World Journal of

Gastroenterology

World Journal of Gastroenterology

Contents

Contents

Contents

ABOUT COVER

Editorial board member of *World Journal of Gastroenterology*, Prof. Antonio Biondi is an Associate Editor of *Updates in Surgery*, the official journal of the Italian Society of Surgery, and a Full Professor of surgery at the School of Medicine, University of Catania, Italy. Prof. Biondi obtained his MD degree from the University of Catania in 1993, and his PhD degree in 2001. He was promoted to Full Professor in the School of Medicine, University of Catania, in 2018. His ongoing research interests are colorectal surgery and laparoscopic procedures. He is a member of the editorial boards and a reviewer of several scientific journals, and has published more than 150 peer-reviewed articles. Prof. Biondi served as elected member of the Italian National University Council (CUN). Currently, he is the Chief of the Laparoscopic Surgery Division, Department of General Surgery and Medical-Surgical Specialties, University Hospital Policlinico Vittorio Emanuele, Catania and Director of the Multidisciplinary Research Center for Diagnosis and Treatment of Rare Diseases, University of Catania.

AIMS AND SCOPE

The primary aim of *World Journal of Gastroenterology* (*WJG*, *World J Gastroenterol*) is to provide scholars and readers from various fields of gastroenterology and hepatology with a platform to publish high-quality basic and clinical research articles and communicate their research findings online. *WJG* mainly publishes articles reporting research results and findings obtained in the field of gastroenterology and hepatology and covering a wide range of topics including gastroenterology, hepatology, gastrointestinal endoscopy, gastrointestinal surgery, gastrointestinal oncology, and pediatric gastroenterology.

INDEXING/ABSTRACTING

The *WJG* is now indexed in Current Contents®/Clinical Medicine, Science Citation Index Expanded (also known as SciSearch®), Journal Citation Reports®, Index Medicus, MEDLINE, PubMed, PubMed Central, and Scopus. The 2020 edition of Journal Citation Report® cites the 2019 impact factor for *WJG* as 3.665 (5-year impact factor: 4.048), ranking *WJG* as 35 among 88 journals in gastroenterology and hepatology (quartile in category Q2).

RESPONSIBLE EDITORS FOR THIS ISSUE

ORIGINAL ARTICLE

Retrospective Cohort Study

Predictors of irreversible intestinal resection in patients with acute mesenteric venous thrombosis

Shi-Long Sun, Xin-Yu Wang, Cheng-Nan Chu, Bao-Chen Liu, Qiu-Rong Li, Wei-Wei Ding

ORCID number: Shi-Long Sun 0000-0002-2943-6655; Xin-Yu Wang 0000-0002-7605-3091; Cheng-Nan Chu 0000-0001-9986-3508; Bao-Chen Liu 0000-0002-6944-1205; Qiu-Rong Li 0000-0002-5470-3161; Wei-Wei Ding 0000-0002-5026-689X.

Shi-Long Sun, Xin-Yu Wang, Cheng-Nan Chu, Bao-Chen Liu, Qiu-Rong Li, Wei-Wei Ding, Division of Trauma and Surgical Intensive Care Unit, Research Institute of General Surgery, Jinling Hospital, Medical School of Nanjing University, Nanjing 210002, Jiangsu Province, China

Corresponding author: Wei-Wei Ding, MD, PhD, Doctor, Division of Trauma and Surgical Intensive Care Unit, Research Institute of General Surgery, Jinling Hospital, Medical School of Nanjing University, No. 305, East Zhongshan Road, Nanjing 210002, Jiangsu Province, China. dingwei_nju@hotmail.com

Abstract

BACKGROUND
Acute mesenteric venous thrombosis (AMVT) can cause a poor prognosis. Prompt transcatheter thrombolysis (TT) can achieve early mesenteric revascularization. However, irreversible intestinal ischemia still occurs and the mechanism is still unclear.

AIM
To evaluate the clinical outcomes of and to identify predictive factors for irreversible intestinal ischemia requiring surgical resection in AMVT patients treated by TT.

METHODS
The records of consecutive patients with AMVT treated by TT from January 2010 to October 2017 were retrospectively analyzed. We compared patients who required resection of irreversible intestinal ischemia to patients who did not require.

RESULTS
Among 58 patients, prompt TT was carried out 28.5 h after admission. A total of 42 (72.4%) patients underwent arteriovenous combined thrombolysis, and 16 (27.6%) underwent arterial thrombolysis alone. The overall 30-d mortality rate was 8.6%. Irreversible intestinal ischemia was indicated in 32 (55.2%) patients, who had a higher 30-d mortality and a longer in-hospital stay than patients without resection. The significant independent predictors of irreversible intestinal ischemia were Acute Physiology and Chronic Health Evaluation (APACHE) II score (odds ratio = 2.368, 95% confidence interval: 1.047-5.357, $P = 0.038$) and leukocytosis (odds ratio = 2.058, 95% confidence interval: 1.085-3.903, $P = 0.027$).

Using the receiver operating characteristic curve, the cutoff values of the APACHE II score and leukocytosis for predicting the onset of irreversible intestinal ischemia were calculated to be 8.5 and 12×10^9/L, respectively.

CONCLUSION
Prompt TT could achieve a favorable outcome in AMVT patients. High APACHE II score and leukocytosis can significantly predict the occurrence of irreversible intestinal ischemia. Therefore, close monitoring of these factors may help with the early identification of patients with irreversible intestinal ischemia, in whom ultimately surgical resection is required, before the initiation of TT.

Key words: Acute mesenteric venous thrombosis; Transcatheter thrombolysis; Irreversible intestinal ischemia; Surgical resection; Acute Physiology and Chronic Health Evaluation II score; Leukocytosis

Core tip: Prompt transcatheter thrombolysis (TT) can achieve early mesenteric revascularization in acute mesenteric venous thrombosis (AMVT) patients. However, irreversible intestinal ischemia still occurs in many cases. We compared AMVT patients with irreversible intestinal ischemia who underwent TT to patients with reversible intestinal ischemia. We demonstrated that the independent predictors of irreversible intestinal ischemia were Acute Physiology and Chronic Health Evaluation II score and leukocytosis and the cutoff values were 8.5 and 12×10^9/L, respectively. Close monitoring of these factors may help with early identification of irreversible intestinal ischemia, which requires surgical resection, before initiation of TT in AMVT patients.

INTRODUCTION

Acute mesenteric venous thrombosis (AMVT) accounts for approximately 5% to 15% of cases of acute mesenteric ischemia and has a mortality of up to 10%[1-3]. AMVT is characterized by an insidious onset, rapid progression, and non-specific abdominal signs in the early stages. The occurrence of irreversible intestinal ischemia impairs the outcomes of AMVT. In the short term, AMVT can cause intestinal necrosis, which predicts a poor outcome[4]. In the long term, postischemic intestinal stenosis (delayed intestinal stricture or non-transmural necrosis) impairs the quality of life[5].

The early diagnosis of AMVT has increased because of the feasible use of abdominal computed tomography (CT), with a specificity of 100% and sensitivity of 93%[6]. The main goal of treatment is early recanalization to prevent irreversible intestinal ischemia[7]. Immediate anticoagulation is the first step and the cornerstone of management strategies. Early anticoagulation has been demonstrated to result in > 80% recanalization and to reduce mortality[8,9]. However, a previous study also showed that systemic anticoagulation was associated with 25% of cases of extrahepatic portal vein hypertension, 18% of cases of transmural bowel infarction, and an elevated risk of bleeding[10,11]. Transcatheter thrombolysis (TT) is the mainstream method used, and it is recommended when there is persistent worsening of abdominal symptoms despite systemic anticoagulation or when there is a high risk of bowel infarction at admission[12]. Prompt recanalization, salvage of additional potentially reversible segments, and decreased intestinal resection can be achieved with endovascular treatment[12,13]. The use of endovascular therapy has increased significantly in the modern era and has altered the management of ASMVT[14]. However, damage control laparotomy including intestinal resection and open abdomen may be ultimately warranted for patients with intestinal necrosis and severe sepsis[15]. Our group previously advocated the establishment of an intestinal stroke center (ISC) and a

multidisciplinary stepwise management strategy for the treatment of AMVT, which have been proven to decrease the mortality and improve the clinical outcomes[16,17].

The mortality rates associated with intestinal resection ranged between 20% and 60%, and severe disability may result from either intestinal infarction or postischemic intestinal stenosis[18,19]. Some researchers revealed that aggressive TT could improve the outcomes[13,17]. However, irreversible intestinal ischemia is still the main reason for poor prognosis. The risk factors for irreversible intestinal ischemia are unknown, especially in AMVT patients treated by TT. The present study aimed to evaluate the clinical outcomes and determine the independent clinical, laboratory, and radiologic factors that can successfully predict irreversible intestinal ischemia leading to resection according to short- and long-term outcomes in AMVT patients treated by TT. The present study also aimed to discriminate patients who develop irreversible intestinal ischemia and who are in need of operative intervention from patients who have reversible bowel ischemia.

MATERIALS AND METHODS

Patients

Prospectively maintained records of patients with AMVT admitted to the ISC during the period from January 2010 to October 2017 were retrospectively reviewed. Ethical approval of the study was obtained from the Institutional Review Board. This study was conducted in accordance with the principles of the Declaration of Helsinki.

The diagnosis of AMVT was based on the following criteria: Acute clinical onset of abdominal symptoms with a duration of less than 4 wk before admission, vascular occlusion of the superior mesenteric vein (SMV) on CT or digital subtraction angiography (DSA) portography, and intestinal wall injury on CT[5,17]. AMVT patients who were treated by TT were included in the study (Figure 1). We excluded AMVT patients (1) whose symptoms improved after anticoagulation only; (2) with contraindications to thrombolysis; (3) who underwent hybrid emergency operation upon admission without TT; (4) who underwent surgical intervention before admission; (5) who participated in follow-up for < 1 year; and (6) with incomplete records or records missing some of the vital data required for the study.

The primary outcome was the resection of irreversible intestinal ischemic injury, defined by laparotomy and/or pathology assessment of bowel necrosis/infarction and postischemic intestinal stenosis (Figure 2). Patients were divided into two groups according to primary outcomes. Patients who recovered from AMVT after TT with no need for intestinal resection after 12 mo of follow-up were considered not to have irreversible intestinal ischemic injury, considering that irreversible intestinal ischemia could be ruled out at this point in follow-up. For primary outcome assessment, patients were followed until the date of irreversible ischemia diagnosis (for patients who underwent surgery), 1 year of follow-up (for patients who did not undergo surgery), or death, whichever came first.

Treatment strategy

A multidisciplinary stepwise management strategy was followed upon admission, aiming to achieve early mesenteric recanalization as described before[17]. Immediate anticoagulation, with the initiation of an unfractionated heparin bolus followed by continuous infusion, was initiated soon after the diagnosis was made. In addition, supportive treatment included broad-spectrum antibiotics, bowel rest, microcirculation improvement, and acidosis correction. Intensive care unit (ICU) treatment, including fluid resuscitation, multi-organ function support, and early enteral nutrition, was initiated when indicated.

Endovascular treatment by transcatheter thrombolysis

Endovascular treatment approaches were chosen depending on the location of the thrombus in the portal vein and superior mesenteric vein as described before[12,17]. For patients with patent or partially patent intrahepatic portal vein branches, a percutaneous transhepatic approach or trans-jugular intrahepatic portosystemic approach was preferred for direct thrombolysis of the portal vein (PV)-SMV thrombosis, and indirect thrombolysis alone *via* the superior mesenteric artery (SMA) was also adopted. Moreover, indirect thrombolysis alone *via* the SMA was adopted for patients with a completely occluded PV or portal vein cavernous transformation associated with superior mesenteric vein thrombosis. A catheter was placed in the vein under the guidance of DSA, and the thrombi were aspirated *via* the venous catheter.
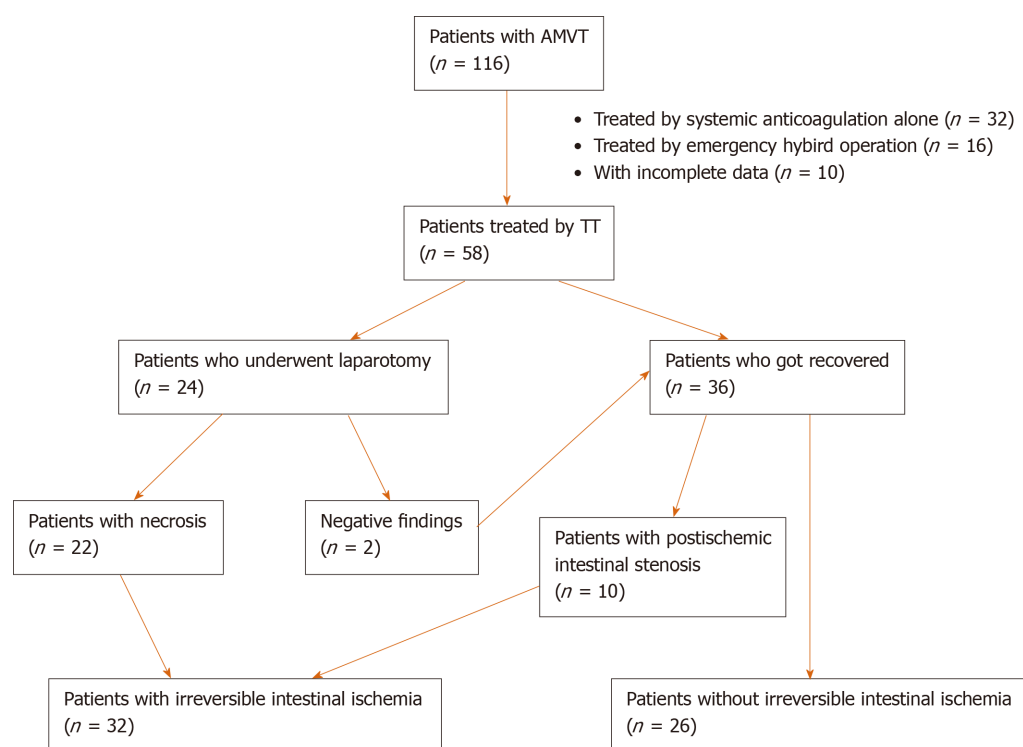
Figure 1 Flow diagram illustrating the management and outcome of patients with acute mesenteric venous thrombosis. AMVT: Acute mesenteric venous thrombosis; TT: Transcatheter thrombolysis.
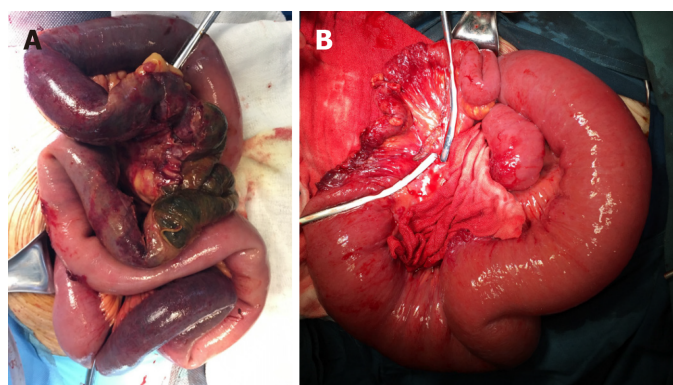
Figure 2 Operative findings of irreversible intestinal ischemia. A: Intestinal necrosis, characterized by gangrenous bowel; B: Postischemic intestinal stenosis, characterized by segmental intestinal stricture.

Low-molecular-weight heparin (4100 U/12 h) was administered as an anticoagulant. Urokinase [(40-60) × 10^4 IU/d] or recombinant tissue plasminogen activator (20 mg/d) was administered for 5 d for thrombolysis before angiography was repeated. If patients had stable vital signs and improved abdominal signs, thrombolytic treatment was continued for 1 wk. Contrast-enhanced abdominal CT and DSA were repeated to assess the abdominal and intestinal integrity. In patients who developed severe/diffuse peritonitis alongside worsening vital signs and hemodynamic instability, surgical intervention was required.

Surgical resection of irreversible intestinal ischemia
Damage control surgery was indicated during or after transcatheter thrombolytic therapy if there were signs of irreversible intestinal ischemia, including intestinal necrosis and postischemic intestinal stenosis[20,21](Figure 2).

Intestinal necrosis(Figure 2A)**:** Surgical procedures included resection of the necrotic bowel and reservation of the suspected necrotic small bowel. To determine the patency of the intestine, distal or proximal stomas were created. In the presence of

intraabdominal hypertension, the abdomen was left open. Abdominal closure was performed once the intraabdominal pressure returned to a normal range. Patients were transferred to the ICU following surgery, where patients received organ support therapy to restore homeostatic balance. A definite intestinal anastomosis was performed after the patient completely recovered from the acute phase and was on a full oral diet.

Postischemic intestinal stenosis(Figure 2B)**:** Close monitoring of postischemic intestinal stenosis was carried out in AMVT patients who got symptom alleviation after TT. Intolerance to enteral nutrition or oral diet, symptoms of ileus, and confirmed intestinal stricture by CT and enterography were used to help with the diagnosis. Close follow-up, anticoagulation, and corrections of malnutrition and water and electrolyte imbalance were initiated. Planned laparotomy was indicated, and resection of the irreversible stricture in the intestine was warranted.

Data collection
The collected data were as follows: Sex, age, thrombosis risk factors (*e.g.*, active smoking, history of thrombosis, history of abdominal surgery, and liver cirrhosis), thrombosis distribution, vital signs, hematochezia, results of abdominal examination, Acute Physiology and Chronic Health Evaluation (APACHE) II score, laboratory test values, findings of abdominal CT scanning on admission or before TT, length of stay, treatment outcomes (*i.e.*, length of resected bowel and 30-d and 1-year mortality) and complications [*i.e.*, sepsis, anastomotic or parastomal leakage, acute respiratory distress syndrome, acute kidney injury, and multiple organ dysfunction syndrome (MODS)].

Statistical analysis
Quantitative variables are expressed as the mean ± SD or median and interquartile range according to distributions after Shapiro-Wilk test. Categorical variables are expressed as absolute and relative frequencies. Comparisons between groups of independent quantitative variables were performed using Student's *t*-tests or Mann–Whitney tests. Comparisons between groups of qualitative variables were performed using the χ^2 test or Fisher's exact test when appropriate. A multivariate analysis of variables was conducted using a binary logistic regression test to determine the independent variables that predicted irreversible intestinal ischemia leading to resection, and the results are shown as odds ratios (ORs) and 95% confidence intervals (CIs). The accuracy of this model was further evaluated using a receiver operating characteristic (ROC) curve. A *P* value less than 0.05 was considered significant. All analyses were performed using SPSS version 17.0 software (SPSS Inc., Chicago, IL, United States).

RESULTS

Patient characteristics
From January 2010 to October 2017, a total of 58 consecutive patients [39 (67.2%) males] were included. The mean age of the patients was 45 ± 12.4 years. The patients' baseline characteristics are described in Table 1.

TT was initiated 28.5 h after systemic anticoagulation. A total of 42 (72.4%) patients underwent arteriovenous combined thrombolysis, and 16 (27.6) underwent arterial thrombolysis alone. After recanalization, exploratory laparotomies were performed in 24 patients, and 22 patients underwent resection of the infarcted intestine. In addition, planned laparotomy was also performed in 10 patients with postischemic intestinal stenosis later, and the involved stenosed bowel was resected. Eventually, 32 (55.2%) patients underwent resection of irreversible ischemic intestines, and 26 (44.8%) did not undergo resection.

There were no significant differences in age or sex between patients with and without irreversible intestinal ischemia (Table 1). Moreover, no significant difference was found in the thrombosis distribution or transcatheter thrombolytic therapy (including the initiation time, choice of thrombolytic approach, and duration of thrombolysis). Compared with patients with reversible ischemia, AMVT patients with irreversible intestinal ischemia had higher APACHE II scores (12.5 ± 3.9 *vs* 8.4 ± 3.5, *P* < 0.001). In addition, no significant difference was found in the associated morbidities or duration of symptoms from onset to admission between these two groups. In terms

Table 1 Characteristics of acute mesenteric venous thrombosis patients treated by transcatheter thrombolysis

Variable	All patients	Without resection	With resection	*P* value
	n = 58	*n* = 26	*n* = 32	
Age, yr, mean ± SD	45 ± 12.4	44.6 ± 10.4	47.6 ± 13.8	0.366
Male, *n* (%)	39 (67.2)	16 (61.5)	23 (71.9)	0.404
Location of thrombosis, *n* (%)				0.752
SMV	12 (20.7)	6 (23.1)	6 (18.8)	
SMV + PV	46 (79.3)	20 (76.9)	26 (81.3)	
Duration of anticoagulation alone before catheter-directed thrombolysis, h, median (IQR)	28.5 (22-54.8)	36 (22.8-72)	27 (18.8-48)	0.143
Thrombolytic approaches, *n* (%)				0.199
PT/TI-PV-SMV + SMA catheterization	42 (72.4)	21 (80.8)	21 (65.6)	
SMA catheterization alone	16 (27.6)	5 (19.2)	11 (34.4)	
Days of thrombolysis, d, mean ± SD	7.1 ± 2.9	6.7 ± 2.9	7.3 ± 2.8	0.421
APACHE II score, mean ± SD	10.6 ± 4.2	8.4 ± 3.5	12.5 ± 3.9	< 0.001
Associated comorbidities, *n* (%)				
Liver cirrhosis/portal hypertension	11 (19.0)	7 (26.9)	4 (12.5)	0.163
Splenectomy	10 (17.2)	7 (26.9)	3 (9.4)	0.078
History of other abdominal surgery	9 (15.5)	5 (19.2)	4 (12.5)	0.481
History of thrombosis	9 (15.5)	2 (7.7)	7 (21.9)	0.138
Active smoking	13 (22.4)	6 (23.1)	7 (21.9)	0.913
Alcohol abuse	7 (12.1)	3 (11.5)	4 (12.5)	0.911
Hypertension	6 (10.3)	2 (7.7)	4 (12.5)	0.550
Diabetes mellitus	2 (3.4)	0 (0)	2 (6.3)	0.197
Duration of symptoms from onset to admission, d, median (IQR)	7 (4-13)	7 (4-15)	7 (4-12)	0.333
Clinical presentation, *n* (%)				
Abdominal pain	53 (91.4)	23 (88.5)	30 (93.8)	0.475
Nausea and vomiting	28 (48.3)	12 (46.2)	16 (50.0)	0.771
Hematochezia	12 (20.7)	6 (23.1)	6 (18.8)	0.686
Local peritonitis	19 (32.8)	5 (19.2)	14 (43.8)	0.048

Quantitative variables are expressed as the mean ± SD or median and interquartile range (IQR). AMVT: Acute mesenteric venous thrombosis; SMV: Superior mesenteric vein; PV: Portal vein; SMA: Superior mesenteric artery; PT: Percutaneous transhepatic; TI: Trans-jugular intrahepatic; APACHE II: Acute Physiology and Chronic Health Evaluation II; IQR: Interquartile range.

of the clinical presentation, local peritonitis was significantly more often in patients with irreversible intestinal ischemia than in those with reversible ischemia (43.8% *vs* 19.2%, *P* = 0.048).

According to the results of the laboratory examinations (Table 2), patients with irreversible intestinal ischemia had significantly higher leukocyte counts as well as C-reactive protein, total bilirubin, serum albumin, serum creatinine, and arterial lactate levels than patients without resection (*P* < 0.05). The hemoglobin, platelet, procalcitonin, alanine aminotransferase, aspartate aminotransferase, and D-dimer levels were not significantly different between the groups of patients with and without irreversible intestinal ischemia. Compared to free intraperitoneal fluid, bowel dilation, bowel wall thickening, and misty mesentery, only decreased bowel wall enhancement (28.1% *vs* 7.7%, *P* = 0.048) was seen more frequently in AMVT patients with irreversible ischemia than in patients with reversible intestinal ischemia on the imaging examination.

Table 2 Laboratory and imaging examinations of acute mesenteric venous thrombosis patients treated by transcatheter thrombolysis

Variable	All patients	Without resection	With resection	*P* value
	n = 58	*n* = 26	*n* = 32	
Laboratory examination				
Total leukocyte count, × 10^9/L, mean ± SD	14.3 ± 8.9	7.1 ± 2.2	20.3 ± 7.9	< 0.001
Hemoglobin, g/L, mean ± SD	114.3 ± 29.8	117.7 ± 27.3	111.5 ± 31.9	0.451
PLT, × 10^9/L, mean ± SD	242.5 ± 160.7	287.8 ± 182.4	204.8 ± 131.4	0.056
Procalcitonin, µg/L, median (IQR)	0.25 (0.09-0.75)	0.14 (0.07-0.62)	0.42 (0.14-0.87)	0.096
CRP, mg/L, median (IQR)	59.8 (17.6-133.2)	19.0 (6.4-40.6)	120 (62.6-148.6)	< 0.001
Total bilirubin, µmol/L, mean ± SD	18.3 ± 15.5	13.6 ± 9.4	22.1 ± 18.4	0.035
ALT, U/L, median (IQR)	27 (36.3-51.9)	28 (17-43)	26 (14.5-38)	0.748
AST, U/L, median (IQR)	28 (20-38.8)	31 (21-42)	25 (19-36)	0.260
Serum albumin, g/L, mean ± SD	33.3 ± 5.2	35.8 ± 5.2	31.2 ± 4.2	0.001
D-dimer, µg/L, median (IQR)	5.6 (3.5-9.5)	3.9 (2.2-7.0)	6.5 (4.1-9.9)	0.081
Creatinine, µmol/L, mean ± SD	67.9 ± 35.6	57.3 ± 28.8	76.5 ± 38.7	0.040
Arterial lactate, mmol/L, mean ± SD	2.8 ± 0.9	2.1 ± 0.5	3.3 ± 0.8	< 0.001
Imaging Examination, *n* (%)				
Free peritoneal fluid	35 (60.3)	13 (50.0)	22 (68.8)	0.147
Bowel loop dilation	25 (43.1)	9 (34.6)	16 (50.0)	0.239
Decreased bowel wall enhancement	11 (19.0)	2 (7.7)	9 (28.1)	0.048
Bowel wall thickening	32 (55.2)	12 (45.2)	20 (62.5)	0.213
Misty mesentery	23 (39.7)	8 (30.8)	15 (46.9)	0.212

Quantitative variables are expressed as the mean ± SD or median and interquartile range (IQR). AMVT: Acute mesenteric venous thrombosis; PLT: Platelet count; CRP: C-reactive protein; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; IQR: Interquartile range.

Clinical outcomes and follow-up

The outcomes of these two groups according to the crude analysis are summarized in Table 3. Five patients died due to sepsis induced MODS during hospitalization and two died from cardiovascular accidents during follow-up. The following poor prognostic indicators demonstrated significantly higher rates in patients with intestinal resection than in those without: Sepsis and MODS (*P* < 0.05). Patients with reversible intestinal ischemia had shorter ICU stays (5.2 ± 3.9 *vs* 12.1 ± 7.7, *P* < 0.001) and hospital stays (16.6 ± 4.7 *vs* 31.9 ± 16.7, *P* < 0.001) than patients with irreversible intestinal ischemia. Although no significant difference was found in 1-year mortality, 30-d mortality showed a trend of higher mortality in patients with irreversible intestinal ischemia than in those without intestinal resection (15.6% *vs* 0; *P* = 0.035).

Predictors of irreversible intestinal ischemia leading to resection

Multivariable analysis using binary logistic regression showed that the significant independent predictors for irreversible intestinal ischemia leading to resection in AMVT patients treated by TT were leukocytosis (higher leukocyte count) (OR = 2.058, 95%CI: 1.085-3.903, *P* = 0.027) and APACHE II score (OR = 2.368, 95%CI: 1.047-5.357, *P* = 0.038) (Table 4). The overall area under the ROC curve of the model was 0.975 (95%CI: 0.936-1.000). Using the ROC curve, the cutoff values of the leukocyte count and APACHE II score for predicting the onset of irreversible intestinal ischemia were 12 × 10^9/L and 8.5, respectively (Table 5).

Table 3 Outcome and complications of acute mesenteric venous thrombosis patients treated by transcatheter thrombolysis

Variable	All patients	Without resection	With resection	P value
	n = 58	*n* = 26	*n* = 32	
Recanalization rate of SMV, *n* (%)				
Complete recanalization	33 (56.9)	16 (61.5)	17 (53.1)	0.520
Partial recanalization	13 (22.4)	6 (23.1)	7 (21.9)	0.913
Invalid	5 (8.6)	0 (0)	5 (15.6)	0.035
Cavernous transformation	7 (12.1)	4 (15.4)	3 (9.4)	0.485
Length of bowel resection, cm, median (IQR)	100 (60-150)	ND	100 (60-150)	ND
Short bowel syndrome, *n* (%)	1 (1.7)	0 (0)	1 (3.1)	0.552
Surgical site infection, *n* (%)	3 (5.2)	0 (0)	3 (9.4)	0.161
Sepsis, *n* (%)	9 (15.5)	1 (3.8)	8 (25.0)	0.028
Hemorrhage, *n* (%)	2 (3.4)	1 (3.8)	1 (3.1)	0.700
Anastomotic or parastomal leakage, *n* (%)	2 (3.4)	0 (0)	2 (6.3)	0.497
AKI, *n* (%)	2 (3.4)	0 (0)	2 (6.3)	0.497
ARDS, *n* (%)	2 (3.4)	0 (0)	2 (6.3)	0.497
Liver dysfunction, *n* (%)	2 (3.4)	0 (0)	2 (6.3)	0.497
MODS, *n* (%)	6 (10.3)	0 (0)	6 (18.8)	0.022
Time of ICU stay, d, mean ± SD	9.1 ± 7.2	5.2 ± 3.9	12.1 ± 7.7	< 0.001
Time of hospital stay, d, mean ± SD	25.2 ± 14.9	16.6 ± 4.7	31.9 ± 16.7	< 0.001
30-d mortality, *n* (%)	5 (8.6)	0 (0)	5 (15.6)	0.035
1-yr mortality, *n* (%)	7 (12.1)	1 (3.8)	6 (18.8)	0.090

Quantitative variables are expressed as the mean ± SD or median and interquartile range (IQR). ND: No data; AMVT: Acute mesenteric venous thrombosis; SMV: Superior mesenteric vein; AKI: Acute kidney injury; ARDS: Acute respiratory distress syndrome; MODS: Multiple organ dysfunction syndrome; ICU: Intensive care unit; IQR: Interquartile range.

Table 4 Binary logistic regression analysis of risk factors associated with irreversible intestinal ischemia leading to resection in acute mesenteric venous thrombosis patients treated by transcatheter thrombolysis

Variable	P value	ORs	95%CI
APACHE II score	0.038	2.368	1.047-5.357
Leukocyte count	0.027	2.058	1.085-3.903
C-reactive protein	0.875	-	-
Arterial lactate	0.661	-	-
Serum albumin	0.547	-	-

AMVT: Acute mesenteric venous thrombosis; APACHE II: Acute Physiology and Chronic Health Evaluation II; ORs: Odds ratio; CI: Confidence interval.

DISCUSSION

Acute mesenteric ischemia is an acute vascular emergency of the intestine that can also extend to involved parts of the colon[22]. Although AMVT is the least common form, accounting for 6% to 9% of acute mesenteric ischemia (AMI), mainly involving the SMV[5,23,24], the distinction between irreversible ischemia and a viable bowel is more difficult than in arterial mesenteric ischemia, and different pathophysiology is involved in these two diseases despite ultimately involving intestinal necrosis[7,21].

Table 5 Diagnostic value of the risk factors for diagnosis of irreversible intestinal ischemia in acute mesenteric venous thrombosis patients treated by transcatheter thrombolysis

Variable	AUC	Cut-off value	Sensitivity	Specificity	PPV	NPV	Youden index
APACHE II score	0.728	8.5	0.933	0.440	0.682	0.833	0.373
Leukocyte count	0.947	12×10^9	0.900	1	1	0.893	0.900

AMVT: Acute mesenteric venous thrombosis; APACHE II: Acute Physiology and Chronic Health Evaluation II; AUC: Area under curve; PPV: Positive predictive value; NPV: Negative predictive value.

Thus, the factors predictive of poor prognosis in AMVT should be distinguished from those in arterial mesenteric ischemia. However, limited to the rarity and the small number of AMI patients, predictors have often been generally analyzed in a large group of AMI patients[25-27]. Moreover, prompt treatment and early recognition of patients who need surgical intervention may help achieve a better outcome[13]. In this study, acute intestinal ischemia was reversed by TT in 26 (44.8%) patients, and the 30-d survival rate was 91.4%. Furthermore, we identified two factors from a multivariate analysis that were independent and easy to assess during the initial workup and were predictive of irreversible intestinal injury and the requirement of surgical resection (APACHE II > 8.5 and leukocytosis > 12×10^9/L). Close monitoring of these factors may help evaluate whether surgical resection of irreversible intestinal ischemia is ultimately required upon admission.

Patients with persistent symptoms, worsened abdominal pain after anticoagulation therapy, the development of signs of peritonitis, or a high risk of bowel infarction should initiate the multidisciplinary stepwise management[7,12]. According to the multidisciplinary stepwise management strategy in our ISC, initial catheter-directed thrombolysis was a preferred alternative for patients with local peritonitis[17]. A high risk of bleeding, confirmed intestinal necrosis or perforation, recent stroke, and primary or metastatic central nervous system malignancies are contraindications to thrombolysis[17]. Despite the beneficial effect of TT, emerging research has revealed the efficiency of preventing intestinal necrosis or salvaging more ischemic segments. Hollingshead *et al*[28] reported 20 patients treated by TT with symptom resolution in 85% of patients, and no patients required bowel resection[28]. In addition, in a series of pilot studies published by the intestinal stroke center in China, prompt endovascular treatment combined with damage control could improve the outcome[11,13,17]. In this research, among all AMVT patients, only those who were treated by TT were included. Although 32 (55.2%) patients, including 22 (37.9%) patients with intestinal necrosis and 10 (17.24%) with postischemic intestinal stenosis, required intestinal resection and approximately 100 cm-long segments of ischemic bowel were irreversibly resected, short bowel syndrome occurred only in 1 (1.7%) patient. Furthermore, the 30-d mortality and 1-year mortality rates were 8.6% and 12.1%, respectively.

The initiation of endovascular treatment is often suggested after 48-72 h of systemic anticoagulation[12]. The conditions of approximately 5% of AMVT patients who receive conservative treatment will deteriorate, and endovascular treatment should be initiated[29]. However, in this research, systemic anticoagulation could not improve conditions in 50% of patients, and TT was initiated 28.5 h after systemic anticoagulation. This may mainly be attributed to the severe conditions in most patients (32.8% of patients with local peritonitis). Signs of peritonitis have traditionally been considered an indication for prompt surgery[10]. However, in our research, we found that patients with local peritonitis could avoid surgical intervention. Patients with irreversible intestinal ischemia showed a significantly higher rate of peritonitis than patients with reversible intestinal injuries, but this higher rate was not independently associated with irreversible intestinal ischemia.

The APACHE II score is a severity-of-disease classification system and was designed to measure the severity of disease and predict mortality in adult patients admitted to the ICU. Fluid resuscitation, multi-organ function support, early enteral nutrition, and other special treatments in the ICU play pivotal roles in AMI treatment. In AMVT patients, the APACHE II score can also be used to evaluate the severity of illness. Wu *et al*[30] reported that a high APACHE II score was significantly associated with a poor prognosis in patients with necrotic bowel-induced hepatic portal venous gas[30]. Hsu *et al*[31] also reported that a high APACHE II score was significantly associated with a poor prognosis in AMI patients[31]. Similar findings in AMVT patients were also reported by Yang *et al*[17]. In this research, we found that a high score

was an independent predictive factor for irreversible intestinal ischemia leading to resection. Clinical awareness should be implemented in AMVT patients with a high APACHE II score (> 8.5) upon admission, even when TT is initiated; ultimately, surgical intervention may also be warranted in these patients.

In terms of the laboratory tests, patients with irreversible intestinal ischemia had higher total leukocyte counts as well as levels of C-reactive protein, total bilirubin, lactate, and creatinine. These results revealed that irreversible intestinal ischemia caused severe tissue hypoxia and that a systemic inflammatory response to irreversible ischemia and organ injury was initiated[25,27]. Moreover, intestinal dysfunction also impairs nutrition, which was reflected by decreased serum albumin levels in patients with irreversible intestinal ischemia. However, only leukocytosis independently predicted the onset of irreversible bowel ischemia in patients with AMVT treated by TT. A similar result was also reported by Emile[27]. Moreover, the onset of bowel ischemia, in general, is associated with profound leukocytosis[32], and a recent study found a total leucocyte count of more than 18000 as a cut-off point for bowel necrosis, as a significant predictor of mortality in AMI[33]. In this research, the cut-off point for irreversible intestinal ischemia was 12×10^9/L.

Although prompt TT can help achieve a better outcome, surgical intervention was still performed in 32 (55.2%) patients. Operative intervention is reserved for patients with severe and diffuse peritonitis and transmural bowel infarction or perforation[34]. In such severe cases, damage control surgery, such as bowel resection with open abdomen, is preferred over complex definitive procedures in order to reduce the second hit phenomenon[12,17,35]. In patients with intestinal necrosis, double-barrel enterostomy allows the observation of the color and vitality of the stoma, which provides an indirect assessment of the intestinal blood supply and avoids a second-look operation. Sometimes, temporary abdominal closure may be applied when there is severe bowel edema with a risk of intra-abdominal hypertension or abdominal compartment syndrome[15,36]. In the long term, AMVT can cause postischemic intestinal stenosis[37]. It tends to progressively worsen and ultimately result in total occlusion[38,39]. Correction of malnutrition and anticoagulation as well as surgical resection can be initiated in patients with postischemic intestinal stenosis[20,38,40]. In this study, 27 (84.4%) patients were discharged and the 1-year survival rate was 81.3%.

This study had some limitations. With regard to the rareness of this disease, a large randomized clinical trial seems difficult but is expected. This study, involving a total of 58 AMVT patients treated by TT, is a relatively large-scale study in the current literature. However, a multicenter prospective study is still warranted. Second, there is a lack of useful parameters that may also predict the onset of irreversible intestinal ischemia leading to resection in these patients. Third, checking for inherited or acquired thrombophilia is also warranted. For the two predictive factors, confirmation by further validation cohorts is necessary to allow clinicians and surgeons to draw generalizable conclusions.

Prompt TT can improve outcomes of AMVT. However, patients with irreversible intestinal ischemia manifest a higher risk of poor prognosis than patients with reversible injuries. The two independent predictors of irreversible intestinal ischemia leading to resection are an APACHE II score > 8.5 and a total leukocyte count > 12×10^9/L. When TT is promptly initiated, close monitoring of these factors can help discriminate AMVT patients in need of ultimately bowel resection from those who can be managed with conservative measures.

ARTICLE HIGHLIGHTS

Research background
Acute mesenteric venous thrombosis (AMVT) can cause a poor prognosis as a result of irreversible intestinal ischemia. Emerging studies revealed that prompt transcatheter thrombolysis (TT) can achieve early mesenteric revascularization and reverse early intestinal injury. However, irreversible intestinal ischemia still occurs in some cases.

Research motivation
Previous studies always involved both arterial and venous mesenteric ischemia. However, compared to arterial mesenteric ischemia, different pathophysiology is involved and it is more difficult to distinguish irreversible ischemia from viable bowels in venous mesenteric ischemia. What's more, AMVT can not only cause intestinal necrosis in the short term but also result in intestinal stenosis in the long

term, requiring intestinal resection. Limited to the rarity of AMVT, few studies have explored the predictive factors for irreversible intestinal ischemia, requiring surgical resection, in AMVT patients treated by TT.

Research objectives

This study aimed to identify predictive factors for irreversible intestinal ischemia in AMVT patients treated by TT.

Research methods

We retrospectively analyzed the data of 58 AMVT patients who underwent TT. To identify the predictive factors, AMVT patients treated by TT were divided into two groups: Patients with irreversible intestinal ischemia and those with reversible intestinal ischemia. Then, group comparisons and a multivariate binary logistic regression analysis were performed.

Research results

Thirty-two (55.2%) patients with irreversible intestinal ischemia had a higher 30-d mortality and a longer in-hospital stay than patients with reversible intestinal injuries. The significant independent predictors of irreversible intestinal ischemia were Acute Physiology and Chronic Health Evaluation (APACHE) II score (odds ratio = 2.368, 95% confidence interval: 1.047-5.357, P = 0.038) and leukocytosis (odds ratio = 2.058, 95% confidence interval: 1.085-3.903, P = 0.027). Using the receiver operating characteristic curve, the cutoff values of the APACHE II score and leukocytosis for predicting the onset of irreversible intestinal ischemia were calculated to be 8.5 and 12 $\times 10^9/L$, respectively.

Research conclusions

Both total leukocyte count and APACHE II score are prognostic factors for irreversible intestinal ischemia in AMVT patients after initiation of TT.

Research perspectives

Both total leukocyte count and APACHE II score are common clinical parameters that are easily available to clinicians upon admission, and may be valuable predictors to discriminate AMVT patients treated by TT who will suffer from irreversible intestinal ischemia from those who can be managed with conservative measures.

REFERENCES

1   **Schoots IG**, Koffeman GI, Legemate DA, Levi M, van Gulik TM. Systematic review of survival after acute mesenteric ischaemia according to disease aetiology. *Br J Surg* 2004; **91**: 17-27 [PMID: 14716789 DOI: 10.1002/bjs.4459]

2   **Clair DG**, Beach JM. Mesenteric Ischemia. *N Engl J Med* 2016; **374**: 959-968 [PMID: 26962730 DOI: 10.1056/NEJMra1503884]

3   **Russell CE**, Wadhera RK, Piazza G. Mesenteric venous thrombosis. *Circulation* 2015; **131**: 1599-1603 [PMID: 25940967 DOI: 10.1161/CIRCULATIONAHA.114.012871]

4   **Kumar S**, Kamath PS. Acute superior mesenteric venous thrombosis: one disease or two? *Am J Gastroenterol* 2003; **98**: 1299-1304 [PMID: 12818273 DOI: 10.1111/j.1572-0241.2003.07338.x]

5   **Singal AK**, Kamath PS, Tefferi A. Mesenteric venous thrombosis. *Mayo Clin Proc* 2013; **88**: 285-294 [PMID: 23489453 DOI: 10.1016/j.mayocp.2013.01.012]

6   **Aschoff AJ**, Stuber G, Becker BW, Hoffmann MH, Schmitz BL, Schelzig H, Jaeckle T. Evaluation of acute mesenteric ischemia: accuracy of biphasic mesenteric multi-detector CT angiography. *Abdom Imaging* 2009; **34**: 345-357 [PMID: 18425546 DOI: 10.1007/s00261-008-9392-8]

7   **Björck M**, Koelemay M, Acosta S, Bastos Goncalves F, Kölbel T, Kolkman JJ, Lees T, Lefevre JH, Menyhei G, Oderich G, Esvs Guidelines Committee, Kolh P, de Borst GJ, Chakfe N, Debus S, Hinchliffe R, Kakkos S, Koncar I, Sanddal Lindholt J, Vega de Ceniga M, Vermassen F, Verzini F, Document Reviewers, Geelkerken B, Gloviczki P, Huber T, Naylor R. Editor's Choice - Management of the Diseases of Mesenteric Arteries and Veins: Clinical Practice Guidelines of the European Society of Vascular Surgery (ESVS). *Eur J Vasc Endovasc Surg* 2017; **53**: 460-510 [PMID: 28359440 DOI: 10.1016/j.ejvs.2017.01.010]

8   **Condat B**, Pessione F, Helene Denninger M, Hillaire S, Valla D. Recent portal or mesenteric venous thrombosis: increased recognition and frequent recanalization on anticoagulant therapy. *Hepatology* 2000; **32**: 466-470 [PMID: 10960436 DOI: 10.1053/jhep.2000.16597]

9   **Condat B**, Pessione F, Hillaire S, Denninger MH, Guillin MC, Poliquin M, Hadengue A, Erlinger S, Valla D. Current outcome of portal vein thrombosis in adults: risk and benefit of anticoagulant therapy. *Gastroenterology* 2001; **120**: 490-497 [PMID: 11159889 DOI: 10.1053/gast.2001.21209]

10 **Bergqvist D**, Svensson PJ. Treatment of mesenteric vein thrombosis. *Semin Vasc Surg* 2010; **23**: 65-68 [PMID: 20298951 DOI: 10.1053/j.semvascsurg.2009.12.008]

11 **Yang S**, Liu B, Ding W, He C, Wu X, Li J. Acute superior mesenteric venous thrombosis: transcatheter

thrombolysis and aspiration thrombectomy therapy by combined route of superior mesenteric vein and artery in eight patients. *Cardiovasc Intervent Radiol* 2015; **38**: 88-99 [PMID: 24934733 DOI: 10.1007/s00270-014-0896-z]

12   **Yang S**, Wu X, Li J. Transcatheter thrombolysis centered stepwise management strategy for acute superior mesenteric venous thrombosis. *Int J Surg* 2014; **12**: 442-451 [PMID: 24704749 DOI: 10.1016/j.ijsu.2014.03.015]

13   **Liu K**, Meng J, Yang S, Liu B, Ding W, Wu X, Li J. Transcatheter thrombolysis combined with damage control surgery for treatment of acute mesenteric venous thrombosis associated with bowel necrosis: a retrospective study. *World J Emerg Surg* 2015; **10**: 50 [PMID: 26516342 DOI: 10.1186/s13017-015-0045-2]

14   **Arthurs ZM**, Titus J, Bannazadeh M, Eagleton MJ, Srivastava S, Sarac TP, Clair DG. A comparison of endovascular revascularization with traditional therapy for the treatment of acute mesenteric ischemia. *J Vasc Surg* 2011; **53**: 698-704; discussion 704-5 [PMID: 21236616 DOI: 10.1016/j.jvs.2010.09.049]

15   **Ding W**, Wang K, Liu B, Fan X, Wang S, Cao J, Wu X, Li J. Open Abdomen Improves Survival in Patients With Peritonitis Secondary to Acute Superior Mesenteric Artery Occlusion. *J Clin Gastroenterol* 2017; **51**: e77-e82 [PMID: 28877534 DOI: 10.1097/MCG.0000000000000799]

16   **Corcos O**, Castier Y, Sibert A, Gaujoux S, Ronot M, Joly F, Paugam C, Bretagnol F, Abdel-Rehim M, Francis F, Bondjemah V, Ferron M, Zappa M, Amiot A, Stefanescu C, Leseche G, Marmuse JP, Belghiti J, Ruszniewski P, Vilgrain V, Panis Y, Mantz J, Bouhnik Y. Effects of a multimodal management strategy for acute mesenteric ischemia on survival and intestinal failure. *Clin Gastroenterol Hepatol* 2013; **11**: 158-65.e2 [PMID: 23103820 DOI: 10.1016/j.cgh.2012.10.027]

17   **Yang S**, Fan X, Ding W, Liu B, Meng J, Xu D, He C, Yu W, Wu X, Li J. Multidisciplinary stepwise management strategy for acute superior mesenteric venous thrombosis: an intestinal stroke center experience. *Thromb Res* 2015; **135**: 36-45 [PMID: 25466834 DOI: 10.1016/j.thromres.2014.10.018]

18   **Plessier A**, Rautou PE, Valla DC. Management of hepatic vascular diseases. *J Hepatol* 2012; **56** Suppl 1: S25-S38 [PMID: 22300463 DOI: 10.1016/S0168-8278(12)60004-X]

19   **Elkrief L**, Corcos O, Bruno O, Larroque B, Rautou PE, Zekrini K, Bretagnol F, Joly F, Francoz C, Bondjemah V, Cazals-Hatem D, Boudaoud L, De Raucourt E, Panis Y, Goria O, Hillaire S, Valla D, Plessier A. Type 2 diabetes mellitus as a risk factor for intestinal resection in patients with superior mesenteric vein thrombosis. *Liver Int* 2014; **34**: 1314-1321 [PMID: 24237969 DOI: 10.1111/liv.12386]

20   **Paraskeva P**, Akoh JA. Small bowel stricture as a late sequela of superior mesenteric vein thrombosis. *Int J Surg Case Rep* 2015; **6C**: 118-121 [PMID: 25544479 DOI: 10.1016/j.ijscr.2014.11.071]

21   **Harnik IG**, Brandt LJ. Mesenteric venous thrombosis. *Vasc Med* 2010; **15**: 407-418 [PMID: 20926500 DOI: 10.1177/1358863X10379673]

22   **Yang S**, Zhao Y, Chen J, Ni Q, Guo X, Huang X, Xue G, Zhang L. Clinical Features and Outcomes of Patients With Acute Mesenteric Ischemia and Concomitant Colon Ischemia: A Retrospective Cohort Study. *J Surg Res* 2019; **233**: 231-239 [PMID: 30502253 DOI: 10.1016/j.jss.2018.08.010]

23   **Rhee RY**, Gloviczki P. Mesenteric venous thrombosis. *Surg Clin North Am* 1997; **77**: 327-338 [PMID: 9146716 DOI: 10.1016/s0039-6109(05)70552-1]

24   **Brunaud L**, Antunes L, Collinet-Adler S, Marchal F, Ayav A, Bresler L, Boissel P. Acute mesenteric venous thrombosis: case for nonoperative management. *J Vasc Surg* 2001; **34**: 673-679 [PMID: 11668323 DOI: 10.1067/mva.2001.117331]

25   **Wang X**, Chu C, Sun S, Xie T, Duan Z, Wang K, Liu B, Fan X, Wu X, Ding W. Outcomes and clinical characteristics of transmural intestinal necrosis in acute mesenteric ischemia. *Scand J Gastroenterol* 2019; **54**: 953-959 [PMID: 31361977 DOI: 10.1080/00365521.2019.1646800]

26   **Nuzzo A**, Maggiori L, Ronot M, Becq A, Plessier A, Gault N, Joly F, Castier Y, Vilgrain V, Paugam C, Panis Y, Bouhnik Y, Cazals-Hatem D, Corcos O. Predictive Factors of Intestinal Necrosis in Acute Mesenteric Ischemia: Prospective Study from an Intestinal Stroke Center. *Am J Gastroenterol* 2017; **112**: 597-605 [PMID: 28266590 DOI: 10.1038/ajg.2017.38]

27   **Emile SH**. Predictive Factors for Intestinal Transmural Necrosis in Patients with Acute Mesenteric Ischemia. *World J Surg* 2018; **42**: 2364-2372 [PMID: 29387956 DOI: 10.1007/s00268-018-4503-3]

28   **Hollingshead M**, Burke CT, Mauro MA, Weeks SM, Dixon RG, Jaques PF. Transcatheter thrombolytic therapy for acute mesenteric and portal vein thrombosis. *J Vasc Interv Radiol* 2005; **16**: 651-661 [PMID: 15872320 DOI: 10.1097/01.RVI.0000156265.79960.86]

29   **Acosta S**, Alhadad A, Svensson P, Ekberg O. Epidemiology, risk and prognostic factors in mesenteric venous thrombosis. *Br J Surg* 2008; **95**: 1245-1251 [PMID: 18720461 DOI: 10.1002/bjs.6319]

30   **Wu JM**, Tsai MS, Lin MT, Tien YW, Lin TH. High APACHE II score and long length of bowel resection impair the outcomes in patients with necrotic bowel induced hepatic portal venous gas. *BMC Gastroenterol* 2011; **11**: 18 [PMID: 21385464 DOI: 10.1186/1471-230X-11-18]

31   **Hsu HP**, Shan YS, Hsieh YH, Sy ED, Lin PW. Impact of etiologic factors and APACHE II and POSSUM scores in management and clinical outcome of acute intestinal ischemic disorders after surgical treatment. *World J Surg* 2006; **30**: 2152-62; discussion 2163-4 [PMID: 17103101 DOI: 10.1007/s00268-005-0716-3]

32   **Sise MJ**. Mesenteric ischemia: the whole spectrum. *Scand J Surg* 2010; **99**: 106-110 [PMID: 20679047 DOI: 10.1177/145749691009900212]

33   **Akıldız HY**, Sözüer E, Uzer H, Baykan M, Oz B. The length of necrosis and renal insufficiency predict the outcome of acute mesenteric ischemia. *Asian J Surg* 2015; **38**: 28-32 [PMID: 25183292 DOI: 10.1016/j.asjsur.2014.06.001]

34   **Riva N**, Donadini MP, Dentali F, Squizzato A, Ageno W. Clinical approach to splanchnic vein thrombosis: risk factors and treatment. *Thromb Res* 2012; **130** Suppl 1: S1-S3 [PMID: 23026649 DOI: 10.1016/j.thromres.2012.08.259]

35   **Jansen JO**, Loudon MA. Damage control surgery in a non-trauma setting. *Br J Surg* 2007; **94**: 789-790 [PMID: 17571297 DOI: 10.1002/bjs.5922]

36   **Waibel BH**, Rotondo MM. Damage control surgery: it's evolution over the last 20 years. *Rev Col Bras Cir* 2012; **39**: 314-321 [PMID: 22936231 DOI: 10.1590/s0100-69912012000400012]

37   **Eugène C**, Valla D, Wesenfelder L, Fingerhut A, Bergue A, Merrer J, Felsenheld C, Moundji A, Etienne

JC. Small intestinal stricture complicating superior mesenteric vein thrombosis. A study of three cases. *Gut* 1995; **37**: 292-295 [PMID: 7557585 DOI: 10.1136/gut.37.2.292]

38   **Takeuchi N**, Naba K. Small intestinal obstruction resulting from ischemic enteritis: a case report. *Clin J Gastroenterol* 2013; **6**: 281-286 [PMID: 23990850 DOI: 10.1007/s12328-013-0393-y]

39   **Yang XY**, Chen CX, Zhang BL, Yang LP, Su HJ, Teng LS, Li YM. Diagnostic effect of capsule endoscopy in 31 cases of subacute small bowel obstruction. *World J Gastroenterol* 2009; **15**: 2401-2405 [PMID: 19452586 DOI: 10.3748/wjg.15.2401]

40   **Nishimura N**, Yamamoto H, Yano T, Hayashi Y, Sato H, Miura Y, Shinhata H, Sunada K, Sugano K. Balloon dilation when using double-balloon enteroscopy for small-bowel strictures associated with ischemic enteritis. *Gastrointest Endosc* 2011; **74**: 1157-1161 [PMID: 21924719 DOI: 10.1016/j.gie.2011.07.024]