DOI: 10.1002/ncp.10687

Clinical Research

An examination of gastrointestinal absorption using the acetaminophen absorption test in critically ill patients with COVID-19: A retrospective cohort study

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Abstract

Objective: Gastrointestinal (GI) dysfunction is prevalent in critically ill patients with coronavirus disease 2019 (COVID-19). The acetaminophen absorption test (AAT) has been previously described as a direct method for assessment of GI function. Our study determines whether the AAT can be used to assess GI function in critically ill COVID-19 patients, compared with traditional measures of GI function.

Design: Retrospective observational study of critically ill patients with COVID-19.

Setting: Three intensive care units at a tertiary care academic medical center.

Patients: Twenty critically ill patients with COVID-19.

Interventions: The results of AAT and traditional measures for assessing GI function were collected and compared.

Measurements and Main Results: Among the study cohort, 55% (11 of 20) of patients had evidence of malabsorption by AAT. Interestingly, all patients with evidence of malabsorption by AAT had clinical evidence of bowel function, as indicated by stool output and low gastric residuals during the prior 24 h. When comparing patients with a detectable acetaminophen level (positive AAT) with those who had undetectable acetaminophen levels (negative AAT), radiologic evidence of ileus was less frequent (20 vs 88%; $P = .03$), tolerated tube-feed rates were higher (40 vs 10 ml/h; $P = .01$), and there was a trend toward lower gastric residual volumes (45 vs 830 ml; $P = .11$).

Conclusion: Malabsorption can occur in critically ill patients with COVID-19 despite commonly used clinical indicators of tube-feeding tolerance. The AAT provides a simple, rapid, and cost-effective mechanism by which enteral function can be efficiently assessed in COVID-19 patients.

KEYWORDS
COVID-19, critical illness, gastrointestinal function, malabsorption

INTRODUCTION

Coronavirus disease 2019 (COVID-19), the disease caused by the novel coronavirus severe acute respiratory distress syndrome coronavirus 2, is a global pandemic having infected > 168 million people worldwide, resulting in > 3.5 million deaths. COVID-19 generally starts as a local upper respiratory tract infection but can spread to affect multiple organ systems, including the gastrointestinal (GI) tract, with consequences that are only now being fully appreciated. A recent study reported that nearly half of critically ill patients with COVID-19 develop GI hypomotility, which results in enteral feeding intolerance.[2] Many of these patients had poor oral intake and anorexia on admission, and a number of these patients had either clinical or radiographic evidence of an ileus/pseudo-obstruction.[3] Among the critically ill COVID-19 patients with severe intestinal dysmotility and concern for bowel ischemia that were taken to the operating room for exploration, there was evidence of small vessel thrombosis, suggesting viral enteroneuropathy as the likely etiology.[3] Increased dosing requirements of sedatives and opioids used to facilitate ventilator synchrony may also contribute to bowel dysfunction in critically ill COVID-19 patients.[4] Delay in providing adequate nutrition to critically ill patients has been associated with increased morbidity and mortality.[5] Early identification of patients who are at risk for malnutrition in the intensive care unit (ICU) can help facilitate early initiation of nutrition support.

European Society for Clinical Nutrition and Metabolism (ESPEN) guidance for nutrition management in critically ill patients with COVID-19 follows previous recommendations for nutrition guidelines in critical care.[6,7] Enteral nutrition should be started immediately in intubated patients with COVID-19 to avoid malnutrition and improve prognosis. Prolonged states of malnutrition have been associated with poor outcomes in critical illness, and current recommendations include initiation of early enteral nutrition within 24–36 h of ICU admission or within 12 h of intubation. Current guidelines recommend transition from enteral to parenteral nutrition in patients with feeding intolerance. Clinical signs of feeding intolerance, including abdominal pain, vomiting, distension, and imaging findings are both limited in critically ill, intubated patient populations and necessitate increased clinical exposure of healthcare workers to potential COVID-19 infection. Additional methods that allow clinicians to understand enteral function in this patient population may aid in decreased delay in adequate nutrition and improved safety of healthcare workers.

The acetaminophen absorption test (AAT) has been previously described as a method to directly assess GI function and absorption in critically ill patients when compared with indirect assessment using gastric residual volume.[8,9] The AAT provides a direct measure of gastric emptying by determining the enteral uptake of orally administered acetaminophen via serum acetaminophen measurements at predefined intervals.[8] We hypothesized that the AAT may allow for rapid, reliable, and safe determination of the effectiveness of enteral absorption capacity in patients who are experiencing the effects of COVID-19–related critical illness.

We performed a retrospective study of enteral absorption in critically ill patients with COVID-19. We hypothesized that patients may have poor GI absorption, as determined by the AAT, even when GI motility appears to be present, as suggested by low gastric residuals and regular stool output. Furthermore, evidence of malabsorption in critically ill patients, as indicated by undetectable acetaminophen levels, may prompt earlier initiation of supplemental parenteral nutrition, thereby improving nutrition and positively impacting patient outcome.

MATERIALS AND METHODS

This retrospective observational study was performed in three ICUs at a tertiary care academic medical center after approval by the institutional review board (protocol number 2020P001354). The study cohort consisted of critically ill adult (aged ≥18 years) patients with COVID-19 who were receiving enteral nutrition via nasogastric tube (NGT) and had received the AAT to assess absorption. For all study patients, the NGT position was confirmed via abdominal x-ray per ICU protocol.

Per ICU practice, and consistent with prior literature, the AAT was performed by administration of 950–1000 mg of acetaminophen liquid suspension through the NGT, which was then clamped for 90 min, after which enteral feeds were resumed if previously held. An acetaminophen of 950–1000 mg was used based on prior literature for adult patients while taking into account the effects of

increased body mass index (BMI) (calculated as weight in kilograms divided by height in meters squared) on acetaminophen pharmacokinetics (8) while accounting for the increased prevalence of elevated liver enzymes in COVID-19 patients. The times of administration were recorded and blood samples were ordered to be drawn at 90 min following acetaminophen administration. Although the timing of the acetaminophen level was scheduled to be at 90 min from administration, the actual time the level was drawn varied based on other patient care needs, as well as efforts to minimize exposure of healthcare workers and conserve personal protective equipment. Acetaminophen plasma levels were then measured via laboratory evaluation (Roche Diagnostics, Indianapolis, IN). Based on prior literature, the test was considered positive for absorption if the plasma acetaminophen concentration was ≥5 mcg/ml (lower limit of the assay) at 90 min following administration.[8–10] The acetaminophen suspension administered was supplied as either a 325-mg/10.15 ml (Precision Dose) or 650-mg/20.3 ml (Pharmaceutical Associates, INC) unit dose product. Gastric residual volumes were checked every 4 h, and the gastric residual volume was not reinfused. The decision to order an AAT was at the discretion of the attending intensivist and was based on clinical suspicion of impaired absorption (ie, low stool output, elevated gastric residual volumes, abdominal distention, or evidence of aspiration).

Data were collected from the institutional electronic medical record, EPIC (EPIC Systems Corporation, Verona, WI). Continuous variables are expressed as median and interquartile range (IQR), as appropriate. Categorical data are expressed as percentages. Continuous variables were compared between the two groups using the Mann-Whitney *U* test. Categorical variables were compared using the Fisher exact test. A two-sided *P*-value of <.05 was considered statistically significant. All statistical analyses and graphs were performed using Microsoft Excel and STATA version 13 (STATA Corp). Radiographic evidence ileus was determined by reviewing the formal abdominal radiograph report read by an attending radiologist who had no knowledge of the study.

RESULTS

Baseline study population characteristics

A total of 20 adult critically ill patients with COVID-19 were included (median age, 56 years [IQR, 38–67; range 32–74]; 35% female) (Table 1). The majority were obese with a median BMI of 35.4 (IQR, 31.5–37.8). The median number of days since hospital admission was 11.5 (IQR, 9–24), and the median Sequential Organ Failure Assessment score at the time of AAT testing was 8.0 (IQR, 7–11). Ninety percent of patients were receiving mechanical ventilation at the time of testing, with 35% receiving a paralytic agent and 35% in the prone position to facilitate ventilation.

Baseline nutrition characteristics of our study population

Among the study cohort, 70% (14 of 20) were receiving enteral nutrition via tube feeding at the time of testing and 30% (6 of 20) were receiving parenteral nutrition (Table 2). Among those receiving tube feeding, the median volume administered, NGT output, and stool volume reported in the 24-h period prior to testing were 190 ml (IQR, 42.5–462.5), 175 ml (IQR, 0–453.75), and 350 ml (IQR, 30–850), respectively.

Relationship between AAT testing and gastric residuals/stool output

The majority of patients received 975 mg of acetaminophen for testing, and the median time between administration and drawing the blood acetaminophen level was 75.5 min (IQR, 59.75–90) (Table 3). There was no association between the time the acetaminophen levels were drawn and whether the levels were detectable (odds ratio [0.99], CI [0.97–1.03]). Among the study cohort, 55% (11 of 20) had evidence of malabsorption indicated by acetaminophen levels <5 mcg/ml (Table 4). There were no significant differences between patients who had evidence of malabsorption (undetectable acetaminophen levels) and absorption (detectable acetaminophen level) with respect to baseline patient or nutrition characteristics (Table 4). Interestingly, all the patients with evidence of malabsorption by AAT had clinical evidence of bowel function, as determined by low gastric residuals and stool output during the prior 24 h (Table 2).

Relationship between AAT testing and radiographic evidence of ileus

A total 65% (13 of 20) of patients had abdominal radiography in the 24 h prior to AAT. The proportion of imaging findings consistent with a diagnosis of ileus on abdominal x-ray evaluation was significantly greater in patients with an undetectable acetaminophen level (negative AAT) compared with patients with a detectable acetaminophen level (positive AAT) (88% vs 20%; $P = .03$) (Table 5). Median tube-feed rates were greater (40 [IQR, 35–45] vs 10 [IQR, 0–30] ml/h; $P = .01$) and there appeared to be a trend toward

TABLE 1 Baseline study cohort characteristics

Patient ID #	Age (years)	Gender	BMI	SOFA score	Mechanical ventilation	Paralytic infusion	Patient positioning	HTN	HLD	DM
1	32	F	38.2	3	No	No	Supine	Yes	No	No
2	32	F	38.2	1	No	No	Supine	Yes	No	No
3	56	M	29.5	13	Yes	No	Prone	Yes	Yes	Yes
4	56	M	29.5	11	Yes	Yes	Supine	Yes	Yes	Yes
5	74	M	35	8	Yes	Yes	Prone	No	Yes	No
6	39	M	35.7	7	Yes	No	Supine	Yes	No	No
7	60	F	24.5	8	Yes	Yes	Prone	Yes	No	No
8	35	M	46.6	8	Yes	Yes	Prone	No	Yes	No
9	68	M	34.8	11	Yes	No	Supine	No	No	No
10	69	F	34.4	7	Yes	Yes	Prone	Yes	Yes	Yes
11	69	M	29.2	8	Yes	Yes	Prone	Yes	Yes	Yes
12	34	M	36.9	13	Yes	No	Supine	No	No	No
13	55	F	32.2	4	Yes	No	Supine	Yes	No	No
14	64	M	35.7	11	Yes	No	Supine	No	Yes	Yes
15	66	M	25.7	7	Yes	Yes	Prone	No	No	No
16	57	F	51.1	11	Yes	No	Supine	Yes	Yes	No
17	74	M	35	9	Yes	No	Supine	Yes	Yes	No
18	47	M	36.6	9	Yes	No	Supine	Yes	No	No
19	34	M	37.6	20	Yes	No	Supine	No	No	No
20	42	F	39.6	7	Yes	No	Supine	No	No	No

Note: BMI was calculated as weight in kilograms divided by height in meters squared.

Abbreviations: BMI, body mass index; DM, diabetes mellitus; F, female; HLD, hyperlipidemia; HTN, hypertension; M, male; SOFA, Sequential Organ Failure Assessment.

TABLE 2 Baseline nutrition characteristics

Patient ID #	TF volume administered in prior 24 h (ml)	NGT output in prior 24 h (ml)	Stool output in prior 24 h (ml)	Receiving PN prior to AAT
1	0	750	0	Yes
2	0	100	150	Yes
3	220	150	350	No
4	160	900	525	Yes
5	222	0	250	No
6	250	0	600	No
7	140	200	0	No
8	150	500	1100	No
9	50	1150	1100	No
10	250	0	400	No
11	55	425	0	No
12	410	0	1100	No
13	620	0	3x unmeasured[a]	Yes
14	0	450	1260 + 1x unmeasured[b]	No
15	785	0	2050	No
16	830	0	550	No
17	0	350	0	Yes
18	940	200	600 + 3x unmeasured[c]	No
19	20	465	0	Yes
20	840	0	210	No

Abbreviations: AAT, acetaminophen absorption test; NGT, nasogastric tube; TF, tube feeds; PN, parenteral nutrition.

[a]Patient 13 did have three bowel movements; none were quantified.

[b]Patient 14 did have one unquantified bowel movement in addition to measured stool output.

[c]Patient 18 did have three unquantified bowel movements in addition to measured stool output.

lower gastric residual volumes (45 [IQR, 7.5–112.5] vs 830 [90–1020] ml; $P = .11$) in patients with a positive AAT. Of note, tube feeds were resumed in 89% of patients with a detectable level vs 73% in patients with an undetectable level.

DISCUSSION

A growing body of literature reports that GI dysfunction is prevalent in critically ill patients with COVID-19.[2,11,12] Given the protracted course of the disease, it is reasonable to assume that many of these patients are nutrition deficient on arrival to the ICU and that these deficiencies may persist during their course of care. Early detection and correction of nutrition deficiency are essential in the care of critically ill patients, as inadequate provision of nutrition has been linked to increased morbidity and mortality.[6,11,13] Common clinical practice for ensuring the provision of adequate enteral nutrition in critically ill patients occurs through administration of an appropriate tube-feed formulation at a designated rate and assessment of tolerance by monitoring gastric residuals and stool output. However, this practice does not ensure that the delivered tube feeding is actually absorbed.

Our study provides evidence that malabsorption is common in critically ill patients with COVID-19 and can occur despite clinical indicators of tube-feed tolerance (ie, low gastric residuals and stool output). Furthermore, this malabsorption can occur many days after hospital admission. In addition to the harm associated with inadequate nutrition, delivery of enteral feeding to a critically ill patient without GI absorption could predispose them to risks such as bowel distention and resulting ischemia, as well as vomiting and aspiration, without clinical benefit. A negative AAT was associated with ileus on radiographic imaging and a lower rate of tube feeds at 24 h, both of which are predictors of GI intolerance and malabsorption. Our findings suggest that the AAT may provide a rapid, safe, and inexpensive method to assess bowel function in critically ill patients with COVID-19. Evidence of malabsorption by AAT may facilitate decision-making regarding

TABLE 3 Acetaminophen absorption testing characteristics

Patient ID #	Acetaminophen dose administered (mg)	Time between administration and level (min)	Acetaminophen concentration (mcg/ml)[a]	Patient received other oral acetaminophen doses in 24 h
1	975	32	7	No
2	975	90	<5.0	No
3	975	63	<5.0	No
4	975	77	<5.0	No
5	1000	50	<5.0	No
6	975	74	<5.0	No
7	975	93	6.7	Yes
8	975	95	<5.0	No
9	975	97	<5.0	No
10	975	92	23.5	Yes
11	975	86	14.4	No
12	975	69	<5.0	Yes
13	975	11	5.2	No
14	975	78	6.5	No
15	975	90	9.7	Yes
16	975	86	5.5	No
17	975	74	<5.0	Yes
18	950	49	6.6	No
19	975	63	<5.0	No
20	975	37	<5.0	No

[a]An acetaminophen serum concentration ≥ 5mcg/ml was considered positive, and an acetaminophen serum concentration < 5 mcg/ml was considered negative.

TABLE 4 Comparison of baseline study population and nutrition characteristics between patients with detectable (positive) and undetectable (negative) AAT result

Characteristic[a]	Undetectable (n = 11)	Detectable (n = 9)	*P*-value[b,c]
Age, years	42 (34–68)	60 (51–67.5)	.33
Male, n (%)	9 (82)	4 (44)	.16
BMI	35.7 (34.8–38.2)	34.4 (27.5–37.4)	.3
Days since hospital admission	10 (10–24)	12 (7.5–24)	.94
SOFA score	9 (7–13)	8 (5.5–10)	.23
Mechanical ventilation, n (%)	10 (91)	8 (89)	1
Supine position, n (%)	8 (73)	5 (56)	.64
Receiving paralytic, n (%)	3 (27)	4 (44)	.64
Receiving enteral nutrition at 24 h, n (%)	7 (64)	8 (89)	.32
Volume of TF administered in prior 24 h (ml)	160 (20–250)	250 (27.5–807.5)	.46
NGT output in prior 24 h (ml)	150 (0–500)	200 (0–437.5)	.66
Stool volume in prior 24 h (ml)	350 (150–1100)	475 (0–1095)	.9
Time of AAT (min)	74 (63–90)	86 (40.5–91)	.88

Note: BMI was calculated as weight in kilograms divided by height in meters squared.

Abbreviations: AAT, acetaminophen absorption test; BMI, body mass index; NGT, nasogastric tube; SOFA, Sequential Organ Failure Assessment; TF, tube feeds.

[a]Data presented as median (interquartile range), unless otherwise stated.

[b]Nonparametric data analyzed using Mann-Whitney *U* test.

[c]Categorical data analyzed using Fisher exact test.

TABLE 5 Association of acetaminophen testing results with standard clinical markers of enteral tolerance

	Detectable acetaminophen concentration (n = 9)		Undetectable acetaminophen concentration (n = 11)		*P*-value
Ileus on imaging, n (%)[a]	n = 5	1 (20)	n = 8	7 (88)	.03
Rate of TFs at 24 h (ml/h), median (interquartile range)	40 (35–45)		10 (0–25)		. 01
Total residuals at 24 h (ml), median (interquartile range)[b]	n = 4	45 (7.5–112.5)	n = 7	830 (115–960)	.11
TFs resumed, n (%)	8 (89)		8 (73)		.59

Abbreviation: TF, tube feeds.

[a]Seven patients did not have abdominal imaging (four patients in the detectable acetaminophen concentration group and three patients in the undetectable acetaminophen concentration group). These individuals were analyzed as missing data.

[b]Nine patients did not have documented gastric residual volumes (five patients in the detectable acetaminophen concentration group and four patients in the undetectable acetaminophen concentration group). These individuals were analyzed as missing data.

introduction or reintroduction of enteral feeding, as well as consideration of earlier initiation of parenteral nutrition.

The AAT has been previously been described as an indicator of malabsorption in intensive care patients.[8,9,14–18] The AAT has not become widely adopted in the practice of critical care despite its simplicity. This lack of adoption appears to be based on the theoretical risks that absorption may be affected by variation in volume of distribution, renal, or hepatic function. In addition, some studies have suggested the use of the area under the curve (AUC) calculations or maximum acetaminophen concentration to derive estimates of enteral absorption, requiring multiple samples at regular intervals, which may be prohibitive in the busy ICU setting.[8,9,14,17,18] Measurement at 90 min likely allows plasma concentrations to be detected even if gastric transit and absorption are delayed given that peak acetaminophen plasma concentration typically occurs between 10 and 105 min in critically ill patients.[8,14,16,17] In our study, there was no association between timing of acetaminophen level being drawn and detectability of said level, supporting use of a single-level test at 90 min in patients with suspected delayed GI transit time when collecting AUC data is not practical.

Acetaminophen uptake occurs in the proximal jejunum, and although volume of distribution does affect plasma concentration, measurement at short time intervals minimizes its impact.[8] In a study of critically ill patients without COVID-19, Cohen et al found that the subgroup of patients who had an abnormal AAT and received enteral feeding did not tolerate reintroduction of feeding. Only after further treatment with prokinetic agents and assessment was enteral feeding well tolerated.[8] Decisions regarding initiation or cessation of tube feeding are often based on residual volume analysis, but in this study, the volume of gastric aspirate did not have a statistically significant association with the results of AAT.[14] A majority (73%) of patients with evidence of malabsorption by AAT in our study had tube feeds restarted, suggesting that current indicators of tube-feed tolerance (ie, low gastric residuals and the presence of stool output) may not be predictive of absorption. Given our results, it is maybe reasonable to start parenteral nutrition when the AAT is negative, and education of ICU clinicians regarding the results may be necessary to guide appropriate management.

Given the protracted clinical course of COVID-19–related illness, patients are likely already suffering from malnutrition on admission.[2,11] Additionally, evidence suggests that GI dysfunction is common in COVID-19–positive patients.[2] Furthermore, many critically ill patients with COVID-19 receive opioids, which may further contribute to GI dysfunction. The AAT in critically ill COVID-19 patients allowed for rapid determination of enteral function in patients in whom GI intolerance was suspected. Of note, the AAT in this study was performed in patients in whom GI intolerance was suspected (ie, low stool output, high gastric residual volumes, abdominal distention, or evidence of aspiration). This is highlighted by the fact that in both the negative and positive AAT groups, none of the patients were receiving full enteral nutrition. Therefore, consideration of AAT in COVID-19 patients represents a possible testing paradigm that can minimize time to initiation of supplemental parenteral nutrition if enteral uptake is not tolerated.

In institutions at which a chest x-ray is routinely performed to confirm gastric tube position, the AAT may also represent a cost-saving procedure when compared with traditional methods of assessing GI function, both to the patient and to the institution. Based on our institutional data, the cost of performing an abdominal radiograph is 325% greater than a single dose of acetaminophen (1000 mg) with serum concentration testing.

Furthermore, performing abdominal radiography necessitates potential viral exposure of 1–2 technicians

per study. In contrast, the AAT can be performed by nursing staff who is already engaged in ongoing patient care, including regular medication administration and obtaining blood samples for laboratory testing. Mitigating the risk of exposure to hospital personal may have significant additional cost benefits for hospital systems when treating patients with high infectivity. Based on the literature and our current findings, we feel that there is a significant opportunity for both direct and indirect cost savings to both the healthcare system and the critically ill COVID-19 patients. However, imaging should be continued to be used in the appropriate clinical context given limitations of the AAT (ie, it cannot confirm or exclude bowel distension, detect free air, etc).

Our findings are consistent with previous literature whereby acetaminophen uptake is well correlated with the ability to tolerate enteral feeding.[8] Our study reveals that a negative AAT result is associated with radiologic imaging findings which are consistent with ileus. Furthermore, all of the patients who had a positive AAT result were able to tolerate enteral feeds. Previous literature has demonstrated that both the rate and total glucose absorption are dependent on a multitude of factors, including but not limited to gastric emptying, the presence of pancreatic enzymes, and serum glucose levels.[19] In contrast to glucose uptake measurements as a proxy for gastric emptying, AAT results may be less impacted by the sequelae of critical illness. In the pandemic environment, in which provider exposure to infectious agents should be minimized, the AAT provides a mechanism for assessment of GI function without the need for repeat imaging or evaluation of gastric residual volume to minimize healthcare worker exposure, medical equipment contamination, healthcare costs, and aspiration risk in patients with already limited pulmonary reserve.

Both ESPEN and American Society for Parenteral and Enteral Nutrition recommendations on nutrition management of critically ill individuals with COVID-19 advocate for early assessment and initiation of enteral nutrition. If enteral nutrition is contraindicated or clinically impossible, parenteral nutrition should be initiated in critically ill patients. Our study findings demonstrate that the correlation between the AAT and traditional assessments of enteral function is high. Given the highly transmissible nature of COVID-19 and significant strain on medical capacity, assessments that minimize superfluous patient contact by additional providers may be beneficial to both healthcare workers and healthcare systems. Therefore, we recommend use of the AAT as an adjunct assessment of enteral function that may allow for improved recognition of enteral dysfunction and facilitate faster progression to adequate nutrition status in critically ill patients secondary to COVID-19 infection.

LIMITATIONS

Our study has several limitations. The study is observational in nature and included a small number of patients from a single institution. Although a multicenter randomized trial would be valuable to confirm our findings, we sought to share this observational data in a time-sensitive manner to aid ICU clinicians in the setting of an ongoing pandemic. Although previous studies have used AUC calculations, which require multiple sample analyses, a single laboratory evaluation was drawn to minimize nursing exposure in the setting of the COVID-19 patient population.

Notably, borderline or negative results represent further decision-making challenges. At the current time, we offer the AAT as a potential adjunct to assessment of GI function rather than as a complete replacement for traditional measures of motility and function. Further work is needed to better delineate how the AAT should be utilized in the context of traditional measures, such as gastric residual volume and imaging evidence of ileus. However, in the setting of a pandemic with high potential risks to healthcare workers and already strained resources, the AAT represents an additional tool for assessment of enteral uptake.

Despite these factors, we posit that rapid assessment of enteral uptake will be useful in these patients as a measure of enteral activity despite multiple medication therapies that may affect outcomes in a conflicting manner.[4,8,15] In addition, a negative test may suggest the need for additional motility agents or increased dosing as part of the treatment strategy. Another limitation of our study is that although the AAT was ordered to be drawn at 90 min, the median time of the laboratory drawn was 75 min (IQR, 56–90), which may confound our findings since critically ill patients with COVID-19 may have delayed gastric emptying. Thus, a negative AAT at even 90 min may not only suggest a lack of absorption but rather markedly delayed absorption that occurs past the 90-min time point. Furthermore, we did not use other absorption tests, such as stable isotopes of proteins or labeled glucose, to confirm the absence of absorption of nutrition components.

One important safety consideration of AAT is whether the test should be initiated in patients with laboratory evidence of liver injury. Liver injury occurs in up to 78% of COVID-19 patients, as manifested by abnormal transaminase levels.[2,20] However, the strategy described above involves a one-time dose of 950–1000 mg acetaminophen. Given the current standards of 24-h maximum acetaminophen dosing of 2000 mg per day in patients with hepatic damage, we feel that the risk of administration is significantly offset by the rapid assessment of enteral feeding capability.

Given the limitations of this small, nonrandomized, and retrospective study, the results can only be viewed as hypothesis-generating. Furthermore, there may be additional confounding variables that are currently unrecognized, which may have impacted the validity of our conclusions.

CONCLUSION

In summary, AAT may provide a useful adjunct to traditional methods for evaluation of GI intolerance in critically ill patients with COVID-19. It is easy to implement, inexpensive, and does not increase provider exposure in the pandemic environment. In patients who already may be nutrition deficient in the setting of a protracted disease course, the AAT may accelerate decision-making regarding whether enteral or supplemental parenteral feeding strategies should be initiated. It is our hope that the AAT will be useful in optimizing the nutrition status of critically ill patients with COVID-19.

AUTHOR CONTRIBUTIONS

Daniel L. Southren, Alexa D. Nardone, Adeniran A. Haastrup, Russel J. Roberts, Marvin G. Chang, and Edward A. Bittner contributed to the conception and design of the research; Daniel L. Southren and Alexa D. Nardone contributed to the acquisition and analysis of the data; Daniel L. Southren, Alexa D. Nardone, Adeniran A. Haastrup, Russel J. Roberts, Marvin G. Chang, and Edward A. Bittner drafted the manuscript. All authors critically revised the manuscript, agree to be fully accountable for ensuring the integrity and accuracy of the work, and read and approved the final manuscript.

FUNDING INFORMATION

None decaled.

ETHICS STATEMENT

The study was approved by the institutional review board (Protocol Number 2020P001354), and consent to participate was waived for the study.

DATA AVAILABILITY STATEMENT

All data generated or analyzed during this study are included in this published article.

CONFLICT OF INTEREST

None declared.

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How to cite this article: Southren DL, Nardone AD, Haastrup AA, Roberts RJ, Chang MG, Bittner EA. An examination of gastrointestinal absorption using the acetaminophen absorption test in critically ill patients with COVID-19: A retrospective cohort study. *Nutr Clin Pract*. 2021;1–10.