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INVITED COMMENTARY

Which Comes First, the Scope or the Cath? Timing of Endoscopy in Patients with Non-variceal Upper Gastrointestinal Bleeding and Non-ST Elevation Myocardial Infarction

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There is a complex interplay linking patients with non-ST elevation myocardial infarction (NSTEMI) and non-variceal upper gastrointestinal bleeding (NVUGIB)—gastrointestinal bleeding can be an inciting event for an NSTEMI by exacerbating cardiac ischemia, further complicated by the medications used to prevent or treat NSTEMI that can cause gastrointestinal bleeding. The mortality rate of patients with concurrent NSTEMI and upper gastrointestinal bleeding is substantially higher than those with NSTEMI alone—30-day mortality rates are as high as 33% in the former compared with 5% in the latter [1]. Although high-risk bleeding lesions can be treated endoscopically while facilitating cardiac management decisions, endoscopy in the setting of NSTEMI can be problematic. Ongoing cardiac complications such as arrhythmias or cardiac failure may require inotropic support; furthermore, the sedation used to perform the endoscopy, as well as the stress response during endoscopy can worsen cardiac ischemia, all of which complicates patient selection and timing of endoscopy in patients with concurrent NVUGIB and NSTEMI.

The decision to perform an endoscopy in the setting of NSTEMI is further confounded by concerns about healthcare resource utilization, requiring the balancing of logistical and economic factors in addition to clinical considerations governing the optimal timing and need. The American College of Gastroenterology (ACG) 2021 guidelines [2] recommend that all patients who are admitted to hospital for upper gastrointestinal bleeding undergo endoscopy within 24 h of presentation. These guidelines also discuss the potential harms if endoscopy is performed prior to appropriate management of active comorbidities. Studies of patients with endoscopically confirmed ulcer bleeding such as the randomized controlled trial performed by Lin et al. [3] have compared outcomes of those with early endoscopy (< 12 h after presentation) versus delayed endoscopy (≥ 12 h), finding no benefit to early endoscopy. There are even fewer studies that address the timing of endoscopy when other active comorbidities may need to be optimized in the setting of NVUGIB. The 2016 American Society of Gastrointestinal Endoscopy (ASGE) guidelines on management of antithrombotic agents [4] discuss endoscopy in the setting of acute coronary syndrome but do not comment on the timing of procedures.

In this issue of *Digestive Diseases and Sciences*, Ali et al. [5] present a study that serves as a starting point into further investigating the timing of endoscopy in relationship to cardiac catheterization in patients who on admission have concurrent NSTEMI and NVUGIB. Using the National Readmission Database, the authors retrospectively compared outcomes between patients who underwent endoscopy before cardiac catheterization (cases) and a matched cohort who underwent endoscopy after cardiac catheterization (controls). The study found the overall inpatient mortality trended higher in the patients undergoing pre-catheterization endoscopy (5.5%) compared with the post-catheterization group (3.9%), with a nonsignificant odds ratio of 1.43; furthermore, the cause of the mortalities was unknown. The authors found that surrogate markers such as admission to the intensive care unit and atrial fibrillation occurrence were higher in cases compared with controls, inferring that patients in the pre-catheterization endoscopy group had inferior outcomes due to hemodynamic instability and cardiac arrhythmias attributed to the early timing of endoscopy. The authors also reported that subjects undergoing pre-catheterization endoscopy had poorer resource utilization outcomes, with longer length and costs of hospital stay compared with the control group.

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Though the advantage of using a national database for the study include utilizing a large sample size with 1592 total patients and use of real-world data where there may also be scheduling and logistical conflicts thus, increasing its generalizability, the study is limited by the information that is provided in the National Readmission Database. The study used matching with propensity scores to assess outcomes. The two groups had no statistical differences in age, gender, cardiac comorbidities, causes of bleeding (with 96% due to peptic ulcer disease) and severity of bleeding; the latter evaluated based on blood transfusion and vasopressor requirements. The database lacks hemodynamic data which would have been useful in calculating risk scores such as the Glasgow-Blatchford score used to assess the severity of bleeding. In addition, since the severity of NSTEMI may affect hemodynamic parameters as well as the magnitude of gastrointestinal bleeding, this issue is exceedingly complex to evaluate.

There may also be other inherent differences not accounted for by the propensity matching between patients who underwent endoscopy before versus after cardiac catheterization, which could confound the results. One pertinent factor is the timing of cardiac catheterization, with those in the pre-catheterization endoscopy group undergoing cardiac catheterization for NSTEMI at a median of six days after admission, compared with the control group who underwent cardiac catheterization at a median of one day. If the endoscopy delayed cardiac catheterization, this may explain the observed poorer outcomes in this group, rather than the timing of the endoscopy per se. The authors acknowledge that further studies are needed to determine this.

Other factors that would have been useful to the analysis that are not included in this study include the cause of death for patients, since death from rebleeding would have different implications when deciding the future timing of endoscopy compared with a cardiac-related death. Documentation of periprocedural events, including hypotension, desaturation, sustained arrhythmias, and knowledge of the stated indication would also help to further interpret the study results. A prior study by Yachimski and Hur [6] found that patients with overt (as opposed to occult) gastrointestinal blood loss had a lower mortality when endoscopy was performed prior to catheterization. It is therefore important to establish the initial magnitude of the suspected gastrointestinal hemorrhage through routine parameters such as the velocity and magnitude of hemoglobin decrease, the presence of hemodynamic instability, and evidence of overt blood loss such as hematemesis and melena since, the acuity and magnitude of blood loss influence the timing for endoscopy. Other factors measured in future studies should include: endoscopic lesion assessment scales such as the Forrest classification; mention of active bleeding at endoscopy; interventions performed during endoscopy; and the medications used peri-procedurally including type of sedation, the use of proton pump inhibitors, and type of antithrombotic agents used for the prevention and treatment of NSTEMI.

In summary, this study addresses an important and common clinical setting of patients with concomitant NSTEMI and NVUGIB. Some of the study data imply that patients undergoing pre-catheterization endoscopy have inferior outcomes to those patients with reversed procedural timing. The authors present a frank discussion of the limitations of their study given the retrospective nature and inherent shortcomings of data availability from the National Readmission Database. Further investigation is needed in this area to answer some of the questions raised above, and by the authors, before this study can influence practice, but it serves as a building block to guide future research.

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