

## ASGE Guideline: the role of endoscopy in the management of variceal hemorrhage, updated July 2005

*This is one of a series of statements discussing the utilization of gastrointestinal endoscopy in common clinical situations. The Standards of Practice Committee of the American Society for Gastrointestinal Endoscopy prepared this text. A previous guideline related to this topic (Gastrointest Endosc 2002;56:618-20) was published in 2002. Since that time, new information has become available which requires an update of this statement and its recommendations. In preparing this update, a MEDLINE literature search was performed, and additional references were obtained from the bibliographies of the identified articles and from the recommendations of expert consultants. When inadequate data existed from well-designed prospective trials, emphasis was given to results from large series and reports from recognized experts.*

*Guidelines for appropriate utilization of endoscopy are based on a critical review of the available data and expert consensus. Controlled clinical studies are needed to clarify aspects of this statement, and revision may be necessary as new data appear. Clinical consideration may justify a course of action at variance from these recommendations.*

Variceal bleeding is a common and serious complication of portal hypertension. Mortality after the index hemorrhage in patients with cirrhosis has been reported to be as high as 50%, with a 30% mortality associated with subsequent bleeding episodes.<sup>1</sup> More recent data suggest an overall threefold decrease in in-hospital mortality over the last 2 decades with the increasing use of vasoactive drugs, endoscopy, and antibiotic prophylaxis.<sup>2</sup> The optimal management of patients with variceal bleeding requires a multidisciplinary approach by a team that includes endoscopists, interventional radiologists, and surgeons. The purpose of this guideline is to provide an updated, practical strategy for the specific use of endoscopy in screening for esophageal varices, prevention of the initial bleeding, and the management of patients with variceal hemorrhage.

### SCREENING FOR ESOPHAGEAL VARICES

Effective prophylactic treatments to prevent variceal bleeding exist for patients with esophageal varices.<sup>3</sup> There are no reliable methods of predicting which cirrhotic patients will have esophageal varices without endoscopy.<sup>4</sup> An American Association for the Study of Liver Diseases guideline suggests that patients with Child's stage A liver cirrhosis and signs of portal hypertension, specifically a platelet count of less than 140,000/mm<sup>3</sup>, and/or enlarged portal vein diameter of greater than 13 mm or those classified as Child's B or C at diagnosis should have screening endoscopy.<sup>5</sup> Patients with cholestatic disease may have portal hypertension with relatively preserved liver function and platelet counts. A retrospective study of 235 patients concluded that patients with either primary biliary cirrhosis or primary sclerosing cholangitis who have a platelet count <200/mm<sup>3</sup>, an albumin level <40 gm/L, and a bilirubin level >20 μmol/L should be screened for esophageal varices.<sup>6</sup> Other groups recommend screening for all patients diagnosed with cirrhosis.<sup>7</sup> The optimal surveillance intervals for esophageal varices have not been determined. For patients found to have no varices on initial screening endoscopy, repeat endoscopy at 3-year intervals has been suggested, whereas patients with small varices should undergo endoscopy in 1 to 2 years.<sup>7</sup> Esophageal varices may grow faster in patients with cirrhosis secondary to alcohol abuse or severe liver impairment and in those with endoscopic stigmata of high risk ("red wale markings"); this subgroup of patients should undergo yearly upper endoscopy.<sup>8</sup>

### PRIMARY PROPHYLAXIS

Because of the high mortality rate associated with the initial variceal hemorrhage, primary prevention is indicated. Non-selective beta-blockers (e.g., propranolol or nadolol), given in doses to reduce the pulse rate by 25%, have been shown to prevent or delay the first episode of variceal bleeding.<sup>9-12</sup> Early beta-blocker therapy may slow the rate of growth of small esophageal varices.<sup>12</sup>

Endoscopic sclerotherapy (EST) is not recommended for primary prophylaxis.<sup>13,14</sup> While several studies have shown benefit, a well-done US study showed an increased mortality rate in the treated group.<sup>15-19</sup>

Endoscopic variceal ligation (EVL) eradicates esophageal varices with fewer complications than EST<sup>20</sup> and has been shown to be as effective as the use of beta-blockers.<sup>21,22</sup> In one recent randomized US study in patients with cirrhosis and a high risk of esophageal varices, propranolol-treated patients had significantly higher rates of first variceal hemorrhage and cumulative mortality than patients who underwent band ligation.<sup>23</sup> In a meta-analysis of eight randomized controlled trials involving 596 patients, EVL reduced the rate of first variceal bleed by 43% compared with beta-blocker use, although there was no effect on mortality.<sup>24</sup> In this meta-analysis, the occurrence of severe adverse events was significantly lower in the EVL group. There was a small risk of initiating a variceal bleeding episode during prophylactic banding. The superiority of EVL over beta-blocker therapy has been questioned, although the two treatments probably have at least equivalent efficacy.<sup>25</sup> In most cases, it is recommended that prophylactic EVL be reserved for patients who cannot tolerate or have contraindications to beta-blocker use, or in those who do not show a reduction in hepatic vein pressure gradient (HVPG) of >20% or <12 mm Hg.<sup>26</sup>

## ENDOSCOPIC TREATMENTS FOR VARICEAL HEMORRHAGE

### Endoscopic variceal ligation

EVL has become the treatment of choice both for controlling variceal hemorrhage and for variceal obliteration in secondary prophylaxis.<sup>27</sup> The results from six randomized prospective trials that have directly compared EVL and EST<sup>28-33</sup> reported that EVL is superior to EST in eradicating varices more rapidly<sup>29,30,32</sup> with less recurrent bleeding<sup>29,31,32</sup> and fewer complications.<sup>28,30,33</sup> Two of the trials have shown a survival advantage in patients treated with EVL.<sup>28,32</sup> A meta-analysis has confirmed the superiority of EVL over EST for all major outcomes (recurrent bleeding, local complications including ulceration and stricture formation, time to variceal obliteration, and survival).<sup>34</sup> In contrast to EST, EVL appears to rarely induce bacteremia. Although antibiotic prophylaxis is indicated for all patients hospitalized for variceal bleeding, the decision to use antibiotic prophylaxis in high-risk patients solely to prevent the infectious complications of EVL should be individualized.<sup>35,36</sup> Recurrence of esophageal varices may develop more frequently in those treated with EVL,<sup>33</sup> and regular endoscopic surveillance remains a critical aspect of management. EVL may be more difficult to use than EST in the presence of active bleeding because of poor visibility or operator inexperience.<sup>37</sup> The introduction of multiple-band firing devices<sup>38,39</sup> has made EVL more widely acceptable and it is favored by many over EST for eradication of esophageal varices. Concomitant treatment with a beta-blocker should be considered as this has been reported to further decrease the rate of

rebleeding from 38% to 14% ( $p = 0.006$ ).<sup>40</sup> The combination of EST and EVL does not appear to be better than EVL alone.<sup>41</sup>

### Endoscopic sclerotherapy

EST is successful in controlling active bleeding in over 90% of patients<sup>42</sup> and can reduce the frequency and severity of recurrent variceal hemorrhage.<sup>43</sup> Gastric varices in continuity with esophageal varices may be treated with EST below the esophagogastric junction. Isolated gastric varices are less amenable to EST. Sclerotherapy may be performed by intravariceal or paravariceal injection of a sclerosant. Several agents (sodium tetradecyl sulfate, sodium morrhuate, ethanolamine oleate, polidocanol, and ethanol) have been used at varying concentrations, volumes, and treatment intervals. More frequent treatments achieve more rapid variceal obliteration than less frequent treatments, but are associated with greater mucosal ulceration.<sup>44-46</sup> Complications of EST include fever, retrosternal discomfort or pain, dysphagia, injection-induced bleeding, esophageal ulceration with delayed bleeding, esophageal perforation, mediastinitis, pleural effusion, bronchoesophageal fistula, adult respiratory distress syndrome, and infectious complications.<sup>47,48</sup> Dysphagia appears to be proportional to the volume of sclerosant used. EST-induced strictures usually respond to dilation.<sup>49,50</sup> Patients with a mechanical prosthetic cardiac valve, a history of endocarditis, a surgically created systemic-pulmonary shunt, or a synthetic vascular graft (placed within the previous year) should receive antibiotic prophylaxis before the procedure. In patients with ascites, antibiotic prophylaxis should also be considered.<sup>36</sup>

## GASTRIC VARICES

Gastric varices are most commonly located in the cardia in continuity with esophageal varices. Isolated gastric varices are most commonly located in the fundus and can be seen in patients with cirrhosis and portal hypertension, as well as in patients with splenic vein thrombosis (e.g., from pancreatic disease) or portal vein thrombosis. Bleeding from gastric varices is typically high volume in nature and can present with massive hematemesis.

In general, endoscopic therapy for the treatment of bleeding gastric varices has been less successful than for esophageal varices. Treatment options that have been studied in prospective trials include injection of cyanoacrylate-based tissue adhesives, alcohol, sclerosants, and the use of band ligation.<sup>51-55</sup> Results from this limited number of small studies have had varying success rates and were uncontrolled, making it difficult to draw definitive conclusions about their efficacy or the superiority of one therapy over another. All techniques appear to be useful, but rebleeding and mortality rates in these studies were high. There are insufficient data to recommend

**TABLE 1. Summary of recommendations for the use of endoscopy in the management of variceal hemorrhage**

| Clinical situation   |  | Management   |
|--|--|--|
| No prior variceal bleeding   |  |  |
| Established cirrhosis, especially in patients with platelet counts $< 140,000/\text{mm}^3$ , or Child's class B or C disease | Perform screening EGD  | Large varices/endoscopic stigmata: treat with beta-blocker; perform EVL if patient is intolerant or has contraindications to beta-blocker use<br><br>Small varices: repeat EGD every 1-2 yrs<br><br>No varices: repeat EGD every 3 yrs |
| Current or prior variceal bleeding from esophageal varices   |  |  |
| Perform EVL  | Repeat every 2-4 weeks until varices are eradicated; perform EST if EVL fails; consider beta-blocker use | Following eradication: perform EGD every 6-12 months; repeat EVL (or EST) if varices recur   |
| Current variceal bleeding from gastric varices   |  |  |
| Attempt endoscopic therapy using cyanoacrylate compounds, sclerotherapy, or EVL with or without detachable snares            |  |  |
| Primary or secondary prophylaxis of gastric varices  |  |  |
| Insufficient data to recommend endoscopic therapy  |  |  |

repeat endoscopic procedures to achieve obliteration or secondary prophylaxis of isolated gastric varices.

Several retrospective analyses of these techniques, as well as on the use of injected fibrin glue, have been performed.<sup>56-64</sup> Clinical success in these studies typically has been higher than in prospective studies, with hemostasis rates ranging from 60% to 100%. Cyanoacrylate-based compounds have not been approved by the Food and Drug Administration for use in the US. Injection of cyanoacrylate-based compounds is associated with the development of bacteremia, and thus antibiotic prophylaxis should be considered in high-risk patients.<sup>65</sup>

## SUMMARY

For the following points: (A), prospective controlled trials; (B), observational studies; (C), expert opinion. (Table 1).

- Bleeding from esophageal or gastric varices is a common cause of morbidity and mortality in patients with portal hypertension (B).
- Patients with cirrhosis and portal hypertension but no prior variceal hemorrhage (especially those with platelet counts  $< 140,000/\text{mm}^3$ , or Child's Class B or C) should undergo screening EGD (B) and treatment with a beta-blocker if large varices are found (A).
- EVL is effective for primary prophylaxis (A), but in most cases it should be reserved for patients who cannot tolerate or who have contraindications to beta-blocker therapy (C).
- Patients with small varices on screening EGD should undergo a repeat procedure every 1 or 2 years, and

those without varices should repeat the EGD every 3 years (C).

- In patients with current or prior bleeding from esophageal varices, EVL is the preferred endoscopic treatment and is superior to EST (A).
- Following an episode of bleeding from esophageal varices, EVL should be performed every 2 to 4 weeks until the varices are eradicated (C). Concomitant beta-blocker therapy should be considered (A).
- Following variceal eradication, EGD should be repeated every 6 to 12 months and recurrent varices should be treated with EVL (C).
- EST should be reserved for patients who fail EVL (C).
- Although endoscopic therapy for actively bleeding isolated gastric varices may be effective, there are insufficient data to recommend a specific type of endoscopic treatment in this setting (C).
- There are not sufficient data to recommend endoscopy for obliteration or as primary or secondary prophylaxis of isolated gastric varices (C).

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