

Original Research Article

Diagnosis and management challenges of acute mesenteric venous thrombosis in patients with liver cirrhosis: a single institution's experience

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ABSTRACT

Background: Acute mesenteric venous thrombosis (MVT) is a dreadful complication of liver cirrhosis that requires prompt diagnosis and aggressive management for better outcome. The aim of this work was to study the diagnostic tools and the optimal management of acute MVT in patients with liver cirrhosis.

Methods: It was a retrospective study including 40 patients with liver cirrhosis who were admitted to the surgical emergency and were eventually diagnosed as acute MVT between May 2011 to September 2016. The preoperative clinicopathological data, operative data and postoperative follow up were recorded.

Results: Forty patients had acute MVT. Twenty five patients (62.5%) had prolonged prothrombin time, 18 patients (45%) had thrombocytopenia and 22 patients (55%) had low protein C. triphasic CT scan was the main diagnostic image in 28 patients, with sensitivity 100% and accuracy 96.9% in detection of intestinal infarction. Ten patients (25%) underwent conservative treatment with anticoagulant, while 30 patients (75%) were surgically explored and 28 patients of them had gangrenous bowel loops and underwent primary resection and anastomosis. Three patients underwent second look operation. Three patients had recurrent symptoms after 1 month of the first presentation. The overall 30- and 90-day mortality was 27.5% and 37.5% respectively.

Conclusions: Cirrhotic patients may have hypercoagulable state and the usual laboratory tests don't accurately assess the coagulation status in these patient. Acute MVT in cirrhotic patients has a high early morbidity and mortality that needs early diagnosis and urgent management with selective surgical intervention and proper anticoagulant.

Keywords: Anticoagulant, Intestinal resection and anastomosis, Liver cirrhosis, Mesenteric venous thrombosis

INTRODUCTION

Acute mesenteric venous thrombosis (MVT) remains a life-threatening condition that requiring rapid diagnosis and aggressive management. It is responsible for only about 3-15% of cases of acute mesenteric ischemia

(AMI), so a high index of suspicion is needed for accurate diagnosis because of the non-specific nature of its presenting signs, symptoms and laboratory tests. For successful diagnosis, physicians must first be aware of MVT and consider it in the differential diagnosis of cases presenting with abdominal pain.¹⁻³

The liver plays several roles in both primary and secondary hemostasis. The complex balance between procoagulant components, anticoagulant and fibrinolytic system is altered in patients with liver cirrhosis resulting in the dominance of one of the two systems' components. This can manifest as hypercoagulable state in some patients and as excessive bleeding in others.^{4,5}

It has now been proven that a state of hypercoagulability can coexist in patients with liver cirrhosis. The investigations that are used for the evaluation of the coagulation cascades are concentrated on the procoagulant components, they neglect the rebalance between the components of the coagulation system so it cannot be used as a reliable test for the evaluation of the patients' coagulation state.^{6,7}

Contrast-enhanced abdominal computed tomography (CT) is the main diagnostic tool for early detection of MVT where anticoagulant drugs can be given early before the ischemic changes and intestinal infarction.⁸ An emergent surgery is indicated in the presence of established ischemia or transmural infarction with signs of peritonitis.^{8,9} The aim of this work was to analyze the early diagnostic tools and the National Liver Institute (NLI) experience for optimal management of acute MVT in patients with liver cirrhosis and the factors that may influence the outcome of these patients.

METHODS

The study was conducted as retrospective study of 40 cirrhotic patients who were diagnosed as acute MVT and admitted at the department of surgery, National Liver Institute, Menoufia University, Menoufia, Egypt between May 2011 and September 2016. The data were collected from an institutional review board (IRB)-approved prospective database. Patients presentation, different diagnostic tools, treatment options, operative details, and postoperative follow up data were collected and analyzed for each patient.

Patients presented by symptoms of abdominal pain "out of proportion to physical finding", sepsis, organ dysfunction or diffuse peritonitis suggesting MVT were evaluated by pelvi-abdominal ultrasound (US) to assess intra-abdominal fluid collections and to have US guided sample if possible. The condition of bowel loops if there is distention, edematous loop or sluggish motility was also assessed. Duplex study of mesenteric vessels was done for confirmation of mesenteric venous thrombosis and extension of thrombus if possible due to its difficulty with bowel gases distension. As by NLI protocol all patient, except for patients who had severe renal impairment, underwent contrast enhanced triphasic CT scan abdomen and pelvis for confirmation of the diagnosis of the presence of complete or partial occlusion of mesenteric veins, assessment of bowel wall thickening, mucosal enhancement, pneumatosis, mesenteric

stranding, ascites, visceral infarction, pneumoperitoneum and exclusion of other causes of acute abdomen.

The conservative treatment was implemented if there was no evidence of intestinal infarction by clinical, radiological and laboratory investigations. The conservative treatment was done by nasogastric tube, and anticoagulant therapy in the form of low molecular weight heparin (LMWH) in therapeutic doses (1ml/kg, twice daily), then started oral anticoagulant (as Warfarin) when oral feeding was tolerated. Oral feeding was restarted gradually after improvement of the general condition.

Patients with clinical signs of peritonitis, abnormal serum parameters and/or evidence of gangrenous bowel loops by contrast enhanced CT portography (bowel loops dilatation and pneumatosis, presence of air in Portal vein, enhancement of the wall of bowel loops with increased wall thickening, and thrombotic occlusion of SMV) were explored surgically, with resection and primary anastomosis or exteriorization of the bowel loop. This was done according to the patients general condition on exploration, the severity of peritonitis and extension of mesenteric thrombosis. Second look exploration was not done as a routine postoperative, it was done only when indicated.¹⁰

All patients with acute MVT discharged on oral anticoagulant, to reduce risk of propagation of thrombus, recurrence, and overall mortality. The oral anticoagulant was taken for at least six months, and was monitored by international normalized ratio (INR) to be between 2-3, and it was followed up every 3 months.¹¹

Follow up of the patients was from the date of surgery to March 2017 with median follow up period of 34 months. The follow up was implemented by abdominal U/S with duplex study on mesenteric vessels every 3 months during first year then every 6 months, and CT scan with CT portography if needed.

Statistical analysis

Data were statistically analyzed by using SPSS version 21 categorical variables were analyzed using Chi-square or Fisher's exact test. Mann Whitney U-test or Student t-test were used for continuous variables, as appropriate. Cox regression analysis was used to determine independent prognostic factors. A Kaplan-Meier curve was plotted for the analysis of survival. The P-value was considered statistically significant if <0.05.

RESULTS

From May 2010 to September 2016, 40 patients were diagnosed as having acute mesenteric venous thrombosis at the National Liver Institute, Menoufia University, Egypt.

The demographic and preoperative data of the patients were listed in Table 1:

Table 1: Demographic and clinicopathological data for patients with MVT.

Parameters	No (%)
Age (year)	
Mean	55.2±11
Range	15-72
Gender	
Male	30 (75%)
Female	10 (25%)
Co morbidity	
DM	5 (12.5%)
HTN	4 (10%)
IHD	1 (2.5%)
Cerebral stroke	1 (2.5%)
Previous abdominal operation	
(Splenectomy)	7 (17.5%)
Causes of liver cirrhosis	
HCV	30 (75%)
HBV	3 (7.5%)
HCV and HBV	3 (7.5%)
Others	4 (10%)
Child-pugh score	
A	15 (37.5%)
B	18 (45%)
C	7 (17.5%)
Meld score	
<10	11 (27.5%)
10-20	22 (55%)
>20	7 (17.5%)
Symptoms and signs	
Abdominal pain	40 (100%)
Distension	32 (80%)
Intestinal obstruction	26 (65%)
fever	25 (62.5%)
Bleeding per rectum/melena	13 (32.5%)
Haematemesis	2 (5%)
Serum creatinine level (n=0.6-1.4 mg/dl)	
Normal	29 (72.5%)
High	11 (27.5%)
Serum urea level (n=15-40mg/dl)	
Normal	16 (40%)
High	24 (60%)
Platelet count (n=150,000-450,000u/l)	
Normal	19 (47.5%)
Low	18 (45%)
High	3 (7.5%)
INR	
Normal	15 (37.5%)
1.3-1.7	16 (40%)
>1.7-2.5	6 (15%)
>2.5	3 (7.5%)
Protein C (n=70-160%)	

Normal	8 (20%)
Low	22 (55%)
Unavailable	10 (25%)
Protein S (n=60-150%)	
Normal	20 (50%)
Low	10 (25%)
Unavailable	10 (25%)
Antithrombin III (n=19-31%)	
Normal	11 (27.5%)
Low	7 (17.5%)
High	9 (22.5%)
Unavailable	13 (32.5%)

MVT (mesenteric venous thrombosis), DM (diabetes mellitus), HTN (hypertension), IHD (ischemic heart disease), MELD (model of end stage liver disease), INR (international normalized ratio), HCV (hepatitis C virus), HB (hepatitis B virus).

Radiological investigations

Ultrasound revealed that 35 patients (87.5%) showed intraabdominal fluid collection. US guided aspiration of the fluid collection was done for 30 (75%) patients. Fluid samples were serosanguinous in 17 patients, purulent in 3 patients and clear ascites in 10 patients. The duplex study of the mesenteric vessels was listed in Table 2.

Table 2: Duplex study and triphasic CT scan for the patients.

Parameter	Number (percentage)
Doppler study (40 patients)	thrombosed PV, SMV and SV
	6 (15%)
	Thrombosed PV and SMV
	6 (15%)
	thrombosis of PV
Triphasic CT scan (28 patients)	6 (15%)
	thrombosis of SMV
	5 (12.5%)
	couldn't be assessed
	17 (42.5%)
Triphasic CT scan (28 patients)	thrombosis of SMV, SV and PV
	7 (25%)
	thrombosed SMV and PV
	13 (46.4%)
	thrombosis of SMV
Triphasic CT scan (28 patients)	8 (28.6%)
	congested and edematous loops
	10 (35.7%)
Triphasic CT scan (28 patients)	gangrenous loops
	18 (64.3%)

CT (computed tomography), SMV (superior mesenteric vein), PV (portal vein), SP (splenic vein).

Triphasic CT scan abdomen and pelvis was done for 28 patients (70%), 9 patients (22.5%) didn't undergo triphasic CT scan because of severe renal impairment, and 3 patients (7.5%) were explored depending on clinical picture and duplex study. Triphasic CT scan revealed the extent of mesenteric vessels thrombosis (Figure 1) and gave an impression about bowel loops status (Table 2). The sensitivity of triphasic CT scan in detection of intestinal infarction with MVT was 100%, 90.9% specificity and accuracy of 96.4%.

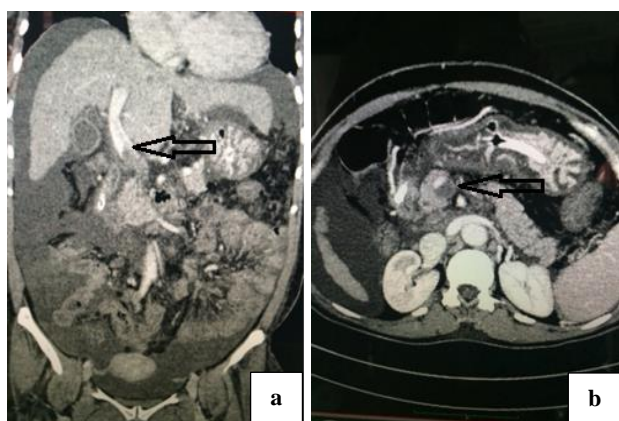


Figure 1: Coronal and axial cuts for a triphasic CT abdomen and pelvis showing thrombosed SMV and extended to PV (black arrow), also cirrhotic liver, ascites, and dilated bowel loops.

Ten patients (25%) underwent conservative treatment, while 30 patients (75%) were explored surgically. Patients with conservative management; oral feeding was started after improvement of clinical condition with a mean of 3 ± 2 days (range 2-6 days) after admission, and they didn't receive total parenteral nutrition (TPN).

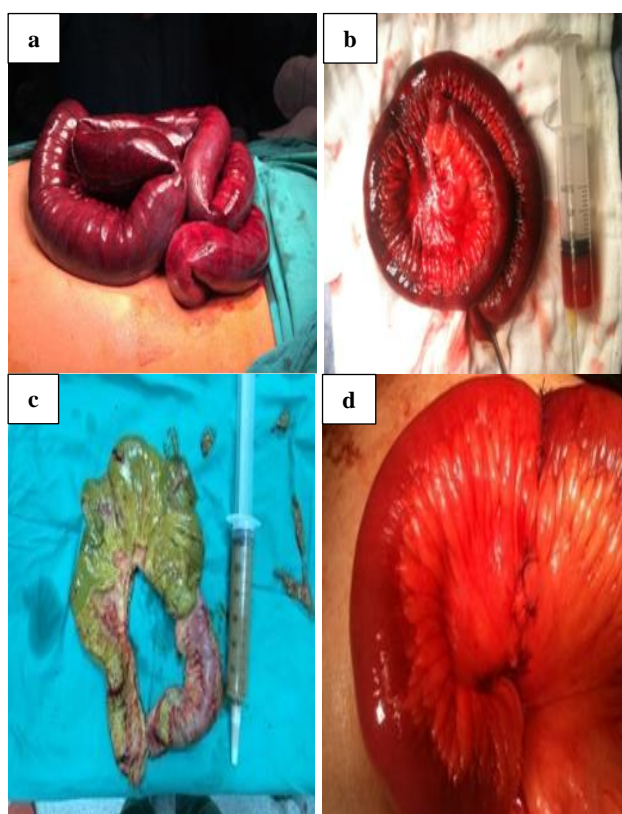


Figure 2: a) Gangrenous jejunal loops; b) resection of gangrenous ileal loop, its length is about 60 cm, and sample of serosanguinous intraperitoneal collection; c) gangrenous and perforated ileal loop with sample of pus and intraperitoneal intestinal contents; d) Primary anastomosis of an ileal loop.

For patients who were offered surgical exploration, the mean time between the manifestations and exploration was 5 ± 2 days (range 1-15 days). Exploration revealed; 2 patients (6.7%) with only congested bowel loop without gangrene and 28 patients (93.3%) with gangrenous bowel loops. The sites of gangrenous loops were; Jejunal loops in 17 patients (60.7%), ileal loops in 6 patients (21.4%) (one of them was perforated), jejunal and ileal loops in 4 patients (14.3%), while gangrenous small intestine from duodeno-jejunal junction down to terminal ileum (about 70 cm before ileocecal junction) was found in one patient (3.6%) (Figure 2).

The mean length of the resected gangrenous loops was 76 ± 119 cm (range: 20-250 cm). Resection and primary anastomosis was done in 27 patients (96.4%) while ileostomy was done in only one patient (3.6%).

Five patients (17.8%) received intra-operative blood transfusion with mean 1 ± 1.5 (range: 1-3), and 7 patients (25%) received plasma transfusion intra-operative with mean 2 ± 1.5 (range: 2-6). The mean of operative time was 140 ± 66 min (range 65-240 min).

Three patients (10%), out of 30 patients who were surgically explored underwent second look exploration; One of them was negative exploration and the second one underwent re-resection and anastomosis to jejunal loop, and the third one underwent ileostomy.

Follow up data and outcomes

Oral feeding was restarted post-operative with mean 4 ± 3 days (range: 2-13). Out of 30 explored patients 15 patients (50%) received postoperative TPN.

All patients whether undergoing conservative or surgical treatment received LMWH in the hospital admission and discharged on oral anticoagulant (warfarin), for at least 6 months.

Early complications were; 13 patients (32.5%) suffered from post-operative liver decompensation in the form of (hepatic encephalopathy, hyperbilirubinemia, or massive ascites), 5 patients (12.5%) suffered from septic shock and severe chest infections, 4 patients (10%) suffered from Systemic Inflammatory Response Syndrome (SIRS), and 3 patients (7.5%) had hematemesis and melena. The management was by liver support in cases with hepatic decompensation, selected antibiotics in cases with different types of infections, and upper endoscopy and resuscitation in patients with hematemesis.

The mean hospital stay for the group who had surgical exploration was 11 ± 7 days (range 6-25 days). Hospital stay for the conservatively treated group was 10 ± 6 days (range 7-17 days).

Three patients experienced recurrence of the symptoms and signs of acute MVT after 1 month of first

presentation, and they were readmitted and two of them were managed conservatively and the other one was explored surgically and underwent resection and anastomosis of a jejunal loop. The overall 30-day mortality was 11 patients (27.5%). The overall 90 days

mortality was 15 patients (37.5%), 11 patients of them after surgical exploration, while 4 patients were from the conservative treatment group. The causes and time of death are listed in Table 3.

Table 3: causes and time of mortality.

Cause of mortality	No.	Time of death
Septic shock	3	4,5,8 days after surgical exploration
Spontaneous bacterial peritonitis and liver failure	2	60days after discharge
		30 days after discharge
Hematemesis and melena	2	6 days after admission
		20 days after surgical exploration
Decompensated liver failure	3	7, 10 days after surgical exploration
		30 days after discharge
Chest infection and liver failure	2	38 days after discharge
		5 days after surgical exploration
Renal impairment	2	3 days after surgical exploration
Myocardial infarction	1	3 days after admission

The 1-, 3- and 5 year overall survival was 62.5%. The 1-, 2-, and 3-year survival in patients who underwent conservative treatment (10 patients) was 60%. The 1-, 3- and 5- year survival in patients with surgical treatment (30 patients) was 63.3% (Figure 3).

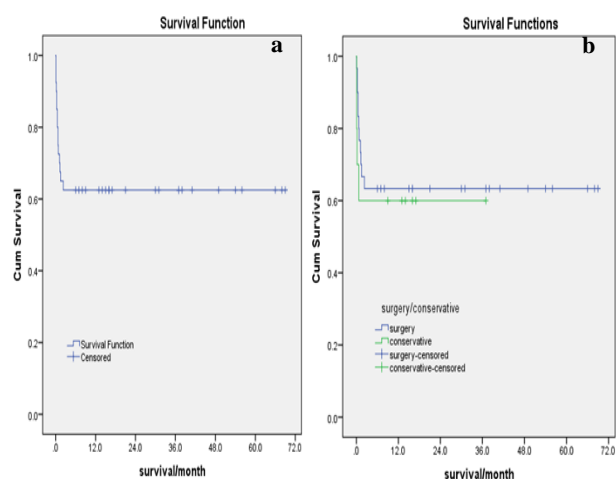


Figure 3: Kaplan-Meier curve for survival; a) Total survival of all the patients, b) Survival of the patients with surgical exploration and conservative treatment.

In the univariate analysis, the risk factors for survival were; Child score ($P=0.02$), high MELD score ($P=0.01$), leukocytosis ($P=0.01$), INR ($P=0.02$), low protein C ($P\leq 0.01$), metabolic acidosis ($P=0.049$), and bleeding per rectum and/or melena at presentation ($P=0.05$). In the multivariate analysis, only leukocytosis was an independent risk factor for survival ($P=0.04$).

DISCUSSION

It is still a challenge to diagnose and determine the underlying causes of MVT. The onset of clinical manifestations is slower than mesenteric arterial occlusion, and early diagnosis can affect the outcome of the patients.^{12,13}

Contrary to the traditional concept in which patients with liver cirrhosis tend usually towards bleeding, MVT and portal vein thrombosis are a complication of cirrhosis, with an incidence of about 10-25%. There is also a higher tendency to venous thrombosis with more severe liver disease.^{14,15} The rebalance between procoagulant (as factor VIII) and anticoagulants (as protein C) shows a paradoxically trend to hypercoagulability in the favor of factor VIII pathway. Reduced portal flow velocity seems also to be an important predictive variable for MVT development in patients with liver cirrhosis.^{16,17}

A major difficulty in the assessment of these patients is that there are no accurate established laboratory tests that reflect the changes in both the procoagulant and anticoagulant systems; therefore, the routine laboratory testing is misleading to the physician for accurate prediction of the coagulation profile. The thrombocytopenia and international normalized ratio (INR) are examples of this type of misleading tests.^{5,18} Present study also proves this concept, as there were 9 patients (22.5%) with INR above 1.7 and 18 patients (45%) with thrombocytopenia and they were presented by acute MVT.

Fayed et al reported that rotational thrombo elastometry (ROTEM) can be one of the accurate diagnostic tools for

hypercoagulability. This can be diagnosed by the ROTEM if the clotting time is short and the maximum clot firmness exceeds 70mm.^{18,19} Portal phase of triphasic CT scan or MRI can be considered the main diagnostic images for patients with suspected MVT. Acosta et al, mentioned that portal phase CT scan was the main diagnostic tool of MVT in 20 patients with abdominal pain, and as a result they had conservative treatment and only one patient underwent surgical exploration.^{20,21} In the current study, triphasic CT was feasible to be done in 28 patients (70%) with suspected MVT, and confirmed the diagnosis of MVT in all of these patients, 10 patients had no intestinal infarction and underwent conservative treatment according to the data of CT scan, with accuracy of 96.9% in detecting intestinal infarction in acute MVT. Yanar et al, showed that the median time between complaining and diagnosis of MVT was three days (range 1-20 days), while in the present study it was five days (range 1-15 day).¹¹

The primary aim of the treatment is to stop the pathological sequence that can lead to intestinal wall necrosis, and peritonitis.²² In our series 10 patients (25%) underwent conservative treatment with anticoagulant therapy with good response to the conservative treatment, and 30 patients (75%) underwent surgical exploration, and 28 patients of them (70%) had intestinal resection and anastomosis. Some studies showed that the non-operative treatment with anticoagulation can resolve the condition in more than 90% of patients.^{22,23} Acosta et al, also showed that conservative management can be effective in 95% of the patients if the CT scan confirmed the diagnosis early.¹⁸ In a study by Yanar et al, only 11 patients (32%) with peritonitis underwent surgical intervention and 23 patients (68%) underwent conservative treatment.¹¹ In another study 21 patients (100%) underwent surgical treatment and 85% underwent intestinal resection and anastomosis.²⁴ Our results are comparable to what is reported by Abu Daff et al that 21 patients (70%) underwent surgical exploration, and 95% of them underwent bowel resection.²⁵

In other series, endovascular treatments with thrombolysis had promising success rate in selected patients with acute MVT, but further studies are still needed for its effectiveness.²⁶⁻²⁸ Some authors recommended a rational for planned 'second-look' operation during the first 2 days postoperative. By doing re-laparotomy we can reassess the suspected viability of any intestinal segments, so decreasing the incidence of initial large segment resection of bowel loops.¹⁰ In one study, a re-exploration was performed in the first 24 hours after the first operation with intestinal resection in nearly 45% of patients with MVT because of concerns regarding questionable intestinal segment viability; all the patients with the second look operation had unviable intestinal segments and required further resection.²⁹

In contrast to previous study, we did not do a routine second look operation, but it was only performed when

necessary depending on clinical manifestations and findings of first exploration. Only 3 patients underwent second look exploration, and 2 of them needed further resection. This comes in agreement to the study of Meng et al, as they reported that the routine use of the second look operation is an aggressive maneuver that may be accompanied with unnecessarily complications.¹⁰

The current study revealed that there was no significant difference between patients who received oral anticoagulant for 6 months (16 patients, 40%) and patients who received it for longer period (9 patients, 22.5%). Other series documented that patients with MVT can receive anticoagulation for 6 months or more, depending on the causes and the underlying risk factors of the disease.^{11,23,26} Mesenteric vein thrombosis has a high rate of recurrence during the first month after presentation and diagnosis.¹¹ In the current study, three patients had recurrence of MVT, shortly after one month of discharge, due to non-compliance to the oral anticoagulant treatment.

Acute MVT has a better prognosis than the other different causes of AMI. In one of large series containing 3700 patients with AMI, who were diagnosed between 1966 and 2002, the overall mortality for patients with MVT was 44, with comparable results to present study (37.5% overall mortality).³⁰ In other study the overall first month mortality rate for patients with MVT was 20%, and it was also comparable to our 30 day mortality (27.5%).³¹ The prognosis of the patients after their discharge depends on the cause of MVT, with poorest survival in patients with associated cancer, Yanar et al noticed that there were no late mortalities related to MVT in their study.^{11,31} Also in the current study, there was no late mortalities.

Further studies with larger series are needed to better comprehensive studying of the early diagnosis and management planes for acute MVT in patients with liver cirrhosis.

CONCLUSION

Patients with liver cirrhosis may have hypercoagulable state and the usual laboratory tests don't accurately assess the coagulation status of the cirrhotic patients. Triphasic CT scan with portal phase can be the corner stone of different diagnostic modalities for MVT. The second look operation is not recommended to be a routine after first exploration, and it should be reserved only for selected cases. Acute MVT still has a high early morbidity and mortality rate especially in cirrhotic patients that needs early diagnosis and urgent management with selective surgical intervention and proper anticoagulant therapy.

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