National consensus on management of peptic ulcer bleeding in Denmark 2014

Stig Borbjerg Laursen, Henrik Stig Jørgensen & Ove B. Schaffalitzky de Muckadell

Introduction

The Danish Society of Gastroenterology and Hepatology have compiled a national guideline for the management of peptic ulcer bleeding. It provides evidence-based recommendations for the assessment and management of peptic ulcer bleeding. Sources of data included published studies up to June 2014. The guideline was approved by the Danish Society of Gastroenterology and Hepatology September 4, 2011. The current version is revised June 2014.

Subject-area delimitation

This guideline deals with the treatment of patients bleeding from chronic peptic ulcerations located in the stomach and/or duodenum.

Background

Peptic ulcer bleeding is a frequent cause of admission to hospital accounts for almost 2000 admissions annually in Denmark.[1] Despite the development of more potent acid-inhibiting drugs and improved endoscopic techniques, mortality has remained unchanged at about 10% for a many years. This is presumably a consequence of increasing age and an increased frequency of comorbidity.

Definitions

Bleeding peptic ulcer is defined as the occurrence of haematemesis and/or melaena and/or an unexplained drop in B-haemoglobin in a patient in whom a subsequent endoscopy documents that the source of bleeding is a chronic peptic ulcer. *Chronic ulcerations* are defined as ulcers with a visible loss of substance that penetrate the lamina propria and lamina muscularis mucosae. Chronic ulcerations will normally have a diameter of more than 5mm and should not be confused with acute erosions.

Review of included topics

1. Admission and circulatory restoration

Initial assessment and treatment of patients with suspected peptic ulcer bleeding is based on the ABCDE principles: Airway, Breathing, Circulation, Disability and Exposure/Environment.[2] Staff should be competent in the recognition of airway problems, use of basic airway manoeuvres, and when to call upon staff trained in advanced airway therapy.

Unobstructed airways and sufficient respiration is secured. Peripheral oxygen saturation should be measured and be ≥ 93%. Oxygen (10-15L/min) should be administered to patients with haemodynamic disturbance in order to secure adequate delivery of oxygen and avoiding global hypoperfusion and tissue hypoxia.[3]

Treatment of circulatory insufficiency is the cornerstone of the initial management. A minimum of two large peripheral IV lines are established and kept open with isotonic NaCl. If the patient is haemodynamically unstable one or more boli of 500-1,000 ml isotonic NaCl, or Ringer acetate, is rapidly infused for stabilization of circulation and ensuring optimal tissue perfusion. A Cochrane review comparing crystalloid and colloid fluid restoration demonstrated no significant statistical difference,[4] and as colloids may interfere with haemostasis, crystalloids are recommended.

Patients with severe bleeding with haemodynamic compromise should as soon as possible receive balanced blood component therapy in the following ratio:

Erythrocytes 3 : fresh frozen plasma 3 : platelets 1 [5]

0 rhesus negative blood can be used until compatible blood becomes available. Platelets are administered from the beginning simultaneously with infusion of fresh frozen plasma and erythrocytes in separate IV lines. The need of volume replacement should be assessed by monitoring blood pressure, heart rate, peripheral perfusion and oxygen saturation.
Care should be taken to avoid overloading, especially in patients with heart failure because of the risk of development of pulmonary oedema.

In patients with circulatory failure, nasogastric lavage may indicate if the circulatory compromise is a result of upper gastrointestinal bleeding. Nevertheless, it is important to underline that even clear gastric aspirate cannot rule out severe bleeding and must

not be used as an argument for postponing upper endoscopy. Nasogastric lavage should not be used routinely because of the lack of consequence and risk of pulmonary aspiration.

The following blood samples are to be taken initially: B-Haemoglobin, B-Platelets, International normalised ratio (INR), P-Na, P-K, P-Albumin, P-Creatinine, P-Urea, Blood-type, BAC test and ECG.

Prognostic factors from case history include a description of the occurrence of coffee-ground vomit/haematemesis, melaena/haematochezia and syncope in conjunction with the aforementioned symptoms. Intake of nonsteroidal anti-inflammatory drugs (NSAIDs), acetylsalicylic acid (ASA), other platelet-inhibiting drugs, anticoagulants, and selective serotonin reuptake inhibitors (SSRI) is registered. Details, or clinical suspicion, of co-morbidity (particularly heart, liver, kidney and pancreas) and previous aortic intervention are important for prognostic reasons, and also of significance for optimal resuscitation and evaluation of the risk of bleeding from varices, aortoenteric fistula or pancreatic pseudocyst.

1.1 Restrictive transfusion strategy
Use of a restrictive transfusion strategy (Transfusion threshold: B-haemoglobin < 7 g/dL) in patients with upper GI bleeding in general seems to be associated with improved survival, lower rate of rebleeding, and lower risk of complications compared with use a more liberal transfusion strategy.[6] Stratified analyses have shown that these advances are not achieved in peptic ulcer bleeding, but mainly in patients with Child-Pugh A or B cirrhosis.[6] Nevertheless, in peptic ulcer bleeding we recommend use of a restrictive transfusion strategy as this is as safe as use of a more liberal transfusion policy and is associated with a lower risk of development of transfusion-related complications.[6]

We recommend that patients with significant ischemic vascular disease (ischemic heart disease, cerebral ischemia (previous stroke or transient ischemic attack), or symptomatic peripheral vasculopathy) are treated with a liberal transfusion policy (Transfusion threshold: B-haemoglobin < 9 g/dL)

1.2 Risk-scoring systems
Risk-scoring systems for the assessment of patients with upper GI-bleeding have two aims: 1. Identification of low-risk patients who can be managed safely as out-patients, and 2. Identification of high-risk patients with increased risk of adverse outcome.

1.2.1 Identification of patients with symptoms of upper GI-bleeding who can be safely managed as outpatients
Around 40% of patients who are admitted to hospital for suspected upper GI-bleeding in Denmark do not need transfusion, or haemostatic intervention, and will survive 30 days after time of presentation.[7]

The Glasgow Blatchford score (GBS) can safely be used for identification of patients suitable for outpatient care.[7,8] The optimal threshold of the GBS is ≤1.[9] Patients with symptoms of upper GI-bleeding and a GBS ≤1 have a risk of 1% of needing transfusion, haemostatic intervention, or death within 30 days.[9] By implementation of a protocol for non-admission of patients with a GBS ≤1 it is expected that 15-20% of all admissions to hospital for suspected upper GI-bleeding can be avoided safely.[9]

We recommend that the GBS is calculated for all patients with upper GI-bleeding. Cases with low clinical suspicion of upper GI-bleeding and a GBS ≤1 can be managed as outpatients if there is no other disease present requiring admission to hospital. We recommend that these patients are offered diagnostic endoscopy within a short time-frame.

1.2.2 Identification of high-risk patients with increased risk of treatment failure
The Rockall score and the GBS is the most validated risk-scoring systems for identification of patients in risk of treatment failure (need of endoscopic treatment, surgery, or death). Both risk-scoring systems have only a limited predictive ability for identification of these high-risk patients.[10] There is no evidence that implementation of a risk-scoring system for identification of high-risk patients is associated with an improved outcome. The Rockall score can be used after endoscopy for a rough estimation of the risk of rebleeding or death. Patients with a Rockall score ≥ 6 have a high risk of rebleeding and death[11] and should be observed closely for development of complications.

2. Monitoring
Patients with upper GI bleeding should be admitted, assessed and managed in a dedicated bleeding unit, which in a cohort study was shown to reduce mortality.[12]

Only a sparse number of studies are available on optimal observation in connection with ulcer bleeding, for which reason the recommendations below are based on consensus.[13]

The vital parameters: Heart rate, blood pressure, oxygen saturation, respiratory rate, diuresis and level of consciousness are monitored at least every 15 minutes until the patient has stabilized, then once an hour. Fluid balance should be documented on specific charts.
During endoscopy the level of consciousness, respiratory rate, blood pressure, heart rate and oxygen saturation are observed continuously. Continuous ECG monitoring may be useful. Supplementary monitoring with invasive arterial/venous pressure measurements and hourly urinary output can be considered in patients in haemodynamic distress.

Following a haemostatic procedure, respiratory rate, heart rate, blood pressure, level of consciousness and oxygen saturation should be recorded at regular intervals with an eye to early identification of rebleeding. Until four hours after haemostasis is achieved, it is recommended checking parameters every half an hour, from 5-12 hours once an hour, from 13-24 hours every four hours and then a minimum of three times a day.

Rebleeding occurs in 10-15%[1] and should be suspected in case of redevelopment of haematemesis, melaena, haematochezia, arterial hypotension, syncope, tachycardia, falling B-Haemoglobin, or if lack of normalization of P-Urea is observed.

3. Timing of endoscopy
Patients with suspected peptic ulcer bleeding should generally be endoscoped within 24 hours of being hospitalized, thereby reducing the need for surgical haemostasis, rebleeding rate and inpatient stay.[14]

On suspicion of serious peptic ulcer bleeding and occurrence of bloody gastric aspirate, endoscopy should be endeavoured within

twelve hours. A randomized study has shown that this is associated with earlier discharge and reduces the need for transfusion.[15]

Endoscopy within 6-8 hours generally leads to an increased risk of poor mucosal overview and pulmonary aspiration, and an increased rate of endoscopic therapy that is not associated with an improved outcome.[14]

Upper endoscopy should be performed immediately on vital indication in patients with circulatory shock despite intensive resuscitation. In patients with haemodynamical instability despite infusion with 1000 – 2000 ml's of crystalloids should have performed gastroscopy within one hour.

4. Endoscopic treatment
4.1 Indication and purpose
Endoscopic treatment is indicated in Forrest I-IIb ulcers. In addition to primary haemostasis, endoscopic treatment of
Forrest I-IIa ulcers will result in a lower rebleeding rate, rate of surgery and mortality.[16] Endoscopic treatment of ulcers with an adherent clot – defined as a coagulum that cannot be removed by vigorous irrigation or suction – is a subject of controversy.[17] A meta-analysis has shown that endoscopic treatment for this type of ulcer does reduce the rate of rebleeding and surgery, but mortality remained unchanged.[18] However, the available studies are, as far as treatment is concerned, methodologically heterogeneous. The most frequently used treatment modality is injection of 5-10 ml of adrenaline-saline (see section 4.2.1) followed by removal of the clot and treatment of any underlying bleeding stigmata with a secondary treatment modality.

4.2 Modalities of therapy
4.2.1 Adrenaline-saline injection
In most instances, treatment with adrenaline-saline injection (1:10,000) is the technique of choice as the first modality, since the method is good for achieving haemostasis[19-22] and creating an overview of the source of bleeding. Three randomized studies have shown a clear correlation between the volume of adrenaline-saline injected and the rebleeding rate.[23-25] The rebleeding rate is halved if the injected volume is increased from 5-10 ml to 13-20 ml.[23] Because development of rebleeding is associated with up to a six fold increase in mortality[11] it is important to inject a sufficient amount of adrenaline-saline. For the purpose of reducing the rebleeding rate a total volume of at least 13 ml adrenaline-saline should be injected, irrespective of already obtained haemostasis. Injecting a total volume greater than 30 ml increases the risk of perforation (5%) and protracted abdominal pain (67%) and should therefore be avoided.[24]

In practice, we recommend quadrant-wise injection of 1-2ml aliquots 2-3mm from the bleeding point (extravasal deposits) until a total volume of 13-30ml is injected.

4.2.2 Contact thermal probe
Treatment with contact thermal probes includes use of heater probe and multipolar electrocoagulation. Both types of thermal probes are effective.[26-28] The mechanism of action is coaptive coagulation.

Coaptive coagulation is best achieved by applying the probe with a steady pressure (compresses the underlying artery and reduces the heat-sink effect) followed by activation of the probe (3x30J if a 10F heater probe is used) and lastly removing the probe while irrigating. In order to remove the blood supply to the bleeding point we recommend initially treatment at 6-8 sites circumferentially around the bleeding point followed by treatment of the bleeding point.

4.2.3 Hemoclips
The aim of treatment with hemoclips is to achieve mechanical haemostasis. Hemoclips are particularly well suited to a visible vessel. However, application of a hemoclip can be technically challenging, especially in retroflexion and in the case of ulcers located to the posterior wall of the duodenal bulb. The evidence for the effectiveness of hemoclips as compared with a contact thermal probe is scanty and in several cases contradictory.[29-31] Overall, the methods seem to be of equal value.[32]

Regarding optimal application of hemoclips we refer to the article by Kaltenbach and colleagues.[33]

4.2.4 Injection with sclerosing drugs
Injection of a sclerosing drug such as polydocanol (Aethoxysclerol) and ethanol used to be employed frequently to obtain haemostasis. However, due to reports on subsequent fatal necrotization[34-35] and the emergence of better alternatives, injection treatment with sclerosing drugs can no longer be recommended for peptic ulcer bleeding.

4.2.5 Argon plasma coagulation
The evidence for efficacy of argon plasma coagulation in the treatment of ulcer bleeding is limited. A randomized trial seem to show that argon plasma coagulation is associated with a higher risk of treatment failure (rebleeding, surgery, or death) when compared with hemoclips (16% versus 6%).[36] The existing evidence in this area is based on populations that are very different from the Danish population, and the underlying studies are characterised by lack of power and a considerable risk of bias. The effectiveness of argon plasma coagulation is presumably limited due to a modest depth effect and lack of coaptive coagulation. Therefore, use of argon plasma coagulation in treatment of peptic ulcer bleeding cannot be recommended.

4.3 Mono versus dual therapy
There are numerous studies, including a number of meta-analyses, comparing different forms of endoscopic therapy. An important aspect in this context is whether monotherapy with a particular form of therapy is associated with the same outcome as dual therapy. Unfortunately, there is divergence between studies in several areas.

Use of adrenaline-saline injection as monotherapy is associated with a rebleeding rate of just under 20%.[37] A Cochrane analysis has shown that by adding a secondary treatment modality it is possible to reduce both rebleeding rate, the rate of surgery, and mortality.[37] Thus, adrenaline-saline injection should always be supplemented with a secondary form of therapy.

Three meta-analyses have compared the effect of monotherapy with contact thermal probes with dual therapy.[38-40] The findings in these studies are diverging, and the conclusions controversial.[41-43] A meta-analysis found that monotherapy with contact thermal probes was associated with a higher rate of rebleeding compared with dual therapy.[40] The evidence in this area is

uncertain but based on the aforementioned study we recommend that treatment with contact thermal probes is combined with another endoscopic treatment modality.

Only few studies have compared monotherapy with hemoclips with endoscopic combination therapy. In the meta-analyses described previously, monotherapy with hemoclips seems to as efficient as combination therapy.[38-40]

5. Invasive procedures
Transcatheter arterial embolization (TAE) and surgery are used in patients with severe bleeding not responding to endoscopic therapy. There are no high-quality trials comparing the outcome of TAE and surgery. Patients treated with TAE seem to have the same survival as patients undergoing surgery despite that patients treated with TAE in general are older and have more co-morbidities.[44] On the other hand surgery seems to be associated with a lower rate of rebleeding than TAE.[44] We recommend that TAE is used as the first line of therapy in patients with bleeding not responding to endoscopic therapy in centres where this treatment is available.

5.1 Transcatheter arterial embolization
If endoscopic haemostasis cannot be achieved, the patient should undergo TAE without delay. Using TAE it is possible to achieve haemostasis in 93% of patients.[45] If no active bleeding is present at time of angiography "blind embolization" can be performed based of knowledge of the ulcer's anatomical location.[45] If possible, a hemoclip should be placed in the edge of the ulcer during the preceding endoscopy, thus facilitating identification of the bleeding vessel. Sodium bicarbonate can be used in azotaemic patients.

5.2 Surgical haemostasis
If endoscopic haemostasis cannot be achieved and TAE is not feasible, an emergency operation must be performed. It is recommended undertaking transfixion of the ulcer and the bleeding vessel rather than gastric resection. Mortality after both interventions is identical [46-47] for which reason the simplest operation should be used. There is no evidence supporting use of a specific access, surgical technique, or suture technique. In patients with Billroth II gastrectomy it is sometimes impossible to suture or staple the duodenum distally to the ulcer. In these cases we recommend that the transfixed ulcer base is left in the posterior wall of the duodenal bulb, the anterior wall is sutured down to the anal part of the fibrous ulcer and a drain inserted into the duodenal lumen for decompression. The drain is best positioned via a separate incision laterally into the descending part of duodenum.[48] In general, extraluminal drains are not necessary after surgery for ulcer bleeding.

6. Rebleeding
At the first episode of rebleeding, therapeutic endoscopy is repeated if considered technically possible. Repeated endoscopic treatment is less effective than surgery in achieving haemostasis, but equal in terms of survival and associated with fewer complications.[49] In the event of repeated rebleeding, treatment with repeat endoscopic therapy, TAE or surgery must be considered on the basis of a case-by-case judgement and local expertise.

7. Medical treatment
7.1 Proton pump inhibitors (PPI)
A Cochrane analysis from 2006 showed that treatment with PPI overall reduces the rebleeding rate and the need for surgical haemostasis as compared with treatment with placebo or histamine-2 receptor antagonists.[50] For ulcers with active bleeding or a visible vessel treated with endoscopic therapy, it was found that infusion of high-dose PPI (80mg bolus followed by 8mg/hour in 72 hours) in addition resulted in reduced mortality. Based on this use of high dose PPI-infusion has been recommended worldwide following endoscopic treatment for peptic ulcer bleeding.

A later Cochrane analysis from 2013 did not find any differences in outcome between use of high dose versus non-high dose PPI following endoscopic therapy for peptic ulcer bleeding.[51] This analysis was associated with considerable risk of bias and a low event rate indicated that patients with severe bleeding were not sufficiently represented.[51,52] Accordingly, the authors concluded that use of high-dose PPI is still recommended following endoscopic therapy for peptic ulcer bleeding.

A Cochrane analysis has shown that treatment with preendoscopy PPI reduces the need for endoscopic therapy.[53] Use of preendoscopy PPI is, however, not associated with a reduced rate of rebleeding, need for surgery, or mortality.[53] Treatment with preendoscopy PPI is not recommended and should not delay the timing of endoscopy.

All patients with ulcer bleeding should be placed on treatment with proton pump inhibitors. Low-risk ulcers (Forrest IIc-III) are treated with oral PPI at a dose equipotent to 20 mg omeprazole daily. We recommend that high-risk ulcers (Forrest I-IIb) should be treated with high dose PPI (80mg of PPI as bolus followed by 8 mg/hour for 72 hours) following endoscopic therapy.

7.2 Pausing treatment with ASA, ADP receptor inhibitors, anticoagulants, NSAIDs and SSRI
The risk of developing arterial thrombosis is almost doubled when discontinuing well-indicated ASA treatment.[54] Premature withdrawal of anti-platelet therapy is the most significant risk factor for stent thrombosis among patients with coronary stents.

A randomized trial has shown that continuation of well-indicated low-dose ASA in patients receiving high-dose intravenous PPI after endoscopic treatment reduces mortality without causing a significant increase in rate of rebleeding.[55] The platelet function in normal subjects is inhibited for up to five days after withdrawal of ASA or adenosine diphosphate (ADP) receptor inhibitors (e.g. clopidogrel), but presumably for a shorter time in bleeding patients. Consequently, both drugs can safely be paused for 24 hours until the bleeding has stopped and the situation is stabilized.

It is recommended pausing treatment with ASA, ADP receptor inhibitors, anticoagulants, NSAIDs, and SSRI in the presence of ulcer bleeding. Low-dose ASA can be resumed after 24 hours if there is no sign of rebleeding. Treatment with ADP receptor inhibitors in patients with coronary stents can be resumed after three days. In case of doubt it is recommended to consult a cardiologist. Unnecessary NSAID intake should be discontinued. Treatment with anticoagulants and SSRI can be resumed after five days.

7.3 Tranexamic acid

A Cochrane analysis has found that treatment with tranexamic acid may reduce mortality when compared to placebo.[56] The analysis did not identify any differences in need for transfusion, rebleeding rate, or need of surgery. As the included studies were very old PPI was only used in one study and sufficient endoscopic therapy according to nowadays standard was not used in any of the studies. Therefore, there is insufficient evidence to recommend the use of tranexamic acid for peptic ulcer bleeding.

7.4 Thrombosis prophylaxis

Deep vein thrombosis is a frequent complication following abdominal surgery (7-45%).[57] A Cochrane analysis has shown that extended treatment with low-molecular heparins (LMH) following major abdominal operations reduces the risk of developing venous thromboembolism without increasing the risk of postoperative bleeding.[58] Supplementary mechanical treatment with graduated compression stockings and early mobilization further reduces the occurrence of thromboembolic events.[59]

We recommend use of LMH and compression stockings following surgical haemostasis. The treatment can beneficially be continued for four weeks.

8. Nutrition

There are only few studies evaluating the importance of nutrition for peptic ulcer bleeding. A randomized study found that resuming oral intake one to two days after endoscopic therapy reduced in-patient stay without affecting the outcome.[60]

It is recommended that patients with endoscopic/endovascular/surgically treated peptic ulcer bleeding are allowed an oral liquid diet for the first 24 hours after the procedure and then a normal diet. Patients with low-risk ulcer disease (Forrest IIc-III) without clinical suspicion of significant bleeding can be given a normal diet once the effect of the analgesia has worn off.

9. Discharge

Several studies have shown that patients at low risk of rebleeding or mortality can be discharged early.[61-63] Thus, patients with low-risk ulcers (Forrest IIc-III) without circulatory distress, or serious competing illness, can often be discharged within 24 hours of endoscopy.

Among patients requiring endoscopic treatment who rebleed within a month, the majority (60-76%) rebleed within 72 hours.[64-66] These patients can normally be discharged after 72 hours of PPI infusion if there is no sign of rebleeding.

10. Aftercare

10.1 Helicobacter pylori infection

All patients with peptic ulcer disease must have the Helicobacter pylori status established and Helicobacter-positive patients should receive eradication therapy in order to reduce the recurrence rate.[67] Reference is made to the DSGH guideline on the diagnosis and treatment of Helicobacter pylori infection.

10.2 Monitoring gastric ulcers

If a satisfactory number of biopsies (5-7) has not been taken from patients with gastric ulcers, or the experienced endoscopist is in doubt regarding the risk of malignancy, follow-up gastroscopy must be performed after 4-6 weeks.[68]

10.3 PPI prophylaxis

Intake of ASA or NSAIDs is associated with an increased relative risk of ulcer complications of 4-7.[69] During ASA treatment, the risk of recurrence of peptic ulcer bleeding is prevented just as effectively with omeprazole 20 mg and Helicobacter pylori eradication, while only PPI prevents recurrence of ulcer bleeding on treatment with NSAIDs.[70] In patients with previous peptic ulcer bleeding, long-term treatment with clopidogrel 75 mg produces 8 times more bleeding recurrences than the combination of ASA 80-100 mg and PPI.[71,72] A combination of PPI and ASA seems safer in terms of preventing bleeding than a combination of PPI and clopidogrel.[73] It is controversial whether pantoprazole should be preferred to other types of PPI in patients treated with clopidogrel.[74] The significance of any PPI-clopidogrel interaction is not clarified.

It is recommended that patients needing continued ASA or NSAIDs treatment are given prophylactic treatment with PPI at standard dosage. The combination of 75 mg ASA and PPI should be given preference over monotherapy with clopidogrel in patients needing platelet-inhibiting treatment on the basis of indications other than coronary stents.

Levels of evidence for clinical recommendations

Admission and circulatory restoration	
Immediate and intensive circulatory stabilization is essential for survival	**Evidence II**
Resuscitation with infusion of colloids is no more effective than crystalloids, for which reason the latter should be preferred	**Evidence Ia**
In the event of circulatory failure, balanced blood component therapy should be initiated as quickly as possible	**Evidence IV**
In stable patients without significant ischemic vascular disease a restrictive transfusion strategy should be used as this is associated with a lower risk of transfusion-related complications	**Evidence Ib**
In patients with circulatory failure highest possible oxygen supplement should be initiated	**Evidence IV**
Nasogastric lavage should not be used routinely	**Evidence IV**
Cases with low clinical suspicion of upper GI-bleeding and a GBS ≤1 can be managed as outpatients if there is no other disease present requiring admission to hospital	**Evidence IIa**
Monitoring	
Patients with upper gastrointestinal bleeding should be managed in a dedicated unit with specially trained staff, thereby reducing mortality	**Evidence II**

Documentation of administration of fluids and blood on dedicated charts	**Evidence IV**
Time intervals for observation following admission, endoscopy and surgery	**Evidence IV**

Timing of endoscopy

Endoscopy should generally be performed within 24 hours, reducing operation rate, rebleeding rate and duration of in-patient stay	**Evidence II**
When serious ulcer bleeding is suspected and blood found in gastric aspirate, endoscopy within 12 hours will result in faster discharge and reduced need for transfusions	**Evidence Ib**
In general, endoscopy within 6-8 hours entails an increased risk of poor mucosal overview due to retained blood, greater risk of aspiration and an increased rate of therapy that will not improve the prognosis.	**Evidence IV**

Endoscopic treatment

Endoscopic treatment is indicated for Forrest Type I-IIb ulcers	**Evidence Ia**
Initial treatment with injection of 13-25 ml adrenaline-saline is efficient in achieving haemostasis and reducing rebleeding rate	**Evidence Ib**
Monotherapy with adrenaline-saline injection or contact thermal devices should be avoided	**Evidence Ia**
Monotherapy with hemoclips is just as effective as endoscopic combination therapy	**Evidence Ia**
Secondary treatment with heater probe or hemoclips is of equal value	**Evidence Ia**

Invasive procedures

TAE and surgery are equal in terms of rebleeding rate and mortality	**Evidence II**
In the case of surgical haemostasis, transfixion of the ulcer is preferred	**Evidence II**

Rebleeding

First rebleeding episode should, if technically possible, be treated endoscopically	**Evidence Ib**

Pharmacological treatment

Treatment with PPI following endoscopy reduces the rebleeding rate and the need for surgical haemostasis	**Evidence Ia**
Following successful endoscopic therapy, PPI treatment should be given as an intravenous bolus followed by continuous infusion	**Evidence IV**
Pause treatment with ASA, ADP receptor inhibitors, anticoagulants, NSAIDs and SSRI	**Evidence III**
Low-dose ASA can be resumed after 24 hours	**Evidence Ib**

Nutrition

Patients with Forrest IIc-III ulcers are allowed a normal diet after endoscopy	**Evidence IV**
Patients who have been treated endoscopically are allowed a liquid diet for the first 24 hours after the procedure and then an unrestricted diet	**Evidence IV**

Discharge

Patients with Forrest IIc-III ulcers and no haemodynamic disturbance or serious comorbidity can often be discharged within a day of completing endoscopy	**Evidence Ib**
Patients with ulcers requiring endoscopic treatment are discharged on the basis of case-by-case judgement after 72 hours of PPI infusion	**Evidence IV**

Aftercare

All patients with peptic ulcer bleeding should be tested for Helicobacter pylori	**Evidence Ia**
If a satisfactory number of biopsies has not been taken from gastric ulcers, or the experienced endoscopist is in doubt regarding the risk of malignancy, follow-up gastroscopy must be performed after 4-6 weeks	**Evidence IV**
Patients in need of continued treatment with ASA or NSAIDs should be put on prophylactic treatment with PPI at standard dosage	**Evidence Ib**
The combination of 75mg ASA and PPI should be preferred to monotherapy with clopidogrel in patients needing antiplatelet therapy on the basis of indications other than coronary stents	**Evidence II**

Quick guide
Admission and initial resuscitation
- Patients are assessed and managed in accordance with the ABCDE principles
- A minimum of two large peripheral IV lines are established
- Haemodynamically unstable patients are treated with rapid infusion of one or more boli of 500-1,000 ml iso-

tonic NaCl, or Ringer acetate, for stabilization of circulation and ensuring optimal tissue perfusion.

- In the event of life-threatening bleeding, balanced blood component therapy in the proportions erythrocytes 3 : fresh frozen plasma 3 : platelets 1 is initiated as quickly as possible.
- In medical history, information about haematemesis, melaena, haematochezia, syncope, NSAIDs/ASA/anticoagulants/SSRI intake, comorbidity or previous intervention on abdominal aorta should be obtained
- Patients with low clinical suspicion of upper GI-bleeding and a GBS ≤1 can be managed as outpatients if there is no other disease present requiring admission to hospital.

Initial monitoring
- Heart rate, blood pressure, saturation, respiratory rate, diuresis and level of consciousness should be monitored every 15 min until the patient has stabilized and then once hourly
- Administration of fluids and blood should be documented on a dedicated chart
- Patients should be assessed and managed in a dedicated unit with specially trained staff

Timing of endoscopy
- Should generally be undertaken within 24 hours
- If severe bleeding is suspected, endoscopy within 12 hours is recommended
- If the patient's circulation cannot be stabilized, urgent endoscopy is performed on vital indication

Endoscopic treatment
- Forrest type I-IIb ulcers should be treated endo-scopically
- In most situations injection of 13-30 ml adrenaline-saline is the technique of choice as the first endoscopic treatment modality
- Endoscopic injection of adrenaline-saline should always be supplemented with a secondary therapeutic modality, usually in the form of a contact thermal probe or hemoclips

Invasive procedures
- In patients with severe bleeding not responding to endoscopic therapy immediate treatment with TAE is recommended
- If TAE is unavailable, immediate laparotomy, transfixion and ligation of the bleeding vessel is performed

Rebleeding
- Rebleeding should initially be treated by repeat endoscopic therapy, if technically possible
- In the event of further rebleeding, TAE, surgery or repeated endoscopic treatment is considered

Initial pharmacological treatment

- Pause any ASA, NSAIDs, ADP receptor inhibitors, anticoagulants, and SSRI treatment
- Low-risk ulcers (Forrest IIc-III) are treated with oral standard-dosage PPI.

- Ulcers requiring endoscopic treatment are treated with high-dose PPI given intravenously as bolus followed by continuous infusion for 72 hours
- Helicobacter pylori positive patients are given eradication therapy
- Patients who have had surgical haemostasis performed must be treated with low-molecular heparin and compression stockings postoperatively

Summary

Description: The Danish Society of Gastroenterology and Hepatology have compiled a national guideline for the management of peptic ulcer bleeding. Sources of data included published studies up to June 2014. Quality of evidence and strength of recommendations have been graded. The guideline was approved by the Danish Society of Gastroenterology and Hepatology September 4, 2011. The current version is revised June 2014.

Recommendations: Recommendations emphasize the importance of early and efficient resuscitation. Use of a restrictive blood transfusion policy is recommended in haemodynamically stable patients without serious ischaemic disease. Endoscopy should generally be performed within 24 hours, reducing operation rate, rebleeding rate and duration of in-patient stay. When serious ulcer bleeding is suspected and blood found in gastric aspirate, endoscopy within 12 hours will result in faster discharge and reduced need for transfusions. Endoscopic hemostasis remains indicated for high-risk lesions. Hemoclips, thermocoagulation, and epinephrine injection are effective in achieving endoscopic hemostasis. Use of endoscopic monotherapy with epinephrine injection is not recommended. Intravenous high-dose proton pump inhibitor (PPI) therapy for 72 hours after successful endoscopic hemostasis is recommended even though the evidence is questionable. Although selected patients can be discharged promptly after endoscopy, high-risk patients should be hospitalized for at least 3 days after endoscopic hemostasis. Patients with peptic ulcer bleeding who require secondary cardiovascular prophylaxis should start receiving acetylsalicylic acid (ASA) within 24 hours from primary endoscopy.

Patients in need of continued treatment with ASA or a nonsteroidal anti-inflammatory drug should be put on prophylactic treatment with PPI at standard dosage. The combination of 75mg ASA and PPI should be preferred to monotherapy with clopidogrel in patients needing anti-platelet therapy on the basis of indications other than coronary stents. Low-risk patients without clinical suspicion of peptic ulcer bleeding who have a Glasgow Blatchford score ≤ 1 can be offered out-patient care, unless hospital admission is required for other reasons.

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