Does COVID-19 provoke aggressive form of acute mesenteric thrombosis? A comparative study

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Received: 21 November 2021
Accepted: 02 January 2022
Published: 10 October 2022

The Egyptian Journal of Surgery 2022, 41:287–295

Background
Coronavirus disease 2019 (COVID-19) elicits thrombotic events, among which acute mesenteric thrombosis (AMT) might be very serious.
Patients and methods
Eligible patients with AMT who presented to Sohag University Hospital (January 2020–August 2021) were retrospectively studied. Patients were classified into group A (without) versus group B (with) COVID-19. Group B was subdivided into B-1 with mild symptoms and B-2 with peritonitis, all received treatment according to 'damage-control' protocol.
Results
Fifteen patients were eligible (nine males and six females) with median age of 66 (range: 38–81) years. Group B patients (10) were admitted during the last 35% of the study period (7 months) and exhibited delayed presentation compared with group A (five patients), *P* value less than 0.05. In group A, three patients with arterial thrombosis underwent laparotomy during which ischemic bowel segments were resected. Two patients had venous thrombosis and recovered under therapeutic anticoagulation. All group B patients suffered from mixed pattern of AMT (arterial and venous). Group B-1 (five patients) received initially anticoagulation, which was successful in two. Peritonitis developed in three, who required either repair of small-bowel perforations or resection of gangrenous segments. All five patients in group B-2 underwent upfront laparotomy due to peritonitis, gangrenous small bowel and colon of variable lengths were found and resected. The overall mortality rate was 33.3% (five patients died). However, death rate was significantly higher in group B (40%) compared with group A (20%), *P* value less than 0.05.
Conclusions
COVID-19 triggers aggressive variety of AMT with worse clinical outcome.

Keywords:
anticoagulation therapy, coronavirus disease 2019, mesenteric thrombosis

Egyptian J Surgery 2022, 41:287–295

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Introduction

Coronavirus disease of 2019 (COVID-19), which develops in response to infection with severe acute respiratory-syndrome coronavirus-2, progressed to a pandemic that represented a worldwide health threat since the end of 2019 [1,2]. Several studies pointed at the relationship between coronavirus-2 and development of potentially fatal thrombotic events, since the early waves of this pandemic [3]. It was strongly suggested that an aggressive coronavirus-2-induced inflammatory reaction is the main trigger of hypercoagulability [4]. The severity of respiratory dysfunction was found to correlate with vascular endothelial injury, hypercoagulability, and failure of fibrinolysis in lung vasculature [5].

Coronavirus-2 gains access to the cells via angiotensin-converting enzyme 2 (ACE2) [6]. Viral surface glycoprotein, known as 'spike,' unites with ACE2 to penetrate into the target cells. Given that ACE2 is most plentiful in type-II alveolar cells, the majority of COVID-19 cases present with respiratory symptoms [7].

However, COVID-19 may affect other systems, among which the digestive tract is frequently embattled due to high expression of ACE2 in the glandular epithelial cells of the stomach, duodenum, and rectum in addition to the small-bowel endothelial cells and enterocytes [8,9]. Gastrointestinal involvement ranges from 9 to 48.5% and could be the initial indicator of infection, even before development of fever or respiratory dysfunction [10].

Acute mesenteric thrombosis (AMT) may result from partial or complete occlusion of the mesenteric arteries and/or veins by thrombi. It is a potentially

fatal disorder with high mortality rate. In addition to thrombosis, blood flow in the mesenteric vessels can be acutely challenged by embolic or nonocclusive mesenteric ischemia [5,11]. During the era of COVID-19 pandemic, AMT was increasingly discovered. The diagnosis is frequently delayed because of lack of prominent abdominal signs before development of infarctions in the bowel wall. Likewise, an additional diagnostic challenge relates to lack of early pathognomonic findings in simple laboratory tests or abdominal imaging [12,13]. This situation becomes more complex in the context of COVID-19 pandemic due to the overwhelming number of patients requiring hospitalization, shortage of medical staff, deficiency in medical supplies and equipment, as well as the hesitancy of patients to ask for medical advice due to the exaggerated fear of catching infection [14]. Therefore, the majority of patients present with complications, requiring laparotomy and resection of variable length of necrotic bowel [15].

In this study, we will address the presentation, diagnosis, management, and mortality among patients with AMT versus without concomitant COVID-19.

Patients and methods

Study design and patient groups

Retrospective analysis of medical records of patients who were presented to the Emergency Unit, Department of Surgery, Sohag University Hospitals, Sohag, Egypt, from January 2020 to August 2021. Eligible patients were adults more than or equal to 18 years with proven AMT. Exclusion criteria entailed embolic occlusion, nonocclusive, and chronic mesenteric ischemia. Patients were classified according to COVID-19 infection into group A (AMT without COVID-19) and group B (AMT with documented COVID-19) infection. We studied the presentation, diagnosis, management of AMT, and related mortality. Every patient provided a written informed consent on all surgical and nonsurgical-related procedures. The study was approved by Sohag Faculty of Medicine Committee on Medical Research Ethics.

Preoperative workup

All patients underwent meticulous medical history evaluation and clinical examination. An array of laboratory investigations, including routine tests (blood-cell count, liver and kidney functions, electrolyte, and hepatitis serology) and COVID-19-relevant tests (complete blood count, ferritin, D-dimer, C-reactive protein, random blood glucose, lactate and dehydrogenase) were done. Chest computed tomography (CT) and abdominal imaging by radiograph and ultrasonography were undertaken in all patients, while contrast-enhanced abdominal CT and angiography were carried out after confirmation of the preserved renal functions.

Management protocol during coronavirus disease 2019 pandemic

During the last wave of COVID-19, we adopted 'damage-control' protocol in response to remarkable shortage in medical personnel, medical supplies, and hospital beds. This protocol entailed anticoagulation therapy, resection of ischemic bowel, and endovascular treatment thereafter. Abdominal exploration was carried out under general anesthesia via generous midline incision in all patients. Second-look laparotomy was carried out within 48 h after the initial exploration with preceding 12-h pause of anticoagulation.

Statistical analysis

Statistical analysis was performed by Graphpad Prism 7. Qualitative data were expressed as number and percentages, whereas quantitative data were shown as median and SD. Student *t* test was used to compare quantitative variables. Differences were considered statistically significant if *P* value was less than 0.05.

Results

Demographics, patient groups, and subgroups

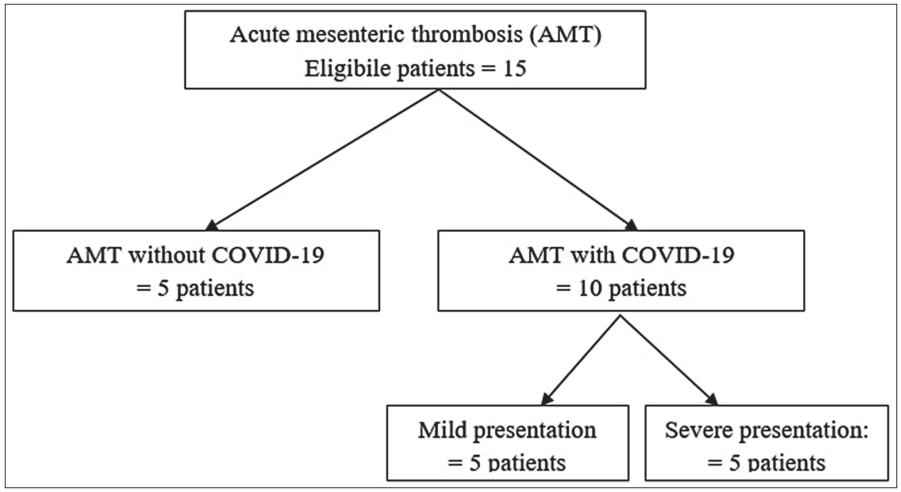
Fifteen patients (nine males and six females) with median age of 66 (range: 38–81) years and confirmed diagnosis of thrombotic acute mesenteric ischemia were enrolled. Diagnostic tests for COVID-19 were negative in five patients (group A), whereas 10 patients (group B) had documented COVID-19 infection, these data are shown in detail in Table 1. According to the severity of presentation, group B was further subdivided into subgroup B-1 (five patients) with mild mesenteric ischemia versus group B-2 (five patients) with peritonitis complicating severe mesenteric ischemia (Fig. 1). Among all patients, there was no history of previous vascular intervention or medical treatment for mesenteric ischemia.

Table 1 Age and sex distribution

	Group A (*N*=5)	Group B (*N*=10)
Males*	3/5 (60)	6/10 (21.7)
Age (years)*	53 (42–81)**	47 (38–73)**

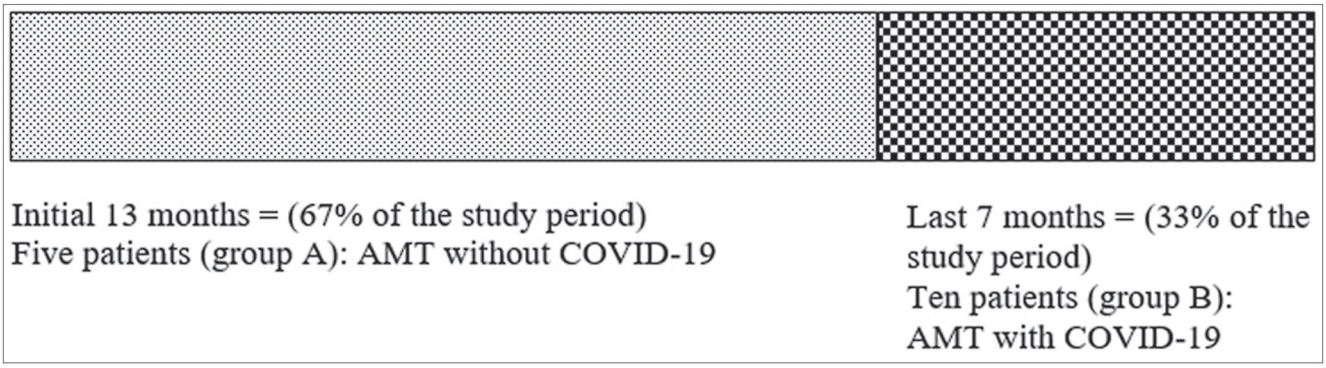
*No significant difference. **Median (range).

Figure 1



Study population, groups, and subgroups.

Figure 2



Distribution of groups A and B across the study period.

Number of patients in relation to the latest coronavirus disease 2019 wave and group B divisions

Five (33%) patients were diagnosed during the earliest 13 months (65%) of the study period, none of them showed any clinical, laboratory, or radiologic evidence of COVID-19.

In contrast, 10 (67%) patients with confirmed COVID-19 were admitted during the last 7 months (35%) of the study period (Fig. 2).

Preoperative clinical data

Patients of group A sought medical advice early within a median of 1 day (range: 1–2 days) after the occurrence of acute postprandial abdominal pain. In contrast, the presentation of group B was delayed. The time lapse between the initial abdominal symptoms and hospital admission was 2–5 (median: 4) days, during which patients received standard COVID-19-treatment regimen for respiratory symptoms with diet restriction and antispasmodics for abdominal pain. The symptoms and risk factors are presented in Table 2. The types of mesenteric thrombosis according to preoperative abdominal CT angiography and duplex studies and the order of treatments applied according to the damage-control protocol are shown in Tables 3 and 4.

Table 2 Symptoms and risk factors

Symptom and risk factors	Group A	Group B
Abdominal pain*	5/5	10/10
Nausea	2/5	7/10
Vomiting	2/5	6/10
Diarrhea	3/5	8/10
Hematochezia	0/5	3/10
Heart disease	2/5	0/10
Smoking	3/5	3/10
Hyperlipidemia	4/5	2/10
Obesity	3/5	2/10
Diabetes mellitus	3/5	2/10
Portal hypertension	1/5	0/10
Hormonal treatment**	1/5	0/10

*Group A showed earlier presentation (median: 1 day, range: 1–2 days) compared with group B (median: 3, range: 2–5 days).
**Oral contraceptive pills.

Management and operative procedures

The choice of primary and subsequent treatment approach was dependent on the severity of presentation and type of AMT. These parameters in addition to the clinical outcome per patient are shown in Table 5.

Group A

In group A, the first patient had multiple atherosclerotic patches in the aorta and iliac arteries with thrombosis of the main trunk of the superior mesenteric artery (Fig. 3a,b). During urgent laparotomy, multiple ischemic areas and necrotic perforations were found across small-bowel segment measuring about 2 m, the distal end was ~80 cm from the ileocecal valve (Fig. 3c,d). Resection and primary anastomosis were carried out (Fig. 3e,f). The second and third patients suffered from thrombosis of small mesenteric arterioles. Emergency laparotomy was performed in both patients because of the development of signs of peritonitis on the second and fourth days after admission, respectively. Ischemic bowel segments (about 50-cm length in one patient and 180 cm in the other) were found with multiple perforations, more than 1 m from the ileocecal valve. In both patients, small-bowel resection and primary anastomosis with proximal enterostomy were undertaken.

Therapeutic anticoagulation was established under strict surveillance of coagulation profile. However, during second-look laparotomy, the third patient showed progression of bowel gangrene, which affected almost the whole small intestine, for which additional resection of the necrotic bowel was carried out.

On the other hand, the fourth and fifth patients (with minor venous thrombosis as diagnosed by CT angiography and duplex examination) recovered successfully under medical treatment with therapeutic anticoagulation.

Table 3 Types of mesenteric thrombosis per group/subgroup

		Group B	
	Group A	Subgroup B-1	Subgroup B-2
Arterial	3	0	0
Venous	2	0	0
Mixed (arterial+venous)	0	5	5
Number of patients per group/subgroup	5	5	5

Table 4 Order of applied treatment modalities

		Group B	
	Group A	Subgroup B-1	Subgroup B-2
Anticoagulation alone	2	2	0
Anticoagulation "" surgery "" anticoagulation	3	3	0
Surgery "" anticoagulation	0	0	5
Number of patients per group/subgroup	5	5	5

All recovered patients had multidisciplinary follow-up, including general and vascular surgeons, endovascular interventionists, and hematologists.

Group B

Subgroup B-1

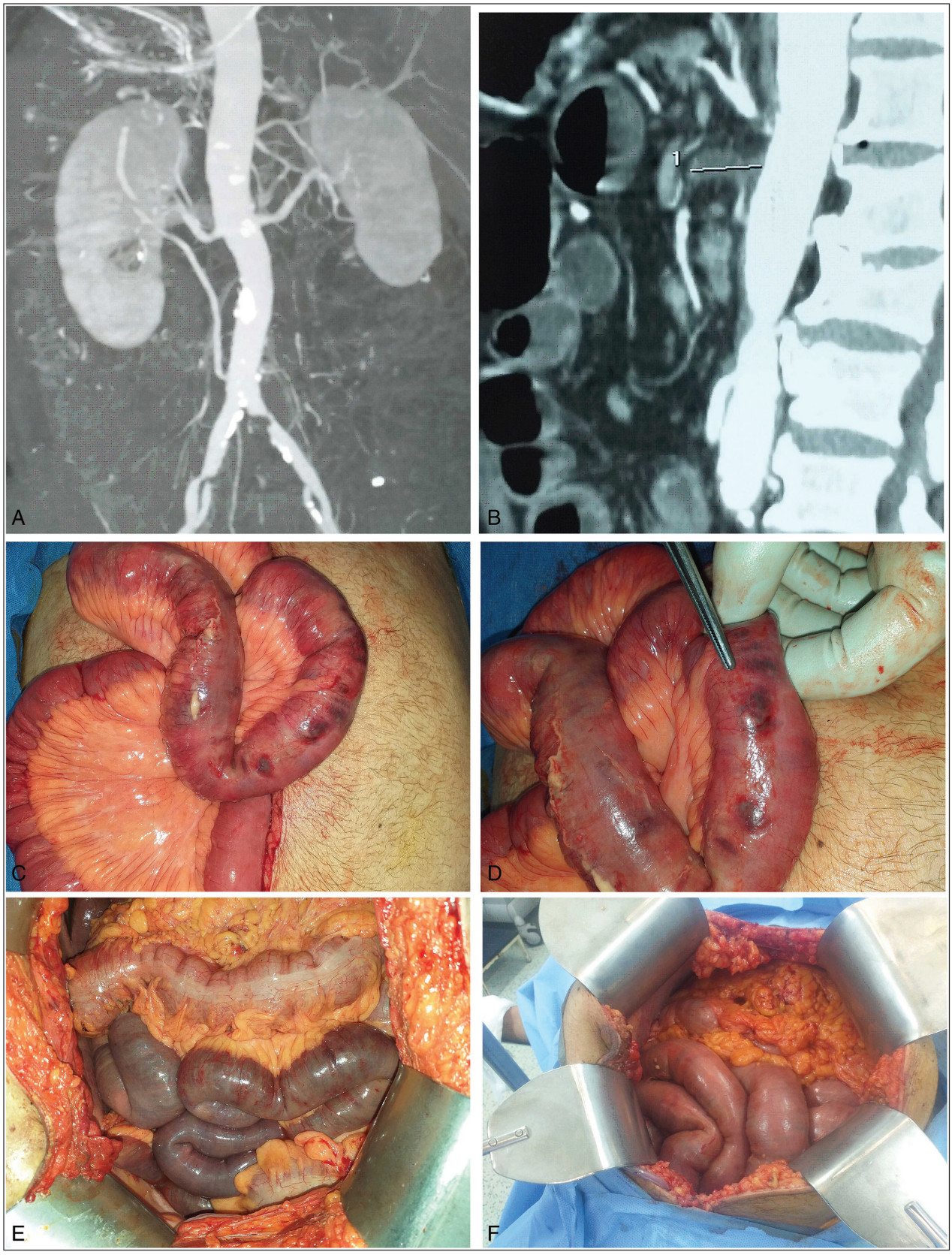
All patients showed mild initial symptoms and borderline laboratory findings. They received therapeutic anticoagulation under stringent observation. Conservative treatment was successful in the first two patients. Nevertheless, laparotomy was carried out in the other three patients who showed evidence of clinical and laboratory deterioration. The third and fourth patients required resection of

Table 5 Site of mesenteric thrombosis, management, and clinical outcome

Groups		Patients #	Site of thrombois	Management	Clinical outcome
Group A		1	SMA	Anticoagulation "" bowel resection "" anticoagulation	Recovery
		2	Mesenteric arterioles	Anticoagulation "" bowel resection "" anticoagulation	Recovery
		3		Anticoagulation "" bowel resection "" anticoagulation	Death
		4	Mesenteric venules	Anticoagulation alone	Recovery
		5		Anticoagulation alone	Recovery
Group B	Subgroup B-1	1	Mixed (mesenteric arterioles and venules	Anticoagulation alone	Recovery
		2		Anticoagulation alone	Recovery
		3		Anticoagulation "" bowel resection "" anticoagulation	Recovery
		4		Anticoagulation "" bowel resection "" anticoagulation	Recovery
		5		Anticoagulation "" bowel resection "" anticoagulation	Death
	Subgroup B-2	1		Bowel resection "" anticoagulation	Death
		2		Bowel resection "" anticoagulation	Death
		3		Bowel resection "" anticoagulation	Death
		4		Bowel resection "" anticoagulation	Recovery
		5		Bowel resection "" anticoagulation	Recovery

SMA, superior mesenteric artery.

Figure 3



Radiologic and operative findings in the first patient in group A. (a) Aortic bifurcation and common iliac arteries narrowed by atheromatous plaques. (b) Superior mesenteric artery filling defect, consistent with thrombotic perforations. (c) Multiple small-bowel necrotic areas and impending perforations. (d) Multiple small-bowel necrotic areas and impending perforations (higher magnification). (e) Small bowel after resection of frankly ischemic segments. Suboptimal perfusion of the small bowel contrary to the well-perfused transverse colon is obvious. The patient was transferred to the ICU for anticoagulation therapy and strict observation. (f) Same patient (e) who improved perfusion of the small bowel is confirmed during second-look laparotomy.

two segments of the small bowel due to ischemic perforations. Second-look laparotomy proved that there is no evidence of further thrombosis. In the fifth patient, mesenteric edema and massive gangrene affecting almost 75% of the small bowel were found, therefore, resection of the gangrenous intestine was done without primary anastomosis. During second-look exploration, further resection of a newly developed 20-cm gangrenous segment of small bowel was performed.

Figure 4

Subgroup B-2, massive bowel gangrene, massive bowel gangrene (small intestinal loops are seen) in a patient with COVID-19 infection complicated with AMT. AMT, acute mesenteric thrombosis; COVID-19, coronavirus disease 2019.

Subgroup B-2

The entire subgroup exhibited obvious signs of peritonitis and sepsis and underwent emergency laparotomy after resuscitation. One patient showed extensive gangrene of the small bowel and right side of the colon down to mid-transverse colon (Fig. 4). Two patients exhibited small-bowel gangrene (except 50 and 70 cm distal to the duodeno–jejunal junction, respectively) and the right colon, representative pictures are shown in Fig. 5a,b. Second-look laparotomy showed progressive gangrene in all three patients who underwent further resection of the newly developed gangrenous bowel. The other two patients underwent resection of 60 and 80 gangrenous segments of the jejunum (Fig. 6a,b) and ileum, respectively, and showed no progression on the second-look laparotomy. Of note, primary anastomosis was not attempted in any patient in group B.

Figure 5

Subgroup B-2, extensive bowel gangrene. (a) Extensive small-bowel gangrene (sparing only about 70 cm distal to the dudeno–jejunal junction), due to concomitant COVID-19 and AMT. (b) Same patient (a) mesenteric edema due to AMT (predominantly venous thrombosis). AMT, acute mesenteric thrombosis; COVID-19, coronavirus disease 2019.

Figure 6

Subgroup B-2, segmental small-bowel gangrene. (a) Segmental small-bowel gangrene in a patient suffering from COVID-19 infection and concurrent AMT. (b) Same patient (a) perfusion down to the distal ileum is borderline. AMT, acute mesenteric thrombosis; COVID-19, coronavirus disease 2019.

Hospital stay, complications, and postoperative mortality

Overall, hospital stay ranged from 5 to 42 (median: 15) days. It was significantly prolonged in group B (range: 9–42, median: 19) in comparison with group A (range: 5–17) (median: 8) days, *P* value less than 0.05. Generally, in-hospital death rate was 33.3% (five out of 15 patients). However, death rate was significantly higher in group B (40%) compared with group A (20%), *P* value less than 0.05. Complication rates (intra-abdominal abscess, multiorgan failure, wound sepsis, postoperative pneumonia, severe malnutrition, and cardiac arrhythmias) were significantly higher in group B ($P<0.05$). In group A, one patient died on the third postoperative day due to severe sepsis. In subgroup B-1, one postoperative death occurred on the seventh postoperative day due to pulmonary-artery thrombosis. In subgroup B-2, three postoperative deaths were reported in relation to progressive sepsis, electrolyte disturbances, and multiorgan failure 3, 6, and 14 days after the second laparotomy.

Follow-up

After discharge, the patients received multidisciplinary care involving specialist general and vascular surgeons, endovascular interventionists, and hematologists for further assessment and possible interventions. Regular follow-up was scheduled in the general-surgery outpatient clinic.

Discussion

In this study, we studied patients with concomitant COVID-19 and AMT during the most aggressive wave of the pandemic in Egypt. Those patients suffered from worse clinical presentation and increased mortality compared with those who were free of COVID-19.

Group B (AMT with COVD-19) included twice the number of patients in group A (AMT with COVID-19), with more serious symptoms. However, this doubled number of patients presented to the hospital during no more than the last third of the study period (7 months), which represents only one-third of the whole study period. The rise of the number of patients with AMT was likely triggered by the overwhelming spread of COVID-19 and high case-fatality rate in Egypt compared with several other heavily infected countries [16,17].

The time of presentation among group B patients was delayed compared with those in group A. This could be related to the heterogeneous and late COVID-19-related thrombotic complications [18]. Likewise, lack of sufficient public awareness that COVID-19 might provoke severe gastrointestinal disorders including AMT, could have contributed to late presentations [1,19–21].

The predisposing factors in group A were obvious. For instance, our patients who suffered from arterial AMT were atherosclerotic, hypertensive, obese, and diabetics. These factors are known to enhance the risk of AMT [22,23]. Mesenteric venous thrombosis occurred in relation to the history of portal hypertension and hormonal contraceptive treatment [24,25]. In sharp contrast, definitive predisposing factors in group B could be barely found. In this context, the contribution of COVID-19 infection to the development of AMT appears reasonable, particularly with the strong evidence that COVID-19 may elicit thrombosis of the aorta, celiac trunk, superior and inferior mesenteric arteries [26–28], peripheral arteries [29], and portal, splenic, and superior mesenteric veins [30,31].

It should be emphasized that damage-control protocol comprised, whenever feasible, initial treatment with therapeutic anticoagulation. However,

complicated presentation with peritonitis or failure of anticoagulation prompted urgent laparotomy. Surgery was performed primarily to resect gangrenous bowel, avoid sepsis, enable application of therapeutic anticoagulation postoperatively in the ICU, and second-look laparotomy within 48 h [32]. Thereafter, appropriate endovascular interventions were planned for successfully rescued patients [33].

In group A, the patients exhibited mild clinical symptoms. Likewise, bowel ischemia affected definitive uninterrupted segments of the small bowel, thus, we were encouraged to carry out primary anastomosis after ischemic bowel resection. Our approach conforms with published reports, which indicated that the options of primary anastomosis or diverting stoma can be applied [34]. Nonoperative resolution occurred in two patients with venous mesenteric thrombosis. This is in line with the reported data on anticoagulation therapy as potentially sufficient sole treatment of mesenteric venous thrombosis [35]. In subgroup B-1, therapeutic anticoagulation has successfully prevented further progression of mesenteric thrombosis in two patients. This could be attributed to predominance of mesenteric venous (not arterial) thrombosis, a situation in which systemic anticoagulation therapy alone might be also enough [11].

Patients in subgroup B-2 presented to the hospital during late stages of the disease. Thus, there was no primary treatment option available for them other than upfront surgery. This group had the worst outcome most likely due to delayed presentation and extensive mesenteric thrombosis [33,36,37].

The overall mortality was 33.3%, which is in accordance with previous studies, which demonstrated mortality rates up to 40–60% [5]. We found that patients with concomitant AMT and COVID-19 had doubled mortality rate (40%) compared with those who were free of COVID-19 (20%). This figure is similar to what has been demonstrated in a series of 13 patients with concurrent COVID-19 and venous AMT [15]. This could be explained by extensive COVID-19-induced cross-talk between inflammation and thrombosis [38].

It should be underlined that the retrospective nature of this study may represent significant shortcomings. However, given the low number of case series published on the outcome of concurrent AMT and COVID-19 infection, this study addressed this important issue on a reasonable number of patients who were treated in a single center.

In conclusion, the current study demonstrated that COVID-19 triggered high numbers and enhanced the severity of AMT. Prompt diagnosis and implementation of multidisciplinary care might improve the clinical outcome in this complicated situation.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

References

1 Wang M-K, Yue H-Y, Cai J, Zhai Y-J, Peng J-H, Hui J-F, *et al*. COVID-19 please supply all of their names. If there are 8 or more authors, please supply the first 6 authors' names then *et al*.] and the digestive system: a comprehensive review. World J Clin Cases 2021; 9:3796–3813.

2 Kumar SU, Madhana Priya NM, Nithya SR, Kannan P, Jain N, Kumar DT, *et al*. A review of novel coronavirus disease (COVID-19): based on genomic structure, phylogeny, current shreds of evidence, candidate vaccines, and drug repurposing. Biotech 2021; 11:198.

3 Jin B, Singh R, Ha SE, Zogg H, Park PJ, Ro S, *et al*. Pathophysiological mechanisms underlying gastrointestinal symptoms in patients with COVID-19. World J Gastroenterol 2021; 27:2341–2352.

4 Avila J, Long B, Holladay D, Gottlieb M. Thrombotic complications of COVID-19. Am J Emerg Med 2021; 39:213–218.

5 Al Mahruqi G, Stephen E, Abdelhedy I, Al Wahaibi K. Our early experience with mesenteric ischemia in COVID-19 positive patients. Ann Vasc Surg 2021; 73:129–132.

6 Beyerstedt S, Casaro EB, Rangel ÉB. COVID-19: angiotensin-converting enzyme 2 (ACE2) expression and tissue susceptibility to SARS-CoV-2 infection. Eur J Clin Microbiol Infect Dis 2021; 40:905–919.

7 Lai CC, Ko WC, Lee PI, Jean SS, Hsueh PR. Extra-respiratory manifestations of COVID-19. Int J Antimicrob Agents 2020; 56:106024.

8 Xu J, *et al*. Digestive symptoms of COVID-19 and expression of ACE2 in digestive tract organs. Cell Death Discov 2020; 6:1–8.

9 Zhang H, *et al*. Specific ACE2 expression in small intestinal enterocytes may cause gastrointestinal symptoms and injury after 2019-nCoV infection. Int J Infect Dis 2020; 96:19–24.

10 Fang LG, Zhou Q Remarkable gastrointestinal and liver manifestations of COVID-19: a clinical and radiologic overview. World J Clin Cases 2021; 9:4969–4979.

11 Bala M, Kashuk J, Moore EE, Kluger Y, Biffl W, Gomes CA, *et al*. Acute mesenteric ischemia: guidelines of the World Society of Emergency Surgery. World J Emerg Surg 2017; 12:38.

12 Copin P, Zins M, Nuzzo A, Purcell Y, Beranger-Gibert S, Maggiori L, *et al*. Acute mesenteric ischemia: a critical role for the radiologist. Diagn Intervent Imag 2018; 99:123–134.

13 Cudnik MT, Darbha S, Jones J, Macedo J, Stockton SW, Hiestand BC, *et al*. The diagnosis of acute mesenteric ischemia: a systematic review and meta-analysis. Acad Emerg Med 2013; 20:1087–1100.

14 Rubin R. Tracking COVID-19 supply shortages. JAMA 2021; 326:1138.

15 Stasyshyn A. Mesenteric thrombosis in patients with coronavirus disease. BJSTR 2021; 34:2.

16 Saied AA, Metwally AA, Madkhali NAB, Haque S, Dhama K. Egypt's COVID-19 recent happenings and perspectives: a mini-review. Front Public Health 2021; 9:1132.

17 Samir A, Elabd AM, Mohamed W, Baess AI, Sweed RA, Abdelgawad MS, *et al*. COVID-19 in Egypt after a year: the first and second pandemic waves from the radiological point of view; multi-center comparative study on 2000 patients. Egypt J Radiol Nucl Med 2021; 52:168.

18 Alemán W, Cevallos LC. Subacute mesenteric venous thrombosis secondary to COVID-19: a late thrombotic complication in a nonsevere patient. Radiol Case Rep 2021; 16:899–902.

19 Alahdal H, Basingab F, Alotaibi R. An analytical study on the awareness, attitude and practice during the COVID-19 pandemic in Riyadh, Saudi Arabia. J Infect Public Health 2020; 13:1446–1452.

20 Galanopoulos M, Gkeros F, Doukatas A, Karianakis G, Pontas C, Tsoukalas N, *et al*. COVID-19 pandemic: pathophysiology and manifestations from the gastrointestinal tract. World J Gastroenterol 2020; 26:4579–4588.

21 Su S, Shen J, Zhu L, Qiu Y, He J-S, Tan J-Y, *et al*. Involvement of digestive system in COVID-19: manifestations, pathology, management and challenges. Therap Adv Gastroenterol 2020; 13:1756284820934626.

22 Franca E, Shaydakov ME, Kosove J. Mesenteric artery thrombosis. Treasure Island, FL: StatPearls Publishing; 2020.

23 Chiu Y-W, Wu C-S, Chen P-C, Wei Y-C, Hsu J-S, Wang S-H, *et al*. Risk of acute mesenteric ischemia in patients with diabetes: a population-based cohort study in Taiwan. Atherosclerosis 2020; 296: 18–24.

24 Intagliata NM, Caldwell SH, Tripodi A. Diagnosis, development, and treatment of portal vein thrombosis in patients with and without cirrhosis. Gastroenterology 2019; 156:1582–1599.

25 Béliard A, Verreth L, Grandjean P. Oral contraceptive and acute intestinal ischemia with mesenteric venous thrombosis: a case report. Open Access J Contracept 2017; 8:9–11.

26 Almeida A, Baixauli J, Cienfuegos JA, Valentí V, Rotellar F. Concomitant aortic, inferior mesenteric artery thrombosis and sigmoid colon perforation in severe COVID-19 disease. Cir Esp 2021; 5:XX. doi:10.1016/j.ciresp.2021.09.013

27 A Beccara L, Pacioni C, Ponton S, Francavilla S, Cuzzoli A. Arterial mesenteric thrombosis as a complication of SARS-CoV-2 infection. Eur J Case Rep Intern Med 2020; 7:001690.

28 Krothapalli N, Jacob J. A rare case of acute mesenteric ischemia in the setting of COVID-19 infection. Cureus 2021; 13:e14174.

29 Costa VDE, Guilherme de Almeida BC, Nicolini EM, Rodrigues GDA, da Costa BMA, Carvalhoe GH, dos Reis ALS, Colen DP. Acute arterial occlusion of the lower limb as the main clinical manifestation in a patient with COVID-19–case report. Int J Surg Case Rep 2020; 77:454–458.

30 Jeilani M, Hill R, Riad M, Abdulaal Y. Superior mesenteric vein and portal vein thrombosis in a patient with COVID-19: a rare case. BMJ Case Rep 2021; 14:e244049.

31 Vidali S, Morosetti D, Granai AV, Legramante JM, Buonomo OC, Argirò R, *et al*. Splenoportal-mesenteric axis thrombosis and splenic artery occlusion as initial presentations of COVID-19 disease. Eur Rev Med Pharmacol Sci 2021; 25:1680–1683.

32 Brillantino A, Lanza M, Antropoli M, Amendola A, Squillante S, Bottino V, Renzi A, Castriconi M. Usefulness of damage control approach in patients with limited acute mesenteric ischemia: a prospective study of 85 patients. Updates Surg 2022; 74:337–342.

33 Lim S, Halandras PM, Bechara C, Aulivola B, Crisostomo P. Contemporary management of acute mesenteric ischemia in the endovascular era. Vasc Endovascular Surg 2019; 53:42–50.

34 Awad S, Tarabay A, Negm A, Althobaiti W, Alorabi F, Dawoud I, Sheishaa M. Primary anastomosis versus diverting stoma as a management of intestinal vascular gangrene: a randomized controlled study. Egypt J Surg 2021; 40:73–82.

35 Acosta S, Salim S. Management of acute mesenteric venous thrombosis: a systematic review of contemporary studies. Scand J Surg 2021; 110:123–129.

36 Wu W, Yang L, Zhou Z. Clinical features and factors affecting postoperative mortality for obstructive acute mesenteric ischemia in China: a hospital-based survey. Vasc Health Risk Manag 2020; 16:479–487.

37 de Macedo VSO, Moreira GB, de Albuquerque ACF, Oliveira SCDS, Aragão Esmeraldo MA, Barbosa FCB. *et al*. Late mesenteric ischemia after Sars-Cov-2 infection: case report. J Vasc Bras 2021; 20:e20200105.

38 Connors JM, Levy JH. COVID-19 and its implications for thrombosis and anticoagulation. Blood 2020; 135:2033–2040.