CHARACTERISTICS AND NATURAL HISTORY OF GASTRIC VARICES IN PORTAL HYPERTENSION

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CERTIFICATE

This is to certify that the dissertation entitled **"CHARACTERISTICS AND NATURAL HISTORY OF GASTRIC VARICES IN PORTAL HYPERTENSION"** is the bonafide original work of **Dr.B.SIVASUBRAMANIAM** in partial fulfillment of the requirements for **D.M (GASTROENTEROLOGY) BRANCH – IV** Examination of the Tamilnadu Dr. M.G.R. Medical University to be held in August 2012.

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DECLARATION

I, **Dr. B.SIVASUBRAMANIAM,** solemnly declare that the dissertation titled, "CHARACTERISTICS AND NATURAL HISTORY OF GASTRIC VARICES IN PORTAL HYPERTENSION" is a bonafide work done by me at Govt. Stanley Medical College & Hospital during 2009-2012 under the guidance and supervision of **Dr. A.R.VENKATESWARAN., M.D., D.M,** Professor and Head, Department of Medical Gastroenterology, Stanley Medical College, Chennai-600 001.

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INTRODUCTION

Portal hypertension can occur due to many reasons. One of the commonest causes for portal hypertension is cirrhosis. Other important causes are non cirrhotic portal fibrosis (NCPF) and extra hepatic portal vein obstruction (EHPVO). Portal pressure increases in cirrhosis initially as a result of an increased resistance to portal flow. This mostly results from fibrous tissue and regenerative nodules formation within the hepatic parenchyma which leads to distortion of the architecture of the liver.[1]

Along with this structural resistance to blood flow, there is an intra-hepatic constriction of the vessels that accounts for twenty to thirty percent of the increase in resistance within the liver. This happens because there is decreased synthesis of nitric oxide endogenously. [2-3] The obstruction to the portal flow is at perisinusoidal level in NCPF but in EHPVO the obstruction is extra hepatic, which is commonly due to the formation of thrombosis in the portal vein.

Porto-systemic collaterals are formed due to the development of portal hypertension. Although the collaterals are formed to relieve the portal pressure portal hypertension persists due to two causes: (1) an increase in portal venous inflow due to splanchnic arteriolar vasodilatation along with the formation of collaterals[4] and (2) inadequate decompression of the portal venous system

through the collaterals since they have a higher resistance than the normal liver.[5] Therefore, an increased portal pressure gradient results from both an increase in portal blood inflow and increase in resistance to portal flow.

Gastroesophageal varices are commonly seen in up to 50% of patients with cirrhosis.[6] Gastric varices are seen in 20-25% of patients with portal hypertension. If the patient is not having varices it will develop at the rate of 8% per annum [8-9] and one who have small varices will develop larger varices at 8% per year.. In few subsets of patients such as in primary biliary cirrhosis and hepatitis C with bridging fibrosis, even in the absence of overt cirrhosis they have propensity to develop varices in up to 16 % of the patients.[6-7] Irrespective of the aetiology, the important and dreadful complication of varices is upper gastrointestinal bleeding.

Prevalence of gastric varices is low when compared to esophageal varices. They are present in 6%-35% of patients with portal hypertension. The incidence of bleeding is about twenty-five percent in 2 years and highest bleeding rate is for fundal varices.[12] Risk factors for gastric variceal haemorrhage include fundal varices size (large varices defined as >10 mm, medium -5-10 mm and small >5 mm), Child-Turcotte-Pugh score, particularly Child C status and endoscopic presence of variceal red spots (defined as localized reddish mucosal area or spots on the mucosal surface of a varix). [11, 13]

Gastric varices are classified into four types. The relationship of gastric varices with that of esophageal varices and the position in the stomach decides the gastroesophageal varices classification. Gastroesophageal varices (GOV) are classified into 2 types. Type 1 gastroesophageal varices are called as GOV1 which runs along the lesser curvature of the stomach and this most frequently seen. Since they are similar to esophageal varices, the management is same to that of esophageal varices. If the varices extend along the fundus, it is called as Type 2 gastroesophageal varices and tends to be longer and more tortuous. [12]

If gastric varices occur without the presence of esophageal varices they are categorized into two types. The first type is IGV1 are located in the fundus and tend to be tortuous and complex and type 2 (IVG2) are located in the body, antrum, or around the pylorus. The presence of IGV1 fundal varices requires excluding the presence of splenic vein thrombosis.

In Indian study by Sarin et al, the incidence of gastric varices is just 4% in cirrhotics patient who has not bled. Others have shown that 25% of cirrhotics had gastric varices at screening endoscopy with 18% of patients having both gastric and esophageal varices.[12] Gastric varices are also more common in NCPH and EHPVO which is present in 25% and 33% of patients respectively.[14]

The risk of bleeding with gastric varices is half that of esophageal varices. The transfusion requirement and mortality are high once the bleeding has occurred particularly for isolated gastric varices (IGV). Large gastric varices patients have a lower portal pressure compared to esophageal varices, which is due to the development of gastrorenal portosysytemic shunts, or large size of the varices resulting in increased wall tension.[15] The type and prevalence of gastric varices varies greatly.

AIM

The aim of this study is to assess

1. The prevalence of gastroesophageal varices in patients with portal hypertension in a tertiary referral centre
2. Characteristics of the gastric varices and
3. Natural history of gastric varices in portal hypertension.

REVIEW OF LITERATURE

Portal hypertension is an important and inevitable complication of cirrhosis of the liver, extrahepatic portal vein obstruction (EHPVO) and non cirrhotic portal fibrosis (NCPF), which leads to various hemodynamic effects. The portal pressure if an increase above 12 mm Hg is usually associated with portal hypertension and upper gastro intestinal bleeding can occur from varices in oesophagus, oesophagogastric junction, stomach, colon and other rare places such as duodenum. In colon, particularly it develops in the rectum.

Gastric varices are commonly classified as GOVs (gastric varices in continuity with esophageal varices) and isolated gastric varices (IGV). Fifty percent of cirrhotic patients will have gastroesophageal varices and gastric varices are seen in approximately 20-25% of patients with portal hypertension.[12]

The prevalence and risk of bleeding of gastric varices are lower than those of esophageal varices but bleeding from gastric varices tends to be more severe, requires more transfusions, and is associated with higher mortality (>45%)

Gastric varices tend to be larger and more tortuous compared with esophageal varices and along with their anatomical location (particularly fundic varices), make endoscopic management more challenging. Current management strategies for gastric varices include pharmacotherapy which includes β-blockers and vasoactive agents, endoscopic therapy (band ligation, thrombin, and tissue adhesives), transjugular intrahepatic portosystemic shunt (TIPS) placement; balloon occluded retrograde transvenous occlusion (BRTO) and ultimately surgical intervention in refractory cases.

Natural History of Varices

The important collaterals at the level of portosystemic circulation are esophageal and gastric varices. If they rupture, severe variceal hemorrhage can occur, the most catastrophic complication of cirrhosis. The direct complication of cirrhosis is the development of varices and bleeding, which is due to portal hypertension. Patients with cirrhosis and gastroesophageal varices have a hepatic venous pressure gradient of ten-twelve mm Hg.

Severity of cirrhosis well correlates with the presence of gastric varices. They are present only 40% of Child A patients but 85% of Child C patients will have varices. If there is no varices at first visit in patients with cirrhosis, it will develop at a rate of eight percent per annum and the strongest predictor for

development of varices in those with cirrhosis who have no varices at the time of initial endoscopic screening is an HVPG >10 mmHg.

Patients with small varices develop large varices at a rate of 8% per year. Decompensated cirrhosis (Child B/C), alcoholic cirrhosis, and presence of red wale marks (defined as longitudinal dilated venules resembling whip marks on the variceal surface) at the time of baseline endoscopy are the main factors associated with the progression from small to large varices. Variceal hemorrhage occurs at a yearly rate of 5%-15%, and the most important predictor of hemorrhage is the size of varices, with the highest risk of first hemorrhage (15% per year) occurring in patients with large varices.

Although bleeding from esophageal varices ceases spontaneously in up to 40% of patients, and despite improvements in therapy over the last decade, it is associated with a mortality of at least 20% at 6 weeks.[16-18] Patients with an HVPG of >20 mmHg (measured within 24 hours of variceal hemorrhage) have been identified as being at a higher risk for early rebleeding (recurrent bleeding within the first week of admission) or failure to control bleeding (83% vs. 29%) and a higher 1-year mortality (64% vs. 20%) compared to those with lower pressure. [19,20]

In approximately 60% of untreated patients late rebleeding occurs, mostly within 1-2 years of the index hemorrhage.[21-22] Variceal wall tension is probably the main factor that determines variceal rupture. Vessel diameter is one of the determinants of variceal tension. At an equal pressure, a large diameter vessel will rupture while small diameter vessels will not rupture. Apart from the vessel diameter, one of the determinants of variceal wall tension is the pressure within the varix, which is directly related to the HVPG. [23]

A reduction in HVPG should lead to a decrease in variceal wall tension, thereby decreasing the risk of rupture. Indeed, variceal hemorrhage does not occur when the HVPG is reduced to ≤12 mmHg. It has also been shown that the risk of rebleeding decreases significantly with reductions in HVPG greater than 20% from baseline. [24, 25]

Patients whose HVPG decreases to ≤12mmHg or at least 20% from baseline levels ("HVPG responders") not only have a lower probability of developing recurrent variceal hemorrhage, but also have a lower risk of developing ascites, spontaneous bacterial peritonitis, and death. [26]

Gastric Varices

Prevalence

Gastric varix (GV) and its association with portal hypertension were first described in 1913.[27] The prevalence of GV in patients with portal hypertension varies from 18% to 70%, although the incidence of bleeding from gastric varices is relatively low ranging from 10% to 36%. [14, 15]

In a study by Khalid Mumtaz et al, the prevalence of GV in patients with portal hypertension was 15% (220/1436) and the incidence of bleeding was 22.7% (50/220). Out of the 50 bleeding GV patients, isolated gastric varices (IGV-I) were seen in 22 (44%), gastro-oesophageal varices (GOV) on lesser curvature (GOV-I) in 16 (32%), and GOV on greater curvature (GOV-II) in 15 (30%). IGV-I was seen in 44% (22/50) patients who had bleeding as compared to 2 3% (39/170) who did not have bleeding ($P < 0.003$). [28]

Gastric varices are less prevalent than esophageal varices and are present in 5%-33% of patients with portal hypertension with a reported incidence of bleeding of about 25% in 2 years, with a higher bleeding incidence for fundal varices.

In a study conducted by Sarin et al, the precise incidence of gastric varices in portal hyper tension is not known, but it has been reported to vary from 2-100 %. Though it is generally believed that gastric varices bleed more severely than esophageal varices, the exact profile of bleeding of gastric varices in the presence or absence of esophageal varices is not known.

Classification

Sarin et al classified gastric varices based on their relationship with esophageal varices as well as their location in the stomach. Gastroesophageal varices (GOV) extend beyond the gastroesophageal junction and associated with esophageal varices and are divided into 2 types. The most common are Type 1(GOV1) varices, which extend along the lesser curvature. They are considered extensions of esophageal varices and should be managed similarly. Type 2 (GOV2) gastric varices extend along the fundus and tend to be longer and more tortuous.

Isolated gastric varices (IGV) occur in the absence of esophageal varices and are also classified into 2 types. Type 1 (IGV1) are located in the fundus and tend to be tortuous and complex, and type 2 (IVG2) are located in the body,

antrum, or around the pylorus. The presence of IGV1 fundal varices requires excluding the presence of splenic vein thrombosis.

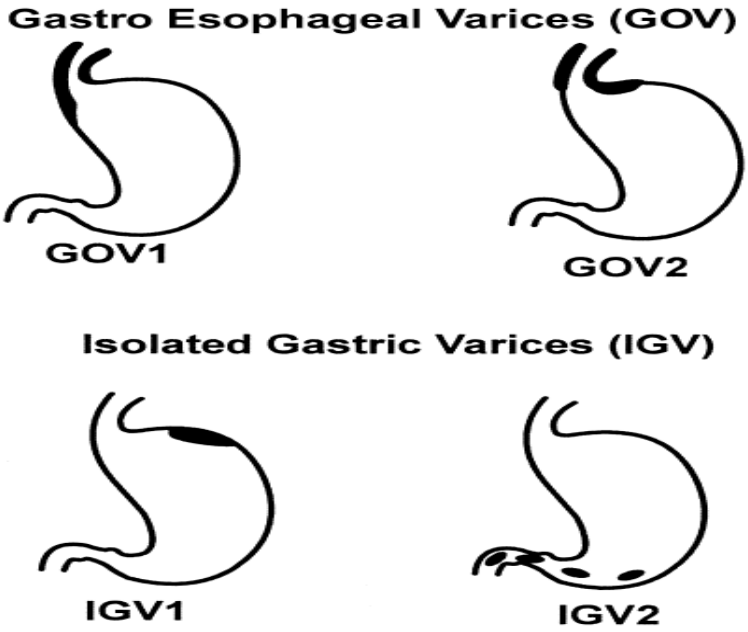

Figure-1.

Sarin classification of gastroesophageal varices

Hashizume *et al*., described the type of gastric varices based on the clinically important findings during endoscopy, and especially from the view point of findings associated with the most risk of varices likely to rupture, similar to the classification of esophageal varices. He categorized the varices based on the findings of gastric varices in endoscopy and according to their form, location, and colour. [29]

The form was classified into three types: tortuous (F1), nodular (F2), and tumorous (F3). The location was classified into five types: anterior (La), posterior (Lp), lesser (Ll) and greater curvature (Lg) of the cardia, and fundic

area (Lf). The location of the gastric varices depends on hemodynamic factors. The colour can be white (Cw) or red (Cr). The glossy, thin-walled focal redness on the varix was defined as red colour spot (RC spot). The Hashizume Group reported that significantly higher risk of gastric variceal bleeding can occur from the RC spot and larger forms.

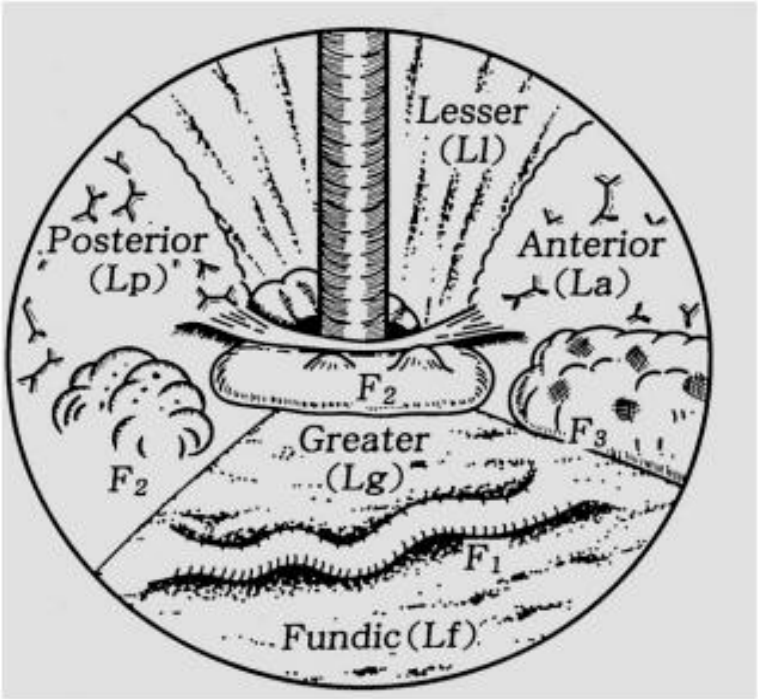

Figure-2 Schematic diagram of endoscopic findings, classified by Hashizume et al

A study by Ryan et al showed that GV also may be considered primary or secondary. Primary GV are those present at initial examination or in a patient who has never had EV endoscopic variceal sclerotherapy (EVS) or endoscopic variceal band ligation (EVL). Secondary GV refer to those that develop after endoscopic therapy (either EVS or EVL) for EV. [30]

Endoscopic treatment of EV can have 2 distinct effects on GV. First, endoscopically evident GV develop in approximately 9% to 20% of patients previously treated with EVS or EVL for EV [12, 31, 35], but using more sensitive techniques such as endoscopic ultrasonography, they have been reported in 26% to 43% of patients so treated. [34] Second, esophageal EVS also can obliterate associated GV (GOV) in a large proportion of patients, depending on the GV type. [12, 36, 37]

Esophageal EVS led to the disappearance of 30% to 60% of GOV1[12, 31] and 20% of GOV2 within 6 months. This is likely to be caused by caudal flow of sclerosant toward the GV. [32, 40, 41] Because of the possibility that GOV1 or GOV2 may disappear after esophageal EVS, it has been recommended that in patients with GOV1/2, the EV should first be treated, and if after 6 months the GV persist, then specific therapy for the GV should be considered if indicated. [12,33]

Hemodynamics

In portal hypertension there is a generalized enlargement of the veins draining the digestive tract. [42-44] In the upper gastrointestinal tract the increased portal pressure is transmitted through two main venous pathways. First, through the right and left gastric veins, which drain varices around the distal oesophagus

and cardia (EV and GOV1) into the portal vein, or if the flow is reversed, the blood flows into the azygous system in cephalad direction.[15, 29]

The second pathway is via the short and posterior gastric veins, which under normal circumstances drain blood from the fundus into the splenic vein. In portal hypertension the flow often is reversed and blood drains from the spleen toward the stomach into fundal varices (GOV2 and IGV1).[15] IGV2 often are caused by dilation of branches of the gastroepiploic veins.

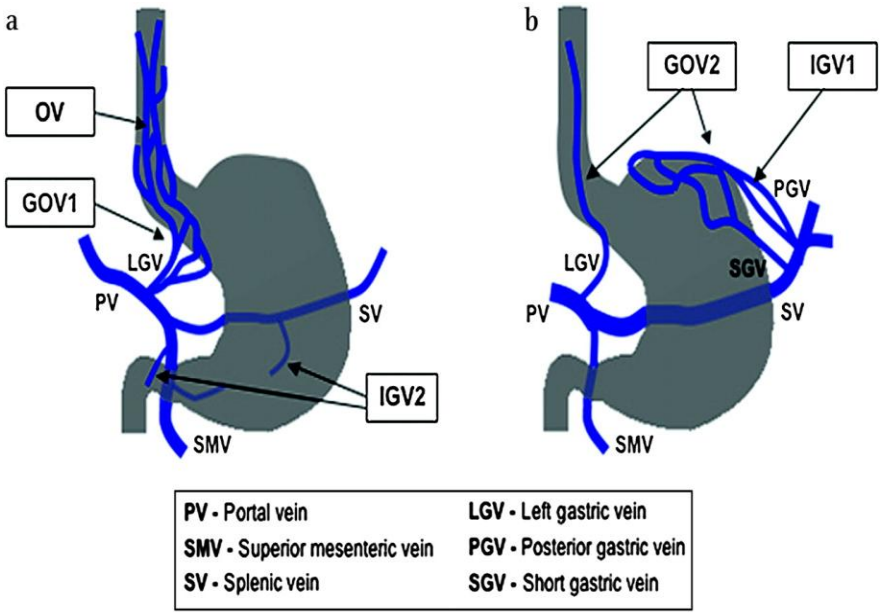

Figure- 3 Showing the type of gastric varices and their corresponding venous drainage a). GOV1, b) GOV2 and IGV1

An essential difference between EV and GV is their position in the gastrointestinal wall. EV form in the lamina propria mucosae and submucosa and GV lie deep in the submucosa under the gastric mucosa, which is relatively thick compared with that of the oesophagus.[45]

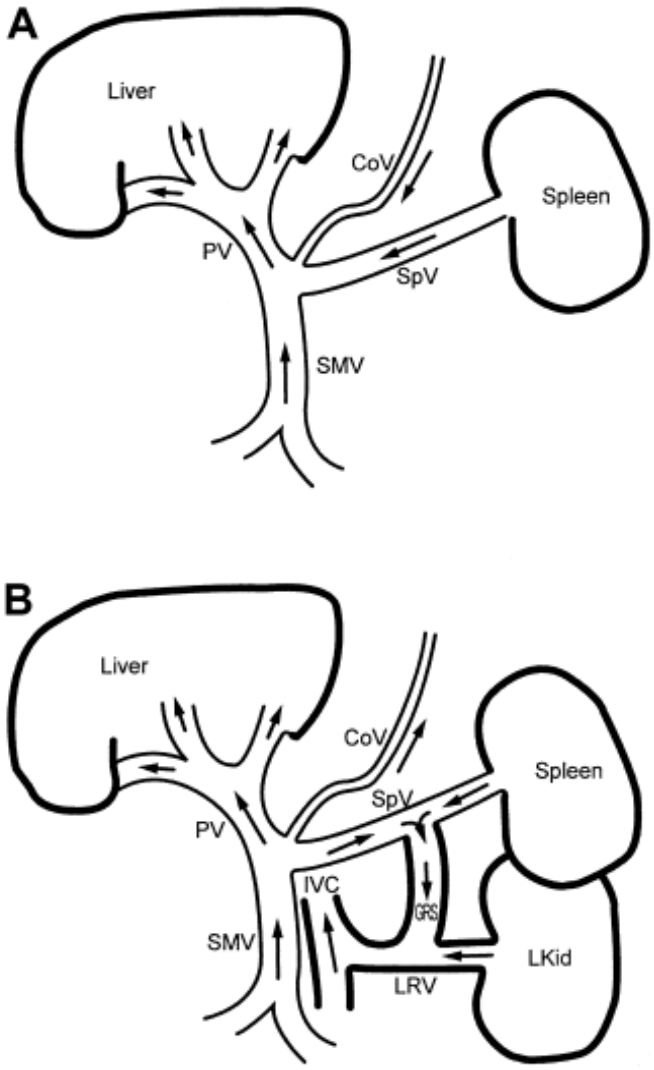

Figure – 4 (A) Normal portal venous blood flow. PV, portal vein; COV,coronary vein; SPV, splenic vein; SMV, superior mesenteric vein.

(B) Portal venous blood flow in the presence of portal hypertension and GRS.

Note reversal of flow in the coronary vein resulting in esophageal varices, and reversal of flow in the splenic vein resulting in gastric varices, which decompress via the GRS.

LKID, left kidney; LRV, leftrenal vein; IVC, inferior vena cava.

Spontaneous portosystemic splenorenal or gastrorenal shunts commonly develop between the splenic vein (splenorenal shunt) and gastric varices, respectively, and connect via the inferior phrenic or suprarenal vein to the left renal vein.[15] Such shunts, collectively termed gastrorenal shunts (GRS), are

more common in GV (60% to 85% of cases) than EV (17% to 21% of cases). [15, 46]

Precisely what determines the predominant collateral pathways that develop in a given individual with PHT remains unknown, however, the size and length of the potential collateral vessel are likely to play a role.[15, 33] Watanabe et al. found that 78% of patients with PHT had predominant collateral flow though the left or right gastric vein, which correlated with the presence of EV or GOV1, while a minority of patients had predominant collateral flow through the short and posterior gastric veins, correlating with the presence of GV.

These frequencies of flow patterns are in good agreement with the observed frequencies of EV and GV. Another study described blood flow patterns in patients with PHT based on the direction of flow in the left gastric vein and the presence or absence of a spontaneous GRS. [46]

Due to the portal and systemic hyperdynamic state in patients with portal hypertension gastroesophageal varices develop as one part of the circulation which is formed by collaterals. Till date, to whom the varices develop is questionable and it is largely unknown. The layer at which the varices develop is submucosal layer at the fundus or cardia of the stomach. The location of the varices in all cases goes along with the porto-systemic shunting boundary line.

This is due to relationship of the retroperitoneum with that off posterior wall of the cardiac or the fundic area, which is fixed to the and lies closest site to the systemic circulation via porto-systemic shunts. The hyperdynamic state of portal hypertension is characterized by the existence of either or both higher arterial and venous inflow. The higher venous outflow vessels associated with a major decrease in peripheral vascular resistance.

The left gastric vein, posterior and short gastric veins are the main supplying vessels to gastric varices, while the gastro-renal shunt is the main drainage vessel. It is important to confirm the supplying vessels and the drainage vessels for the management of the gastric varices. Local hemodynamics of the gastric varices is very important in selecting the best choice for the effective treatment of the gastric varices.

The diameter of huge gastro-renal shunt is about one to three centimetres. The volume of blood flowing through the shunt and the velocity of the porto-systemic shunt are extraordinarily large. This is one reason why conventional endoscopic injection sclerotherapy (EIS) is usually not sufficient to obliterate the varices and can lead to serious complications such as pulmonary embolism or massive ulcer bleeding.

Recently, multidirection-computer tomography (MD-CT) provides the precise information such as the vascular architecture of the gastric varices without angiography[47, 48] to know the hemodynamics of the portal circulation, including the supply and the drainage vessels and it is very helpful in selecting the best treatment choice for each patient with gastric varices.

In patients, especially in Japan with gastrorenal shunts, balloon-occluded retrograde transvenous obliteration (B-RTO) is the most promising and the most effective treatment although it is mostly applied to prophylactic cases. [49-51]

Rick factors

Precisely it is unclear what triggers a bleed from gastric varices. In EV, a decrease in varix wall thickness and an increase in diameter predispose to rupture.[52-54] Similar factors are likely to be at play in GV but the overlying gastric mucosa is much thicker. Although fundal varices form in the submucosa, they do penetrate through the muscularis mucosae and lamina propria at sites where they protrude into the stomach lumen; these vulnerable positions are where rupture occurs, possibly triggered by a mechanical insult or an ulcer overlying the GV, although this remains unproven.

Few studies have prospectively examined the risk for bleeding and mortality from GV.[12, 13] In one study, the 2-year risk for bleeding from GV was 25%,

which is similar to the 20% to 40% two-year risk for bleeding from EV [55]. GV bled more severely than EV, requiring significantly more transfusions. Fundal varices, however, had a significantly higher bleeding incidence (78% for IGV1 and 55% for GOV2), than GOV1 and IGV2 (10%). In other smaller studies also similar bleeding rates were found. [56]

A number of risk factors for GV bleeding have been identified, they include:

1. Red color spots
2. Larger nodular GV
3. Fundal location.

Kim et al [13] found that advanced Child–Pugh class, varix 5 mm or more in size, and the presence of a red spot were associated with an increased risk for a first bleed. In that study the estimated 1-year risk for GV bleeding in patients ranged from 4% to 65% in the lowest risk and highest risk categories, respectively. Factors not associated with bleeding risk included classification as primary or secondary, concomitant EV, underlying cause of liver disease, and presence of encephalopathy, among others. A PPG of ≥12 mm Hg is not necessary for development of, or bleeding from, GV.

Clinical presentation:

GV are discovered most commonly during screening of PHT patients for varices, or at the time of a first variceal bleed, at which time the bleeding usually is caused by associated EV and uncommonly originates from bleeding GV.[12] Considerable number of patients with GV also may present with hepatic encephalopathy. Watanabe et al. showed that encephalopathy was more common in GV (25%) than EV (3%) patients, probably attributable to the increased prevalence of GRS in GV patients.[15]

Diagnosis

There are various methods to diagnose the gastric varices namely upper gastrointestinal endoscopy, ultrasonography, computed tomography, magnetic resonance imaging and endoscopic ultrasonography.

Upper Gastrointestinal Endoscopy

Upper endoscopy is usually the initial investigation in patients with suspected fundal varices although the distinction between fundal varices and gastric folds, particularly in patients with hypertensive gastropathy may be difficult. The current consensus is that all patients with cirrhosis of the liver, extrahepatic portal vein obstruction and non cirrhotic portal fibrosis should be screened for esophageal varices by endoscopy. In patients in whom no varices are detected

on initial endoscopy, endoscopy to look for varices should be repeated in 2 to 3 years.

If small varices are detected on the initial endoscopy, endoscopy should be repeated in 1 to 2 years.[57, 58] None of the various non-invasive methods of determining which patients benefit most from endoscopic screening are accurate enough to recommend for routine use in clinical practice.[59] The role of non-invasive markers in predicting the risk of large gastroesophageal varices requires study in large multicenter trials.[60] Preliminary data suggest that wireless video capsule endoscopy and computed tomography (CT) imaging are alternative screening modalities in patients who are not candidates for upper endoscopy. Moreover, CT screening may be more cost-effective than endoscopy. [61]

Gastroesophageal varices are diagnosed on retroflexion during upper gastrointestinal endoscopy and classified according to Sarin.

Ultrasonography

Ultrasound examination of the liver with Doppler study of the vessels has been used widely to assess patients with portal hypertension. Features suggestive of portal hypertension on ultrasonography include splenomegaly, portosystemic collateral vessels, and reversal of the direction of flow in the portal vein (hepatofugal flow). Few studies have demonstrated that a portal vein diameter

greater than 13 mm and the absence of respiratory variations in the splenic and mesenteric veins are sensitive but nonspecific markers of portal hypertension. [62, 63]

These criteria are not used routinely in clinical practice in most centres. Ultrasound examination can detect thrombosis of the portal vein, which appears as nonvisualization or cavernous transformation (a cavernoma) of the portal vein; the latter finding indicates an extensive collateral network in place of the portal vein.[64] Splenic vein thrombosis also can be demonstrated. Portal blood flow can be measured by Doppler ultrasonography, which is the easiest research method for detecting postprandial increases in splanchnic blood flow .[65]

Although Doppler ultrasonography is clinically useful in the initial evaluation of portal hypertension, the technique is not widely used to provide quantitative assessments of the degree of portal hypertension. Transient elastography may be useful in detecting portal hypertension but is not sufficiently sensitive to recommend as a modality to monitor decreases in portal pressure in patients on pharmacotherapy.[66]

Computed Tomography

Computed tomography (CT) is useful for demonstrating many features of portal hypertension, including abnormal configuration of the liver, ascites, splenomegaly, and collateral vessels. Detection of varices may be an emerging

indication for CT. Diagnosis of fundal varices by multidetector row CT (MDCT) is at least as accurate as endoscopic ultrasonography.

CT is especially helpful in distinguishing submucosal from perigastric fundal varices [67] and is considered a less invasive alternative to conventional angiographic portography in assessing portosystemic collaterals. At present, however, CT is not a recommended screening method for detecting large esophageal varices, but it may be a cost-effective method of screening for varices and preferred to endoscopy by patients.[61]

The computed tomography (CT) angiography is gaining increasing acceptance as a minimally invasive technique for imaging the abdominal vascular system, which allows visualization of small visceral vessels by offering shorter acquisition times, less motion artefacts and increased spatial resolution.[51, 68, 69]

These features may be useful in order to assess the gastric fundus for the presence and differentiation of submucosal and perigastric varices. In a study by Willmann et al, it is mentioned that Multi-detector row CT (MDCT) angiography is gaining increasing acceptance as a minimally invasive technique for imaging the abdominal vascular system.[67]

Magnetic Resonance Imaging

Gadolinium-enhanced magnetic resonance imaging (MRI) is becoming recognized as a potentially useful method of detecting esophageal varices.[70] In addition, MRI can be used to measure portal and azygous blood flow, which is increased in patients with portal hypertension.[71] MRI provides excellent detail of the vascular structures of the liver and can detect portal venous thrombosis and spleen stiffness in patients with portal hypertension, but the role of MRI in the assessment of portal hypertension requires further study. Unlike transient elastography using ultrasound, MRI can accurately assess the stiffness of even fatty livers.[72]

Endoscopic Ultrasonography

Currently, endoscopic ultrasound (EUS) is considered most useful in the evaluation and diagnosis of submucosal fundal varices which allows visualization of the different layers of the gastric wall and permits differentiation between submucosal and perigastric fundal varices.[73-75] However, EUS is invasive, not widely available, and examiner dependent. Hence a non-invasive imaging modality would be preferable in these high risk patients.

Endoscopic ultrasound examination (EUS) using radial or linear array echo-endoscopes or endoscopic ultrasound mini-probes passed through the working

channel of a diagnostic endoscope has been applied as an investigational tool in the evaluation of patients with varices.

EUS can be combined with endoscopic measurement of transmural variceal pressure to allow estimation of variceal wall tension, which is a predictor of variceal bleeding.[76-78]

Splenoportography or percutaneous transhepatic portography

The role of splenoportography or percutaneous transhepatic portography is limited in the distinction between submucosal and perigastric fundal varices, although this modality allows good assessment of the portal venous system and its collaterals.[79]

Management:

Although variety of treatments have been developed for esophageal varices since the 1940s including porto-caval shunts, selective shunts, or esophageal transaction, as well as endoscopic treatments, the management of gastric varices still remains a therapeutic challenge. Most approaches have been performed successfully and clinical results have been acceptable when the indications have been appropriately applied. Because there are few controlled clinical trials, much less confidence can be placed on guidelines for the management of gastric varices than for their esophageal counterparts.[80]

Most studies that have investigated the effect of β-blocker in primary prevention have contained few patients with GV.[81-85] GOV1 seem to behave similarly to EV and should be treated accordingly. RCTs investigating β-blockade in primary prophylaxis of GV bleeding need to be performed. However, until such time that conclusive data from RCTs suggest otherwise, it seems reasonable to give β-blockers empirically in primary prevention of GV bleeding, although their value is not proven.

Since the mortality of GV hemorrhage is high, it has been suggested that the patients at high risk for bleeding with an annual risk of 16% [86] should undergo primary prophylactic eradication of the GV.[87] Although this approach is embraced in Asia; it remains contentious and is not standard accepted practice in most western centres. Well-designed RCTs are required before this approach can be propounded universally.

Management of Acute Bleeding and Prevention of Rebleeding

Bleeding should be considered to have arisen from GV if there is (1) active spurt or ooze, (2) adherent clot, or (3) presence of large GV, no EV, and no other source of bleeding evident.[88]

The modalities of therapy available include the following:

1. Pharmacotherapy & antiboitics
2. Balloon tamponade with Sengstaken Blackmore or Linton Nachlas tube
3. Endoscopic variceal sclerotherapy
4. Endoscopic variceal obturator therapy with N-Butyl-2- Cyanoacrylate and thrombin
5. Endoscopic variceal ligation using snares, bands and endoloops
6. Endoscopic variceal ligation–injection sclerotherapy
7. Interventional radiology such as BRTO and TIPSS
8. Shunt surgery

Pharmacotherapy

There is little data concerning the efficacy of somatostatin or vasopressin or their analogues in the control of acute GV bleeding.[89] However, given the similar pathophysiology and anatomy, GOV1 should be treated as for EV. Octreotide has been shown to have a beneficial effect on acute bleeding from portal hypertensive gastropathy, but it is likely that the often voluminous bleeding from GV might not be controlled by pharmacologic measures.[90]

The role of β-blockers and nitrates in secondary prevention of GV bleeding has not been studied extensively. A small open-label trial of -blocker and nitrate therapy reported that although these agents conferred no significant benefit in terms of risk for rebleeding or overall survival.

Antibiotics

Antibiotics should be administered as early as possible in acute variceal bleeding because, bacterial infection occurs in 20% of cirrhotic patients [91] within 2 days of an acute variceal bleed and is associated with a worsening of prognosis.[92,93] Bacterial translocation may be spontaneous or due to instrumentation. A recent meta-analysis showed that antibiotic prophylaxis significantly reduced infection rates and was associated with a better short-term prognosis.[94]

Fluoroquinolones such as ciprofloxacin have been shown to significantly reduce infection in several studies.[95] and oral or intravenous ciprofloxacin prophylaxis at a dose of 1 g/day has been recommended.[89] RCTs comparing systemic vs. oral nonabsorbable antibiotics are needed.[96]

Balloon Tamponade

The commonly used Sengstaken–Blakemore or Minnesota tubes are not usually efficacious in controlling bleeding from fundal varices, owing to

the small volume of the gastric balloon (200 mL). The Linton– Nachlas tube has a 600-mL volume single gastric balloon and seems to be more effective in controlling fundal variceal bleeding in up to 50% of patients, although 20% subsequently will rebleed.[97,98] Balloon tamponade should be used only as a stopgap to definitive treatment for gastric varices.

Endoscopic Therapy

Endoscopic Variceal Sclerotherapy (EVS)

Traditional endoscopic variceal sclerotherapy involves injection of sclerosants such as ethanolamine oleate or absolute alcohol intra- or perivariceally (or both) which results in endothelial damage and thrombosis of blood and subsequent sclerosis of the varix. This has been very successful in the treatment of EV bleeding and in eradication of EV.[99,100] it has been less successful in the treatment of GV, probably because of the high-volume blood flow through GV compared with EV, resulting in rapid flushing away of the sclerosant in the bloodstream.

Typically, EVS of GV requires larger volumes of sclerosant than for EV, and fundal varices (GOV2 and IGV1) require significantly more sclerosant than GOV1. This may be associated with more side effects after EVS for GV than for EV. The commonly seen side effects are retrosternal, abdominal pain and

fever.[101]. In acute GV bleeding, EVS controlled bleeding in 60% to 100% of cases, depending on the report [102], but has been associated with unacceptably high rebleeding rates of up to 90%.

It appears to be least successful in controlling acute fundal variceal bleeding.[103] Differences observed between studies may reflect different injection techniques, different mixes of GV subtypes, but also inclusion of different patient populations; half of the patients in one study had noncirrhotic PHT [104], whereas in the other studies more patients had cirrhosis and associated hepatic synthetic dysfunction.

EVS achieved secondary prophylactic variceal eradication in 40% to 70% of all GV patients treated electively [105], but Sarin et al. found that this success was weighted heavily by high efficacy in GOV1 (95% eradication) and was less effective for GOV2 and IGV1. In that study, rebleeding after elective EVS was less than 20% for patients with GOV1 and GOV2 but it was high in patients with IGV1 (53%). Most bleeds were related to ulcers at the injection site reflecting the large amounts of sclerosant often needed.

EVS is an effective and appropriate treatment for both treatment of acute GOV1 hemorrhage and for attempting secondary prophylactic GOV1 obliteration. However it is not appropriate for patients with fundal varices (GOV2 or IGV1)

because of the low rate of primary hemostasis, the low success rate for secondary variceal eradication, and the high rate of rebleeding.

Endoscopic variceal obturation therapy:

Endoscopic variceal obturation (EVO) refers to the injection of agents such as n-butyl-2-cyanoacrylate (Histoacryl), isobutyl-2-cyanoacrylate (Bucrylate), or thrombin, which solidify and/or induce thrombosis in the varix [106] with ultimate sloughing off of the glue cast weeks to months post injection, resulting in late ulceration. At present, these agents are not approved for use in GV in many countries, but it is available in other countries including India and in a study by Khalid Mumtaz et al the success rate for achieving primary haemostasis with glue was 90-100% without recurrent bleeding within 48 hrs. The same result was also observed in a study in India conducted by Shiv K Sarin et al in acute GV bleeding.

EVO has emerged as the initial treatment of choice for acute GV bleeding and for secondary eradication of GV. Two small RCTs have shown that EVO is superior to both EVS and EVL 107 in the treatment of acute GV bleeding, achieving haemostasis in 90% of cases compared with 62% for EVS [107]and 40% for EVL. Sarin et al. found a similar rebleeding rate (22% to 25%) in both EVS and EVO groups, but the overall success of EVO was better (78% vs. 38%) because of the higher rate of initial haemostasis. A number of large case series

or nonrandomized trials also have shown that cyanoacrylates successfully control acute GV bleeding in over 90% of cases.[108-111]

Thrombin also has been used to control fundal variceal bleeding with a relatively good success rate of up to 75% [112] and a rebleeding rate of 0% to 30% in the small reported series. To date, no RCTs of thrombin injection therapy for bleeding GV have been performed. Eradication rates between 50% and 100% have been reported with an average of about 75%. In the long term, GV rebleeding occurs in 23% to 50% of patients, with the vast majority occurring in the first year.

Side effects of EVO include pyrexia and abdominal discomfort, which are usually mild and transient. Uncommon side effects associated with the use of acrylates include cerebral, pulmonary and portal vein embolism, retroperitoneal abscess, splenic infarction, and portal and splenic vein thrombosis. The systemic emboli probably occur in patients with large GRS and hepatopulmonary syndrome.

Hepatopulmonary syndrome is found in up to 20% of patients with cirrhosis and is characterized by pulmonary microvasculature dilatation with consequent right-to-left shunting potentially facilitating entry of the glue-like substance into the systemic circulation. Avoidance of this technique in patients with known

large GRS or hepatopulmonary syndrome may help avoid embolic complications.

Embolic and thrombotic phenomena have been associated with a larger volume of injected material and it is recommended that no more than 2 mL. of compound should be injected in a session. Precautions to prevent damage to the scope must be taken when using this agents.[113] Given the high rate of primary haemostasis and lower rate of rebleeding compared with EVS, EVO with acrylates is now used as standard first-line treatment of bleeding fundal GV and in secondary prophylactic eradication of GV.

Endoscopic variceal ligation:

EVL with nylon or stainless steel snares or standard rubber bands has been used in treatment of bleeding GV. GV smaller than 2 cm in diameter can be ligated with standard rubber bands, whereas larger-diameter GV require the use of larger detachable snares. The literature is sparse on this topic and only one RCT has been reported comparing GV EVL using rubber bands against EVO.

Barbera Ryan et al found that EVL was less effective than EVO in controlling acute GV (45% vs. 87%) and had a higher rebleeding rate (54% vs. 31%), although the ability to eradicate varices was similar (45% vs. 51%). A number of case series, however, have shown EVL to be safe and highly efficacious in

terms of achieving haemostasis in acute GV bleeding (83% to 100%), low rebleeding rate (0% to 19%), and eradication of GV (77% to 100%).[114]

Active bleeding was controlled in 83% (10/12) of patients, one acute bleeder died and one bleeder required rescue EVO. The rebleeding rate was low and often was caused by ulceration at the ligation site. GV were eradicated successfully in almost all patients initially, but all patients subsequently developed recurrent GV within 2 years. Most of the recurrences were treated with EVO or EVS owing to difficulties in snaring the varices in fibrosed mucosa.

Higher GV recurrence post-EVL compared with post- EVO may be owing to a lesser degree of deep fibrosis after EVL compared with EVO.[115] Future RCTs are required to compare EVL with the gold standard of EVO and to define the long term outcome of this therapy.

Endoscopic variceal ligation–injection sclerotherapy:

A combination technique of EVS and EVL, called endoscopic variceal ligation injection sclerotherapy, has been reported by Japanese endoscopists.[116] Using this technique, a detachable snare is placed around the varix and partially tightened to cause stasis of blood.

The sclerosant (ethanolamine oleate) is then injected into the varix, followed by tightening and release of the snare around the varix. Uncontrolled data from a total of 22 patients treated with endoscopic variceal ligation injection sclerotherapy for acute GV bleeding reported haemostasis in 100%, a low rebleeding rate of 0% to 8%, and a GV eradication rate of 85% up to 2 years posttreatment.[117]

The better long-term eradication rates than EVL alone may reflect the added fibrosing effect of the sclerosant.

Interventional Radiologic Treatment

TIPSS- Transvenous intrahepatic portosystemic shunt therapy

Most published series of TIPS contain relatively few GV patients. For management of EV bleeding, meta-analysis comparing TIPS with endoscopic treatment has shown that TIPS is associated with a reduction in rebleeding, a higher risk for encephalopathy, and a similar overall survival rate.[118]

British Society of Gastroenterology guidelines for the management of variceal hemorrhage in cirrhotic patients recommended TIPS or shunt surgery as second-

line therapy for control of acute GV bleeding when standard endoscopic measures have failed. Appropriate patient selection for TIPS is critical.[89]

Prognosis is worst in Child–Pugh class C, but the majority of candidates for TIPS fall within this category. Other factors shown to be associated with poor outcome after TIPS in patients with advanced liver disease include higher serum bilirubin and creatinine levels, underlying chronic viral hepatitis as opposed to chronic alcohol-induced cirrhosis, variceal hemorrhage necessitating emergent TIPS, and high international normalized ratios.[119]

TIPS in acute GV bleeding.

The current role of TIPS in acute GV bleeding is as second-line rescue therapy when EVO has failed. In GV, TIPS has been shown to control acute refractory GV bleeding in 90% to 100% of cases.[120] Rebleeding occurs in 10% to 30% of patients within 1 year. Early rebleeding (within the first week) and late rebleeding (after 1 week) can occur due to recurrent variceal bleeding and stent failure (stenosis or occlusion) respectively. New-onset encephalopathy develops in 3% to 16% of patients after TIPS.

After control of GV bleeding by TIPS, reported survival rates vary from 50% to 85% at 1 month, to 58% to 79% at 1 year.[121] The most common causes of mortality are sepsis, multiorgan failure, and recurrent hemorrhage.

TIPS for prevention of GV rebreeding.

In an early study, Spahr et al. found that the post-TIPS rebleeding rate was higher from GV (53%) than from EV (11%).[122] Stanley et al., however, found no difference in rebleeding from GV (13%) and EV (17%) during a follow-up period of approximately 1 year.

An interesting finding of the study of Tripathi et al. concerns the role of PPG in GV and EV bleeding. They found that 35% of GV bleeders had a PPG of ≤12 mm Hg at the time of TIPS compared with only 8% of EV patients. In patients who had pre-TIPS PPG of ≤12 mm Hg, a decrease in PPG after TIPS did not affect the risk for rebleeding, suggesting that in this subgroup of patients, PPG may not be the critical determinant of bleeding risk. In contrast, in the group in which pre-TIPS PPG was ≥12 mm Hg, a clear relationship was shown between post-TIPS risk for rebleeding and higher post-TIPS PPG, suggesting that in this group, PPG plays a central role in determining the risk for bleeding.[123]

TIPS stent surveillance.

Pseudointimal hyperplasia leading to stent occlusion is a major drawback of TIPS. Studies have shown that stent insufficiency occurs in 30% to 80% and 47% to 90% of patients by 1 and 2 years post-TIPS, respectively. When clinical signs herald stent insufficiency, then clearly re-intervention is indicated. The

optimal post-TIPS surveillance regimen has not yet been defined and there are arguments for and against both a more- or less-invasive approach.[124]

Doppler ultrasound is 70% sensitive and 90% specific in predicting stent dysfunction. Surveillance portal angiography every 6 months has been advocated.[124] Computed tomography angiography and magnetic resonance angiography also offer excellent images of the portal vasculature and can be used to monitor the shunt anatomy (but not function) post-TIPS.[44]

TIPS is currently indicated for treating refractory GV bleeding and for prevention of rebleeding although further RCTs are required. One year post-TIPS, the rebleeding rate is between 10% and 30%, the incidence of new-onset encephalopathy is 3% to 18%, and the overall 1-year survival ranges from 58% to 80%, depending mainly on the severity of the underlying liver disease. Appropriate patient selection is critical and the severity of the underlying liver disease must be taken into consideration.

Balloon-Occluded Retrograde Transvenous Obliteration and Balloon-Occluded Endoscopic Injection Sclerotherapy

A number of interventional radiologic techniques have been developed in Japan for the treatment of GV. These therapies have been used predominantly in

primary prophylactic GV eradication, but also to treat acute GV bleeding and in secondary preventive GV eradication.

Primary GV eradication in patients with high-risk GV is not standard accepted practice outside Asia. To date, there is no experience of these techniques outside of Japan and almost all data emanate from case series. Balloon-occluded retrograde transvenous obliteration (B-RTO) is technically feasible only in patients with a known GRS, which accounts for almost 85% of GV patients.

Treatment and short-term outcome of 188 patients treated with BRTO has been reported in the literature.[46] Haemostasis was achieved in 100% (16/16) of patients for acute bleeding and the rebleeding rate was 0% during almost 2 years of follow-up evaluation. The majority of literature, however, pertains to eradication of high-risk GV, for which B-RTO was reported to eradicate 85% to 100% of GV and to have a low rate of rebleeding.

The most common complications reported were hemoglobinuria, abdominal pain, transient fever, pleural effusion, and transient worsening in liver biochemistry, but more serious complications also have been reported including shock and atrial fibrillation.

A potentially problematic long-term sequelae of B-RTO is the observed development or worsening of EV in up to 50% of patients thus treated, although on the whole EV are managed more easily than GV.[46] Balloon-occluded endoscopic injection sclerotherapy, another vascular interventional technique developed in Asia, can be performed in patients with or without a GRS, but it is more invasive.[125]

Reports of fewer than 20 patients suggest that it is a potentially effective means of eradicating GV and it seems similar to B-RTO in terms of safety and efficacy. RCTs comparing B-RTO and balloon-occluded endoscopic injection sclerotherapy with standard therapies for acute GV bleeding need to be performed.

Surgery

Portocaval shunts can be either nonselective (diversion of portal blood flow into the systemic circulation, bypassing the liver) or selective (such as distal splenorenal shunts (Warren) that drain varices into the systemic system without affecting liver blood flow). Most reported studies included mainly EV patients. A meta-analysis has shown that although shunt surgery was associated with a significant reduction in variceal bleeding (not categorized as GV or EV), incidence of hepatic encephalopathy and mortality were increased significantly.[126]

With the advent of other therapeutic options, and considering the reduction in survival, primary prophylactic shunt surgery is not recommended. Bleeding GV were treated by selective shunt surgery in one study of 30 patients with good liver function. In this study only 6 of the patients had cirrhosis (Child's A or B) and the remainder had portal vein thrombosis or portal fibrosis. Bleeding was controlled in 87% (26/30) of cases.[127] Two patients (7%) died (both had cirrhosis) and 2 patients developed shunt thrombosis. In the context of prevention of rebleeding, again little specific GV information exists.

Clearly data on the role and efficacy of shunt surgery in patients with GV is lacking. Moreover, the role of shunt surgery in patients with already existing spontaneous GRS, so common in GV patients, is not known. In a RCT published by Roberto et al showed that a subgroup of patients with good liver function, DSRS with a correct portal-azygos disconnection more effectively prevents variceal rebleeding than ES.

BSG guidelines suggest that shunt surgery should be considered as an alternative to TIPS for prevention of GV rebleeding or as second-line treatment of refractory acute GV bleeding.[89]

The proposed algorithm for the treatment of Gastric varices

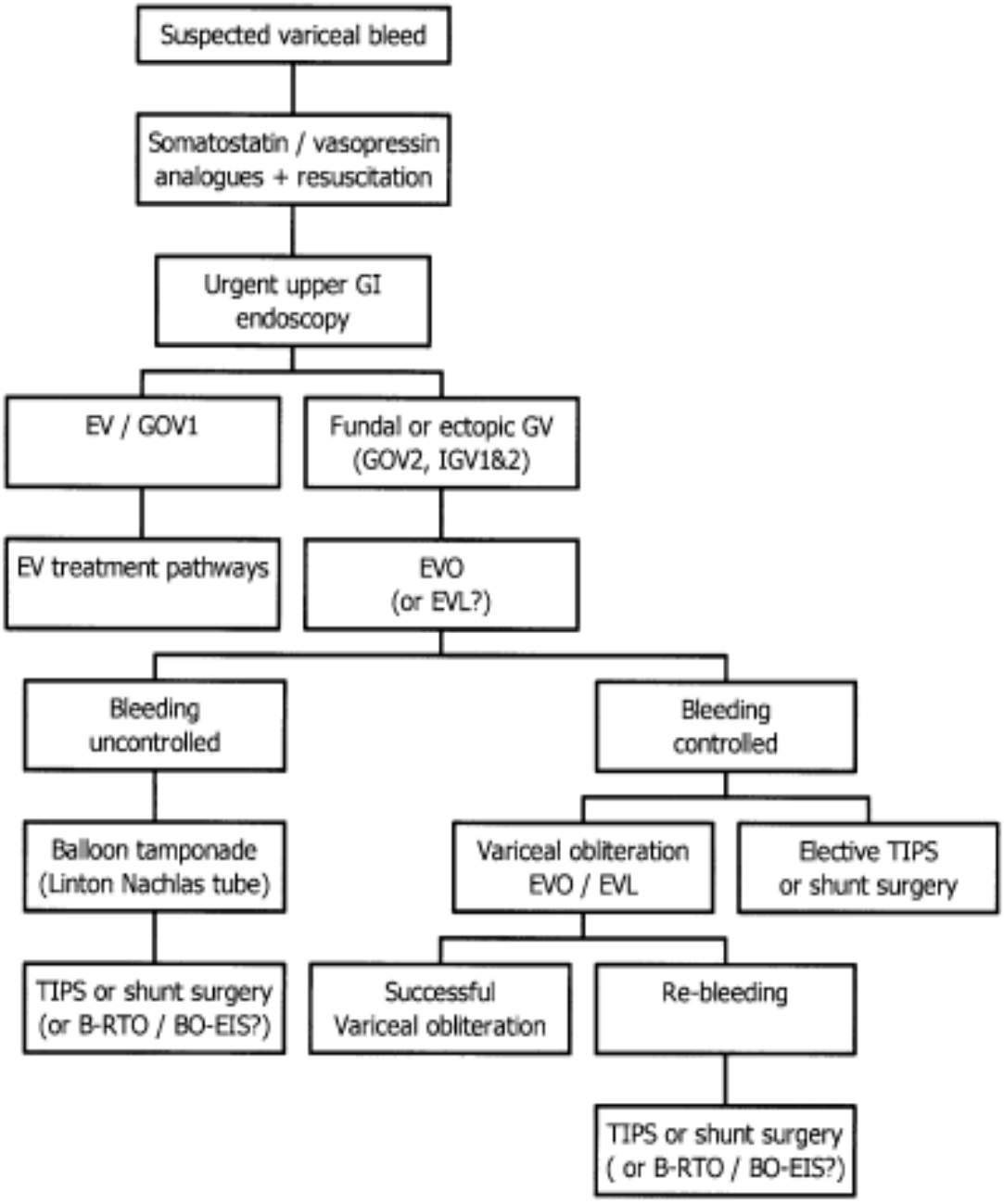

Figure-5 Proposed simple algorithm for the management of gastric varices.

EVO-Endoscopic variceal obturation , BO-EIS- Balloon occluded endoscopic injection sclerotherapy.

To conclude, primary GV are found in approximately 20% of patients with PHT, and a further 10% to 20% of PHT patients will develop GV after endoscopic therapy of EV. Accurate classification of GV is essential in determining the optimal management of these patients. GOV1 should be treated as for EV, whereas fundal varices do not respond well to therapeutic modalities used in EV.

GOV1 have a low risk for hemorrhage, but the risk for bleeding from fundal varices can be as high as 65% within 1 year, comparable with the risk for EV bleeding. GV bleeding tends to be more profuse and to require more transfusions. A PPG of ≥12 mm Hg is not required for GV bleeding to occur and a large proportion (35%) bleed below this threshold, probably related to the high incidence of spontaneous gastrorenal shunts among GV patients.

The optimum acute and long-term management of GV has not been determined and the Reston–Baveno group have highlighted the need for RCTs for various GV treatment options. Endoscopic variceal obliteration has a proven track record in treating acute GV bleeding and should be used as first-line treatment of acute fundal GV bleeding, whereas other treatment modalities need further evaluation.

TIPS is a valuable adjunct to management of acute refractory or recurrent GV bleeding, but its role in managing patients with a PPG of ≤12mm Hg and its appropriateness in patients with advanced liver disease remains to be

clarified. A number of radiologic or combination endoscopic-radiologic techniques have been pioneered in Japan and need further trials.

MATERIALS AND METHODS

It is a prospective study conducted between April 2010 and October 2011 where consecutive patients with the diagnosis of cirrhosis, NCPF and EHPVO undergoing oesophagogastroduodenoscopy (OGD) scopy as a routine evaluation and for upper gastrointestinal bleeding were included. Patients with cirrhosis and NCPH are subjected to endoscopy in which if there are gastric varices, they are included in this study.

If the patient diagnosed to have cirrhosis and NCPH who had already undergone this investigation and found to have gastric varices are also included. Grading of the varices and diagnosing the fundal varices are carried out by experts in endoscopy technique. Among the 1083 patients who underwent OGD scopy, 81 patients were found to have gastric varices and those were included in the study. A non bleeder was defined as any patient without a history of hematemesis or melena.

A written consent was obtained from all the patients. Institute ethical committee has approved the study. All patients with gastric varices were included in the study. All the patients had baseline investigations such as Complete blood count, Liver function test, Prothrombin time, International normalized ratio, Renal function test, HBsAg, Anti-HCV and ultra sonogram. Cirrhosis was

diagnosed by clinical, imaging and biochemical values. EHPVO and NCPF have been diagnosed by ultra sonogram and Portal vein Doppler study. Baseline demographic details such as age, gender, literacy, socio economic status, alcohol intake, smoking, religion and occupation were collected.

A detailed history about the upper gastrointestinal bleeding was obtained from all the patients such as age at the time of diagnosis, duration of illness, cause of portal hypertension, index bleed , subsequent bleed with dates, volume of blood vomiting, presence of liver cell failure feature at the time of bleed, use of Sengstaken Blackmore tube to arrest bleeding, use of vasopressors drugs, application of endoscopic sclerotherapy, endoscopic variceal ligation and glue, surgery details in case of failure of endotherapy and outcome after the bleed.

A detailed clinical examination was also performed in all patients which includes pallor, jaundice, pedal edema, fever, asterixis, clubbing, cyanosis , presence of liver cell failure features such as Parotidomegaly, Gynaecomastia, Spider angioma, Dupuytran’s contarcture , Palmar erythema, Testicular atrophy in males and on per abdomen examination abdominal veins, liver and spleen enlargement and ascites. Per rectal examination, proctoscopy and examination of other systems was also done.

Upper gastrointestinal endoscopy and grading of the varices have been done in all patients. Grading of varices was done by using Sarin's classification. In his classification, four types of gastric varices have been described.

1. GOV1- Extend 2 to 5 cm below the gastroesophageal junction and are in continuity with esophageal varices
2. GOV2 - Gastroesophageal varices are in the cardia and fundus of the stomach and in continuity with esophageal varices
3. IGV1 - Varices that occur in the fundus of the stomach in the absence of esophageal varices are called isolated gastric varices type
4. IGV2 - Varices that occur in the gastric body, antrum, or pylorus

Exclusion Criteria:

1. Patients with only esophageal varices
2. Child- Turcotte-Pugh score >10
3. Patients with diagnosis other than Cirrhosis, NCPF and EHPVO.

Patients presented with bleed were admitted in the hospital and appropriate resuscitative measures have been done including the use of SBT tube, use of octreotide, endoscopy therapy and surgery. Glue injection to obliterate the

varices in suitable patients. The patients are followed after treatment for the varices and if they will have subsequent bleed, they are admitted again to assess the nature of the fundal varices.

Further course of the illness is also observed carefully. Follow up endoscopy was done regularly initially at 3rd month and later at 6 months intervals. Patients were followed up minimum for a period of 3 months. During the follow up outcome of the patient was monitored. Patients with uncontrolled bleeding and from remote places where endoscopic therapy is inaccessible were given the option to undergo surgical treatment if they are willing, to prevent recurrent bleeding in future. Propranolol therapy was continued in all patients as a primary as well as for secondary prophylaxis.

Statistical analysiss

Quantitative data were expressed in Mean and Standard deviation. Qualitative data were given in frequencies with their percentage. The association between various factors like age, gender, literacy, per capita income, alcohol consumption, aetiology of portal hypertension, index bleed, subsequent bleed, treatment given to bleed, clinical examination details and type of varices were

analyzed by using Pearson Chi square test/ student independent test as appropriate. P value less than 0.05 was taken as statistically significant.

OBSERVATION AND RESULTS

A total of 1083 patients underwent upper gastro intestinal endoscopy during the study period. 81 patients had gastroesophageal varices and those were taken for analysis. Mean age of the patient is 41.23 ± 15.4 years. The aetiology for the gastroesophageal varices was:

1) Cirrhosis in 49.4%.

2) Extrahepatic portal vein obstruction in 27.2%.

3) Non cirrhotic portal fibrosis in 23.5%.

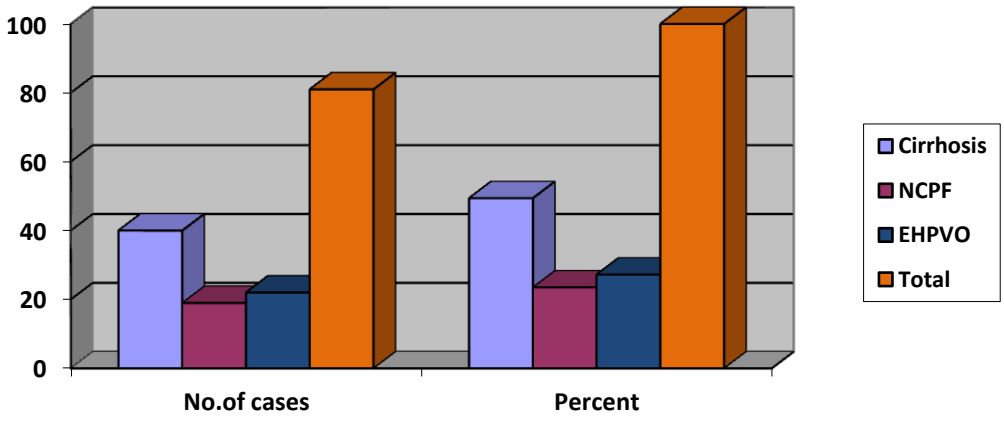

Figure-1. Graphical representation of various aetiologies for gastric varices.

Among the 81 patients, (Table-1) 75 (92.6%) patients had history of upper gastrointestinal bleeding and 6 (7.4%) patients had no history of bleeding. Subsequent bleed was observed in 58% (47) of the patients who has bled initially. 4 (4.9%) patients had bleed in the form of melena. All other patients (77) developed hematemesis during the index bleed.

Table-1.Demographic characteristics of the study population

Characteristics			n (%)
Total No of cases			81
Male			50(61.8%)
Female			31(38.2%)
Mean age (Years)			41.23± 15.4
Literacy status	Yes		68 (84%)
	No		13 (16%)
Per capita income		≤ 5000	74(91.3%)
		≥5000	7(8.7%)
Aetiology of portal hypertension			
Cirrhosis			40 (49.4%)
EHPVO			22 (27.2%)
NCPF			19 (23.5%)
Bleeder			75(92.6%)
Non bleeder			6(7.4%)
Outcome	Alive		74(91.4%
	Dead		7(8.6%)
HBsAg positive			4(4.9%)
Anti-HCV positive			3(3.75%)

Table-2.Bleed details

GOV1	40(49.4%)
GOV2	14(17.3%)
IGV1	14(17.3%)
IGV AND ESOPHAGEAL VARICES	12(14.8%)
GOV1&2	1(1.2%)
Index bleed cases	75(92.6%)
Subsequent bleed cases	47(58%)
Transfusions requirement	71(87.7%)
Mean volume of blood given (L)	2.28
Rectal varices	1(1.2%)

Among the bleeders (Table-2) blood transfusion required in 87.7 % of the patients. The mean volume of units of blood given to the bleeding patients was 2.28L. The number of patients underwent surgery for the bleeding episodes were 19 (23.5%).

Rectal varix was seen in only one patient. GOV 1 was the commonest type which was seen in 40% of patients. Index bleed was present in 92.6% patients and subsequent bleed was seen in 58% of patients.

Table-3 Characteristics of bleeders and non bleeders

Characteristics	Bleeder n (%) n=75	Non bleeder n (%) n=6	P value*
Age (mean)	40.8	44.8	0.306
Gender			
Male	48	1	0.197
Female	27	5	
Type of gastric varices			
GOV1	37	3	0.701
GOV2	13	1	0.636
IGV1	12	2	0.782
IGV & Esophageal Varices	12	Nil	---
GOV1&2	1	Nil	---
Aetiology of portal hypertension			
Cirrhosis	35	5	0.193
NCPF	19	Nil	0.105
EHPVO	21	1	0.184
Hepatic encephalopathy	14	8	0.307

Table-4 Index and subsequent bleed

Characteristics	Index bleed (P value)	Subsequent bleed (P value)
Alcohol consumption	0.423	0.017
Age at diagnosis	0.235	0.002
Quantity of bleed	0.001	0.003
Cause of PHT	0.193	0.005
Duration of illness	0.452	0.001
Follow up	0.023	0.001
No.of Transfusions	0.001	0.001
SBT	0.266	0.006
EVL	0.046	0.001
EST	0.080	0.001
Surgery	0.159	0.008

Table-4 compares the characteristics of index bleed and subsequent bleed with significance of the variables between the two. Quantity of bleed, follow up, No. of transfusions and EVL has got significant p value in both groups. Alcohol consumption and other parameters have significant p value in subsequent bleed.

Table-5 Mean value of the blood investigations

Variables	Mean	Standard deviation
Total Count	6081.48	3382.31
Haemoglobin	7.92	2.45
Platelets	112575.31	92737.55
Sugar	118.12	57.15
Urea	28.0	15.49
Creatinine	0.8623	0.2999
Prothrombin time	18.05	5.25
INR	1.54	2.44
Total Bilirubin	2.23	2.71
Conjugated Bilirubin	1.34	1.92
Albumin	3.01	0.626
Globulin	3.1	0.83
Aspartate transaminase	48.65	29.09
Alanine transaminase	37.95	26.33
Serum alkaline phosphatase	197.95	172.92

Table-6 Complications

Complications	Total No. of cases n (%)
Ascites	34 (42)
Hepatic encephalopathy	14(17.2)
Spontaneous bacterial peritonitis	4(4.9)
Hepatorenal syndrome	2(2.5)
Coagulopathy	15(18.5)

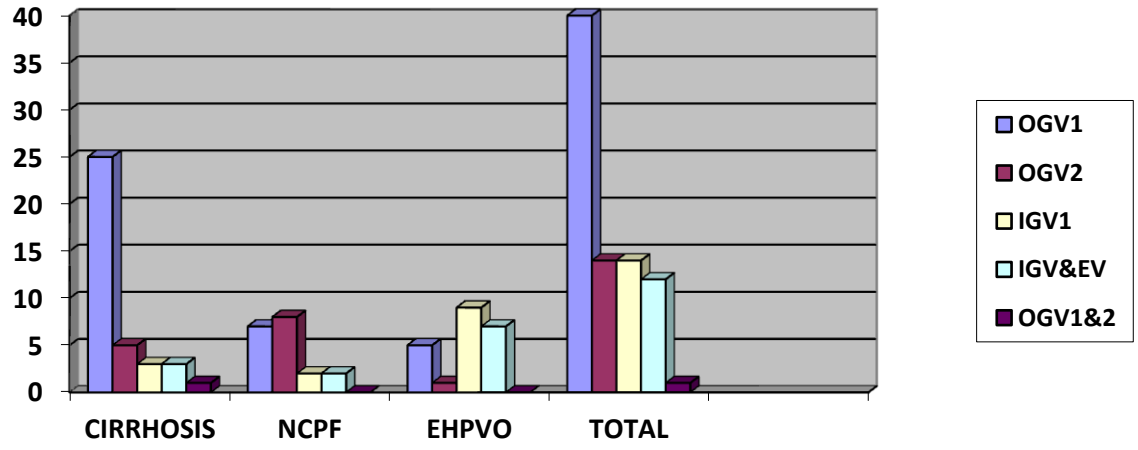

Figure-2 Distribution of type of varices in various aetiologies

The type of varices commonly seen in cirrhosis (Figure-2) is GOV1, in EHPVO IGV1 is more frequently seen and GOV2 is mostly in NCPF.

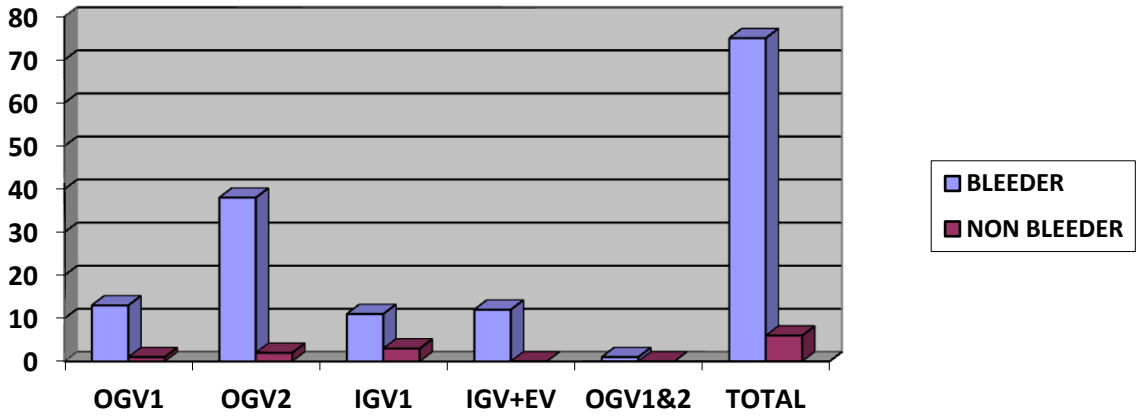

Figure- 3. Frequency of bleeding with different type of gastric varices

The patients with GOV2 had more number of bleed episodes and severe bleed when compared to other types (Figure-3)

Table – 7 Treatment details

Characteristics		n (%)
Pharmacotherapy with Octreotide		74(91.3)
Sengstaken Blackmore tube		13(16)
Endoscopic variceal sclerotherapy		26(32.1)
Endoscopic variceal ligation		45(55.6)
Glue injection		22(27.2)
Surgery	Devascularization with splenectomy	2(2.46)
	Shunt surgery	17(20.9)

There is no significant difference between the bleeders and non-bleeders with regards to age (p=0306), gender (p=0.197), type of gastric varices- OGV1 (p=0.701), OGV2 (p=0.636), IGV1 (p=0.782), aetiology of portal hypertension-Cirrhosis (p=0.193), NCPF (p= 0.106) and EHPVO (p= 0.184).

The index bleed parameters (Table-4) such as quantity of bleed (p=0.001), follow up in months (p=0.023), no of transfusions (p=0.001), EVL(0.046) had significant p value in index bleed group

Variables such as alcohol consumption (p=0.017), age at diagnosis (p=0.001), quantity of bleed(P=0.003), cause of PHT(P=0.005), duration of illness (p=0.001), follow up in months (p=0.001), No. of transfusions(p=0.001), EVL(p=0.001), EST(p=0.001) and surgery(p=0.008) had significant p value in subsequent bleed group.

DISCUSSION

Gastric varices are common in all types of portal hypertension. Primary gastric varices were seen up to 20 % in patients with portal hypertension.[12] The pathogenesis of portal hypertension influences the prevalence of gastric varices. Gastric varices were more common in segmental portal hypertension due to EHPVO than in generalized portal hypertension due to cirrhosis.[14] This is probably due to more direct transmission of increased portal pressure to the short gastric and posterior gastric varices in EHPVO. In our study the prevalence of gastric varices is 7.5%.

Gastric varices were approximately five times more common in bleeders than in non bleeders. This indicates that the gastric varices develop at a more advanced stage of portal hypertension.[12] The most common type is GOV1, constitutes 75% of all primary varices. In our study we have encountered of GOV1 varices in 49.4% patients. Other workers have also found GOV1 to be the most common type of gastric varix .[15]

GOV2 constituted in 14(17.3%) patients. IGV1 was also observed in 14 (17.3%) patients. Watanabe et al found them in 3% of their patients.[15] IGV1 and esophageal varices were simultaneously seen in 12 patients. These varices

develop because of dilatation of short gastric and posterior gastric varices in patients with EHPVO [128] or because of direct anastomotic veins between the gastric and retroperitoneal veins in patients with cirrhosis. Only one patient had GO1 and GOV2 in combination. In our study only one patient had colonic varices in the form of rectal varices. Table -8 shows the incidence of gastric varices in different aetiologies.[12]

Table-8 Study by Sarin et al.

Pathogenesis of PHT	GOV1 (%)	GOV2 (%)	IGV1 (%)	IGV2 (%)	Total (%)
Cirrhosis n=301	38(12.6)	16(5.3)	3(1)	8(2.7)	65(21.6)
NCPF n=115	16(13.9)	10(8.7)	2(1.7)	7(6.1)	35(30.4)
EHPVO n=117	29(24.8)	5(4.3)	4(3.4)	7(6.0)	45(38.5)
HVOO n=35	2(5.7)	--	--	--	2(5.7)
Total	85(14.9)	31(5.5)	9(1.6)	22(3.9)	147(20.9)
Our study	40(49.4%)	14(17.3%)	14(17.3%)	Nil	68(80%)

According to Sarin et al, the common type of varices observed was GOV1 and it was seen in more number of cirrhotic patients.

Another study by Khalid et al (Table-9) showed the similar frequency of cases in each type of gastric varices except for GOV1&2.

Table-9

Type of varices	Khalid et al	**Our study**
GOV1 (%)	78(35)	40(49.4)
GOV2 (%)	56(25)	14(17.3)
IGV1 (%)	59(27)	14(17.3)
IGV2 (%)	6(3)	Nil
GOV1&2(%)	14(6)	1(1.2)

Regarding the treatment details considered in our study, vasopressor therapy with octreotide has been administered in all 81 patients. Sengstaken Blackmore tube was used in 13(16%) patients. Endoscopic variceal sclerotherapy and endoscopic variceal ligation were applied in 32.1% and 55.6% of patients. Glue injection was given to 22(27.2%) patients and 19 patients were referred for surgery. Table – 10, shows the few randomized trials of endoscopic treatment. In all these studies the gastroesophageal obliteration therapy was the major mode of treatment.[80]

Table-10

Author	Classification GOV1/GOV2/IGV1	Treatment
Sarin et al (2002)	0/8/28	GVS(n=17) GVO(n=20)
Tan et al(2006)	53/25/19	GVL(n=48) GVO(n=49)
Lo et al(2007)	36/33/0	TIPS(n=35) GVO(n=37)
Mishra et al(2010)	0/all GOV2 or IGV1	GVO(n=33) β –blocker(n=34)
Our study	40/14/14	GVO=22,GVL=45

In 17 patients, proximal splenorenal shunt (PSRS) was performed as per institute policy. All these patients were subjected for splenectomy also. 2 patients have undergone devascularisation with splenectomy. In a randomized control trial by Roberto Santambrogio et al, it was concluded that in a sub group of patients with good liver function, DSRS with a correct portal- azygos disconnection more effectively prevents variceal rebleeding than endoscopic sclerotherapy with N-Butyl-2-Cyanoacrylate.[129]

In our study, most number of bleed has occurred in GOV2 type (44.4%), which was followed by GOV1 in 14 (17.2%) patients. In a study by Sarin et al, [12] GOV1 patients had more bleeding incidence.

The re bleeding rate was low in patients treated with N-butyl 2-Cyanoacrylate (NBC). Among the 22 patients 7 patients had no rebleeding and 7 patients had only one episode of bleeding. This is being similar to the study published by Khalid Mumtaz et al, in her study the rate for primary haemostasis with NBC is consistent with the reported rate of 90 %- 97% in other studies.[13,28,111]

Table-11

Author	Mortality (%)
Sarin et al	45
Trudeau and Pindiville	55
Our study	8.6%

Mortality related to bleeding from gastric varices in a series by Sarin et al [12] was 45%. (Table-11) Trudeau and Pindiville [130] reported 55% mortality after GV bleeding. In our study totally 7 patients (8.6%) expired. 6 of them were bleeders and 1 of them was non bleeder. This non bleeding death was due to hepatic encephalopathy. Among the death, **GOV2 patients had higher mortality**. The low mortality rate in our study might be due to short duration of follow up.

SUMMARY

In the present study,

1) The prevalence of gastric varices is 7.5% among the various aetiologies.

2) The commonest type of gastroesophageal varices is GOV1 which is followed by GOV2 and IGV1 which is well correlated with various studies.

3) Index bleed is seen in 92.6% of patients and subsequent bleed is seen in 58% of the patients.

4) Among the aetiology, cirrhosis is the most common cause and EHPVO is the next common cause for gastroesophageal varices.

5) There is no significant difference between the bleeders and nonbleeders with regards to age, gender, type of gastric varices- GOV1, GOV2, IGV1, aetiology of portal hypertension (Cirrhosis, NCPF and EHPVO), and complication such as hepatic encephalopathy.

6) Nineteen patients (19/81 - IGV1-14, OGV2-5) have undergone surgical treatment to arrest the recurrent bleeding.

7) The index bleed parameters such as quantity of bleed, follow up in months, no of transfusions, EST and EVL had **significant p value** in index bleed group.

8) The subsequent bleed parameters - alcohol consumption, age at diagnosis, quantity of bleed, cause of PHT, duration of illness, follow up in months, no. of transfusions, SBT, EVL, EST and surgery had **significant p value** in subsequent bleed group.

9) In our study mortality is less (8.6%), when compared to other studies.

CONCLUSION

In conclusion, the results of our study confirm that the prevalence of gastroesophageal varices was low but within the range when compared with various studies.

The type of the varices in Our study tallies with the international classification and the common type is GOV1 as denoted by many studies.

GOV1 is relatively have a benign course and requires treatment only in the form of gastric variceal sclerotherapy if they bleed.

For most GOV2 varices, endoscopic variceal obliteration therapy with N-Butyl 2- Cyanoacrylate is quite useful in arresting the bleeding and achieving the variceal obliteration.

Although endoscopic therapy was effective in treating some patients with IGV1 varices, surgery was required in significant no. of patients to prevent re bleeding.

In our study, the surgery was contemplated for such patients and also for other type of gastric varices because those patients were from far remote places where the immediate endoscopic intervention may not be feasible always.

IGV2 cases were less in Our study and it might require long term follow up to identify such patients.

Because the gastric varices have the potential to cause severe upper GI bleeding, its recognition is very important to manage the cases appropriately.

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