



# Colon ischemia in patients with severe COVID-19: a single-center retrospective cohort study of 20 patients

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## Abstract

**Purpose** Thromboembolic complications due to COVID-19 are common in patients requiring critical care and are associated with high morbidity and mortality rates. The aim of this study was to evaluate clinical manifestations and postoperative outcomes after colectomy for COVID-19-associated colonic ischemia in the first versus the second wave of the pandemic.

**Methods** A retrospective cohort study of patients with severe COVID-19 at our institution between 1 March 2020 and 31 January 2021 was performed. All patients with severe COVID-19, requiring critical care and surgical treatment of colonic ischemia, were included. The main outcomes were surgical complications and mortality rate.

**Results** A total of 190 patients were included of whom 20 (10.5%) patients underwent surgery for colon ischemia. Preoperatively, D-dimer was elevated, especially in the first wave (median 15.24 (interquartile range 6.00–32.00) vs. 2.09 (1.42–4.28) mg/L,  $p=0.025$ ). Twelve (60%) patients underwent a (sub)total colectomy, 7 (35%) a right hemicolectomy, and one patient (5%) an ileocecal resection. Grade 3b complications occurred in one of 5 patients (20%) in the first and in 9 of 15 patients (60%) in the second wave. The overall in-hospital mortality was similar in both waves (40% vs. 47%), with death occurring after a median stay of 21 days.

**Conclusion** In this cohort study of patients with severe COVID-19 and colonic ischemia, clinical presentation and laboratory findings varied. However, the majority of patients required (sub)total colectomy. Despite a lower threshold to surgery in the second wave, mortality remained high.

**Keywords** Colon ischemia · COVID-19 disease · SARS-CoV-2 · Colectomy · Mortality

## Introduction

The novel coronavirus disease 2019 (COVID-19) is known to predispose to acute thromboembolic complications, and up to half of the patients with severe thromboembolic events are not salvageable.

After clinicians world-wide observed cases with COVID-19-associated thromboembolism, the awareness regarding hypercoagulability has been raised in the course of the pandemic. The management has therefore been optimized to prevent thromboembolic events. However, there is data that almost one-third of critically ill patients with COVID-19 suffer thromboembolic complications despite systemic thromboprophylaxis [1]. If colon ischemia occurs, colectomy is usually inevitable.

The aim of this study was to review clinical courses of patients with COVID-19 and colon ischemia with a special focus on the therapeutic management in the first wave compared to the second wave of the pandemic.

## Methods

We performed a single-center retrospective study (local ethical advisory board ID 2021–802) of all consecutive patients with PCR-confirmed COVID-19 who were mechanically

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ventilated and underwent surgery for colon ischemia between 1 March 2020 and 31 January 2021 (in Germany, the first wave lasted from March 2020 until June 2020 and the second wave from October 2020 until January 2021 [2]).

To identify all eligible patients, we searched our clinical information system for the ICD Codes U07.1, K55.-, K55.0, K55.1, K55.8, and K55.9 and the OPS-Codes 5–453.2 and 5–455.0 to 5–455.y and 5–456 to 5–456.y. Data were managed using REDCap (Research Electronic Data Capture) electronic data capture tools hosted at University Medicine Mannheim.

Quantitative variables are presented by their median values together with the quartiles  $Q_1$  and  $Q_3$ ; for qualitative factors, counts and percentages are given. In order to compare two groups, Mann–Whitney  $U$  test or Fisher's exact test was performed, as appropriate. The result of a statistical test was considered significant for  $p < 0.05$ . All statistical calculations were done with SAS software, release 9.4 (SAS Institute Inc., Cary, North Carolina, USA).

## Results

We extracted data from 582 consecutive patients with PCR-proven COVID-19 (exclusively wild type SARS-CoV-2) between 1 March 2020 and 31 January 2021 of whom 190 required intensive care treatment. Twenty (10.5%) patients underwent surgery for colon ischemia. In the first wave 5 of 29 patients (17%) and in the second wave, 15 of 161 patients (9%) underwent colectomy. Baseline characteristics are summarized in Table 1.

At the time of surgery, 6 patients required extracorporeal membrane oxygenation (ECMO) therapy. Immediately preoperatively, the infection parameters were significantly elevated. D-dimer was also increased, especially in patients of the first wave (15.24 (6.00–32.00) mg/L vs. 2.09 (1.42–4.28) mg/L,  $p = 0.025$ ). Only a few patients presented with gastrointestinal symptoms. Most patients (16/20) underwent surgery for increasing levels of catecholamines indicating rapid hemodynamic deterioration without further identifiable causes. Computed tomography scan was performed in 95% of the patients, showing colonic wall thickening (1/19), pneumatosis or portal venous gas (3/19), perforation (1/19), distension of colon (10/19), SMA (superior mesenteric artery), or celiac thrombosis (1/19). Preoperative colonoscopy was performed in 8 patients (40%), with no pathological findings in 4 patients. Only one patient had signs of mucosal ischemia in the colonoscopy. The diagnostic parameters are summarized in Table 1.

A (sub)total colectomy was necessary in 12 patients (60%), a right hemicolectomy in 7 patients (35%) and an ileocecal resection in one patient (5%). The pathological examination of the colectomy specimens confirmed the

finding of colonic ischemia in all cases. Postoperative surgical complications occurred in 10 patients, and revision surgery was also needed in 10 patients: completion colectomy (2/10), small bowel resections for ischemia (2/10), cholecystectomy (1/10), operative wound therapy (5/10).

Among the whole study cohort, we recorded an in-hospital mortality rate of 45% in comparison to an overall mortality of 37% in all COVID-19-positive patients who required critical care (70/190). Deaths occurred after a median of 21 days from admission.

## Discussion

As awareness of the inherent thromboembolism risk in patients with COVID-19 increased during the pandemic, we hypothesized that there may have been fewer thromboembolic complications in the second wave because of improved prevention strategies.

During the studied period, 190 patients were treated for severe COVID-19 at our intensive care units. Of these, 20 patients had to undergo colectomy due to colonic ischemia. Considering the cohort as a whole, some aspects stand out: the median body mass index (BMI) was 31 kg/m<sup>2</sup> corresponding to class 1 obesity, a known risk factor for a complicated course of COVID-19. As a meta-analysis of 12 studies including 405,359 patients revealed, the pooled risk of COVID-19 severity is 1.31 times higher among overweight patients [3]. Another interesting finding was that one-fourth of the patients (5/20, 25%) were under anticoagulant therapy, which raises the question of whether these patients were already at an increased risk of thrombosis before SARS-CoV-2 infection. One could hypothesize that preexisting individual hypercoagulability in addition to COVID-19-induced hypercoagulable state could have increased the risk for thromboembolic events in this subgroup despite prophylactic continuous heparin infusion.

Taking a focused look at the preoperative laboratory values, there are some conspicuous features that are worthy of discussion: first, the D-dimer was relevantly increased, especially in the first wave cohort. Of course, elevated D-dimer levels are common in severe sepsis and disseminated intravascular coagulation due to COVID-19 [4]; nevertheless, the significantly higher values may indicate that patients in the first wave were already in a more progressive septic deterioration and that colonic ischemia was already more advanced when it was diagnosed than in patients in the second wave. Similar trends are seen with respect to procalcitonin, lactate, leucocytes, and C-reactive protein. This could indicate that colonic ischemia was diagnosed earlier in the second wave which led to a faster indication for surgery. In addition, the establishment of a daily ward round by a surgical attending in the medical COVID-19 ICU has certainly contributed to a

**Table 1** Baseline characteristics, diagnostic workup, and postoperative outcomes

	First wave ( <i>n</i> = 5)	Second wave ( <i>n</i> = 15)	<i>P</i> value	Total ( <i>n</i> = 20)
Age (years), median (Q1–Q3)	68 (63–69)	69 (61–72)	0.717	69 (62–72)
Gender (male/%)	2 (40%)	13 (87%)	0.073	15 (75%)
Body mass index (kg/m <sup>2</sup> )	32 (27.8–33.2)	31.1 (28.1–34.6)	0.782	31.2 (28–33.9)
30–35	2 (40%)	7 (47%)		9 (45%)
35–40	0	2 (13%)		2 (10%)
> 40	1 (20%)	1 (7%)		2 (10%)
Duration ICU stay (days), median (Q1–Q3)	27 (17–31)	26 (17–44)	0.626	26.5 (17–42)
Home medication, <i>n</i> (%)				
Home medication, overall	2 (40%)	14 (93%)	<b>0.032</b>	16 (80%)
Anticoagulants	1 (20%)	8 (53%)	0.319	9 (45%)
Leucocyte count, 10E12/L, median (Q1–Q3)	24.3 (14.4–29.5)	20.3 (15.7–24.4)	0.800	20.6 (15.6–25.0)
CRP, mg/L, median (Q1–Q3)	204 (164–268)	208 (91–274)	1.000	206 (96.5–271)
PCT, µg/L, median (Q1–Q3)	4.28 (4.28–4.28)	1.82 (1.18–2.27)	0.546	1.87 (1.18–4.28)
D-dimer, mg/L, median (Q1–Q3)	15.24 (6.00–32.00)	2.09 (1.42–4.28)	<b>0.025</b>	2.18 (1.97–6.00)
Platelet count, 10E9/L, median (Q1–Q3)	288 (211–306)	167 (130–280)	0.063	187.5 (144.5–297)
PTT, s, median (Q1–Q3)	68.1 (33.7–71.0)	45.5 (40.6–62.3)	0.600	45.8 (39.7–67.0)
Antithrombin activity, %, median (Q1–Q3)	82 (75–87)	66 (61–80)	0.179	75 (62–85)
Lactate, mmol/L, median (Q1–Q3)	4.2 (2.0–6.3)	2.4 (1.3–6.5)	0.599	3.3 (1.4–6.4)
Abdominal imaging				
Radiography	0	5 (33.3%)	0.266	5 (25%)
CT-scan	5 (100%)	14 (93%)	1.000	19 (95%)
MRI	0	0	n.c	0
Imaging findings, <i>n</i> (%); Patients with CT-scan ( <i>n</i> = 19)				
Colonic or rectal wall thickening	0	1 (7%)	1.000	1 (5%)
Pneumatosis or PV gas	1 (20%)	2 (14%)	1.000	3 (16%)
Perforation	1 (20%)	0	0.263	1 (5%)
Distension of colon	1 (20%)	8 (57%)	0.303	10 (53%)
SMA or celiac thrombosis	0	1 (7%)	1.000	1 (5%)
Preoperative colonoscopy	2 (40%)	6 (40%)	1.000	8 (40%)
Endoscopic findings, <i>n</i> (%)				
No pathological findings	1 (50%)	3 (50%)	1.000	4 (50%)
Mucosal ischemia	0	1 (16.6%)	1.000	1 (12.5%)
Transmural ischemia	0	0		0
Bowel dilatation	1 (50%)	3 (50%)	1.000	4 (50%)
Other	1 (50%)	1 (16.6%)	0.464	2 (25%)
Norepinephrine level	5.5 (1.1–9.5)	4.7 (0.7–6.5)	0.483	5.1 (0.9–6.5)
Extent of colon surgery, <i>n</i> (%)			0.230	
Right hemicolectomy	2 (40%)	5 (33.3%)		7 (35%)
(Sub)total colectomy	2 (40%)	10 (66.7%)		12 (60%)
Ileocecal resection	1 (20%)	0		1 (5%)
Revisional surgery, <i>n</i> (%)				
Revisional surgery, overall	1 (20%)	9 (60%)	0.303	10 (50%)
Completion colectomy	0	2		2
Small bowel resection	1	1		2
Cholecystectomy	0	1		1
Other	0	5		5
Surgical complications, <i>n</i> (%)	2 (40%)	7 (47%)	1.000	9 (45%)
Further ischemia	1	2		3
Gastrointestinal leakage	0	0		0

**Table 1** (continued)

	First wave ( <i>n</i> = 5)	Second wave ( <i>n</i> = 15)	<i>P</i> value	Total ( <i>n</i> = 20)
SSI	0	2		2
Other	2	5		7
Clavien Dindo classification, <i>n</i> (%)			0.182	
Grade 1	0	0		0
Grade 2	1 (20%)	0		1 (5%)
Grade 3a	0	0		0
Grade 3b	1 (20%)	9 (60%)		10 (50%)
Grade 4a	0	0		0
Grade 4b	0	0		0
Grade 5	0	0		0
Mortality	2 (40%)	7 (47%)	1.000	9 (45%)

*P* values in bold type indicate statistical significance. D-dimer conversion factor to SI Unit nmol/l is 5.476. Leucocyte count conversion factor to SI Unit  $10^9$  is 1000.

*CRP* C reactive protein, *CT* computed tomography, *ECMO* extracorporeal membrane oxygenation, *GI* gastrointestinal, *ICU* intensive care unit, *n.c.* not calculable, *PCT* procalcitonin, *PTT* partial thromboplastin time, *PV* portal venous, *SSI* surgical site infection.

faster diagnosis, and the implementation of an extra COVID-19 operating room has shortened the interval between the decision to operate and the beginning of the operation at our institution.

That the earliest possible diagnosis of advancing irreversible colonic ischemia is still a challenge becomes evident looking at our results on clinical symptoms and diagnostic workup. Signs of gastrointestinal failure are by far not present in all patients and are sometimes difficult to determine in ventilated patients. Our data is in accordance with a small case series from Spain which found similar gastrointestinal clinical signs in three COVID-19 patients with colon ischemia [5]. This leads to a relatively low threshold to perform diagnostic imaging. However, though 90% of patients received a CT scan, the findings were often not typical of colonic ischemia. In contrast to this, a review of 22 studies including 31 patients with COVID-19-related gastrointestinal ischemia found that contrast-enhanced abdominal CT scan identified macrovascular thrombosis in almost half of the patients [6]. Similarly, Abdelmohsen reports that in 27 of 40 patients (67.5%), a CT scan revealed acute vascular pathologies. Therefore, the authors highlight the importance of abdominal CT imaging in COVID-19 patients [7]. Considering the high mortality rate in case of delayed surgery, the therapeutic algorithm for COVID-19 patients should include a rapid indication for surgery, if there are clinical or radiological signs of ischemia.

Comparing the colectomy rates between the first and the second wave, more patients required colectomy in the first wave. This could speak for an optimized management with regard to the prevention of thromboembolic events. However, the pooled colectomy rate among our patient cohort of 10.5% (20/190) is remarkably higher than the reported

colectomy rate in ICU patients with admission diagnoses other than COVID-19: a large Finnish retrospective cohort study of 22,936 patients admitted to the ICU showed a colectomy rate of only 0.4% [8].

Remarkably, right hemicolectomy was necessary in 7 patients (35%) and a (sub)total colectomy in 12 patients (60%), whereas there was no case of isolated left-sided colonic resection. The reasons for this distribution of ischemia location are unknown. Sotiriadis reports that isolated right colon ischemia accounts for about 10% of all cases of colon ischemia and has a worse prognosis than non-right-sided colon ischemia; however, it is unclear whether this can be applied to COVID-19 patients [9].

Interestingly, almost one third of the patients with right hemicolectomy had to undergo completion colectomy due to progressive ischemia of the left colon. This leads to the conclusion that in the case of clinical deterioration of patients who had initially undergone only partial colectomy, one must always consider ischemia of the residual colon and should therefore indicate revisional surgery with a low threshold.

The in-hospital mortality rate in our study population was 45%. This is in line with other reports on patients with COVID-19-related acute respiratory distress syndrome [10], and it is also in accordance with the reported in-hospital mortality among patients undergoing colectomy for acute ischemic colitis without an association with COVID-19 [11]. Karagiannidis reports a mortality rate of 53% of mechanically ventilated patients during the first wave, and this remained unchanged throughout the second wave despite an improvement of the overall management of COVID-19 patients [12].

In summary, mortality in COVID-19 patients with colonic ischemia remains high despite improved management and a low threshold to surgery.

## Declarations

**Competing interests** The authors declare no competing interests.

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