

Gastrointestinal Endoscopy

Outcomes of symptom screening and universal COVID-19 reverse transcription polymerase chain reaction testing prior to endoscopy in a community-based ambulatory surgery center --Manuscript Draft--

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Abstract:	<p>Background and Aims: Elective endoscopy resumed in our outpatient ambulatory center after instituting the pre-procedure policy of a confirmed negative COVID-19 reverse transcription polymerase chain reaction (RT-PCR) status performed 72 hours prior to a scheduled procedure as mandated by the state of Illinois. In addition, all patients were required to contemporaneously complete the ASGE COVID-19 risk screening questionnaire published April 28, 2020 as outlined in the ASGE guidance document for reopening GI endoscopy during the COVID-19 pandemic. 1 The aim of our study is to report the outcomes of 1000 patients who successfully completed the clinical aspects of the ASGE COVID-19 risk screening questionnaire and whose RT-PCR tests were valid for interpretation.</p> <p>Methods: Data was retrospectively collected from patient medical records for demographics, symptom responses to the pre-procedure ASGE COVID-19 risk screening questionnaire, and RT-PCR test results of patients scheduled to undergo an elective outpatient endoscopy at Rockford Gastroenterology Associates from May 22 through June 28, 2020. Descriptive statistics and standard calculation methods to determine both positive and negative predictive values were employed for data analysis.</p> <p>Results: Eight of the 1000 patients included in the study tested positive for COVID-19. Three of the eight patients reported one or more symptoms on the ASGE COVID-19 risk screening questionnaire. One hundred and nineteen additional patients reported symptoms on the ASGE COVID-19 risk screening questionnaire but tested negative for COVID-19. The positive (PPV) and negative predictive value (NPV) of the ASGE COVID-19 risk screening questionnaire were 2.46% and 99.43%, respectively.</p> <p>Conclusions: The low incidence of COVID-19 infection in a community-based ambulatory surgery center is supported by a positive RT-PCR test rate of 0.80%. Absence of symptoms to the ASGE COVID-19 risk screening questions was highly predictive of a negative RT-PCR test (99.43% NPV), whereas the PPV was low (2.46%) in symptomatic patients. A positive RT-PCR test was invaluable in preventing 5 asymptomatic patients from undergoing endoscopy. Similarly, 119 symptomatic</p>

	patients underwent endoscopic evaluation who would have otherwise been excluded without RT-PCR testing. Symptom based screening alone should not be the primary pre-procedural assessment tool in selecting patients for undergoing endoscopy during the COVID-19 pandemic.
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9/25/2020

Michael B. Wallace MD, MPH, FASGE
3300 Woodcreek Drive
Downers Grove, IL 60515

Manuscript No. GIE-D-20-01928


Dear Dr. Wallace,

Thank you for reviewing our manuscript , **“Outcomes of symptom screening and universal COVID-19 reverse transcription polymerase chain reaction testing prior to endoscopy in a community-based ambulatory surgery center.”**

Attached is a revised version of the manuscript, which incorporates the recommended editorial changes.

Thank you again for your continued attention to this manuscript.

Yours sincerely,

A handwritten signature in black ink, appearing to read 'Brad A. Bowyer', with a long, sweeping horizontal stroke extending to the left.

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Running title: Outcomes of symptom screening and universal COVID-19 reverse transcription polymerase chain reaction testing prior to endoscopy in a community-based ambulatory surgery center

Keywords: COVID-19, screening, questionnaire, testing, pre-procedure, endoscopy

Conflict of Interest Statement: The authors have no conflict of interest to disclose.

Evaluations:

At this time, please check your submitted Disclosure and Attestation form carefully to ensure that it is complete and accurate for ALL authors. GIE takes this very seriously; please be sure all authors have disclosed all conflicts of interest.

Reviewer #1: This study looked at the PPV and NPV of the ASGE screening questionnaire in patients in a busy practice in Illinois.

1. The goal of the study is not clear. Is it to assess the ASGE questionnaire? The ASGE questionnaire is a simple set of questions based on recommendations. The goal is to identify patients at higher risk. Are the authors trying to validate it? If so, they need to a priori define the threshold at which they would consider the questionnaire acceptable.

Our aim is to report outcomes of the symptom component of the ASGE questionnaire (questions 2, 3 and 4) in conjunction with universal COVID-19 test results prior to endoscopy. The objective is not to validate the questionnaire because we accepted the simplicity and relevance of the questions at face value.

2. What should the performance of the questionnaire be in a given population? Of course, that will depend on the prevalence of disease. So, the questionnaire may have a higher PPV in an area with higher prevalence of COVID-19.

Establishing an acceptable performance threshold is arbitrary and indeed is dependent upon disease prevalence as well as the pre-test probability of an individual being infected based on their symptoms as well as exposure risk. As the pre-test probability of disease decreases, the NPV of the questionnaire will approach 100 percent. The opposite holds true for the PPV. Of course, this is assuming the metric by which the questionnaire is judged has an acceptable performance in clinical practice. To our knowledge, there is no published data on the sensitivity of currently FDA approved assays for COVID-19 in asymptomatic patients (1)

1. Woloshin S, Patel N, Kesselheim A. False Negative Tests for SARS-CoV-2 Infection-Challenges and Implications. N Engl J Med 2020;383: e38 DOI: 10.1056/NEJMp2015897

3. Since the study only looked at patients who had both ASGE questionnaire and COVID-19 testing it did not collect data patients who might have had fever or symptoms that were positive on the ASGE questionnaire and then maybe did not get COVID-19 testing. How many patients had ASGE questionnaires who did not get COVID-19 testing? Were those patients more likely to have COVID-19 symptoms?

Twenty-six of the 163 excluded patients completed a questionnaire for review. Twenty-five reported no symptoms. One patient or 3.8 % of those who completed the questionnaire reported symptoms (nausea and vomiting) compared to 12.2 % who reported symptoms in our study group. Details of a positive questionnaire with negative COVID-19 PCR in our study have now been included in the manuscript. The paucity of highly suspicious symptoms (fever and respiratory symptoms) for COVID-19 in the 12.2% with a positive questionnaire suggests that patients with an acute respiratory illness defer scheduling an elective endoscopic procedure precluding them from participating in our questionnaire interview process. In reviewing the charts of the excluded patients, we identified an error in the number reported in the manuscript. Instead of 207 excluded patients, there were 163 which did not meet inclusion criteria. This error will be reflected in our revised submission.

4. The PPV and NPV depend on the prevalence of disease. A PPV of 2.4% in a population that has a disease prevalence of 0.8% is actually not bad. I don't consider that a poor value. For a screening questionnaire that asks simple questions this is actually pretty good.

Agreed, low percent positivity within a population would be anticipated to have a high NPV and low PPV. Our use of the word poor in this context was inappropriate in the statistical sense and was intended to point out that the usefulness of predicting disease based on the presence of symptoms is low. That is, in our patients who reported symptoms we would predict a positive COVID-19 test in 2.4 percent which we believe is not useful in the clinical setting. On the contrary, an NPV of 99.42 % seems quite good given limitations of the standard by which it is measured as outlined above.

5. The major impact of COVID19 testing has been the ability to re-start endoscopy and do it safely. Patients, nurses, technicians, and endoscopists have been protected even in low risk areas. The benefits are difficult to measure unless one performs surveys of patients, endoscopy personnel and endoscopists. Similarly, cost effectiveness assessment would be challenging as it needs to factor in impact of not testing on endoscopic services. Prior to testing all endoscopy was shut down.

Safety is a priori in resumption of elective endoscopy during the pandemic. The psychological benefits for patients and endoscopy staff alike cannot be underestimated by universal testing as reported by the Stanford group (reference 5 in the manuscript). Assessing medical cost effectiveness would be quite challenging; however, Corral et al. (2) published a detailed economic analysis demonstrating COVID-19 PCR testing to be an effective means of reopening endoscopy during the pandemic, although they did point out that the frequency of testing would be determined by local resources and disease prevalence. Anecdotally, we have experienced a number of patients who have elected to forego recommended endoscopic procedures because of COVID-19 testing and or the requisite pre procedure 72-hour quarantine. The medical consequences of not providing necessary endoscopy either from not testing as we experienced during the shut-down or from the current barriers created from universal testing has significant negative implications as well. How to achieve the balance of maximum procedural access while maintaining safety and minimizing over-utilization of valuable testing resources during an unpredictable pandemic is indeed challenging. Additional research is needed to address these urgent concerns. Clearly, there are limitations of a risk screening questionnaire as well as PCR testing, albeit, this is our current standard of care while we all attempt to safely open our endoscopy centers. We anticipate this will not be an indefinite strategy as the trajectory of the pandemic wanes over time and when wide scale vaccinations or treatments become available. During that transition, as more data becomes available, we may have an acceptable performance threshold when a negative risk screening questionnaire is coupled with selective PCR testing for those individuals with a higher pre-test probability of disease.

2. Corral JE, Hoogenboom SA, Kroner PT et al. COVID-19 polymerase chain reaction testing before endoscopy: an economic analysis. *Gastrointestinal Endoscopy* Volume 92, No. 3: 2020

Reviewer #2: Summary: The authors evaluated the performance of the ASGE COVID-19 risk screening questionnaire compared with COVID-19 TR PCR results in 1000 patients undergoing procedures at an ambulatory outpatient endoscopy center, of which 8 testing positive for COVID-19. They found the questionnaire to have a positive predictive value of 2.46% and a negative predictive value of 99.43%.

1. The questionnaire only was positive in 3/8 patients who actually had active COVID-19 infection. This suggests that in this population the questionnaire is not helpful as a substitute for COVID RT-PCR testing, if the goal is to detect all cases and ensure the safety of staff and other patients.

We have no argument that the current standard for detecting the presence of disease is with real time COVID-19 RT-PCR testing. The risk screening questionnaire is not a substitute for PCR testing at this time. Nonetheless, while the analytic (laboratory) performance of these assays is known, to our knowledge, there is no published data on their accuracy in the clinical setting. If the risk screening questionnaire was highly suggestive of active disease despite a negative PCR test, the clinician may elect to defer elective endoscopy and repeat the PCR when the symptoms have resolved. The clinical decision to offer an endoscopic procedure is multifaceted and should not rely on a single metric. There is much needed research with regard to the in vivo performance of our current COVID-19 PCR test kits. The false reassurance that universal PCR testing is 100 percent accurate may lead to inappropriate relaxation of safety protocols initiated at the outset of the pandemic unnecessarily exposing endoscopy personnel to an individual with a false negative PCR test. Moreover, false positive tests would delay patients from indicated endoscopic procedures. The importance of the clinical performance of current PCR testing has been discussed by Woloshin et al. (1) and Corral et al. (2)

1. Woloshin S, Patel N, Kesselheim A. False Negative Tests for SARS-CoV-2 Infection-Challenges and Implications. *N Engl J Med* 2020;383: e38 DOI: 10.1056/NEJMp2015897

2. Corral JE, Hoogenboom SA, Kroner PT et al. COVID-19 polymerase chain reaction testing before endoscopy: an economic analysis. *Gastrointestinal Endoscopy* Volume 92, No. 3: 2020

2. The very low positive predictive value (PPV) also suggests that if this were only used most patients with a positive questionnaire result would be falsely excluded from endoscopy (if testing were not available) or would be falsely worried that they had COVID-19 (if testing were available).

We are in agreement that the questionnaire alone is not adequate in the absence of PCR testing limited by the assumption that this metric by which the questionnaire is judged has limitations as outlined above. A high PPV would be more useful in areas of greater disease prevalence, yet the non-specific symptoms of COVID-19 infection overestimates the pre-test probability of disease as suggested by the number of false positive questionnaires in our study. As you aptly stated, PCR testing would decrease those falsely excluded from endoscopy and reassure those patients whose PCR was negative.

3. Although the authors discuss the community prevalence of COVID-19 during the last week of the study, this is not a result of this and would be better off in the discussion section. Furthermore, it would be much more helpful to have an overall community prevalence rate to compare than just the last week as we do not know if this is representative of the study period.

We contacted the administrator of the Winnebago County Health Department directly to assist in accessing data not published on their website for the average percent positivity rate during our study period. The average percent positive rate for our study period was 8.37 %. The manuscript will be amended to reflect this information.

Agree, this should not have been in the results section and our revision will reflect this change.

4. It would be useful if the authors provide the full ASGE COVID-19 risk screening questionnaire, either as a Table or a supplement.

Agree. We have added the ASGE COVID-19 risk screening questionnaire to the revised manuscript highlighting the symptom related questions (2, 3, and 4) which was required for completion as an inclusion criterion for our study.

5. The top half of Table 1 does not add anything and can be deleted. The main points that should be included are Race and Age.

Agree. We have deleted those items from Table 1 for the revised manuscript.

6. It is interesting to note that 5/8 patients with COVID-19 were younger than age 45 which represented only 14% of the population and one additional patient was 45. Perhaps COVID-19 RT-PCR testing of those under 50 would be most beneficial as more likely to have asymptomatic infection, whereas older patients may be more likely to be symptomatic.

This is a keen point and remains a distinct possibility pending the results of widespread testing throughout the US, and, in particular, from our college campuses.

7. I would like a more complete break-down of which symptoms were positive in those patients with positive questionnaires but negative RT-PCR testing.

A chart detailing this information by age has been added to the manuscript.

For instance, were patients undergoing EGD for known diarrhea, nausea and/or vomiting? If so, these questions would not be surprising to be falsely positive.

This statement is quite true. Our data support the expectation that patients would present with a higher incidence of symptoms prompting procedural evaluation. Known nausea, chest pain and cough accounted for 22.6 % of the procedural indications for upper endoscopy while known diarrhea accounted for 60.4 % of the procedural indications for colonoscopy.

In summary, the indication for 21 of the 84 patients who underwent EGD were: nausea (19), chest pain (1) and cough (1). Indications for the remaining 63 patients were: dysphagia (25), dyspepsia/abdominal pain (13), GERD (7), abnormal imaging (5), Barrett's surveillance (3), varices screening/surveillance (3), assess healing (2), iron deficiency anemia (2), melena (1), hematemesis (1) and pre-op gastric sleeve (1). The indication for 26 of the patients who underwent colonoscopy was diarrhea. Indications for colonoscopy of the remaining 43 patients were: colon cancer screening (18), polyp surveillance (10), rectal bleeding (7), iron deficiency anemia (3), fecal incontinence (2), positive Cologuard (1), Crohn's colitis surveillance (1) and abnormal imaging (1).

Furthermore, how many of the false positives were in the high-risk groups of health care providers or employees of a daycare facility, senior living location, adult daycare or extended care or rehabilitation care facility?

We are unable to answer this question as our protocol required answers only to the symptom aspects of the ASGE risk screening questionnaire (questions 2, 3, and 4).

8. The conclusion of the discussion that routine COVID-19 testing is not valuable is not supported by the study results, as the data suggests that routine RT-PCR will detect the cases of COVID-19, whereas the ASGE COVID-19 risk screening questionnaire was overall not helpful.

We whole heartedly concur with your assessment that currently there is no substitute for universal COVID-19 testing as the standard in selecting patients for elective procedures despite the lack of published sensitivity data on asymptomatic patients as recently reviewed in the NEJM by Woloshin et al. (1) It was not the intent of our conclusion that COVID-19 PCR testing be abandoned but simply to consider the strategy of the questionnaire's utility in the setting of very low disease prevalence when universal PCR testing has less value. In such a scenario, where local resources are limited, PCR testing could be reserved for patients with symptoms highly suggestive of disease or have risk factors such as health care workers, younger age, and residents or personnel from facilities known to increase the pre-test probability of infection.

1. Woloshin S, Patel N, Kesselheim A. False Negative Tests for SARS-CoV-2 Infection-Challenges and Implications. N Engl J Med 2020;383: e38 DOI: 10.1056/NEJMp2015897)

9. Would not include in the abbreviation RGA in the abstract.

Agree. This will be deleted from the abstract.

10. In Table 3 can delete height, weight and all categories starting with smoker extending to cirrhosis.

The tables will be changed accordingly.

11. How do the authors think the ASGE COVID-19 risk screening questionnaire should be used in clinical practice? How should this vary depending on prevalence of COVID-19 disease?

Currently, with the uncertain trajectory of the COVID-19 pandemic, we believe the questionnaire should be used in conjunction with COVID-19 testing for all patients undergoing elective procedures. Larger series from endoscopy centers throughout the US in varying degrees of disease prevalence and demographic spectra may give additional insights into the performance of the questionnaire. In addition, PCR performance, by which the questionnaire is measured, will further our understanding of the questionnaire's usefulness in various clinical scenarios. As disease prevalence wanes, the value of PCR testing decreases which may increase the value of a risk screening questionnaire. In certain circumstances, the ASGE COVID-19 risk screening questionnaire alone may suffice if the disease prevalence within a community becomes extremely low and the NPV becomes nearly 100%. In such a scenario, COVID-19 testing could be limited to only those individuals whose questionnaire is highly suspicious for disease, in younger patients who may be asymptomatic, and in those individuals from high risk groups (health care providers, residents or employees of a daycare/senior living /adult daycare/ and rehabilitation facilities) . We believe the questionnaire has value for practices with very low disease prevalence and limited testing capabilities in those states where universal COVID-19 testing prior to elective procedures is not mandatory. Whichever pre-procedural strategy is adopted, strict adherence to standard safety protocols of hand hygiene, disinfection and PPE use should remain universal in endoscopy centers irrespective of the disease prevalence.

GIE follows ICMJE recommendations for Original Article titles, including NOT to use questions in the title. Please change your title accordingly.

Our title has been changed in accordance with ICMJE recommendations for Original Article titles to:

Outcomes of symptom screening and universal COVID-19 reverse transcription polymerase chain reaction testing prior to endoscopy in a community-based ambulatory surgery center

~~Is pre-procedure COVID-19 testing necessary in patients whose risk screening questionnaire is negative? Results of 1000 cases in an outpatient community-based endoscopy center~~

~~Outcomes of symptom screening and universal COVID-19 reverse transcription polymerase chain reaction testing prior to endoscopy in a community-based ambulatory surgery center~~

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Running title: ~~Is pre-procedure COVID-19 testing necessary in patients whose risk screening questionnaire is negative? Results of 1000 patients in an outpatient community-based endoscopy center.~~

~~Outcomes of symptom screening and universal COVID-19 reverse transcription polymerase chain reaction testing prior to endoscopy in a community-based ambulatory surgery center~~

Keywords: COVID-19, screening, questionnaire, testing, pre-procedure, endoscopy

Conflict of Interest Statement: The authors have no conflict of interest to disclose.

Background and Aims: Elective endoscopy resumed in our outpatient ambulatory center after instituting the pre-procedure policy of a confirmed negative COVID-19 ~~RT-PCR~~ reverse transcription polymerase chain reaction (RT-PCR) status performed 72 hours prior to a scheduled procedure as mandated by the state of Illinois. In addition, all patients were required to contemporaneously complete the ASGE COVID-19 risk screening questionnaire published April 28, 2020 as outlined in the ASGE guidance document for reopening GI endoscopy during the COVID-19 pandemic.¹ The aim of our study is to report the outcomes of 1000 patients who successfully completed the clinical aspects-of the ASGE COVID-19 risk screening questionnaire and whose ~~COVID-19 RT-~~ PCR tests were valid for interpretation.

Methods: Data was retrospectively collected from patient medical records for demographics, ~~past medical history~~, symptom responses to the pre-procedure ASGE COVID-19 risk screening questionnaire, and ~~COVID-19 RT-~~ PCR test results of patients scheduled to undergo an elective outpatient endoscopy at Rockford Gastroenterology Associates (~~RGA~~) from May 22 through June 28, 2020. Descriptive statistics and standard calculation methods to determine both positive and negative predictive values were employed for data analysis.

Results: Eight of the 1000 patients included in the study tested positive for COVID-19. Three of the eight patients reported one or more symptoms on the ASGE COVID-19 risk screening questionnaire. One hundred and nineteen additional patients reported symptoms on the ASGE COVID-19 risk screening questionnaire but tested negative for

COVID-19. The positive (PPV) and negative predictive value (NPV) of the ASGE COVID-19 risk screening questionnaire were 2.46% and 99.43%, respectively.

Conclusion: The ~~rarity~~ low incidence of COVID-19 infection in a community-based ambulatory ~~outpatient community endoscopy surgery~~ center is supported by a positive RT-PCR test rate of 0.80%. Absence of symptoms to ~~The~~ the ASGE COVID-19 risk screening ~~questionnaire questions~~ was highly predictive of a negative COVID-19 RT-PCR test ~~in the asymptomatic patient~~ (99.43% NPV), ~~The poor positive predictive value of the ASGE COVID-19 risk screening questionnaire may be explained by the nonspecific nature of symptoms manifested by COVID-19 infection shared by a host of other organic as well as functional etiologies.~~ whereas the PPV was low (2.43 %) in symptomatic patients. A positive COVID-19 RT-PCR test was invaluable in preventing 5 asymptomatic patients from undergoing endoscopy. Similarly, 119 symptomatic patients underwent endoscopic evaluation who would have otherwise been excluded without RT-PCR testing. Symptom based screening alone should not be the primary pre-procedural assessment tool in selecting patients for undergoing ~~elective~~ endoscopy during the COVID-19 pandemic.

Introduction:

During the height of the Coronavirus (COVID-19) pandemic, a joint statement by the US gastroenterology professional societies recommended performing only those endoscopic procedures that were deemed urgent or emergent.² This was done as part of the public

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4 health response to mitigate infection spread ~~and to divert resources by diverting~~
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6 resources to unburden the supply chain ~~and for~~ health care delivery systems.
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11 In the state of Illinois, elective endoscopic procedures could begin on May 11, 2020
12 provided the facility was in compliance with the April 24, 2020 Illinois Department of Public
13 Health's (IDPH) guideline of self-quarantine and confirmed negative status of a COVID-
14 19 RT-PCR 72 hours prior to the scheduled procedure.³ On April 28, 2020, the ASGE
15 recommended adopting a pre-procedural COVID-19 risk screening questionnaire, but did
16 not endorse pre-procedural COVID-19 testing until the assays were ~~widely available, and~~
17 ~~standardized, and assay performance had been validated~~ standardized, validated and
18 ~~widely available~~¹ Rockford Gastroenterology Associates (RGA) developed stringent
19 policies to meet the Illinois Department of Public Health's mandate including adoption of
20 the ASGE pre-procedure COVID-19 risk screening questionnaire. (Appendix A) ~~Limited~~
21 ~~Inadequate~~ local resources for high volume ~~and rapid COVID-19 RT-PCR test results,~~
22 ~~testing with rapid result turnaround time~~ prompted our development of an onsite outdoor
23 ~~COVID-19 testing~~ facility limited to RGA patients in order to meet the requirements set
24 forth by the IDPH.
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48 **Methods:**

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52 The study protocol was designed as a retrospective review of existing records from
53 patients within our practice who were 18 to 85 years of age and scheduled to undergo
54 an endoscopic procedure from May 22 through June 28, 2020. To be included in this
55 study, these patients must have fulfilled the inclusion criteria of responses to the
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4 presence or absence of symptoms contained in the ASGE pre-procedure COVID-19
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6 Risk Screening Questionnaire (RSQ) as well as an RGA onsite 72 hour pre-procedure
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8 real time nasopharyngeal ~~COVID-19-RT~~-PCR test result that was valid for
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10 interpretation. Patients with invalid ~~COVID-19- RT~~-PCR test results, such as insufficient
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12 quantity of specimen, were removed from this study. Patient demographics for age,
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14 race, gender-and pertinent history pertaining to procedural indication and risks
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16 ~~indication and medical history of current smoking status, Angiotensin Converting~~
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18 ~~Enzyme/Angiotensin II Receptor Blocker use, hypertension, diabetes, coronary artery~~
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20 ~~disease, chronic obstructive pulmonary disease, and cirrhosis~~ were extracted from the
21
22 medical record. The protocol was reviewed and approved by the Institutional Review
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24 Board of the University of Illinois College of Medicine (Rockford, IL). The RSQ required
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26 yes or no responses to the following symptoms: fever of 100.4 degrees (38 C) or higher,
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28 difficulty breathing, cough, loss of sense of smell or taste, shortness of breath, chest
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30 pain, sore throat, new onset of fatigue or lack of energy, nausea with or without
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32 vomiting, and diarrhea. Answers to those questions on the RSQ were obtained via
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34 telephone or an in-person interview by a limited number of trained RGA medical
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36 personnel. Likewise, the nasopharyngeal specimens were collected by a select group of
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38 RGA registered nurses and physicians who had completed methodological training in
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40 the handling and acquisition of the sample for subsequent analysis by the FDA-
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42 approved (for use under Emergency Use Authorization) Roche COBAS 6800/8800 real-
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44 time RT-PCR COVID-19 test for the detection of SARS-CoV-2 RNA and pan-
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46 Sarbecovirus including SARS-CoV-2.^{4,5} The performance characteristics of the test
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48 were verified by Poplar Healthcare which is regulated under CLIA as qualified to
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perform high-complexity testing.⁶ ~~The Winnebago County Health Department's published percent positivity rate was used as a marker for disease prevalence within our community of Winnebago County, Illinois.~~

Percent positivity rates obtained from the Winnebago County Health Department served as a marker for disease prevalence within our community.

Results:

~~1000 of 1207 patients met inclusion criteria for evaluation. Patient demographics and pertinent medical history are summarized in Table 1. Of the 1000 patients included in this study, 8 tested positive for COVID-19, of whom only 3 reported symptoms in the RSQ as illustrated in the 2 x 2 contingency Table 2 (infection rate of 0.80%). Calculations from the 2 x 2 contingency table for negative and positive predictive values were 99.43% and 2.46%, respectively. Demographics, medical history, and symptom specifics of the 8 COVID-19 positive patients are summarized in Table 3. Two patients reported only nausea. One patient reported chest pain, sore throat, and loss of taste or smell. None of the COVID-19 positive patients had a past medical history of hypertension, diabetes, coronary artery disease, chronic obstructive pulmonary disease, or cirrhosis in contrast to the COVID-19 negative group which included 44.4% with hypertension, 18.8% with diabetes, 7.0% with coronary artery disease, 3.6% with chronic obstructive pulmonary disease, and 2.9% with cirrhosis. The demographics of the COVID-19 positive patients were similar to the COVID-19 negative patients. Based on data published by the Winnebago County Health Department's seven day rolling average, the positivity rate for our service area of Winnebago County, Illinois during the last week of this study was 4.5%.⁴ Percent positivity rates for Winnebago County were initially made public by the health department at the end of June. Recognizing that we do not have this data for the entirety of the study, our assumption is that the~~

~~number of new cases began to plateau earlier in the study and there would not have been a marked difference in the percent positivity rate at the initiation of our study compared to the end. The percent positivity rate in Winnebago County (4.5%) was notably higher than the infection rate in our patient cohort (0.80%).~~

1000 of 1163 patients met inclusion criteria for evaluation. Patient demographics are summarized in Figure 1. Of the 1000 patients included in this study, 8 tested positive for COVID-19, of whom 3 reported symptoms in the RSQ as shown in the 2 x 2 contingency tabulation (Table 1). Calculations from the 2 x 2 contingency table for negative and positive predictive values were 99.43% and 2.46%, respectively. Age and reported symptoms of the 8 RT-PCR positive patients are summarized in Figure 2. Two patients reported nausea. One patient reported chest pain, sore throat, and the loss of taste or smell.

Details of symptoms by age for the 8 PCR positive patients and the 119 PCR negative symptomatic patients (false positives) are shown Figures 2 and 2b, respectively. Three of the five asymptomatic RT-PCR positive patients were less than 45 years old. Patients less than 45 years of age represented 13.9 % of all patients enrolled in the study. In the false positive group, diarrhea was the most commonly reported symptom (62) followed by nausea and or vomiting (41), shortness of breath, chest pain, difficulty breathing (38), cough (11), new onset fatigue (11), sore throat (7), loss of taste or smell (7), and fever (2). Known nausea, chest pain, and cough accounted for 22.6% of the procedural indications for upper endoscopy while known diarrhea accounted for 60.4% of the procedural indications for colonoscopy. Symptom frequency was independent of race and gender in both the PCR positive and false negative groups.

Discussion:

This is the first study of outcomes for pre-risk screening followed by universal COVID-19 testing in patients undergoing elective endoscopic procedures within a community-based gastroenterology practice. Of the 1000 patients who underwent both the ASGE risk screening questionnaire (RSQ) and subsequent COVID-19 RT-PCR testing, 8 patients had a positive COVID-19 RT-PCR test result. Only 3 of these patients reported symptoms as assessed by the RSQ.

Based on the data collected from our cohort, the PPV of the RSQ was 2.46% and NPV was 99.43%. The infection rate of COVID-19 detected in our cohort of patients presenting for endoscopic procedures was 0.80%. This was similar to the infection rates noted in patients presenting for endoscopic procedures from academic centers in Stanford, California (0.14%)⁵ and New York City, New York (0.96%).⁶ Of note, disease prevalence may be variable depending on resources available for COVID-19 testing as well as the number of asymptomatic individuals tested within a population. Pre-procedure COVID-19 testing in areas of higher viral prevalence would be expected to detect higher rates of infection. This was not supported by our study nor in the findings of Podboy, et al.⁵ where the infection rate in Santa Clara County, California was 4.34%. Likewise, the infection rate in New York City, New York was 6.27% as reported by Dolinger, et al.⁶ The marked similarity of low infection rates in patients presenting for endoscopic procedures in moderate to high prevalence communities at coastal academic centers and our midwestern outpatient endoscopy center is not readily explained. Perhaps, patients seeking to undergo elective endoscopy during the pandemic have practiced social

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4 distancing, hand hygiene, and wore face masks to a greater degree than their
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6 counterparts within the community.
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14 The benefits of universal COVID-19 testing cannot be understated. Indeed, recent
15 findings from the research of Podboy, et al. demonstrated a significant decrease in
16 anxiety amongst patients and endoscopy unit staff after implementation of universal pre-
17 procedure testing for COVID-19.⁵ Nonetheless, universal COVID-19 testing has
18 significant limitations. It is burdensome for patients who are required to schedule a
19 preceding appointment for testing, potentially interfering with work and childcare
20 responsibilities. This prerequisite creates a barrier to timely medical care and the potential
21 consequence of esophageal and colon cancer deaths due to delays in diagnosis.⁷ Implicit
22 to testing is the mandate for subsequent patient self-quarantine for 72 hours until the time
23 of the endoscopy. However, this is nearly impossible to enforce and creates an additional
24 barrier for patients when considering an elective endoscopy during the COVID-19
25 pandemic.
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45 From a health care facility standpoint, universal COVID-19 testing may also be
46 problematic. Many institutions have limited access to testing which can be compounded
47 by concerns regarding delays in result reporting as well as the accuracy of testing. In
48 addition, the availability of testing in many areas of the US is still inadequate. Universal
49 testing in asymptomatic patients may further lead to a shortage of a limited and valuable
50 resource. Staffing of a testing center is challenging, costly, and diverts provider resources
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4 from patient care. Additionally, the wide use of outdoor COVID testing can be onerous to
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6 the medical staff and patients in the setting of weather extremes which presents yet
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8 another barrier for elective endoscopy.
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14 This is the first outcomes study for pre-procedure symptom screening followed by
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16 universal COVID-19 RT-PCR testing in patients undergoing endoscopic procedures
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18 within a community-based ambulatory surgery center. Eight of the 1000 patients had a
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20 positive RT-PCR test result. Four of the 5 asymptomatic RT-PCR positive patients were
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22 45 years old or less in age suggesting the potential for a higher incidence of asymptomatic
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24 infection in younger patients. None of the three symptomatic RT-PCR patients reported
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26 symptoms highly suggestive of infection (fever, cough, shortness of breath, or difficulty
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28 breathing). Nausea, vomiting, and diarrhea accounted for the most frequent symptoms in
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30 all age categories as anticipated in a gastroenterology practice.
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41 was 99.43%. The RT-PCR positivity rate was 0.80%. In reference to published⁷ and
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43 unpublished data obtained from the Winnebago County Health Department (S. Martell,
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45 personal communication, September 1st and 9th, 2020), the calculated average positivity
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47 rate for our service area of Winnebago County, Illinois during this study was 8.37%. The
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49 percent positivity rate in Winnebago County (8.37%) was notably higher than the infection
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51 rate in our patient cohort (0.80%).
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Our findings were comparable to infection rates observed in patients presenting for endoscopic procedures from academic centers in Stanford, California (0.14%)⁸ and New York City, New York (0.96%)⁹. Pre-procedure RT-PCR testing in areas of higher viral prevalence would be expected to detect higher rates of infection. This was not supported by our findings (8.37%) in comparison to the infection rate of New York City, New York (6.27%) as reported by Dolinger, et al.⁹ The marked similarity of low infection rates in patients presenting for endoscopic procedures from coastal academic centers and our midwestern community-based ambulatory surgery center is not readily explained; however, we suspect that patients who have symptoms highly suggestive of COVID-19 are unlikely to schedule an elective endoscopy precluding requisite RT-PCR testing. This is supported by the paucity of fever, cough, loss of sense of smell or taste, new onset fatigue, and sore throat in our 119 patients with a false positive RSQ. In addition, health conscious individuals desirous of surveillance or screening endoscopy may have practiced social distancing, hand hygiene, and worn face masks to a greater degree than their counterparts within the community which in turn would have comparatively reduced their risk of infection.

The benefit of universal COVID-19 testing should not be underestimated. In our study, 5 asymptomatic patients were prevented from undergoing endoscopy as a result of positive RT-PCR testing, while procedures were performed on 119 patients with symptoms not highly suggestive of COVID-19 as a result of their negative RT-PCR tests. Nearly 12% of our patients scheduled to undergo endoscopy would have been unnecessarily excluded from indicated procedures if symptom screening alone were the primary tool in

determining the likelihood of infection. Of course, the overall clinical suspicion of COVID-19 in this group was low since many presented with known gastrointestinal symptoms. The reassurance of a negative RT-PCR test is important for those patients who were worried that exacerbation of their gastrointestinal symptoms was related to COVID-19. Indeed, recent findings from the research of Podboy, et al. demonstrated a significant decrease in anxiety amongst patients and endoscopy unit staff after implementation of universal pre-procedure testing.⁸ Furthermore, in a detailed economic analysis, Corral et al. recently reported PCR testing to be an effective strategy for the resumption of endoscopy during the pandemic.¹⁰

The limitations of universal PCR testing are nonetheless relevant. Although the analytic performance in a laboratory setting of currently available assays for detecting SARS-CoV-2 RNA can be determined, to our knowledge, there is no published data on the sensitivity of such assays in clinical practice. Recent publications from two research groups have emphasized the implications of false negative and false positive test results related to imperfect diagnostic performance of currently used assays.^{10,11} Although RT-PCR testing is the primary metric for determining the presence or absence of disease, the uncertainty of its accuracy should not be ignored. Disease prevalence and the pre-test suspicion of infection based on symptoms and known risks factors for disease are major determinants in assessing test results in the absence of validated reference standards. Clinical discernment is critical when RT-PCR results conflict with the pre-test assessment for risk of infection. Universal RT-PCR testing and pre-requisite 72-hour pre-procedure quarantine create barriers for timely elective and semi-urgent procedures. Researchers from the United Kingdom reported an estimated 15.3-16.6% increase in colorectal cancer deaths related to delays in diagnosis during the pandemic.¹² From a health care facility standpoint, universal PCR testing is disruptive and diverts provider resources from patient

care. Outdoor testing facilities face significant challenges during inclement weather which presents an additional barrier for procedural access.

~~In conclusion, the benefit of routine COVID-19 testing in asymptomatic patients before elective endoscopy in areas of moderate to high disease prevalence may be outweighed by the negative impacts on healthcare resources and delays in gastrointestinal cancer diagnoses. Further studies are needed to confirm the validity of pre-procedure COVID-19 testing in patients whose risk screening questionnaire is negative.~~

Conclusion

Our study is the first to report the outcomes of pre-procedure symptom screening followed by universal COVID-19 RT-PCR testing in patients undergoing endoscopy within a community-based ambulatory surgery center. Although universal COVID-19 testing presents logistical obstacles for patients as well as health care facilities, and the in vivo diagnostic accuracy of RT-PCR is unclear, we believe this remains the best strategy for minimizing exposure risk in endoscopy centers while avoiding delays in diagnosis for those RT-PCR negative symptomatic patients. As practices resume scheduling of elective and semi-urgent endoscopy, they must attempt to balance safety and optimal procedural access within the context of their disease prevalence and local testing capabilities. In our study, the absence of symptoms was predictive of a negative RT-PCR in 99.42% of patients, while the presence of symptoms predicted RT-PCR positivity in only 2.46%. Additional studies are needed to determine in vivo accuracy of RT-PCR tests as well as an acceptable performance threshold for symptom-based screening.

References

1. <https://www.asge.org/docs/default-document-library/asge-guidance-for-reopening-4-28-2020.pdf>. Accessed August 2020. Google.
2. Joint Society Message on Endoscopy During COVID-19-
<https://gi.org/2020/04/01/joint-gi-society-message-on-endoscopy-during-covid-19>. Accessed August 2020. Google.
3. https://www.dph.illinois.gov/sites/default/files/Elective_Surgery_04.24.20.pdf. Accessed August 2020. Google.
4. https://www.wchd.org/images/June_29_2020_WCHD_COVID19Report.pdf. Accessed August 2020. Google.
5. Pedboy A, Cholanteril G, Gianfichi L, Guzman Jr. E, Ahmed A, Banerjee S, **Implementation and Impact of Universal Pre-procedure Testing of Patients for COVID-19 prior to Endoscopy**, *Gastroenterology* (2020), doi: <https://doi.org/10.1053/j.gastro.2020.06.022>.
6. Dolinger MT, Kumta NA, Greenwald DA, Dubinsky MC. **Outcomes of universal pre-procedure COVID-19 testing prior to endoscopy in a tertiary care center in New York City**. *Gastroenterology* (2020), doi: <https://doi.org/10.1053/j.gastro.2020.07.015>.
7. Maringe C, Spicer J, Morris M, et al. **The impact of the COVID-19 pandemic on cancer deaths due to delays in diagnosis in England, UK: a national, population-based, modeling study**. *Lancet Oncol*. 2020; 1023-1034. doi:10.1016/S1470-2045(20)303888-0.

References

1. <https://www.asge.org/docs/.default-document-library/asge-guidance-for-reopening-4-28-2020.pdf>. Accessed August 2020. Google.
2. Joint Society Message on Endoscopy During COVID-19-
<https://gi.org/2020/04/01/joint-gi-society-message-on-endoscopy-during-covid-19>.
Accessed August 2020. Google.
3. https://www.dph.illinois.gov/sites/default/files/Elective_Surgery_04.24.20.pdf.
Accessed August 2020. Google.
4. Cobas SARS-CoV-2 test. 2020.
<https://diagnostics.roche.com/global/en/products/params/cobas-sars-cov-2-2-test.html>
Accessed September 2020. Google.
5. Fact sheet for healthcare providers, coronavirus disease 2019 (COVID-19), Cobas SARS-CoV-2, Molecular systems, Inc. US. Food and Drug Administration, 2020.
<https://www.fda.gov/media/136047/download>. Accessed September 2020. Google.
6. Poplar Healthcare, 3495 Hacks Road, Memphis, Tennessee 38125-
<https://www.poplarhealthcare.com>. Accessed September 2020. Google.
7. https://www.wchd.org/images/June_29_2020_WCHD_COVID19Report.pdf.
Accessed September 2020. Google.
8. Podboy A, Cholankeril G, Cianfichi L, Guzman Jr. E, Ahmed A, Banerjee S, Implementation and Impact of Universal Pre-procedure Testing of Patients for COVID-19 prior to Endoscopy, *Gastroenterology* (2020).

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4 9. Dolinger MT, Kumta NA, Greenwald DA, Dubinsky MC, Outcomes of universal pre-
5 procedure COVID-19 testing prior to endoscopy in a tertiary care center in New York
6 City, *Gastroenterology* (2020), doi: <https://doi.org/10.1053/j.gastro.2020.07.015>.
7
8
9

10
11 10. Corral JE, Hoogenboom SA, Kroner PT et al. COVID-19 polymerase chain reaction
12 testing before endoscopy: an economic analysis. *Gastrointestinal Endoscopy* Volume
13 92, No. 3: 2020
14
15
16

17
18 11. Woloshin S, Patel N, Kesselheim A. False Negative Tests for SARS-CoV-2
19 Infection-Challenges and Implications. *N Engl J Med* 2020;383: e38 DOI:
20 10.1056/NEJMp2015897
21
22
23

24
25
26 12. Maringe C, Spicer J, Morris M, et al. The impact of the COVID-19 pandemic on
27 cancer deaths due to delays in diagnosis in England, UK: a national, population-based,
28 modeling study. *Lancet Oncol.* 2020; 1023-1034. doi:10.1016/S1470-2045(20)303888-0.
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Table 4

	Yes	No	Not Reported
Current Smoker	10.7%	47.8%	41.5%
ACE/ARB	30%	67.9%	2.1%
Hypertension	44.4%	54.3%	1.3%
Diabetes	18.8%	81.2%	n/a
CAD	7%	91.5%	1.5%
COPD	3.6%	96.4%	n/a
Cirrhosis	2.9%	95.9%	1.2%

Gender	55% Female — 45% Male
Race	76.1% White 7.1% African American 0.3% Asian 0.5% Other 16% Not declared
BMI	1.4% Underweight — BMI < 18.5 29% Normal Weight — BMI 18.5-25 25.4% Overweight — BMI 25-30 44.2% Obese — BMI > 30

AGE	3.0% 18-24	13.9 % 18-44
	3.7% 25-34	
	7.2% 35-44	
	19.4% 45-54	48.3 % 45-64
	28.9% 55-64	
	27.9% 65-74	
	9.9% 75-85	37.8 % 65-85

Table 2. 1.Contingency table

	Positive COVID-RT- PCR	Negative COVID RT- PCR	Total
Positive Questionnaire	3	119	122
Negative Questionnaire	5	873	878
Column Totals	8	992	1000

Table 3

RT-PCR Positive Patients

Symptoms reported on questionnaire Y/N	Which symptom(s) reported Symptom Reported	COVID-19 test results pos/neg	height (in)	weight (lb.)	BMI	Gender	Race	Age	Current Smoker Y/N	Taking ACE/ARB Y/N	Hypertension Y/N	Diabetes Y/N	CAD Y/N	COPD Y/N	Cirrhosis Y/N
Nausea	nausea	pos	73	227	29	M	NRND	31	Y	N	N	N	N	N	N
Loss of taste or smell, chest pain, sore throat	loss of smell or taste, chest pain, sore throat	pos	61	130	25	F	C	47	NR	N	N	N	N	N	N
Nausea	nausea	pos	73	225	29	M	NRND	20	N	N	N	N	N	N	N
N	n/a	pos	68	236	36	F	C	29	N	N	N	N	N	N	N
N	n/a	pos	64	157	27	M	NRND	30	N	N	N	N	N	N	N
N	n/a	pos	65	192	31	M	C	64	NR	NR	N	Y	N	N	N
N	n/a	pos	64	337	57	F	AA	45	NR	N	N	Y	N	N	N
N	n/a	pos	65	275	46	F	C	41	N	N	N	N	N	N	N

*Caucasian **African American ***Not reported/declared

APPENDIX A

COVID-19 Questionnaire (suggested; adapt as needed)

1. Have you had testing for COVID-19? Clarify if this was a direct viral test (e.g., swab, saliva) or serologic (blood antibody) test.

a. Was your test positive or negative?

2. Do you have any of the following? (yes or no)

a. Fever to 100.4 degrees(38C) or higher

b. Cough

c. Shortness of breath, difficulty breathing, chest pain d. sore throat

e. Loss of sense of smell or taste

f. New onset of fatigue or lack of energy

3. Do you have nausea with or without vomiting?

4. Do you have diarrhea?

The top impacted states in the United States and hot spots around the world

5. Have you recently traveled to any current COVID-19 hot spot? If so, where?

can be found in the *New York Times Coronavirus Map: Tracking the Global* ^a

Outbreak.

6. In the past 14days, have you come into close contact (within 6 feet/2 meters)?

with someone who has a laboratory-confirmed COVID-19 diagnosis?

7. Are you a first responder, healthcare worker, or do you work or volunteer at a hospital or health care facility?

8. Are you an employee of a daycare facility, senior living location, adult day care or extended care or rehabilitation care facility?

Answering “yes” to any of the above symptom questions (1-4) should result in referral to a primary care provider for assessment and possible testing. Answering “yes” to any other question should trigger COVID-19 testing performed less than 72 hours prior to the procedure.

^a Coronavirus Map: Tracking the Global Outbreak, *New York Times*,
<https://www.nytimes.com/interactive/2020/world/coronavirus-maps.html>.

April 28, 2020

Questions 2, 3, 4 and required responses for study inclusion

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4 Background and Aims: Elective endoscopy resumed in our outpatient ambulatory center after
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6 instituting the pre-procedure policy of a confirmed negative COVID-19 reverse transcription
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8 polymerase chain reaction (RT-PCR) status performed 72 hours prior to a scheduled procedure
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10 as mandated by the state of Illinois. In addition, all patients were required to contemporaneously
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12 complete the ASGE COVID-19 risk screening questionnaire published April 28, 2020 as outlined
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14 in the ASGE guidance document for reopening GI endoscopy during the COVID-19 pandemic.¹
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16 The aim of our study is to report the outcomes of 1000 patients who successfully completed the
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18 clinical aspects of the ASGE COVID-19 risk screening questionnaire and whose RT-PCR tests
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20 were valid for interpretation.
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27 Methods: Data was retrospectively collected from patient medical records for demographics,
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29 symptom responses to the pre-procedure ASGE COVID-19 risk screening questionnaire, and RT-
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31 PCR test results of patients scheduled to undergo an elective outpatient endoscopy at Rockford
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33 Gastroenterology Associates from May 22 through June 28, 2020. Descriptive statistics and
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35 standard calculation methods to determine both positive and negative predictive values were
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37 employed for data analysis.
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43 Results: Eight of the 1000 patients included in the study tested positive for COVID-19. Three of
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45 the eight patients reported one or more symptoms on the ASGE COVID-19 risk screening
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47 questionnaire. One hundred and nineteen additional patients reported symptoms on the ASGE
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49 COVID-19 risk screening questionnaire but tested negative for COVID-19. The positive (PPV)
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51 and negative predictive value (NPV) of the ASGE COVID-19 risk screening questionnaire were
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53 2.46% and 99.43%, respectively.
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59 Conclusions: The low incidence of COVID-19 infection in a community-based ambulatory surgery
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61 center is supported by a positive RT-PCR test rate of 0.80%. Absence of symptoms to the ASGE
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COVID-19 risk screening questions was highly predictive of a negative RT-PCR test (99.43% NPV), whereas the PPV was low (2.46%) in symptomatic patients. A positive RT-PCR test was invaluable in preventing 5 asymptomatic patients from undergoing endoscopy. Similarly, 119 symptomatic patients underwent endoscopic evaluation who would have otherwise been excluded without RT-PCR testing. Symptom based screening alone should not be the primary pre-procedural assessment tool in selecting patients for undergoing endoscopy during the COVID-19 pandemic.

Introduction

During the height of the Coronavirus (COVID-19) pandemic, a joint statement by the US gastroenterology professional societies recommended performing only those endoscopic procedures that were deemed urgent or emergent.² This was done as part of the public health response to mitigate infection spread by diverting resources to unburden the supply chain for health care delivery systems.

In the state of Illinois, elective endoscopic procedures could begin on May 11, 2020 provided the facility was in compliance with the April 24, 2020 Illinois Department of Public Health's (IDPH) guideline of self-quarantine and confirmed negative status of a COVID-19 RT-PCR 72 hours prior to the scheduled procedure.³ On April 28, 2020, the ASGE recommended adopting a pre-procedural COVID-19 risk screening questionnaire, but did not endorse pre-procedural COVID-19 testing until the assays were standardized, validated, and widely available.¹ Rockford Gastroenterology Associates (RGA) developed stringent policies to meet the Illinois Department of Public Health's mandate including adoption of the ASGE pre-procedure COVID-19 risk screening questionnaire. (Appendix A) Inadequate local resources for high volume rapid RT-PCR test results, prompted our development of an onsite outdoor testing facility limited to RGA patients in order to meet the requirements set forth by the IDPH.

Methods

The study protocol was designed as a retrospective review of existing records from patients within our practice who were 18 to 85 years of age and scheduled to undergo an endoscopic procedure from May 22 through June 28, 2020. To be included in this study, these patients must have fulfilled the inclusion criteria of responses to the presence or absence of symptoms contained in the ASGE pre-procedure COVID-19 Risk Screening Questionnaire (RSQ) as well as an RGA onsite 72 hour pre-procedure real time nasopharyngeal RT-PCR test result that was valid for interpretation. Patients with invalid RT-PCR test results, such as insufficient quantity of specimen, were removed from this study. Patient demographics for age, race, gender, and pertinent history pertaining to procedural indication and risks were extracted from the medical record. The protocol was reviewed and approved by the Institutional Review Board of the University of Illinois College of Medicine (Rockford, IL). The RSQ required yes or no responses to the following symptoms: fever of 100.4 degrees (38 C) or higher, difficulty breathing, cough, loss of sense of smell or taste, shortness of breath, chest pain, sore throat, new onset of fatigue or lack of energy, nausea with or without vomiting, and diarrhea. Answers to those questions on the RSQ were obtained via telephone or an in-person interview by a limited number of trained RGA medical personnel. Likewise, the nasopharyngeal specimens were collected by a select group of RGA registered nurses and physicians who had completed methodological training in the handling and acquisition of the sample for subsequent analysis by the FDA-approved (for use under Emergency Use Authorization) Roche COBAS 6800/8800 real-time RT-PCR COVID-19 test for the detection of SARS-CoV-2 RNA and pan-Sarbecovirus including SARS-CoV-2.^{4,5} The performance characteristics of the test were verified by Poplar Healthcare which is regulated under CLIA as qualified to perform high-complexity testing.⁶ Percent positivity rates obtained from the Winnebago County Health Department served as a marker for disease prevalence within our community.

Results

1000 of 1163 patients met inclusion criteria for evaluation. Patient demographics are summarized in Figure 1. Of the 1000 patients included in this study, 8 tested positive for COVID-19, of whom 3 reported symptoms in the RSQ as shown in the 2 x 2 contingency tabulation (Table 1). Calculations from the 2 x 2 contingency table for negative and positive predictive values were 99.43% and 2.46%, respectively. Age and reported symptoms of the 8 RT-PCR positive patients are summarized in Figure 2. Two patients reported nausea. One patient reported chest pain, sore throat, and the loss of taste or smell.

Details of symptoms by age for the 8 PCR positive patients and the 119 PCR negative symptomatic patients (false positives) are shown Figures 2 and 2b, respectively. Three of the five asymptomatic RT-PCR positive patients were less than 45 years old. Patients less than 45 years of age represented 13.9 % of all patients enrolled in the study. In the false positive group, diarrhea was the most commonly reported symptom (62) followed by nausea and or vomiting (41), shortness of breath, chest pain, difficulty breathing (38), cough (11), new onset fatigue (11), sore throat (7), loss of taste or smell (7), and fever (2). Known nausea, chest pain, and cough accounted for 22.6% of the procedural indications for upper endoscopy while known diarrhea accounted for 60.4% of the procedural indications for colonoscopy. Symptom frequency was independent of race and gender in both the PCR positive and false negative groups.

Discussion

This is the first outcomes study for pre-procedure symptom screening followed by universal COVID-19 RT-PCR testing in patients undergoing endoscopic procedures within a community-based ambulatory surgery center. Eight of the 1000 patients had a positive RT-PCR test result. Four of the 5 asymptomatic RT-PCR positive patients were 45 years old or less in age suggesting the potential for a higher incidence of asymptomatic infection in younger patients. None of the

three symptomatic RT-PCR patients reported symptoms highly suggestive of infection (fever, cough, shortness of breath, or difficulty breathing). Nausea, vomiting, and diarrhea accounted for the most frequent symptoms in all age categories as anticipated in a gastroenterology practice.

Based on the data collected from our cohort, the PPV of the RSQ was 2.46% and NPV was 99.43%. The RT-PCR positivity rate was 0.80%. In reference to published⁷ and unpublished data obtained from the Winnebago County Health Department (S. Martell, personal communication, September 1st and 9th, 2020), the calculated average positivity rate for our service area of Winnebago County, Illinois during this study was 8.37%. The percent positivity rate in Winnebago County (8.37%) was notably higher than the infection rate in our patient cohort (0.80%).

Our findings were comparable to infection rates observed in patients presenting for endoscopic procedures from academic centers in Stanford, California (0.14%)⁸ and New York City, New York (0.96%)⁹. Pre-procedure RT-PCR testing in areas of higher viral prevalence would be expected to detect higher rates of infection. This was not supported by our findings (8.37%) in comparison to the infection rate of New York City, New York (6.27%) as reported by Dolinger, et al.⁹ The marked similarity of low infection rates in patients presenting for endoscopic procedures from coastal academic centers and our midwestern community-based ambulatory surgery center is not readily explained; however, we suspect that patients who have symptoms highly suggestive of COVID-19 are unlikely to schedule an elective endoscopy precluding requisite RT-PCR testing. This is supported by the paucity of fever, cough, loss of sense of smell or taste, new onset fatigue, and sore throat in our 119 patients with a false positive RSQ. In addition, health conscious individuals desirous of surveillance or screening endoscopy may have practiced social distancing, hand hygiene, and worn face masks to a greater degree than their counterparts within the community which in turn would have comparatively reduced their risk of infection.

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hour pre-procedure quarantine create barriers for timely elective and semi-urgent procedures. Researchers from the United Kingdom reported an estimated 15.3-16.6% increase in colorectal cancer deaths related to delays in diagnosis during the pandemic.¹² From a health care facility standpoint, universal PCR testing is disruptive and diverts provider resources from patient care. Outdoor testing facilities face significant challenges during inclement weather which presents an additional barrier for procedural access.

Conclusion

Our study is the first to report the outcomes of pre-procedure symptom screening followed by universal COVID-19 RT-PCR testing in patients undergoing endoscopy within a community-based ambulatory surgery center. Although universal COVID-19 testing presents logistical obstacles for patients as well as health care facilities, and the in vivo diagnostic accuracy of RT-PCR is unclear, we believe this remains the best strategy for minimizing exposure risk in endoscopy centers while avoiding delays in diagnosis for those RT-PCR negative symptomatic patients. As practices resume scheduling of elective and semi-urgent endoscopy, they must attempt to balance safety and optimal procedural access within the context of their disease prevalence and local testing capabilities. In our study, the absence of symptoms was predictive of a negative RT-PCR in 99.43% of patients, while the presence of symptoms predicted RT-PCR positivity in only 2.46%. Additional studies are needed to determine in vivo accuracy of RT-PCR tests as well as an acceptable performance threshold for symptom-based screening.

References

1. <https://www.asge.org/default-document-library/asge-guidance-for-reopening> 4-28-2020.pdf.

Accessed August 2020. Google.

2. Joint Society Message on Endoscopy During COVID-19-
<https://gi.org/2020/04/01/joint-gi-society-message-on-endoscopy-during-covid-19>.

Accessed August 2020. Google.

3. https://www.dph.illinois.gov/sites/default/files/Elective_Surgery_04.24.20.pdf.

Accessed August 2020. Google.

4. Cobas SARS-CoV-2 test. 2020.

<https://diagnostics.roche.com/global/en/products/params/cobas-sars-cov-2-2-test.html>

Accessed September 2020. Google.

5. Fact sheet for healthcare providers, coronavirus disease 2019 (COVID-19), Cobas SARS-CoV-2, Molecular systems, Inc. US. Food and Drug Administration, 2020.

<https://www.fda.gov/media/136047/download>. Accessed September 2020. Google.

6. Poplar Healthcare, 3495 Hacks Road, Memphis, Tennessee 38125-

<https://www.poplarhealthcare.com>. Accessed September 2020. Google.

7. https://www.wchd.org/images/June_29_2020_WCHD_COVID19Report.pdf.

Accessed September 2020. Google.

8. Podboy A, Cholankeril G, Cianfichi L, Guzman Jr. E, Ahmed A, Banerjee S, Implementation and Impact of Universal Pre-procedure Testing of Patients for COVID-19 prior to Endoscopy, *Gastroenterology* (2020).

9. Dolinger MT, Kumta NA, Greenwald DA, Dubinsky MC, Outcomes of universal pre-procedure COVID-19 testing prior to endoscopy in a tertiary care center in New York City, *Gastroenterology* (2020), doi: <https://doi.org/10.1053/j.gastro.2020.07.015>.

10. Corral JE, Hoogenboom SA, Kroner PT et al. COVID-19 polymerase chain reaction testing before endoscopy: an economic analysis. *Gastrointestinal Endoscopy* Volume 92, No. 3: 2020

1
2
3
4 11. Woloshin S, Patel N, Kesselheim A. False Negative Tests for SARS-CoV-2
5 Infection-Challenges and Implications. N Engl J Med 2020;383: e38 DOI:
6 10.1056/NEJMp2015897
7
8

9
10 12. Maringe C, Spicer J, Morris M, et al. The impact of the COVID-19 pandemic on
11 cancer deaths due to delays in diagnosis in England, UK: a national, population-based,
12 modeling study. Lancet Oncol. 2020; 1023-1034.doi:10.1016/S1470-2045(20)303888-0.
13
14
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Table 1. Contingency table

	Positive RT-PCR	Negative RT-PCR	Total
Positive Questionnaire	3	119	122
Negative Questionnaire	5	873	878
Column Totals	8	992	1000

APPENDIX A

COVID-19 Questionnaire (suggested; adapt as needed)

1. Have you had testing for COVID-19? Clarify if this was a direct viral test (e.g., swab, saliva) or serologic (blood antibody) test.
 - a. Was your test positive or negative?
2. Do you have any of the following? (yes or no)
 - a. Fever to 100.4 degrees(38C) or higher
 - b. Cough
 - c. Shortness of breath, difficulty breathing, chest pain
 - d. sore throat
 - e. Loss of sense of smell or taste
 - f. New onset of fatigue or lack of energy
3. Do you have nausea with or without vomiting?
4. Do you have diarrhea?

The top impacted states in the United States and hot spots around the world

5. Have you recently traveled to any current COVID-19 hot spot? If so, where?

can be found in the *New York Times Coronavirus Map: Tracking the Global* ^a

Outbreak.

6. In the past 14days, have you come into close contact (within 6 feet/2 meters)?
with someone who has a laboratory-confirmed COVID-19 diagnosis?

7. Are you a first responder, healthcare worker, or do you work or volunteer at a hospital or health care facility?
8. Are you an employee of a daycare facility, senior living location, adult day care or extended care or rehabilitation care facility?

Answering “yes” to any of the above symptom questions (1-4) should result in referral to a primary care provider for assessment and possible testing. Answering “yes” to any other question should trigger COVID-19 testing performed less than 72 hours prior to the procedure.

^a Coronavirus Map: Tracking the Global Outbreak, *New York Times*,
<https://www.nytimes.com/interactive/2020/world/coronavirus-maps.html>.

April 28, 2020

Questions 2, 3, and 4 required responses for study inclusion

Figure 1. Cohort demographics: gender, race, age

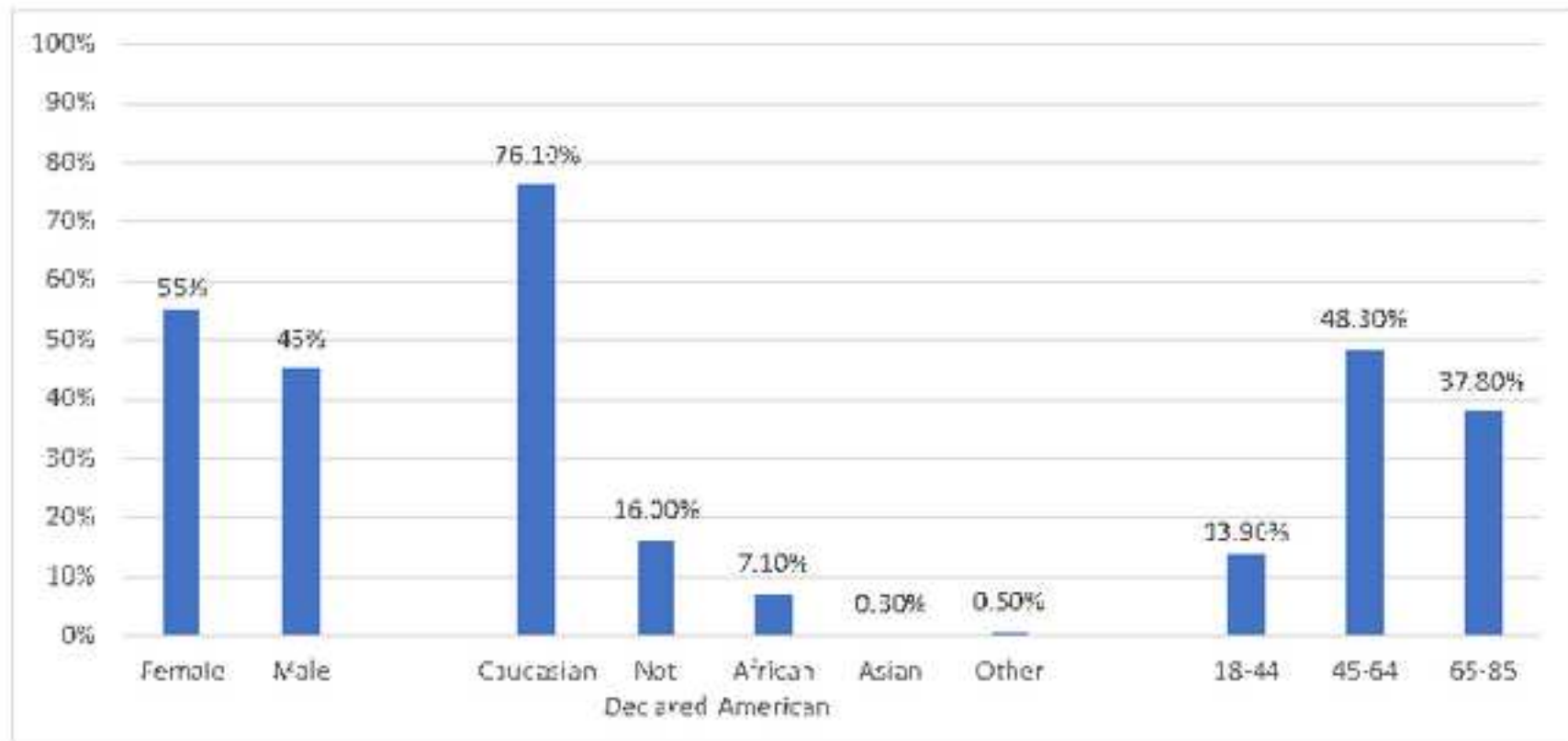


Figure 2. Symptoms By Age of Patients With a Positive RT-PCR

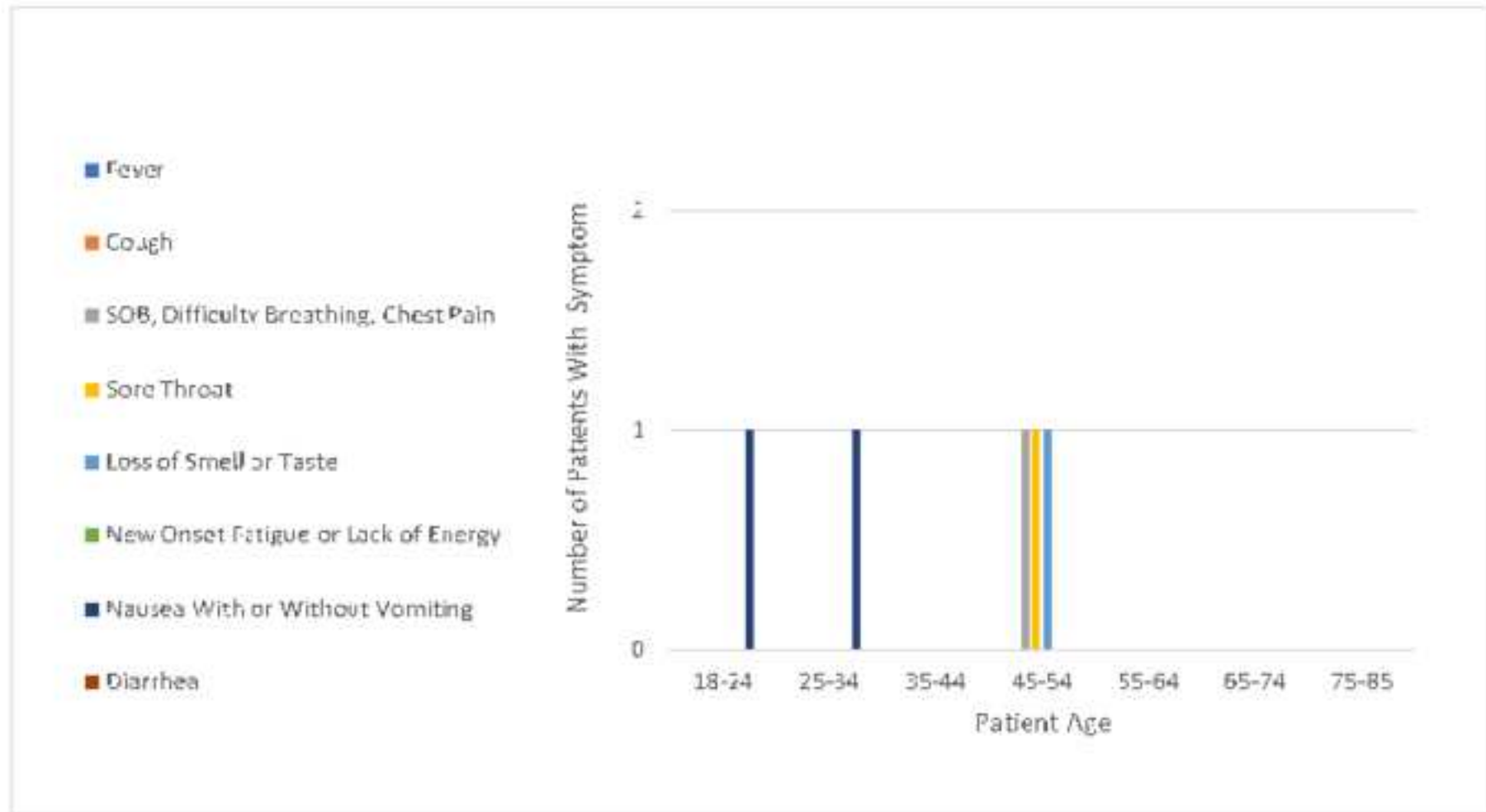
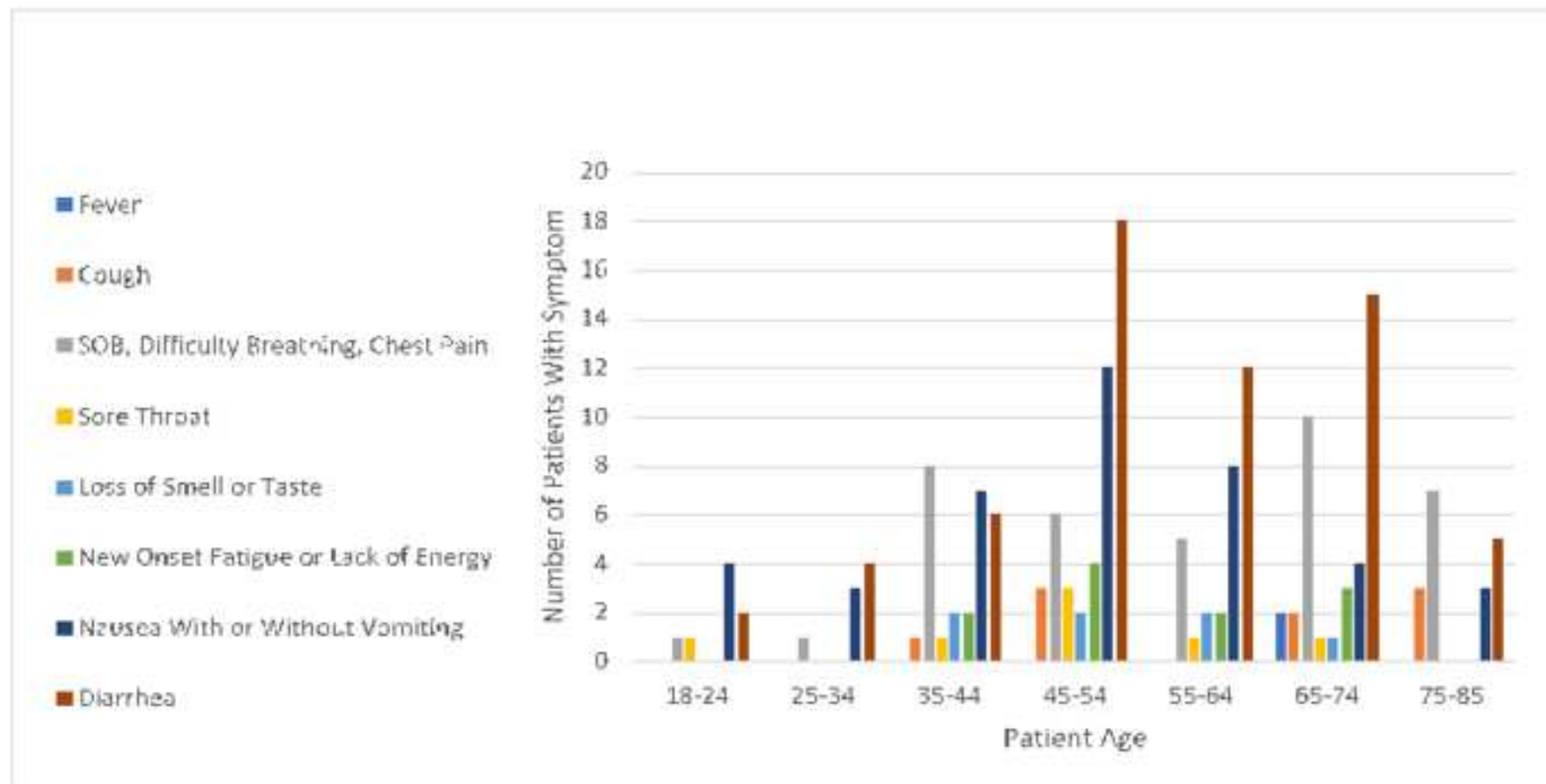


Figure 2b. Symptoms By Age of Patients With a Negative RT-PCR



Acronyms and Abbreviations included in this paper

- SARS-CoV-2 - Severe Acute Respiratory Syndrome Coronavirus 2
- COVID-19 – CO (corona)VI (virus) D (disease)
- RGA – Rockford Gastroenterology Associates, Ltd.
- ASGE – American Society for Gastrointestinal Endoscopy
- NPV – Negative predictive value
- PPV – positive predictive value
- IDPH – Illinois Department of Public Health
- RT-PCR – Real-time Reverse Transcription Polymerase Chain Reaction
- RSQ – Risk Screening Questionnaire
- FDA – Food and Drug Administration
- CLIA – Clinical Laboratory Improvement Amendments
- ACE – Angiotensin converting enzyme inhibitors
- ARB – Angiotensin receptor blockers
- CAD – Coronary Artery Disease
- COPD – Chronic Obstructive Pulmonary Disease
- n/a – Not Applicable



Journal CME Conflict of Interest: Disclosure and Attestation

Lead Author: Brad Bowyer MD

Article: Is pre-procedure COVID-19 testing necessary in patients whose risk screening questionnaire is negative? Results of 1000 cases in an outpatient community-based endoscopy center

Date: August 18, 2020

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