# Portal Hypertension and Esophageal Varices — Symptoms and Causes

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**The development of varices in the esophagus and the gastrointestinal tract is only one of the 3 complications caused by increased pressure within the portal system, the others being ascites and hepatic encephalopathy. All of these conditions are essentially brought about by diseases that impair the flow of blood through the liver such as in liver cirrhosis. The presence of collateral blood vessels in the portosystemic circulation allows for normal blood flow into and out of the liver. However, these collateral do not hold blood well in times of increased portal pressure, making them vulnerable to massive dilatation and rupture.**

## Normal Portal Circulation

In normal circumstances, the **portal venous system** exists to drain blood from the lower esophagus, stomach, intestines, spleen, and pancreas.

The **portal vein** is formed by the junction of the splenic vein and the superior mesenteric artery, both of which are made up of tributaries that drain the majority of the digestive system. Upon reaching the hilum of the liver, the portal vein divides into the **left and right portal veins**, which branch out to eventually drain into hepatic sinusoids of each hepatic lobule.

The blood then exits the lobules by draining into the **centrilobular veins**, which eventually forms the **hepatic veins**. Blood from these vessels enters the central circulation by entering the **inferior vena cava about 4 cm before it enters the right atrium**. Blood passing through this system comprises about 75% of the blood flow to the liver, the rest being from the hepatic artery.

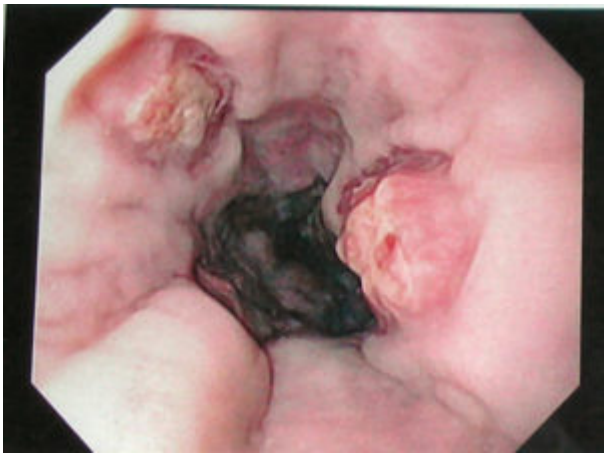

Image: “Esophageal ulcers after banding, posted in public domain with permission of patient.” by Samir – own work, License: Public domain

In the absence of complications, the pressure in the portal circulation is maintained within its highly-compliant and low-resistance nature. Blood vessels are able to accommodate slight increases in blood volume, such as when you just had a big meal. This is partly because of the compliant hepatic sinusoids. In situations where there is a decrease in the portal system input to the liver such as in **portal vein blockage**, the hepatic artery compensates by supplying more blood to the liver than it used to. This mechanism is termed **hepatic arterial response**.

The open-vessel characteristic of the **sinusoids** with fenestrated, discontinuous endothelium (See fenestration-endothelial-transport/) that serves as a location for mixing of the oxygen-rich blood from the hepatic artery and the nutrient-rich blood from the portal vein normalizes the pressure in the highly vascular portal system. Other substances are also known to influence the pressure regulatory mechanisms. Some of the few naturally occurring chemicals that are known to dilate or constrict the vasculature in the system are the following:

- **Nitric oxide (NO)** derived from **endothelial NO synthase (eNOS)** – dilator
- **Endothelin-1 (ET-1)** produced by **hepatic stellate cells** – constrictor

## Portal Hypertension

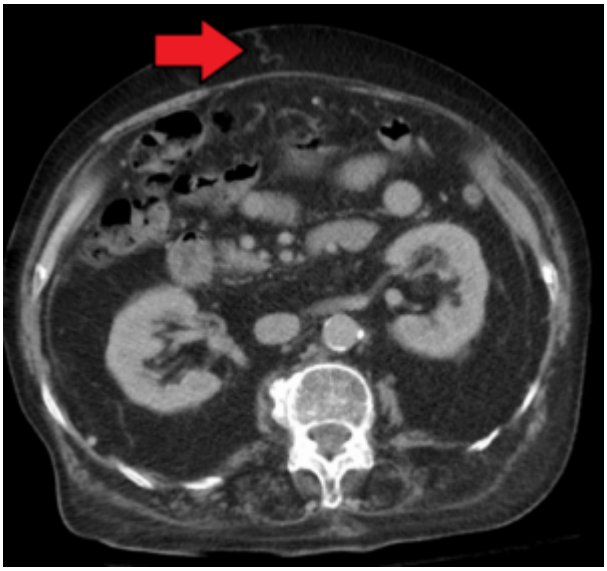

Image: “Portal hypertension due to cirrhosis resulting in revascularization of the umbilical vein” by James Heilman, MD – Own work, License: CC BY-SA 4.0

In situations where there is an increase in the pressure in the portal system, such as in **liver cirrhosis**, the changes in the pressure are caused by the alterations in the major determinants of blood pressure in the circulation: **resistance and blood flow**. This can be exemplified by the formula used to denote Ohm’s law:

**ΔP = F x R**

In this equation, ΔP denotes the change in pressure while F and R are blood flow and resistance, respectively.

## Increased intrahepatic resistance

There are many factors that lead to an increase in the resistance to the blood flow within the cirrhotic liver. These factors cause increased resistance in the tributaries all the way to the major vessels at the hilum of the liver. Liver cirrhosis causes increased intrahepatic vascular resistance by the following factors :

- Regenerative nodules
- Fibrotic bands
- Capillarization of the sinusoids ( decreased fenestrations and gaps)
- Hepatocyte and Kupffer cell enlargement

The resistance in the portal circulation can be pictured out using the law of Poiseuille:

$$R = 8\eta L/\pi r^4$$

R represents resistance, ηL is the product of blood viscosity and the length of the vessel and r is the radius of the blood vessel (the bigger the vessel radius, the lower the resistance).

Another contributory phenomenon that could result in an increase in the resistance of the blood vessels in the portal circulation is the **imbalance between NO and ET-1 synthesis and degradation**. A decrease in the former in cases of cirrhosis is said to be caused by the poor activation of eNOS brought about by the increased production of its inhibitor **caveolin-1.** eNOS phosphorylation may also be reduced when there is a decreased level of **AKT,** a protein kinase B, and an increase in **GRK** or **G protein-**

**coupled receptor kinase,** an eNOS inhibitor.

Both the decrease in NO or increase in ET-1 are thought to cause the hepatic stellate cells to become activated and highly contractile, further contributing to the increase in the resistance.

## Hyperdynamic circulation

In contrast to the increase in the resistance occurring intrahepatically, there is actually an increase in the total blood flow coming into the portal circulation. This does not have to mean that there is an increased flow of blood in the portal vein, though.

It has been thought to be caused by the **vasodilatation of the splanchnic blood vessels** in the presence of the excess NO produced by their endothelial cells. As a result, arteriolar relaxation and **hyperemia** are maintained, keeping most of the blood in the body pooled away from the peripheries. The hyperdynamic circulation manifests as reduced mean arterial pressure and increased cardiac output.

## Development of esophageal and gastrointestinal varices

Under high portal pressures due to the increased resistance of the portal vessels and the hyperdynamic inflow of blood to the portal circulation, the **collateral vessels** connecting the portal vein and the systemic circulation expand to somehow accommodate blood and thereby relieve the whole system of the pressure.

However, since there is higher pressure in the portal circulation as compared to the systemic venous circulation, the blood flow in these collaterals becomes reversed, causing further **engorgement** in distal areas that normally drain into these vessels. With these, varices form in response to the constant engorgement caused by cirrhosis. The most common sites of varix formation are the following:

- rectum
- umbilicus
- retroperitoneum
- distal esophagus and proximal stomach (the major collaterals)

The veins located between the **gastroesophageal junction** and the **lower esophageal region** are the most prone to bleeding. The lower esophageal region serves as a watershed for both the portal and the systemic circulation. Here, there are significant changes in intraluminal pressures because of the sudden difference between positive pressures in the abdominal veins and negative pressures in the thorax. The veins run longitudinally along the esophagus and are found in groups that are placed parallel to each other.

Unfortunately, in cases such as cirrhosis, the increasing pressure in the portal circulation does not improve despite the accommodation of blood by the collaterals. In fact, it could even get worse as the obstruction along the portal circulation becomes more pronounced, as the inflow of blood continues to rise and as the collaterals themselves begin to gain resistance.

# Causes of Portal Hypertension

The causes of the development of portal hypertension are usually classified according to the location where there is increased resistance: prehepatic, intrahepatic, and

posthepatic. However, a more useful classification of the causes is clinically based. Causes can be either common or less common:

- **Common Causes**

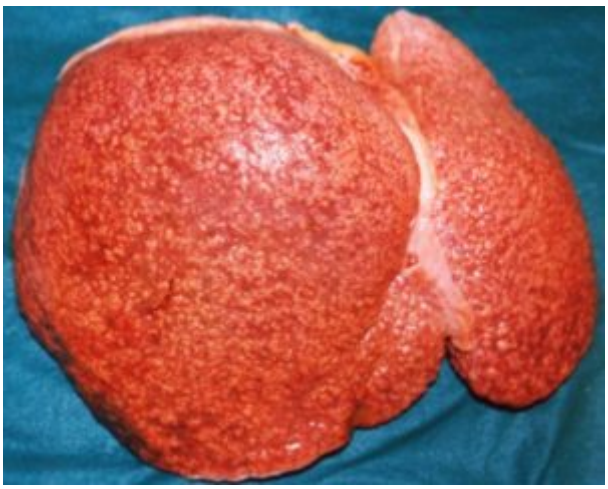

Image: “Macroscopic image of micronodular (liver) cirrhosis caused by alcohol consumption” by Amadalvarez – Own work, License: CC BY-SA 4.0

    - cirrhosis
    - schistosomiasis
    - extrahepatic portal vein thrombosis
    - idiopathic portal hypertension
- **Less Common Causes**
    - nodular regenerative hyperplasia
    - partial nodular transformation of the liver
    - fibropolycystic liver disease
    - sarcoidosis
    - malignancy
    - splanchnic arteriovenous fistula
    - hereditary hemorrhagic telangiectasia

## Approach to Patients with Variceal Bleeding

In recent years, it has been a standard operating procedure for patients with liver cirrhosis to undergo diagnostic procedures such as **endoscopy** to screen for esophageal and gastrointestinal varices. True enough, about 1/3 of all the diagnosed cases of cirrhosis do have some degree of variceal formation anywhere in the highly prone areas. 1/3 of this number is also expected to develop bleeding at one point. The factors that could identify the risk for bleeding include:

- the severity of cirrhosis as measured by standard scoring systems e.g. Child’s classification
- level of wedged hepatic venous pressure (WHVP)
- size and location of the varices
- endoscopic indicators such as red wale signs, hematocytic spots, diffuse erythema, bluish color, cherry red spots or white-nipple spots

# Esophageal Varices

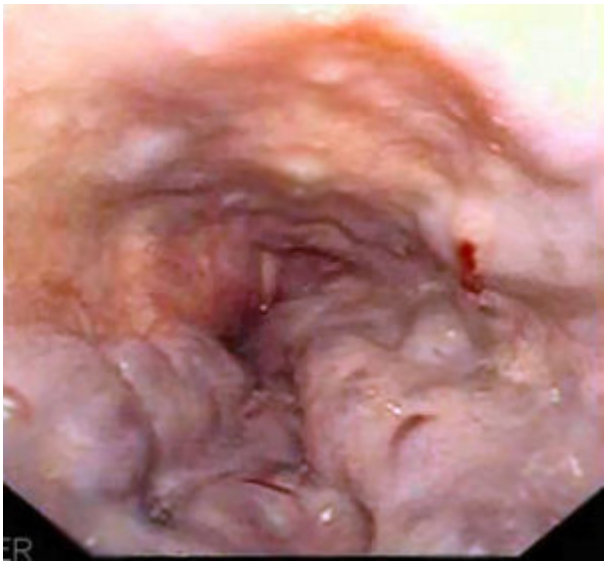

Image: “Gastroscopy image of esophageal varices with prominent red wale spots.” by Samir at English Wikipedia – created by author, originally from en.wikipedia, License: Public Domain

## Prophylaxis

Beta-blockers may be used to prevent the development or the enlargement of varices, although their efficacy is yet to be determined. Prophylactic therapy is emphasized among patients with large varices in order to avert bleeding, regardless of the presence of endoscopic visual changes in the esophagus. Beta-blockers are frequently used and have been demonstrated to produce positive results. However, what keeps these drugs from being used long term among cirrhotic patients is their **cardiovascular side effects**.

Unless there is **gastrointestinal bleeding**, patients on beta-blockers are generally not recommended for follow-up endoscopy. Instead, a **hepatic venous pressure gradient** should be measured a month after starting the drug regimen.

Unfortunately, only a third of all the patients taking beta-blockers respond well to the pharmacological prophylaxis. In this case, a preventive endoscopic procedure such as **variceal band ligation** should be done.

## Control of acute bleeding

Bleeding from an esophageal varix is automatically considered as an **emergency** and should be addressed immediately. The airway should be maintained early on. After establishing a **patent intravenous line**, the **hematocrit** is maintained by transfusing packed red blood cells. **Antibiotics** are also administered to prevent **bacteremia** and **sepsis**.

It has been proven that the use of pharmacology and endoscopic methods is superior to either one of them used alone. Drugs that are used to control the bleeding include **somatostatin**, **octreotide**, **terlipressin**, and **vassopressin with nitroglycerin**.

Once the hemodynamics is stabilized, the patient is subjected to **endoscopic ligation**.

**Prophylactic ligation** of the other varices that have not yet ruptured is also done by this time. For patients awaiting a definitive diagnosis, the use of a **balloon tamponade** may be employed to temporarily control the bleeding. Ultimately, **portosystemic shunts** are created in order to normalize the pressure in the portal circulation, thereby preventing further rupture of varices and bleeding.

# Gastric Varices

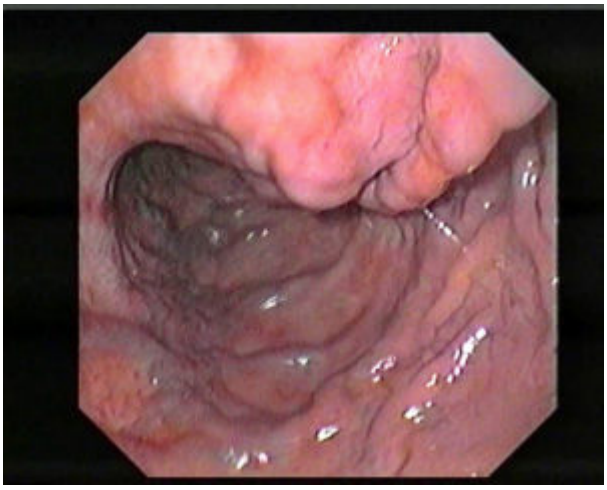

Image: “Gastric varices” by Jeremias – Own work, License: CC BY-SA 3.0

## Prophylaxis

Sadly, there is no recommended therapy for the prevention of bleeding gastric varices. Instead, the guidelines used for the management of esophageal varices are used to manage unruptured gastric varices. The risk of bleeding for patients with varices is also carefully identified and monitored. The use of endoscopic treatments is not recommended as a prophylactic measure.

## Control of acute bleeding

The same recommendations used to control the bleeding and stabilize the patient in the presence of an acutely bleeding esophageal varix is used in the control of a patient with a bleeding gastric varix. Since the diagnosis of a bleeding gastric varix is challenging due to the obliteration of the area by the pooled blood, certain indicators can be used instead in coming up with the diagnosis. These include:

- bleeding is noted from a gastric varix
- blood is present at the gastroesophageal junction or fundus
- (+) white nipple sign upon endoscopy
- no lesions are present other than varices

Instead of ligation, the most common endoscopic therapy used to control bleeding is the **injection of cyanoacrylate polymers and other chemicals** that serve as adhesives, sealing off the breaks in the varices. However, for varices up to 20 mm and for those located near the cardiac portion of the stomach, ligation may still be used.

In cases where bleeding still continues despite the above-mentioned measures, **multi-lumen tubes** may be inserted to temporarily control the situation. Tubes such as the

**Linton-Nachlas, Minnesota** and **Sengstaken-Blakemore tubes** are commonly used in practice while awaiting definitive therapeutic procedures such as the placement of portosystemic shunts.

## References

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Notes