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Name of Journal: World Journal of Gastrointestinal Surgery

Manuscript NO: 89754

Manuscript Type: ORIGINAL ARTICLE

Retrospective Study

Effectiveness of TIPS in the Treatment of Cirrhotic Esophageal-Gastric Variceal Bleeding and Its Impact on Patient Prognosis

Efficacy of TIPS in treating cirrhotic EGVB

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Abstract

BACKGROUND

Esophageal-gastric variceal bleeding (EGVB) represents a severe complication among patients with cirrhosis, often culminating in fatal outcomes. Interventional therapy, a rapidly developing treatment modality over the past years, has found widespread application in clinical practice due to its minimally invasive characteristics. Nevertheless, whether transjugular intrahepatic portosystemic shunt (TIPS) treatment exerts an impact on patients' prognosis remains controversial.

AIM

This research is dedicated to probing the efficacy of TIPS in treating cirrhotic EGVB and its influence on the prognosis of patients afflicted by the disease.

METHODS

A retrospective study was conducted on ninety-two patients presenting with cirrhotic esophageal-gastric variceal bleeding (EGVB) who were admitted to our hospital between September 2020 and September 2022. Based on the different modes of treatment, the patients were assigned to the study group (TIPS received, n = 50) and the control group [percutaneous transhepatic varices embolization (PTVE) received, n = 42]. Comparative analyses were made between the two groups preoperatively and one month postoperatively in the following aspects: varicosity status, hemodynamics parameters [portal vein flow velocity (PVV), portal vein diameter (PVD)], platelet count (PLT), red blood cell count (RBC), white blood cell count (WBC), and hepatic function [albumin (ALB), total bilirubin (TBIL), and glutamic oxalacetic transaminase (AST)]. The questionnaire of Generic Quality of Life Inventory-74 (GQOLI-74) was utilized in assessing the life of quality in the two groups, and their 1-year postoperative rebleeding and survival rates were juxtaposed.

RESULTS

Following the surgical intervention, there was an improvement in varicosity compared to the preoperative status in both cohorts. Notably, the study group exhibited more pronounced enhancements in comparison to the control group (P<0.05). PVV increased, and PVD decreased compared to preoperative levels, with the study cohort achieving better outcomes (P<0.05). PLT and WBC were elevated postoperatively in the two groups, with the study cohort displaying higher levels (P<0.05). No differences were discerned between the two groups in ALB, TBIL, or AST levels both preoperatively and postoperatively (P<0.05). Postoperative scores across all dimensions of life quality surpassed preoperative levels, with the study cohort achieving higher scores (P<0.05). The one-year postoperative re-bleeding rate in the study cohort, at 22.00%, demonstrated a significant reduction compared to the control group's rate of 42.86% (P<0.05); conversely, no remarkable disparity was observed in the 1-year postoperative survival rate between the two cohorts (P>0.05).

CONCLUSION

TIPS, demonstrating robust efficacy in managing cirrhotic EGVB, remarkably alleviates varicosity and improves hemodynamics in patients. This intervention not only presents a safer profile but also contributes significantly to a more favorable prognosis.

Key Words: liver cirrhosis; esophagogastric variceal bleeding; transjugular intrahepatic portosystemic shunt; prognosis

Hu X, Dai J, Lu J, Li G, Wang J, Deng Y, Feng R, Lu KP. Effectiveness of TIPS in the Treatment of Cirrhotic Esophageal-Gastric Variceal Bleeding and Its Impact on Patient Prognosis. *World J Gastrointest Surg* 2023; In press

Core Tip: Esophageal-gastric variceal bleeding (EGVB) constitutes a severe and lifethreatening complication associated with cirrhosis. The implementation of Transjugular Intrahepatic Portosystemic Shunt (TIPS) emerges as an effective strategy for both the treatment and prophylaxis of EGVB. The objective of this study is to evaluate the effectiveness of TIPS in terms of cirrhosis-triggered EGVB treatment and to probe its impact on patient prognosis. The research outcomes contribute valuable insights into the management of acute variceal bleeding and the enhancement of long-term prognostic outcomes for individuals with advanced hepatopathy. A comprehensive understanding of the benefits and potential risks associated with TIPS is pivotal for the development of personalized strategies in the treatment of variceal bleeding attributed to cirrhosis.

INTRODUCTION

Portal hypertension constitutes a cluster of clinical syndromes stemming from elevated pressure within the portal venous system, primarily attributed to cirrhosis triggered by diverse factors [1]. The fundamental pathophysiological features of portal hypertension include obstruction of blood flow and/or increased blood flow in the portal venous system, augmented intravascular static pressure in the portal vein and its branches, as well as the formation of collateral circulation. The gastroesophageal varices (GEV) in the gastric fundus are the predominant collateral vessels. As portal hypertension intensifies, GEV will expand and ultimately rupture, leading to esophageal-gastric variceal bleeding (EGVB). EGVB stands as one of the most prevalent gastrointestinal emergencies and a primary contributor to mortality in patients with cirrhosis [2]. Cirrhotic EGVB patients typically present with symptoms such as hematemesis and melena. Approximately 30% to 50% of cirrhosis patients succumb to this condition within six weeks following their initial esophageal variceal bleeding episode [3]. These complications pose a significant burden on global public health, leading to a severely compromised quality of life for affected individuals and an increased mortality rate. Hence, a proactive exploration of treatment modalities for EGVB assumes paramount significance.

Presently, therapeutic strategies for EGVB encompass pharmacotherapy, triple-lumen dual-balloon catheters for pressure hemostasis, endoscopic therapy, as well as

interventional and surgical procedures. Among these modalities, interventional treatment is highly regarded by clinical practitioners due to its straightforward procedural execution, minimal trauma, and prompt hemostatic outcomes [4]. Interventional treatments primarily involve partial splenic embolization (PSE), percutaneous transhepatic variceal embolization (PTVE), balloon-occluded retrograde transvenous obliteration (BRTO), and transjugular intrahepatic portosystemic shunt (TIPS). Nonetheless, given the somewhat unsatisfactory progress in domestic technology at present, certain scholars fail to allocate adequate attention to this field and tend to favor a one-sided emphasis on decompression. On the other hand, the lack of appropriate interventional equipment and the numerous complications correlated with BRTO, coupled with its limited indications, have hindered the development of PSE and BRTO within the country. Currently, PTVE and TIPS are the commonly employed interventional treatments for cirrhotic EGVB. PTVE involves percutaneous puncture of the intrahepatic portal vein branch under ultrasound guidance, followed by selective entry into variceal branches such as the coronary and short gastric veins, where embolization materials are injected to obstruct bleeding and varices in the esophagus and stomach, serving the purpose of treatment and prevention of variceal hemorrhage. Nonetheless, PTVE is not without its drawbacks, as it bears the risk of exacerbating hypersplenism due to heightened portal venous pressure [5]. TIPS, on the other hand, establishes a shunt channel between the portal vein and hepatic vein within the liver parenchyma via the internal jugular vein, diverting blood flow from the portal venous system directly back into the systemic circulation via the channel, thus attenuating portal veinous pressure [6]. In recent years, the clinical efficacy of TIPS has gained recognition, attributed to the implementation of endovascular stent grafts and refined modulation of shunt diameters [7]. In summary, interventional treatments offer advantages like minimal trauma, short preoperative preparation time, rapid hemostasis, and a broad range of indications. Nevertheless, there remains ongoing debate in the clinical realm regarding the impact of these two methods on liver function and

prognosis in cirrhotic EGVB patients. Thus, this article endeavors to thoroughly investigate the efficacy of these two approaches.

MATERIALS AND METHODS

2.1 General data

A retrospective examination was conducted on the clinical data of 92 patients diagnosed with cirrhotic EGVB, who were admitted to our institution between September 2020 and September 2022. Inclusion criteria comprised: (1) Individuals diagnosed with GEVB through gastroscopy; (2) Age equal to or greater than 18 years; (3) Unsatisfactory response to conservative treatments, including medications and endoscopy; (4) First-time TIPS or PTVE procedures; (5) Availability of complete data, capability to read, comprehend, and provide informed consent. Exclusion criteria encompassed: (1) Clear indications of mental illness; (2) Pregnant or lactating women; (3) Contraindications for surgery; (4) Systemic infection, fever, or organic heart disease; (5) Severe hepatic encephalopathy, hepatic space-occupying lesions, or hepatic diabetes; (6) Total bilirubin (TBIL) levels exceeding three times the upper limit of normal; (7) Portal vein obstruction or stenosis; (8) Gastrointestinal bleeding attributed to other cirrhosis-linked factors. The patients were further allocated into the study group (n = 50) and the control group (n = 42) based on distinct treatment modalities.

2.2 Methods

Within the study cohort, TIPS procedure was executed as follows: Patients were placed in a supine position, subjected to standard aseptic draping, and local anesthesia was administered. Under X-ray guidance, the right internal jugular vein underwent puncture, and a Rups-100 guidewire was inserted into the right hepatic vein, positioned approximately 1 cm distal to its confluence with the inferior vena cava. Following the measurement of right atrial pressure, a puncture needle was harnessed to access the right branch of the portal vein from the right hepatic vein. A guidewire was then advanced into the main portal vein, and portal veinous pressure was gauged. After

obtaining the portal systemic collateral circulation pressure gradient, a guidewire was introduced into the splenic vein for angiographie portale. A balloon was inflated and placed through the shunt channel. Variceal vein embolization was performed using a spring coil. A Gore stent was introduced over a guidewire, and the status of the stent as well as the patency of the shunt tract were reassessed through repeat angiography. Upon confirmation of favorable conditions, the postoperative portal systemic collateral circulation pressure gradient was reassessed, and the guiding catheter was subsequently removed, thereby concluding the procedure.

Within the control cohort, PTVE was performed as follows: Patients were placed in a supine position, standard aseptic draping was applied, and local anesthesia was administered. Under the guidance of ultrasound, percutaneous liver puncture was performed to access the portal vein branch. A super-smooth guidewire was placed, followed by a 4F introducer sheath. Portal vein angiography was conducted to validate portal venous pressure and evaluate the magnitude of varices. A suitable quantity of absolute ethyl alcohol was infused to induce solidification of the blood vessels. Variceal vein embolization was carried out using a spring coil. After embolization, a repeat angiography was performed to verify the absence of abnormalities. Pressure measurements were once again obtained, and the catheter was removed. The puncture route was sealed using a spring coil and gelatin sponge, completing the procedure.

2.3 Evaluation of indicators

2.3.1 Varicosity status

Following relevant guidelines, the evaluation of variceal status in the patient cohorts was conducted both preoperatively and one month postoperatively. Variceal conditions were categorized into four classes, including absence of varices, mild varices (presenting as linear formations), moderate varices (exhibiting sinuous tortuosity and elevation), and severe varices (manifesting as bead-like, nodular, or tumorous formations).

2.3.2 Hemodynamics

With the assistance of Doppler ultrasonography, the hemodynamic conditions of the portal vein were examined in the two groups preoperatively and one month postoperatively. The parameters under consideration encompassed portal vein flow velocity (PVV) and portal vein diameter (PVD).

2.3.3 Peripheral blood cell count

Before the surgical procedure and one month thereafter, 1 mL of fasting venous blood was drawn from both cohorts. After centrifugation at 3500 r/min, the supernatant was harvested for further analysis. Platelet count (PLT), red blood cell count (RBC), and white blood cell count (WBC) were ascertained with the use of a fully automatic hematology analyzer.

2.3.4 Liver function

Preoperatively and one month postoperatively, 3 mL of fasting venous blood was drawn from both patient cohorts. Following centrifugation at 3500 r/min, the supernatant was collected for subsequent analysis. Serum albumin (ALB), TBIL, and glutamic oxalacetic transaminase (AST) levels were gauged employing enzyme-linked immunosorbent assay (ELISA).

2.3.5 Quality of life

The Generic Quality of Life Inventory-74 (GQOLI-74) questionnaire was harnessed to evaluate the overall quality of life in the two groups preoperatively and one month postoperatively. This instrument comprises four dimensions, wherein social function, psychological function, and physical function are assessed on a scale ranging from 20 to 100 points each, while material life condition is appraised on a scale ranging from 16 to 80 points. Elevated scores indicate an enhanced quality of life.

2.3.6 Re-bleeding and survival rates

All patients underwent bi-weekly follow-up appointments at the designated portal hypertension outpatient clinic. The follow-up period for the two cohorts extended to one year postoperatively, with no instances of study withdrawal, resulting in a 100% follow-up rate. Throughout the one-year timeframe, occurrences of recurrent bleeding and survival status for each patient were meticulously documented.

2.4 Statistical analysis

Data analysis was performed with the assistance of SPSS25.0 software. Measurement data were represented as mean \pm standard deviation, while enumeration data were exhibited as n (%). For data conforming to normal distribution, the analysis encompassed one-way analysis of variance (ANOVA) and t-tests, whereas enumeration data analysis adopted the χ^2 test. The rank sum test was performed for ranked data analysis. Statistical significance was set at P<0.05.

RESULTS

3.1 Comparison of general data between the two groups

The study cohort consisted of a total of 50 patients, comprising 29 males and 21 females, with an average age of 54.62 ± 7.17 years. Within the control cohort, there existed 42 individuals, comprising 26 males and 16 females, with an average age of 55.18 ± 6.95 years. Statistical analysis revealed no significant differences between the two cohorts with respect to gender, age, and the etiology of liver cirrhosis (P>0.05). See Table 1.

3.2 Comparison of variceal status between the two groups

Preceding surgical intervention, the rates of absence, mild, moderate, and severe varices within the study group were 0.00% (0/50), 18.00% (9/50), 40.00% (20/50), and 42.00% (21/50) respectively. In comparison to the control cohort with rates of 0.00% (0/42), 11.90% (5/42), 40.48% (17/42), and 47.62% (20/42), the differences revealed no statistical significance (P>0.05). Post-surgery, the study group exhibited rates of 38.00% (19/50), 32.00% (16/50), 18.00% (9/50), and 12.00% (6/50) for absence, mild, moderate,

and severe varices, respectively. This was superior to the control group rates of 9.52% (4/42), 50.00% (21/42), 23.81% (10/42), and 16.67% (7/42) (P<0.05). Refer to Table 2.

3.3 Comparison of hemodynamics between the two groups

Before the surgical intervention, there were no substantial differences in PVV and PVD between the two cohorts (P>0.05). Postoperatively, PVV increased, while PVD decreased in the two groups, with the study cohort demonstrating superior outcomes compared to the control cohort (P<0.05) (Table 3).

3.4 Comparison of serum parameters between the two groups

Preoperatively, no statistically significant differences were observed in PLT, RBC, and WBC between the two patient cohorts (P>0.05). Postoperatively, the study group displayed a PLT count of $134.17\pm22.35\times10^9/L$ and a WBC count of $5.54\pm0.92\times10^9/L$, which were higher than the PLT count ($134.17\pm22.35\times10^9/L$) and WBC count (5.08 ± 0.86) within the control group. This disparity held statistical significance (P<0.05). Nevertheless, with regard to RBC, the study cohort had an RBC count of $3.31\pm0.65\times10^{12}/L$, whereas the control cohort had an RBC count of $3.29\pm0.67\times10^{12}/L$, and no remarkable difference was detected between the two groups (P=0.885) (Table 4).

3.5 Comparison of liver function between the two groups

Preoperatively, there were no discernible differences in levels of ALB, TBIL, and AST between the two cohorts of patients (P>0.05). Postoperatively, the study group displayed ALB levels of 32.41±4.96 g/L, TBIL levels of 34.81±7.79 µmol/L, and AST levels of 75.39±9.81 U/L. The control group exhibited ALB levels of 33.74±6.62 g/L, TBIL levels of 33.01±8.11 µmol/L, and AST levels of 74.47±8.25 U/L. No difference was detected between the two patient cohorts (P>0.05) (Table 5).

3.6 Comparison of quality of life between the two groups

Preceding surgery, there existed no differences in the scores of various dimensions of quality of life between the two cohorts (P>0.05). Subsequent to surgery, scores for each dimension of quality-of-life surpassed preoperative values in both groups. Specifically, within the study cohort, social function, psychological function, physical function, and material life condition scores were 78.36 ± 3.81 , 70.16 ± 5.83 , 65.25 ± 7.39 , and 63.81 ± 6.78 , respectively. These scores were all higher than those within the control cohort, which stood at 75.50 ± 3.66 , 65.28 ± 5.19 , 60.67 ± 6.98 , and 60.62 ± 5.75 , respectively. The differences contained statistical significance (P<0.05). Refer to Table 6.

3.7 Comparison of re-bleeding and survival rates between the two groups

One year postoperatively, the re-bleeding rate within the study group amounted to 22.00% (11/50), demonstrating a statistically significant reduction compared to the rebleeding rate observed in the control group, which stood at 42.86% (18/42) (P<0.05). The one-year survival rate within the study cohort was 62.00% (31/50), and when contrasted to the control group's survival rate of 52.38% (22/42), the difference contained no statistical significance (P>0.05). Refer to Table 7.

DISCUSSION

In the context of liver cirrhosis, hepatic tissues undergo diffuse fibrosis, culminating in impedance of portal venous drainage, augmented pressure, and the initiation of EGVB [8]. While pharmacological interventions can proficiently manage bleeding in individuals with cirrhotic EGVB, they encounter challenges in eradicating varices and are linked to extended treatment durations, thereby yielding suboptimal efficacy [9]. Endoscopic treatments fall short of providing a definitive resolution for recurrent bleeding among EGVB patients, often necessitating repeated interventions, which may hinder patient acceptance [10]. Despite the efficacy of surgical procedures in managing esophageal-gastric variceal bleeding (EGVB), their application is constrained by significant trauma, a heightened incidence of postoperative complications, and their inapplicability to individuals with severely impaired preoperative liver function.

Consequently, these factors limit their clinical utility ^[8]. With recent advancements in medical technology, interventional therapies have gradually found application in the treatment of cirrhotic EGVB and have garnered significant attention from clinicians ^[11-13]. Consequently, the search for an effective interventional treatment modality holds substantial significance in improving patient prognosis.

TIPS is classified as an interventional therapy, entailing the establishment of a shunt channel between the portal and hepatic veins to embolize varicose veins. This process brings about a reduction of portal veinous pressure and alleviation of variceal severity, effectively controlling bleeding [14-16]. PTVE is also categorized as an interventional therapy, utilizing liquid embolism agents to occlude varicose veins and employing a spring coil to embolize the main trunk of the gastric coronary vein, achieving hemostasis [17-19]. In this research, postoperative variceal conditions within the study cohort were superior to both preoperative conditions and the control group, reflecting that TIPS may be more efficacious in ameliorating variceal conditions in patients with cirrhotic EGVB. Concerning the rationales, PTVE accomplishes hemostasis by modifying the distribution of portal vein blood flow, leading to an elevation in portal vein blood flow and intensification of portal venous pressure, thereby yielding a suboptimal enhancement in varicose veins. On the other hand, TIPS achieves hemostasis by establishing a shunt channel between the portal and hepatic veins, diverting a portion of blood in the portal vein into the systemic circulation. This process promotes a decline in portal veinous pressure, thereby alleviating the severity of varicose veins [20-23]. Colombato L et al found that TIPS demonstrated excellent hemostatic efficacy (95%) and a low rebleeding rate (<20%) [24]. In our work, the postoperative PVV within the study cohort was heightened compared to both preoperative levels and the control group, whereas PVD was lowered compared to both preoperative levels and the control group. These findings are aligned with the aforementioned study, suggesting that TIPS is more effective than PTVE in improving the portal venous hemodynamics of cirrhotic EGVB patients. This may be attributed to TIPS inducing a reduction in portal veinous pressure by establishing a shunt channel,

consequently abating vascular resistance and augmenting blood flow velocity. The utilization of a GORE stent enables precise control over the size of the shunt channel, thereby facilitating optimal blood flow dynamics within the channel [25-27]. Studies have pinpointed that cirrhotic EGVB patients experience splenomegaly due to elevated portal veinous pressure, leading to hypersplenism and attenuated levels of PLT, WBC, and other parameters [28]. In our research, postoperative PLT and WBC levels within the study group were elevated compared to both preoperative values and the control group, suggesting that TIPS, compared to PTVE, is more effective in ameliorating cirrhotic EGVB patients' splenic function and heightening PLT and WBC levels. This improvement can bear a relation to the ability of TIPS to bring down portal vein pressure, thereby alleviating or preventing hypersplenism [29-32]. Cirrhotic EGVB patients inherently suffer from impaired liver function, and the stress and inflammatory response substances elicited during and subsequent to interventional treatments need to be cleared by the liver. Hence, interventional treatments might exacerbate the burden on patients' liver function [33]. Notwithstanding, in our research, no differences were discerned in preoperative and postoperative levels of ALB, TBIL, and AST between the two cohorts, unraveling that both TIPS and PTVE have certain safety profiles in the treatment of cirrhotic EGVB patients and do not significantly impact liver function. Here, the postoperative quality of life scores across all dimensions within the research cohort surpassed both preoperative scores and those of the control group, hinting the superior efficacy of TIPS over PTVE in enhancing the postoperative quality of life for cirrhotic EGVB patients. This improvement may be associated with TIPS being more effective in mitigating the severity of varices, bolstering recovery [34-36]. Furthermore, o our investigation unveiled a 22.00% re-bleeding rate within the research cohort at the one-year mark, contrasting with the 42.86% rate observed in the control group. This implies that TIPS exhibits greater efficacy than PTVE in reducing the one-year postoperative re-bleeding rate in cirrhotic EGVB patients. This effect may be related to the improvement of portal veinous pressure and hemodynamics by TIPS. Additionally, our endeavor uncovered no substantial difference in one-year postoperative survival rates between the two cohorts, indicating a favorable prognosis for both TIPS and PTVE in the treatment of patients afflicted by cirrhotic EGVB.

CONCLUSION

To sum up, in the management of EGVB in cirrhotic patients, TIPS stands out as an effective and safe therapeutic option. It dramatically mitigates the severity of varices and hemodynamics, aiding cirrhotic patients in alleviating their condition, averting the onset of complications, elevating the quality of life, and attaining superior treatment outcomes. Our study establishes a theoretical foundation for advocating Transjugular Intrahepatic Portosystemic Shunt (TIPS) as a primary intervention for patients afflicted with cirrhosis complicated by esophageal-gastric variceal bleeding (EGVB). However, it is essential to acknowledge the limitations inherent in our investigation. Firstly, this study adopts a retrospective design rather than a randomized controlled trial, thereby introducing the potential for selection bias and confounding factors. Secondly, the absence of long-term follow-up represents a notable limitation, as sustained observation is imperative for comprehending alterations in patient survival and quality of life in the context of TIPS treatment.

ARTICLE HIGHLIGHTS

Research background

Transjugular intrahepatic portosystemic shunt (TIPS) is one of the important methods for treating upper gastrointestinal bleeding (UGB) caused by portal hypertension (PHT) in patients with liver cirrhosis. Nevertheless, additional research endeavors are requisite to elucidate the precise therapeutic efficacy of TIPS in managing variceal bleeding and to discern its implications for patient prognosis.

Research motivation

The primary objective of this study is to scrutinize the efficacy of TIPS in the management of esophageal-gastric variceal bleeding in individuals with cirrhosis and

to evaluate its consequential influence on patient prognosis. The study endeavors to meticulously assess the advantageous outcomes associated with TIPS, aiming to furnish evidence-based insights that can inform and enhance clinical decision-making processes.

Research objectives

Through in-depth research on the therapeutic effect and prognosis of TIPS treatment, this paper aims to provide more comprehensive information for clinical doctors in order to better guide treatment decision-making and improve disease management for patients.

Research methods

A retrospective study was undertaken, encompassing 92 patients afflicted with cirrhotic EGVB who were admitted to our hospital during the period spanning from September 2020 to September 2022. The patient cohort was dichotomized into two groups based on distinct treatment modalities: the TIPS treatment group (n = 50) and the PTVE treatment group (n = 42). Comparative analyses were conducted on varicosity status, hemodynamic parameters, and quality of life for both groups, both preoperatively and postoperatively. Additionally, a comparative examination was undertaken to evaluate the 1-year re-bleeding and survival rates between the two treatment groups.

Research results

Postoperative varicosity improved in both groups, with the study group showing better outcomes. PVV increased and PVD decreased postoperatively, again with the study group demonstrating superior results. Postoperative PLT and WBC levels were higher in both groups, and the study group had higher scores in all dimensions of life quality. Furthermore, the study group exhibited a notably lower one-year re-bleeding rate in comparison to the control group, although no significant difference was discerned in the one-year postoperative survival rate between the two cohorts.

Research conclusions

TIPS treatment has demonstrated robust efficacy in the management of cirrhotic EGVB by significantly diminishing varicosity and enhancing hemodynamics in affected patients. This intervention not only presents a safer alternative but also contributes to a more favorable prognosis in this clinical context.

Research perspectives

Cirrhosis, as a grave and chronic ailment, exerts a profound influence on both the quality of life and the life expectancy of afflicted individuals. Consequently, a thorough exploration of treatment modalities and prognosis pertaining to esophageal-gastric variceal bleeding induced by cirrhosis assumes paramount importance, offering invaluable insights and reference points for clinicians engaged in clinical practice.

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