

World Journal of *Clinical Cases*

World J Clin Cases 2021 February 16; 9(5): 999-1246



Contents

Thrice Monthly Volume 9 Number 5 February 16, 2021

MINIREVIEWS

- 999 Remote nursing training model combined with proceduralization in the intensive care unit dealing with patients with COVID-19

Wang H, Kang K, Gao Y, Yang B, Li J, Wang L, Bi Y, Yu KJ, Dai QQ, Zhao MY

ORIGINAL ARTICLE

Case Control Study

- 1005 Metabolic syndrome, ApoE genotype, and cognitive dysfunction in an elderly population: A single-center, case-control study

Wang JY, Zhang L, Liu J, Yang W, Ma LN

- 1016 Serum neuron-specific enolase: A promising biomarker of silicosis

Huang HB, Huang JL, Xu XT, Huang KB, Lin YJ, Lin JB, Zhuang XB

Retrospective Study

- 1026 Biochemical recurrence of pathological T2+ localized prostate cancer after robotic-assisted radical prostatectomy: A 10-year surveillance

Yang CH, Lin YS, Ou YC, Weng WC, Huang LH, Lu CH, Hsu CY, Tung MC

Observational Study

- 1037 Clinical characteristics of perineal endometriosis: A case series

Liang Y, Zhang D, Jiang L, Liu Y, Zhang J

- 1048 Safety of gastrointestinal endoscopy in patients with acute coronary syndrome and concomitant gastrointestinal bleeding

Elkafrawy AA, Ahmed M, Alomari M, Elkaryoni A, Kennedy KF, Clarkston WK, Campbell DR

SYSTEMATIC REVIEWS

- 1058 Clinical features of SARS-CoV-2-associated encephalitis and meningitis amid COVID-19 pandemic

Huo L, Xu KL, Wang H

CASE REPORT

- 1079 Neuropathy and chloracne induced by 3,5,6-trichloropyridin-2-ol sodium: Report of three cases

Ma Y, Cao X, Zhang L, Zhang JY, Qiao ZS, Feng WL

- 1087 Effect of rifampicin on anticoagulation of warfarin: A case report

Hu YN, Zhou BT, Yang HR, Peng QL, Gu XR, Sun SS

- 1096 Severe lumbar spinal stenosis combined with Guillain-Barré syndrome: A case report

Xu DF, Wu B, Wang JX, Yu J, Xie JX

- 1103** Treatment of pediatric intracranial dissecting aneurysm with clipping and angioplasty, and next-generation sequencing analysis: A case report and literature review
Sun N, Yang XY, Zhao Y, Zhang QJ, Ma X, Wei ZN, Li MQ
- 1111** Imaging characteristics of a rare case of monostotic fibrous dysplasia of the sacrum: A case report
Liu XX, Xin X, Yan YH, Ma XW
- 1119** Primary aldosteronism due to bilateral micronodular hyperplasia and concomitant subclinical Cushing's syndrome: A case report
Teragawa H, Oshita C, Orita Y, Hashimoto K, Nakayama H, Yamazaki Y, Sasano H
- 1127** Management of corneal ulceration with a moisture chamber due to temporary lagophthalmos in a brain injury patient: A case report
Yu XY, Xue LY, Zhou Y, Shen J, Yin L
- 1132** Bronchoscopy for diagnosis of COVID-19 with respiratory failure: A case report
Chen QY, He YS, Liu K, Cao J, Chen YX
- 1139** Pembrolizumab as a novel therapeutic option for patients with refractory thymic epithelial tumor: A case report
Wong-Chong J, Bernadach M, Ginzac A, Veyssière H, Durando X
- 1148** Successful bailout stenting strategy against rare spontaneous retrograde dissection of partially absorbed magnesium-based resorbable scaffold: A case report
Liao ZY, Liou JY, Lin SC, Hung HF, Chang CM, Chen LC, Chua SK, Lo HM, Hung CF
- 1156** Chronic myelomonocytic leukemia-associated pulmonary alveolar proteinosis: A case report and review of literature
Chen C, Huang XL, Gao DQ, Li YW, Qian SX
- 1168** Obturator nerve impingement caused by an osteophyte in the sacroiliac joint: A case report
Cai MD, Zhang HF, Fan YG, Su XJ, Xia L
- 1175** Venetoclax in combination with chidamide and dexamethasone in relapsed/refractory primary plasma cell leukemia without t(11;14): A case report
Yang Y, Fu LJ, Chen CM, Hu MW
- 1184** Heterochronic triple primary malignancies with Epstein-Barr virus infection and tumor protein 53 gene mutation: A case report and review of literature
Peng WX, Liu X, Wang QF, Zhou XY, Luo ZG, Hu XC
- 1196** Negative conversion of autoantibody profile in chronic hepatitis B: A case report
Zhang X, Xie QX, Zhao DM
- 1204** Dumbbell-shaped solitary fibrous tumor in the parapharyngeal space: A case report
Li YN, Li CL, Liu ZH
- 1210** Spontaneous small bowel perforation secondary to *Vibrio parahaemolyticus* infection: A case report
Chien SC, Chang CC, Chien SC

- 1215** Management protocol for Fournier's gangrene in sanitary regime caused by SARS-CoV-2 pandemic: A case report
Grabińska A, Michalczyk Ł, Banaczyk B, Syryło T, Ząbkowski T
- 1221** Infective bicuspid aortic valve endocarditis causing acute severe regurgitation and heart failure: A case report
Hou C, Wang WC, Chen H, Zhang YY, Wang WM
- 1228** Endoscopic repair of delayed stomach perforation caused by penetrating trauma: A case report
Yoon JH, Jun CH, Han JP, Yeom JW, Kang SK, Kook HY, Choi SK
- 1237** Bilateral musculocutaneous neuropathy: A case report
Jung JW, Park YC, Lee JY, Park JH, Jang SH

ABOUT COVER

Editorial Board Member of *World Journal of Clinical Cases*, Dr. Antonio Corvino is a PhD in the Motor Science and Wellness Department at University of Naples "Parthenope". In 2008, he obtained his MD degree from the School of Medicine, Second University of Naples. Then, he completed a residency in Radiology in 2014 at University Federico II of Naples. In 2015, he undertook post-graduate training at Catholic University of Rome, obtaining the 2nd level Master's degree in "Internal Ultrasound Diagnostic and Echo-Guided Therapies". In 2016-2018, he served on the directive board of Young Directive of Italian Society of Ultrasound in Medicine and Biology. His ongoing research interests involve ultrasound and ultrasound contrast media in abdominal and non-abdominal applications, etc. (L-Editor: Filipodia)

AIMS AND SCOPE

The primary aim of *World Journal of Clinical Cases* (WJCC, *World J Clin Cases*) is to provide scholars and readers from various fields of clinical medicine with a platform to publish high-quality clinical research articles and communicate their research findings online.

WJCC mainly publishes articles reporting research results and findings obtained in the field of clinical medicine and covering a wide range of topics, including case control studies, retrospective cohort studies, retrospective studies, clinical trials studies, observational studies, prospective studies, randomized controlled trials, randomized clinical trials, systematic reviews, meta-analysis, and case reports.

INDEXING/ABSTRACTING

The WJCC is now indexed in Science Citation Index Expanded (also known as SciSearch®), Journal Citation Reports/Science Edition, Scopus, PubMed, and PubMed Central. The 2020 Edition of Journal Citation Reports® cites the 2019 impact factor (IF) for WJCC as 1.013; IF without journal self cites: 0.991; Ranking: 120 among 165 journals in medicine, general and internal; and Quartile category: Q3. The WJCC's CiteScore for 2019 is 0.3 and Scopus CiteScore rank 2019: General Medicine is 394/529.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: Jia-Hui Li; Production Department Director: Yu-Jie Ma; Editorial Office Director: Jin-Lai Wang.

NAME OF JOURNAL

World Journal of Clinical Cases

ISSN

ISSN 2307-8960 (online)

LAUNCH DATE

April 16, 2013

FREQUENCY

Thrice Monthly

EDITORS-IN-CHIEF

Dennis A Bloomfield, Sandro Vento, Bao-gan Peng

EDITORIAL BOARD MEMBERS

<https://www.wjgnet.com/2307-8960/editorialboard.htm>

PUBLICATION DATE

February 16, 2021

COPYRIGHT

© 2021 Baishideng Publishing Group Inc

INSTRUCTIONS TO AUTHORS

<https://www.wjgnet.com/bpg/gerinfo/204>

GUIDELINES FOR ETHICS DOCUMENTS

<https://www.wjgnet.com/bpg/GerInfo/287>

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH

<https://www.wjgnet.com/bpg/gerinfo/240>

PUBLICATION ETHICS

<https://www.wjgnet.com/bpg/GerInfo/288>

PUBLICATION MISCONDUCT

<https://www.wjgnet.com/bpg/gerinfo/208>

ARTICLE PROCESSING CHARGE

<https://www.wjgnet.com/bpg/gerinfo/242>

STEPS FOR SUBMITTING MANUSCRIPTS

<https://www.wjgnet.com/bpg/GerInfo/239>

ONLINE SUBMISSION

<https://www.f6publishing.com>

Observational Study

Safety of gastrointestinal endoscopy in patients with acute coronary syndrome and concomitant gastrointestinal bleeding

Ahmed A Elkafrawy, Mohamed Ahmed, Mohammad Alomari, Ahmed Elkaryoni, Kevin F Kennedy, Wendell K Clarkston, Donald R Campbell

ORCID number: Ahmed A Elkafrawy 0000-0002-9114-1399; Mohamed Ahmed 0000-0001-6947-6849; Mohammad Alomari 0000-0003-1201-0866; Ahmed Elkaryoni 0000-0001-9615-1396; Kevin F Kennedy 0000-0003-3941-166X; Wendell K Clarkston 0000-0002-1783-3194; Donald R Campbell 0000-0003-0436-0380.

Author contributions: Campbell DR and Clarkston WK were the study's senior authors; they contributed to interpreting the data, writing, critical reviewing, and editing of the manuscript; Elkafrawy AA contributed to the conception, study design, literature review, and drafting of the manuscript; Ahmed M and Alomari M performed the literature review and drafted the manuscript; Elkaryoni A contributed to the study design and to develop the analytic plan; Kennedy KF extracted the data and performed the statistical analysis; all authors reviewed and approved the final manuscript.

Institutional review board

statement: The study population was identified from the Healthcare Cost and Utilization Project databases (HCUP). The HCUP databases are sponsored by the Agency for Healthcare Research

Ahmed A Elkafrawy, Digestive Disease and Surgery Institute, Cleveland Clinic Foundation, Cleveland, OH 44195, United States

Ahmed A Elkafrawy, Mohamed Ahmed, Internal Medicine, University of Missouri Kansas City School of Medicine, Kansas City, MO 64108, United States

Mohammad Alomari, Department of Gastroenterology and Hepatology, Cleveland Clinic Florida, Weston, FL 33331, United States

Ahmed Elkaryoni, Division of Cardiovascular Medicine, Loyola University Medical Center and Stritch School of Medicine, Maywood, IL 60153, United States

Kevin F Kennedy, Mid America Heart Institute, Saint Luke's Health System, Kansas City, MO 64111, United States

Wendell K Clarkston, Donald R Campbell, Department of Gastroenterology, Saint Luke's Hospital/University of Missouri Kansas City, Kansas City, MO 64111, United States

Corresponding author: Ahmed A Elkafrawy, MD, Academic Fellow, Digestive Disease and Surgery Institute, Cleveland Clinic Foundation, 9500 Euclid Avenue, A50, Cleveland, OH 44195, United States. ahmed.aly.kafrawy@gmail.com

Abstract

BACKGROUND

Gastrointestinal bleeding (GIB) is a major concern in patients hospitalized with acute coronary syndrome (ACS) due to the common use of both antiplatelet medications and anticoagulants. Studies evaluating the safety of gastrointestinal endoscopy (GIE) in ACS patients with GIB are limited by their relatively small size, and the focus has generally been on upper GIB and esophago-gastroduodenoscopy (EGD) only.

AIM

To evaluate the safety profile and the hospitalization outcomes of undergoing GIE in patients with ACS and concomitant GIB using the national database for hospitalized patients in the United States.

METHODS

and Quality. The Nationwide Inpatient Sample (NIS) database is the largest HCUP database, and it contains unweighted data from over 7 million hospital admission each year. The data represent a 20% random sample of participating hospital discharges from 46 states. The NIS database is de-identified and available to the public. Thus, it is not considered human subject research and is exempted from review by the institutional review board.

Informed consent statement: The study population was identified from the Healthcare Cost and Utilization Project databases (HCUP). The HCUP databases are sponsored by the Agency for Healthcare Research and Quality. The Nationwide Inpatient Sample (NIS) database is the largest HCUP database, and it contains unweighted data from over 7 million hospital admission each year. The data represent a 20% random sample of participating hospital discharges from 46 states. The NIS database is de-identified and available to the public. Thus, no informed consents were required or obtained.

Conflict-of-interest statement: The authors declare that they have no conflict-of-interest.

Data sharing statement: The study was conducted from the Nationwide Inpatient Sample Database (NIS). The NIS is a public database that contains de-identified data from hospitalized patients in the US. There is no risk of identification of patients.

STROBE statement: The authors have read the STROBE checklist, and the manuscript was prepared and revised according to the STROBE checklist.

Open-Access: This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0)

The Nationwide Inpatient Sample database was queried to identify patients hospitalized with ACS and GIB during the same admission between 2005 and 2014. The International Classification of Diseases Code, 9th Revision Clinical Modification was utilized for patient identification. Patients were further classified into two groups based on undergoing endoscopic procedures (EGD, small intestinal endoscopy, colonoscopy, or flexible sigmoidoscopy). Both groups were compared regarding demographic information, outcomes, and comorbidities. Multivariate analysis was conducted to identify factors associated with mortality and prolonged length of stay. Chi-square test was used to compare categorical variables, while Student's *t*-test was used to compare continuous variables. All analyses were performed using SAS 9.4 (Cary, NC, United States).

RESULTS

A total of 35612318 patients with ACS were identified between January 2005 and December 2014. 269483 (0.75%) of the patients diagnosed with ACS developed concomitant GIB during the same admission. At least one endoscopic procedure was performed in 68% of the patients admitted with both ACS and GIB. Patients who underwent GIE during the index hospitalization with ACS and GIB had lower mortality (3.8%) compared to the group not undergoing endoscopy (8.6 %, $P < 0.001$). A shorter length of stay (LOS) was observed in patients who underwent GIE (mean 6.59 ± 7.81 d) compared to the group not undergoing endoscopy (mean 7.84 ± 9.73 d, $P < 0.001$). Multivariate analysis showed that performing GIE was associated with lower mortality (odds ratio: 0.58, $P < 0.001$) and shorter LOS (-0.36 factor, $P < 0.001$).

CONCLUSION

Performing GIE during the index hospitalization of patients with ACS and GIB was correlated with a better mortality rate and a shorter LOS. Approximately two-thirds of patients with both ACS and GIB undergo GIE during the same hospitalization.

Key Words: Gastrointestinal endoscopy; Gastrointestinal bleeding; Acute coronary syndrome; Safety; Outcomes; Mortality

©The Author(s) 2021. Published by Baishideng Publishing Group Inc. All rights reserved.

Core Tip: Less than 1% of hospitalized patients have concomitant acute coronary syndrome (ACS) and gastrointestinal bleeding (GIB). However, the combination of these two conditions is reported to be associated with increased morbidity and mortality. Studies evaluating the safety and hospitalization outcomes of gastrointestinal endoscopy (GIE) in patients with ACS and GIB are limited and conflicting. This analysis was designed to evaluate GIE safety and efficacy in patients with ACS and GIB. This study concluded that GIE in patients hospitalized with ACS and GIB is both safe and associated with lower mortality as well as a shorter hospital stay.

Citation: Elkafrawy AA, Ahmed M, Alomari M, Elkaryoni A, Kennedy KF, Clarkston WK, Campbell DR. Safety of gastrointestinal endoscopy in patients with acute coronary syndrome and concomitant gastrointestinal bleeding. *World J Clin Cases* 2021; 9(5): 1048-1057

URL: <https://www.wjgnet.com/2307-8960/full/v9/i5/1048.htm>

DOI: <https://dx.doi.org/10.12998/wjcc.v9.i5.1048>

INTRODUCTION

Gastrointestinal bleeding (GIB) is associated with increased morbidity and mortality^[1]. The annual incidence of upper GIB in the United States is estimated to be 65 per 100000 individuals^[2], and between 0.7% and 3% of patients with acute coronary syndrome (ACS) develop GIB^[3-6]. GIB in patients with ACS is associated with a higher 30-d mortality rate (9.6%) as compared to ACS patients without GIB (1.4%)^[3]. Studies

license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Unsolicited manuscript

Specialty type: Gastroenterology and hepatology

Country/Territory of origin: United States

Peer-review report's scientific quality classification

Grade A (Excellent): 0
Grade B (Very good): B, B
Grade C (Good): C, C, C
Grade D (Fair): 0
Grade E (Poor): 0

Received: July 24, 2020

Peer-review started: July 24, 2020

First decision: September 14, 2020

Revised: October 1, 2020

Accepted: January 6, 2021

Article in press: January 6, 2021

Published online: February 16, 2021

P-Reviewer: Chen YD, Guo JS, Ju SQ, Karayiannakis AJ, Wang K

S-Editor: Zhang H

L-Editor: A

P-Editor: Xing YX



evaluating the safety of gastrointestinal endoscopy (GIE) in ACS patients with GIB are limited by their relatively small size, and the focus has generally been on upper GIB and esophagogastroduodenoscopy (EGD) only. The current study aims to evaluate the safety and outcomes of undergoing GIE (EGD, enteroscopy, colonoscopy, or flexible sigmoidoscopy) in patients with concomitant ACS and acute GIB (upper and lower GIB) using the Nationwide Inpatient Sample (NIS) database.

In patients with GIB, it may be difficult to determine whether the source is in the upper or lower GI tract. Emergent EGD is frequently the initial diagnostic study used to evaluate patients with GIB^[7]. However, its safety and utility, in the setting of ACS, present a common management dilemma^[8]. Patients with ACS are at a higher risk of arrhythmias, heart failure, further ischemic events, and death. The stress of undergoing endoscopic procedures with procedural sedation can theoretically precipitate cardiac complications and increase procedural risk^[9-12].

Antiplatelet therapy, dual antiplatelet therapy, anticoagulation therapy, and mechanical revascularization are well-established treatment modalities for ACS. However, these strategies are associated with an increased risk of precipitating gastrointestinal hemorrhage^[13,14]. These therapies, especially when used together or when used in patients with comorbidities (*e.g.*, prior peptic ulcer disease, renal failure, *etc.*) may precipitate GIB^[15,16].

Endoscopic studies of the upper and/or lower GI tract are frequently required to: (1) Identify the anatomic site of bleeding; (2) Identify the lesion; and (3) Intervene to control bleeding^[17].

The dilemma endoscopists often face is determining how safe an endoscopic procedure is in a patient with ACS. The current study was designed to evaluate on a large scale the safety and outcomes associated with the performance of endoscopic procedures during the same hospitalization with ACS and concomitant GIB.

MATERIALS AND METHODS

Patients older than 18 years of age with the diagnosis of ACS and GIB (upper and/or lower GIB) during the same index admission were included in the study. ACS was defined as acute myocardial infarction, subendocardial infarction, and acute coronary occlusion without infarction. Patients with chronic ischemic heart disease without an ACS associated diagnosis, peptic ulcer without hemorrhage, acute duodenal ulcer without hemorrhage, gastric ulcer without hemorrhage, and esophageal varices without bleeding were excluded.

The study population was identified from the Healthcare Cost and Utilization Project databases (HCUP). The Agency for Healthcare Research and Quality sponsors the HCUP databases. The NIS database is the largest HCUP database, and it contains unweighted data from over seven million hospital admission each year. The data represent a 20% random sample of participating hospital discharges from 46 states. The NIS database is de-identified and available to the public. Thus, it is not considered human subject research and is exempted from review by the institutional review board. To assure a meaningful study cohort, the investigators agreed upon a minimum study cohort of 250000 admissions. International Classification of Diseases (ICD)-9 codes were transitioned to ICD-10 codes in the last quarter of 2015. To assure consistency and data integrity, the study was designed only to include ICD-9 codes. Therefore, the study population and variables of interest ([Table 1](#)) between January 2005 and December 2014 were evaluated as in subsequent years, ICD-10 codes were used to populate the NIS database.

Patients undergoing single or multiple endoscopic procedures (esophago-gastro-duodenoscopy, small intestinal endoscopy, colonoscopy, or flexible sigmoidoscopy) were compared to those not undergoing endoscopic procedures in the same hospital encounter. Demographic data, including age, gender, race, payer status, geographic region, hospital size, and academic affiliation were evaluated. Mortality, length of stay (LOS), blood transfusion requirement, shock, mechanical ventilation, and commonly associated comorbidities were compared between both groups. Commonly associated comorbidities obtained from the NIS database were defined by the Agency for Healthcare Research and Quality and included thirty categories of comorbidity^[18] ([Supplementary Table 1](#)). Analyses of mortality and LOS in ACS patients with GIB were further adjusted for comorbidities. All ICD-9 CM and ICD-9 PCS codes are detailed in Appendix-1, [Supplementary material](#).

Table 1 Comparison between 2 groups regarding undergoing gastrointestinal endoscopy

	Total (n = 269483)	Patients underwent endoscopy (n = 183409)	Patients without endoscopy (n = 86073)	P value
Mean age at admission	72.32 ± 11.72	72.82 ± 11.41	71.27 ± 12.29	< 0.001
Males	178111 (66.1)	120040 (65.4)	58070 (67.5)	< 0.001
Females	91372 (33.9)	63369 (34.6)	28003 (32.5)	
Race				< 0.001
Caucasian	185713 (79.1)	127623 (79.5)	58089 (78.1)	
African American	17453 (7.4)	11555 (7.2)	5898 (7.9)	
Hispanic	16362 (7.0)	10710 (6.7)	5652 (7.6)	
Other	15338 (6.5)	10639 (6.6)	5652 (7.6)	
Mortality	14448 (5.4)	7027 (3.8)	7421 (8.6)	< 0.001
Length of stay	6.99 ± 8.49	6.59 ± 7.81	7.84 ± 9.73	< 0.001
Primary expected payer				< 0.001
Medicare	198925 (73.9)	137580 (75.1)	61344 (71.4)	
Medicaid	12590 (4.7)	7864 (4.3)	4726 (5.5)	
Private	45991 (17.1)	30558 (16.7)	15433 (18.0)	
Self-pay	6407 (2.4)	3900 (2.1)	2507 (2.9)	
No charge	578 (0.2)	318 (0.2)	261 (0.3)	
Other	4642 (1.7)	2971 (1.6)	1672 (1.9)	
Location/teaching status of hospital				< 0.001
Rural	26040 (9.7)	19100 (10.5)	6939 (8.1)	
Urban nonteaching	119321 (44.5)	82796 (45.4)	6939 (8.1)	
Urban teaching	122779 (45.8)	80650 (44.2)	42129 (49.2)	
Region of hospital				0.022
Northeast	49463 (18.4)	34252 (18.7)	15212 (17.7)	
Midwest	64974 (24.1)	44079 (24.0)	20895 (24.3)	
South	100860 (37.4)	68653 (37.4)	20895 (24.3)	
West	100860 (37.4)	68653 (37.4)	17759 (20.6)	
Shock	24171 (9)	13172 (7.2)	10999 (12.8)	< 0.001
Mechanical ventilation	24705 (9.2)	12736 (9.2)	11969 (13.9)	< 0.001
Blood transfusion	145939 (54.2)	102484 (55.9)	43455 (50.5)	< 0.001

Table 1 compares demographics and main outcomes between patients who underwent gastrointestinal endoscopy and the group who did not undergo endoscopy. Values are presented as *n* (%).

Statistical analysis

Continuous variables were described using mean ± SD, while categorical variables were described using proportion (percentage). Chi-square test was used to compare categorical variables, while Student's *t*-test was used to compare continuous variables. Multivariate analysis was done using logistic regression models to decrease bias and adjust for possible confounding factors. Statistical analysis was performed by a biomedical statistician. All analyses were performed using SAS 9.4 (SAS Institute Inc., Cary, NC, United States).

RESULTS

General characteristics

A total of 35612318 patients with ACS were identified between January 2005 and December 2014, and 269483 (0.75%) of the patients with ACS developed GIB during the same index admission. At least one GIE procedure was performed in 183248 (68%) patients with concomitant GIB and ACS, and outcomes in these patients were compared to the 86235 patients who did not undergo any endoscopic procedures (Figure 1). Males comprised 66.1% of the study population, while females comprised 33.9%. The mean age of the study population was 72.3 years, 79.1% were Caucasian, 7.4% African American, and 7.0% were Hispanic.

Outcomes

In the study cohort, undergoing GIE procedure was associated with reduced mortality (3.8%) in comparison to (8.6 %) in the group not having an endoscopic procedure (95%CI: -5.2, -4.4), ($P < 0.001$). Hospital length of stay (LOS) was shorter in patients who underwent gastrointestinal endoscopic procedures (mean 6.59 ± 7.81 d) in comparison to the group who did not undergo endoscopy (mean 7.84 ± 9.73 d) (95%CI: -1.42, -1.10), ($P < 0.001$). Shock was present in 7.2% of patients undergoing GIE compared to 12.8% in patients not undergoing endoscopy (95%CI: -6.1, -5.1), ($P < 0.001$) while 6.9% of patients were mechanically ventilated from the first group as compared to 13.9% in the group not undergoing endoscopy (95%CI: -7.5, -6.5), ($P < 0.001$). 55.9 % of patients who underwent GIE received blood transfusions in comparison to 50.5% of patients not undergoing endoscopic procedures (95%CI: 4.5, 6.3) ($P < 0.001$). Refer to Table 1 for comparison between both groups. Other compared comorbidities are detailed in Supplementary Table 1.

Multivariate analysis

Multivariate logistic regression models were used to predict factors associated with increased mortality and LOS. GIE was associated with less mortality; odds ratio (OR) of 0.58 (95%CI: 0.53-0.63) ($P < 0.0001$). Coagulopathy, shock, and mechanical ventilation were associated with higher mortality, OR of 1.76, 3.03, and 9.16, respectively ($P < 0.0001$). Regarding LOS, performing endoscopy was associated with a shorter LOS by -0.36 factor (beta weight) (95%CI: -0.56, -0.16) ($P < 0.001$). Congestive heart failure, shock, and mechanical ventilation were associated with prolonged LOS by 1.57, 3.16, 8.48 factor, respectively (beta weight). Refer to Tables 2 and 3 for all variables included in the logistic regression models.

DISCUSSION

Similar to previous studies, the results of this analysis found that 0.75% of patients admitted during a ten-year period with ACS develop GIB. Previous studies estimated the prevalence of GIB in ACS patients between 0.7% and 3%^[3-5]. Performing GIE (EGD, small intestinal endoscopy, colonoscopy, or flexible sigmoidoscopy) in patients with ACS and GIB was associated with significantly lower mortality and a shorter hospitalization stay in comparison to the group not undergoing endoscopic procedure. The selection of endoscopic procedures depended on the clinical impression of the gastroenterologist. Since patients with hematochezia may be experiencing brisk upper GIB or lower GI hemorrhage, some patients required evaluation with more than one endoscopic procedure. For that reason, all types of endoscopic procedures commonly used in the management of GIB were included in this study without stratification. One of the challenges in this study was to determine whether the patients who did not undergo GIE were at excessive risk for an endoscopic procedure or whether they developed complications (shock, respiratory failure, *etc.*) as a result of not having had an endoscopic procedure performed. A temporal relationship between performing endoscopy, presence of shock, mechanical ventilation, and other comorbid confounding factors could not be evaluated in this database. However, the association between performing GIE and better outcomes was statistically significant in the logistic regression models in the presence of these comorbidities.

GIB complicating ACS is a complex clinical scenario with sparse data to direct evidence-based guidelines on proper management. A recent study reported that the use of antiplatelet therapy, malignancy, renal impairment, heart failure, previous peptic ulcer disease, and abnormal activated partial thromboplastin time were predictors of GIB following ACS^[19]. Pioppo *et al*^[20] concluded that non-variceal upper

Table 2 Predictors of mortality (multivariate analysis)

	Odds ratio, 95%CI	P value
GIE	0.58 (0.53, 0.63)	< 0.0001
Age	1.03 (1.03, 1.03)	< 0.0001
Female	0.99 (0.9, 1.08)	0.7729
Race (Caucasian)	0.9 (0.83, 0.99)	0.0225
DM	0.71 (0.64, 0.79)	< 0.0001
CHF	1.13 (1.02, 1.26)	0.0186
Coagulopathy	1.76 (1.57, 1.98)	< 0.0001
Anemia	0.85 (0.76, 0.96)	0.0069
Liver disease	1.75 (1.51, 2.02)	< 0.0001
Renal failure	1.32 (1.2, 1.44)	< 0.0001
Diagnosis of cancer	1.76 (1.41, 2.19)	< 0.0001
Shock	3.03 (2.72, 3.38)	< 0.0001
Mechanical ventilation	9.16 (8.33, 10.07)	< 0.0001
Blood transfusion	0.9 (0.82, 0.99)	0.0314
Tobacco smoking	0.71 (0.63, 0.8)	< 0.0001
Alcohol abuse	1.19 (1.01, 1.41)	0.0400

Multivariate logistic regression model for predictors of mortality in patients hospitalized with acute coronary syndrome and concomitant gastrointestinal bleeding. Performing gastrointestinal endoscopy was included along with other variables and comorbidities that can affect mortality. GIE: Gastrointestinal endoscopy; DM: Diabetes mellitus; CHF: Congestive heart failure.

GIB in hospitalized patients with ACS was correlated with higher mortality, a longer length of stay, and increased hospitalization charges. Several studies have evaluated the safety of upper endoscopy shortly after ACS (usually within 30 d) and concluded it could be safely performed^[21-24]. The current study assessed the safety of endoscopic procedures during the same admission as ACS, and those admissions averaged approximately eight days. Al-Ebrahim *et al*^[25] reported complications occurred in 25% of patients undergoing endoscopy. However, mortality was not reported in that study, and only a small number of patients met the inclusion criteria. Lim *et al*^[21] evaluated major and minor complications following performing EGD within 30 d of ACS. They found no major complication, while minor complications occurred in 31% of the patients.

Another study concluded that undergoing upper GIE before cardiac catheterization was associated with a lower death rate when done for overt upper GIB^[24]. Additionally, Modi *et al*^[26] found that colonoscopy performed in the same admission for patients with STEMI and concomitant GIB was associated with lower mortality as compared with no intervention.

A meta-analysis by Cena *et al*^[27] evaluated the safety and benefits of performing GIE after myocardial infarction. It demonstrated that endoscopic procedures are safe and beneficial in stable patients with GIB after recent MI and should be performed without delay. A more recent meta-analysis found higher rates of cardiac complications following endoscopy in ACS patients^[28]. However, that study included endoscopic retrograde cholangiopancreatography and endoscopic ultrasound, which may have increased the rates of complications.

Several predictors of GIB in patients with ACS have been identified, including; older age, diabetes, hypertension, previous peptic ulcer disease, and dual antiplatelet therapy^[3,5,29]. In the study reported herein, the presence of coagulopathy, chronic heart failure, liver disease, renal failure, shock, and mechanical ventilation are associated with increased mortality.

A recently published study concluded that performing endoscopy in ACS patients was associated with better outcomes. However, it was not limited to the patients with GI hemorrhage and included other indications for performing endoscopy^[30]. The current analysis highlights the safety and superior outcomes of undergoing

Table 3 Factors associated with length of stay (multivariate analysis)

Label	Beta weight, 95%CI for LOS	P value
GIE	-0.36 (-0.56, -0.16)	< 0.001
Age	-0.01 (-0.02, 0)	0.0059
Sex (female)	0.34 (0.2, 0.48)	< 0.0001
Race (Caucasian)	-0.47 (-0.62, -0.32)	< 0.0001
DM	-0.8 (-0.95, -0.66)	< 0.0001
CHF	1.57 (1.35, 1.8)	< 0.0001
Coagulopathy	1.39 (1.04, 1.74)	< 0.0001
Anemia	0.07 (-0.11, 0.26)	0.4333
Liver disease	0.28 (-0.05, 0.61)	0.0945
Renal failure	1.41 (1.24, 1.59)	< 0.0001
Diagnosis of cancer	0.56 (0.08, 1.04)	0.0228
Shock	3.16 (2.73, 3.59)	< 0.0001
Mechanical ventilation	8.48 (7.96, 9)	< 0.0001
Blood transfusion	-0.69 (-0.9, -0.49)	< 0.0001
Tobacco smoking	-1.58 (-1.77, -1.38)	< 0.0001
Alcohol abuse	-0.77 (-1.08, -0.47)	< 0.0001

Multivariate logistic regression model for predictors of length of stay (LOS) in patients hospitalized with acute coronary syndrome and concomitant gastrointestinal bleeding. Performing gastrointestinal endoscopy was included along with other variables and comorbidities that can affect LOS. LOS: length of stay; GIE: Gastrointestinal endoscopy; DM: Diabetes mellitus; CHF: Congestive heart failure.

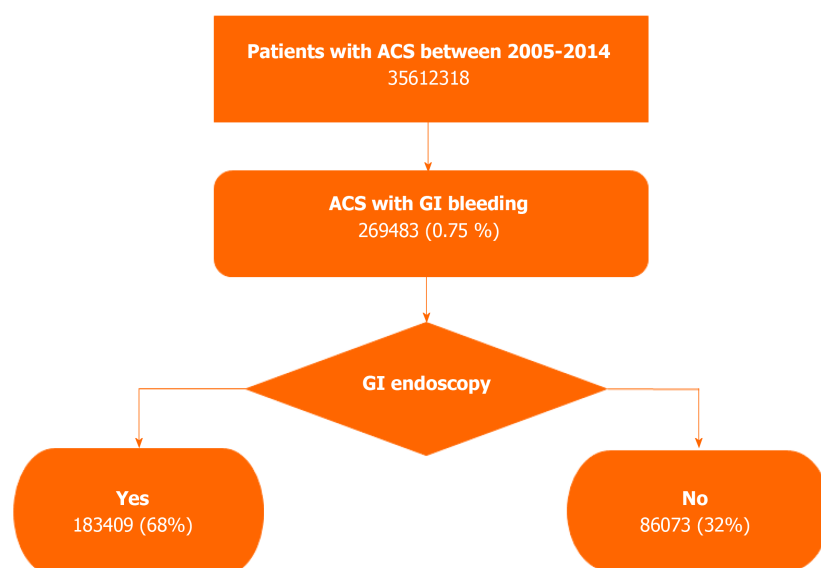


Figure 1 Diagram illustrating the number and percentage of patients with acute coronary syndrome and concomitant gastrointestinal bleeding in the same admission and also shows the number and percentage of patients who underwent gastrointestinal endoscopy. ACS: Acute coronary syndrome; GI: Gastrointestinal.

gastrointestinal endoscopic procedures in the specific setting of ACS and GIB.

Limitations

Like all retrospective database studies, the usual concerns apply (selection bias, confounding, reliability of data, *etc.*). The diagnoses of diseases, comorbidities,

outcomes, and procedures were identified using ICD-9 CM and ICD-9 PCS codes. Coding accuracy and missing data are potential sources of bias. The inability to review the individual medical records to validate the data may have led to inaccuracies. The temporal relationship between the performance of endoscopic procedures and confounding comorbidities could not be evaluated. However, the logistic regression models allowed for evaluation for comorbidities and minimization of possible confounding factors. Despite these limitations, the large sample size (269483 patients with concomitant ACS and GIB), wide geographic representation, variable size, and type of hospital (community vs. academic) enhance the generalizability of the findings.

CONCLUSION

This large retrospective analysis found that over a ten year period, 0.75% of patients admitted with ACS developed significant GIB. An endoscopic procedure was performed during the same hospitalization in the majority of the 269483 patients experiencing ACS and gastrointestinal hemorrhage. Patients with ACS who underwent GIE had lower mortality (3.8%) compared to patients who did not undergo endoscopic procedures (8.6%). Undergoing GIE in these patients during the same hospitalization was not only safe but was also correlated to lower mortality and a shorter hospital stay. The study confirms GIE can be safely performed in the majority of patients with ACS and concomitant GIB. The analysis highlights the need for future prospective controlled studies to determine the optimal time for intervention in patients with concomitant ACS and GIB and whether different modalities of endoscopy are equally safe. However, it's unlikely such a study will ever be completed given the requisite enrollment numbers combined with current and other studies demonstrating the safety and superior outcomes with the same hospitalization endoscopy.

ARTICLE HIGHLIGHTS

Research background

Gastrointestinal bleeding (GIB) in patients with acute coronary syndrome (ACS) is reported to be associated with increased morbidity and mortality.

Research motivation

Large scale studies investigating the safety profile and hospitalization outcomes of undergoing gastrointestinal endoscopic (GIE) procedure in hospitalized patients with ACS and GIB are limited and conflicting.

Research objectives

This large scale study assesses the safety and utility of performing GIE in hospitalized patients with concomitant ACS and GIB.

Research methods

The Nationwide Inpatient Sample database was queried to identify patients hospitalized with ACS and GIB during the same admission between 2005 and 2014 using ICD-9 codes. The study cohort was further categorized into two groups based on undergoing GIE. Outcomes of interest were compared between both groups. Multivariate analysis was conducted to predict factors associated with increased mortality and prolonged length of stay.

Research results

Patients with both ACS and GIB during the same admission who underwent GIE had a lower mortality rate (3.8%) in comparison to the group without endoscopy (8.6 %). Patients who underwent GIE had a shorter hospital stay (mean 6.59 ± 7.81 d) contrasted to those not undergoing endoscopic procedure (mean 7.84 ± 9.73 d). Multivariate regression analysis showed that undergoing GIE in this cohort was an independent predictor of lower mortality and shorter hospital stay.

Research conclusions

Undergoing GIE in patients presenting with ACS and GIB during the same index

admission was associated with lower mortality as well as a shorter hospital stay.

Research perspectives

Future prospective studies are needed to evaluate the optimal time for intervention in patients with concomitant ACS and GIB and whether different modalities of endoscopy and endoscopic interventions are equally safe.

REFERENCES

- 1 **Kim JS**, Kim BW, Kim DH, Park CH, Lee H, Joo MK, Jung DH, Chung JW, Choi HS, Baik GH, Lee JH, Song KY, Hur S. Guidelines for Nonvariceal Upper Gastrointestinal Bleeding. *Gut Liver* 2020; **14**: 560-570 [PMID: [32921639](#) DOI: [10.5009/gnl20154](#)]
- 2 **Wuerth BA**, Rockey DC. Changing Epidemiology of Upper Gastrointestinal Hemorrhage in the Last Decade: A Nationwide Analysis. *Dig Dis Sci* 2018; **63**: 1286-1293 [PMID: [29282637](#) DOI: [10.1007/s10620-017-4882-6](#)]
- 3 **Nikolsky E**, Stone GW, Kirtane AJ, Dangas GD, Lansky AJ, McLaurin B, Lincoff AM, Feit F, Moses JW, Fahy M, Manoukian SV, White HD, Ohman EM, Bertrand ME, Cox DA, Mehran R. Gastrointestinal bleeding in patients with acute coronary syndromes: incidence, predictors, and clinical implications: analysis from the ACUITY (Acute Catheterization and Urgent Intervention Triage Strategy) trial. *J Am Coll Cardiol* 2009; **54**: 1293-1302 [PMID: [19778672](#) DOI: [10.1016/j.jacc.2009.07.019](#)]
- 4 **Collins RT 2nd**, Doshi P, Onukwube J, Fram RY, Robbins JM. Risk Factors for Increased Hospital Resource Utilization and In-Hospital Mortality in Adults With Single Ventricle Congenital Heart Disease. *Am J Cardiol* 2016; **118**: 453-462 [PMID: [27291967](#) DOI: [10.1016/j.amjcard.2016.05.020](#)]
- 5 **Al-Mallah M**, Bazari RN, Jankowski M, Hudson MP. Predictors and outcomes associated with gastrointestinal bleeding in patients with acute coronary syndromes. *J Thromb Thrombolysis* 2007; **23**: 51-55 [PMID: [17186397](#) DOI: [10.1007/s11239-006-9005-8](#)]
- 6 **Gaglia MA Jr**, Torguson R, Gonzalez MA, Ben-Dor I, Maluenda G, Collins SD, Syed AI, Delhaye C, Wakabayashi K, Belle L, Mahmoudi M, Hanna N, Xue Z, Kaneshige K, Suddath WO, Kent KM, Satler LF, Pichard AD, Waksman R. Correlates and consequences of gastrointestinal bleeding complicating percutaneous coronary intervention. *Am J Cardiol* 2010; **106**: 1069-1074 [PMID: [20920640](#) DOI: [10.1016/j.amjcard.2010.06.011](#)]
- 7 **Cader MZ**, Di Pietro M. Acute Upper GIB: Good Night, Sleep Tight, Endoscopy Can Wait until Morning Light. *Gastroenterology* 2020; **159**: 1990-1991 [PMID: [32918914](#) DOI: [10.1053/j.gastro.2020.09.006](#)]
- 8 **Mehran R**, Pocock S, Nikolsky E, Dangas GD, Clayton T, Claessen BE, Caixeta A, Feit F, Manoukian SV, White H, Bertrand M, Ohman EM, Parise H, Lansky AJ, Lincoff AM, Stone GW. Impact of bleeding on mortality after percutaneous coronary intervention results from a patient-level pooled analysis of the REPLACE-2 (randomized evaluation of PCI linking angiogram to reduced clinical events), ACUITY (acute catheterization and urgent intervention triage strategy), and HORIZONS-AMI (harmonizing outcomes with revascularization and stents in acute myocardial infarction) trials. *JACC Cardiovasc Interv* 2011; **4**: 654-664 [PMID: [21700252](#) DOI: [10.1016/j.jcin.2011.02.011](#)]
- 9 **Gangi S**, Saidi F, Patel K, Johnstone B, Jaeger J, Shine D. Cardiovascular complications after GIE: occurrence and risks in a large hospital system. *Gastrointest Endosc* 2004; **60**: 679-685 [PMID: [15557942](#) DOI: [10.1016/s0016-5107\(04\)02016-4](#)]
- 10 **Kounis NG**, Zavras GM, Papadaki PJ, Kouni SN, Batsolaki M, Gouvelou-Deligianni GV, Markoglou C, Goudevenos JA, Mallioris CN, Kokkinis C, Kalokairinou K, Grapsas N, Kounis GN, Koutsojannis CM. Electrocardiographic changes in elderly patients during endoscopic retrograde cholangiopancreatography. *Can J Gastroenterol* 2003; **17**: 539-544 [PMID: [14532927](#) DOI: [10.1155/2003/620564](#)]
- 11 **McAlpine JK**, Martin BJ, Devine BL. Cardiac arrhythmias associated with upper gastrointestinal endoscopy in elderly subjects. *Scott Med J* 1990; **35**: 102-104 [PMID: [2237385](#) DOI: [10.1177/003693309003500403](#)]
- 12 **Yazawa K**, Adachi W, Koide N, Watanabe H, Koike S, Hanazaki K. Changes in cardiopulmonary parameters during upper gastrointestinal endoscopy in patients with heart disease: towards safer endoscopy. *Endoscopy* 2000; **32**: 287-293 [PMID: [10774967](#) DOI: [10.1055/s-2000-7377](#)]
- 13 **Huang KW**, Luo JC, Leu HB, Huang CC, Hou MC, Chen TS, Lu CL, Lin HC, Lee FY, Chang FY. Risk factors for upper gastrointestinal bleeding in coronary artery disease patients receiving both aspirin and clopidogrel. *J Chin Med Assoc* 2013; **76**: 9-14 [PMID: [23331775](#) DOI: [10.1016/j.jcma.2012.09.004](#)]
- 14 **Abraham NS**, Yang EH, Noseworthy PA, Inselman J, Yao X, Herrin J, Sangaralingham LR, Ngufor C, Shah ND. Fewer gastrointestinal bleeds with ticagrelor and prasugrel compared with clopidogrel in patients with acute coronary syndrome following percutaneous coronary intervention. *Aliment Pharmacol Ther* 2020; **52**: 646-654 [PMID: [32657466](#) DOI: [10.1111/apt.15790](#)]
- 15 **Wallace MC**, Rankin J, Forbes GM. Acute gastrointestinal bleeding after percutaneous coronary intervention. *Expert Rev Gastroenterol Hepatol* 2012; **6**: 211-221 [PMID: [22375526](#) DOI: [10.1111/j.1751-2975.2012.02611.x](#)]

- 10.1586/egh.11.104]
- 16 **Abraham NS**, Hlatky MA, Antman EM, Bhatt DL, Bjorkman DJ, Clark CB, Furberg CD, Johnson DA, Kahi CJ, Laine L, Mahaffey KW, Quigley EM, Scheiman J, Sperling LS, Tomaselli GF; ACCF/ACG/AHA. ACCF/ACG/AHA 2010 expert consensus document on the concomitant use of proton pump inhibitors and thienopyridines: a focused update of the ACCF/ACG/AHA 2008 expert consensus document on reducing the gastrointestinal risks of antiplatelet therapy and NSAID use. *Am J Gastroenterol* 2010; **105**: 2533-2549 [PMID: [21131924](#) DOI: [10.1038/ajg.2010.445](#)]
 - 17 **Strate LL**, Gralnek IM. ACG Clinical Guideline: Management of Patients With Acute Lower Gastrointestinal Bleeding. *Am J Gastroenterol* 2016; **111**: 755 [PMID: [27151132](#) DOI: [10.1038/ajg.2016.155](#)]
 - 18 **Elixhauser A**, Steiner C, Harris DR, Coffey RM. Comorbidity measures for use with administrative data. *Med Care* 1998; **36**: 8-27 [PMID: [9431328](#) DOI: [10.1097/00005650-199801000-00004](#)]
 - 19 **Zheng W**, Zhang YJ, Liu R, Zhao XD, Ai H. Prediction of gastrointestinal bleeding events in patients with acute coronary syndrome undergoing percutaneous coronary intervention: An observational cohort study (STROBE compliant). *Medicine (Baltimore)* 2020; **99**: e21312 [PMID: [32791719](#) DOI: [10.1097/MD.00000000000021312](#)]
 - 20 **Pioppo L**, Bhurwal A, Reja D, Tawadros A, Mutneja H, Goel A, Patel A. Incidence of Non-variceal Upper Gastrointestinal Bleeding Worsens Outcomes with Acute Coronary Syndrome: Result of a National Cohort. *Dig Dis Sci* 2020 [PMID: [32328894](#) DOI: [10.1007/s10620-020-06266-7](#)]
 - 21 **Lim RG**, Cobell WJ, Theivanayagam S, Kilgore TW, Matteson ML, Puli SR, Bechtold ML. Endoscopy after acute myocardial infarction: an evaluation of safety. *South Med J* 2013; **106**: 545-549 [PMID: [24096947](#) DOI: [10.1097/SMJ.0000000000000001](#)]
 - 22 **Mumtaz K**, Ismail FW, Jafri W, Abid S, Hamid S, Shah H, Dhakam S. Safety and utility of oesophago-gastro-duodenoscopy in acute myocardial infarction. *Eur J Gastroenterol Hepatol* 2008; **20**: 51-55 [PMID: [18090991](#) DOI: [10.1097/MEG.0b013e3282f16a3a](#)]
 - 23 **Lin S**, Konstance R, Jollis J, Fisher DA. The utility of upper endoscopy in patients with concomitant upper gastrointestinal bleeding and acute myocardial infarction. *Dig Dis Sci* 2006; **51**: 2377-2383 [PMID: [17151907](#) DOI: [10.1007/s10620-006-9326-7](#)]
 - 24 **Yachimski P**, Hur C. Upper endoscopy in patients with acute myocardial infarction and upper gastrointestinal bleeding: results of a decision analysis. *Dig Dis Sci* 2009; **54**: 701-711 [PMID: [18661236](#) DOI: [10.1007/s10620-008-0403-y](#)]
 - 25 **Al-Ebrahim F**, Khan KJ, Alhazzani W, Alnemer A, Alzahrani A, Marshall J, Armstrong D. Safety of esophagogastroduodenoscopy within 30 days of myocardial infarction: a retrospective cohort study from a Canadian tertiary centre. *Can J Gastroenterol* 2012; **26**: 151-154 [PMID: [22408766](#) DOI: [10.1155/2012/841792](#)]
 - 26 **Modi RM**, Li F, Mumtaz K, Hinton A, Lilly SM, Hussan H, Levine E, Zhang C, Conwell DL, Krishna SG, Stanich PP. Colonoscopy in Patients With Postmyocardial Infarction Gastrointestinal Bleeding: A Nationwide Analysis. *J Clin Gastroenterol* 2019; **53**: 23-28 [PMID: [28858942](#) DOI: [10.1097/MCG.0000000000000902](#)]
 - 27 **Cena M**, Gomez J, Alyousef T, Trohman RG, Pierko K, Agarwal R. Safety of endoscopic procedures after acute myocardial infarction: a systematic review. *Cardiol J* 2012; **19**: 447-452 [PMID: [23042306](#) DOI: [10.5603/cj.2012.0083](#)]
 - 28 **Dorreen A**, Moosavi S, Martel M, Barkun AN. Safety of Digestive Endoscopy following Acute Coronary Syndrome: A Systematic Review. *Can J Gastroenterol Hepatol* 2016; **2016**: 9564529 [PMID: [27446879](#) DOI: [10.1155/2016/9564529](#)]
 - 29 **Shalev A**, Zahger D, Novack V, Etzion O, Shimony A, Gilutz H, Cafri C, Ilia R, Fich A. Incidence, predictors and outcome of upper gastrointestinal bleeding in patients with acute coronary syndromes. *Int J Cardiol* 2012; **157**: 386-390 [PMID: [21277643](#) DOI: [10.1016/j.ijcard.2010.12.081](#)]
 - 30 **Hoffman GR**, Stein DJ, Moore MB, Feuerstein JD. Safety of Endoscopy for Hospitalized Patients With Acute Myocardial Infarction: A National Analysis. *Am J Gastroenterol* 2020; **115**: 376-380 [PMID: [32022723](#) DOI: [10.14309/ajg.0000000000000528](#)]



Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA

Telephone: +1-925-3991568

E-mail: bpgoffice@wjgnet.com

Help Desk: <https://www.f6publishing.com/helpdesk>

<https://www.wjgnet.com>

