

Management of Gastric Varices

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ABSTRACT

Upper gastrointestinal bleeding is one of the emergency conditions in the field of gastroenterology and variceal bleeding is the most common cause of it. Gastric varices accounts only 5% to 10% of all causes of upper gastrointestinal bleeding respectively, but it could be fatal and difficult to control despite provision of adequate therapy. Early diagnosis and appropriate management may decrease the morbidity and mortality of gastric variceal bleeding.

Keywords: Gastric varices, upper gastrointestinal bleeding, endoscopy

INTRODUCTION

Upper gastrointestinal bleeding is one of emergency conditions in the field gastroenterology. In the US, it had caused 10,000-20,000 deaths per year with the prevalence of 150 per 100,000 populations. In Cipto Mangunkusumo General National Hospital we found respectively 200-300 cases of upper gastrointestinal bleeding with mortality rate of 26% in 1998.¹ The most common cause of these was variceal bleeding which had high morbidity and mortality rate. More than 30% of initial variceal bleeding would be fatal and the rest 70% would have recurrence of bleeding.² Most of variceal bleeding caused by rupture of esophageal varices, while gastric varices was responsible only 5% of all cases.³ However, gastric variceal bleeding may become fatal and difficult to control even by endoscopic treatment.⁴ The management of variceal bleeding prevention consists of 3 phases as follows:⁴

1. Primary prevention is to prevent the occurrence of initial variceal bleeding
2. Secondary prevention is to prevent the recurrence of bleeding
3. Tertiary prevention is to stop the active bleeding

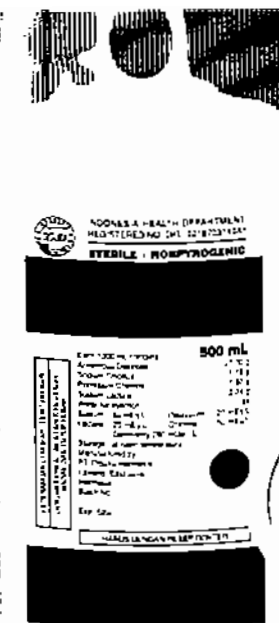
DEFINITION AND CLASSIFICATION

Gastric varices is defined as dilatation of gastric collateral vein in the submucosa.^{3,5} Collateral system in the portal vein has important role in the pathogenesis of gastric varices. Portal vein originates from splenic vein, superior mesenteric vein and inferior mesenteric vein and left gastric vein. Superior mesenteric vein receive blood from colon and intestine, while the inferior mesenteric vein and hyllus joint short gastric vein in caudal part of pancreas. Left gastric vein will receive the blood flow from esophagus and stomach.^{6,7}

Gastric varices is classified as gastroesophageal varices or isolated gastric varices. Type I gastroesophageal varices is the continuity of esophageal varices and only covers 2-5 cm below the gastroesophageal junction, while gastroesophageal varices type two lines up until gastric fundus. Isolated gastric varices type 1 is placed on gastric fundus while the type two widen until gastric antrum.⁷

PATHOGENESIS

Several theories of mechanism may explain the pathogenesis of gastric varices. First theory is thrombosis in splenic vein that causes isolated gastric varices. The etiology of splenic vein thrombosis was

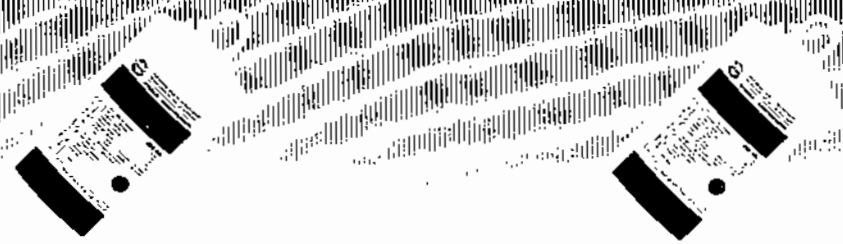


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1. Cohn, J.N. et al. New Guidelines for Potassium Replacement in Clinical Practice. Arch. Intern. Med. 2000;160:2429 - 2436



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associated with some pathological condition such as neoplasma, pancreatitis, trauma, pseudocyst, hypercoagulable state, etc. If the obstruction is at the distal of left gastric vein, the collateral circulation will cross short gastric vein to gastric fundus.⁶⁻⁸ Other condition that may cause gastric varices is portal hypertension. The portal hypertension might be cirrhotic or non cirrhotic.

In portal hypertension the obstruction of portal blood flow may occur as well as the vascular resistance. In addition, hyper-dynamic circulation in liver cirrhosis and collateral system cause increased cardiac output and increased intra variceal pressure. Renin-Angiotensin-Aldosterone system, endothelin and nitric oxide implicate on vasodilatation of splanchnic vascular. Apart from that, collagenation of liver stellate cell would also affect the increase of portal pressure.⁴

Non cirrhotic portal hypertension is a pathological condition of increased portal pressure caused by intrahepatic or prehepatic lesions without liver cirrhosis. Common lesion found in portal hypertension and liver cirrhosis is vascular disorder in the portal vein or perisinusoidal region.⁹

Common causes of non cirrhotic portal hypertension can be seen as follows:⁵

1. Extra-hepatic obstruction of portal vein
2. Non cirrhotic portal fibrosis or idiopathic portal hypertension
3. Schistosomiasis
4. Primary or secondary biliary cirrhosis
5. Congenital hepatic fibrosis
6. Veno-occlusive disease
7. Nodular regenerative hyperplasia
8. Partial nodular transformation
9. Hepatoportal sclerosis
10. Peliosis hepatitis

Gastric varices may arise due to complication of sclerotherapy treatment of esophageal varices.⁴

DIAGNOSIS

Clinical Manifestation

The important clinical manifestation of gastric varices is upper gastrointestinal bleeding and it is also the advanced complication.^{1,10} Blood that is vomited is usually dark colored and does not coagulate due to contamination of gastric acid. However, if the vomit is containing fresh blood, it indicates massive bleeding. Calculation of blood loss is important for appropriate management. Intestinal lumen has the reserve capacity

of blood before it is vomited or expelled from the anus. Postural hypotension describes the possibility of blood loss about 40%. Serial evaluation of hemoglobin and hematocrit can be used to calculate amount of blood transfusion needed.^{1,10}

Other symptoms that might be found are splenomegaly and ascites as sign of portal hypertension. Physical examination is important to find out the underlying cause of portal hypertension to be cirrhotic or non cirrhotic. The presence of spider nevi, palmar erythema and jaundice suggest chronic liver disease. The liver function test and abdominal ultrasound are also needed. The diagnosis of liver cirrhosis is confirmed by liver biopsy.⁴

Angiography is performed to evaluate thrombosis and blood flow in portal or splenic vein. Left gastric vein is the main vessel forming the esophageal varices. The posterior and short gastric veins are the main vessels involved in the formation of gastric varices.^{5,7} Splenoportography can also be used to evaluate thrombus in splenic or portal vein.⁷

Endoscopy

Endoscopy is the main diagnostic tool to confirm diagnosis of gastroesophageal varices. It has important role to determine the source of bleeding as well as therapeutic modality for variceal bleeding.^{1,11} Gastric varices may be more difficult to identify at endoscopy because they are generally situated deeper than esophageal varices and may resemble rugal folds.³ In acutely bleeding patients, the fundus is frequently obscured by a pool of blood and small gastric varices may not be easily detected. Endoscopy examination revealed red spot as localized erythematous area in gastric mucosa. Histologic features of red spot are not very clear. The presence of red spot indicates trauma in gastric mucosa and risk of bleeding in gastric varices.¹²

Vascular structure of gastric varices is different compare to esophageal varices. Red-color sign is not commonly found in gastric varices. Red-color sign indicates dilatation of vessel aligning mucosal epithelium of esophageal varices, while gastric varices is usually placed in the submucosal layer. Based on its size, gastric varices are classified into several categories:¹²

1. Small, if the size less than 5 mm
2. Medium, if the size between 5 and 10 mm
3. Large, if the size more than 10 mm

MANAGEMENT OF GASTRIC VARICES

1. Primary Prevention to Prevent Bleeding of Varices

The most important pharmacologic therapy to prevent variceal bleeding is the one that has the capacity to reduce portal hypertension. The drugs which are able to decrease portal vein collateral or intrahepatic vascular resistance can be used such as beta blockers, nitrates, alpha blocker, spirinolacton and pentoxiphyllin. Variceal bleeding will not occur if the hepatic vein pressure gradient is less than 12 mmHg, so the therapeutic goal is to reduce the pressure as closer as possible to that number.²

Beta blockers will reduce portal pressure, splanchnic and collateral blood flow. The non-selective beta blockers like propranolol and nadolol are more useful because the blocking effect on β_1 adrenergic receptor cause splanchnic vasoconstriction. Decrease of portal vein pressure by 20% or hepatic vein pressure gradient less than 12 mmHg was associated with significant protection from bleeding. If the equipment to measure hepatic vein pressure gradient is not available, beta blockers can be titrated until heart rate at rest reach 55 beats per minute or there is 25% reduction from baseline heart rate.^{2,13} Nadolol can also be used in primary prevention. The advantage of nadolol is that it can be given as single dose.^{4,14}

The effectiveness of beta blockers for primary prevention had been shown in several controlled studies. Meta-analysis showed significant decrease in risk of bleeding and mortality rate.¹³ Beta blockers should be given carefully in severe and active bleeding because they might disturb resuscitation process and precipitate hepatic encephalopathy.¹⁵

Other drug can be used is isosorbid mononitrates. The mechanism of nitrates remains unclear. It is assumed that nitrate has the capacity to reduce intrahepatic pressure, decrease portal pressure due to splanchnic vasoconstriction as response to peripheral vasodilatation.²

Unfortunately, nitrate can not be used as monotherapy. However, study by *Angelico et al* observed the use of isosorbid mononitrate as monotherapy in comparison to propranolol in primary prevention. The results showed that nitrate was as effective and safe as propranolol.¹⁶

Several studies had showed that the use combination of isosorbid mononitrate and propranolol had given better result than each drug used as monotherapy.^{2,4,17}

2. Controlling Active Bleeding

General Management

The principal management of acute bleeding due to gastric varices is the same as management of other upper gastrointestinal bleeding. First measure to be done is to improve the general condition and stabilize vital signs. Fluid resuscitation using crystalloid such as normal saline (NaCl) or ringer lactate and plasma expander such as colloid if needed. Blood transfusion of packed red cell is given after fluid resuscitation. It may be necessary to consider giving coagulation factors such as fresh frozen plasma especially for patients with liver cirrhosis. Whole blood can be used in massive bleeding.¹

Gastric lavage using the iced water or NaCl solution is useful as diagnostic tool and therapeutic intervention. Appropriate gastric lavage technique is important to prevent trauma at upper gastrointestinal mucosa.^{1,18}

Endoscopic exploration is necessary to find the source of bleeding and confirm the diagnosis. There are two alternatives, emergency endoscopy or early endoscopy. Emergency endoscopy may be able to locate the source of acute bleeding and perform therapeutic intervention concomitantly. Emergency endoscopy is technically difficult and need high competency, adequate equipment and completes resuscitation team.¹

Early endoscopy is done when patient's condition has been stable. Vasoactive drugs are given either to stop or to prevent bleeding.

Vasoactive drugs

Vasoactive drugs used for this condition:^{1,2,6,7,18}

1. Vasopressin
This drug attenuates bleeding by splanchnic vasoconstriction and cause reduction portal pressure and blood flow. The recommended dose is 0.2-0.4 unit/minute for 1 to 24 hours. Vasopressin is given by intravenous continuously due to its short half-life. The side effect of this drug is systemic vasoconstriction that can cause myocardial infarction and mesenteric ischemia. Thus, it should be very careful when giving it to elderly patient and it is contraindicated in patients with heart disease.
2. Somatostatin and octreotide
These drugs have been used commonly in upper gastrointestinal bleeding due to its effect in decreasing splanchnic and portal pressure without significant complications. In addition, they can also

inhibit the secretion of gastric acid and pancreatic enzyme as well as decrease the blood flow to the stomach. The recommended doses are:

- Somatostatin: 250 mcg bolus followed by continuous infusion of 250 µg/h
- Octreotide: continuous infusion of 50 µg/h

Endoscopic Treatment

Sclerotherapy and ligation for gastric varices are not as effective as for esophageal varices in controlling acute bleeding because gastric varices is localized deeper in the gut wall. The treatment of choice is injection of glue cyanoacrylate. It will make contact to blood and form plaque on site of bleeding. This glue contains lipiodol mixture delayed polymeration. If the needle has been inserted into the varices, glue cyanoacrylate will be injected and lipiodol will be used to assist the glue reaching the source of bleeding. In addition, a small non-controlled study had showed that endoscopic ligation with detachable minisnare is also effective to control bleeding due to gastric varices.² Experience using rubber band ligation in our hospital had indicated satisfying result.¹

Balloon Tamponade

Balloon used for gastric varices called Linton-Nicholas is a single, large size gastric balloon (600 cc). This balloon was commonly used to stop acute bleeding due to fundal varices. Balloon tamponade was actually effective in controlling bleeding, but the incidence of rebleeding was high. The common complications were rupture, respiratory tract obstruction and aspiration. Balloon tamponade still can be used for patients who are failed to endoscopic treatment or rebleed after endoscopic treatment.⁸

Transjugular Intrahepatic Portosystemic Shunt (TIPS)

TIPS is a percutaneous treatment making the connection between portal vein and hepatic vein. The methods used were to implant metal stent as the bridge between portal vein and hepatic vein via transjugular vein.⁶ The goal of this treatment is decompression of portal system to systemic vein without conducting surgical treatment.

Among complications of TIPS are hepatic encephalopathies, portal stenosis or stent occlusion. Stenosis were more common than occlusion due to intimal hyperplasia.¹³ The advantage of TIPS in comparison to surgical procedure is the low mortality rate.⁸ In addition, 5% to 10% patients with refractory acute variceal bleeding including gastric varices would response very well and stop the bleeding.¹⁹ Mortality

rate of TIPS were high in elderly patients and those who have multi organ failure reaching almost 100%.²

3. Secondary Prevention to Prevent Rebleeding

Secondary prevention is done to prevent the recurrence of variceal bleeding. Two of three patients would rebleed in 6 weeks after first episode. Clinical predictor for bleeding recurrence are bleeding severity in initial bleeding, stage of liver decompensation, the presence of encephalopathy hepaticum and decreased renal function.²

Pharmacologic Therapy

Decrease portal pressure of more than 20% will decrease bleeding recurrence. Some drugs have been used to decrease portal pressure as secondary prevention. One of them, non selective beta blocker had been used commonly and its effectiveness had been proved by several studies. The combination of beta blocker and isosorbide mononitrate in patients with liver cirrhosis child A-B was superior compare to those with sclerotherapy.¹⁴ Other study showed more effective pharmacologic therapy compare to ligation in patients with liver cirrhosis child A, B.²⁰

Endoscopic Treatment

Sclerotherapy and ligation are not effective for gastric varices. The best management of patients with bleeding recurrence due to gastric varices is N-buthyl-cyanoacrylate injection.²

Transjugular Intrahepatic Portosystemic Shunt (TIPS)

TIPS is more effective in prevention of bleeding recurrence compare to endoscopic treatment. Significant increased incidence of hepatic encephalopathy in 25% patients after shunting. Besides, TIPS did not increase life expectancy compare to endoscopic treatment in patients with advanced liver disease and gave bad result after shunting. TIPS could be used as bridging therapy before liver transplantation in patients with advanced liver disease.² TIPS gave better result and was less expensive compare to distal splenorenal shunt. However, TIPS is recommended mainly for child A liver cirrhosis due to high incidence of TIPS complication.²¹

Surgical Therapy

Surgery is conducted as emergency or elective procedure. Emergency surgery is indicated in patients of 1st and 2nd degree of criticalness. The classifications of criticalness are as follows:²⁰

- 1st degree of criticalness : need blood transfusion more than two liters in the first 8 hours to maintain adequate circulation.
- 2nd degree of criticalness : need blood transfusion more than two liters in the first 24 hours to maintain adequate circulation
- 3rd degree of criticalness : bleeding still active after 72 hours since hospital admission

Elective surgery to prevent rebleeding due to gastric varices is usually performed after six weeks after bleeding has stopped. Surgical procedure in portal hypertension is divided into categories as follows:

1. Shunt decompression, classified into total, partial and selective decompression.

a. Total Portal Systemic Shunt

One of technique had been used was portocaval shunt that can be conducted end to end or side to side. In portocaval shunt, the portal vein is connected to inferior cava vein and caused decreased portal pressure and hepatic vein pressure to increase the hepatic artery blood flow.^{7,15} Recently, portocaval shunt technique is rarely used due to high incidence of complications.

Other technique used in total-portal systemic shunt is mesocaval shunt which makes the connection between superior mesenteric vein and inferior cava vein using Dacron graft. This technique is not difficult and portal vein will stay open, although direction of blood flow cannot be determined. Shunt occlusion commonly occurs and usually followed by bleeding recurrence.⁶ The most popular mesocaval technique was H-graft shunt by Drapanas and Cameron. Graft connected mesenteric superior vein that placed inferior of pancreas with inferior cava vein that placed below insertion of renal vein.

b. Partial Porto Systemic Shunt

This technique is based on principal to limit portal systemic shunt while conducting decompression to control bleeding, thus it will keep maintaining relatively sufficient blood flow to portal system in the liver.⁷ Central splenorenal shunt is one of technique with the same goal, but according to Sharfen et al, the definition of partial shunt is shunt interposition between portal vein and inferior cava vein with diameter of 8 mm. The

difficulty of this technique is maintaining size of shunt without causing thrombosis or stenosis. The advantage of the technique is the lower incidence of hepatic encephalopathy compare to total shunt.

c. Selective Varices Decompression

There are two types of selective shunt. The most commonly used is the distal splenorenal shunt which could selectively decompress spleen and gastroesophageal to the left lienalis vein, superior mesenteric vein and portal vein to maintain portal blood flow. The other type is coronary caval shunt which was popularized by Inokuchi. It makes anastomosis of left gastric vein and inferior cava vein and usually splenectomy is also conducted.⁷

2. Devascularisation procedure

This technique is suggested if the shunt operation is difficult to be done. Sugiura and Futugawa had popularized the esophagogastric devascularization with splenectomy and trisection of esophagus. It is an alternative therapy for patient with liver cirrhosis who is not eligible for shunt procedure or those with extrahepatic portal vein thrombosis.²¹

CONCLUSION

Upper gastrointestinal bleeding is an emergency condition in the field of gastroenterology with high morbidity and mortality rate. One of the causes of upper gastrointestinal bleeding is the rupture of gastric varices which can be fatal and difficult to control although it is relatively small in frequency. The pathogenesis of gastric varices is thrombosis of splenic vein and cirrhotic or non-cirrhotic portal hypertension. Endoscopy is the main modality in making diagnosis of gastric varices.

The management of gastric varices is divided into three phases: primary prevention, control active bleeding and secondary prevention by pharmacologic therapy, endoscopy, TIPS or surgical treatment.

REFERENCES

1. Makmun D. Tatalaksana pendarahan saluran cerna bagian atas pada sirosis hati. Dalam: Alwi I, Bawazier LA, Kolopaking MS, Syam AF, Gustaviani R. Simposium penatalaksana kedaruratan di bidang Ilmu Penyakit Dalam II, Jakarta. Pusat Informasi dan Penerbitan, IPD FKUI 2002.h.85-97
2. Sharara AI, Rockey DC Gastroesophageal variceal hemorrhage. *N Engl J Med* 2001;345:669-81
3. Khan AN, Ali M. Portal Hypertension. <http://www.emedicine.com/radio/topic570.htm.2002>
4. Akbar N. Terapi farmakologis pada hipertensi portal. Dalam: Setiati S, Alwi I, Kasjmir YI, Atmakusuma D, Lydia A, Syam

- AF. Current diagnosis and treatment in Internal Medicine, Jakarta. Pusat Informasi dan Penerbitan, IPD FKUI 2001.h.19-18
5. Arakawa M, Masuzaki T, Okuda K. Pathology of gastric varices, pathology of fundic varices of the stomach and rupture. *J Gastroenterol Hepatol* 2002;17:1064-69
 6. Sherlock S, Dooley J. The portal venous system and portal hypertension. Sherlock S, Dooley J, editors. *Disease of the liver and biliary system*. 10th ed. Oxford. Blackwell Sci 1997.p.132-75
 7. Boyer TD, Henderson JM. Portal hipertension and bleeding esophageal varices. In: Zakim D, Boyer TD, editors. *Hepatology a text book of liver disease*. Vol I, 3th ed. Philadelphia: WB Saunders Co 1996.p.720-55
 8. Chung S. Advances in endoscopy, management of bleeding in the cirrhotic patient. *J Gastroenterol Hepatol* 2002;17:355-60
 9. Sarin SK, Kapoor D. Non-cirrhotic portal fibrosis: Current concepts and management. *Gastroentero-Hepatology* 2002;17:256-34
 10. Djojoningrat D. Hematemesis Melena. Dalam: Alwi I, Syam AF, Mansjoer A. *Simposium Penatalaksanaan Kedaruratan di bidang Ilmu Penyakit Dalam*, Jakarta. Pusat Informasi dan Penerbitan, IPD FKUI 2001.h.85-89
 11. Thahir GA. Varices esofagus: endoskopi dalam bidang gastroentero-hepatologi. Hadi S, Thahir G, Daldijono, Rani A, Akbar N, Jakarta. *Perhimpunan Endoskopi Gastrointestinal Indonesia*, Balai Penerbit FKUI.h.61-68
 12. Kim T, Shijo H, Kokawa H, Tokumitsu H. Risk factors for hemorrhage from gastric fundal varices. *Hepatology* 1997;25:307-11
 13. D'Amico G, Pagliaro L, Bosch J. The treatment of portal hypertension: a metaanalytic review. *Hepatology* 1995;22:332-54
 14. Villanueva C, Balanzo J, Novella M, Soriono G. Nadolol plus isosorbide mononitrate compared sclerotherapy for the prevention of variceal bleeding. *N Engl J Med* 1995;334:1624-29
 15. Kusmubroto H. Pendarahan non-varises pada sirosis hati. Dalam: Lesmana LA, Gani RA, Hasan I, Wijaya IK, Mansjoer A. *Abstrak liver update 2000. Perkembangan terkini diagnosis dan penatalaksanaan penyakit hati dan saluran empedu*. Jakarta. Pusat Informasi dan Penerbitan, IPD FKUI 2002.h.71
 16. Angelico M, Carli L, Pial C. Isosorbide-5-mononitrate versus propanolol in the prevention of first bleeding in cirrhosis. *Gastroenterology* 1993;104:1460-65
 17. Rani A. Peranan nitrat pada pencegahan pendarahan varises esofagus akibat hipertensi portal. Dalam: Lesmana LA, Gani RA, Hasan I, Wijaya IK, Mansjoer A. *Abstrak liver update 2002, perkembangan terkini diagnosis dan penatalaksanaan penyakit hati dan saluran empedu*. Jakarta. Pusat Informasi dan Penerbitan, IPD FKUI 2002.h.68-70
 18. Peterson WL. Gastrointestinal bleeding. In: *Gastrointestinal disease, pathophysiology diagnosis management*. 4th ed. Philadelphia: WB Saunders Co 1989.p.397-414
 19. Djojoningrat D, Hardjodisastro D. Hematemesis melena. Dalam: *Pedoman diagnosis dan terapi di bidang Ilmu Penyakit Dalam*. Pusat Informasi dan Penerbitan, IPD FKUI 2000.h.22-23
 20. Orozco H, Mercado MA. The evaluation of portal hypertension surgery. *Arch Surg* 2000;135:389-93
 21. Zacks SL, Sandler RS, Biddle AK. Decision analysis of transjugular intrahepatic portosystemic shunts versus distal splenorenal shunt for portal hypertension. *Hepatology* 1999.p.1399-1405