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Progress and Prospects of Surgical Treatment of Portal Hypertension

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Abstract

Portal hypertension is a group of syndrome characterized by splenic hyperfunction, esophageal and gastric varices and ascites caused by abnormal portal vein hemodynamics. Among them, upper gastrointestinal bleeding caused by esophageal and gastric varices is the most dangerous complication, which often threatens the lives of patients. After half a century of development, the treatment of portal hypertension is divided into two categories: medical drug therapy, endoscopic therapy and surgical treatment. With the understanding of portal hypertension and the continuous development of medical technology, the surgical operation of portal hypertension has also been greatly improved, reducing postoperative complications and improving the quality of life of patients after operation. However, at present, there is no surgical method that can completely cure portal hypertension. This article reviews the progress of surgical treatment of portal hypertension in recent years, in order to provide reference for the surgical treatment of portal hypertension.

Keywords

Portal Hypertension, Surgical Treatment, Devascularization, Shunt, Transjugular Intrahepatic Portosystemic Shunt, Liver Transplantation

1. Introduction

Portal hypertension is a syndrome of elevated portal vein pressure caused by abnormal portal vein blood flow system, which is common in hepatocirrhosis, schistosomiasis, portal vein occlusion and so on. According to statistics, the global number of deaths from liver cirrhosis reached 13.229 million in 2017, while the number of deaths from liver cirrhosis increased by 15% from 2007 to 2017 [1], of which patients with liver cirrhosis and portal hypertension ac-

counted for 50% [2]. Portal hypertension can cause serious complications such as esophageal and gastric varices bleeding, hypersplenism, ascites, hepatorenal syndrome, hepatopulmonary syndrome, hepatic encephalopathy and so on. Esophageal and gastric varices bleeding is the leading cause of death in patients with liver cirrhosis and portal hypertension [3] [4] [5] [6]. At present, the mainstream international guidelines [7] and consensus [8] regard drug therapy and endoscopic ligation as the first-line treatment of portal hypertension, weakening the role of surgical treatment, but in China, surgery still plays an important and indispensable role in the treatment of portal hypertension. The main purpose of surgical treatment of portal hypertension is to treat patients with acute upper gastrointestinal bleeding who are ineffective in drug treatment and endoscopic therapy, as well as the prevention of bleeding and secondary prevention of esophageal and gastric varices bleeding. This paper gives a comprehensive overview of the pathogenesis and surgical treatment of portal hypertension.

2. The Pathogenesis of Portal Hypertension

The portal vein mainly collects blood from the superior mesenteric vein, inferior mesenteric vein and splenic vein, and then extends from the hepatoduodenal ligament to the hepatic hilum to supply the left and right branches to the left and right half of the liver, respectively. 80% of the blood supply and 20% of the oxygen supply to the liver is supplied by the portal vein, which also provides important nutritional factors to the liver. Normally, the portal vein pressure fluctuates between 5 and 10 mmHg [9], As the most important and accurate parameter to evaluate the bleeding risk and severity of patients with portal hypertension, hepatic vein pressure gradient (hepatic venous pressure gradient, HVPG) can replace portal vein pressure to evaluate the pressure and bleeding risk of esophagogastric vein, Under normal circumstances, HVPG is between 1 and 4 mmHg. When HVPG > 5 mmHg, portal hypertension can be diagnosed. When HVPG > 10 mmHg, it can not only cause esophageal and gastric varices, but also damage liver function and increase the risk of liver cancer. When HVPG > 12 mmHg, the patient's liver function is decompensated at this time and is at high risk for upper gastrointestinal bleeding. Mortality increased significantly when HVPG > 16 mmHg in portal hypertension patients with impaired liver function [10] [11]. At present, the pathogenesis of portal hypertension is not completely clear. At present, there are mainly "passive hyperemia theory" and "active congestion theory". According to the theory of passive hyperemia, the increase of portal vein outflow tract resistance leads to portal vein passive congestion, depending on the location of the increase in resistance. Portal hypertension can be divided into three types: prehepatic type (splenic vein, mesenteric vein, extrahepatic portal vein obstruction or compression, etc.), intrahepatic type (liver cirrhosis, schistosomiasis, congenital liver fibrosis, congenital non-cirrhotic portal hypertension, etc.), and posthepatic type (hepatic vein obstruction, pericarditis, right heart failure, etc.). In addition, liver fibrosis and regenerative hepatocyte nodules

squeeze intrahepatic blood vessels, resulting in stenosis or even occlusion, resulting in reduced liver blood flow, impaired liver sinusoidal endothelial cell function, increased release of vasoconstrictor factors (mainly endothelin-1, cyclooxygenase-1, prostaglandin, etc.), and decreased release of relaxing factors (mainly NO) [12]. Which further increases portal outflow tract resistance. The theory of active congestion is related to visceral hyperdynamic circulation, portal blood flow increase and portal venous active congestion. Studies have shown that in patients with liver cirrhosis and portal hypertension, the changes of circulating fluid transmitters, the increase of vasoactive substances and the relative decrease of vasoconstrictive substances, and the decrease of vascular response to endogenous vasoconstrictive substances, these factors make visceral vasodilation, portal vein blood flow increased and portal vein pressure further increased.

3. Development of Surgical Procedures for Portal Hypertension

The early and middle period of the 20th century was the period of pre-clinical trials and data accumulation of surgical treatment; at the beginning of the 20th century, the surgical treatment of portal hypertension developed rapidly. In 1900, Preble found that gastrointestinal bleeding in patients with portal hypertension came from esophageal varices and described the opening of communicating branches between portosystemic veins during portal hypertension. In 1903, Vidal tried out the first human portacaval shunt, and the operation was successful. The successful portacaval shunt performed by Whipple and Blakmore in 1945 ushered in a new era of surgical treatment of portal hypertension [13]. Since then, the rise of enterocaval shunt, proximal splenocaval shunt, proximal splenorenal shunt and the application of restrictive shunt have compensated for the disadvantages of excessive shunt portal blood flow in total portal-systemic shunt, which is called partial portal-systemic shunt. By 1967 Warren [14] put forward the concept of regional shunt and designed distal splenorenal shunt (DSRS). Theoretically, this operation not only maintains the blood flow pressure of the mesenteric portal vein and the portal vein to the liver, but also reduces the blood flow pressure of the gastrosplenic vein area, so as to achieve the purpose of treating esophageal and gastric fundus variceal bleeding. Since then, distal splenorenal shunt, distal splenocaval shunt and coronary shunt have been produced as selective shunts different from portosystemic shunt.

In 1970, Hasab [15] adopted the devascularization method of pericardial devascularization, which is called Hassab operation. In 1973, Sugiura [16] cut off the esophagus in the first half of the week and sutured all the varicose vessels on the basis of the Hassab operation, making the devascularization more complete, known as the Sugiura operation. Since then, there have been many improved devascularization procedures, but their purpose is to prevent gastroesophageal variceal bleeding caused by portal hypertension.

Since the beginning of surgical treatment of portal hypertension in China in the 1950s, shunt was advocated before 1978, but it was mainly devascularization

from ten years later to 1989. Since then, the advantages and disadvantages of devascularization and shunt have been discussed. At the Seventh Symposium on Portal Hypertension in 1999, due to the rapid development of drug therapy, endoscopic therapy and interventional therapy at that time, the treatment of portal hypertension tended to consider non-operative and surgical treatment in terms of overall efficacy. Since 1990s, with the maturity of organ transplantation technology, liver transplantation has been recognized as the only surgical treatment for primary liver disease and portal hypertension. At this point, the treatment of portal hypertension has entered a diversified and individual treatment stage, such as medicine, endoscopy, intervention, traditional surgery and liver transplantation.

4. Current Status of Surgical Procedures for Portal Hypertension

At present, the main purpose of surgical treatment of portal hypertension is to prevent and treat variceal bleeding and ascites [17]. Surgical treatment is still the best choice for patients with upper gastrointestinal bleeding in portal hypertension. The surgical treatment of portal hypertension is mainly devascularization, shunt, (Transjugular intrahepatic portosystemic shunt, TIPS), liver transplantation and so on.

4.1. Devascularization vs. Shunt

Devascularization has developed from initial splenectomy combined with esophagogastric variceal devascularization (Hassab), transthoracic and abdominal lower esophagostomy (Sugiura) and its modified procedure to selective pericardial devascularization combined with splenectomy. The surgical trauma has been continuously reduced, and the postoperative complications and mortality have been reduced. The principle of devascularization is to prevent and control the bleeding of esophageal and gastric varices by severing the collateral circulation of the fundus of esophagus and stomach caused by portal hypertension. This method not only prevents the abnormal blood flow between portal azygos veins, but also has a considerable hemostatic effect in the near future. At the same time, it ensures the supply of blood flow into the liver, which is conducive to the improvement of liver function, thus enhancing the metabolism of ammonia in the body and reducing the occurrence of hepatic encephalopathy. However, because this operation is only symptomatic treatment, there are still some disadvantages: 1) there is no real relief of portal hypertension, the postoperative long-term recurrence and rebleeding rate of varicose veins is relatively high (20% Rue 50%) [18]; 2) due to blocking part of the gastric fundus collateral circulation, it will further aggravate portal hypertensive gastropathy; 3) portal vein thrombosis may be caused after splenectomy. At present, the selective cardiac devascularization proposed by Yang Zhen [19] in China can avoid the above disadvantages to a certain extent, The characteristics of the operation are as fol-

lows: 1) To perform accurate portal-azygous devascularization by dissecting the esophageal cardia region and gastric coronary vein more carefully and deeply, only to sever the perforating vessels outside the serosa of the esophageal cardia region, to maintain the integrity of the main vessels, so as to achieve the goal of complete devascularization and preservation of spontaneous shunt of the body; 2) through the retroperitoneal fixation of the greater omentum, the collateral circulation between the porta azygos was promoted and the portal vein pressure was reduced. The operation has been widely popularized in China, and the clinical therapeutic effect can be affirmed. In addition, the timing of operation for patients with portal hypertension and upper gastrointestinal bleeding is still controversial. Some scholars suggest elective surgery because emergency surgery increases mortality and postoperative complications. Some scholars suggest emergency surgery, because acute upper gastrointestinal bleeding not only aggravates the damage of liver and renal function, but also aggravates shock. Emergency surgery can quickly stop bleeding and reduce the mortality of patients [20].

The principle of shunt is to reduce the portal vein blood pressure and control bleeding by shunting most or part of the blood flow of the portal system. The advantage of this operation is that it fundamentally shunts part of the portal vein blood flow, reduces the portal vein pressure, and then reduces the blood flow load of esophageal and gastric varices to prevent rupture and bleeding. Among the many shunt methods, distal splenorenal shunt has the advantages of selectivity and regional shunt, so it has become the leading surgical method to control gastrointestinal varicose bleeding. However, its limitations lie in: 1) Reducing the normal blood flow of the portal vein to the liver, thus damaging the liver function in the long run; 2) The occurrence of hepatic encephalopathy because the shunt portal vein blood flow is not detoxified by the liver; 3) Thrombus may form at the anastomotic stoma, which may affect the shunt effect or even be abandoned. Shunt can be divided into non-selective portosystemic shunt and selective portosystemic shunt. Although non-selective portosystemic shunt effectively reduces portal pressure, it also significantly reduces hepatic blood flow and liver perfusion, which is easy to induce hepatic encephalopathy and liver failure [21]; Moreover, due to the destruction of the anatomical structure of the first hepatic porta, it is difficult for liver transplantation in the future. Compared with non-selective portosystemic shunt, selective operation reduces the incidence of hepatic encephalopathy, but it is easy to produce a large amount of ascites after operation [22], so patients with large amount of ascites and small diameter of splenic vein generally do not choose this method. Galambos *et al.* [23] compared the effects of selective shunt and non-selective shunt, there was no difference in operative mortality, incidence of anastomotic obstruction and rebleeding rate between the two groups. But the incidence of hepatic encephalopathy in selective shunt group was better than that in non-selective shunt group, and the maintenance of liver function in selective shunt group was better than

that in non-selective shunt group. The study of Rikkers *et al.* [24] also drew similar conclusions, and there was no difference in the long-term anastomotic occlusion rate between the two groups by angiography.

Due to the different design principles of devascularization and shunt, there are differences in surgical results. Zong *et al.* [21] conducted a meta-analysis of the related studies on devascularization and shunt in the treatment of portal hypertension, suggesting that: The incidence of hepatic encephalopathy and ascites in the disconnection group was significantly lower than that in the shunt group, and the postoperative rebleeding rate in the disconnection group was significantly higher than that in the shunt group. There was no significant difference in operative mortality and long-term survival rate between the two groups. There are differences in the results of comparison, but a basic consensus can be reached: 1) shunt is better than devascularization in reducing portal pressure and preventing rebleeding; 2) devascularization is more effective in maintaining blood perfusion after liver surgery than shunt, which is helpful to maintain liver function [25] and reducing the incidence of postoperative hepatic encephalopathy. Therefore, the choice of devascularization and shunt should be optimized according to the individual situation of the patient and the indication of surgery.

4.2. TIPS

TIPS uses the method of interventional radiation to establish a channel between portal vein and hepatic vein or inferior vena cava through jugular vein and place stent to form portosystemic shunt. It is characterized by: 1) less surgical trauma and rapid postoperative recovery; 2) it can significantly reduce portal pressure; 3) improve the survival rate of liver transplantation. At present, TIPS has developed into an important method for the treatment of portal hypertension-related complications. Its main indications [26] [27] [28] are: 1) As a second-line treatment, it can be used to prevent variceal rebleeding in portal hypertension. The success rate can reach 59.4% - 91.0%, and the postoperative rebleeding rate can reach 9.0% - 23.0%; 2) Acute massive upper gastrointestinal bleeding which is ineffective by drug or endoscopic therapy; 3) To treat intractable ascites that can not be controlled by abdominal drainage; 4) To prepare for liver transplantation in patients with portal hypertension. However, TIPS can significantly damage the liver function of patients with portal hypertension, and the risk of postoperative hepatic encephalopathy is higher. Therefore, TIPS is not recommended for patients with old age, poor liver function and cardiovascular disease.

4.3. Liver Transplantation

As an effective surgical treatment for patients with end-stage liver disease, liver transplantation not only replaces the diseased liver, but also restores the hemodynamics of the portal system. It not only cured the related complications of portal hypertension, but also eradicated the related etiology. Compared with other surgical treatments, liver transplantation reduces postoperative complications and improves the 5-year survival rate [22] [29]. At present, liver transplan-

tation mainly includes orthotopic liver transplantation, backpack liver transplantation, living partial liver transplantation and split liver transplantation. Among them, living donor partial liver transplantation has become one of the most promising surgical methods because of reasonable donor selection, short waiting time, short donor liver ischemia time and high success rate. However, due to the high requirements for surgical techniques, lack of donor resources, lifelong use of immunosuppressants and high surgical costs, liver transplantation can not become the first choice for patients with portal hypertension.

5. Reflections and Perspectives

5.1. Whether the Spleen Is Preserved or Not

Splenectomy is generally performed in patients with portal hypertension complicated with hypersplenism, which has the following significance [30] [31] [32]. First, splenectomy can relieve hypersplenism and correct decreased triplet cells in peripheral blood. Patients can tolerate low platelets caused by antiviral therapy with interferon. At the same time, splenectomy can also reduce 40% of the blood supply of the portal vein, thus reducing the pressure of the portal vein. Splenectomy can also cut off the short blood vessels of the stomach, which can reduce the state of high pressure in the gastric fundus and cardia to a certain extent, and relieve portal hypertensive gastropathy in a short time. However, with the further understanding of the hemodynamics of the portal vein system and the development of splenic surgery, more and more scholars believe that the complications of traditional devascularization are mostly related to splenectomy, especially many complications of devascularization caused by portal vein thrombosis are actually the complications of splenectomy, because under portal hypertension, the splenic vein and its branches are connected with the coronary vein and retroperitoneal Retzius vein. An important collateral circulation pathway was constructed. Splenectomy will destroy the extensive collateral circulation that has been formed around the spleen. Not only the risk of operation is high, there is more bleeding during the operation, but also the risk of postoperative portal vein thrombosis is significantly increased. Which easy to induce postoperative portal vein thrombosis and rebleeding [33] [34] [35]. Some scholars have proposed that devascularization does not necessarily require splenectomy, but should depend on the situation. The more difficult the splenectomy is, the more varicose blood vessels are around the spleen, indicating that extensive collateral circulation has been established around the spleen, and the less it should be removed [36]. For patients with PHT whose spleen function is not hyperactive and whose peripheral blood cells are not reduced, the spleen can be preserved. But for hypersplenism patients with significantly decreased peripheral blood triple system, spleen preservation should not be carried out blindly. As the most significant complication after splenectomy, portal vein thrombosis often leads to further increase of portal vein pressure and poses a threat to patients' life. Anticoagulant therapy is routinely given after surgery to avoid this compli-

cation. In addition, the popular partial splenectomy in recent years is also a good choice for PHT patients, which can not only preserve part of the spleen to maintain the patient's immune function, but also effectively solve the hypersplenism. But how much of the spleen should be preserved, and will the remaining spleen continue to grow and become hyperplenic? Whether the spleen is preserved or not? More clinical trials and basic research are needed to verify it.

5.2. Timing of Preventive Surgery

In recent years, with the development of endoscopic technology and radiation intervention, endoscopic therapy and interventional therapy tend to be the first-line treatment of patients with portal hypertension. Its biggest advantage is that it can reduce the damage of liver function caused by surgical trauma. Surgeons generally do not advocate preventive surgery, but for severe splenomegaly (grade III splenomegaly), severe hypersplenism with esophageal and gastric varices, severe varices or red sign, in the absence of other effective treatment, preventive surgery can be considered for patients at high risk of upper gastrointestinal bleeding in a short period of time.

5.3. Prospects for Surgical Treatment of Portal Hypertension

The portal hypertension consensus of Baveno VII [8] in 2021 and the Mexican Consensus [37] emphasize the necessity of individualized treatment and multidisciplinary diagnosis and treatment of patients with portal hypertension. Due to the complexity and severity of portal hypertension, as well as the differences in etiology, liver function classification and varicose veins, the diagnosis and treatment of portal hypertension involves many disciplines. It is very suitable for multi-disciplinary collaborative diagnosis and treatment and the implementation of individual precision treatment. As an important part of multidisciplinary diagnosis and treatment, surgical treatment also needs continuous innovation to reduce surgical trauma and postoperative complications. Through the popularization of intelligent robot assisted surgical treatment, the in-depth research of stem cells and the maturity of artificial organ technology, it brings good news for the treatment of patients with portal hypertension.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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