Guidelines in the Management of Upper Gastro-Intestinal Tract Bleeding

The College of Surgeons of Sri Lanka 2007

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Section 1 Introduction

Upper Gastrointestinal Bleeding (UGIB) has a wide spectrum of presentations which range from occult bleeding to massive life threatening haemorrhage leading to circulatory failure. Therefore management priorities would differ depending on the mode of presentation which can be broadly categorized into 3 groups:

1. Occult bleeding
2. Bleeding in trivial amounts
3. Significant bleeding

Occult bleeding will essentially present with signs and symptoms of anaemia or be detected by screening and will not be discussed in these guidelines.

Trivial UGIB is a warning symptom of underlying pathology. These patients should be investigated to identify the source and the cause of bleeding. Definitive management of these patients would depend on the cause of bleeding. Recommendations for initial management of such patients are given under a separate chapter in the guideline.

Major bleeders are those who need resuscitation, blood transfusions and therapeutic interventions to control bleeding. Management guidelines are mainly aimed at this group of patients.

Evidence for recommendations is given with respective rating whenever evidence is available. (see appendix 1)
Section 2  Level of Care

All patients with UGIB should have access to cost effective evidence based care. Care delivery that can be provided to patients is subjected to limitations depending on the grade of the institution to which the patient initially presents. Sri Lanka has a tiered health care system through which a patient can ascend to a higher level of institution to obtain the services of health care professionals and resources.

There are, however, a few major drawbacks in this system.

(1) Inappropriate referrals
This leads to overloading of tertiary care hospitals by patients who can be managed at the primary care level. On the other hand, patients who need comprehensive care may not be referred promptly.

(2) Delay in the process of referral

(3) Poor communication between centres

(4) Lack of proper grading of institutions based on the resources available

(5) Poor maintenance of available resources

One of the aims of this guideline is to rectify some of these limitations and to provide a practical approach to promote the implementation of cost-effective evidence-based care in settings between which resources vary widely.

The approach adopted has been to advice on two levels of care:

1) Primary care
Management of a patient with UGIB who presents to a health centre until the patient is prioritised and standard care arranged. The essential components at this level include initial treatment
with or without resuscitation, clinical assessment and prioritisation, and referral for standard care.

2) Comprehensive care

This form of care is required for patients who present with significant bleeding and those who need investigations for diagnosis. In order to achieve these goals one needs endoscopic facilities, blood transfusion services, and surgical care services. Patients should be prioritised based on the need for:

<table>
<thead>
<tr>
<th>PRIORITY</th>
<th>A - Emergency transfer</th>
<th>B - Early referral</th>
<th>C - Routine referral</th>
</tr>
</thead>
<tbody>
<tr>
<td>P A</td>
<td>Unstable patients with major bleeding who may need blood transfusions and emergency therapeutic interventions. (Endoscopy/ Surgery) These patients may be transferred to specialised centres on an emergency basis after communication.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>P B</td>
<td>Stable patients who need expert opinion and early treatment. However these patients should be referred after communicating with the tertiary care centre, preferably during day time.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>P C</td>
<td>Need endoscopy and other specialized investigations to arrive at a definite diagnosis. These patients could be referred to specialized clinics.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Section 3 Delivery of Care

All patients with major bleeding should be managed in an institution with appropriate resources. Following is a useful protocol for such patients. Details are discussed in relevant chapters.

(1) Clinical assessment
(2) Resuscitation
(3) Risk categorization.
(4) Basic investigations
(5) Specialized investigations
(6) Therapeutic interventions
(7) Follow up
(8) Rehabilitation
Section 4 Clinical Assessment

Presentations and differential diagnosis

UGIB is defined as bleeding derived from a source proximal to the ligament of Treitz. Haematemesis and melaena are the most common presentations of acute UGIB, and patients may present with either one, or both symptoms. Occasionally, a brisk UGIB manifests as haematochezia.

A complete history should be obtained from all patients with UGIB along with full physical examination in order to:
- Assess severity of bleeding – see page 12
- Do a risk assessment
- Diagnose the pathology.

A meta-analysis documented the incidence of presenting symptoms in patients with UGIB as follows. (1)

**History and physical examination findings in acute UGIB at presentation**
- Haematemesis 40-50%
- Melaena 70-80%
- Haematochezia 15-20%
- Either haematochezia or melaena 90-98%
- Syncope 14.4%
- Presyncope 43.2%
- Symptoms 30 days prior to admission No percentages available
- Dyspepsia - 18%
- Epigastric pain - 41%
- Heartburn - 21%
- Diffuse abdominal pain - 10%
- Dysphagia - 5%
- Weight loss - 12%
• Jaundice - 5.2%

These clinical signs may also be indicators of the potential source of the GI bleeding, as noted in the following table (1).

**Table 1.** Probable Source of bleeding within the gut

<table>
<thead>
<tr>
<th>Clinical Indicator</th>
<th>Probability of Upper GI Source</th>
<th>Probability of Lower GI Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hematemesis</td>
<td>Almost certain</td>
<td>Rare</td>
</tr>
<tr>
<td>Melena</td>
<td>Probable</td>
<td>Possible</td>
</tr>
<tr>
<td>Hematochezia</td>
<td>Possible</td>
<td>Probable</td>
</tr>
<tr>
<td>Blood-streaked stool</td>
<td>Rare</td>
<td>Almost certain</td>
</tr>
<tr>
<td>Occult blood in stool</td>
<td>Possible</td>
<td>Possible</td>
</tr>
</tbody>
</table>

**Differential Diagnosis for UGIB**

- Gastric ulcer
- Duodenal ulcer
- Oesophageal varices or Gastric varices
- Mallory-Weiss tear
- Oesophagitis
- Neoplasm
- Haemorrhagic gastritis
- Dieulafoy lesion
- Angiodysplasia
- Haemobilia
- Pancreatic pseudocyst
- Pancreatic pseudoaneurysm
• Aorto-enteric fistula

The above sources of UGIB are broadly divided into two categories:-

1. Variceal bleeding

2. Non-variceal bleeding
Section 5 Resuscitation

5.1 Airway

Prevent aspiration: Use an NG tube if copious vomiting

Semiconscious and unconscious patients need securing of airway: Consider-
- Left lateral. Position (X)
- Oro-pharyngeal airway (X)
- Endo-tracheal tube

Monitoring adequacy of respiration
- Pulse oxymeter (Y)
- Blood gas analysis(Y)

5.2 Circulation

Intravenous access-Preferably two large bone (14 G) cannulae (X)

Rapid infusion of Fluid
- Crystalloids (Normal saline/ Hartman’s)
- Colloids
- Blood transfusion – when available

Monitor adequacy of resuscitation
- Pulse rate (should come down with resuscitation)
- Blood Pressure (should increase)
- Urine output
- CVP if available (useful in patients with cardiovascular and renal co-morbidity)

**Aims**

- Euvolaemic resuscitation
  (Guided by urine output – maintain 0.5 to 1 ml/kg/hr)

In most patients 1-2 litres of saline will correct volume losses. If, after this, the patient remains shocked, plasma expanders are needed as at least 20% of the blood volume has been lost.

Adequately resuscitated patients have a urine output of more than 30 ml/h and a central venous pressure of 5-10 cm H₂O.

**Transfuse blood (as red cell concentrate) when**

- a) Bleeding is extreme, as judged by active haematemesis and/or haematemesis with or without shock. (O negative blood can be given in extreme circumstances)

- b) When the haemoglobin concentration is less than 80 g/l

Although it is reasonable to avoid blood transfusion at this level in patients who have chronic anaemia for those who present with acute bleeding this haemoglobin concentration is an indication for blood transfusion.
**Table 2** Estimated Fluid and Blood Losses in Shock

<table>
<thead>
<tr>
<th></th>
<th>Class I</th>
<th>Class 2</th>
<th>Class 3</th>
<th>Class 4</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Blood Loss, ml</strong></td>
<td>Up to 750</td>
<td>750-1500</td>
<td>1500-2000</td>
<td>&gt;2000</td>
</tr>
<tr>
<td><strong>Blood Loss,% blood volume</strong></td>
<td>Up to 15%</td>
<td>15-30%</td>
<td>30-40%</td>
<td>&gt;40%</td>
</tr>
<tr>
<td><strong>Pulse Rate, beats per min</strong></td>
<td>&lt;100</td>
<td>&gt;100</td>
<td>&gt;120</td>
<td>&gt;140</td>
</tr>
<tr>
<td><strong>Blood Pressure</strong></td>
<td>Normal</td>
<td>Normal</td>
<td>Decreased</td>
<td>Decreased</td>
</tr>
<tr>
<td><strong>Respiratory Rate</strong></td>
<td>Normal or Increased</td>
<td>Decreased</td>
<td>Decreased</td>
<td>Decreased</td>
</tr>
<tr>
<td><strong>CNS (Mental Status)</strong></td>
<td>Slightly anxious</td>
<td>Mildly anxious</td>
<td>Anxious, confused</td>
<td>Confused, lethargic</td>
</tr>
<tr>
<td><strong>Fluid Replacement, 3-for-1 rule</strong></td>
<td>Crystallloid</td>
<td>Crystallloid</td>
<td>Crystallloid and blood</td>
<td>Crystallloid and blood</td>
</tr>
</tbody>
</table>
Section 6 Investigations

1. **Laboratory studies**
   - Cross match of blood
   - Hb & PCV
   - WBC, Platelets
   - PT
   - Urea/electrolytes
   - Liver enzymes (ALT, AST, ALP, GGT)

2. **Endoscopy**
   Two major categories of UGIB are differentiated by early endoscopy.
   - Variceal bleeding
   - Non-variceal bleeding

3. **Special investigations**
   Highly specialised investigations beyond endoscopy are required rarely and patients needing such investigation can be referred to tertiary care centres as routine cases.

Examples of such patients include those patients diagnosed as, or suspected of having:
- Malignancy
- Multiple Endocrine Neoplasia Syndrome
- Pre and post sinusoidal portal hypertension
- Haemobilia
- Bleeding from the pancreatic duct
- Bleeding from an unidentified source
- Coagulopathy
Section 7 Management of Non-variceal bleeding

7.1 Risk categorization

Assessment of severity of bleeding
Severity of bleeding can be assessed clinically and an estimate of the amount of blood that has been lost at the time of admission made. (see Table 2)

Risk categorization
It is essential to categorise patients at the time of admission into high or low risk of death. Rockall et al defined independent risk factors which were subsequently shown to accurately predict death (4)(grade A). Clinical features associated with a high risk of recurrent bleeding, need for surgery, and increased mortality are listed below.

Clinical risk factors for poor outcomes (3)
- Older age (>60 years)
- Severe co morbidity
- Active bleeding (witnessed haematemesis, red blood per nasogastric tube, haematochezia)
- Hypotension or shock
- Red blood cell transfusion >6 units
- Inpatient status at time of bleed
- Severe coagulopathy
*Recurrent bleeding, need for endoscopic haemostasis or surgery, or mortality.

7.2 Endoscopic management of Non-variceal bleeding

Risk categorization / Prognostication of Non-variceal bleeding by endoscopy
- low risk
7.2.1 Early endoscopy (within the first 24 hours) with risk classification by clinical and endoscopic criteria allows for:

1. Safe and prompt discharge of patients categorized as low risk: 
   Recommendation: A; Evidence: I)

2. Improves patient outcomes for patients classified as high risk 
   (Recommendation: C; Evidence: II-2);

3. Reduces resource utilization for patients classified as either low or 
   high risk (Recommendation: A; Evidence: I).

4. Cost reduction (evidence 7.2.1 section 9)

7.2.2 Endoscopic findings: (5, 6.)
Low risk of rebleeding and death (Recommendation A)
- Normal upper gastrointestinal endoscopy
- Mallory Weiss tear
- ulcer with a clean base

In contrast, active bleeding from a peptic ulcer in a shocked patient carried an 80% risk of continuing bleeding or of death 
(7) (Recommendation A). A non-bleeding visible vessel is 
associated with a 43% risk of rebleeding in hospital (7, 8) 
(Recommendation A). These risk factors are shown in table 3.

Patients with liver disease are special cases and separate 
guidelines are required for their management. Their prognosis 
is related to the severity of liver disease rather than to the 
magnitude of haemorrhage.
**Table 3: Ulcer Characteristics and Correlations (10)**

<table>
<thead>
<tr>
<th>Ulcer Characteristics</th>
<th>Prevalence Rate, %</th>
<th>Rebleeding Rate, %</th>
<th>Surgery Rate, %</th>
<th>Mortality Rate, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clean base</td>
<td>42</td>
<td>5</td>
<td>0.5</td>
<td>2</td>
</tr>
<tr>
<td>Flat spot</td>
<td>20</td>
<td>10</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>Adherent clot</td>
<td>17</td>
<td>22</td>
<td>10</td>
<td>7</td>
</tr>
<tr>
<td>Visible vessel</td>
<td>17</td>
<td>43</td>
<td>34</td>
<td>11</td>
</tr>
<tr>
<td>Active bleeding</td>
<td>18</td>
<td>55</td>
<td>35</td>
<td>11</td>
</tr>
</tbody>
</table>

**Low risk group**

A finding of low-risk endoscopic stigmata (a clean-based ulcer or a flat spot in an ulcer) is **not an indication** for endoscopic haemostatic therapy. (Recommendation A) (Evidence 1 in section 9)

**High risk group**

A finding of a clot in an ulcer bed warrants targeted irrigation in an attempt at dislodgment, with appropriate treatment of the underlying lesion. A finding of high risk endoscopic stigmata (active bleeding or a visible vessel in an ulcer bed) is **an indication** for immediate endoscopic haemostatic therapy (Recommendation A)

**Endoscopic therapeutic options available for peptic ulcers**

A range of endoscopic treatments are available for treating patients who have major stigmata of recent haemorrhage. A meta-analysis of trials showed that endoscopic therapy reduced
rebleeding, need for surgical intervention, and mortality (Recommendation A). Endoscopic therapies can be classified as those based on injection, application of heat, or mechanical clips.

(i) Injection
A disposable injection needle is used to inject a 1:10 000 adrenaline solution in normal saline. Injection is undertaken in quadrants around the bleeding point, then into the bleeding vessel using a total of 4-16 ml. This approach will achieve primary haemostasis in up to 95% of patients although bleeding will recur in 15—20% of these (Recommendation A).

(Evidence 2 in chapter 9)

(ii) Application of heat.
Thermal haemostasis is achieved using either the heater probe or multipolar coagulation. The heater probe is applied at settings of 20—30 joules repeatedly until haemostasis is achieved and a blackened area is formed. Haemostasis is achieved by a combination of pressure (tamponade) and heat application and is as effective as adrenaline injection.
(Recommendation A).

(Evidence 3 in section 9)

(iii) Mechanical clips. Mechanical clips can be applied to bleeding points in clinical trials these perform well (Recommendation B). Clips are particularly useful for actively bleeding large vessels but may be difficult to apply to awkwardly placed ulcers. The placement of clips is a promising endoscopic haemostatic therapy for high-risk stigmata.
(Evidence 4 in section 9)
B. Other Conditions

**Mallory Weiss tears.** These almost always stop bleeding spontaneously but occasional endoscopic therapy is needed to arrest severe haemorrhage. Endoscopic injection using adrenaline or thermal methods are almost always effective (Recommendation C).

**Vascular malformations:** (including telangiectasia and gastric antral vascular ectasia.) These are probably best treated by application of heat using the Argon Plasma Coagulator or heater probe (Recommendation B). Multiple sessions may be required before complete haemostasis is achieved.

**Dieulafoi lesion** is often difficult both to diagnose and treat. A range of therapeutic endoscopic modalities have been examined but no comparisons have been published. Uncontrolled series report success with band ligation, injection, and thermal methods (Recommendation C).

**Drug Therapy in Non-variceal Bleeding**

1. H2 receptor antagonist are not recommended in acute Upper GI bleeding. (Evidence 5 in section 9)

2. Proton-pump inhibitors – IV bolus and infusion

   An intravenous bolus followed by continuous-infusion proton-pump inhibitor is effective in decreasing rebleeding in patients who have undergone successful endoscopic therapy. In patients awaiting endoscopy, empirical therapy with a high-dose proton pump inhibitor should be considered.

   (Evidence 6 in section 9)
This recommendation recognizes the excellent safety profile of proton-pump inhibitors. The panel did not explicitly endorse an optimal route of administration, although some advocated an intravenous route for patients at high risk and an oral route for those at low risk. Proton-pump inhibitor infusion is not a replacement for urgent endoscopy and haemostasis, where appropriate.

3. Somatostatin and Octreotide

Somatostatin and octreotide are not recommended in the routine management of patients with acute nonvariceal upper GI bleeding (Recommendation C) (Evidence 7 in section 9)

4. Antifibrinolytic drugs

Antifibrinolytic drugs cannot be recommended until further studies are available. (Evidence 8 in section 9)

5. H. Pylori eradication

Patients with upper GI bleeding should be tested for Helicobacter pylori and receive eradication therapy if infection is present. (Recommendation A)
   Testing (CLO test)
   Eradication treatment for two weeks:
   Amoxycillin 1g b.d
   Metranidazole 400mg b.d
   Omeprazole 20mg b.d.
6. Discontinuation of NSAIDS

All of the preceding recommendations also apply to patients who have ulcers associated with non steroidal anti-inflammatory drugs.

**Surgical Treatment:**

Indications:
1. Haemorrhage that can not be controlled by other measures.
2. Perforated Ulcer
3. Gastric outlet obstruction.

- **For Gastric Ulcers**:
  Recommendation:
  1) Excision of the Ulcer
  2) Partial Gastrectomy

  (Procedure depends on the size and the location of the ulcer)

(Evidence 10 in section 9)

- **For Duodenal Ulcers**:

  Recommendation:
  1) Distal gastrectomy to include duodenal ulcer with Billroth I or Billroth II reconstruction, has the lowest rebleeding rate
  2) Under running the bleeding ulcer with specific ligation of Gastro duodenal and right gastro-epiploic arteries.
(Evidence 11 in section 9)
Section 8. Management of Variceal Bleeding

Portal hypertension causing variceal bleeding can be due to several causes such as:

Table 4

<table>
<thead>
<tr>
<th>Presinusoidal</th>
<th>Sinusoidal</th>
<th>Postsinusoidal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Extrahepatic</td>
<td>Cirrhosis</td>
<td>Hepatic veins</td>
</tr>
<tr>
<td>Congenital</td>
<td></td>
<td>Budd-Chairi syndrome</td>
</tr>
<tr>
<td>Umbilical sepsis</td>
<td></td>
<td>Veno-occlusive disease</td>
</tr>
<tr>
<td>Trauma</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypercoagulation state</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malignant occlusion</td>
<td></td>
<td>-</td>
</tr>
<tr>
<td>Intrahepatic</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

A) Management of acute variceal bleeding.

Management options available include:

- Pharmacological therapy
- Endoscopic therapy
- Tamponade
- Decompression – Surgical / Radiological
- Liver transplantation.

Recommendation:
Diagnosis of Variceal bleeding due to portal hypertension is often identified at the initial endoscopy. However until endoscopic evaluation is performed, specific therapy for variceal bleeding may be considered based on the clinical evaluation and the available previous health records.

**Control of bleeding:**

**Recommendations**

1) **Pharmacotherapy:**
   
   - **Vasopressin:** Bolus 20 units in 200ml of normal saline, followed by continuous infusion 0.2 – 0.4 units / minutes.
   
   Caution: Needs cardiac protection for ischemic heart disease patients. Nitroglycerin infusion 40 mcg/ min along with vasopressin ) ( Evidence 12 in section 9)

   - **Somatostatin / Octreotide**

   - **Recombinant coagulation factor VII**

   This is a synthetic coagulation factor that is currently used to treat acute bleeding episodes in patients with haemophilia. It has recently been trialled in randomized studies as an adjunct to standard methods of controlling variceal haemorrhage. Patients in end-stage liver disease lose the synthetic capacity to produce these coagulation factors, most notably factor VII 87. As a result, it has been postulated that replacing factor VII in cirrhotics may aid in controlling acute variceal haemorrhage.

   (Evidence 13 in chapter 9)
2) Tamponade:
This option is not available in many centres in Sri Lanka.

(Evidence 14 in section 9)

3) Endoscopic treatment:

Recommendation:

Variceal banding
Endoscopic variceal banding ligation consists of the placement of a rubber band around the varix. This technique is performed by first sucking the varix into a sheath attached to the distal end of the endoscope. Once the varix is suctioned into the sheath, a trigger device allows the deployment of a rubber band around the varix, a procedure that strangulates the varix.

Sclerotherapy
Endoscopic sclerotherapy involves injecting a sclerosing agent, such as ethanolamine or polidocanol, into the lumen of the varix (intravariceal) or immediately adjacent to the vessel (paravariceal) to create fibrosis in the mucosa overlying the varix, which leads to haemostasis. (Evidence 15 in section 9)

Cyanoacrylate glue:
The other available endoscopic option is the use of tissue adhesives, which are useful for both oesophageal and gastric varices. Native cyanoacrylate is a liquid tissue adhesive used frequently in Europe. It has a consistency similar to water, which makes it easy to manipulate down the endoscope. After injecting the substance into the varix, the blood mixes with the adhesive agent and rapidly polymerizes into a hard glue. The cyanoacrylate then plugs the lumen of the varix and creates haemostasis. Several weeks (i.e., 2 wk to 3 months) after the
initial injection, the overlying mucosa sloughs off and the adhesive cast is passed through the GI tract.
(Evidence 16 in section 9)

4) Surgical treatment:

Indications:
- Failure of endoscopic therapy.
- In patients who have no access to endoscopy treatment.

Surgical shunts
Surgery for bleeding oesophagogastric varices is the most reliable method to control acute haemorrhage and is associated with recurrent bleeding rates of less than 10% (88). The goal of a surgical shunt is to effectively decrease the portal venous hypertension and its adverse effects without compromising liver function.

Liver transplantation
The need for liver transplantation should also be considered during the initial evaluation of patients with UGIB and portal hypertension. For patients with Child class A or B cirrhosis with preserved liver function, portal decompression is preferable to transplantation. For patients with Child class C cirrhosis, the TIPS procedure can be used as a temporizing measure to provide a bridge until transplantation can be arranged. (Evidence 17 in section 9)

B) Prevention of re-bleeding
In patients who have minor rebleeding after variceal obliteration by endoscopic techniques, especially those who have not bled until 1-2 years later, a repeat endoscopic banding procedure is a more reasonable approach.
Section 9 – Notes on evidence and evidence base for the recommendations

Rating of evidence

Categorization of evidence

Categories and grade Description

Quality of evidence

Level I Evidence obtained from at least I properly randomized, controlled trial.
Level II - 1 Evidence obtained from well-designed controlled trials without randomization
Level II - 2 Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than 1 centre or research group.
Level II - 3 Evidence obtained from comparisons between times or places with or without the intervention, or dramatic results in uncontrolled experiments.
Level III Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

Classification of recommendations
A There is good evidence to support the procedure or treatment.
B There is fair evidence to support the procedure or treatment.
C There is poor evidence to support the procedure or treatment, but recommendations may be made on other grounds
D There is fair evidence that the procedure or treatment should not be used.
E There is good evidence that the procedure or treatment should not be used.
Evidence 7.2.1
The definition of *early endoscopy* varies widely among studies, from 2 to 24 hours after presentation to the emergency department (11, 12-16). In the UGBE cohort, first endoscopy in “real life” was performed within 24 hours of presentation in 76% of patients (mean [±SD], 23 ± 38 hours) (17). This was similar to the rate of 78% reported in a survey in the Amsterdam area (18). The consensus panel agreed to define *early* as within the first 24 hrs.

Several observational studies (19, 20, 15, 21-23) and a systematic review (24) support the use of early endoscopic stratification for all risk groups. Studies in-risk patients have shown no major complications in those triaged to outpatient care with early endoscopy (25, 20, 12, 14, 21, 22, 26, 27). A retrospective cohort trial found reductions in both length of hospital stay and need for surgery with early endoscopy in unselected patients (15). In a randomized controlled trial, early endoscopy and endoscopic therapy reduced transfusion requirements and length of hospitalization in patients with bloody nasogastric aspirate but not in those with clear or coffee grounds aspirate (13). Studies in patients with at low risk (28, 12, 14), at high risk (14), and unselected patients (29, 15, 26) have demonstrated statistically significant reductions in length of hospital stay. In patients at low risk two randomized controlled trials have demonstrated cost reductions of 43% to 91% with the use of early endoscopy (12, 14).

Evidence 7.2.3 A
Two meta-analyses have demonstrated the benefits of endoscopic therapy in patients with high-risk rather than low-risk stigmata, with resultant statistically significant decreases in rates of further bleeding, surgery, and mortality (30, 31). Modern endoscopic haemostasis techniques were reviewed more recently in meta-analyses of 56 studies. Bardou and colleagues (32, 33) showed that, compared with drug or placebo treatment, endoscopic treatment was associated with statistically significant absolute decreases in rates of rebleeding, surgery, and mortality.

The optimal management of adherent clots has long been controversial, since this finding obscures underlying stigmata that may be at high or low risk for rebleeding. The risk for rebleeding...
with clots that remained adherent after washing has been reported as only 8% in one study (34) but as high as 25% to 29% in others (35, 36). Two recent studies found that endoscopic therapy for adherent clots statistically significantly reduced the rate of rebleeding compared with medical therapy alone (37, 38).

Evidence: 1
On the basis of the favorable natural history we do not recommend any endoscopic treatment for patients with low-risk endoscopic stigmata (a clean-based ulcer or a flat spot in an ulcer bed). Two meta-analyses have demonstrated the benefits of endoscopic therapy in patients with high-risk rather than low-risk stigmata, with resultant statistically significant decreases in rates of further bleeding, surgery, and mortality (30, 31). Modern endoscopic haemostasis techniques were reviewed more recently in meta-analyses of 56 studies. Bardou and colleagues (32, 33) showed that, compared with drug or placebo treatment, endoscopic treatment was associated with statistically significant absolute decreases in rates of rebleeding, surgery, and mortality.

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Evidence 2:
No single solution for endoscopic injection therapy is superior to another for haemostasis. The meta-analyses by Bardou and colleagues (32, 33) which included 38 relevant studies and demonstrated no statistically significant benefits of one solution over another for endoscopic injection. In individual trials, no statistically significant differences were seen for epinephrine alone versus distilled water (39), cyanoacrylate (40), thrombin (41, 42), sodium tetradecyl sulfate (43), or ethanol (44, 45). In one study, no statistically
significant differences were seen in treatment with normal saline, hypertonic saline (3% NaCl), 50% glucose in water solution, or pure alcohol 46.

Injection of absolute alcohol into the bleeding point does not confer advantages over adrenaline and also risks clinical perforation. Injection of agents which directly stimulate clot formation such as fibrin glue or thrombin have been shown to be effective 47,48 but are not freely available.

**Evidence 3:**
Most individual randomized studies have shown no differences in rates of rebleeding, surgery, and mortality among coagulative therapy with heater probe thermocoagulation, multipolar electrocoagulation, or neodymium yttrium—aluminium—garnet laser when compared with injection therapy, although some studies have shown differences in rates of haemostasis 49 - 55. Laser therapy is no longer commonly used for acute management of high-risk patients because of high costs and poor portability of the equipment.

**Evidence 4**
Several randomized, controlled trials have investigated the use of endoscopic clips, alone 56 or in combination 56 for endoscopic haemostasis. Endoscopic clips have shown superiority over heater probe 57 or injection therapy 56 in 2 trials but higher failure rates compared with injection therapy 58 in another. Studies of the combination of injection plus endoscopic clips have demonstrated no statistically significant benefit over injection alone 58 or clips alone 56. The finding of increased rebleeding with the combination of injection and clips compared with clips alone 56,58 requires further study.

The variable success of endoscopic clips may reflect difficulty with their placement. Some studies report outcomes only of patients in whom clips were successfully placed, rather than performing an intention-to-treat analysis. It is likely that further improvement in the clips and their ease of placement will lead to more widespread use.
Monotherapy, with injection or thermal coagulation, is an effective endoscopic haemostatic technique for high-risk stigmata; however, the combination is superior to either treatment alone. Evidence: I Previous meta-analyses of injection or thermal endoscopic haemostatic therapies reported statistically significant relative decreases in rebleeding rates and mortality compared with standard therapy. The more recent McGill University meta-analyses by Bardou and colleagues found statistically significant reductions in the absolute rates of rebleeding and mortality with endoscopic treatment compared with placebo or pharmacotherapy (see previously discussed recommendations). Combination therapy with both injection and coaptive therapy has shown superiority over medical therapy. Bardou and colleagues investigated combinations of 2 endoscopic methods in 6 studies: epinephrine injection plus thermal treatment in 5 studies, epinephrine injection plus laser treatment in 2 studies, and epinephrine injection plus clips in one study. Combination treatment was associated with statistically significant reductions in absolute rates of rebleeding compared with injection alone, thermal treatment alone, or pharmacotherapy. Similar reductions in rebleeding were not observed when the combination was compared with haemoclip therapy alone, despite statistically significant reductions in surgery rates. In an analysis of the 3 studies combining thermal methods with injection, combination treatment was associated with statistically significant reductions in absolute rates of rebleeding compared with pharmacologic, injection, or thermal treatment alone. The absolute mortality rates were statistically significantly lower with combination therapy than with pharmacologic or injection therapy.

Evidence 5:
H₂-receptor antagonists are not recommended in the management of patients with acute upper GI bleeding. Meta-analysis by Collins and Langman, which included 27 randomized trials with more than 2500 patients, suggested that H₂-receptor antagonist treatment might reduce the rates of rebleeding, surgery, and death by approximately 10%, 20%, and 30%,
respectively, compared with placebo or usual care. However, these results were statistically significant only for surgery and death, and it appeared that the benefit was confined to patients with bleeding gastric ulcers. A meta-analysis by Selby and associates, which included 21 studies and 3566 patients treated with H2-receptor antagonists or proton-pump inhibitors, demonstrated statistically significant reductions in rates of rebleeding and surgery but not mortality compared with placebo. Another recent meta-analysis by Levine and coworkers concluded that intravenous H2-receptor antagonists provided no additional benefit in bleeding duodenal ulcers but provided small but statistically significant absolute risk reductions in rebleeding (7.2%), surgery (6.7%), and death (3.2%) in patients with bleeding gastric ulcer compared with placebo. In the McGill University meta-analyses by Bardou and colleagues, which included 16 relevant studies assessing H2-receptor antagonist therapy, no statistically significant improvement in outcomes was noted compared with other pharmacotherapy or endoscopic therapy. However, the results were not stratified according to H2-receptor antagonist dosing regimens or ulcer location. Recent meta-analyses have found proton-pump inhibitors to be more effective than H2-receptor antagonists. Given the proven benefit of proton-pump inhibitors and the inconsistent and at best, marginal benefits of H2-receptor antagonists, the latter are not recommended for the management of acute upper GI bleeding.

Evidence 6:

Four randomized trials specifically assessing high-dose bolus and continuous-infusion of proton-pump inhibitors, largely in patients with high-risk stigmata following endoscopic therapy, have shown decreased rebleeding and, in some cases, reduced need for surgery compared with H2-receptor antagonists or placebo. Two recent meta-analyses demonstrated that intravenous proton-pump inhibitors were more effective than H2-receptor antagonists in preventing persistent or recurrent bleeding. Only one showed a decrease in surgery rates, and neither demonstrated a decrease in mortality rates. The McGill University meta-analyses
found that high-dose proton-pump inhibitor therapy after successful endoscopic therapy led to a statistically significant reduction in the absolute rate of rebleeding compared with H2-receptor antagonists alone, H2-receptor antagonists in combination with somatostatin, or placebo. Intravenous proton-pump inhibitors also statistically significantly reduced absolute mortality rates compared with placebo and surgery rates compared with placebo or a combination of H2-receptor antagonists and somatostatin. Among 156 patients with non-bleeding visible vessels and adherent dots, a recent randomized trial by Sung and colleagues demonstrated the superiority of a combination of intravenous high-dose omeprazole infusion and endoscopic haemostasis over intravenous high-dose treatment alone.

Both the rationale for the use of proton-pump inhibition and the existing data suggest that this is a class effect and that the improvement in rebleeding can be achieved by using either intravenous omeprazole or pansoprazole, 80-mg bolus followed by 8 mg/h for 72 hours after endoscopic therapy. It is unclear what the threshold, or lowest effective dose, would be and whether it would differ among proton-pump inhibitors.

In patients awaiting endoscopy, empirical therapy with a high-dose proton pump inhibitor should be considered Evidence: III

This recommendation is based primarily on consensus among the panel and best available evidence. One study of the use of intravenous proton-pump inhibitors before endoscopic therapy in unselected patients with upper GI bleeding found no difference compared with placebo, despite an improvement in endoscopic stigmata. However, doses of proton-pump inhibitors (omeprazole, 80-mg bolus plus 40 mg intravenously every 8 hours for 1 day, followed by 40 mg orally every 12 hours for 4 days) may have been sub-optimal. Two studies in Asia compared oral omeprazole, 40 mg every 12 hours for 5 days, with either placebo (without endoscopic therapy) or endoscopic injection of alcohol for high-risk lesions. A third study compared the same omeprazole dosage after endoscopic injection therapy with placebo. All showed decreased rebleeding with or without decreased rates of surgery.
Evidence 7:

In the McGill University meta-analyses by Bardou and colleagues \(^{32,33}\), neither somatostatin nor octreotide improved outcomes compared with other pharmacotherapy or endoscopic therapy. Several studies have shown octreotide to be similar to or better than ranitidine in terms of rebleeding but statistically significantly less effective than endoscopic haemostatic therapy \(^{35,76,77}\). In other studies, somarostatin was no more effective than ranitidine \(^{78}\).

Evidence 8:

A meta-analysis has shown that tranexamic acid therapy, while not reducing ulcer rebleeding, does appear to reduce the need for surgical intervention and tends to reduce mortality in ulcer bleeding patients. This meta-analysis was probably disproportionately skewed by inclusion of an extremely large trial in which the mortality in cimetidine treated patients was surprisingly high. Further studies of tranexamic acid are necessary before it can be recommended as routine therapy.

Evidence 9:

Post-treatment \textit{H. pylori} infection status has been shown to be an independent \textit{predictor} of rebleeding \(^{82}\). In many randomized, controlled trials \(79—81\), eradication of \textit{H. pylori} has been demonstrated to reduce the rate of ulcer recurrence and rebleeding in complicated ulcer disease. Most tests of active infection may exhibit increased false-negative rates in the context of acute bleeding. Although the optimal diagnostic approach remains unclear, it may include acute testing for \textit{H. pylori} infection, followed by, if results are negative, by a confirmatory test outside the acute context of bleeding. There is no rationale for urgent intravenous eradication therapy; oral therapy
can be initiated either immediately or during follow-up in patients found to have *H. pylori* infection.

**Evidence 10:**
No Controlled clinical trials are available to support any particular form of Surgery. Decision should be made by an individual basis by an experience Surgeon. (Evidence III)

**Evidence 11:**
There is only one clinical trial of different surgical procedures for bleeding duodenal ulcers. The rebleeding rate was lowest in patients having a gastrectomy to include the ulcer either with Billroth I or Billroth II reconstruction compared with those subjected to more conservative operations. However, the bile leak rate following gastrectomy was much higher and the overallmortality in the two randomised groups was the same. The same study suggests that when a bleeding duodenal ulcer is under run, specific ligation of the gastroduodenal and right gastroepiploic arteries reduced the rebleeding rate to a similar level as a gastrectomy.

**Evidence 12:**
A meta-analysis from 1995 reviewed vasopressin versus untreated controls and revealed that vasopressin was dearly superior in arresting haemorrhage but showed no survival benefit. In Europe, a newly developed pro-drug called terlipressin has been used that has advantages over vasopressin. Terlipressin has a longer half-life with a biphasic vasoconstriction profile. The drug first has systemic vascular effects that are then steadily converted into a more effective vasoconstriction of the splanchnic bed. Randomized control trials comparing terlipressin with placebo have shown clear benefit in terms of bleeding control and survival. This drug is not yet available in Sri Lanka.

**Evidence 13:**
A recent double-blind trial has shown increased success at controlling bleeding endpoints in more severe cirrhotics (classes B and C) treated with factor VII compared to placebo.\textsuperscript{87}

**Evidence 14:**
Since the 1990s, the use of balloon tamponade for the emergent control of oesophageal variceal bleeding has steadily decreased and is now usually indicated for only the 10\% of patients whose acute bleeding episode is not controlled endoscopically.\textsuperscript{88} The use of these tubes can be a life-saving manoeuvre when medical and endoscopic efforts fail to control the bleeding. Although temporary control of the bleeding is effective in 85\% of cases, recurrent bleeding with release of the tamponade occurs in most patients.\textsuperscript{89} In addition to their limited effectiveness, the tubes are associated with a 20\% complication rate that includes airway obstruction, aspiration, and oesophageal necrosis with rupture.\textsuperscript{89} Because of the severe life-threatening complications and limited use, the tubes are used only as a temporary measure while the patient is resuscitated. The tubes act as a bridge to help stabilize the patient until a time when the patient is prepared for either a repeat endoscopy procedure or a portal pressure decompression through a radiological or surgical method.

**Evidence 15:**
A recent meta-analysis of all the randomized controlled trials comparing sclerotherapy with variceal banding found significantly lower mortality rates, variceal rebleeding, oesophageal perforation, and stricture formation with variceal banding therapy.\textsuperscript{90} In addition, evidence accumulating in the literature documents the safety of endoscopic banding in prophylactic therapy for patients at high risk for oesophageal variceal haemorrhage.\textsuperscript{91} This benefit has not been established with endoscopic sclerotherapy. The single potential downside to endoscopic variceal banding is poor visualization of the varices when massive bleeding is present. This is due to the 30\% reduction in the field of vision through the endoscope caused by the plastic sheath used to deploy the rubber band.\textsuperscript{92} The drawback to sclerotherapy is its potential for life-
threatening complications such as perforation, ulceration, and stricture of the oesophagus.

The initial success in arresting haemorrhage comparing the 2 techniques is comparable—as high as 95% in some studies. Variceal rebleeding rates are lower with band ligation compared to sclerotherapy, which has rebleeding rates as high as 50% (84).

In summary, endoscopic variceal banding is a more effective technique resulting in faster variceal eradication and fewer complications than endoscopic sclerotherapy. Endoscopic surveillance at 3-month intervals during the first year is important to detect recurrent and new varices when they are small and have a low risk of bleeding. 88

Evidence 16:
Cyanoacrylate is 90% successful in achieving haemostasis in patients with acute bleeding from either gastric or esophageal varices 93. The early rebleeding rate is 0-28%. The risks of using these adhesive agents are the potential systemic effects and permanent damage to the endoscope from exposure to the adhesives at the lens of the scope 94. Oho et al performed a prospective randomized trial involving 53 patients that compared cyanoacrylate glue to sclerotherapy in patients with acute gastric variceal bleeding. Cyanoacrylate was more effective in achieving haemostasis (93% vs 67%).

The potential systemic effects are related to the risk of thrombotic complications. Cerebral stroke from anomalous right-to-left shunts, fatal pulmonary embolization, portal vein embolization, splenic infarction, and retrogastric abscess have all been reported in the literature 94.

The need for emergent surgical intervention was also reduced in patients initially injected with the glue tissue adhesive. Other agents used include bovine fibrin or fibrin glue. Polidocanol, a 2-component fibrin glue, has shown promise as an effective agent with a decreased incidence in mucosal damage or post therapy ulceration that is characteristic of sclerosants and tissue adhesives 95.

Evidence 17
Practitioners may well ask whether one shunt is superior to the others and whether one shunt controls bleeding better than the others. Each type of shunt has a bleeding control rate greater than 90%\(^8\). The difference between shunts is the incidence of encephalopathy and the risk of worsening ascites.

Depending on whether the shunt completely decompresses the portal venous system, porto-systemic shunts can be classified as non-selective, selective, or partial. The goal of selective or partial shunts, in addition to decreasing portal venous hypertension, is to preserve portal blood flow to the liver in order to avoid compromising liver perfusion and function. Data from many randomized control trials that have compared the various types of shunts indicate that encephalopathy occurs in 10-15% of patients after a selective shunt (distal splenorenal), in 10-20% after a partial shunt, and in 30-40% after a total shunt\(^8\). The differences in survival between all the different shunts are not significantly different, with mortality rates of approximately 5%\(^8\).
Section 10 References


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