Surgical Shunting Versus TIPS for Recurrent Variceal Bleeding in Liver Cirrhosis: An Evidence-Based Case Report

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ABSTRACT

Background: *Variceal bleeding is a portal hypertension complication, often leading to a fatal outcome. With mortality of about 30-50%, those who survived are at increased risk of re-bleeding. Therefore, secondary prevention is needed,*

Objective: *To determine whether the surgical shunt is better than the trans jugular intrahepatic portosystemic shunt to prevent re-bleeding in patients with portal hypertension due to liver cirrhosis.*

Methods: Literature searching was performed in 4 online databases, Cochrane, PubMed, Embase, and SCOPUS. Three meta-analyses were appraised critically.

Results: *Of all meta-analyses included, the internal validities were poor and only included a small number of trials. However, the results show that surgical shunt is better for preventing variceal re-bleeding with varied heterogeneities.*

Conclusion: *Surgical shunts may have benefits over TIPS in preventing variceal re-bleeding.*

Keywords: *portal hypertension, secondary prevention, Surgical portosystemic shunt, Trans-jugular Intrahepatic Portosystemic Shunt (TIPS), Variceal re-bleeding*

INTRODUCTION

Variceal bleeding is a portal hypertension complication, often leading to a fatal outcome. It is estimated that 50% of patients with portal hypertension will develop gastroesophageal varices, and one-third will have bleeding. At the first episode, the mortality of variceal bleeding could reach 30-50%.[1] However, those who survived are at increased risk of re-bleeding (> 60% in a year).[1,2]

The primary treatment of variceal bleeding is a combination of pharmacological and endoscopic intervention (use of a long tube fitted with a camera to locate and occlude the varices with elastic bands).[3] It is proven effective in controlling the bleeding at the first episode.[2] But, since the morbidity of having re-bleeding is enormous, secondary prevention is mandatory.[4] Those who have refractory bleeding or re-bleeding despite adequate medical therapy will need a liver transplant or decompression shunting (tubes that divert blood from portal circulation directly to the heart, either by surgical or with the help of an ultrasound, i.e., Trans Jugular Intrahepatic Portosystemic Shunt (TIPS)).[2] However, since the availability of donor organs is scarce, shunting is often proposed as an attractive option. However, both shunts (surgical and TIPS) have their benefit and harm. This evidence-based case report determined whether a surgical shunt is better than a radiologic shunt for preventing re-bleeding in patients with portal hypertension due to liver cirrhosis.

CASE ILLUSTRATION

A 47-year-old male presented with recurrent episodes of upper gastrointestinal bleeding in the past year. He had liver cirrhosis with Child-Pugh classification grade A and Hepatitis B, treated with tenofovir for four months. His HBV DNA was not

detected. However, upper gastrointestinal endoscopy revealed grade three esophageal varices, and he was treated with the optimal dose of non-selective beta blocker and frequent variceal ligations. We try to find another effective treatment to improve his condition and prevent variceal re-bleeding.

CLINICAL QUESTION

In the adult population with portal hypertension due to liver cirrhosis, is a surgical shunt better at preventing re-bleeding than Trans-jugular Intrahepatic Portosystemic Shunt (TIPS)?

METHODS

Search Strategies

The literature search was conducted on September 1, 2022, using four databases: Cochrane, PubMed, Embase, and SCOPUS. The following are the keywords used in each database (Table 2):

Eligibility criteria

Inclusion criteria:

1. Randomized clinical trial (RCT) design or meta-analysis of RCTs
2. The article is written in English or Bahasa
3. Human subjects
4. Published within the last ten years

Table 2. Search strategies

Database	Keyword	Hit
Cochrane	((Adult) AND (Hypertension, Portal)) AND (Portosystemic Shunt, Surgical) AND (Portosystemic Shunt, Transjugular Intrahepatic)) AND (Hemorrhage)	2
PubMed	((Hypertension, Portal[MeSH Terms]) AND (((Splenorenal Shunt, Surgical[MeSH Terms]) OR (Portacaval Shunt, Surgical[MeSH Terms])) AND (Portosystemic Shunt, Transjugular Intrahepatic[MeSH Terms]))) AND (Hemorrhage[MeSH Terms])	30
Embase	('portal vein thrombosis'/exp OR 'idiopathic non-cirrhotic portal hypertension' OR 'Budd Chiari syndrome'/exp OR 'Budd Chiari syndrome' OR 'Chiari syndrome'/exp OR 'Chiari syndrome' OR 'Chiaris syndrome' OR 'syndrome, cruveilhier-baumgarten' OR 'cruveilhier baumgarten syndrome'/exp OR 'cruveilhier baumgarten syndrome' OR 'cruveilhier-baumgarten syndrome'/exp OR 'cruveilhier-baumgarten syndrome' OR 'portal hypertensions' OR 'portal hypertension'/exp OR 'portal hypertension' OR 'hypertensions, portal' OR 'non-cirrhotic portal hypertension' OR 'non-cirrhotic portal vein hypertension' OR 'portal vein hypertension' OR 'portal vein thrombosis') AND ('portacaval shunt, surgical' OR 'portacaval anastomosis' OR 'anastomoses, portacaval' OR 'surgical portacaval shunt' OR 'portacaval shunts, surgical' OR 'portacaval shunts' OR 'portacaval shunt' OR 'Eck fistula' OR 'shunt, portacaval' OR 'surgical portacaval shunts' OR 'anastomosis, portacaval' OR 'shunt, surgical portacaval' OR 'shunts, portacaval' OR 'shunts, surgical portacaval' OR 'portacaval anastomoses' OR 'fistula, Eck' OR 'splenorenal shunt, surgical' OR 'shunt, splenorenal' OR 'surgical splenorenal shunts' OR 'splenorenal shunt' OR 'splenorenal shunts, surgical' OR 'surgical splenorenal shunt' OR 'shunt, surgical splenorenal' OR 'shunts, splenorenal' OR 'shunts, surgical splenorenal' OR 'splenorenal shunts' OR 'dsrs' OR 'psrs') AND ('tips' OR 'trans jugular intrahepatic portosystemic' OR 'trans jugular intrahepatic portosystemic shunt' OR 'portosystemic shunt' OR 'trans jugular intrahepatic shunt' OR 'trans jugular intrahepatic portosystemic' OR 'tipss') AND ('hemorrhages' OR 'hemorrhage' OR 'bleeding')	204
Scopus	(TITLE-ABS-KEY ("TIPS" OR "Trans jugular Intrahepatic Portosystemic" OR "Trans jugular Intrahepatic Portosystemic Shunt" OR "Portosystemic Shunt" OR "Trans jugular Intrahepatic Shunt" OR "Trans jugular Intrahepatic Portosystemic" OR "TIPSS")) AND (TITLE-ABS-KEY ("Portacaval Shunt, Surgical" OR "Portacaval Anastomosis" OR "Anastomoses, Portacaval" OR "Surgical Portacaval Shunt" OR "Portacaval Shunts, Surgical" OR "Portacaval Shunts" OR "Portacaval Shunt" OR "Eck Fistula" OR "Shunt, Portacaval" OR "Surgical Portacaval Shunts" OR "Anastomosis, Portacaval" OR "Shunt, Surgical Portacaval" OR "Shunts, Portacaval" OR "Shunts, Surgical Portacaval" OR "Portacaval Anastomoses" OR "Fistula, Eck" OR "Splenorenal Shunt, Surgical" OR "Shunt, Splenorenal" OR "Surgical Splenorenal Shunts" OR "Splenorenal Shunt" OR "Splenorenal Shunts, Surgical" OR "Surgical Splenorenal Shunt" OR "Shunt, Surgical Splenorenal" OR "Shunts, Splenorenal" OR "Shunts, Surgical Splenorenal" OR "Splenorenal Shunts" OR "DSRS" OR "PSRS")) AND (TITLE-ABS-KEY ("Hemorrhages" OR "Hemorrhage" OR "Bleeding")) AND (TITLE-ABS-KEY ("portal vein thrombosis" OR "idiopathic non-cirrhotic portal hypertension" OR "Budd Chiari Syndrome" OR "Chiari Syndrome" OR "Chiaris Syndrome" OR "Chiaris Syndrome" OR "Syndrome, Cruveilhier-Baumgarten" OR "Cruveilhier Baumgarten Syndrome" OR "Cruveilhier-Baumgarten Syndrome" OR "Portal Hypertensions" OR "Portal Hypertension" OR "Hypertensions, Portal"))	240

Exclusion criteria:

1. Studies whose participants did specify to portal hypertension population
2. Included subjects aged below 18 years old
3. Not comparing surgical shunts and TIPS

Article selection

Literature searching was performed in four online databases, Cochrane, PubMed, Embase, and SCOPUS, using previously mentioned keywords (table 2). The next step is screening document duplication and applying inclusion and exclusion criteria. Five articles were selected for full-text reading. Two articles were excluded as they were included in the systematic review/meta-analysis were included in this review. Finally, three articles were used in this EBCR and further appraised using tools from the Center for Evidence-Based Medicine guidelines of the University of Oxford.[5]

RESULTS

Three studies were critically appraised from the article selection, which were systematic reviews/ meta-analyses of RCTs. The internal validity of all included studies is presented in Table 3. Huang L,[6] and Zhou GP,[7] showed poor internal validity in finding all relevant evidence. Also, Huang L did not describe the inclusion criteria of selected studies, and Zhou GP did not perform a sub-group analysis to explain the heterogeneity of their results.[6,7] Moreover, all of the meta-analyses included non-high-quality studies since the nature of the comparing interventions could not be blinded (Table 4). The results showed that compared with TIPS, surgical shunting was associated with a low risk of variceal re-hemorrhage and variceal re-bleed with varieties of heterogeneity (Table 5).

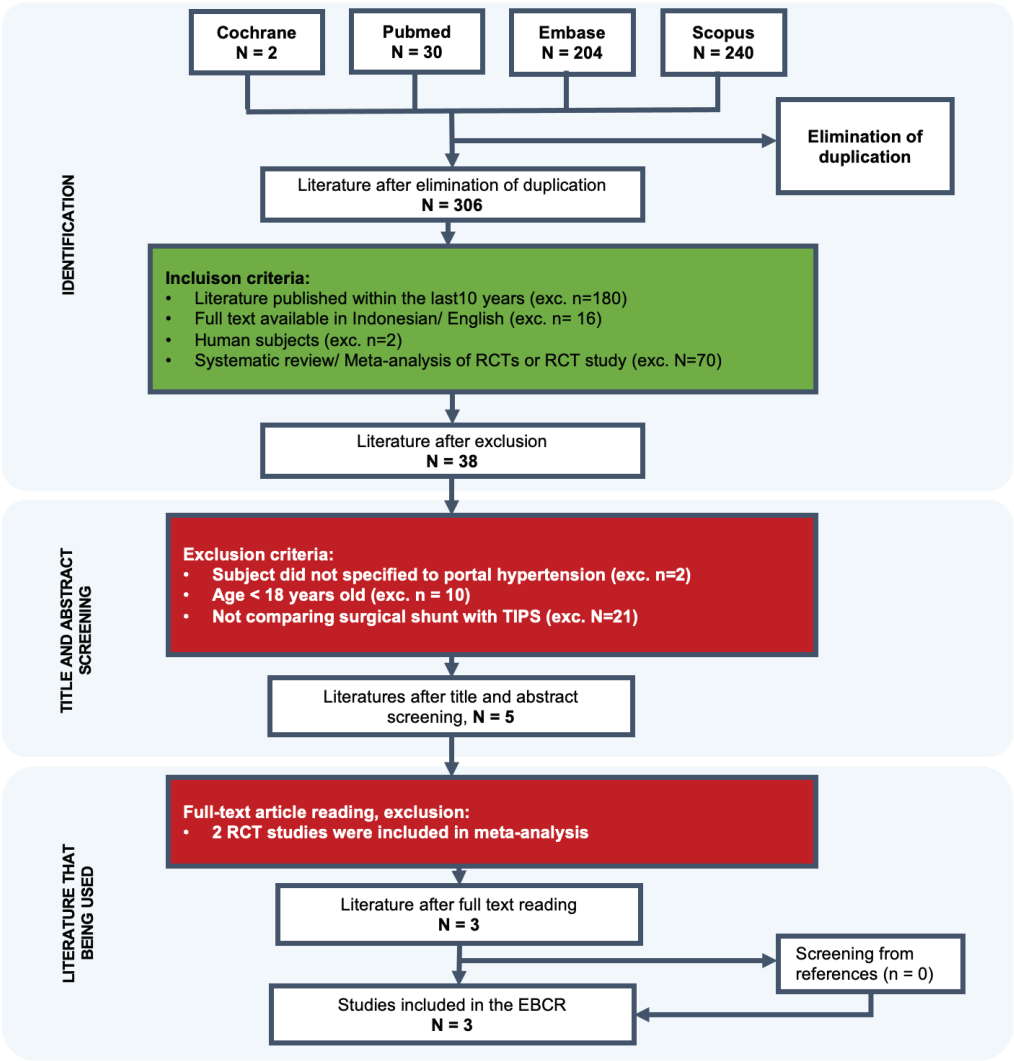

Figure 1. Search Strategy Flowchart

Table 4. Internal Validity

Validity Question	Huang L et al. (2015)[6]	Brand M et al. (2018)[2]	Zhou GP et al. (2019)[7]
Does the systematic review address a focused question (PICO)?	Yes	Yes	Yes
Does the systematic review address a focused question (PICO) and use it to direct the search and select articles for inclusion?	No	Yes	Yes
Did the search find all the relevant evidence?	No	Yes	No
Have the studies been critically appraised?	Yes	Yes	Yes
Did they only include high-quality studies?	No	No	No
Have the results been totaled up with appropriate summary tables and plots?	Yes	Yes	Yes
Have the results been totaled up with appropriate summary tables, plots, and heterogeneity between studies assessed and explained?	Yes	Yes	No

Table 5. Summary of included studies

Parameters	Huang L et al. (2015)[6]	Brand M et al. (2018)[2]	Zhou GP et al. (2019)[7]
Title of article	Trans jugular Intrahepatic Portosystemic Shunt Versus Surgical Shunting in the Management of Portal Hypertension	Surgical portosystemic shunts versus trans jugular intrahepatic portosystemic shunt for variceal bleeding in people with cirrhosis (Review)	Comparison between portosystemic shunts and endoscopic therapy for prevention of variceal re-bleeding: a systematic review and meta-analysis
Study design	Systematic review/ Meta-analysis of RCTs	Systematic review/ Meta-analysis of RCTs	Systematic review/ Meta-analysis of RCTs
Population/ problems	Portal hypertension	Cirrhotic portal hypertension with documented refractory or recurrent variceal bleeding following pharmacologic and endoscopic interventions.	Cirrhotic portal hypertension aged > 16 years with at least one documented variceal bleeding that had subsequently stabilized
Intervention	TIPS	Surgical portosystemic shunt: small diameter H-graft shunt (mesocaval/ portocaval shunt), DSRS, PCS, Central splenorenal shunt, 16 mm diameter H-graft shunt (mesocaval/ portocaval shunt)	Surgical portosystemic shunt
Comparison	Surgical shunting group; DSRS, HGPCS, and PCS	TIPS	TIPS
Outcome			
Variceal re-bleeding	OR 7.45, 95% CI 3.93 to 14.15; participants = 493; studies =4; I^2: 62.8%, P: 0.04 X^2: 8.07 df: 3 (definite heterogeneity)	RR 0.18, 95% CI 0.07 to 0.49; participants = 496; studies = 4; I2 = 0%; P: 0.72 X^2: 1.4 df: 3 (Heterogeneity unlikely)	RR 0.21; 95% CI 0.07 to 0.60; participants = 496; studies = 4; I2 = 60%, P: 0.06, X^2: 7.57 df: 3 (Possible heterogeneity)
Level of Evidence	-	1a	-

CI: Confidence Interval; DSRS: Distal splenorenal shunt; HGPCS: H-graft portocaval shunt; PCS: Portocaval shunt; OR: Odds Ratio; RCTs: randomized controlled trials; RR: Risk Ratio

DISCUSSION

We identified only three meta-analyses with poor internal validity and small included trials comparing surgical shunts with TIPS for preventing re-bleeding in patients with portal hypertension due to cirrhosis. As the number of TIPS performed has increased, the number of surgical shunts has decreased, and the result is only small trials available comparing both interventions.[8] In this EBCR, all meta-analyses included four trials of mostly the same studies (Orloff, Rosemurgy, and Henderson).[9-12] Of all meta-analyses, the results were in favor of surgical shunt with varied heterogeneities.[2,6,7]

By definition, portal hypertension is a pathologically increased pressure within the portal venous system.[13] It is determined by measuring the pressure gradient between the portal and hepatic vein, known as a hepatic venous portal gradient (HVPG).[14] portal hypertension becomes clinically significant when the gradient exceeds 10 mm mercury (Hg).[14,15] It is developed when the resistance to portal blood flow and portal venous in-flow increases. It leads to decompensation of liver function, with clinical manifestations such as ascites, jaundice, hepatic encephalopathy, hepatorenal syndrome, and variceal bleeding.[3]

A systematic review reported variceal bleeding as the second most common cause of death in liver

cirrhosis patients.[16] The gastroesophageal varices develop when the natural portosystemic collateral enlarges to compensate for the elevated portal pressure. These portosystemic collaterals form when the HVPG is 10-12 mmHg over the threshold. Moreover, variceal bleeding is a time-dependent phenomenon. According to Frank's modification of Laplace law, the likelihood of rupture in varices is directly proportional to the difference between intra-variceal (VAp) and luminal (LUp) pressures and variceal radius (R) and inversely proportional to variceal wall thickness (L). The study reported that any existing varices in liver cirrhosis patients would enlarge over time (higher R).[3] Furthermore, the increased flow and portal pressure will cause thinning of the vessel walls (lower L). If not adequately managed, VAp also tends to increase along with increased portal vein pressure. In conclusion, variceal bleeding occurs when wall tension exceeds the elastic limit of the variceal wall, with the advanced progression of liver cirrhosis.[3]

Since the prevalence and mortality of variceal bleeding are massive, prophylactic variceal bleeding is needed. However, once patients have experienced the first episode of variceal bleeding, they have a 60% chance of experiencing secondary bleeding within a year.[2] With the factor of re-bleeding being the same as the first episode and only 3-10% of cirrhosis patients with bleeding will undergo a liver transplant, different therapies are available, including decompression shunting.[8] By reducing the portal pressure either by TIPS or surgical shunts, it is hoped that it will ultimately reduce HVPG and decrease the likelihood of variceal bleeding.

TIPS is the percutaneous-radiologic guided procedure that aims to create a conduit from the portal venous system to the hepatic venous system. Since its first implantation in humans in 1981, TIPS has evolved, improved, and become the standard treatment of choice for portal decompression in the western world.[8] According to the systematic review, the primary indication of TIPS are liver cirrhosis and variceal bleeding (as salvage TIPS, early TIPS, or re-bleeding despite optimal secondary prophylaxis) or refractory ascites.[17] Unfortunately, Indonesia cannot perform this intervention due to the non-availability of the operator. However, despite its advantage as a minimally invasive intervention, there are reports where complications and re-interventions concerning TIPS are high. The parenchymal and vascular trauma during the TIPS procedure can increase bleeding risk in patients with coagulopathy.[18] Also, there are concerns that TIPS might accelerate hepatic deterioration and hepatic failure by diverting nutrient-effective hepatic blood flow away from already compromised hepatocytes.[2] It is also reported that creating a portosystemic shunt, there was a large-volume blood shift from the splanchnic to the systemic circulation, leading to an abrupt increase in cardiac output and proper heart pressures.[17] Even though it is usually transient, patients with cirrhotic cardiomyopathy might experience post-TIPS cardiac failure, and it might occur in about 20% of patients.[17]

Before the introduction and widespread adoption of TIPS, surgical shunts were a viable treatment for treating variceal bleeding. The surgical shunts are divided into non-selective and selective shunts. Non-selective shunts divert all portosystemic circulation into the systemic circulation (i.e., portocaval shunt, central splenorenal shunt, and the large diameter H-graft shunt).[2] While selective surgical shunt (i.e., distal splenorenal shunt and the small diameter H-graft shunt) maintains some hepatic perfusion while providing adequate portal decompression.[2] Both interventions are available in Indonesia. However, it is not commonly performed considering perceived increased periprocedural morbidity and mortality rates, especially in patients with advanced cirrhosis. Brand et al. reported that the all-cause mortality rate, especially the mortality due to variceal bleeding, was significantly lower in surgical shunts.[2] This evidence-based case report also shows that the risk of variceal re-bleeding was lower in surgical shunt compared to TIPS.

Despite the harm and benefit of both procedures, our confidence in estimates of intervention effect on preventing variceal re-bleed is low due to poor internal validity in most included studies. This judgment was because non-high-quality studies were included in all of the meta-analyses. In addition, although the nature of the interventions made the RCT unrealistic for blinding the subject or personnel, the risk of bias can be reduced by blinding the outcome assessment. However, this is not performed in most of the included trials.[9,10] Hence, the lack of blinding in RCTs could overestimate the results.

Moreover, there is a tendency that not-all available RCTs comparing TIPS with surgical shunts were included in the meta-analyses, which might lead to imprecision and publication bias.[6,7] Furthermore, since the sample size was small (minimal RCTs included, small sample size of the individual trials, and few events), there are possibilities that the results were affected by chance. This could be seen as a wide range

of confidence intervals in the included meta-analyses.

Finally, we found a variation of heterogeneities of all included meta-analyses. There was a possible reason for this finding, including the type of surgical shunt (i.e., selective vs. non-selective) and the indication of shunting (i.e., salvage shunting or in an emergency setting).[2,6] Moreover, since there is a paucity of available trials, the risk of random errors in all meta-analyses was high. This finding strengthens the need for more extensive trials comparing both interventions.

CONCLUSION

In conclusion, we found evidence suggesting that surgical shunts may have a benefit over TIPS in preventing variceal re-bleeding in patients with portal hypertension due to liver cirrhosis. However, considering the low certainty of the evidence and the high risk of chance, we have very little confidence in this report. Therefore, further multicentered RCT with a large sample size is recommended to produce an actual intervention effect.

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