Communication from the ASGE Standards of Practice Committee

GUIDELINE

The role of endoscopy in the management of variceal hemorrhage

This is one of a series of statements discussing the use of GI endoscopy in common clinical situations. The Standards of Practice Committee of the American Society for Gastrointestinal Endoscopy prepared this text. In preparing this document, a search of the medical literature was performed by using PubMed. Additional references were obtained from the bibliographies of the identified articles and from recommendations of expert consultants. When limited or no data exist from well-designed prospective trials, emphasis is given to results from large series and reports from recognized experts. Recommendations for appropriate use of endoscopy are based on a critical review of the available data and expert consensus at the time the guidelines are drafted. Further controlled clinical studies may be needed to clarify aspects of this document. This document may be revised as necessary to account for changes in technology, new data, or other aspects of clinical practice. The recommendations were based on reviewed studies and were graded on the strength of the supporting evidence (Table 1).[1]

This document is intended to be an educational device to provide information that may assist endoscopists in providing care to patients. It is not a rule and should not be construed as establishing a legal standard of care or as encouraging, advocating, requiring, or discouraging any particular treatment. Clinical decisions in any particular case involve a complex analysis of the patient's condition and available courses of action. Therefore, clinical considerations may lead an endoscopist to take a course of action that varies from these recommendations.

Variceal bleeding is a common and serious adverse event of portal hypertension. Mortality after an index hemorrhage in patients with cirrhosis had been previously reported to be as high as 50%, with a 30% mortality rate associated with subsequent bleeding episodes.[2] Although more recent data demonstrate improvement in mortality with the increasing use of vasoactive drugs, endoscopy, and antibiotic prophylaxis, bleeding from esophageal varices is still associated with 20% mortality rate at 6 weeks.[3-6] The optimal management of patients with variceal bleeding requires a multidisciplinary approach by a team that includes gastroenterologists, interventional radiologists, and surgeons. The purpose of this document is to update a previous ASGE Standards of Practice publication providing a practical strategy for the specific use of endoscopy in screening for esophageal and gastric varices, prevention of variceal bleeding, and the management of patients with variceal hemorrhage.[7]

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ESOPHAGEAL VARICES

Screening for esophageal varices

Effective prophylactic treatments exist for patients with esophageal varices to prevent variceal bleeding.[8] There are no reliable methods for predicting which cirrhotic patients will have esophageal varices without endoscopy.[9] The most recent American Association for the Study of Liver Disease (AASLD) and Baveno V consensus guidelines suggest that all patients who have been diagnosed with cirrhosis undergo screening endoscopy to assess for esophageal and gastric varices.[10,11] If esophageal varices are identified on endoscopy, they should be graded as small or large (>5 mm) and the presence of red wales or spots should be noted because these findings have been identified as risk factors for future bleeding.[2,12] The optimal surveillance intervals for esophageal varices have not been determined. For patients with compensated cirrhosis found to have no varices on initial screening endoscopy, repeat endoscopy every 2 to 3 years has been suggested, whereas patients with small varices should undergo repeat endoscopy every 1 to 2 years.[2,13] Esophageal varices may develop faster in patients with cirrhosis secondary to alcohol abuse, decompensated liver disease, and in those with small varices with high-risk stigmata (red wale marks or red spots) on endoscopic examination. This subgroup of patients should undergo yearly upper endoscopy, even when no or only small varices are seen on initial screening.[2,12,13]

Endoscopy and primary prophylaxis

Endoscopy plays an essential role in the management of patients with cirrhosis because it identifies patients who will benefit from primary prophylaxis to prevent initial variceal hemorrhage and helps guide specific therapies. Nonselective β-blockers (eg, propranolol or nadolol) have been shown to prevent or delay the first episode of variceal bleeding in patients found to have large varices and patients who have small varices with advanced liver disease (Child-Pugh class B or C) or the presence of high-risk stigmata on varices.[14-18]

Endoscopic variceal ligation (EVL) is highly effective in eradicating esophageal varices and has been shown

TABLE 1. GRADE system for rating the quality of evidence for guidelines[1]

Quality of evidence	Definition	Symbol
High quality	Further research is very unlikely to change our confidence in the estimate of effect	⊕⊕⊕⊕
Moderate quality	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate	⊕⊕⊕◯
Low quality	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate	⊕⊕◯◯
Very low quality	Any estimate of effect is very uncertain	⊕◯◯◯

Adapted from Guyatt et al.[1]

to be as effective as β-blockers in preventing first variceal hemorrhage in 3 large randomized, controlled trials.[19-21] A single randomized U.S. study in patients with cirrhosis and high-risk esophageal varices demonstrated that propranolol-treated patients had a significantly higher rate of first variceal hemorrhage (12.9% vs 0%, $P = .04$) and cumulative mortality (12.9% vs 0%, $P = .04$) than patients who underwent prophylactic EVL.[22] However, this study was criticized for premature discontinuation because of an interim analysis showing a significantly higher number of treatment failures (variceal bleeding and severe adverse effects) in the propranolol group compared with the EVL group, which limited the follow-up to a median of 18 months.[23] In a meta-analysis of 8 randomized, controlled trials involving 596 patients, EVL compared with β-blockers reduced the rate of first variceal bleed (relative risk [RR], 0.57; 95% CI, 0.38-0.85), although there was no effect on mortality.[24] In this meta-analysis, severe adverse events in the propranolol group were more common than in the EVL group (RR, 0.34; 95% CI, 0.17-0.69); however there were 2 fatalities from ligation-induced ulcer bleeding in the EVL group. A recent Cochrane review comparing EVL with nonselective β-blockers for primary prophylaxis in esophageal varices included 19 randomized trials and demonstrated that EVL reduced variceal bleeding compared with β-blocker therapy (RR, 0.67; 95% CI, 0.53-1.39) with no difference in mortality.[25] Despite the results of these meta-analyses, the consensus of experts is that the 2 treatments are likely to have similar efficacy.[10,11] It is recommended that in most cases, prophylactic EVL be reserved for patients who cannot tolerate or who have contraindications to β-blockers or patients who have large varices with high-risk stigmata or Child-Pugh class B or C cirrhosis.[10,11] In addition, if primary prophylaxis with EVL is performed, it is recommended that β-blocker therapy not be used because combination therapy does not appear to further decrease the risk of initial variceal bleeding or mortality and is associated with increased side effects.

Current guidelines recommend that patients undergoing EVL for primary prophylaxis have repeat endoscopy with EVL every 1 to 2 weeks until documentation of variceal obliteration.[10] However, studies evaluating EVL for primary prophylaxis have used variable intervals for repeat EVL, ranging from 1 to 8 weeks.[19-22,26-28] A randomized, controlled trial of bimonthly versus biweekly EVL in 63 cirrhotic patients for both primary and secondary prophylaxis, the majority of whom were enrolled for primary prophylaxis (87.5% in the biweekly arm, 81% in the bimonthly arm), found that 3 sessions of EVL bimonthly had a higher total eradication rate, lower recurrence rate, and lower rate of additional treatment than 3 sessions of biweekly EVL.[29] Thus, repeat EVL for primary prophylaxis can be safely performed at 1- to 8-week intervals until variceal eradication is achieved. Surveillance EGD should be performed 1 to 3 months after eradication, and every 6 to 12 months thereafter to assess for variceal recurrence.[10,26] If recurrent varices are noted on surveillance examinations, additional attempts at eradication should be undertaken.

A potential adverse event of EVL is ligation-induced ulcers, reported to occur in 0.5% to 3% of cases, and is a major cause of concern when considering EVL for prophylactic therapy.[30,31] Studies of EVL for primary prophylaxis have variably used a proton pump inhibitor (PPI) after EVL, and PPIs can be considered as adjunctive therapy.[22,32]

Endoscopic treatments for acute esophageal variceal hemorrhage

Initial management and therapy before endoscopy. Patients with acute esophageal variceal hemorrhage should be stabilized in an intensive care unit before undergoing endoscopy. Obtaining adequate intravenous (IV) access with cautious blood volume resuscitation should be performed to maintain hemodynamic stability and achieve a hemoglobin concentration of approximately 7 to 8 g/dL.[11] Aggressive resuscitation with blood products and crystalloid should be avoided as it theoretically can increase portal pressures, leading to increased risk of rebleeding and mortality.[33-35] In patients with significant coagulopathy or thrombocytopenia, transfusion of fresh frozen plasma and/or platelets should be considered.

In addition, prophylactic antibiotics (oral or IV quinolone or IV ceftriaxone) should be administered to cirrhotic