnosis of MVT was made by demonstration of intraluminal occlusion in the spleno-porto-mesenteric venous territory on preoperative imaging, intraoperative assessment by the surgeon, and/or histological study.

After surgery, in critically ill patients, sodium heparin therapy was initiated: bolus injection of 5000 U intravenously, followed by continuous infusion with dose adjustment to maintain an activated partial thromboplastin time value of 1.5 to 2.5. In stable patients, enoxaparin was administered at therapeutic doses: 1 mg/kg/12 hours subcutaneously for 5 to 7 days, and then 1.5 mg/kg/24 hours.

All patients were maintained on subcutaneous enoxaparin at therapeutic doses after hospital discharge, under control by hematology. During follow-up, patients were offered to continue with the same therapeutic regimen or switch to oral acenocoumarol, under strict international normalized ratio control (maintained between 2.0 and 3.0), or direct oral anticoagulants.

Patients were divided into two groups: patients with primary MVT (patients with hematological hypercoagulability disorders or idiopathic MVT) and patients with MVT secondary to a known triggering factor, mainly neoplasms, cirrhosis, or intra-abdominal infections.

Patients with secondary MVT were maintained on anticoagulation therapy for 3 months and then discontinued if the intercurrent disease was controlled.

Patients with primary MVT were maintained on anticoagulation for 6 months and re-evaluated on a case-by-case basis. After this period, if there was no thrombotic recurrence, anticoagulation therapy was discontinued, and a thrombophilia study was performed.

Antiphospholipid antibodies (lupus anticoagulant and anticardiolipin antibody) were determined in all patients. In nonelderly patients, disorders such as factor V Leiden mutation, prothrombin gene mutation, protein C and S deficiency, activated protein C resistance, antithrombin III deficiency, or hyperhomocysteinemia were investigated.

Finally, if a hypercoagulable state was detected, permanent anticoagulation with acenocoumarol or direct oral anticoagulant was prescribed.

The following variables were collected:

- *Sociodemographic characteristics*: age, gender, comorbidity measured by the Charlson comorbidity index.[21,22]
- *Clinical findings:* abdominal pain, abdominal distension, peritonitis, fever, shock (defined as systolic blood pressure below 90 mm Hg despite fluid therapy, which requires drugs to maintain mean arterial pressure above 65 mm Hg).
- *Intervals:* symptoms evolution (<24 hours, 24-48 hours, and >48 hours) and the interval between the first assessment by a surgeon and surgery (<6 hours, 6-12 hours, and >12 hours).
- *Laboratory:* hemoglobin, leukocytes/mm^3, platelets, blood glucose, creatinine, creatinine phosphokinase, amylasemia, and pH.
- *Radiological tests*: computed tomography (CT) abdomen and arteriography.
- *Surgical findings and procedures:* massive intestinal necrosis (defined as a situation where the amount of bowel remaining after resection is less than 100 cm, usually incompatible with life), small bowel and/or colon involvement, bowel resection, primary anastomosis, and second-look reoperation.
- *Postoperative complications:* according to the Clavien-Dindo classification,[23] this variable was categorized

ARTICLE HIGHLIGHTS

- **Type of Research:** Single-center, retrospective, observational study
- **Key Findings**: Fifty-five patients were operated on for acute mesenteric ischemia of venous origin. The operative mortality was 23.6%, mainly related to massive ischemic necrosis. The cumulative probability of survival at 5 years was 51.0%. The independent predictors of long-term survival in multivariate analysis were age ($P = .002$) and comorbidity ($P = .019$).
- **Take Home Message:** In terms of long-term survival, age and comorbidity play a fundamental role. Likewise, patients with primary mesenteric venous thrombosis (hypercoagulability disorders and idiopathic cases) tend to have more favorable outcomes than patients with secondary venous thrombosis.

into no complications, mild complications (grades I and II), and serious complications (grades III and IV), including death (grade V).
- *Origin of venous thrombosis:* primary vs secondary MVT and patients with hypercoagulability vs patients without hypercoagulability status (idiopathic MVT).
- *Operative mortality:* defined as death occurring within 30 days after surgery or later if due to a postoperative complication.
- *Long-term survival:* all surviving patients were followed up for at least 2.5 years (mean follow-up: 6 years) by medical history or telephone interview.

Statistical analysis. The SPSS 17.0 statistical package for Windows (SPSS Inc) was used for data analysis. For the descriptive analysis of the sample, frequencies and percentages were obtained for categorical variables. Continuous quantitative variables were expressed using medians and interquartile ranges (IQRs) because they usually followed a nonparametric distribution. Survival curves were calculated using the Kaplan-Meier method. For univariate analysis, the χ^2 test or the Fisher exact test was used in the case of categorical variables. For normally distributed numerical variables, the Student *t*-test was used to compare means. The Mann-Whitney *U* test was used for non-normal distribution.

Cox regression was performed to highlight the variables that behaved as independent prognostic factors for long-term survival. The most clinically revealing variables that were statistically significant in the univariate analysis were introduced into the model. A significance level of $P < .05$ was considered, and the odds ratio and hazard ratio (HR) were used as measures of the magnitude of the association.

RESULTS

Of the 55 patients operated on for mesenteric ischemia of venous origin during the study period, the mean age was 66.7 years (standard deviation: ±18.0 years), 36 (65.5%) men and 19 (34.5%) women ($P < .001$).

The median Charlson index was 1.0 (IQR: 1.0-3.0). According to this index, 28 (50.9%) patients had no comorbidity, 9 (16.4%) patients had low comorbidity, and 18 (32.7%) patients had high comorbidity. Among their comorbidities, the following stood out: arterial hypertension in 35 (63.6%) cases, heart disease in 17 (30.9%) cases, diabetes mellitus in 16 (29.1%) cases, chronic renal failure in 8 (14.5%) cases, liver disease in 8 (14.5%) cases, and chronic obstructive pulmonary disease in 5 (9.1%) cases. Five patients (9.1%) had a preoperative diagnosis of deep venous thrombosis and were anticoagulated with acenocoumarol or low-molecular-weight heparin at the time of MVT. In addition, 13 patients (23.6%) were on antiplatelet therapy.

The clinical findings, symptom course, laboratory values, and surgical aspects of the patients in the sample are listed in Table I.

In our series, no patients underwent surgical or endovascular venous revascularization procedures, such as mechanical thrombectomy or local thrombolysis.

Based on radiological, surgical, and histopathological findings, MVT was found to involve the superior mesenteric vein or its branches in 32 (58.2%) patients, the mesenteric-portal venous axis in 9 (16.4%), the splenoportal axis plus superior mesenteric vein in 9 (16.4%), the splenoportal axis in 3 (5.5%), the superior and inferior mesenteric venous systems in 1 (1.8%), and isolated portal vein thrombosis in 1 (1.8%) patient. In one patient the exact localization of the affected venous segment could not be reported. No patient had isolated inferior mesenteric vein thrombosis.

A total of 14 patients (25.5%) were reoperated: 9 second look planned since the first surgery, 3 reinterventions due to deterioration of the patient with progression of the ischemia, 1 anastomosis dehiscence, and 1 upper gastrointestinal bleeding.

Only 6 patients (10.9%) had no complication, 17 patients (30.9%) presented minor complications, and 32 patients (58.2%) presented severe complications according to the Clavien-Dindo classification.

The median length of stay was 14.0 days (IQR: 9.0-30.0 days).

Operative mortality was 23.6% (13 patients): 4 cases due to massive ischemia, 1 ischemia progression, 1 multifactorial multiorgan failure, 3 decompensated cirrhosis, 1 stroke, 2 pneumonia, and 1 peritoneal carcinomatosis.

A total of 41 (74.5%) patients were classified as primary MVT, and 14 (25.5%) patients as secondary MVT. Table II lists the related pathologies. Within the first group, in 11 (36.7%) patients, a hypercoagulability status was detected, and 19 (63.3%) patients had idiopathic MVT. It is noteworthy that in 4 of the 11 patients with hypercoagulability status, more than one thrombophilia factor coexisted. The hematological study could not be performed in 11 patients (2 missing, 7 postoperative deaths, and 2 early deaths during follow-up).

At the end of the follow-up, 31 patients (56.4%) had died and 24 (43.6%) remained alive. The probability of being alive at 1, 3, and 5 years was 66.4%, 57.9%, and 51.0%, respectively.

In only seven of the deceased patients was death correlated with progression or direct complication of MVT (massive pulmonary thromboembolism, extensive MVT to the splenoportal axis, multiple vascular thrombosis, complication with extensive arterial thrombosis, and necrotizing vasculitis). Patients with primary MVT (with and without hypercoagulability) had 0% operative mortality. At the end of follow-up, only 2 of the 11 patients had died (18%), none of them with apparent relation to the previous MVT process (one patient due to congestive

Table I. Baseline characteristics of the patients included in the sample

Clinical findings	Values
Abdominal pain	54 (98.2)
Abdominal distension	30 (54.5)
Signs of peritonitis	39 (70.9)
Fever	5 (9.1)
Shock	18 (32.7)
Evolution of the symptoms	
Duration of symptoms, hours	
<24	13 (23.6)
24-48	10 (18.2)
>48	32 (58.2)
Time elapsed from surgeon assessment to surgery, hours	
<6	14 (25.5)
6-12	22 (40.0)
>12	19 (34.5)
Laboratory values	
Hemoglobin, g/dL	14.2 (12.1-15.6)
Leukocytes/mm^3	17,000 (14,200.0-25,300.0)
Platelet count/mm^3	237,000 (174,000-327,500)
Creatinine, mg/dL	1.13 (0.80-1.52)
Glycemia, mg/dL	175 (126-223)
Serum creatine phosphokinase, U/L	90 (38-248.5)
Serum amylase, U/L	69 (36.5-125.0)
Radiological tests	
Computed tomography	33 (60)
Angiography	3 (5.4)
Surgical aspects	No. (%)
Small bowel involvement	49 (89.1)
Large bowel involvement	14 (25.5)
Segmental resection	44 (80.0)
Primary anastomosis	29 (52.7)
Massive intestinal necrosis	4 (7.3)

IQR, Interquartile range.
Data are shown as number (%) and median (IQR).

heart failure and another with associated dilated cardiomyopathy and endometrial carcinoma).

Table III shows the results of the univariate analysis of operative mortality. Only comorbidity ($P = .019$) and massive ischemia ($P = .002$) were related to mortality.

Patients with primary MVT presented better mortality rates compared with the group of patients with secondary MVT, almost statistically significant ($P = .058$). However, there were no differences between those who presented hypercoagulability and those who did not (0% mortality in both cases). Multivariate analysis could not be performed because of the low number of postoperative deaths (0%) in one of the included variables in the model (type of MVT).

Table IV shows the results of the univariate analysis of survival. The variables age ($P < .001$), comorbidity measured by the Charlson comorbidity index ($P < .001$), and type of MVT ($P = .003$) were related to long-term survival (Fig 1). Of note, the existence of an underlying neoplasm was not related to long-term survival ($P = .175$) (Table IV). After excluding the 11 patients in whom the hypercoagulability study could not be performed, no statistically significant differences were observed in long-term survival between patients with hypercoagulability and patients with idiopathic MVT ($P = .116$). However, survival curves (Fig 2) show a clear trend toward a better prognosis for patients with hypercoagulability as the follow-up time progresses.

In the multivariate analysis of long-term survival, age ($P = .002$; HR: 1.05, 95% confidence interval: 1.02-1.09) and comorbidity ($P = .019$; HR: 1.28, 95% confidence interval: 1.04-1.57) behaved as independent prognostic factors for survival.

DISCUSSION

Current treatment of mesenteric thrombosis is mainly directed toward early anticoagulation.[24-26] However, 20% to 30%[27,28] of patients will require surgical intervention. From this subgroup of patients undergoing surgery, it is difficult to find studies with a sufficient volume of patients to draw any robust conclusions.

Numerous studies in patients with intestinal ischemia have shown that age is associated with a poor prognosis.[29,30] In our sample of patients with MVT, age behaved as an independent prognostic factor for long-term survival.

According to the Charlson score,[21,22] 33% of our patients had severe comorbidity. We found that comorbidity was shown to be a predictor of a poor prognosis for both operative mortality and survival. For each point increase in the Charlson index, the risk of death increased by 43%. Other authors[28] have also associated comorbidity with an increased risk of requiring surgery and 30-day mortality.

In a previous study by our group,[30] focused on a series of 186 patients with acute mesenteric ischemia (25 with MVT), we found that the age-adjusted Charlson score was also shown to be an independent predictor of perioperative mortality and long-term survival. Other studies that have assessed the Acute Physiology and Chronic Health Evaluation (APACHE) II severity score[31] at admission, to predict a prognosis in MVT,[32,33] have found a high score as an independent predictor of irreversible bowel ischemia.

Regarding clinical findings, in line with most of published reports, abdominal pain is the most frequent symptom (98%).[9] It has been reported that the presence of peritonitis is a risk factor for requiring surgical intervention and perioperative mortality.[28] Our study showed a high percentage of patients with peritonitis (71%)

Table II. Concurrent conditions related to mesenteric venous thrombosis (*MVT*) in 27 patients in whom an underlying etiology could be identified

Underlying conditions related to MVT	Values
Hypercoagulability status	11[a] (20.0)
Protein C and S deficiencies	5
Factor V Leiden mutation	3
Prothrombin gene mutation	2
Lupus anticoagulants	2
Activated protein C resistance	1
Antithrombin III deficiency	1
Antiphospholipid antibodies	1
Hyperhomocysteinemia	1
Monoclonal gammopathy	1
Sickle cell disease	1
Neoplasia	7 (12.7)
Sigmoid cancer	1
Colon cancer	1
Neuroendocrine carcinomatosis	1
Non-Hodgkin's lymphoma	1
Endometrial cancer	1
Lung cancer	1
Breast cancer	1
Intra-abdominal infection	4 (7.3)
Appendicitis with pylephlebitis	2
Pancreatitis	1
Cholecystitis	1
Liver cirrhosis	3 (5.5)
Recurrent pulmonary thromboembolism	1 (1.8)
Previous deep venous thrombosis	1 (1.8)

Data are shown as number (%).
[a]In 4 of the 11 patients with hypercoagulability status, more than one thrombophilia factor coexisted.

compared with other series, because ours only included surgical MVT.

Laboratory markers for the early diagnosis of MVT are not yet available.[17] In our cases, none of these parameters showed statistically significant association with operative mortality or survival. Other authors[12] have found leukocytosis to be a predictor of irreversible intestinal ischemia in MVT.

CT has improved early diagnosis, with a specificity of 100% and a sensitivity of 93%,[34] and is the "gold standard" diagnostic procedure.[35] In our series, the difference in mortality between patients with and without CT almost reached statistical significance. It is possible that the progressive standardization of the early use of diagnostic CT may have influenced the reduction in mortality. In fact, mortality in this series is 10 points lower than the mortality observed in our surgical patients with MVT before 2002, when comparatively fewer CT scans were performed.[36] Acosta and Salim[26] highlight that early diagnosis with urgent CT and anticoagulation are two important elements for a successful nonoperative outcome.

For most patients with MVT, at least one predisposing hematological risk factor is recognized. The frequency of idiopathic cases ranges from 21%[37] to 49%.[38] In our series, we could not establish a clear triggering factor for MVT in 19 (35%) cases. There have been series that identify a precipitating hematological risk factor in up to 80% of patients with MVT.[16] We believe that surgical patients constitute a subgroup of MVT in which the precipitating factors are often unclear. In addition, the higher perioperative mortality precludes an appropriate deferred hematological workup. In our patients, a diagnosis of hematological thrombophilia was only possible in the few cases in which it was known before the episode of MVT and in those patients who survived and were able to undergo the study.

An increasing number of factors that may influence the occurrence of MVT have been described: hereditary thrombophilias (antithrombin III deficiency, factor V Leiden mutation, hemorrhage-telangiectasia, hyperfibrinogenemia, JAK2VI6F mutation, plasminogen deficiency, protein C deficiency, protein S deficiency, prothrombin G 20210 mutation, and HbS sickle cell disease); acquired thrombophilias (antiphospholipid antibodies, disseminated intravascular coagulation, essential thrombocythemia, hyperhomocysteinemia, monoclonal gammopathy, polycythemia vera, and paroxysmal nocturnal hemoglobinuria); hypercoagulable states related to systemic disorders, hormones, or drugs (nephrotic syndrome, cancer, pregnancy, oral contraceptives, estrogens, puerperium, etc); local intra-abdominal processes (splenectomy, diverticulitis, trauma, pancreatitis, intra-abdominal infection, cirrhosis, portal hypertension, splenomegaly, inflammatory bowel disease, abdominal postoperative state, etc); or history of previous deep venous thrombosis, among other factors.[9,11]

Thrombophilia can be described as an abnormal predisposition to form clots within the vascular system.[39] The most frequent thrombophilic disorder in our series was protein C and S deficiency (45%) followed by factor V Leiden mutation (27%). It should be noted that patients with prothrombin and factor V Leiden mutation appear more prone to recurrent venous thrombosis in unusual locations and at an early age.[40,41] Salim et al[10] found a prevalence of factor V Leiden mutation without cancer of 27% in MVT and 39% in systemic venous thromboembolism and suggest considering screening for thrombophilia in both groups of patients. MVT has also been described after bariatric surgery.[42] Cases of COVID-19-acquired thrombophilia have also been identified with MVT.[43,44] In a previous study by our group,[36] we found that MVT could be associated with hypercoagulability status in up to 33% of cases. Patients with

Table III. Univariate analysis of operative mortality

Variables	Alive (n = 42, 76.4%)	Deaths (n = 13, 23.6%)	*P* values	OR (95% CI)
Age, years, mean ± SD	64.8 ± 19.0	73.0 ± 12.8	.085	1.03 (0.99-1.08)
Gender, No. (%)			.336	1.91 (0.54-6.82)
Male	29 (69.0)	7 (53.8)		
Female	13 (31.0)	6 (46.2)		
Charlson comorbidity index, median (IQR)	1.0 (0.0-3.0)	3.0 (1.0-5.0)	**.019**	1.53 (1.07-2.17)
Peritonitis, No. (%)			.486	0.57 (0.15-2.11)
No	11 (26.2)	5 (38.5)		
Yes	31 (73.8)	8 (61.5)		
Shock, No. (%)			.070	3.29 (0.91-11.94)
No	31 (73.8)	6 (46.2)		
Yes	11 (26.2)	7 (53.8)		
Hemoglobin, gr%, mean ± SD	13.8 ± 2.7	13.8 ± 2.6	.969	0.99 (0.79-1.26)
Leukocytes/mm^3, mean ± SD	18,705.0 ± 10,382.8	19,396.92 ± 11,175.9	.834	1.00 (1.00-1.00)
Creatinine, mg%, median (IQR)	1.0 (0.8-1.6)	1.4 (1.0-3.0)	.194	1.23 (0.90-1.70)
Glycemia, mg%, median (IQR)	169.5 (121.8-205.8)	207.0 (138.0-283.5)	.323	1.00 (0.10-1.00)
CPK, U/L, median (IQR)	90.0 (37.5-257.0)	84.0 (37.0-193.5)	.614	1.00 (0.10-1.00)
Amylasemia, U/L, median (IQR)	65.0 (34.5-116.0)	92.5 (44.8-197.3)	.364	1.00 (0.10-1.01)
CT abdomen, No. (%)			.070	0.31 (0.08-1.13)
No	14 (32.6)	8 (61.5)		
Yes	28 (66.7)	5 (38.5)		
Symptom evolution time, hours, No. (%)			.852	0.93 (0.45-1.95)
<24	11 (26.2)	2 (15.4)		
24-48	5 (11.9)	5 (38.5)		
>48	26 (61.9)	6 (46.2)		
Small intestine involvement, No. (%)			.181	1.36 (1.15-1.61)
No	6 (14.3)	0 (0.0)		
Yes	36 (85.7)	13 (100.0)		
Colon involvement, No. (%)			.722	1.38 (0.35-5.46)
No	31 (75.6)	9 (69.2)		
Yes	10 (24.4)	4 (30.8)		
Massive ischemia, No. (%)			**.002**	0.18 (0.10-0.32)
No	42 (100.0)	9 (69.2)		
Yes	0 (0.0)	4 (30.8)		
Intestinal resection, No. (%)			.106	0.27 (0.07-1.10)
No	6 (14.3)	5 (38.5)		
Yes	36 (85.7)	8 (61.5)		
Primary anastomosis, No. (%)			.512	0.61 (0.16-2.26)
No	14 (37.8)	6 (50.0)		
Yes	23 (62.2)	6 (50.0)		
Underlying neoplasm, No. (%)			.664	1.35 (0.23-7.92)
No	37 (88.1)	11 (84.6)		
Yes	5 (11.9)	2 (15.4)		
Type of MVT, No. (%)			.058	3.64 (0.96-13.84)
Primary	34 (81.0)	7 (53.8)		
Secondary	8 (19.0)	6 (46.2)		
Primary MVT,[a] No. (%)			N.A.[b]	N.A.[b]
Idiopathic	19 (63.3)	0 (0.0)		
Hypercoagulability	11 (36.7)	0 (0.0)		

CI, Confidence interval; *CPK*, creatine phosphokinase; *CT*, computed tomography; *IQR*, interquartile range; *MVT*, mesenteric venous thrombosis; *OR*, odds ratio; *SD*, standard deviation.
Boldface *P* values represent significance $P < .05$.
[a]Excluding 11 patients in whom the hypercoagulability study could not be performed.
[b]Not applicable due to "0" values observed among dead patients.

coagulation disorders had lower mortality than those without it. Some studies[27,38] have found coagulopathy to be a condition associated with MVT that confers a higher risk of requiring surgery and more aggressive management. Andraska et al[45] point out that lactic acidosis and confirmed genetic thrombophilia were strong predictors of the need for bowel resection. This does not contradict our results, as the cohort of our study is the surgical patients. These patients, despite being a subpopulation at higher risk of mortality compared with patients who do not need surgery, once they arrive in the operating theatre, in the case of having hereditary thrombophilia, seem to have better evolution and outcomes than the rest of patients with surgical MVT linked to other causes. Our patients with primary MVT had 0% operative mortality. At the end of follow-up, 2 of 11 patients with hypercoagulability had died, none of them apparently related to the previous MVT process. The high mortality, with increased risk of intestinal infarction[45] and risk of recurrence[41] of MVT linked to thrombophilia, compared with overall mortality from MVT, makes it advisable to systematically screen these patients for thrombophilia and to consider lifelong anticoagulant therapy, especially in the absence of a reversible risk factor.[10] We consider personal or family history of peripheral venous thrombosis as a risk factor for MVT, especially in the absence of a known underlying disease, as reported in the literature.[37,46]

Among the pathogenic mechanisms of MVT categorized by Zarrouk et al[5] as "local venous congestion," we found three patients with liver cirrhosis, a comorbidity with an obvious poor prognosis in our series, where 100% of patients died in the perioperative period. Patients with MVT have a different risk factor profile than patients with systemic thromboembolism,[10] showing a higher prevalence of cancer. Malignancy has long been

Table IV. Univariate survival analysis

Variables	Alive (n = 24, 43.6%)	Deaths (n = 31, 56.4%)	*P* values	HR (95% CI)
Age, years, mean ± SD	54.6 ± 18.3	76.1 ± 10.9	**<.001**	1.06 (1.03-1.10)
Gender, No. (%)			.502	1.28 (0.62-2.65)
Male	17 (70.8)	19 (61.3)		
Female	7 (29.2)	12 (38.7)		
Charlson comorbidity index, median (IQR)	1 (0.0-1.8)	2.0 (1.0-4.0)	**<.001**	1.43 (1.18-1.73)
Small intestine involvement, No. (%)			.268	2.25 (0.54-9.48)
No	3 (12.5)	2 (6.5)		
Yes	21 (87.5)	29 (93.5)		
Colon involvement, No. (%)			.592	1.24 (0.57-2.69)
No	19 (79.2)	22 (71.0)		
Yes	5 (20.8)	9 (29.0)		
Intestinal resection, No. (%)			.178	0.51 (0.19-1.37)
No	6 (25.0)	5 (16.1)		
Yes	18 (75.0)	26 (83.9)		
Underlying neoplasm, No. (%)			.175	1.86 (0.76-4.57)
No	23 (95.8)	25 (80.6)		
Yes	1 (4.2)	6 (19.4)		
Type of MVT, No. (%)			**.003**	3.12 (1.46-6.66)
Primary	22 (91.7)	19 (61.3)		
Secondary	2 (8.3)	12 (38.7)		
Primary MVT,[a] No. (%)			.116	0.30 (0.06-1.47)
Idiopathic	12 (57.1)	7 (77.8)		
Hypercoagulability	9 (42.9)	2 (22.2)		

CI, Confidence interval; *HR*, hazard ratio; *IQR*, interquartile range; *MVT*, mesenteric venous thrombosis; *SD*, standard deviation.
Significance level and HR obtained by the Cox regression.
Boldface *P* values represent significance $P < .05$.
[a]Excluding 11 patients in whom the hypercoagulability study could not be performed.

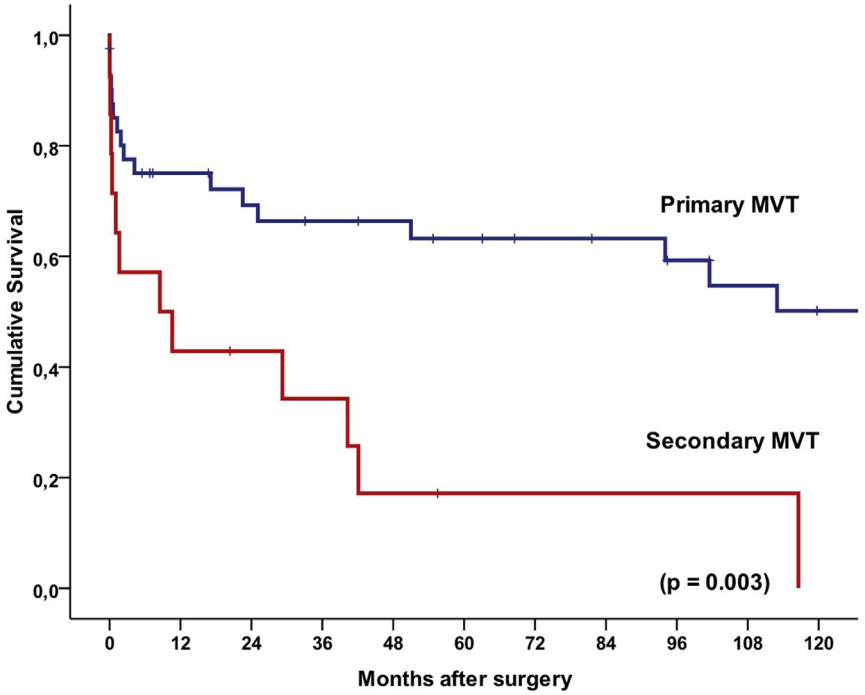

Fig 1. Comparative survival curves between patients with primary and secondary mesenteric venous thrombosis (*MVT*) ($P = .003$; HR: 3.12, 95% CI: 1.46-6.66). *CI*, Confidence interval; *HR*, hazard ratio.

recognized as a risk factor for hypercoagulability and has been reported to be present in 4% to 16% of patients with acute MVT.[9] An occult neoplasia must be excluded in these patients. Sometimes the cancer is already present at the time of MVT diagnosis, as occurred in five of our patients. Other times, it is diagnosed in the early postoperative period. All our neoplastic patients with MVT died during follow-up except for one patient

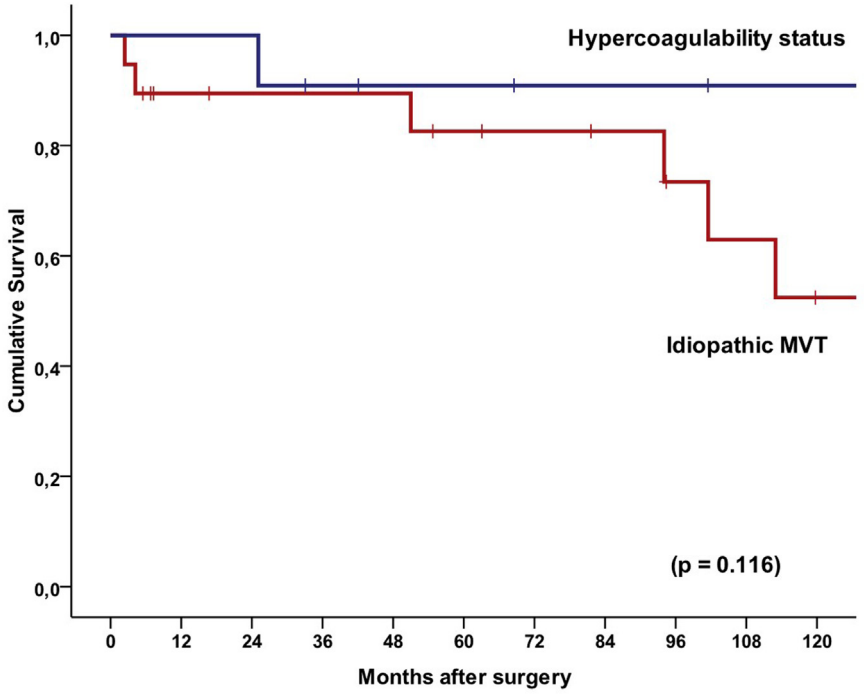

Fig 2. Comparative survival curves of patients with hypercoagulability and patients with idiopathic mesenteric venous thrombosis (*MVT*) ($P = .116$; HR: 0.30, 95% CI: 0.006-1.17). *CI*, Confidence interval; *HR*, hazard ratio.

with breast cancer. Therefore, liver cirrhosis and cancer may be conditions associated with a worse prognosis in surgical MVT, although we have failed to demonstrate statistically this relationship probably due to the small number of patients in our sample. Other authors have reached the same conclusion.[28]

Overall, operative mortality of surgical MVT ranges from 9% to 60%, depending on the series,[9] with a mean 30-day mortality of 32% in severe cases.[47] Mortality of nonsurgical MVT is generally low, with 30-day mortality figures ranging from 1.2% to 4.9%.[27,48-50] Our study showed that surgical MVT leads to high mortality and relatively low long-term survival. More than half of the patients (56.4%) in our series had died by the end of follow-up. However, of the 31 patients who died during follow-up, only 7 could be correlated with progression or direct complication of MVT.

Surprisingly, our study also found that patients with MVT and underlying malignancies did not show significant differences in long-term survival compared with those without malignancies. This may be explained by the fact that in the group of non-neoplastic patients, in addition to patients with hypercoagulability, several patients with very severe disease and poor prognosis were included.

The probability of being alive in our series ranged around 50%, the overall median of the sample being 7.8 years. These survival figures are only slightly lower than those of other MVT series including medically and surgically treated patients. Feldman et al[33] obtained a 5-year survival of 57.9% and an overall median survival of 7.1 years.

Limitations. Because of the nature of this pathology and the low prevalence, a large-volume study of patients and prospective randomization is not possible. As it was a single-center study with a relatively small sample, despite an extensive period of time and follow-up, the limited statistical power of the study could have altered the results.

Nonsurgical MVTs managed conservatively, which are the majority, have not been included in this study, so this is an analysis of a very specific group, with a worse prognosis a priori and whose conclusions cannot be generalized to all MVTs, with a more benign overall management. On the other hand, patients with early postoperative mortality could not undergo a hypercoagulability study. This could have biased the results.

Finally, coagulation tests (prothrombin time, activated partial thromboplastin time, thrombin time, and international normalized ratio) to assess blood coagulation function were not collected in this study, which was more focused on surgical aspects. Therefore, it could not be verified whether the ability to maintain therapeutic levels of anticoagulation could affect the final outcome.

CONCLUSIONS

Patients with MVT who are not amenable to conservative treatment and who end up in surgery represent a subgroup with high lethality. Primary MVT has more favorable outcomes compared with other causes of surgical MVT.

AUTHOR CONTRIBUTIONS

Conception and design: MA, JM
Analysis and interpretation: MA, DO, AS, JM
Data collection: MA, DO, AS, MP, AR, RB
Writing the article: MA
Critical revision of the article: MA, DO, AS, MP, AR, RB, JM
Final approval of the article: MA, DO, AS, MP, AR, RB, JM
Statistical analysis: JM
Obtained funding: Not applicable
Overall responsibility: MA

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