

National Consensus on Management of Non-Variceal Upper Gastrointestinal Tract Bleeding in Indonesia

The Indonesian Society of Gastroenterology

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ABSTRAK

Pengurus Besar Perkumpulan Gastroenterologi Indonesia (PB PGI) menyusun suatu konsensus nasional mengenai tatalaksana perdarahan saluran cerna bagian atas non-variseal (Non-variceal upper gastrointestinal bleeding/NVUGIB). Hal ini merupakan upaya untuk meningkatkan kualitas pelayanan pasien NVUGIB terkait ulkus peptikum. Adapun penyusunan konsensus ini merujuk pada tiga konsensus terbaru dalam tatalaksana NVUGIB dengan melakukan modifikasi dari proses Delphi untuk menyusun panduan klinis. Ketiga konsensus yang menjadi rujukan tersebut, antara lain: The International Consensus Recommendations on the Management of Patients with Non-variceal Upper Gastrointestinal Bleeding (ICON-UGIB), 2010; Asia-Pacific Working Group consensus on non-variceal upper gastrointestinal bleeding, 2011; dan Management of Patients With Ulcer Bleeding, ACG guidelines, 2012.

Konsensus ini disusun agar menjadi rujukan bagi para praktisi medis di seluruh Indonesia dalam penatalaksanaan pasien dengan perdarahan saluran cerna bagian atas non-variseal terkait ulkus peptikum. Namun, teknik pelaksanaannya sangat tergantung dengan fasilitas diagnostik dan terapeutik yang ada pada masing-masing pusat pelayanan kesehatan.

Kata kunci: endoskopi, perdarahan, perdarahan saluran cerna bagian atas non-variseal/NVUGIB, ulkus peptikum.

ABSTRACT

The Indonesian Society of Gastroenterology has compiled a national consensus guideline for the management of non-variceal upper gastrointestinal bleeding (NVUGIB). It is an endeavor to raise the quality of service for NVUGIB patients associated with peptic ulcer. The references for developing this consensus include three recent consensus guidelines on the management of NVUGIB and a modification of Delphi process was done to develop clinical guidelines. The three references are: The International Consensus Recommendations on the Management of Patients with Non-variceal Upper Gastrointestinal Bleeding (ICON-UGIB), 2010; Asia-Pacific Working Group consensus on non-variceal upper gastrointestinal bleeding, 2011; and Management of Patients with Ulcer Bleeding, ACG guidelines, 2012.

The consensus is compiled as a reference for Indonesian medical practitioners all across the country on the management of patients with non-variceal upper gastrointestinal bleeding associated with peptic ulcer. However, the technical implementation extremely depends on diagnostic and therapeutical facilities available in each health care center.

Key words: endoscopy, bleeding, non-variceal upper gastrointestinal bleeding/NVUGIB, peptic ulcer.

INTRODUCTION

Non-variceal upper gastrointestinal bleeding Perdarahan saluran cerna bagian atas non-variseal is a quite common clinical condition; however in general, the incidence tends to decline in peptic ulcer disease.

There are 3 recent consensus guidelines on this topic, which are: The International Consensus Recommendations on the Management of Patients with Non-variceal Upper Gastrointestinal Bleeding (ICON-UGIB), 2010¹; Asia-Pacific Working Group consensus on non-variceal upper gastrointestinal bleeding, 2011²; and Management of Patients With Ulcer Bleeding, ACG guidelines, 2012.³ Those consensus guidelines have used the most recent data about the management of NVUGIB by modifying the Delphi process in order to compile a clinical guideline. Although the guidelines do provide a comprehensive recommendation and utilize the most recent data from literatures, The International Consensus Recommendations of 2010 and the ACG guidelines 2012, but there is no room for specific needs of limited-resources countries and ethnic differences.

As an example, the use of proton pump inhibitors to reduce the degree of endoscopic lesion and the needs of interventional endoscopy are recommended by the ICON-UGIB. This gives a great financial burden to Asia Pacific countries, which have limited resources. Moreover, there is no well-defined recommendation about the route of administration for PPI, either by intravenous or oral route. Furthermore, it is realized that there are great differences on the degree of *Helicobacter pylori* infection, drug metabolism and the use of anti-thrombotic drugs, which may affect the management of NVUGIB.^{1,2} Most of the abovementioned issues have been addressed attentively when compiling the Asia Pacific guideline and Indonesia has also participated during the development of the guideline. However, it is also realized that Indonesia has great differences from other countries regarding the limited availability of medical facilities and infrastructures for NVUGIB management.

The major limitation is the availability of endoscopy, which is the back bone issue in NVUGIB management. Therefore, the task force

in the Organizing Committee of Indonesian Society of Gastroenterology has attempted to develop a national consensus on the management of UGIB associated with peptic ulcer. It is an endeavor to bridge the varied availability of medical facilities and infrastructure in Indonesia in order to raise the quality of service for patients who have UGIB associated with peptic ulcer. Moreover, the consensus may also serve as a professional recommendation for all medical practitioners in Indonesia regarding the management of patients with non-variceal upper gastrointestinal bleeding that associated with peptic ulcer. However, the technical implementation extremely depends on diagnostic and therapeutical facilities available in each health care center.

EPIDEMIOLOGY

An endoscopic study in patients with dyspepsia symptoms that has been conducted in several big cities in Indonesia demonstrates that peptic ulcer, i.e. gastric and duodenal ulcers, is listed in the top five causes of dyspepsia.⁴

The incidence of UGIB indicates that there are great geographical variations, starting from 48 to 160 cases per 100,000 populations with a higher incidence in male and elderly patients. It can be explained due to various causes including the different definition of UGIB, population characteristics, different prevalence of drug-induced ulcer and *Helicobacter pylori*.^{5,6} Despite the optimal management using therapeutical endoscopy and treatment using gastric acid suppressants, the overall mortality of UGIB remains stable in recent decades, which ranges between 6-14%. Nevertheless, most deaths are not caused directly by massive blood loss, but much more by intolerance to blood loss, shock, aspiration and therapeutical procedures.

The mortality due to UGIB is associated with elderly age and severe comorbidity. The risk of mortality is also increased by recurrent bleeding, which is a major outcome parameter.^{5,7} There is a wide range of recurrent bleeding in patients with UGIB from 5% to more than 20%, which depends on several factors, i.e.: 1) The etiology of bleeding – it is more common due to variceal bleeding and rarely due to small

mucosal lesion such as Mallory-Weiss tear.⁸ 2) Timing and adequate treatment of endoscopy – recurrent most likely occurs in early period of treatment and 24 hours are considered to be the most optimal time for endoscopic treatment.^{7,9}

Peptic ulcer bleeding (PUB) is the most common cause of UGIB. The incidence ranges between 31% and 67% of all cases, which is followed by erosive gastritis, variceal bleeding, esophagitis, malignancy and Mallory-Weiss tear.

In a subgroup of patients with PUB, the incidence of bleeding due to duodenal ulcer is slightly higher than that caused by gastric ulcer.^{5,9} In Indonesia, there is a different distribution, the old data revealed that approximately 70% UGIB is caused by ruptured esophageal varices. Nevertheless, since there are increased care on chronic liver disease and raising population of elderly patients, it is estimated that the proportion of bleeding caused by peptic ulcer will also increase.^{8,10,11}

Data from one of hospitals in Indonesia (Sanglah Hospital, Bali) reveal that the most common cause of gastrointestinal bleeding is peptic ulcer, which is followed by erosive gastritis.¹² Based on a retrospective study, which was performed in 4,154 patients who underwent endoscopy in 2001-2005 at the Endoscopic Center of Cipto Mangunkusumo Hospital, Jakarta, there are about 807 (20.15%) patients who have experienced UGIB. The study also demonstrates that the most common cause of UGIB is ruptured esophageal varices (280 cases; 33.4%) followed by peptic ulcer bleeding (225 cases; 26.9%), and erosive gastritis (219 cases; 26.2%) (Table 1).¹³

Table 1. The most common causes of UGIB in patients who underwent endoscopy at the Endoscopic Center of Cipto Mangunkusumo Hospital in 2001-2005

Causes	Cases	Percentage (%)
Ruptured esophageal varices	280	33.4
Peptic ulcer bleeding	225	26.9
Erosive gastritis	219	26.2
Not found	38	4.5
Others	45	9.0
Total	807	100

RISK FACTORS FOR PEPTIC ULCER

As seen in Figure 1, *H. pylori* infection is a major factor in the development of ulcers, both duodenal and gastric ulcers. The data were taken from studies on western countries populations. Although they may have a list with similar order, it is estimated that in developing countries, *H. pylori* plays a more significant role.¹⁴

The evaluation of clinical staging is an important early management step. Elderly age, multiple comorbidity and hemodynamic instability call for aggressive treatment. Regardless of the general clinical guideline, a systematical staging has been developed.

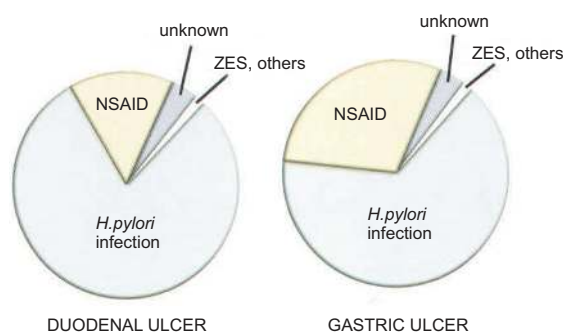


Figure 1. Proportion of risk factors for peptic ulcer.¹⁴

RISK STRATIFICATION FOR RECURRENT BLEEDING AND MORTALITY

Rockall Scoring System is the most utilized scoring system, which provides an estimation risk for bleeding and mortality. The scoring system is developed based on three clinical factors and two endoscopic factors. These factors are presented in Table 2.

Rockall scoring system may range between 0-11; while the score of 0-2 is associated with good prognosis. Another scoring system, which is the Blatchford scoring system only utilizes laboratory and clinical factors and therefore, it is recommended for Asian patients in the recent Asia-Pacific consensus guideline.² Unlike Rockall Scoring System, the major outcomes of this scoring system may predict the needs of clinical intervention such as endoscopy, surgery or blood transfusion. Blatchford Scoring System (Table 3) ranges between 0-23; which the scores of 6 or higher are considered to require intervention.

Table 2. Rockall scoring system¹

Variables	Score 0	Score 1	Score 2	Score 3
Age (year)	<60	60-79	>80	-
Shock	None	Pulse Rate >100x/minute, BP normal	Pulse Rate >100x/minute, Systolic BP <100 mmHg	-
Comorbidity	None	-	Ischemic heart disease, congestive heart failure, and any major comorbidity	Renal failure, hepatic failure, metastasis
Endoscopy diagnosis	Mallory-Weiss Tear, no lesion observed, no stigmata of recent hemorrhage	Peptic ulcer, esophagitis, or erosive disease	Malignancy of upper GI tract	-
Stigmata of endoscopic or recent hemorrhage	Clean ulcer base, flat pigmented spot	-	Blood in upper GI tract, active bleeding, visible vessel without bleeding or adherent clot	-

Table 3. The Blatchford scoring system to determine the needs of intervention⁵

Variables	Points	Variables	Points
Systolic blood pressure (mmHg)		Hemoglobin (male; g/dL)	
- 100-109	1	- 12.0-12.9	1
- 90-99	2	- 10.0-11.9	3
- <90	3	- <10.0	6
Urem (mg/dL)		Hemoglobin (female; g/dL)	
- 36.5-44.5	2	- 10.0-11.9	1
- 44.6-55.5	3	- <10.0	2
- 55.6-139.9	4		
- >140	6		
Other variables			
- Pulse rate >100	1		
- Presentation with melena	1		
- Hepatic disease	2		
- Heart failure	2		
Total			

Some risk factors are also associated with bad prognosis after the bleeding incident associated with peptic ulcer (**Table 4**). If this occurs, clinicians must be more aggressive in determining the management that will be carried out.

DIAGNOSIS

History Taking

The most common signs and symptoms of upper gastrointestinal tract bleeding are

Table 4. Risk factors that characterize bad prognosis in patients with peptic ulcer bleeding¹⁴

Age >60 years
Bleeding onset at the hospital
Comorbid medical
Shock or orthostatic hypotension
Fresh blood in nasogastric tube
Coagulopathy
Requirement of repeated transfusion
Ulcer at the upper part of lesser curvature (near the left gastric artery)
Ulcer at the posterior duodenal bulb (near the gastroduodenal artery)
Endoscopic findings of arterial bleeding or visible blood vessel

hematemesis (vomiting of blood), coffee ground emesis and melena (black tarry stool). About 30% of patients with ulcer bleeding present with hematemesis, 20% with melena and 50% with both. Hematochezia (fresh blood in stool) usually indicates that the source of bleeding is in the lower gastrointestinal tract as the upper gastrointestinal bleeding will turn into black and tarry color during their passage through the GI tract resulting in melena. However, 5% of patients who experienced ulcer bleeding may present with hematochezia, which characterizes severe bleeding that usually is more than 1,000 mL. Patients who present with hematochezia and other hemodynamic instability signs such as syncope, postural hypotension, tachycardia and shock must be considered as patients with upper gastrointestinal tract bleeding.

Non-specific signs and symptoms including nausea, vomiting, epigastric pain, vasovagal phenomenon and syncope as well as the most common comorbidities (such as diabetes mellitus, coronary heart disease, stroke, chronic kidney disease and arthritis) and the history of medication must also be identified.^{5,8,14}

Physical Examination

Evaluation on hemodynamic status (pulse rate and blood pressure), respiratory rate, level of consciousness, pale conjunctiva, slow capillary refill time and no stigmata of chronic liver cirrhosis, which are the early symptoms, must be identified immediately.

Tachycardia on rest and orthostatic hypotension indicate a considerably large amount of blood loss. Low urine output, dry lips and collapse of jugular veins are relatively useful signs. It should be noted that tachycardia may not appear if the patient is on medication with beta blocker drugs, which are commonly used for patients with heart failure and liver cirrhosis.^{5,8,14}

Further Assessment

Although it is not a routine procedure for peptic ulcer bleeding, inserting nasogastric tube (NGT) and evaluating the aspirate are usually useful for early clinical assessment. If bright red blood is detected, then the patient needs immediate endoscopic evaluation and should be managed at the intensive care unit. Reduced hemoglobin level of 1g/dL is associated with 250 mL blood loss. If there is any coffee ground emesis, then the patient needs hospitalization and endoscopic evaluation within 24 hours. However, normal aspirate does not exclude gastrointestinal tract bleeding. About 15% of patients with normal aspirate remain to have active gastrointestinal tract bleeding or high risk for recurrent bleeding.^{5,8,14} Endoscopy detects not only peptic ulcer, but also can be utilized to evaluate stigmata associated with increased risk of recurrent bleeding (**Figure 2**).

Forrest Classification is used to categorize findings during endoscopic evaluation with following description: Ulcer with active spurting (Forrest IA); Ulcer with oozing bleeding (Forrest IB); Ulcer with non-bleeding visible vessel (Forrest IIA); Ulcer with adherent clot (Forrest

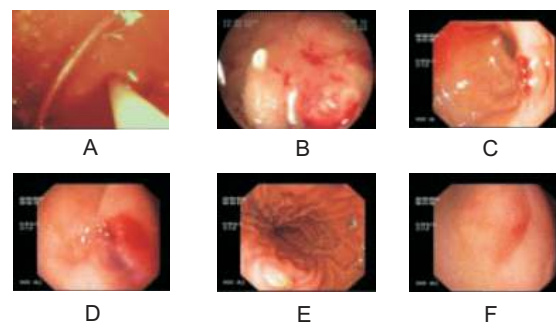


Figure 2. Endoscopic stigmata of recent hemorrhage of a peptic ulcer. A. active bleeding with spurting; B. Oozing bleeding; C. Visible vessel with an adjacent clot; D. Adherent clot. E. Based pigmented spot; F. a clean-based ulcer.

IIB); Ulcer with flat pigmented spot (Forrest IIC); and Clean-based ulcers (Forrest III).

Patients at high risk of rebleeding without treatment are those with active arterial bleeding (90%), the occurrence of a non-bleeding visible vessel (50%) an adherent clot (33%).^{5,8,14}

COMPLICATION

Complication that may occur due to peptic ulcer bleeding is hypovolemic shock, which may be followed with acute renal failure, multi organ failures and death.

TREATMENT

Early Management

An appropriate early evaluation and resuscitation are important measures that should be carried out for patients with UGIB, especially for those who present with hematemesis, massive hematochezia, melena or progressive anemia. We suggest early management with multidisciplinary approach involving an internist/gastroenterologist, an interventional radiologist and a surgeon/digestive surgeon.^{9,14,15}

Stratification of the patient into low or high risk category for recurrent bleeding and mortality may be carried out using Blatchford and Rockall Scoring System (in keeping with the availability of endoscopy facility). Patients with high risk for recurrent bleeding and mortality should be hospitalized in Intensive Care Unit.^{5,14}

Nasogastric tube (NGT) is inserted for the assumed ongoing bleeding, which is accompanied

with hemodynamic instability. The purpose of NGT insertion is to prevent aspiration, provide gastric decompression and evaluate bleeding; therefore, it is not necessarily performed in all patients with bleeding.³ Nasogastric or orogastric lavage can be performed in patients with upper gastrointestinal tract bleeding in certain circumstances. Ice water is not recommended for gastric lavage.³

Resuscitation measures include administration of intravenous fluid, oxygen supplementation, correction of severe coagulopathy and blood transfusion as needed.

The threshold for blood transfusion depends on general medical condition and vital signs of the patients, but it is usually set at a hemoglobin level of ≤ 7.0 g/dL unless if there is ongoing or massive bleeding and there is comorbidity of coronary heart disease, hemodynamic instability (hypotension and tachycardia) and elderly age.⁹

The minimal hemoglobin level required for endoscopy is 8 mg/dL and if a therapeutical endoscopy will be provided, the minimal hemoglobin level is 10 mg/dL and the patient should have a stable hemodynamic status. Pre-endoscopic PPI therapy can be recommended (1B recommendation) for patients with PUB. The acidic environment may cause inhibition of platelet aggregation and plasma coagulation, which may also result in lysis of the already formed clots. Administration of PPI therapy can rapidly neutralize intraluminal gastric acid, which results in stabilization of blood clot. In long term, antisecretory therapy also promotes mucosal healing. A recent study shows that pre-endoscopic PPI therapy has significantly reduced high-risk stigmata at early endoscopy (37% vs. 46%, OR 0.67; 95% CI 0.54-0.84). However, it shows no effect on recurrent bleeding, mortality and surgery.¹⁶

When endoscopy will be delayed and can not be performed, an intravenous PPI therapy is recommended to reduce further bleeding.³

Timing of Endoscopy

Endoscopy has become a major tool of diagnosis and treatment of UGIB. This procedure allows identification of the bleeding source and provides treatment in the same session. Emergency endoscopy allows for early

hemostasis, but it can potentially lead to blood aspiration and oxygen desaturation in unstable patients. In addition, excessive amounts of blood and clots may disturb targeted therapy for bleeding focus, which may cause the necessary repeated endoscopic procedures.^{3,9,14}

The international consensus and Asia Pacific guidelines recommend early endoscopy within 24 hours after the patients have been hospitalized, as this treatment significantly reduces the length of hospital stay and improve clinical outcome. The very early endoscopy (<12 hours) so far has not been shown to give additional advantages in terms of reduced risk for recurrent bleeding, surgery and mortality. However, emergency endoscopy should be considered in patients with severe bleeding. In patients with clinical manifestation of greater risks (such as tachycardia, hypotension, hematemesis or bright red blood in NGT), an endoscopy within 12 hours may increase clinical outcome.¹⁻³

In patients with stable hemodynamic status and without any serious comorbidity, endoscopy should be performed first before discharging the patient from hospital.³

Endoscopic Therapy for PUB

The aim of therapeutic endoscopy is to stop active bleeding and prevent recurrent bleeding. Several techniques, including injection, ablative and mechanical treatment have been developed over recent decades. The selection of treatment can be adjusted according to the appearance of bleeding focus and related risk for persistent and recurrent bleeding (**Figure 3**). In PUB, patients with active bleeding or non-bleeding visible vessel in ulcer beds are at the highest risk for recurrent bleeding; therefore, they need immediate endoscopic hemostatic therapy. Patients with low-risk stigmata (a clean-based ulcer or a pigmented spot in ulcer beds) do not need endoscopic therapy.^{3,7}

Patients with clean-based ulcers may have a soft diet and be discharged after endoscopy assuming they have a stable hemodynamic status, adequate hemoglobin level and they have no other medical problems.³ Patients with active ulcer bleeding, hemostasis therapy should be given in combination (epinephrine in addition to other modalities such as hemoclip placement,

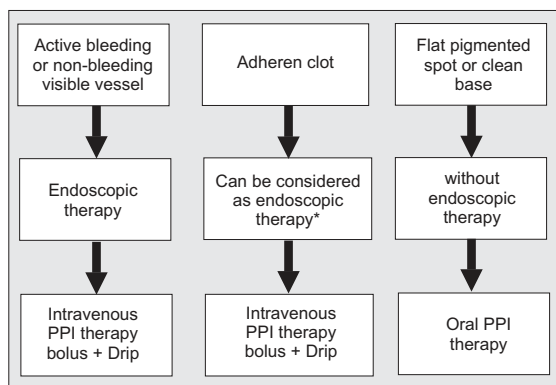


Figure 3. The management options including endoscopic and intravenous PPI treatment for patients with UGIB associated with peptic ulcer. PPI = proton pump inhibitor. *If the endoscopic therapy facility is optimal.

thermocoagulation and electrocoagulation). Epinephrine injection is not recommended as single therapy. Injection with clip placement is recommended as it may reduce the incidence of recurrent bleeding.^{3,14}

Patients who endoscopically have high-risk stigmata (active bleeding, visible vessels, clots (according to the Forrest Classification)) are generally hospitalized for 3 days if there is no recurrent bleeding and no other indication for hospitalization. The patients can have clear liquid diet soon after the endoscopy and the diet should be customized gradually.³ Patients with recurrent bleeding can usually be managed with endoscopic therapy. However, emergency surgery or angiographic embolization may be needed under certain circumstances, such as: spurting bleeding that can not be stopped by endoscopy, non-visible bleeding spot due to massive active bleeding, and recurrent bleeding that occurs after the second therapeutic endoscopy.

POST-ENDOSCOPIC MANAGEMENT

Antisecretory Therapy

Pharmacotherapy plays a second major role in the treatment of UGIB due to peptic ulcer. PPI therapy is more superior compared

to the histamine-2 receptor antagonist. PPI can be administered orally or intravenously depending on the bleeding stigmata (Forrest Classification). Available data have recommended the administration of high-dose continuous intravenous PPI therapy for PUB patients with high-stigmata risks.

Patients with PUB should also be discharged with a prescription for a single-daily-dose oral PPI to reduce the risk of recurrent bleeding. The duration and dose of PPI depend on the etiology and any other medication use. In patients with idiopathic (non-*H.pylori*, non-NSAID) ulcers can be recommended to have long-term antiulcer therapy (such as daily PPI). In patients with low-dose aspirin-associated bleeding ulcers, the urgent need for aspirin should be re-assessed.^{1,2,14}

H. pylori Eradication Therapy

H. pylori test is recommended in all patients with PUB. The test is subsequently followed with eradication therapy for all patients who have positive results, continuous monitoring to assess the results of this therapy and renewed treatment for those with failed eradication.

The triple therapy eradication has a successful rate of 80% or even 90% in peptic-ulcer patients without any significant side effects and has a minimal effect on antibiotic resistance. Furthermore, regarding the evaluation of ulcer healing by endoscopy, it is found that the success rate of one-week PPI therapy reaches 80–85%. After eradication of *H. pylori* has been confirmed, no maintenance therapy of PPI is necessary unless in patients who are NSAIDs or antithrombotic users.

Diagnostic test for *H. pylori* has a low negative predictive value in acute UGIB. It may be due to technical difficulties to perform a representative biopsy or inaccuracy of the test in an alkaline environment caused by the blood. Negative results of biopsy obtained in the acute setting must be carefully interpreted and when necessary, repetition of the test should be performed during the follow up.^{1-3,9,17}

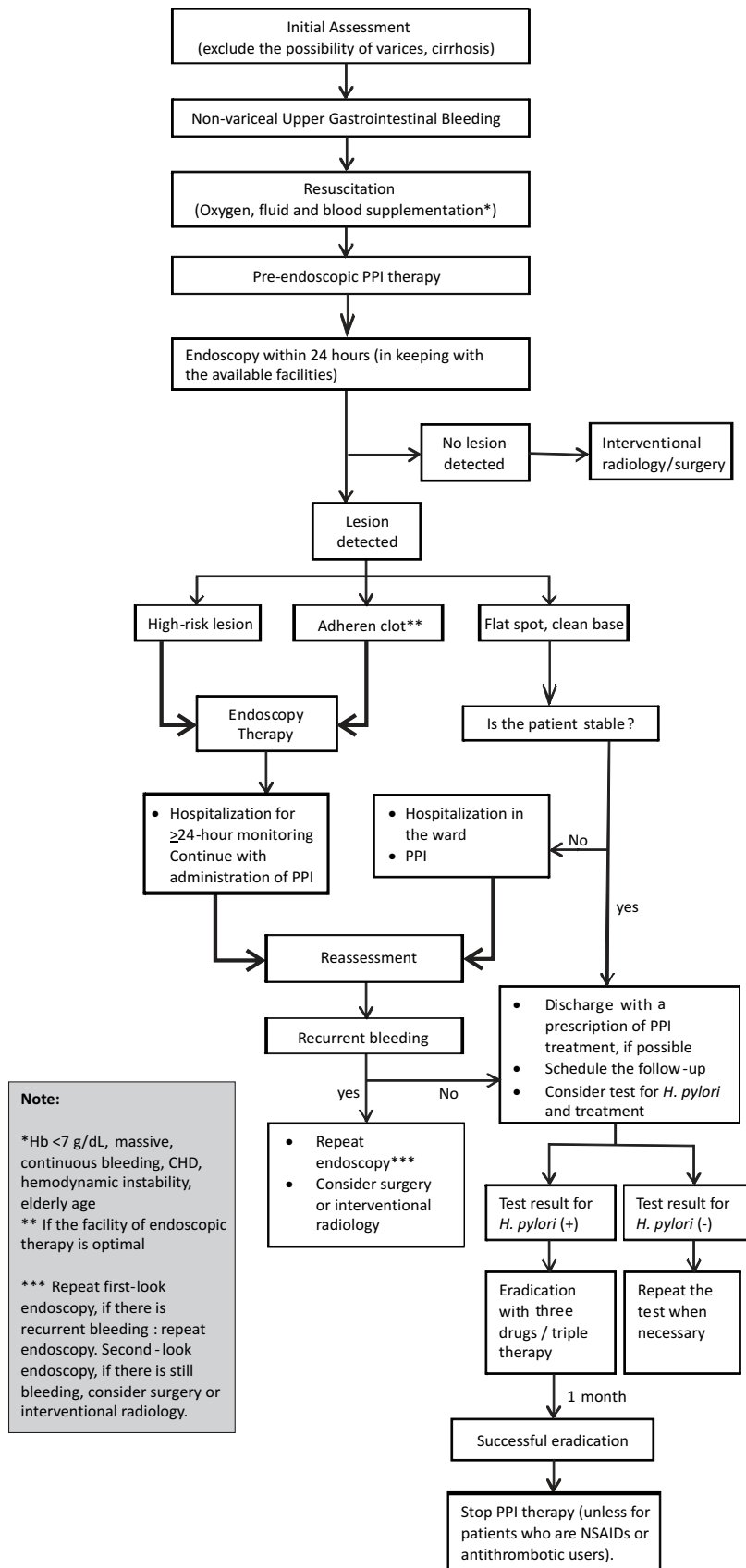


Figure 4.

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