www.nature.com/ctg

Early Sigmoidoscopy or Colonoscopy Is Associated With Improved Hospital Outcomes in Ulcerative Colitis-Related Hospitalization

Kenneth Obi, MD¹, Alice Hinton, PhD², Lindsay Sobotka, DO³, Razvan Arsenescu, MD, PhD⁴, Somashekar G. Krishna, MD¹, Edward J. Levine, MD¹ and Cheng Zhang, MD, PhD¹

OBJECTIVES: Performing a sigmoidoscopy or colonoscopy is recommended for assessment of disease activity, excluding infection, and guiding medical treatment during ulcerative colitis (UC)-related hospitalizations. However, it is unknown whether the timing of endoscopy impacts clinical outcomes. The objective of our study was to determine the impact of timing of endoscopy on hospital outcomes in patients with UC-related hospitalizations.

METHODS: This is a cross-sectional study using data from the Nationwide Inpatient Sample database (2006–2013). Adult inpatients (\geq 19 years) with UC-related hospitalizations were identified using appropriate International Classification of Diseases, Ninth revision, Clinical modification codes (ICD-9-CM). Hospital outcomes stratified by disease severity were compared between patients receiving early (<3 days after admission) and delayed endoscopies (between 3 and 7 days after admission). The primary clinical outcomes included mortality, frequency of large intestine surgery, length of stay (LOS), and hospital cost. Results were analyzed using univariate and multivariate analyses.

RESULTS: Of a total of 84,359 patients with UC-related hospitalizations, 67.2% (56,657) underwent an early endoscopy and 32.8% (27,702) underwent a delayed endoscopy. Delayed endoscopy was associated with higher mortality (adjusted odds ratio: 1.76 (95% confidence interval (CI): 1.08, 2.88)), prolonged LOS (adjusted coefficient: 2.69 (95% CI: 2.61, 2.77)), and higher hospital cost (adjusted coefficient: \$3,394 (95% CI: 3,234, 3,554)). In UC patients with intermediate disease severity, delayed endoscopy was associated with an increased frequency of large intestine surgery (adjusted odds ratio: 1.60 (95% CI: 1.01, 2.53)).

CONCLUSIONS: In UC-related hospitalizations, the timing of endoscopic procedures impacts outcomes. Early endoscopy is associated with decreased mortality and better health-care utilization (LOS and hospital cost) compared with delayed endoscopy. In UC patients with intermediate disease severity, early endoscopy is also associated with a decreased frequency of large intestine surgery.

Clinical and Translational Gastroenterology (2016) 7, e203; doi:10.1038/ctg.2016.61; published online 1 December 2016 Subject Category: Inflammatory Bowel Disease

INTRODUCTION

Hospitalization rates for ulcerative colitis (UC) are increasing.^{1,2} In this era of value-based medicine, it is important to identify factors that decrease health-care resource utilization and mortality while maintaining good outcomes. Currently, it is not known whether the timing of endoscopic evaluation during hospitalization impacts hospital outcomes in patients with UC-related admissions. Many experts recommend performing a flexible sigmoidoscopy or colonoscopy as soon as possible or within 72 h to assess the endoscopic severity and differentiate overlapping diagnoses such as *Clostridium difficile (C. difficile)* colitis and cytomegalovirus (CMV) colitis.^{3,4} Whereas, some experts suggest that endoscopy may be more appropriate after the response to steroids has been measured, typically on or after day 3 of hospitalization.³

To help clinicians understand the differences in health-care outcomes between early and delayed endoscopy, we studied the in-hospital mortality, length of hospital stay (LOS), hospital cost, and frequency of large intestine surgery among patients with UC-related hospitalizations in relation to the timing of endoscopy performance.

METHODS

Data source. Data were extracted from the National Inpatient Sample (NIS) between 2006 and 2013. The NIS is maintained as part of the Healthcare Cost and Utilization Project sponsored by the Agency for Healthcare Research and Quality. This is the largest all-payer inpatient care database in the United States.⁵ This database reflects a 20% sample of nonfederal, acute-care hospitals in the United

¹Division of Gastroenterology, Hepatology and Nutrition, The Ohio State University, Wexner Medical Center, Columbus, Ohio, USA; ²Division of Biostatistics, College of Public Health, The Ohio State University, Columbus, Ohio, USA; ³Department of Medicine, The Ohio State University, Wexner Medical Center, Columbus, Ohio, USA and ⁴Department of Gastroenterology, Morristown Medical Center, Morristown, New Jersey, USA

Correspondence: Cheng Zhang, MD, PhD, Division of Gastroenterology, Hepatology and Nutrition, The Ohio State University, 395W. 12th Ave, 2nd Floor, Columbus, Ohio 43210, USA. E-mail: cheng.zhang@osumc.edu

Received 25 February 2016; accepted 1 September 2016

States. Each data entry includes a unique identifier, demographic variables (including age, gender, and race/ethnicity), type of admission (emergent, urgent, or elective), source of admission (emergency room, another hospital, or long-term facility), day of admission (weekend or weekdays), primary and secondary diagnoses (up to 25), primary and secondary procedures (up to 15), primary insurance payers, hospital cost, and LOS.⁶

The Ohio State Data and Specimen Policy and Human Subjects Research policy does not require Institutional Review Board approval for population-based public data set. The data contained within the data set are neither identifiable nor private and do not meet the federal definition of "human subject" as expressed in 45 Code of Federal Regulations (CFR 46.101).

Study population, definition of variables, and outcomes.

Our study population consisted of all adult discharges aged 19 years or older of UC-related hospitalizations. UC-related hospitalizations were selected using appropriate International Classification of Diseases, Ninth revision, Clinical modification codes (ICD-9-CM) (Supplementary Table 1). The discharges were considered to be UC-related if they had a principle diagnosis of UC. These criteria have been used previously.⁷

Endoscopic procedures included flexible sigmoidoscopy, rigid sigmoidoscopy, and colonoscopy according to the appropriate ICD-9-CM codes (Supplementary Table 1).⁸ We classified the timing of endoscopy as early if the endoscopy occurred within 2 days of hospitalization and delayed if the endoscopy occurred between the third day and the seventh day of hospitalization. If patients had undergone two endoscopies during the same hospitalizations, only the day of the first endoscopy was used.

Patient variables included age, gender, race, and insurance status. Race was categorized as White, Black, Hispanic, and other. Insurance status was categorized as Medicare, Medicaid, Private, and other based on the primary payer listed on the discharge record. Comorbidities for risk adjustment were derived from the Agency for Healthcare Research and Quality comorbidity measures using the Elixhauser score, a widely used and validated measure of comorbidity in hospitalized patients.9 The comorbidity burden was stratified based on the presence of <3 comorbidities as reference vs. ≥3 comorbidities. Hospital variables included bed size, type, inflammatory bowel disease (IBD) admission volume, and admission day. Hospital bed size was classified as small, medium, or large. Hospital type was categorized as rural, urban non-teaching, and urban teaching. IBD admission volume was classified as lowvolume (1-50 hospitalizations), medium-volume (50-150 hospitalizations), and high-volume (more than 150 hospitalizations) hospitals depending on their annual volume of IBD-related hospitalizations as described and validated in a previous study.5

UC-specific severity scores were calculated on the basis of the presence of certain complications such as anemia, malnutrition, requirement for blood transfusion, or total parenteral nutrition (Supplementary Table 2a).¹⁰ The scores ranged from 0 to 7 with higher scores representing greater severity of disease, and thus a higher likelihood of colectomy. The disease-specific severity score has been shown to predict the outcome of interest in derivation and validation cohorts from the NIS and could be used to stratify hospitalizations into low, intermediate, and high severity strata.^{10,11}

Coexisting CMV infection^{12–16} can indicate or trigger severe inflammation in UC patients and is associated with worse outcomes. Baseline characteristics of all patients included the status of CMV infection.

The primary outcomes were in-hospital mortality, frequency of large intestine surgery, LOS, and hospital cost. The latter two are collectively referred to as health-care resource utilization.

Exclusions. Patients who were younger than 19 years old, carried diagnoses of both Crohn's disease and UC, were electively admitted, had coexisting *C. difficile* infection, or were transferred from other hospitals were excluded.

Validity of ICD-9-CM coding in two tertiary referral hospitals. To validate the accuracy of the ICD-9-CM codes for UC, 154 charts with UC as the principle discharge diagnosis (date range 2011–2014) in the Ohio State University affiliated hospitals were reviewed using clinical, pathological, and radiological findings. This study has been approved by the institutional review board of the Ohio State University Medical Center. One hundred forty four patients with principle discharge ICD-9-CM codes of UC (93.5%) presented with symptoms of acute flare of UC on admission.

Statistical analysis. SAS 9.4 (SAS Institute, Cary, NC) was used to perform all analyses, employing appropriate survey estimation commands and strata weights. Categorical variables were tested for statistical significance with χ^2 tests, whereas differences in continuous variables were analyzed with *t*-test. Statistical significance was defined by P < 0.05. Linear regression was used to evaluate the effect of timing of endoscopies on LOS and hospital cost and logistic regression was used to calculate odds ratios (OR) and corresponding 95% confidence intervals (CI) for in-hospital mortality and large intestine surgery. Multivariate regression models adjusted for variables significantly associated with endoscopy timing at $P \le 0.1$ on univariate analysis.

RESULTS

Patient characteristics. Of the 84,359 patients with UC-related hospitalizations during the study period, 67.2% (56,657) underwent an early endoscopy and 32.8% (27,702) underwent a delayed endoscopy (Table 1). There were 16,537 patients excluded. The patients who underwent an early endoscopy were younger (45.89 vs. 48.57, P<0.001), had less severe disease (72.80% vs. 66.54%, P<0.001), fewer comorbidities (69.46% vs. 58.83%, P<0.001), and were less likely to have CMV infection (0.37% vs. 0.62%, P=0.033), compared with the patients in the delayed group. There were also significant differences in sex (P<0.001),

	<3 Days to endoscopy (<i>n</i> =56,657)		≥3 Days to endoscopy (27,702)		P value	
Age (mean, CI) ^a	45.89 (45.43, 46.35)		48.57 (47.92, 49.23)		< 0.001	
Sex Male Female	27,083 29,361	47.98% 52.02%	12,176 15,482	44.02% 55.98%	<0.001	
Race White Black Hispanic Other	37,233 5,769 5,965 2,897	71.79% 11.12% 11.50% 5.59%	17,852 3,492 3,158 1,443	68.81% 13.46% 12.17% 5.56%	< 0.001	
<i>Hospital bed size</i> Small Medium Large	6,716 14,312 35,333	11.92% 25.39% 62.69%	3,137 7,065 17,350	11.39% 25.64% 62.97%	0.645	
Hospital type Rural Urban non-teaching Urban teaching	4,570 25,510 26,280	8.11% 45.26% 46.63%	2,127 11,426 14,000	7.72% 41.47% 50.81%	< 0.001	
Insurance Medicare Medicaid Private Other	13,662 6,398 28,115 8,366	24.16% 11.32% 49.72% 14.80%	8,248 3,553 11,878 3,962	29.84% 12.85% 42.97% 14.33%	<0.001	
Elixhauser score <3 ≥3	39,354 17,303	69.46% 30.54%	16,298 11,404	58.83% 41.17%	< 0.001	
<i>IBD admission volume</i> Low (0–50) Medium (51–150)	41,185 12,378	72.69% 21.85%	19,527 6,373	70.49% 23.01%	0.030	
High (>150)	3,094	5.46%	1,802	6.51%		
<i>Admission day</i> Weekday Weekend	44,898 11,759	79.25% 20.75%	20,913 6,789	75.49% 24.51%	< 0.001	
<i>Severity score</i> Low Intermediate High	41,029 13,436 1,896	72.80% 23.84% 3.36%	18,333 7,650 1,569	66.54% 27.77% 5.69%	< 0.001	
CMV No Yes	56,445 211	99.63% 0.37%	27,531 171	99.38% 0.62%	0.033	

Table 1 Univariate analysis of demographic and hospital characteristics, and comorbidities among patients with ulcerative colitis-related hospitalizations who underwent early or delayed endoscopy

Categorical variables were expressed as weighted frequency (percentage) and differences between groups were analyzed by χ^2 tests. Continuous variables were expressed as mean (confidence interval) and differences were analyzed with t-tests. Data are numbers and percentages unless otherwise indicated. Percentages may not sum to 100 due to rounding, 2006-2013 were combined for all of the above analyses ^aMean with 95% confidence interval.

race (P < 0.001), insurances types (P < 0.001), admission day (P < 0.001), IBD admission volume (P = 0.03), and hospital type (P<0.001) (Table 1).

Severity score analysis. UC-specific severity scores were calculated to stratify patients into low, intermediate, and high severity groups. Univariate analysis of the conditions that comprise the severity score revealed that there were statistically significant differences in anemia (P<0.001), blood transfusion (P<0.001), malnutrition (P<0.001), parenteral nutrition (P<0.001), and admission to teaching hospitals (P < 0.001) across the two cohorts, with the delayed endoscopy group having the higher percentage of patients with those characteristics (Supplementary Table 2a-b).

3

Outcomes

In-hospital mortality. Multivariate analysis was performed to compare patients with UC-related hospitalization who underwent early and delayed endoscopies and was stratified by disease severity (Table 2). After we adjusted for all variables in Table 1 with $P \le 0.1$ on the univariate analysis, patients in the delayed endoscopy group had higher mortality overall compared with the early endoscopy group (adjusted OR: 1.76 (95% CI: 1.08, 2.88)). The mortality benefits of early endoscopy were mainly seen in the intermediate severity strata (adjusted OR: 2.39 (95% CI: 1.15, 4.96)).

Length of stay (LOS). Multivariate analysis was performed to evaluate the difference in LOS among these two cohorts after adjusting for all variables in Table 1 with $P \le 0.1$ on univariate analysis (Table 3). Overall, the delayed endoscopy group had about 3 days longer in LOS compared with the early endoscopy group (adjusted coefficient: 2.69 (95% CI: 2.61, 2.77) P<0.001). The findings were consistent across the low, intermediate, and high severity strata (P<0.001) (Table 3).

Hospital cost. Similarly, multivariate analysis of hospital cost demonstrated that patients in the delayed endoscopy group incurred significantly higher hospital cost compared with the early endoscopy group (adjusted coefficient: \$3,394 (95% CI: 3,234, 3,554) P<0.001). The findings were unchanged across the low, intermediate, and high severity strata (P<0.001) (Table 4).

Large intestine surgery. Multivariate analysis of frequency of large intestine surgery demonstrated that overall the frequency of large intestine surgery was similar between the delayed and early endoscopy groups. However, in the intermediate severity strata, delayed endoscopy was associated with higher odds of large intestine surgery (adjusted OR: 1.60 (95% CI: 1.01, 2.53)) (Table 5).

DISCUSSION

In this study, for patients with UC-related hospitalization, we have demonstrated that early sigmoidoscopy or colonoscopy, defined as endoscopy within the first 2 days of hospitalization, was associated with favorable hospital outcomes including decreased in-hospital mortality, lesser hospital cost, and shorter LOS compared with delayed endoscopy. To our knowledge, this is the first study of this magnitude to demonstrate favorable clinical outcomes that are independently associated with the timing of endoscopy.

The benefits of endoscopy in UC-related hospitalizations include the assessment of endoscopic severity, evaluating for infections such as CMV infections, and other conditions Obi et al.

	Number of events ^a	Percentage of total $^{\rm a}$	Adjusted OR^{b}	95% CI	P value
Overall					0.024
<3 Days	165	0.29%	Reference		
≥3 Days	207	0.75%	1.76	(1.08, 2.88)	
Low severity					0.201
<3 Davs	68	0.16%	Reference		
≥3 Days	70	0.38%	1.65	(0.77, 3.57)	
Moderate severitv					0.020
<3 Davs	63	0.46%	Reference		
≥3 Days	99	1.27%	2.39	(1.15, 4.96)	
Hiah severitv					0.560
<3 Davs	34	1.54%	Reference		
≥3 Days	38	2.25%	1.33	(0.51, 3.43)	

Table 2 Multivariate analysis of in-hospital mortality among patients with UC-related hospitalizations who had either early or delayed endoscopy by disease severity

CI, confidence interval; OR, odds ratio.

4

2006-2013 were combined for all of the above analyses.

^aData are numbers and percentages unless otherwise indicated.

^bAdjusted for age, sex, race, hospital size, hospital type, insurance, Elixhauser score, IBD admission volume, admission day, severity score, year, and CMV.

Table 3 Multivariate analysis of LOS among patients with UC-related hospitalizations who had either early or delayed endoscopy by disease severity

	Days ^a	AC ^b	95% CI	P value
Overall				< 0.001
<3 Days	4.86 (4.78, 4.95)	Reference		
≥3 Days	7.93 (7.78, 8.07)	2.69	(2.61, 2.77)	
Low severity				< 0.001
<3 Days	4.21 (4.14, 4.28)	Reference		
≥3 Days	6.93 (6.80, 7.05)	2.59	(2.53, 2.66)	
Moderate severitv				< 0.001
<3 Days	5.96 (5.76, 6.15)	Reference		
≥3 Days	8.92 (8.62, 9.22)	2.83	(2.45, 3.21)	
Hiah severitv				< 0.001
<3 Days	10.37 (9.57, 11.16)	Reference		
≥3 Days	13.98 (13.00, 14.96)	3.49	(2.29, 4.70)	

AC, adjusted coefficient; CI, confidence interval; LOS, length of stay; UC, ulcerative colitis.

2006-2013 were combined for all of the above analyses.

^aMean with 95% confidence interval.

^bAdjusted for age, sex, race, hospital size, hospital type, insurance, Elixhauser score, IBD admission volume, admission day, severity score, year, and CMV.

Table 4 Multivariate analysis of total hospital cost among patients with UC-related hospitalizations who had either early or delayed endoscopy by disease severity

	Cost (\$) ^a	AC ^b	95% CI	P value
Overall				< 0.001
<3 Days	8,912 (8,718, 9,106)	Reference		
≥3 Days	13,031 (12,658, 13,405)	3,394	(3,234, 3,554)	
Low severity				< 0.001
<3 Days	7,658 (7,490, 7,825)	Reference		
≥3 Days	10,915 (10,599, 11,231)	3,024	(2,888, 3,159)	
Moderate severity				< 0.001
<3 Days	10,997 (10,577, 11,417)	Reference		
≥3 Days	15,047 (14,338, 15,755)	3,736	(2,851, 4,621)	
High severity				< 0.001
<3 Davs	19.535 (17.610, 21.460)	Reference		< 0.001
≥3 Days	26,148 (23,546, 28,751)	6,799	(3,570, 10,028)	

AC, adjusted coefficient; CI, confidence interval; UC, ulcerative colitis.

2006–2013 were combined for all of the above analyses.

^aMean with 95% confidence interval.

^bAdjusted for age, sex, race, hospital size, hospital type, insurance, Elixhauser score, IBD admission volume, admission day, severity score, year, and CMV.

	Number of events ^a	Percentage of total ^a	AOR ^b	95% CI	P value
Overall					0.293
<3 Days	703	1.24%	Reference		
≥3 Days	510	1.84%	1.16	(0.88, 1.53)	
Low severity					0.885
<3 Days	306	0.74%	Reference		
≥3 Days	163	0.88%	0.97	(0.62, 1.52)	
Moderate severity					0.047
<3 Days	215	1.56%	Reference		
≥3 Days	197	2.53%	1.60	(1.01, 2.53)	
High severity					0.557
<3 Days	182	8.31%	Reference		
≥3 Days	149	8.69%	0.86	(0.52, 1.42)	

Table 5 Multivariate analysis of frequency of large intestine surgery among patients with UC-related hospitalizations who had either early or delayed endoscopy by disease severity

AOR, adjusted odds ratio; CI, confidence interval; UC, ulcerative colitis.

2006–2013 were combined for all of the above analyses.

^aData are numbers and percentages unless otherwise indicated.

^bAdjusted for age, sex, race, hospital size, hospital type, insurance, Elixhauser score, IBD admission volume, admission day, severity score, year, and CMV.

that could mimic UC, such as ischemic colitis. In addition, the findings of endoscopy might also prompt the early decision of using rescue medical therapy, such biological therapy. The degree of endoscopic activity may also predict the severity of the disease course.^{3,17} Previous studies have shown that clinical outcomes and the need for colectomy were clearly linked to the presence and extent of deep colonic ulcerations. Severe endoscopic lesions were independent predictors for treatment failure.^{18,19} Therefore, performing an early endoscopy would enable health-care providers to make timely and appropriate clinical decisions. Early introduction of biological medications and timely surgical consultation have the potential to significantly alter the disease course.

In our study, the overall frequency of large intestine surgery, such as colectomy, was similar between the early and delayed endoscopy groups. However, when patients were stratified into three subgroups on the basis of the disease severity, early endoscopy was associated with less requirement of large intestine surgery in patients with intermediate disease severity. In addition, the mortality benefit of early endoscopy was also mainly seen in the patients with intermediate disease severity. It suggests that the outcomes of UC patients with intermediate disease severity would be more significantly impacted by early endoscopy because the clinical course of these patients is more likely influenced by the implementation of rescue medical therapy on time.

The 2012 consensus statement of the Canadian Association of Gastroenterology recommends an early flexible sigmoidoscopy with biopsies to assess endoscopic severity, *C difficile* infection, or CMV colitis on hospitalized patients with severe UC.³ They recommend that performing this evaluation at the time of admission would be appropriate. The British Society of Gastroenterology 2011 guidelines advocate for flexible sigmoidoscopy and biopsy within 72 h (ideally within 24 h) of an acute severe UC admission to confirm the diagnosis and exclude CMV.⁴ To our knowledge, neither the American College of Gastroenterology nor the American Gastroenterological Association have guidelines or consensus statements that specifically address this question. In our study. 94.3% of patients who received early endoscopy and 93.8% of patient who received delayed endoscopy underwent biopsies. In addition, we also performed an analysis to compare the hospital outcomes of UC patients receiving colonoscopy with those receiving sigmoidoscopy. In the early endoscopy group, colonoscopy was associated with less mortality and hospital cost, shorter LOS, and less frequency of large intestine surgery when compared with sigmoidoscopy. But in the delayed endoscopy group, the outcomes were similar between colonoscopy and sigmoidoscopy (Supplementary Tables 3a-b). These findings might be partially due to the bias of endoscopists because patients receiving sigmoidoscopy might have more severe endoscopy findings, which prevent the completion of a full colonoscopy. However, this also suggests that in some patients with UC-related hospitalization, colonoscopy is still a safe procedure to be performed. This large sample-size study will contribute to the existing literature as it supports the recommendations of gastroenterology societies to perform an early endoscopy for patients with UC-related hospitalizations. As a result, it may impact future clinical practice and guidelines on the management of hospitalized UC patients.

Our study had several limitations. An important limitation of this study is that because we used administrative data in the study, the accuracy of ICD-9-CM coding could not be verified by medical charts, owing to privacy safeguards. However, an analysis by the Agency for Healthcare Research and Quality comparing the NIS and other national databases demonstrated good reliability.²⁰ In addition, misclassification of ICD-9-CM coding should be distributed uniformly and non-differentially across all groups.²¹ Furthermore, administrative discharge codes have been widely used and validated for the analysis of various diseases and their outcomes. The discharge codes in our study have been used by several previous studies.^{7,11} We have also performed a chart review

within our tertiary referral medical centers. Our review revealed that the principle discharge code of UC accurately represented symptoms of acute UC flare on admission (93.5%) in our medical centers. There were probably more patients with steroid-refractory or steroid non-responded IBD in the delayed endoscopy group. In our study, the disease-specific severity was stratified into low, intermediate, and high severity strata on the basis of variables available in the administrative databases. Although the variables did not include detailed clinical or laboratory data, the method of stratification has been previously validated and has been shown to predict the severity of UC-related hospitalization.9-11 In our multivariate models, we adjusted for the status of CMV infection, which was expected to contribute to disease severity in patients with UC.¹²⁻¹⁶ Given the structure of the NIS, we could not obtain the information of medication use, laboratory, and endoscopy findings. In our study, the majority of the patients underwent biopsy during endoscopy, suggesting the importance of endoscopy with biopsy in hospitalized UC patients. The hospital outcomes of the subgroup patients who have undergone biopsy during the endoscopy were similar to our main results (data not shown). Because of the cross-sectional design of the study, we could only determine the association between early endoscopy and better outcomes in patients with UC-related hospitalizations. However, to determine causality, a prospective study would be required.

Despite the above limitations, our study also has strengths. The NIS database provides a large number of patients with a discharge diagnosis of UC who have undergone endoscopies, which otherwise would not be possible from smaller single center or multicenter studies. The benefit of using the NIS database is that the results represent the current national inpatient health-care utilization of patients with UC-related hospitalizations.

In conclusion, early colonoscopy or sigmoidoscopy, within 2 days of admission, is associated with improved outcomes in patients with UC-related hospitalizations. Although these findings need to be validated in prospective studies, nevertheless, our study supports the recommendations of gastroenterology societies to perform an early endoscopy for patients with UC-related hospitalizations.^{3,4}

CONFLICT OF INTEREST

Guarantor of the article: Cheng Zhang, MD, PhD. **Specific author contributions**: Kenneth Obi, Razvan Arsenescu, and Cheng Zhang participated in study design and paper writing. Alice Hinton and Cheng Zhang performed biostatistics analysis. Lindsay Sobotka and Cheng Zhang performed chart review and revised the manuscript. Somashekar Krishna and Edward Levine actively participated in the discussion and paper writing.

Financial support: None.

Potential competing interests: None.

Acknowledgments. The authors are grateful to Dr Alan Moss, associate professor, the Harvard Medical School, and Dr Darwin Conwell, professor, the Ohio State University for provision of comments and suggestions on the manuscript.

Study Highlights

WHAT IS CURRENT KNOWLEDGE

- ✓ Performing a sigmoidoscopy or colonoscopy is recommended for assessment of disease activity, excluding infection, and guiding medical treatment during ulcerative colitis (UC)-related hospitalizations.
- ✓ It is unknown whether the timing of sigmoidoscopy or colonoscopy impacts clinical outcomes.

WHAT IS NEW HERE

- ✓ Early sigmoidoscopy or colonoscopy (<3 days) is associated with favorable hospital outcomes including decreased in-hospital mortality, shorter length of stay (LOS), and less hospital cost in UC-related hospitalizations, compared with delayed endoscopy (between the third day and the seventh day after admission).
- ✓ Early sigmoidoscopy or colonoscopy (<3 days) is associated with a decreased frequency of large intestine surgery in UC patients with intermediate disease severity.
- Smyth CM, Picha SB, Rathore O et al. Increasing rates and changing patterns of hospital admissions for patients with inflammatory bowel disease in Ireland: 1996–2001. Ir J Med Sci 2005; 174: 28–32.
- Skrzydło-Radomariska B, Radwan P, Radwan-Kwiatek K. Retrospective analysis of hospital admissions of patients with ulcerative colitis and Crohn's disease from semi-rural and rural regions in the Department of Gastroenterology in Lublin between 2000–2006. Ann Agric Environ Med 2008; 15: 193–197.
- Bitton A, Buie D, Enns R et al. Treatment of hospitalized adult patients with severe ulcerative colitis: Toronto consensus statements. Am J Gastroenterol 2012; 107: 179–194.
- Mowat C, Cole A, Windsor A et al. Guidelines for the management of inflammatory bowel disease in adults. Gut 2011; 60: 571–607.
- (NIS), H.N.I.S. Healthcare Cost and Utilization Project (HCUP) Agency for Healthcare Research and Quality: Rockville, 2006, 2007, 2008, 2009, 2010, 2011, 2012.
- Nguyen GC, Kaplan GG, Harris ML *et al.* A national survey of the prevalence and impact of Clostridium difficile infection among hospitalized inflammatory bowel disease patients. *Am J Gastroenterol* 2008; **103**: 1443–1450.
- Ananthakrishnan AN, McGinley EL, Binion DG. Does it matter where you are hospitalized for inflammatory bowel disease? A nationwide analysis of hospital volume. *Am J Gastroenterol* 2008; 103: 2789–2798.
- Navaneethan U, Njei B, Venkatesh PG et al. Timing of colonoscopy and outcomes in patients with lower GI bleeding: a nationwide population-based study. Gastrointest Endosc 2014; 79: 297–306.
- Elixhauser A, Steiner C, Harris DR et al. Comorbidity measures for use with administrative data. Med Care 1998; 36: 8–27.
- Ananthakrishnan AN, McGinley EL, Binion DG et al. Simple score to identify colectomy risk in ulcerative colitis hospitalizations. Inflamm Bowel Dis 2010; 16: 1532–1540.
- Ananthakrishnan AN, McGinley EL, Binion DG et al. A nationwide analysis of changes in severity and outcomes of inflammatory bowel disease hospitalizations. J Gastrointest Surg 2011; 15: 267–276.
- Kishore J, Ghoshal U, Ghoshal UC *et al.* Infection with cytomegalovirus in patients with inflammatory bowel disease: prevalence, clinical significance and outcome. *J Med Microbiol* 2004; **53**: 1155–1160.
- Kandiel A, Lashner B. Cytomegalovirus colitis complicating inflammatory bowel disease. *Am J Gastroenterol* 2006; **101**: 2857–2865.
- Berk T, Gordon SJ, Choi HY et al. Cytomegalovirus infection of the colon: a possible role in exacerbations of inflammatory bowel disease. Am J Gastroenterol 1985; 80: 355–360.
- Cottone M, Pietrosi G, Martorana G *et al.* Prevalence of cytomegalovirus infection in severe refractory ulcerative and Crohn's colitis. *Am J Gastroenterol* 2001; 96: 773–775.
- Kambham N, Vij R, Cartwright CA *et al.* Cytomegalovirus infection in steroid-refractory ulcerative colitis: a case-control study. *Am J Surg Pathol* 2004; 28: 365–373.

- Alemayehu G, Järnerot G. Colonoscopy during an attack of severe ulcerative colitis is a safe procedure and of great value in clinical decision making. *Am J Gastroenterol* 1991; 86: 187–190.
- 18. Modigliani R. Medical management of fulminant colitis. Inflamm Bowel Dis 2002; 8: 129-134.
- Carbonnel F, Gargouri D, Lémann M et al. Predictive factors of outcome of intensive intravenous treatment for attacks of ulcerative colitis. *Aliment Pharmacol Ther* 2000; 14: 273–279.
- Whalen D, Houchens R, Elixhauser A. 2002 HCUP Nationwide Inpatient Sample (NIS) Comparison Report. U.S. Agency for Healthcare Research and Quality 2005: 1–89.
- Nguyen GC, Bayless TM, Powe NR *et al.* Race and health insurance are predictors of hospitalized Crohn's disease patients undergoing bowel resection. *Inflamm Bowel Dis* 2007; 13: 1408–1416.

Clinical and Translational Gastroenterology is an openaccess journal published by Nature Publishing Group. This work is licensed under a Creative Commons Attribution-NonCommercial-NoDerivs 4.0 International License. The images or other third party material in this article are included in the article's Creative Commons license, unless indicated otherwise in the credit line; if the material is not included under the Creative Commons license, users will need to obtain permission from the license holder to reproduce the material. To view a copy of this license, visit http:// creativecommons.org/licenses/by-nc-nd/4.0/

Supplementary Information accompanies this paper on the Clinical and Translational Gastroenterology website (http://www.nature.com/ctg)