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Geoffrey M. Ginter
Wayne State University, gginter@med.wayne.edu

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Indications for esophagogastroduodenoscopy in anemic patients without overt signs of upper gastrointestinal bleeding

GEOFFREY M. GINTER, Wayne State University School of Medicine, gg8581@wayne.edu

ABSTRACT

A clinical decision report using:


for a patient with a complicated presentation of severe anemia.

Keywords: gastrointestinal bleeding, anemia, endoscopy

Clinical-Social Context

John Davis [pseudonym], a 64-year-old male with a past medical history significant for subacute left cerebellar infarction in the previous year, hypertension, gastroesophageal reflux disorder, and alcohol and tobacco use disorder, presented to the Emergency Department (ED) with a three-day history of paroxysmal dizziness, blurry vision, and weakness in his bilateral lower extremities. He describes the episodes of dizziness as “like the room is spinning,” with each lasting greater than one minute. He remarked that these symptoms were similar to those of his previous infarct. Mr. Davis said, “I’ve been having trouble walking and feeling dizzy past three days. I am worried that I’m having another stroke.” He lives alone with minimal social contact, and he expressed concern that his worsening debility would severely hinder his ability to function independently. Mr. Davis is unemployed and supported by Supplemental Security Income. His highest educational attainment is middle school. He has a 15 pack-year smoking history and a history of multiple emergency department visits for severe alcohol intoxication. His home medications included aspirin, a statin, and metoprolol. CT of the head was negative for new infarcts; Mr. Davis refused an MRI of the head due to severe claustrophobia. A complete blood count (CBC) following fluid resuscitation revealed macrocytic anemia with an MCV of 109 fL with low folate and a hemoglobin of 11 g/dL. Vitamin replenishment was begun, but over the next several days, his hemoglobin continued to decrease to 7 g/dL, at which time concern was raised for occult bleeding. Throughout this period, Mr. Davis was asked daily about melena, hematochezia, hematuria, and hematemesis, which he denied aside from a single episode of minimal hematuria. He did not endorse gastrointestinal symptoms at any point in the hospital course. A fecal occult blood test and urinalysis were ordered, but before they could be completed, Mr. Davis was found down at his bedside with large-volume coffee-ground emesis and melena; hemoglobin at this time was 4.3 g/dL. Emergent esophagogastroduodenoscopy revealed an actively-bleeding 1 cm x 4 mm ulcer with a visible vessel. Hemostasis was achieved, after which he was stabilized in the MICU and discharged to subacute rehabilitation.

GEOFFREY M. GINTER is a 4th-year medical student at the Wayne State University School of Medicine.
Clinical Question

What factors can be used to predict the presence of a bleeding upper gastrointestinal lesion in an anemic patient without clinical symptoms of gastrointestinal bleeding?

Research Article


Description of Related Literature

Survey of the existing literature consisted of a PubMed search using the “advanced search” function. The search was initially conducted using the terms “anemia” AND “gastrointestinal” AND “endoscopy,” which returned 2,194 results. The search was determined to be overly broad, so to narrow the search to studies pertaining to preemptive diagnosis of bleeding ulcers, the term AND “predictors” was added, resulting in a final query of “anemia” AND “gastrointestinal” AND “endoscopy” AND “predictors,” which yielded 57 results. Two of the curated papers were review articles and were therefore excluded. Of the 55 remaining articles, 14 pertained to conditions of the small bowel and colon; these articles were excluded to ensure only papers regarding upper gastrointestinal bleeding were included. No additional filters were applied to the search. Manual review of the abstracts of these 41 papers yielded 27 articles related directly to the pre-endoscopy prediction of bleeding lesions in the upper gastrointestinal tract. Studies which were limited to specific populations, such patients with ST-elevation myocardial infarction, left ventricular assist devices, coagulopathy, and chronic NSAID exposure, were excluded due to their limited applicability.

The remaining studies reflected the body evidence regarding pretest predictors of bleeding ulcers in the upper gastrointestinal tract. Of these, only four papers studied patients without overt symptoms of gastrointestinal bleeding. Tong et al. conducted a retrospective cohort study of 934 anemic patients without symptomatic bleeding who had undergone capsule endoscopy to determine the diagnostic yield of the procedure and predictors of a positive test. The study was strengthened by a relatively large sample size, but only patients with a previous negative EGD were included in the sample, which made the results inapplicable to the clinical question. Cilona et al. studied 140 patients with iron deficiency anemia without symptomatic bleeding comparing the diagnostic yield of fecal-immunohistochemical testing (FIT) compared to the gold standard EGD. Positive FIT was found to be an independent predictor of a bleeding lesion, but the scope of the study was limited to only the predictive value of FIT and therefore did not adequately assess other possible predictive factors. Ioannu et al. studied 637 hospitalized anemic patients without evidence of acute bleeding to determine which factors predicted if the patients would receive laboratory workup or endoscopy. While the study did analyze multiple possible predictive factors, the endpoint was which patients received further workup, not which patients had bleeding lesions, which rendered the paper unsuitable for addressing the clinical question.

The paper that was ultimately selected for critical appraisal, Majid et al., was chosen for its pertinence to the clinical question. Of the literature produced by the search, the paper by Majid and colleagues was the only one which directly addressed the clinical question as to whether any factors can predict the presence of bleeding lesions on endoscopy in anemic patients who lack symptoms of gastrointestinal bleeding. After identifying Majid et al. as the most appropriate candidate, the “similar articles” function was used to generate a list of related literature. The function identified 260 results; limiting the search to full text articles yielded 219 results. Manual review of the abstracts of these papers did not elicit any articles more relevant to the clinical question than Majid et al. Annibale et al. was similar in scope, focusing on the outcomes of endoscopy in patients who were suspected to have gastrointestinal bleeding without clinical symptoms of bleeding. However, the study explored the underlying etiologies that may cause asymptomatic gastrointestinal bleeding, not factors that predict the presence of bleeding.

Majid et al. was therefore selected for critical appraisal. As a study focused on probabilistic diagnostic outcomes, this article meets SORT level 3 criteria.
Critical Appraisal

This study was a cross-sectional study of 95 patients with iron-deficiency anemia diagnosed by laboratory studies without gastrointestinal symptoms. A randomized control trial design was not used, as the study did not entail a treatment condition. Participants underwent EGD, and multivariable logistic regression was performed to ascertain the odds ratio for several independent variables including age, gender, hemoglobin level, mean corpuscular volume (MCV), serum iron, fecal occult blood testing (FOBT), family history of cancer, weight loss, previous treatment for anemia, and use of NSAIDs. Of all patients studied, actively bleeding lesions were found in 53%. The only significant variables that predicted a bleeding lesion on endoscopy were age ≥ 55 (OR = 4.8, 95% CI = 1.9-11.9, p < 0.001), NSAID use (OR = 2.8, 95% CI = 1.0-8.2, p = 0.04), hemoglobin ≤ 9 g/dL (OR = 4.7, 95% CI = 1.5-14.4, p = 0.004), MCV ≤ 60 fl (OR = 3.6, 95% CI = 1.5-8.4, p = 0.003), and positive FOBT (OR = 15.3, 95% CI = 4.2-56.1, p < 0.001).

The most apparent critique of this paper is the sample which was studied. The sample size was limited at 95 participants, which is small for a cross-sectional study. Further, the study was a single-site project at a hospital in Karachi, Pakistan. A smaller, single-center study is not as easily generalizable as a multicenter study in a larger sample of patients. The generalizability of the study was also limited by the cross-sectional design, which only allowed for establishing associations between the risk factors and the outcomes without identifying the temporal relationship between these factors. The study population may also not be comparable to other populations, as Pakistan has among the highest prevalence of Helicobacter pylori in the world at 81.0% compared to 35.6% in the United States. The increased prevalence of H. pylori in Pakistan compared to other nations may provide a source of confounding, as this may increase the pretest probability of a bleeding ulcer.

The study does benefit from the analysis of broad selection of predictive variables. Ten different variables were assessed, most of which were clinically relevant. Factors such as age, gender, NSAID use, and recent weight loss are all pieces of information that can be readily obtained while taking a detailed history. Measurable factors such as a hemoglobin below 9 g/dL or MCV below 60 fl also allow for prediction of bleeding lesions based on the results of a complete blood count. However, the inclusion of FOBT may have been redundant, as a positive test indicates the presence of gastrointestinal bleeding, which would always prompt endoscopic evaluation. This redundancy renders the predictive value of a positive FOBT less clinically valuable, even though it is statistically significant.

As a study focused on probabilistic diagnostic outcomes, this study meets SORT level 3 criteria. The study does not focus on patient-centered outcomes such as morbidity or mortality, and the quality of the study would be greatly strengthened by further data detailing if any of the predictive variables led to earlier detection of bleeding gastrointestinal lesions and if, consequently, this led to improved patient outcomes. However, the findings of this study provide potentially valuable information for the early detection of occult gastrointestinal bleeding, as well as a foundation for further study into the practical value of such predictive factors.

Clinical Application

Mr. Davis presented with stroke-like symptoms and no findings suggestive of gastrointestinal bleeding. Throughout his hospital course, Mr. Davis never developed gastrointestinal symptoms or any signs of bleeding such as melena, hematuria, or hematemesis. Suspicion was raised for gastrointestinal bleeding was raised when his hemoglobin fell to 7 g/dL; however, before FOBT could be completed, the ulcer had ruptured, and he had already developed precipitous bleeding. As a 64-year-old with a history of chronic aspirin use and a hemoglobin below 9 g/dL, Mr. Davis fit three of the criteria shown to predict a bleeding lesion elucidated in the paper by Majid et al., and it is possible that if his MCV were not obscured by macrocytosis from his folate deficiency that he may have also met the MCV criterion. It is likely that use of these predictive factors may have led to an earlier diagnosis and ultimately reduced the likelihood that he would have developed profuse hemorrhage.

Mr. Davis’s social determinants of health also likely contributed to the difficulty in detecting the bleeding ulcer. His history of alcohol use disorder was determined to be the source of his folate deficiency, which obscured the possibility of upper gastrointestinal bleeding, and the alcohol itself may have contributed to the formation of the ulcer that ultimately ruptured. Mr. Davis was unemployed, living alone, and had minimal community interaction, all of which suggest he had minimal, if any, social support. Unfortunately, the lack of social support likely contributed to the severity of his alcohol use disorder, which was the precipitating factor for his subsequent hemorrhage. Mr. Davis also mentioned that he “had a hard time getting to appointments,” due to both his
financial limitations and impaired mobility from his previous stroke, which may have resulted in inadequate follow-up for his aspirin therapy and possibly missing the opportunity to identify him as a bleeding risk at an earlier stage of the disease. It is also possible that Mr. Davis’s financial status may have influenced the decision to pursue aspirin treatment instead of more expensive, non-NSAID antiplatelet therapy that would have required follow-up appointments to refill.

New Knowledge Related to Clinical Decision Science

This case demonstrates the value of assessing pretest probability when attempting to diagnose difficult to detect conditions such as occult gastrointestinal bleeding, as well as the importance of a thorough history, especially as it relates to the social context of the patient. The selected article by Majid and colleagues identifies several possible factors that, if present, increase the pretest probability of a bleeding gastrointestinal lesion. Such information should be taken into consideration when evaluating an anemic patient, even in the absence of bleeding symptoms. This clinical decision-making report highlights the need for such predictive factors, as the complexity of Mr. Davis’s medical and social histories made identifying the lesion in a timely manner more difficult. The set of criteria to initiate endoscopic evaluation in the absence of gastrointestinal symptoms identified by Majid et al. will be invaluable for the prevention of possibly life-threatening hemorrhage in patients with otherwise low clinical suspicion for gastrointestinal bleeding.

Conflict Of Interest Statement

The author declares no conflicts of interest.

References
