BMJ Open

Bowel ischaemia in COVID-19 infection: a scoping review protocol

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To cite: Zhao Y, Teh JJ, Kung V, *et al*. Bowel ischaemia in COVID-19 infection: a scoping review protocol. *BMJ Open* 2022;**12**:e060566. doi:10.1136/bmjopen-2021-060566

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2021-060566).

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Received 27 December 2021
Accepted 22 August 2022

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ABSTRACT

Introduction COVID-19 disease was declared as a pandemic by WHO since March 2020 and can have a myriad of clinical presentations affecting various organ systems. Patients with COVID-19 are known to have an increased risk of thromboembolism, including cardiovascular, pulmonary and cerebral ischaemic events. However, an increasing number of case studies have reported that COVID-19 infection is also associated with gastrointestinal ischaemia. This scoping review aims to collate the current evidence of COVID-19-related gastrointestinal ischaemia and raise awareness among healthcare professionals of this lesser known, but serious, non-pulmonary complication of COVID-19 infection.

Methods The proposed scoping review will be conducted as per the Arksey and O'Malley methodological framework (2005) the Joanna Briggs Institute methodology for scoping reviews. A systematic search will be undertaken on different databases including EMBASE, PubMed and MEDLINE. Two independent reviewers will screen titles, abstracts and full-text articles according to the inclusion criteria and extract relevant data from the included articles. Results will be presented in a tabular form with a narrative discussion.

Ethics and dissemination Ethical approval will not be required for this scoping review. This scoping review will provide an extensive overview of the association between COVID-19 infection and bowel ischaemia. Further ethical and methodological challenges will also be discussed in our findings to define a new research agenda. Findings will be disseminated through peer-reviewed publications and presentations at both national and international conferences.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ There is paucity of literature characterising small bowel ischaemia in patients with COVID-19 infection and our study has attempted to address this.
⇒ This scoping review will conform to the rigorous methodology manual by the Joanna Briggs Institute.
⇒ The identification and synthesis of data will be limited to published articles found on the PubMed, EMBASE and MEDLINE and databases.
⇒ The review will be limited to studies published in English language only.
⇒ Owing to the nature of a scoping review, formal quality assessment and risk of bias will not be undertaken on the included studies in this review.

BACKGROUND

Since the first report of SARS-CoV-2 in Wuhan City in China in December 2019, the WHO has declared COVID-19 disease as a pandemic in March 2020.[1 2] A wide array of clinical manifestations have been reported with COVID-19, which include the more common pulmonary manifestations and the less common extra-pulmonary gastrointestinal manifestations of nausea, abdominal pain, vomiting and diarrhoea.[3 4] COVID-19 infection has been reported to be associated with abnormal coagulation parameters with resultant complications and poor prognosis.[5–7] Coagulopathy and vascular endothelial dysfunction are now recognised complications of COVID-19 infection.[8 9] The most common of such thrombotic events are deep vein thrombosis and myocardial infarction.[10] A hypercoagulation state, suggested by elevated D-dimer, prothrombin time (PT) and activated partial thromboplastin time has been reported in patients with COVID-19 infection. Furthermore, elevations of D-Dimer and PT have been reported as significant indicators of severe COVID-19 disease associated with poor prognosis, as excessive coagulation leads to disseminated intravascular coagulation and multiple organ dysfunction syndromes.[11 12]

COVID-19-related venous thromboembolism is common. More than 20% of patients admitted for secondary management have thrombotic complications, including microvascular thrombosis that includes bowel ischaemia.[13 14] Mesenteric ischaemia can lead to infarction and perforation and has a high mortality rate (50%–69%). Mortality rates are even higher when this is associated with COVID-19.[15 16]

Data are limited on the incidence of gastrointestinal ischaemia related to COVID-19.[17] Eighteen per cent of patients with COVID-19 infection present with gastrointestinal symptoms, approximately half of which (9.2%) with abdominal pain.[18] A proportion of these patients with atypical presentation of COVID-19 disease may have, or develop

Table 1 Data collection items

Item no	Data title	Data type
1	Year of publication	Study characteristic
2	Study authors	Study characteristic
3	Study design	Study characteristic
4	Patient population	Demographics
5	Methodology/methods	Methodology
6	Clinical context and medical history	Outcome
7	Laboratory confirmed COVID-19 infection	Outcome
8	Presence of gastrointestinal (GI) symptoms	Outcome
9	Laboratory results on coagulation	Outcome
10	Radiological investigations confirming GI ischaemia	Outcome
11	Treatment—surgical, anticoagulation	Outcome
12	Prognosis	Outcome

mesenteric ischaemia, and can pose as a diagnostic challenge to clinicians.

Preliminary searches of MEDLINE, PubMed and EMBASE databases revealed that the current literature has been focusing on the symptoms of COVID-19-related bowel ischaemia.[19] To facilitate timely recognition and prompt interventions to improve prognosis, there is a need to adopt a multifaceted approach to diagnose COVID-19-related bowel ischaemia, using a combination of clinical symptoms, imaging and laboratory investigations such as parameters of coagulation.

Protocol design

The proposed scoping review will be conducted in accordance with the Joanna Briggs Institute methodology for scoping review and the methodological framework proposed by Arksey and O'Malley.[20 21] The present protocol and future corresponding scoping review are reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses extension for Scoping Review (PRISMA-ScR) flow diagram.[22] This review will follow five of the six stages: (1) identification of the research question; (2) identification of relevant studies; (3) selection of eligible studies; (4) charting the data and (5) collating, summarising and reporting of the results. There is an optional stage 6 (consultation with stakeholders) to identify additional references about potential studies to include and to collect feedback about the findings uncovered by the review, but this is excluded due to time constraint.

Stage 1: identification of the research questions

1. What are the common clinical parameters manifested in COVID-19 patients with bowel ischaemia?
2. What are the clinical symptoms in patients with gastrointestinal ischaemia with COVID-19 disease?
3. What are the coagulation parameters in such patients?
4. What are the radiological findings in such patients?

We aim to review the clinical presentation and results of laboratory and radiological investigations to establish whether there are any correlations with the disease severity and patient outcomes in COVID-19-related bowel ischaemia. The secondary aim of this study is to review the treatment offered to the included patients.

Stage 2: identifying relevant studies

An initial limited search of PubMed was undertaken to identify articles on the topic. The text words contained in the titles and abstracts of relevant articles, and the index terms used to describe the articles were used to develop a full search strategy for EMBASE, PubMed and MEDLINE (see online supplemental appendix 1). The search strategy, including all identified keywords and index terms, will be adapted for each included database and/or information source. The reference list of all included sources of evidence will be screened for additional studies.

Only studies published in the English language since November 2019 will be included.

Following the search, all identified citations will be collated and uploaded into Rayyan and duplicate removed.[23] Following a pilot test, titles and abstracts will then be screened by two independent reviewers for assessment against the inclusion criteria for the review. The full text of selected citations will be assessed in detail against the inclusion criteria by two independent reviewers. Reasons for exclusion will be recorded and reported in the scoping review. Disagreements between the reviewers at each stage of the selection process will be resolved through discussions, or with an additional reviewer. The results of the search and the study inclusion process will be reported in full in the final scoping review and presented in a PRISMA-ScR flow diagram.[22]

Data will be extracted from the included studies by two independent reviewers using a data extraction tool. The extracted data will include specific details about the participants, concept, context, study methods and key findings relevant to the review question. The planned start date for this review will be August 2022 with an aim to complete by the end of January 2023.

Stage 3: selection of eligible studies

This review will include all adult patients diagnosed with COVID-19 with clinically and radiologically proven bowel ischaemia. Non-human studies, articles on paediatric populations, and articles focusing on thromboembolic events in other parts of the body (such as cardiac, cerebral or pulmonary thromboembolism) will be excluded. Literature that does not discuss the impact of COVID-19 infection or focuses on other types of coronaviruses will also be excluded.

The concept of coagulopathy affecting the gastrointestinal tract secondary to COVID-19 infections will be explored in this review. There are several exchangeable terms when concerning the 'bowel' such as 'mesenteric' and 'intestinal'. Likewise, this study will review patients with 'ischaemia', 'embolism, 'thromboembolism' and 'thrombosis' collectively as they all refer to the loss of blood supply to the bowel. The generated data will help differentiate disease severity and identify the evidence gaps in the management of COVID-19 patients with bowel ischaemia.

This review involves patients with COVID-19 infection who developed bowel ischaemia. Bowel ischaemia is defined as at least a 75% reduction in intestinal blood flow for more than 12 hours.[20] The clinical presentation and management described in the literature will be reviewed and reported.

This scoping review will consider both experimental and quasi-experimental study designs including randomised controlled trials, non-randomised controlled trials, before-and-after studies and interrupted time-series studies. In addition, analytical observational studies including prospective and retrospective cohort studies, case–control studies and analytical cross-sectional studies will be considered for inclusion. This review is anticipated to mainly consider descriptive observational study designs including case series, individual case reports and descriptive cross-sectional studies for inclusion.

Qualitative studies will also be considered that focus on qualitative data including, but not limited to, designs such as phenomenology, grounded theory, ethnography, qualitative description, action research and feminist research.

Stage 4: charting the data

Using Rayyan, two independent reviewers will conduct this process. Relevant studies will be selected from the remaining papers in order to develop agreement on the type of information to be extracted. This scoping review will be focusing on the clinical parameters and radiological reports of bowel ischaemia in COVID-19 infection. Then, data extraction will be performed after defining critical appraisal criteria and results will be stored in table 1 as follows:

Stage 5: collating, summarising and reporting of the results

The purpose of this scoping review is to collect the findings and present and overview of the research as opposed to evaluate the quality of the studies. Therefore, the overall assessment of the strength of the evidence will be narrative instead of using quantitative methods. The extracted data will be presented in tabular form that aligns with the review questions. A narrative summary will accompany the tabulated results and will describe the current state of the research evidence and whether recommendations have been made about the diagnosis and management of bowel ischaemia in COVID-19 patients.

Patient and public involvement

No patient involved

ETHICS AND DISSEMINATION

This study will constitute the first step in reporting the identification and management of bowel ischaemia in COVID-19 infection. The results of this scoping review will guide future research into the extensive research to better inform the healthcare professionals in this topic.

Since the scoping review methodology consists of reviewing and collecting data from publicly available materials, this study does not require ethics approval.

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Contributors SM created the study concept. SM, YZ and JJT provided inputs to the methods and designed the search strategy. YZ and JJT drafted the manuscript. VK and SM provided supervision during the study and critically revised the manuscript. All authors have read and agreed to the published version of the manuscript.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

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REFERENCES

1 Huang C, Wang Y, Li X, *et al*. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *The Lancet* 2020;395:497–506.
2 Kiwango F, Mremi A, Masenga A, *et al*. Intestinal ischemia in a COVID-19 patient: case report from Northern Tanzania. *J Surg Case Rep* 2021;2021:rjaa537.
3 Perisetti A, Gajendran M, Mann R, *et al*. COVID-19 extrapulmonary illness – special gastrointestinal and hepatic considerations. *Disease-a-Month* 2020;66:101064.
4 Gholami A*et al*. Prevalence of different pain patterns in patients with COVID-19: a systematic review and meta-analysis. *Anaesth Pain Intensive Care* 2020;24:141–50.
5 Tang N, Li D, Wang X, *et al*. Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. *J Thromb Haemost* 2020;18:844–7.
6 COVID-19-White-Paper-04-17-2020-FINAL-1.pdf

7 Klok FA, Kruip MJHA, van der Meer NJM, *et al*. Incidence of thrombotic complications in critically ill ICU patients with COVID-19. *Thromb Res* 2020;191:145–7.
8 Zhou F, Yu T, Du R, *et al*. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet* 2020;395:1054–62.
9 Oxley TJ, Mocco J, Majidi S, *et al*. Large-vessel stroke as a presenting feature of Covid-19 in the young. *N Engl J Med* 2020;382:e60.
10 Bikdeli B, Madhavan MV, Jimenez D, *et al*. COVID-19 and thrombotic or thromboembolic disease: implications for prevention, antithrombotic therapy, and follow-up. *J Am Coll Cardiol* 2020;75:2950–73.
11 Long H, Nie L, Xiang X, *et al*. D-Dimer and prothrombin time are the significant indicators of severe COVID-19 and poor prognosis. *Biomed Res Int* 2020;2020:e6159720
12 Cohen B, Meilik B, Weiss-Meilik A, *et al*. Intraoperative factors associated with postoperative complications in body contouring surgery. *J Surg Res* 2018;221:24–9.
13 Abou-Ismail MY, Diamond A, Kapoor S, *et al*. The hypercoagulable state in COVID-19: incidence, pathophysiology, and management. *Thromb Res* 2020;194:101–15.
14 Varga Z, Flammer AJ, Steiger P, *et al*. Endothelial cell infection and endotheliitis in COVID-19. *The Lancet* 2020;395:1417–8.
15 Gartland RM, Velmahos GC. Bowel necrosis in the setting of COVID-19. *J Gastrointest Surg* 2020;24:2888–9.
16 Yang C, Hakenberg P, Weiß C, *et al*. Colon ischemia in patients with severe COVID-19: a single-center retrospective cohort study of 20 patients. *Int J Colorectal Dis* 2021;36:2769–73.
17 Abeysekera KWM, Karteszi H, Clark A, *et al*. Spontaneous portomesenteric thrombosis in a non-cirrhotic patient with SARS-CoV-2 infection. *BMJ Case Rep* 2020;13:e238906.
18 Cheung KS, Hung IFN, Chan PPY, *et al*. Gastrointestinal manifestations of SARS-CoV-2 infection and virus load in fecal samples from a Hong Kong cohort: systematic review and meta-analysis. *Gastroenterology* 2020;159:81–95.
19 Patel S, Parikh C, Verma D, *et al*. Bowel ischemia in COVID-19: a systematic review. *Int J Clin Pract* 2021;75:e14930.
20 JBI Global Wiki. JBI Manual for Evidence Synthesis. Available: https://jbi-global-wiki.refined.site/space/MANUAL
21 Arksey H, O'Malley L. Scoping studies: towards a methodological framework. *Int J Soc Res Methodol* 2005;8:19–32.
22 Tricco AC, Lillie E, Zarin W, *et al*. PRISMA extension for scoping reviews (PRISMA-ScR): checklist and explanation. *Ann Intern Med* 2018;169:467–73.
23 Ouzzani M, Hammady H, Fedorowicz Z, *et al*. Rayyan—a web and mobile APP for systematic reviews. *Syst Rev* 2016;5:210.