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Current standards in the management of acute peptic ulcer bleeding

Ostre krwawienie z wrzodu trawiennego – aktualne standardy postępowania

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Summary

Acute peptic ulcer bleeding remains one of the most frequent medical emergency in internal medicine, with significant risk of mortality and severe complications. Appropriately organized multidisciplinary management, based on clinically proven algorithms, helps to control this clinical situation and improve outcomes in this group of patients. It should be noted crucial role of endoscopy, which done in a proper time and under optimal conditions, is the basis for the planning of further procedures, helps in determining prognosis and allows effective control of bleeding.

This paper aims to outline most important recommendations for the management of patients with overt upper gastrointestinal bleeding due to gastric or duodenal ulcers. The recommendations are based on the current practice guidelines, accepted and published by the American College of Gastroenterology (1) in 2012 and Polish guidelines published in 2008 (2).

Streszczenie

Ostre krwawienie z wrzodu trawiennego pozostaje jednym z częstszych stanów nagłych w chorobach wewnętrznych, z istotnym ryzykiem zgonu i wystąpienia ciężkich powikłań. Odpowiednio zorganizowane, zespołowe postępowanie w tej grupie pacjentów, oparte na dobrze udokumentowanych algorytmach, ułatwia opanowanie sytuacji klinicznej i chroni chorych przed niekorzystnymi konsekwencjami krwotoku. Należy zwrócić uwagę na kluczowe znaczenie badania endoskopowego, które wykonane w odpowiednim czasie i optymalnych warunkach stanowi podstawę dla planowania dalszego postępowania, pomaga w określeniu rokowania oraz umożliwia wykonanie w większości przypadków skutecznego tamowania krwawienia.

W artykule zawarto najważniejsze informacje dotyczące aktualnie rekomendowanych na świecie standardów postępowania z pacjentami z ostrym krwawieniem z wrzodu trawiennego, w oparciu o bieżące zalecenia przyjęte i opublikowane w 2012 r. przez American College of Gastroenterology (1). Część z tych wiadomości jest zawarta w wytycznych polskiej grupy roboczej konsultanta krajowego w dziedzinie gastroenterologii, opublikowanych w 2008 roku (2).

INTRODUCTION

Gastric and duodenal ulcers are the most common cause of acute upper gastrointestinal bleeding (UGIB). Patients with bleeding should be hospitalized and treated under emergency conditions. Despite the broad availability of modern diagnostic and therapeutic procedures such as endoscopy and the use of acid suppressing drugs, it still remains a potentially fatal condition with mortality of up to 10% and high rate of severe complications. Application of clinically proven recommendations leads to diminution of patients mortality and morbidity and improvement in clinical outcomes. These may also result in shorter hospital stay resulting in better cost-effectiveness.

Key issues related to management of patients with overt UGIB presenting with hematemesis, melena and also hematochezia will be discussed in this article.

First section of the article presents initial management of UGIB due to ulcers in patients without suspicion of liver disease associated with esophageal varices. Second part provides information about the role of endoscopic therapy and the third part summarizes post-endosopic management including further treatment, time of hospital stay and re-bleeding prevention.

MULTIDISCIPLINARY WORK-UP

Health care facilities admitting patients with UGIB should be properly equipped and prepared for diagnostic and therapeutic steps in this condition. It is necessary to organize a collective and synchronized management algorithms within units that may be involved in treating this condition. Such integrated approach should involve Emergency Department, Endoscopy Unit, General or Gastrointestinal Surgical Unit with Operating Room, Intensive Care Unit and General or Gastrointestinal Medicine Unit. Furthermore, the role of other, supporting units including hospital laboratory providing blood products, hospital pharmacy and Radiology Unit is of primary relevance.

INITIAL ASSESSMENT

A primary goal in management of a patient with overt UGIB is assessing clinical condition focusing on hemodynamic status. In patients with clinical signs of shock or ongoing bleeding with high risk of hemodynamic collapse resuscitation measures should be immediately initiated. Peripheral venous access (more than one in some cases) enabling transfusion of intravenous fluids should be obtained. **Fast transfusion of red blood** cells compatible with patient's original blood group should be required when hemoglobin level is lower than 7 g/dl (3). In patients with cardiovascular comorbidities, like coronary heart disease, blood transfusion may be considered even with higher hemoglobin level (4). It is also necessary to withdraw the blood specimen for respective blood tests (blood group when no documentation is available, complete blood count, routine biochemistry and coagulation panel). It is obligatory to monitor vital parameters such as heart rate, blood pressure, arterial blood saturation and urine output.

After stabilizing the patient it is necessary to assess the risk of bleeding using one of available scoring systems, such as pre-endoscopic Rockall score (range 0-7, higher value indicates higher risk of death and recurrent bleeding). It uses simple clinical data available immediately at presentation: heart rate, systolic blood pressure, patients age and comorbidities (tab. 1). Rockall scoring system facilitates the delivery of the appropriate level of care to patients and may assist in initial decisions such as timing of endoscopy, need for surgical intervention and time of discharge.

Thus, patients with the highest score (Rockall score 6-7) should be immediately admitted to Intensive Care Unit, while patients with lower Rockall score values may be treated within General Internal Medicine or Surgical Unit. Those with the lowest score (Rockall score 0-1) may be discharged from the emergency department usually within 24 hours just after receiving necessary evaluation including endoscopy showing no active or recent hemorrhage (5).

PRE-ENDOSCOPIC MEDICAL THERAPY

Basic pre-endoscopic pharmacologic treatment include acid suppressant agents like proton-pump inhibitors (PPIs). **Providing 80 mg omeprazole bolus followed** by continuous 8 mg/h infusion is recommended. Such a treatment increases the chances of spontaneous hemostasis, diminishing the risk of early re-bleeding and also the need for endoscopic and surgical intervention (6).

Intravenous infusion of 250 mg erythromycin given approximately 30-minutes before endoscopy may be considered in bleeding patients. The prokinetic effect of this drug accelerates gastric emptying from residual content (blood, clots and remaining food) improving efficiency in localizing the bleeding source, therefore decreasing the need for repeat endoscopy (7-10).

Current recommendations, based on reliable clinical trials, do not support routine application of nasogastric tube or gastric lavage (1).

ENDOSCOPY

Timing of endoscopy

Vast majority of patients with UGIB should undergo gastroscopy within 24 h of admission. As mentioned before, first endoscopy should always be preceded by assessment of general clinical condition and bleeding risk stratification. Proper medical therapy including intravenous fluids, transfusion of red blood cells and acid suppressing therapy with PPIs should be undertaken to achieve clinical stabilization. In stable, low-risk patients without severe comorbidities endoscopy can be performed in a non-emergent setting, therefore in the first available occasion within normal endoscopy unit work schedule, usually next day in the morning. This setting is especially important for the lowest-risk patients (Rockall score 0-1) of whom most can be safely discharged same day after endoscopy with ambulatory follow-up. Higher-risk patients (Rockall score $\geq$ 5), hemodynamically unstable or with clinical evidence of ongoing bleeding need endoscopy in emergency setting within first hours after admission.

Table 1. Pre-endoscopic Rockall scoring system.

Variable	Score 0	Score 1	Score 2	Score 3
Age	< 60 years	60-79 years	> 80 years	
Blood pressure fall (Shock)	No shock SBP > 100 and pulse < 100/min	Tachycardia SBP > 100 and pulse > 100/min	Hypotension SBP < 100 and pulse > 100/min	
Co-morbidity	No major comorbidity		IHD, HF, any major comorbidity	Renal or liver failure, disseminated malignancy

SBP – systolic blood pressure; HF – heart failure; IHD – ischemic heart disease
Total range of the scoring system, which is a summary of particular lines, is between 0 to 7.
First letters of variables arrange in an easy-to-remember ABC scheme.

Anesthesiologist assistance and tracheal intubation for prevention of aspiration blood or clots may be necessary. To improve the visualization of all gastric walls when the stomach is filled with residual content (food particles, blood, clots) changing patient's position (for example turning on the back or the right side) during the procedure may be helpful. If endoscopic intervention is not available, urgent surgery is obligatory.

Endoscopic diagnosis

Endoscopy of upper gastrointestinal tract performed within 24 hours after admission enables to confirm (or exclude) initial diagnosis of bleeding due to peptic ulcer (11, 12). **When active bleeding from erosion or ulcer is detected, whether spurting or oozing, endoscopic hemostatic therapy is required.** In case when no active bleeding is visible, it is necessary to describe the appearance of ulcer base in terms of so called stigmata of recent hemorrhage (SRH). These include visible (non-bleeding) vessel, adherent clot or flat, pigmented spot in the basis of the ulcer. Identifying particular SRH and corresponding Forrest et al. classification value (13, 14) (tab. 2), enables to predict the risk of re-bleeding within the next 2-3 days of hospital stay.

These may also indicate the need for surgical treatment which is associated with growing risk of severe complications and death. Respectively, active bleeding (Forrest IA and IB) holds a 50% risk of re-bleeding, mortality of 10% and need for surgical treatment in about 35% of the cases. Identifying visible vessel in the basis of the ulcer (Forrest IIA) holds a lower re-bleeding risk of 40%, but similar mortality rate and need for surgery. In case of adherent clot (Forrest IIB) the re-bleeding risk decreases to 20%, mortality to 5-7% and need for surgery to 10%. Even lower values of these indicators (< 10%) are seen in patients with pigmented spot in the basis of ulcer (Forrest IIC) or clean base (Forrest III). Furthermore, Forrest et al. classification complement already mentioned Rockall clinical scoring system (tab. 3).

Patients in whom gastroscopy revealed active bleeding or high risk stigmata of hemorrhage (Rockall score > 4) are requiring careful monitoring of clinical status, further treatment including continuous PPI i.v. infusion and endoscopic therapy, but also readiness for urgent surgery. Lower risk patients (Rockall score 1-3) may be discharged within 2-3 days with recommendation of standard oral antisecretive treatment (omeprazole 2 x 20 mg) with further treatment and supervision under ambulatory conditions.

In case of visible clot on the base of the ulcer, it is recommended to irrigate the clot using water pomp device or a syringe. Effective irrigation enables to wash away the clot revealing the base of the ulcer, which enables to assess the risk of re-bleeding using Forrest et al. classification. In some of the cases water irrigation may activate bleeding mandating endoscopic therapy (1).

Endoscopic evaluation of bleeding site (active or recently underwent) is not an ideal tool for prognosis. Marked differences in interpretation of endoscopic image can be seen between endoscopists often related to level of their experience and underwent training. Therefore, proper interpretation and use of Forrest et al. classification should be part of basic endoscopic training.

Table 2. Forrest et al. classification; endoscopic picture and prognosis (14-15).

Endoscopic picture	Grade	Incidence	Rebleeding	Emergency Surgery	Mortality
Active spurting bleeding	IA	12%	55%	35%	11%
Active oozing bleeding	IB				
Visible non-bleeding vessel	IIA	8%	43%	34%	11%
Adherent clot	IIB	8%	22%	10%	7%
Haematin on ulcer base (flat pigmented spot)	IIC	16%	10%	6%	3%
Clean ulcer base with no bleeding	III	55%	5%	0.5%	2%

Table 3. Complete Rockall scoring system (with post-endosopic part including Forrest et al. classification).

Variable	Score 0	Score 1	Score 2	Score 3
Age	< 60 years	60-79 years	> 80 years	
Blood pressure fall (Shock)	No shock SBP > 100 and pulse < 100/min	Tachycardia SBP > 100 and pulse > 100/min	Hypotension SBP < 100 and pulse > 100/min	
Co-morbidity	No major comorbidity		IHD, HF, any major comorbidity	Renal or liver failure, disseminated malignancy
Diagnosis	Mallory-Weiss tear or no lesion and no SRH	All other diagnoses (erosion, ulcer)	Gastrointestinal malignancy	
Evidence of bleeding (Forrest classification)	III	IIC	IA-B, IIA-B	

SBP – systolic blood pressure; HF – heart failure; IHD – ischemic heart disease; SRH – stigmata of recent hemorrhage
Total range of the scoring system, which is a summary of particular lines, is between 0 to 11.
First letters of variables arrange in an easy-to-remember ABCDE scheme.

Endoscopic hemostasis treatment

Current recommendations are indicating that endoscopic therapy should be provided to all patients with active bleeding (Forrest IA and IB) or a non-bleeding visible vessel in the base of the ulcer (Forrest IIA). This treatment is not required in patients who have an ulcer with a clean base or a flat pigmented spot (Forrest IIC and III). Endoscopic therapy can be broadly categorized into mechanical, thermal and injection therapy. The combined approach is proven to be more efficacious than monotherapy. Injection with solutions of diluted epinephrine (1:10 000) is widely used because of its simplicity. Thetamponade effect induced by the volume of injected solution and vasoconstrictive effect of epinephrine enables better evaluation of bleeding site and more effective appliance of supplementary therapy – for example hemoclips, thermal treatment like argon plasma coagulation (APC) or additional injection of sclerotizing agents.

If the *Helicobacter pylori* status is not established, testing for its presence should be performed at the end of endoscopic procedure. Endoscopic tests for *Helicobacter pylori* include biopsies for histologic examination or for rapid urease testing.

POST-ENDOSCOPIC TREATMENT

After successful endoscopic hemostasis of active bleeding, intravenous PPI therapy with 8 mg/h continuous infusion for 72 hours should be given. This pharmacological therapy should be also applied to patients in whom visible non-bleeding vessel or adherent clot was found (Forrest IIA and IIB). They may be fed with clear fluids soon after endoscopy. Patients with pigmented spot or clean ulcer base (Forrest IIC and III) may be treated with standard oral PPI therapy (omeprazole 2 x 20 mg). No restriction in dietary regiments are necessary.

In patients without clinical evidence of recurrent bleeding current guidelines do not recommend repeat endoscopy within 24 hours. **Such an approach should be performed in case of clinical evidence of ongoing bleeding.** In case of failure in achieving hemostasis in repeated endoscopic intervention patient may have to undergo urgent interventions such as surgery or interventional radiology with transcathether arterial embolization.

After achieving hemostasis in patients with active bleeding (Forrest IA and IB) or presence of SRH (Forrest IIA and IIB) hospitalization for at least 3 days is required. After that time, if no recurrent bleeding occurs and there are no other medical indications for prolonged hospitalization, these patients may be discharged with continuing antisecretory oral therapy (PPI).

LONG-TERM PREVENTION OF RECURRENT BLEEDING

Bleeding patients with *Helicobacter pylori* associated ulcers should receive eradication treatment (15). After documented successful eradication, maintaining antisecretory therapy is not needed, unless the patient also requires non-steroidal antiinflammatory drugs (NSAIDs) or antiplatelet therapy. The same applies to patients with idiopathic (non *Heclicobacter pylori*, non NSAIDs) ulcers.

To prevent recurrent bleeding in patients staying on NSAIDs treatment it is recommended to carefully asses the need for such treatment. Change of dosing or type of drug may be considered.

In order to minimalize cardiovascular and cerebrovascular risk in patients requiring acetylic acid for secondary prevention, this kind of treatment should be resumed as soon as possible (usually at the time of discharge), preferably within 1-3 days and certainly within 7 days (16, 17).

BIBLIOGRAPHY

1. Laine L, Jensen DM: Management of Patients With Ulcer Bleeding. Am J Gastroenterol 2012; 107: 345-360.
2. Marek T, Baniukiewicz A, Wallner G et al.: Wytyczne postępowania w krwawieniu z górnego odcinka przewodu pokarmowego pochodzenia nieżylakowego. Przegląd Gastroenterologiczny 2008; 3(1): 1-22.
3. Villanueva C, Colomo A, Bosch A et al.: Transfusion strategies for acute upper gastrointestinal bleeding. N Engl J Med 2013; 368: 11-21.
4. Hebert PC, Wells G, Blajchman MA et al.: A multicenter, randomized, controlled clinical trial of transfusion requirements in critical care. Transfusion Requirements in Critical Care Investigators, Canadian Critical Care Trials Group. N Engl J Med 1999; 340: 409-417.
5. Rockall TA, Logan RFA, Devlin HB et al.: Risk assessment after acute upper gastrointestinal haemorrhage. Gut 1996; 38: 316-321.
6. Lau JY, Leung WK, Wu JCY et al.: Omeprazole before endoscopy in patients with gastrointestinal bleeding. N Engl J Med 2007; 356: 1631-1640.
7. Sreedharan A, Martin J, Leontiadis GI et al.: Proton pump inhibitor treatment initiated prior to endoscopic diagnosis in upper gastrointestinal bleeding. Cochrane Database Syst Rev 2010 (7): CD005415.
8. Barkun AN, Bardou M, Martel M et al.: Prokinetics in acute upper GI bleeding: a meta-analysis. Gastrointest Endosc 2010; 72: 1138-1145.
9. Altraif I, Handoo FA, Aljumah A et al.: Effect of erythromycin before endoscopy in patients presenting with variceal bleeding: a prospective, randomized, double-blind, placebo-controlled trial. Gastrointest Endosc 2011; 73: 245-250.
10. Pateron D, Vicaut E, Debuc E et al.: Erythromycin infusion or gastric lavage for upper gastrointestinal bleeding: a multicenter randomized controlled trial. Ann Emerg Med 2011; 57: 582-589.
11. Spiegel BM, Vakil NB, Ofman JJ: Endoscopy for acute nonvariceal upper gastrointestinal tract hemorrhage: is sooner better? A systematic review. Arch Intern Med 2001; 161: 1393-1404.
12. Tsoi KKF, Ma TKW, Sung JJY: Endoscopy for upper gastrointestinal bleeding: How urgent is it? Nat Rev Gastroenterol Hepatol 2009; 6: 463-469.
13. Forrest JA, Finlayson ND, Shearman DJ: Endoscopy in gastrointestinal bleeding. Lancet 1974; 2: 394-397.
14. Enestvedt BK, Gralnek IM, Mattek N et al.: An evaluation of endoscopic indications and findings related to nonvariceal upper-GI hemorrhage in a large multicenter consortium. Gastrointest Endosc 2008; 67: 422-429.
15. Gisbert JP, Khorrami S, Carballo F et al.: Meta-analysis: *Helicobacter pylori* eradication therapy vs. antisecretory non-eradication therapy for the prevention of recurrent bleeding from peptic ulcer. Aliment Pharmacol Ther 2004; 19: 617-629.
16. Sung JJY, Lau JWY, Ching JYL et al.: Continuation of low-dose aspirin therapy in peptic ulcer bleeding: a randomized trial. Ann Intern Med 2010; 152: 1-9.
17. Derogar M, Sandblom G, Lundell L et al.: Discontinuation of Low-Dose Aspirin Therapy After Peptic Ulcer Bleeding Increases Risk of Death and Acute Cardiovascular Events. Clinical Gastroenterology and Hepatology 2013; 11: 38-42.

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