



## Complete Summary

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### GUIDELINE TITLE

Prevention and management of gastroesophageal varices and variceal hemorrhage in cirrhosis.

### BIBLIOGRAPHIC SOURCE(S)

Garcia-Tsao G, Sanyal AJ, Grace ND, Carey W, Practice Guidelines Committee of the American Association for the Study of Liver Diseases, Practice Parameters Committee of the American College of Gastroenterology. Prevention and management of gastroesophageal varices and variceal hemorrhage in cirrhosis. *Hepatology* 2007;46(3):922-38. [135 references]

### GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Grace ND. Diagnosis and treatment of gastrointestinal bleeding secondary to portal hypertension. *Am J Gastroenterol* 1997;92:1081-1091.

### \*\* REGULATORY ALERT \*\*

### FDA WARNING/REGULATORY ALERT

**Note from the National Guideline Clearinghouse (NGC):** This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- [July 08, 2008, Fluoroquinolones \(ciprofloxacin, norfloxacin, ofloxacin, levofloxacin, moxifloxacin, gemifloxacin\)](#): A BOXED WARNING and Medication Guide are to be added to the prescribing information to strengthen existing warnings about the increased risk of developing tendinitis and tendon rupture in patients taking fluoroquinolones for systemic use.

### COMPLETE SUMMARY CONTENT

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## SCOPE

### **DISEASE/CONDITION(S)**

Gastroesophageal varices and variceal hemorrhage in cirrhosis

### **GUIDELINE CATEGORY**

Diagnosis  
Management  
Prevention  
Treatment

### **CLINICAL SPECIALTY**

Gastroenterology  
Internal Medicine

### **INTENDED USERS**

Advanced Practice Nurses  
Physician Assistants  
Physicians

### **GUIDELINE OBJECTIVE(S)**

To provide a data-supported approach to the management of patients with gastroesophageal varices and variceal hemorrhage

### **TARGET POPULATION**

Patients with cirrhosis and portal hypertension who have or who are at risk of developing gastroesophageal varices

### **INTERVENTIONS AND PRACTICES CONSIDERED**

1. Esophagogastroduodenoscopy (EGD)
2. Grading of varices
3. Non-selective beta-blockers (propranolol, nadolol) for prevention of variceal hemorrhage
4. Endoscopic variceal ligation (EVL)
5. Intravascular volume support and blood transfusion for acute gastrointestinal (GI) hemorrhage

6. Antibiotic prophylaxis (oral norfloxacin, intravenous ciprofloxacin, intravenous ceftriaxone) in patients with GI hemorrhage
7. Pharmacological therapy (somatostatin, octreotide, vapreotide, terlipressin) for variceal hemorrhage
8. EGD with EVL or sclerotherapy for treating hemorrhage
9. Transjugular intrahepatic portosystemic shunt (TIPS)
10. Balloon tamponade in patients with uncontrollable bleeding
11. Endoscopic variceal obturation for gastric varices using tissue adhesives such as cyanoacrylate
12. Secondary prophylaxis to prevent recurrence of variceal hemorrhage
  - Beta-blocker plus EVL
  - TIPS
  - Surgical shunt
13. Referral for transplant

The following interventions were considered but not recommended: non-selective beta-blockers for the prevention of varices; nitrates (alone or in combination with beta-blockers), shunt therapy, and sclerotherapy for primary prophylaxis of variceal hemorrhage.

#### **MAJOR OUTCOMES CONSIDERED**

- Incidence of variceal hemorrhage
- Portal in-flow, portal resistance, and portal pressure
- Cost-effectiveness of treatment
- Side effects of treatment

## **METHODOLOGY**

#### **METHODS USED TO COLLECT/SELECT EVIDENCE**

Hand-searches of Published Literature (Primary Sources)  
 Hand-searches of Published Literature (Secondary Sources)  
 Searches of Electronic Databases

#### **DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE**

These recommendations are based on the following: (1) formal review and analysis of the recently published world literature on the topic (Medline search); (2) several consensus conferences among experts; (3) the American College of Physicians' Manual for Assessing Health Practices and Designing Practice Guidelines; (4) guideline policies, including the American Association for the Study of Liver Diseases' Policy Statement on Development and Use of Practice Guidelines and the American Gastroenterological Association's Policy Statement on the Use of Medical Practice Guidelines; and (5) the authors' years of experience caring for patients with cirrhosis and varices.

#### **NUMBER OF SOURCE DOCUMENTS**

Not stated

## **METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE**

Weighting According to a Rating Scheme (Scheme Given)

## **RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE**

### **Level of Evidence**

**Level A:** Data derived from multiple randomized clinical trials or meta-analyses.

**Level B:** Data derived from a single randomized trial, or nonrandomized studies.

**Level C:** Only consensus opinion of experts, case studies, or standard-of-care.

## **METHODS USED TO ANALYZE THE EVIDENCE**

Review of Published Meta-Analyses  
Systematic Review

## **DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE**

Not stated

## **METHODS USED TO FORMULATE THE RECOMMENDATIONS**

Expert Consensus

## **DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS**

Practice guidelines for the diagnosis and treatment of gastroesophageal variceal hemorrhage, endorsed by the American Association for the Study of Liver Diseases (AASLD), American College of Gastroenterology (ACG), American Gastroenterological Association (AGA), and American Society of Gastrointestinal Endoscopy (ASGE), were published in 1997. Since then, a number of randomized controlled trials have advanced the approach to managing variceal hemorrhage. Three international consensus conferences have been held (Baveno III in 2000, Baveno IV in 2005, and an AASLD/European Association for the Study of Liver Disease (EASL) single topic conference in 2007) in which experts in the field have evaluated the changes that have occurred in the understanding of the pathophysiology and management of gastroesophageal hemorrhage. In this updated practice guideline the authors have reviewed the randomized controlled trials and meta-analyses published in the last decade and have incorporated recommendations made by consensus.

## **RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS**

### **Grading System for Recommendations**

**Class I:** Conditions for which there is evidence and/or general agreement that a given diagnostic evaluation, procedure or treatment is beneficial, useful, and effective.

**Class II:** Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a diagnostic evaluation, procedure or treatment.

**Class IIa:** Weight of evidence/opinion is in favor of usefulness/efficacy.

**Class IIb:** Usefulness/efficacy is less well established by evidence/opinion.

**Class III:** Conditions for which there is evidence and/or general agreement that a diagnostic evaluation/procedure/treatment is not useful/effective and in some cases may be harmful.

## **COST ANALYSIS**

The following cost information is provided:

- Cost-effective analyses using Markov models have suggested either empiric beta-blocker therapy for all patients with cirrhosis or screening endoscopy for patients with compensated cirrhosis, and universal beta-blocker therapy without screening esophagogastroduodenoscopy (EGD) for patients with decompensated cirrhosis. Neither of these strategies considers a recent trial showing that beta-blockers do not prevent the development of varices and are associated with significant side effects, nor do they consider endoscopic variceal ligation as an alternative prophylactic therapy. Until prospective studies validate these approaches, screening EGD is still the recommended approach.
- A cost-effectiveness study comparing nonselective beta-blockers, sclerotherapy, and shunt surgery shows that beta-blockers were the only cost-effective form of prophylactic therapy.
- A recent trial showed that, even though pharmacological (propranolol plus nitrates) therapy was less effective than transjugular intrahepatic portosystemic shunt (TIPS) in preventing rebleeding, it was associated with less encephalopathy, identical survival, and more frequent improvement in Child-Pugh class with lower costs than TIPS. Therefore, TIPS should not be used as a first-line treatment, but as a rescue therapy for patients who have failed pharmacological plus endoscopic treatment.

## **METHOD OF GUIDELINE VALIDATION**

Peer Review

## **DESCRIPTION OF METHOD OF GUIDELINE VALIDATION**

This guideline was produced in collaboration with the Practice Guidelines Committee of the American Association for the Study of Liver Diseases and the Practice Parameters Committee of the American College of Gastroenterology. These committees provided extensive peer review of the manuscript.

## RECOMMENDATIONS

### MAJOR RECOMMENDATIONS

The class of recommendations (I, II, IIa, IIb, III) and the levels of evidence (A–C) are defined at the end of the "Major Recommendations."

#### Diagnosis of Varices and Variceal Hemorrhage

1. Screening esophagogastroduodenoscopy (EGD) for the diagnosis of esophageal and gastric varices is recommended when the diagnosis of cirrhosis is made (**Class IIa, Level C**).
2. On EGD, esophageal varices should be graded as small or large (>5 mm) with the latter classification encompassing medium-sized varices when 3 grades are used (small, medium, large). The presence or absence of red signs (red wale marks or red spots) on varices should be noted (**Class IIa, Level C**).

#### Management Recommendations

##### Patients with Cirrhosis and No Varices

3. In patients with cirrhosis who do not have varices, nonselective beta-blockers cannot be recommended to prevent their development (**Class III, Level B**).
4. In patients who have compensated cirrhosis and no varices on the initial EGD, it should be repeated in 3 years (**Class I, Level C**). If there is evidence of hepatic decompensation, EGD should be done at that time and repeated annually (**Class I, Level C**).

##### Patients with Cirrhosis and Small Varices That Have Not Bled

5. In patients with cirrhosis and small varices that have not bled but have criteria for increased risk of hemorrhage (Child B/C [see Table 2 in the original guideline document for Child-Pugh classification of the severity of cirrhosis] or presence of red wale marks on varices), nonselective beta-blockers should be used for the prevention of first variceal hemorrhage (**Class IIa, Level C**).
6. In patients with cirrhosis and small varices that have not bled and have no criteria for increased risk of bleeding, beta-blockers can be used, although their long-term benefit has not been established (**Class III, Level B**).
7. In patients with small varices that have not bled and who are not receiving beta-blockers, EGD should be repeated in 2 years (**Class I, Level C**). If there is evidence of hepatic decompensation, EGD should be done at that time and repeated annually (**Class I, Level C**). In patients with small varices who receive beta-blockers, a follow-up EGD is not necessary.

##### Patients with Cirrhosis and Medium/Large Varices That Have Not Bled

8. In patients with medium/large varices that have not bled but have a high risk of hemorrhage (Child B/C [see Table 2 in the original guideline document] or variceal red wale markings on endoscopy), nonselective beta-blockers

- (propranolol or nadolol) or EVL may be recommended for the prevention of first variceal hemorrhage (**Class I, Level A**).
9. In patients with medium/large varices that have not bled and are not at the highest risk of hemorrhage (Child A patients [see Table 2 in the original guideline document] and no red signs), nonselective beta-blockers (propranolol, nadolol) are preferred and EVL should be considered in patients with contraindications or intolerance or non-compliance to beta-blockers (**Class I, Level A**).
  10. If a patient is placed on a nonselective beta-blocker, it should be adjusted to the maximal tolerated dose; follow-up surveillance EGD is unnecessary. If a patient is treated with EVL, it should be repeated every 1-2 weeks until obliteration with the first surveillance EGD performed 1 to 3 months after obliteration and then every 6 to 12 months to check for variceal recurrence (**Class I, Level C**).
  11. Nitrates (either alone or in combination with beta-blockers), shunt therapy, or sclerotherapy should not be used in the primary prophylaxis of variceal hemorrhage (**Class III, Level A**).

### **Patients with Cirrhosis and an Acute Episode of Variceal Hemorrhage**

12. Acute gastrointestinal (GI) hemorrhage in a patient with cirrhosis is an emergency that requires prompt attention with intravascular volume support and blood transfusions, being careful to maintain a hemoglobin of ~8 g/dL (**Class I, Level B**).
13. Short-term (maximum 7 days) antibiotic prophylaxis should be instituted in any patient with cirrhosis and GI hemorrhage (**Class I, Level A**). Oral norfloxacin (400 mg twice a day [BID]) or intravenous ciprofloxacin (in patients in whom oral administration is not possible) is the recommended antibiotic (**Class I, Level A**). In patients with advanced cirrhosis intravenous ceftriaxone (1 g/day) may be preferable particularly in centers with a high prevalence of quinolone-resistant organisms (**Class I, Level B**).
14. Pharmacological therapy (somatostatin or its analogues octreotide and vapreotide; terlipressin) should be initiated as soon as variceal hemorrhage is suspected and continued for 3 to 5 days after diagnosis is confirmed (**Class I, Level A**).
15. EGD, performed within 12 hours, should be used to make the diagnosis and to treat variceal hemorrhage, either with EVL or sclerotherapy (**Class I, Level A**).
16. Transjugular intrahepatic portosystemic shunt (TIPS) is indicated in patients in whom hemorrhage from esophageal varices cannot be controlled or in whom bleeding recurs despite combined pharmacological and endoscopic therapy (**Class I, Level C**).
17. Balloon tamponade should be used as a temporizing measure (maximum 24 hours) in patients with uncontrollable bleeding for whom a more definitive therapy (e.g., TIPS or endoscopic therapy) is planned (**Class I, Level B**).

### **Gastric Varices**

18. In patients who bleed from gastric fundal varices, endoscopic variceal obturation using tissue adhesives such as cyanoacrylate is preferred, where available. Otherwise, EVL is an option (**Class I, Level B**).

19. A TIPS should be considered in patients in whom hemorrhage from fundal varices cannot be controlled or in whom bleeding recurs despite combined pharmacological and endoscopic therapy (**Class I, Level B**).

### **Patients with Cirrhosis Who Have Recovered from Acute Variceal Hemorrhage**

20. Patients with cirrhosis who survive an episode of active variceal hemorrhage should receive therapy to prevent recurrence of variceal hemorrhage (secondary prophylaxis) (**Class I, Level A**).
21. Combination of nonselective beta-blockers plus EVL is the best option for secondary prophylaxis of variceal hemorrhage (**Class I, Level A**).
22. The nonselective beta-blocker should be adjusted to the maximal tolerated dose. EVL should be repeated every 1-2 weeks until obliteration with the first surveillance EGD performed 1 to 3 months after obliteration and then every 6 to 12 months to check for variceal recurrence (**Class I, Level C**).
23. TIPS should be considered in patients who are Child A or B (see Table 2 in the original guideline document) who experience recurrent variceal hemorrhage despite combination pharmacological and endoscopic therapy. In centers where the expertise is available, surgical shunt can be considered in Child A patients (**Class I, Level A**).
24. Patients who are otherwise transplant candidates should be referred to a transplant center for evaluation (**Class I, Level C**).

### **Definitions:**

#### **Level of Evidence**

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#### **Grading System for Recommendations**

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**Class III:** Conditions for which there is evidence and/or general agreement that a diagnostic evaluation/procedure/treatment is not useful/effective and in some cases may be harmful.

## CLINICAL ALGORITHM(S)

None provided

## EVIDENCE SUPPORTING THE RECOMMENDATIONS

### TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is specifically stated for each recommendation (see "Major Recommendations" field).

## BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

### POTENTIAL BENEFITS

Appropriate prevention and management of gastroesophageal varices and variceal hemorrhage in cirrhosis

### POTENTIAL HARMS

- The most common side effects related to beta-blockers in cirrhosis are lightheadedness, fatigue, and shortness of breath.
- Beta-blockers should not be used in the acute setting as they will decrease blood pressure and will blunt a physiologic increase in heart rate associated with bleeding.
- Adverse events reported with endoscopic variceal ligation (EVL) include bleeding from ligation-induced esophageal ulcers and overtube-induced esophageal perforation. This last complication is currently less likely to occur given the use of multi-band ligation devices that minimize the use of overtubes for band placement.

## CONTRAINDICATIONS

### CONTRAINDICATIONS

Relative contraindications to the use of beta-blockers include asthma, insulin-dependent diabetes (with episodes of hypoglycemia), and peripheral vascular disease.

## QUALIFYING STATEMENTS

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Intended for use by healthcare providers, these recommendations suggest preferred approaches to the diagnostic, therapeutic, and preventive aspects of care. As with other practice guidelines, this guideline is not intended to replace clinical judgment but rather to provide general guidelines applicable to the majority of patients. They are intended to be flexible, in contrast to standards of care, which are inflexible policies designed to be followed in every case.

## IMPLEMENTATION OF THE GUIDELINE

### DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

### IMPLEMENTATION TOOLS

Personal Digital Assistant (PDA) Downloads

For information about [availability](#), see the "Availability of Companion Documents" and "Patient Resources" fields below.

## INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

### IOM CARE NEED

Getting Better  
Living with Illness  
Staying Healthy

### IOM DOMAIN

Effectiveness

## IDENTIFYING INFORMATION AND AVAILABILITY

### BIBLIOGRAPHIC SOURCE(S)

Garcia-Tsao G, Sanyal AJ, Grace ND, Carey W, Practice Guidelines Committee of the American Association for the Study of Liver Diseases, Practice Parameters Committee of the American College of Gastroenterology. Prevention and management of gastroesophageal varices and variceal hemorrhage in cirrhosis. *Hepatology* 2007;46(3):922-38. [135 references]

### ADAPTATION

Not applicable: The guideline was not adapted from another source.

### DATE RELEASED

1997 (revised 2007 Sep)

### GUIDELINE DEVELOPER(S)

American Association for the Study of Liver Diseases - Private Nonprofit Research Organization  
American College of Gastroenterology - Medical Specialty Society

## **SOURCE(S) OF FUNDING**

American Association for the Study of Liver Disease

## **GUIDELINE COMMITTEE**

Practice Guidelines Committee of the American Association for the Study of Liver Diseases

Practice Parameters Committee of the American College of Gastroenterology

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## **FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST**

Potential conflict of interest: Nothing to report

## **GUIDELINE STATUS**

This is the current release of the guideline.

This guideline updates a previous version: Grace ND. Diagnosis and treatment of gastrointestinal bleeding secondary to portal hypertension. *Am J Gastroenterol* 1997;92:1081-1091.

## **GUIDELINE AVAILABILITY**

Electronic copies: Available in Portable Document Format (PDF) from the [American Association for the Study of Liver Diseases Web site](#).

Print copies: Available from the American Association for the Study of Liver Diseases, 1729 King Street, Suite 200; Alexandria, VA 22314; Phone: 703-299-9766; Web site: [www.aasld.org](http://www.aasld.org); e-mail: [aasld@aasld.org](mailto:aasld@aasld.org).

## **AVAILABILITY OF COMPANION DOCUMENTS**

This guideline is available as a Personal Digital Assistant (PDA) download via the APPRISOR™ Document Viewer from [www.apprisor.com](http://www.apprisor.com).

## **PATIENT RESOURCES**

None available

## **NGC STATUS**

This summary was completed by ECRI Institute on September 18, 2007. The information was verified by the guideline developer on October 10, 2007. This summary was updated by ECRI Institute on July 28, 2008 following the U.S. Food and Drug Administration advisory on fluoroquinolone antimicrobial drugs.

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