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Conflicts of interest

The authors disclose no conflicts.

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Reply. We thank Kidambi et al¹ for their interest in and insightful feedback regarding our work “Yield and Implications of Pre-Procedural COVID-19 PCR Testing on Routine Endoscopic Practice.”² Resumption of elective endoscopy in the coronavirus disease 2019 (COVID-19) era has been challenging due to a lack of evidence-based guidance; conflicting levels of input from federal, state, and local governments; and widely variable COVID-19 prevalence rates by region. We previously reported our experience using a routine pre-procedure COVID-19 testing strategy for maintaining the safety of patients and staff.² During our study, outpatients with upcoming endoscopic procedures were contacted via telephone and asked a COVID-19 screening questionnaire regarding symptoms, exposures, and travel. Those with negative verbal screening underwent nasopharyngeal polymerase chain reaction (PCR) testing 48 to 72 hours before the planned procedure and, if negative, proceeded with their procedure as planned. We found 1 of 396 patients had a positive PCR test result after initial negative questionnaire screening (positive test rate 0.25%; 95% confidence interval, 0.01%–1.40%) in our intermediate-prevalence area at the time of the initial study period. Given this result, we concluded that while ideal if readily available, pre-procedure COVID-19 testing of asymptomatic individuals may be relatively low-yield when coupled with screening questionnaires in a low to intermediate prevalence settings. As such, we advocated a tailored approach to testing based on available resources and disease prevalence.

Our findings were particularly important for practices at an early stage in the pandemic, when resources such as PCR tests and personal protective equipment were limited. As highlighted by Kidambi et al,¹ there is a well-documented potential for asymptomatic spread of COVID-19; however, multiple studies of pre-procedure PCR COVID-19 testing have now demonstrated that asymptomatic carriers are rare in low prevalence areas.^{1–3} In addition, PCR testing results may vary based on disease prevalence, prompting recent guidelines by the American Gastroenterology Association recommending against a pre-procedure testing strategy in low- or high-prevalence areas due to high false-positive or false-negative rates, respectively.⁴

Since proceeding with phased reopening in May 2020, Miami-Dade County has experienced an extensively publicized increase in COVID-19 prevalence, during which time

Florida encountered the highest COVID-19 cases per capita in the nation.⁵ In order to further evaluate yield of routine pre-procedure COVID-19 testing of asymptomatic individuals, we continued to follow our PCR testing positivity rate within the context of our region’s transition from an intermediate to high prevalence area. In a retrospective cohort study of all patients with endoscopic procedures scheduled at our facility between April 13, 2020 and July 17, 2020, the proportion of positive tests pre and at each month post societal re-opening were compared. Post reopening, we encountered 17 of 1415 positive tests (1.22%; 95% confidence interval, 0.07%–1.94%). This rate is not statistically different from our previous positivity rate when Miami was an intermediate prevalence area (0.25% vs 1.22%; $P = .09$). There was no significant change in test positivity rates in the month after re-opening (2 of 565 = 0.35%; $P > .99$); however, a significant change was noted during month 2 (14 of 573 = 2.44%; $P = .01$). The inflection point for significance coincided with the community test positive rate of approximately 20%.

As concluded by Kidambi et al,¹ the implications of even 1 positive patient in the endoscopy unit could result in catastrophic consequences. Despite the overwhelming rise in positive COVID-19 cases in our community, we continued to perform elective and semi-elective endoscopic procedures in a manner that proved safe both for patients and staff using our continued approach of pre-procedure screening questionnaires and PCR testing in addition to physical distancing, full barrier personal protective equipment, and hand hygiene. Our positivity rates among all prevalence levels have remained acceptably low and significantly lower than the positivity rate of the surrounding population. This suggests that screening questionnaires are in fact effective tools for selecting high-risk patients. Despite disease prevalence, it has been our experience that PCR testing provides a useful and crucial adjunct to screening questionnaires by decreasing the likelihood of staff exposures to asymptomatic or pre-symptomatic patients, and we continue to advocate for pre-procedure PCR testing whenever resources permit. Our practice pattern and PCR positivity results demonstrate that an endoscopy unit can continue to operate safely in a high prevalence COVID-19 region. Ultimately, we continue to recommend an approach guided by available resources, and our findings can be cited as justification to mitigate the deleterious and potentially catastrophic effects of medical distancing on the health of our communities.

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Intestinal Ischemic Manifestations of COVID-19



Dear Editors:

We read with interest the article by Norsa et al¹ on intestinal ischemia in patients with coronavirus disease 2019 (COVID-19). They further highlight the coagulopathy known to cause vascular obstructions in patients with severe COVID-19, in whom microthrombi are typically found in the lung circulation; however, also myocardial infarction and ischemic stroke were reported, particularly in the late phase of the disease. The patients reported by Norsa et al had either small or large bowel ischemia, splenic infarct, or pulmonary thromboembolism, which were fatal in 4 of the 7 cases. The mechanisms involved in COVID-19 coagulopathy were analyzed by Grobler et al,² who stressed the importance of early recognition of risk factors for the subsequent development of abnormal clot formation. They concluded that patients need to be treated early in the disease, when high levels of von Willebrand factor and fibrinogen are already present and may interact with activated endothelial cells.² Nicolai et al³ observed that platelets are activated in severe cases of COVID-19, and may be critically involved in neutrophil extracellular trap (NET) formation, a central element of immunothrombosis.³ NETs have high procoagulant potential and could therefore serve as a link to explain altered blood coagulation and microvascular thrombosis in severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. Indeed, elevated markers of NETosis have been found to correlate with disease severity in COVID-19.³ It remains, however, difficult to understand why only a relatively small proportion of individuals with the coronavirus-defined SARS-CoV-2 will develop a hypercoagulable state.

We were puzzled by similar mechanisms occurring in a different infection known to cause binding of platelets to von Willebrand factor and the vessel wall,⁴ activate endothelial cells⁵ (which will hence release von Willebrand factor), and cause aggregation of platelets to granulocytes,⁶ namely infection by pathogenic strains of *Helicobacter pylori*.^{4–6} This pathogen secretes a protein called

neutrophilic activation factor that attracts neutrophils and causes their oxidative burst. In addition, neutrophilic activation factor is a Toll-like receptor 2 agonist able to induce the expression of interleukin-12 and interleukin-23 by neutrophils and monocytes, cause a remarkable increase in the number of interferon-gamma-producing T cells and decrease of interleukin-4-secreting cells, shifting the cytokine profile of antigen-activated human T cells from Th2 to the Th1 cytotoxic phenotype.⁷ This problem was also reported to be involved in the cytokine storm aggravating COVID-19. Due to antigen mimicry, *H pylori* was also shown to elicit autoantibodies against several human tissues and cells, including platelets; such autoantibodies can disappear after eradication of the infection.⁸ The bacterium is also able to induce autoantibodies against the vessel wall, which can in turn facilitate platelet and granulocyte aggregation and worsen vascular obstruction. Other autoantibodies known to occur in *H pylori* infection are those against phospholipids, leading to an antiphospholipid syndrome that subsides after eradication. As COVID-19 can result in ominous outcomes, every avenue should be pursued in an attempt to reduce its burden. Given their common mechanisms, we believe that pathogenic strains of *H pylori* might contribute to the severity of COVID-19, at least in some cases.

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