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REVIEW ARTICLE

Diagnosis and treatment of variceal bleeding

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Summary

Portal hypertension is defined as an increase in the hepatic venous pressure gradient, most commonly resulting from liver cirrhosis and leading to the development of portosystemic collaterals, particularly esophageal varices. At the time of cirrhosis diagnosis, approximately 50% of patients have esophageal varices, and variceal bleeding represents one of the most severe and life-threatening complications in gastroenterology.

Esophagogastroduodenoscopy is the cornerstone for both diagnosis and treatment of acute variceal bleeding. Therapeutic options include endoscopic hemostasis, pharmacological therapy, balloon tamponade, interventional radiology procedures, and surgical interventions. Endoscopic band ligation is the preferred first-line endoscopic treatment, while sclerotherapy, involving intravariceal or paravariceal injection of sclerosant agents, is now used less frequently.

Pharmacological management includes splanchnic vasoconstrictors such as octreotide, terlipressin, vapreotide, and somatostatin analogues, along with supportive measures including fluid resuscitation, blood product transfusion, and correction of coagulopathy. Prophylactic antibiotic therapy, most commonly with fluoroquinolones or cephalosporins, is mandatory in cirrhotic patients with variceal bleeding.

Balloon tamponade using devices such as Sengstaken–Blakemore, Minnesota, or Linton–Nachlas tubes serves as a temporary rescue therapy. In cases refractory to standard treatment, transjugular intrahepatic portosystemic shunt (TIPS) or surgical management may be considered in carefully selected patients. Management of variceal bleeding requires intensive care and a multidisciplinary approach.

Keywords: varices, bleeding, portal hypertension

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INTRODUCTION

Portal hypertension represents the central pathophysiological impairment in the development of gastroesophageal varices and their bleeding (1-3). It occurs as a result of increased hepatic blood flow resistance, most often associated with liver cirrhosis, but also with other liver diseases (1-3). Regardless of etiology, the progression of fibrosis and nodular transformation of the liver parenchyma increases intrahepatic vascular resistance and augments portal pressure, thereby initiating the development of portosystemic collaterals (2, 4). In addition to these architectural changes, splanchnic circulatory alterations, partly mediated by nitric oxide, contribute to changes in portal and systemic hemodynamics in patients with liver cirrhosis (5).

Esophageal and gastric varices represent the most important clinical manifestation of portal hypertension, especially because of their high risk of rupture (3, 6). It has been noted that approximately half of patients with liver cirrhosis have varices at the time of diagnosis, while their number and size increase with disease progression (1). The risk of first-episode variceal bleeding is 4-15% annually and depends on the size of varices, the degree of portal hypertension, and the presence of endoscopic high-risk stigmata, such as red wale marks and cherry-red spots (1). Several classifications have been developed to assess the size of esophageal varices, including the Westaby, Paquet, Japanese Research Society for Portal Hypertension, and North Italian Endoscopic Club systems. In routine clinical practice, a simpler classification into small and large varices, with a diameter cut-off of 5 mm, is most commonly used (2). This approach is particularly useful for evaluating the risk of a first variceal bleeding episode. Acute variceal bleeding is one of the most dramatic and urgent conditions in gastroenterology and hepatology (6, 7). A high risk of hemodynamic instability follows it, the development of acute complications, and fatal outcomes. Despite all efforts and advances regarding prophylaxis and treatment of esophageal variceal bleeding, the rebleeding and mortality rates remain high, and it is still one of the main causes of death in patients with decompensated liver cirrhosis. The mortality associated with variceal bleeding is 15–20% (1). Patients with decompensated liver cirrhosis who experience variceal bleeding have a high one-year mortality of approximately 57% (1). Early rebleeding occurs in 30–40% of patients within the first six weeks after an episode of variceal bleeding. However, with appropriate therapy, this can be reduced to around 20%, which still represents a significant clinical burden (1, 2). The modern concept of managing variceal bleeding is based on an integrated approach that involves early identification of patients with portal hypertension, preventive measures, prompt initial management in the acute bleeding phase, and timely use of endoscopic and pharmacological therapies (2, 8). Secondary prophylaxis is of special importance, given the high risk of recurrent bleeding in the absence of adequate therapy (2, 8). Research has shown through analyses of therapy outcomes that variceal bleeding is a complex process and that there is a need for an individualized, multidisciplinary approach to treating patients with chronic liver diseases (9-11). This narrative review provides an overview of current principles in the diagnosis and treatment of variceal bleeding, emphasizing evidence-based strategies, clinical guidelines, and the role of a multidisciplinary approach in optimizing patient outcomes.

METHODS

A comprehensive search of the PubMed database was conducted using the following keywords: "variceal bleeding AND diagnosis," "variceal bleeding AND treatment," "liver cirrhosis," and "portal hypertension." The search focused on review articles, clinical trials, and meta-analyses published in English over the last 15 years, with particular emphasis on studies published within the last 5 years. Only studies involving human subjects and available in full text were considered. Articles were included if they addressed the diagnosis, management, or treatment outcomes of variceal bleeding in patients with liver cirrhosis or portal hypertension. Studies were excluded if they were case reports, non-English publications, or not directly relevant to the topic.

DIAGNOSTIC METHODS FOR VARICEAL BLEEDING

Clinical assessment and initial treatment

The diagnostic process in patients with suspected variceal bleeding begins with a thorough clinical assessment. The most common symptoms include hematemesis, melena, dizziness, weakness, and syncope, while signs of hypovolemic shock predominate in more severe cases. Particular attention should be paid to the assessment of mental status, as the presence of hepatic encephalopathy may indicate more advanced underlying liver disease. Concurrently with the clinical evaluation, initial management should be initiated in accordance with the principles of airway protection, adequate oxygenation, and hemodynamic stabilization. In patients with massive bleeding or impaired consciousness, early endotracheal intubation should be considered to prevent aspiration (2, 7, 8).

Laboratory assessment

Laboratory tests play an important role in evaluating bleeding severity and the patient's overall condition. The standard laboratory panel includes complete blood count, coagulation parameters, biochemical liver and kidney

function tests, and electrolyte levels. The assessment of preexisting coagulopathy and thrombocytopenia is of significant value, as they are common in patients with liver cirrhosis. In patients with chronic liver diseases, rotational thromboelastometry is of great clinical importance (7). The restrictive transfusion approach, with target hemoglobin values of 7-8 g/dL, has been associated with a more favorable outcome than the liberal transfusion strategy, as it reduces the risk of increased portal pressure and recurrent bleeding (2, 8, 12). When adopting a restrictive approach to red blood cell transfusion, caution is required in patients with significant comorbidities, particularly those with cardiovascular disease and reduced coronary reserve (7).

Endoscopic diagnostics

Esophagogastroduodenoscopy is the key diagnostic and therapeutic method in the treatment of variceal bleeding. It is also important in patients presenting with anemia, as studies have shown that a small proportion (1.2%) of these patients may have underlying esophageal varices, highlighting the role of endoscopy in detecting both variceal and non-variceal sources of gastrointestinal bleeding (13). This procedure ensures direct visualization of varices **(Figure 1)**, identification of active or recent bleeding, and exclusion of other potential causes of upper gastrointestinal bleeding. It is recommended to perform urgent endoscopy within 12–24 hours of patient admission after the initial stabilization (2, 8). Prompt endoscopic diagnostics enable risk stratification and the selection of an optimal therapeutic strategy. The literature emphasizes the significance of urgent endoscopy availability in the medical centers that treat patients with portal hypertension.

Figure 1. Non-bleeding esophageal varices

Non-invasive methods and radiological evaluation

Non-invasive methods for assessing portal hypertension, such as liver and spleen elastography, as well as various clinical and laboratory scores, are increasingly used in everyday clinical practice (4, 14-16). Although they do not play a role in the acute phase of bleeding, these methods are important for the early identification of patients at high risk of developing varices. Radiological diagnostic methods, including Doppler ultrasound, computed tomography, and magnetic resonance imaging, are used to evaluate the anatomy of the portal venous system, detect portal vein thrombosis, and plan interventional procedures. These modalities are particularly important in patients with refractory bleeding, in whom consideration is being given to a transjugular intrahepatic portosystemic shunt (TIPS) or other interventions (17-19). The use of TIPS in patients with liver cirrhosis and variceal bleeding is associated with a reduction in treatment failure and mortality (19).

PROPHYLAXIS AND THERAPY OF VARICEAL BLEEDING

Primary prophylaxis of variceal bleeding

Primary prophylaxis seeks to prevent the occurrence of the first episode of variceal bleeding in patients with already established portal hypertension and esophageal varices. The therapeutic approach includes the administration of nonselective beta-blockers, which decrease portal pressure, along with endoscopic band ligation in patients with high-risk varices (2,8,20). In addition to propranolol, carvedilol or nadolol are also recommended for primary prophylaxis (2, 21). The choice of method depends on the size of the varices, the presence of endoscopic high-risk stigmata for bleeding, and the patient's overall condition (2, 8). Numerous studies have demonstrated that adequate primary prophylaxis significantly reduces the risk of the first bleeding and improves the prognosis in patients with liver cirrhosis (2, 8). The need to individualise the preventive approach has been suggested, taking into account patients' comorbidities and therapy tolerance.

Therapy of acute bleeding from esophageal and gastric varices

The treatment of acute variceal bleeding represents a medical emergency that requires the simultaneous use of multiple therapeutic modalities. The goals of therapy are rapid hemodynamic stabilization of the patient, control of active bleeding, prevention of early complications, and reduction of the risk of recurrent bleeding (2, 8, 11).

Initial management and hemodynamic stabilization

Initial management includes securing venous access, fluid resuscitation, and blood transfusion according to a restrictive transfusion protocol (12). Particular attention is paid to maintaining adequate blood pressure and perfusion of vital organs while avoiding excessive volume replacement that could increase portal pressure. In patients with massive bleeding, altered mental status, or respiratory insufficiency, early endotracheal intubation is considered to protect the airway and prevent aspiration. Correction of coagulopathy and thrombocytopenia is performed selectively, depending on the clinical condition and laboratory parameters (2).

Pharmacological therapy

Pharmacological therapy with splanchnic vasoconstrictors should be initiated immediately when variceal bleeding is suspected, even before endoscopic confirmation of the diagnosis (22). Terlipressin and somatostatin analogues reduce splanchnic blood flow and portal pressure, thereby facilitating bleeding control (22). Their use in combination with endoscopic therapy significantly increases the rate of successful hemostasis (22, 23). Prophylactic antibiotic therapy is an integral component of the management of acute variceal bleeding (24). Infections are common in these patients and are associated with an increased risk of early rebleeding and mortality. Broad-spectrum antibiotics are most commonly used in accordance with local recommendations. The most widely used antibiotics for these indications are cephalosporins (e.g., ceftriaxone) and fluoroquinolones (24, 25).

Endoscopic therapy

Endoscopic therapy represents a cornerstone in the up-to-date concept of treatment for acute variceal bleeding, with a key role in achieving initial hemostasis and preventing early recurrent bleeding episodes. Recent international guidelines recommend urgent endoscopy within 12-24 hours of hospital admission, after initial hemodynamic resuscitation and ongoing pharmacological therapy (2, 8).

Endoscopic band ligation (EBL) is the method of choice for treatment of esophageal variceal bleeding (26). This technique relies on applying elastic bands around varices, which mechanically occlude blood vessels, stop blood flow, and lead to variceal thrombosis **(Figure 2)**. When compared with earlier predominant sclerotherapy, band ligation demonstrated greater efficiency in acute bleeding control, a reduced rate of early rebleeding, and a significantly decreased risk of early complications, such as ulcerations, esophageal strictures, and perforations (26-28). The efficacy of EBL increases further when combined with splanchnic vasoconstrictors, which constitute the standard of contemporary therapy according to Baveno VII and EASL guidelines (8, 11). The procedure could be repeated during the same endoscopy if there are more actively bleeding varices or varices with high-risk stigmata (29).

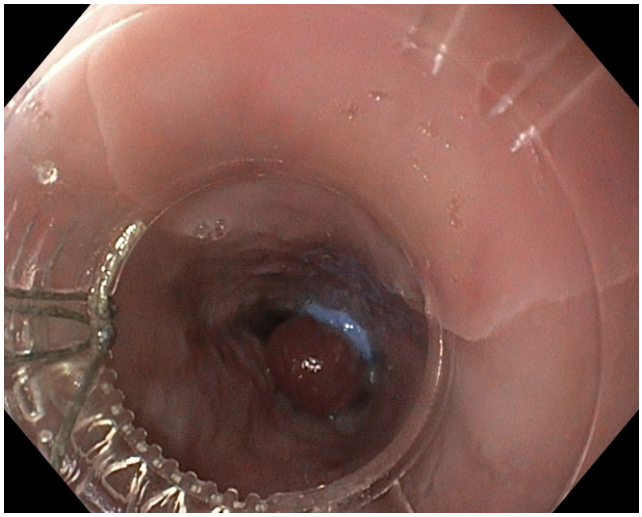

Figure 2. Esophageal varix with a rubber band in situ following endoscopic band ligation

Endoscopic sclerotherapy involves the intravariceal or paravariceal application of sclerosing agents and has a limited role today. Its use is most often considered when EBL is technically infeasible, such as when the esophageal lumen is very small or when anatomical variations are present. Numerous studies have shown that sclerotherapy is associated with a greater number of local and systemic complications; therefore, it is not recommended as the first-line treatment (2, 8, 11). In gastric variceal bleeding, standard EBL often is not adequate (except for GOV-1 varices) due to the different anatomy and hemodynamic characteristics of these varices. In these cases, endoscopic therapy comprises the use of tissue glues, such as cyanoacrylate, or other specialized techniques (30-32). These methods ensure efficient hemostasis, but demand experience and technical expertise due to the risk of embolization-related complications (32). Studies suggest the importance of timely and properly performed endoscopic therapy as part of a multidisciplinary treatment approach in patients with portal hypertension, emphasizing that treatment outcomes depend in great measure on experienced endoscopists and the organization of an emergency endoscopic department (32).

Balloon tamponade represents a temporary measure for bleeding control in patients with uncontrolled hemorrhage in whom endoscopic therapy has failed or is not immediately available (32). This method provides transient hemostasis through mechanical compression of varices; however, it is associated with a risk of serious complications and is used exclusively as a short-term bridge therapy until definitive management can be achieved (38,39). The most commonly used tube for balloon tamponade is

the Sengstaken–Blakemore tube, but the Minnesota or Linton–Nachlas tube has also been used (7).

Interventional radiology and surgical methods

TIPS represents an efficient therapy option in patients with refractory or early recurrent variceal bleeding (19, 32). This procedure leads to a significant reduction of portal pressure and a high rate of bleeding control. Still, it demands careful patient selection due to the high risk of hepatic encephalopathy development (32). In patients with bleeding from gastric varices, Balloon-occluded Retrograde Transvenous Obliteration (BRTO) can also be used, with reported success rates of up to 95% (33). Surgical treatment nowadays has a limited role and is considered only in strictly indicated cases, when other therapy options have not yielded results. Up-to-date therapy algorithms favor minimally invasive methods other than classical surgical procedures (34).

Secondary prophylaxis of variceal bleeding

The goal of secondary prophylaxis of variceal bleeding is to prevent recurrent bleeding episodes in patients who have already survived acute variceal bleeding. The risk of rebleeding in the absence of adequate therapy is extremely high, and it is estimated to be more than 60% in the first year, along with significant mortality (35-37). Therefore, secondary prophylaxis is considered an obligatory part of long-term treatment of these patients. The cornerstone of secondary prophylaxis comprises the combination of pharmacological therapy and endoscopic procedures (2, 8, 11). Nonselective beta-blockers are used to permanently reduce portal pressure, with careful titration to the maximally tolerated dose (38). Their efficacy in reducing the risk of rebleeding and improving overall survival has been confirmed in numerous clinical studies (38). EBL is performed in series at regular time intervals until complete eradication of varices (39). Controlled endoscopies play an important role in assessing treatment success and the timely detection of variceal recurrence. In patients in whom beta-blockers are not tolerated or in whom rebleeding occurs despite optimal combined therapy, TIPS can be considered for secondary prophylaxis (39). This procedure is highly effective in preventing further rebleeding episodes, but it requires proper patient selection because of the increased risk of hepatic encephalopathy and other complications (24, 40, 41). Secondary prophylaxis must be individualized and adjusted to the patient's clinical condition, the severity of liver dysfunction, and the presence of comorbidities (42). The literature emphasizes the importance of long-term follow-up of patients with portal hypertension and continuous evaluation of therapeutic strategies to achieve optimal outcomes (42).

Special aspects of gastric variceal bleeding

Bleeding from gastric varices represents a distinct clinical entity within portal hypertension, characterized by different pathophysiological features and therapeutic approaches compared with esophageal varices. Gastric varices are less common but are frequently associated with more massive bleeding that is more difficult to control **(Figure 3)** (43, 44, 45). Their localization, hemodynamic characteristics, and close association with the splenic vein necessitate specific diagnostic and therapeutic strategies (45). Endoscopic management of gastric varices primarily involves the use of tissue adhesives or other specialized techniques, whereas standard band ligation is often inadequate. Gastric varices are classified according to the Sarin classification into gastroesophageal varices (GOV) and isolated gastric varices (IGV) (43). GOV are subdivided into GOV-1, which are extensions of esophageal varices along the lesser curvature of the stomach, and GOV-2, which extend towards the greater curvature or fundus (43). IGV are located in the stomach without connection to esophageal varices, with IGV-1 localized in the gastric fundus and IGV-2 in other gastric regions (43). EBL can be used to treat bleeding from GOV-1 varices. The role of interventional radiology, including TIPS and BRTO, is particularly important in this patient population (44, 45).

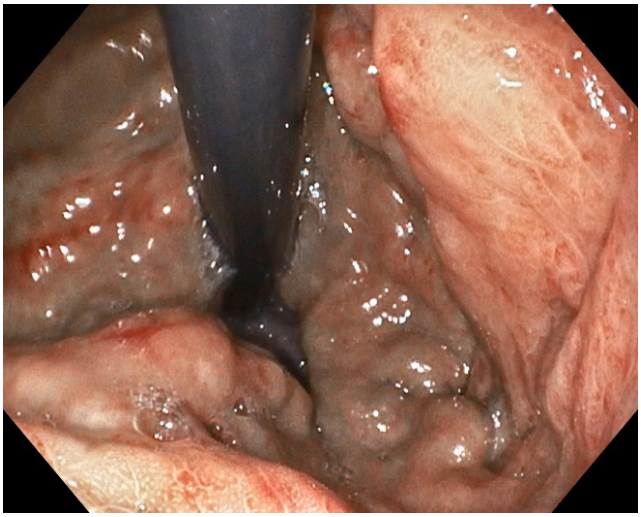

Figure 3. Gastric varices in the fundus, associated with severe portal hypertensive gastropathy

PROGNOSIS AND RISK FACTORS

The prognosis of the patient with variceal bleeding depends on multiple factors, including the severity of liver disease, the promptness and success rate of bleeding control, and the presence of comorbidities. Validated prognostic scores for assessment of mortality risk and treatment outcome are being used in everyday clinical practice, first and foremost Child-Pugh score, Model for

End-Stage Liver Disease (MELD) score, and Age, Blood urea nitrogen, Mental status, Systolic blood pressure, and 65 years or older (AIMS65) score, as well as most recent models that integrate hemodynamic and laboratory parameters, which enable more precise risk stratification and the optimal therapy strategy choice (46, 47-49). Additionally, recent studies highlight the utility of clinical and biomarker-based scoring systems in predicting short-term mortality in advanced cirrhosis complicated by systemic inflammatory response (50). Hematological indices, such as those reflecting anemia, leukocyte counts, and platelet abnormalities, have also been shown to predict complications and adverse outcomes in patients with liver cirrhosis, providing an accessible adjunct to established prognostic models (51). Furthermore, non-invasive scores such as Aspartate Aminotransferase to Platelet Ratio Index (APRI), MELD, Albumin-Bilirubin (ALBI) score, and Platelet-Albumin-Bilirubin (PALBI) score have demonstrated usefulness in predicting the presence of esophageal varices and the risk of variceal bleeding, with MELD being particularly predictive of short-term mortality (52).

SPECIAL POPULATION OF PATIENTS

The treatment of variceal bleeding in elderly patients, patients with renal insufficiency, or those with hepatocellular carcinoma represents an additional challenge. In these populations, therapy decisions must be individualized, taking into account the increased risk of complications, the limited organ reserve, and the potential impact of therapy on overall survival and quality of life (53-55).

FUTURE RESEARCH DIRECTIONS

Despite significant advances in understanding and treating variceal bleeding, open questions remain regarding the optimal timing for applying certain therapeutic methods and the identification of new pharmacological targets. The development of non-invasive methods for assessing portal hypertension is an important direction for future research. Particular attention is directed to the development of non-invasive methods for assessing portal hypertension, including advanced elastography techniques and serum biomarkers, which could replace invasive measurement of the hepatic venous pressure gradient (HVPG) in certain clinical situations (17, 56). Also, the use of artificial intelligence and machine learning to analyze clinical, laboratory, and endoscopic data is a useful tool for predicting bleeding risk and personalizing therapy in patients with liver cirrhosis (57, 58).

Overall, prognostic assessment, careful evaluation of comorbidities, and consideration of patient-specific factors are essential for optimizing therapy and improving outcomes in variceal bleeding.

CONCLUSION

Variceal bleeding remains one of the most severe and life-threatening complications of portal hypertension in patients with liver cirrhosis. Despite advances in diagnostic and therapeutic strategies, it is still associated with significant morbidity and mortality. Early recognition and prompt diagnosis, primarily via esophagogastroduodenoscopy, are essential for effective management and improved outcomes.

A multidisciplinary and multimodal approach combining endoscopic therapy, vasoactive pharmacological agents, antibiotic prophylaxis, and supportive care is recommended. Endoscopic band ligation has become the cornerstone of endoscopic management due to its efficacy and safety, while pharmacological therapy remains an important adjunct. Rescue therapies, including balloon tamponade and TIPS, are reserved for selected cases of refractory bleeding.

Ongoing improvements in risk stratification, early intervention, and adherence to evidence-based guidelines have contributed to better survival. Future research should focus on optimizing individualized treatment, refining timing and selection for advanced interventions, and reducing recurrent bleeding. A coordinated, multidisciplinary approach is essential to achieve optimal outcomes in patients with variceal bleeding.

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Ethical approval: N/A

Informed consent: The presented endoscopic photographs belong to the personal archive of the first author and have not been previously published elsewhere. The images do not reveal the identity of the patient and contain no identifiable personal information.

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DIJAGNOZA I TERAPIJA VARIKSNOG KRVARENJA

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Sažetak

Portna hipertenzija se definiše kao povećanje hepatovenskog gradijenta pritiska (HVPG), najčešće nastalog kao posledica ciroze jetre, što dovodi do razvoja portosistemskih kolaterala, naročito variksa jednjaka. U trenutku postavljanja dijagnoze ciroze jetre, približno 50% pacijenata ima varikse jednjaka, a variksno krvarenje predstavlja jednu od najtežih i najdramatičnijih stanja u gastroenterologiji.

Ezofagogastroduodenoskopija predstavlja osnovnu dijagnostičku i terapijsku metodu u variksnom krvarenju. Terapijske mogućnosti obuhvataju endoskopsku hemostazu, farmakoterapiju, balon tamponadu, interventne radiološke procedure i hirurško lečenje. Endoskopska band ligacija je metoda prvog izbora, dok se skleroterapija, koja podrazumeva intravaricealnu ili paravaricealnu primenu sklerozantnih sredstava, danas znatno ređe koristi.

Farmakološko lečenje uključuje primenu splanhičkih vazokonstriktora, poput somatostatinskih analoga i terlipresina, uz obavezne suportivne mere koje podrazumevaju nadoknadu tečnosti, transfuziju krvnih derivata i korekciju koagulopatije. Kod pacijenata sa cirozom jetre i variksnim krvarenjem neophodna je profilaktička primena antibiotika, najčešće fluorohinolona ili cefalosporina.

Balon tamponada, primenom Sengstaken–Blakemore, Minnesota ili Linton–Nachlas sondi, koristi se kao privremena mera hemostaze. U slučajevima refraktornim na standardno lečenje, može se razmotriti transjugularni intrahepatični portosistemski šant (TIPS) ili hirurško lečenje kod pažljivo odabranih pacijenata. Lečenje variksnog krvarenja zahteva zbrinjavanje u jedinicama intenzivne nege i multidisciplinarni pristup.

Ključne reči: variksi, krvarenje, portna hipertenzija

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