

Comparison of Effects of Devascularization versus Shunt on Patients with Portal Hypertension: A Meta-Analysis

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Rezumat

Comparație între efectele devascularizării și șuntului la pacienții cu hipertensiune portală - Metaanaliză

Obiectiv: De a evalua sistematic eficiența devascularizării și șuntului la pacienții cu hipertensiune portală.

Metode: Studii relevante comparând devascularizarea și șuntul în tratamentul hipertensiunii portale au fost identificate prin consultarea bazelor de date PubMed, Embase, Elsevier, CNKI (China National Knowledge Infrastructure) și Cochrane Trial Register până în decembrie 2013. Date de interes privind devascularizarea și șuntul, inclusiv hemoragii postoperatorii recurente, encefalopatie hepatică postoperatorie, ascită, rata mortalității operatorii și rata supraviețuirii pe termen lung, au fost supuse metaanalizei.

Rezultate: Unsprezece studii au fost incluse în studiul nostru, rezultatele metaanalizei menționând că toate au demonstrat o rată a sângerării recurente postoperatorii mai ridicată în grupul tratat prin devascularizare decât în cel tratat prin șunt (Odds Ratio = 2,14, 95% CI = [1,42, 3,21], P = 0,0003), rata encefalopatiei hepatice în grupul de devascularizare a fost mai scăzută decât în cel de șunt (Odds Ratio = 0,56, 95% CI = [0,38, 0,82], P = 0,003); metaanaliza noastră efectuată pe 3 studii clinice a revelat că reducerea ascitei în grupul de devascularizare a fost semnificativ mai mică decât în grupurile de

șunt (Odds Ratio = 0,48, 95% CI = [0,26, 0,89], P = 0,02), rata mortalității intraoperatorii nu a fost semnificativ diferită între cele două grupuri (Odds Ratio = 1,54, 95% CI = [0,91, 2,63], P = 0,11), la fel și supraviețuirea pe termen lung (Odds = 1,13, ratio, 95% CI = [0,64, 1,99], P = 0,68).

Concluzii: Devascularizarea și șuntul au avantaje, respectiv dezavantaje, diferite, ce se reflectă în complicațiile postoperatorii și supraviețuirea pe termen lung.

Cuvinte cheie: devascularizare, șunt, hipertensiune portală, metaanaliză

Abstract

Objective: To systematically evaluate the effectiveness of devascularization and shunt on patients with portal hypertension.

Methods: Relevant studies compared devascularization and shunt for the treatment of portal hypertension were identified searching the PubMed, Embase, Elsevier, CNKI (China National Knowledge Infrastructure) database and Cochrane Trial Register searches until December 2013. Data of interest for devascularization and shunt including postoperative recurrent bleeding, postoperative hepatic encephalopathy, ascites, operative mortality rate, and long term survival rate were subjected to meta-analysis.

Results: Eleven studies were included in the study, the results of the meta-analysis showed that all eleven clinical studies demonstrated a significantly higher postoperative recurrent bleeding rate with devascularization group than with shunt group (Odds Ratio = 2.14, 95% CI = (1.42, 3.21), P = 0.0003), the rate of hepatic encephalopathy in the devascularization group was significantly lower compared with the shunt group

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(Odds Ratio = 0.56, 95% CI = (0.38, 0.82), $P = 0.003$); Our meta-analysis of three clinical studies revealed that the reduction of ascites in the devascularization group was significantly less than the shunt groups (Odds Ratio = 0.48, 95% CI = (0.26, 0.89), $P = 0.02$), the operative mortality rate was not significantly different between the devascularization group than for shunt group (Odds Ratio = 1.54, 95% CI = (0.91, 2.63), $P = 0.11$). And the long-term survival rate was not significantly different between the devascularization and shunt groups (Odds = 1.13, ratio, 95% CI = (0.64, 1.99), $P = 0.68$). **Conclusions:** Devascularization and shunt have different advantages and disadvantages respectively which reflected in postoperative complications and long term survival rate.

Key words: devascularization, shunt, portal hypertension, meta-analysis

Introduction

Portal hypertension (PHT) is a clinical syndrome defined by a portal venous pressure gradient between the portal vein (PV) and inferior vena cava exceeding 5mmHg (1). Patients with portal hypertension are often asymptomatic and the only clinical evidence of portal hypertension may be splenomegaly. Clinical features of chronic liver disease are usually present (2). Several of the life-threatening complications of chronic liver disease result from the development of portal hypertension, such as Gastro-esophageal varices, hepatic encephalopathy, ascites, hepatorenal syndrome, Spontaneous bacterial peritonitis et al (3-5).

Mere presence of PHT is not an indication for an active treatment other than simple supportive measures. Main indication of an operation is gastroesophageal bleeding and rarely surgery may be done for hypersplenism, intractable ascites or portal biliopathy (6). Devascularization and shunting are the two widely accepted approaches for treatment of portal hypertension especially for control of variceal bleeding (7,8).

To date, several studies, including randomized controlled trials (RCTs), have compared clinical outcomes and postoperative complications between devascularization and shunt (9-12). However, no definite consensus has been reached regarding the merits and demerits of two kinds of operations. To demonstrate an objective advantage for the devascularization and shunt, thus we performed a meta-analysis to compare devascularization with shunt for portal hypertension in terms of postoperative outcomes.

Methods

Literature Search

The PubMed, Embase, Elsevier, CNKI (China National

Knowledge Infrastructure) database and Cochrane Trial Register searches were performed to identify all the eligible papers. The search terms were used as the following: portal hypertension, shunt and devascularization. The publication languages were restricted to English and Chinese. Moreover, potentially relevant studies were evaluated by reviewing the titles and abstracts, and studies matching the criteria were carefully retrieved. If more than one study was published using the same data, only the study with a larger population was included. The literature search was updated on December, 2013. This systematic review was planned, conducted, and reported in adherence to standards of quality for reporting meta-analyses.

Inclusion and exclusion criteria

Studies were included in the meta-analysis if they met all of the following criteria: (1) investigation of comparison of devascularization with shunt for treatment about portal hypertension between 1980 and 2013; (2) patients with no serious cardiopulmonary diseases, and with no other liver disorders except cirrhosis; (3) presence of raw data including most of the following: postoperative recurrent bleeding, postoperative hepatic encephalopathy, ascites, operative mortality rate, and long term survival rate. Exclusion criteria were (1) no devascularization or shunt group as a control; (2) duplicate publication or provision of insufficient data. (3) reviews, case report, editorial or comment.

Quality assessment of studies

Full copies of studies were independently assessed for methodologic quality by both authors using the Jadad score (13) This 5-point quality scale awards points for randomization (randomized¼ 1 point, table of random numbers or computer-generated randomization¼ an additional 1 point), double-blinding (double-blind¼ 1 point, use of a placebo¼ additional 1 point), and follow-up (numbers and reasons for withdrawal in each group are stated¼ 1 point) within the report of an RCT. Final scores of 0 to 2 point were considered low quality, whereas final scores ≥ 3 point were regarded as representing studies of high quality (Table 2). Sensitivity analysis was performed by excluding low quality studies (Jadad score < 3).

Risk of bias assessment

Assessment of methodological quality was performed using the risk of bias assessment tool by the Cochrane Collaboration indicating the following bias domains: selection bias (random sequence generation, allocation concealment), performance/detection bias (blinding of participants and personnel/blinding of outcome assessment), attrition bias (incomplete data outcome), reporting bias (selective reporting), and other bias. Studies which were deemed as "adequate" in all principal domains were considered to be of low risk of bias. Studies, in which there was no clear judgment concerning the procedures in one or more key domains, were considered to be at least of

medium risk of bias. Studies with clearly inadequate procedures in one or more of the key domains were considered to be of high risk of bias. In this context, blinding of operators was impossible and blinding of patients meaningless. However, RCTs were evaluated as medium risk of bias when blinding of participants and outcome assessors, concealment of allocation, or randomization method were unclear. For each RCT, the risk of bias was independently assessed by two authors. The summary assessments of risk of bias were evaluated not only for each RCT across outcomes but also specifically for meta-analyses. RCTs with unclear or high risk of bias were not excluded from meta-analyses. However, meta-analyses including such RCTs were explicitly indicated. As mentioned above, nonrandomized prospective trials and nonrandomized retrospective analyses were excluded from meta-analysis.

Data extraction

Three researchers extracted data from each study by using a structured sheet and entered the data into a database. The following data were extracted from each study: the first author's last name, publication year, source journal, research design, study duration, retention and drop-out rate, surgical methods, patient's sex and age, sample size, postoperative rebleeding, postoperative hepatic encephalopathy, ascites, operative mortality rate and long term survival rate. Postoperative rebleeding defined as cases with a history of variceal bleeding before surgery, or variceal bleeding during the follow-up after surgical treatment, operative mortality was defined as death within 30 days of surgery or death occurring in the same hospitalization as surgery. Long-term survival rate was defined as 5-year survival rate (14).

Statistical analysis

For each outcome measure of interest, a meta-analysis was performed to determine the pooled effect of the intervention in terms of weighted mean differences between the postintervention (or differences in means) values of the devascularization and shunt groups. Combining both the post-intervention values and difference in means in one meta-analysis is an accepted method described by the Cochrane Collaboration (15). All data were analyzed using Review Manager 5.0 software (The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark). In this meta-analysis, odds ratios (ORs) were used for dichotomous variable. Heterogeneity among trial results was tested with a standard chi-square test. The I^2 parameter was used to quantify any inconsistency: $I^2 = [(Q - df)/Q] \times 100\%$, where Q is the chi-square statistic. A value for $I^2 > 50\%$ was considered to represent substantial heterogeneity (16). To consider heterogeneity, the random-effects model was used to estimate weighted mean differences with 95% CIs. Forest plots were generated to illustrate the study-specific effect sizes along with 95% CIs. To determine the presence of publication bias, we assessed the symmetry of the funnel plots in which mean differences were plotted against their corresponding standard errors. In this

study, 95% confidence intervals (CIs) were calculated. P values 0.05 were considered to indicate statistical significance.

Results

Eleven clinical studies fulfilled the inclusion criteria and were included in the meta-analysis (9-12,17-23). There were a total of 1716 portal hypertension cases (770 undergone devascularization and 946 undergone shunt). The search and exclusion strategy is displayed in Fig. 1. The characteristics of the eleven clinical studies which were all retrospective studies are shown in Table 1. There were no significant difference between devascularization group and shunt group about the age, gender, and etiology Classification of patients. The assessment of methodological quality about the eleven clinical studies can be seen in Table 2, and each study has a score of ≥ 3 points except the study from Wang (11) and Vons (22).

Postoperative recurrent bleeding

All eleven clinical studies demonstrated the rate of postoperative recurrent bleeding, and all showed a significantly higher with devascularization group than with shunt group (Odds Ratio = 2.14, 95% CI = (1.42, 3.21), $P = 0.0003$; Fig. 2).

Postoperative hepatic encephalopathy

Seven studies showed data on postoperative hepatic encephalopathy, our study shows that the rate of hepatic encephalopathy in the devascularization group was significantly lower compared with the shunt group [Odds Ratio = 0.56, 95% CI = (0.38, 0.82), $P = 0.003$; Fig. 3].

Ascites

Our meta-analysis of three clinical studies revealed that the reduction of ascites in the devascularization group was significantly less than the shunt groups [Odds Ratio = 0.48, 95% CI = (0.26, 0.89), $P = 0.02$; Fig. 4].

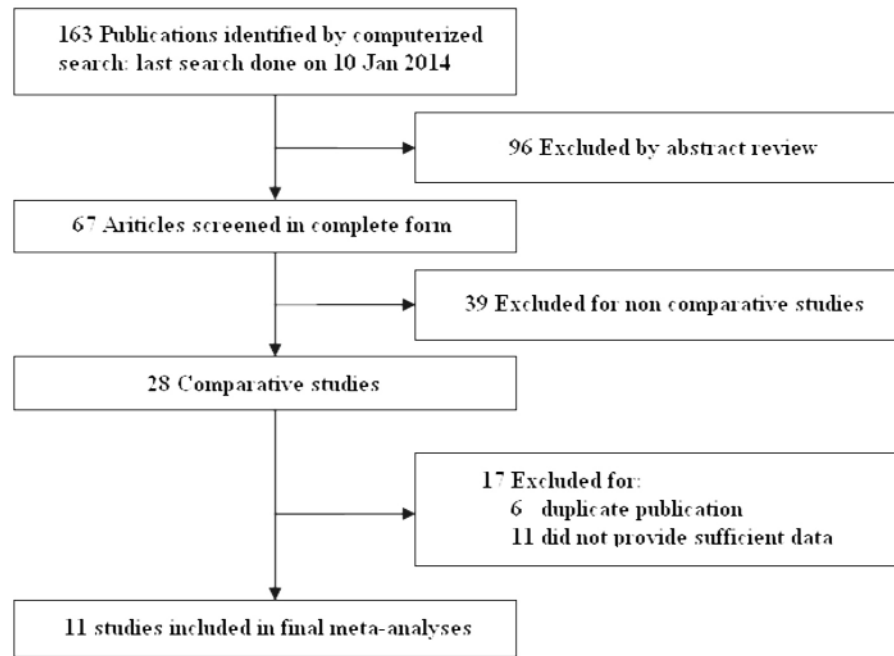
Operative mortality rate

This meta-analysis of six clinical studies revealed that the operative mortality rate was not significantly different between the devascularization group than for shunt group [Odds Ratio = 1.54, 95%CI = (0.91, 2.63), $P = 0.11$; Fig. 5]. A total of fifty-one patients died. The major cause of death was mesenteric venous thrombosis (fourteen cases), abdominal bleeding (twenty-six cases) and septicemia (eleven cases).

Long term survival rate

Long term survival rate was reported in six studies. Our meta-analysis shows that the long-term survival rate was not significantly different between the devascularization and shunt groups (Odds ratio = 1.13, 95%CI = (0.64, 1.99), $P = 0.68$; Fig. 6).

Figure 1. Systematic search and selection strategy



Assessment of publication bias

The funnel plot of standard of error by effect size for the measurements of postoperative recurrent bleeding, postoperative hepatic encephalopathy, operative mortality rate and long-term survival rate (the studies about ascites were less than five) showed an equal distribution of studies around

the middle line, indicating that publication bias were not evident (Fig.7 - Fig.10).

Sensitivity analysis

Sensitivity analysis was performed by excluding low quality studies (Jadad score < 3). ORs, 95% CIs and P values for post-

Table 1. Characteristics of the eleven clinical studies

Study (ref.) Year	Group	Gender		Age (year)	Etiology Classification (cirrhosis)	Follow-up time
		Male	Female			
Mercado et al. 2001 (17)	devascularization shunt	87 61	50.1+8.6	87 61	4years	
Orozco et al. 1994 (9)	devascularization shunt	32 62	23 39	unclear	55 101	13 years
Borgonovo et al. 1996 (10)	devascularization shunt	22 21	5 6	53.6+9.3 51.0+9.4	27 27	3 years
Xu et al. 2005 (18)	devascularization shunt	106 267	123 89	40.8	229 356	5 years
Ezzat et al. 1990 (19)	devascularization shunt	87 120	9 3	36+11 36+11	96 123	6.5 years
Huang et al. 2005 (20)	devascularization shunt	30 45	10 11	46+12	40 56	4.7 years
Zhou et al. 2009 (21)	devascularization shunt	85 64	50.2±10.7 44.9±9.8	85 64	5years	
Wang et al. 2002 (11)	devascularization shunt	24 22	8 6	48.8±9.7 47.2±10.1	32 28	1 year
Vons et al. 1996(22)	devascularization shunt	9 6	51+8	9 6	0.5year	
da Silva et al. 1986 (12)	devascularization shunt	23 40	9 22	30.7+8.9 31.6+9.2	29 57	more than 5 years
Xie et al. 2002 (23)	devascularization shunt	62 52	19 15	49.1±10.0 50.5±8.8	unclear	7 years

Table 2. Assessment of methodological quality

Study (ref.)	Randomization method	Allocated concealment	Baseline control	Eligibility criteria	Loss to follow-up described	Study quality (Jadad score)
Mercado et al. (17)	RCT	Unclear	Adequate	yes	yes	3
Orozco et al. (9)	RCT	Unclear	Adequate	yes	yes	3
Borgonovo et al. (10)	RCT	Unclear	Adequate	yes	yes	4
Xu et al. (18)	RCT	Unclear	Adequate	yes	yes	4
Ezzat et al. (19)	RCT	Unclear	Adequate	yes	yes	4
Huang et al. (20)	RCT	Unclear	Adequate	yes	yes	3
Zhou et al. (21)	RCT	Unclear	Adequate	yes	yes	3
Wang et al. (11)	RCT	Unclear	Adequate	yes	no	2
Vons et al. (22)	RCT	Unclear	Adequate	yes	yes	2
da Silva et al. (12)	RCT	Unclear	Adequate	yes	yes	4
Xie et al. (23)	RCT	Unclear	Adequate	yes	yes	3

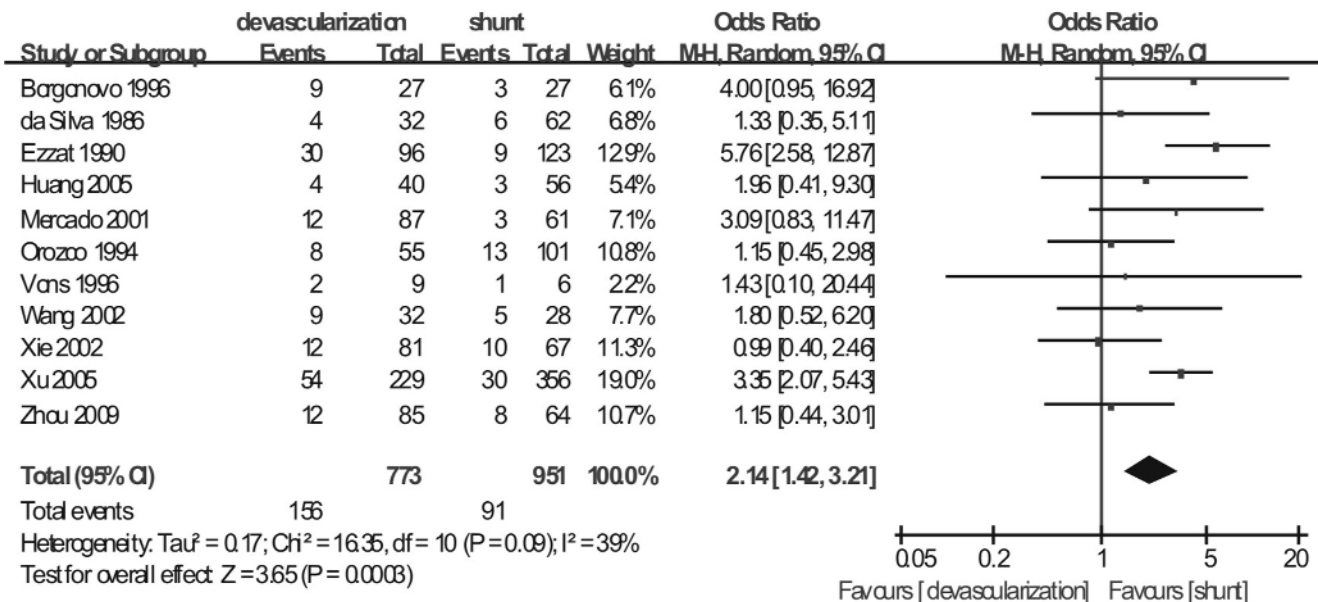
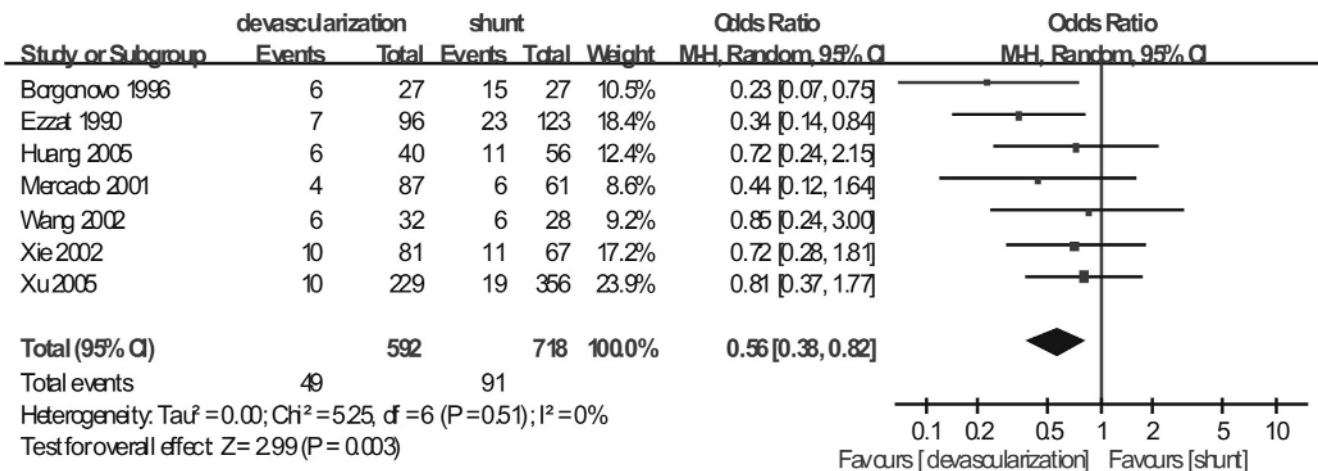
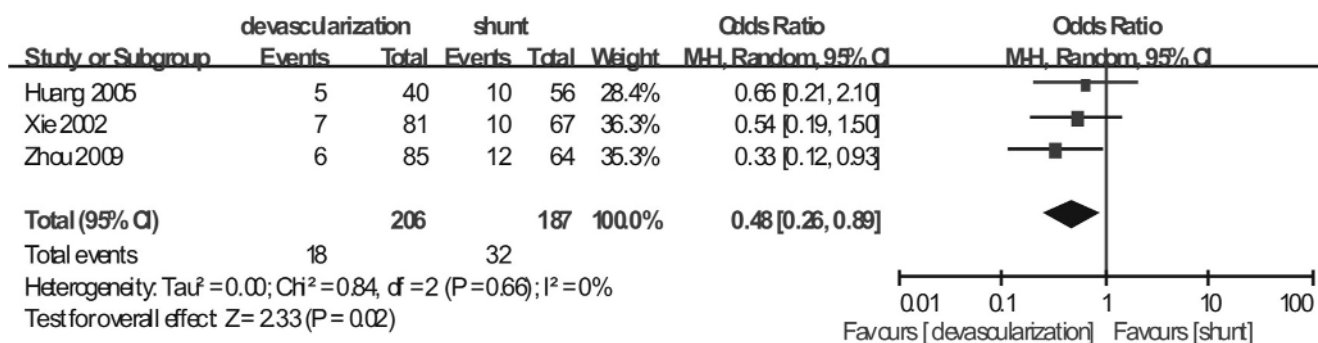
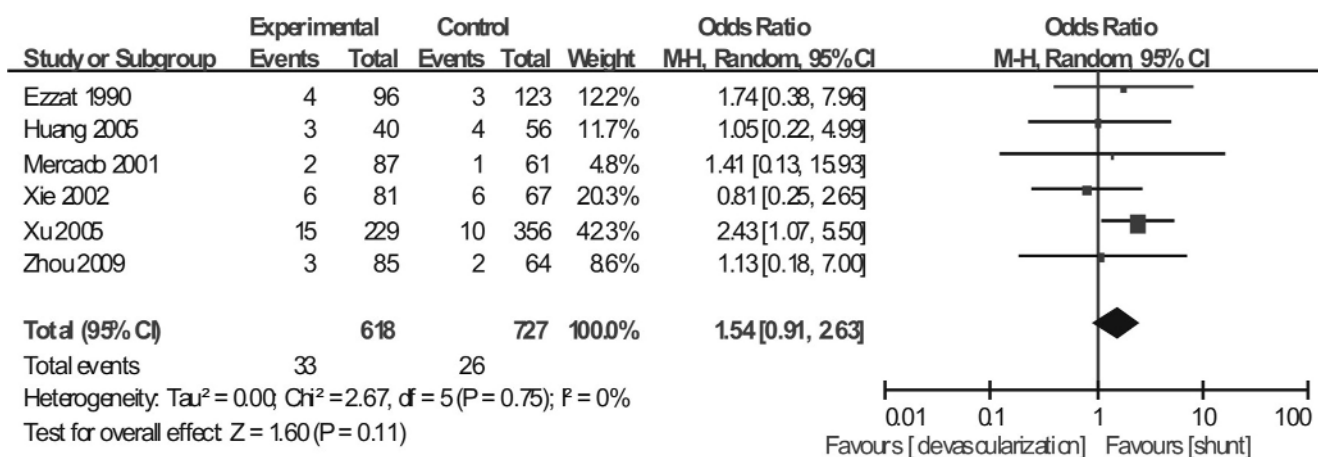
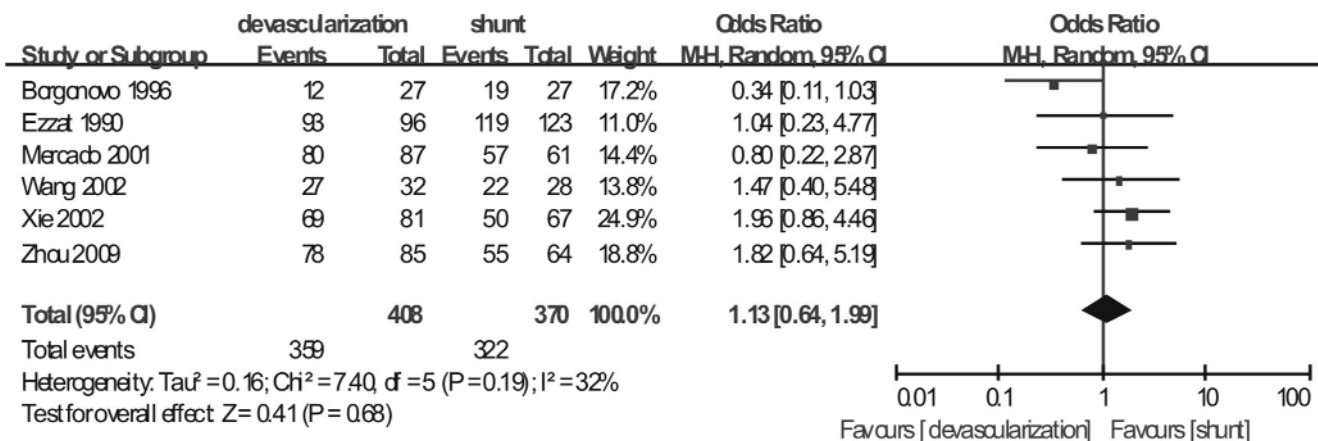
Figure 2. Meta-analysis of devascularization and shunt groups for postoperative recurrent bleeding**Figure 3.** Meta-analysis of devascularization and shunt groups for postoperative hepatic encephalopathy.

Figure 4. Meta-analysis of devascularization and shunt groups for ascites**Figure 5.** Meta-analysis of devascularization and shunt groups for operative mortality rate**Figure 6.** Meta-analysis of devascularization and shunt groups for Long term survival rate

operative recurrent bleeding, postoperative hepatic encephalopathy and long-term survival rate were still similar to results before exclusion of low-quality studies (Table 3). This indicates that low-score RCTs had no bias on results of our meta-analyses.

Discussion

Portal hypertension is primarily a consequence of liver cirrho-

sis, which can result in serious complications, such as bleeding gastro-esophageal varices, thrombocytopenia, and ascites. Many patients have to be treated each year. The treatment of portal hypertension include several scenarios with different prognostic and therapeutic implications (24). These include treatment of the acute bleeding episode (a major medical emergency requiring the combined effort of hepatogastro-enterologists, endoscopists and surgeons), the elective treatment (prevention of rebleeding in patients who have survived a bleeding episode

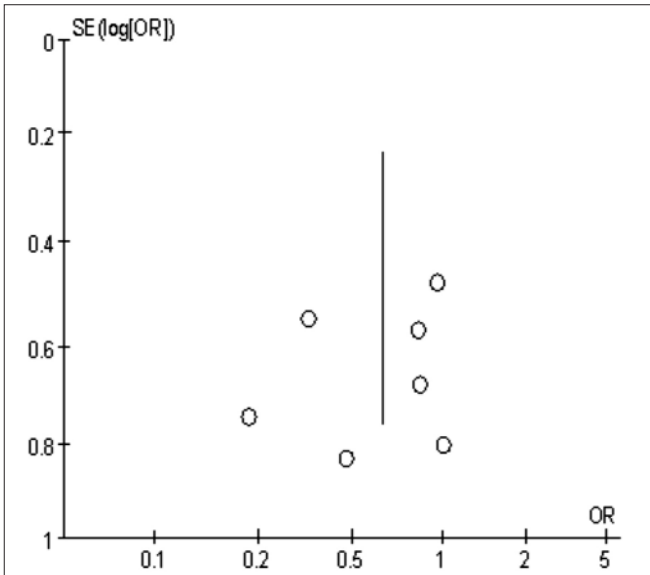


Figure 7. Funnel plot for the results from the studies comparing postoperative recurrent bleeding in patients undergoing devascularization with shunt of portal hypertension

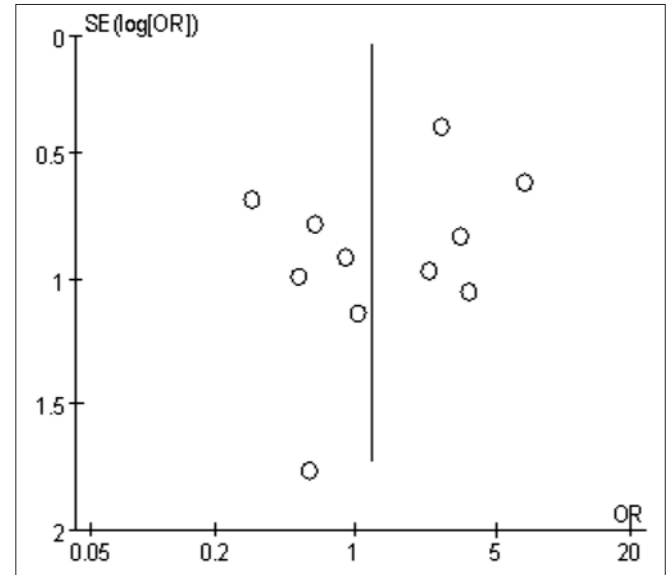


Figure 8. Funnel plot for the results from the studies comparing postoperative hepatic encephalopathy in patients undergoing devascularization with shunt of portal hypertension

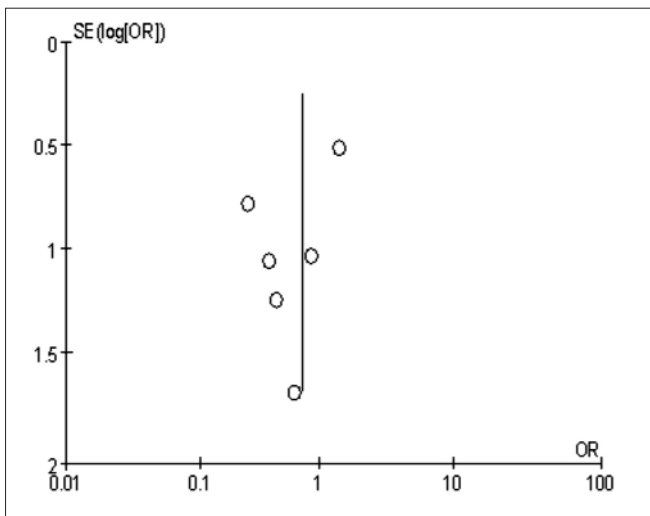


Figure 9. Funnel plot for the results from the studies comparing operative mortality rate in patients undergoing devascularization with shunt of portal hypertension

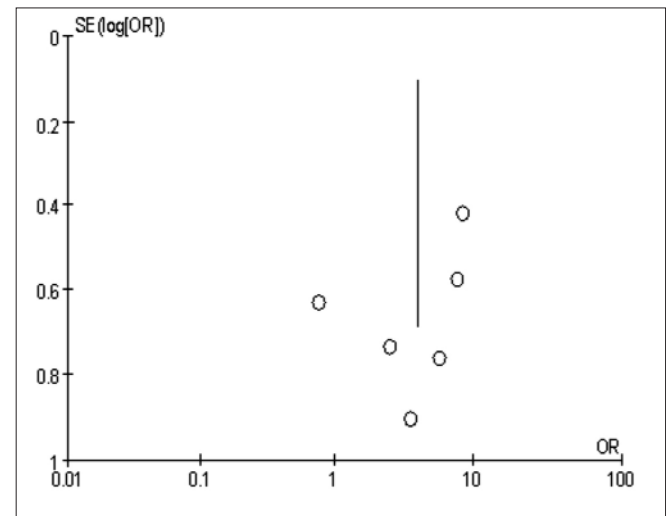


Figure 10. Funnel plot for the results from the studies comparing long-term survival rate in patients undergoing devascularization with shunt of portal hypertension

Table 3. Pooled estimates of effect size and 95% CIs expressed as odd ratio (OR) for the effects of devascularization with shunt on portal hypertension in 11 studies

Outcomes	Number. of patients		No. of studies	OR	95% CI	P- value
	devascularization	shunt				
recurrent bleeding	732	917	nine	2.37	(1.21,2.98)	0.001
hepatic encephalopathy	560	690	six	0.72	(0.31,0.76)	0.008
long-term survival rate	376	342	five	1.62	(0.58,1.73)	0.52

CI = confidence interval; OR= odds ratio

from esophageal or gastric varices) and the so-called primary prophylaxis (prevention of the first variceal hemorrhage in patients who have never bled)(25,26).

The methods of treating portal hypertension with with variceal hemorrhage included pharmacological therapy such as β -adrenergic blockers and nitrates, interventional radiological therapy such as transjugular intrahepatic portosystemic shunt (TIPS), endoscopic therapy such as band ligation and surgical therapy. Surgical treatment remains the best treatment choice for patients with portal hypertension because of a lower rebleeding rate compared with other forms of treatment (27).

In 1945, Allen Whipple reported a series of portacaval and central splenorenal shunts, the selective shunting including the distal splenorenal shunt and the coronary-caval shunt were developed by Warren and Inokuchi thereafter (28-30). In the last two decades, Surgical shunt procedures including partial portal-systemic shunts and improved methods for selective shunts were appeared (31,32). Devascularization procedures were introduced by several groups in the 1950s and compromised components of devascularization procedures with the modifications of variceal ligation, oesophageal transection and splenectomy (33). Sugiura and Futagawa in 1973 reported a two-stage procedure involving both transthoracic and transabdominal approaches for interruption of gastroesophageal varices while still maintaining flow through other portal-azygous collaterals (34). Yammamoto modified this procedure to be performed through the transabdominal approach only (35). The emergence of liver transplantation in the 1980s as a clinical reality has provided definitive treatment of the underlying liver disease and is the ultimate treatment for portal hypertension (36). Among all the surgical procedures performed, devascularization and shunt are the most common elective procedure. Several systematic reviews have indicated that devascularization and shunt is an effective procedure for the treatment of portal hypertension (37-39). However, The role of devascularization and shunt in portal hypertension remains a topic of debate (40). The choice of surgical treatment for these patients have to balance out the risks of recurrent bleeding, hepatic encephalopathy, and other complications.

In this meta-analysis, we collected eleven clinical studies that compared devascularization with shunt to investigate the advantages and disadvantages of the two surgical procedures in the treatment of portal hypertension, and evaluate their role in the elective and emergent settings. The heterogeneity of

different lesion sites, different lesion types, and different study types was overcome by sensitivity analysis to combine the data more effectively.

The esophagus lower extremity position is deep, the collateral circulation is rich, periphery also has the abdomen aorta, the diaphragm and so on the important internal organs. In practice, surgeon can encounter hyperblastosis, edema, vein conglobation, adhesion, and increased blood loss which make the operation more difficult. In such cases, it will be difficult to perform extensive devascularization, specially to interrupt the top tributaries of gastric coronary vein -perch rami esophagei and the rear gastric veins, after the operational procedure also can occur bleeds again (41-44). On the other hand, the procedure of devascularization can emphasize esophagus-fundus ventriculi vein backflow barrier, aggravate organization's dropsy and lacks the blood, the oxygen deficit. after the procedure, the gastric mucosal may bleed (45,46). The patients undergone shunt may not be faced with the above. Xie et al (23) reported that rebleeding rate is about 10% after a shunt but is very high to the extent of 30-40% after a devascularisation procedure, Our meta-analysis results are similar to it. The main reason of rebleeding after shunt are stress ulcer hemorrhage and anastomotic thrombosis. Rebleeding in shunt surgery is directly proportional to shunt occlusion rate. In case of rebleed after a shunt operation, endoscopic management of the varices is probably the best alternative (47).

Hepatic encephalopathy describes a chronic neuropsychiatric syndrome secondary to chronic liver disease. The mechanism of hepatic encephalopathy is unknown. Recent evidence supports the concept of neurochemical disturbances arising in the brain after detoxification of ammonia in the astrocytes (48). In patients with portal hypertension, hepatic encephalopathy often occurs following a surgical procedure. In our meta-analysis, the rate of hepatic encephalopathy in the devascularization group was significantly lower compared with the shunt group. This may be due to the change of portal vein blood flow. Shunt can results in a large number of portal vein blood flow bypassing the liver cells, then toxic substances such as ammonia, mercaptans, γ -aminobutyric acid) can not be metabolized and detoxicated, and enter into the blood circulation directly (49,50). Thereby the toxic effects on the brain may be increased.

Our meta-analysis further shows that the reduction of ascites was significantly different between study groups. The

mechanisms of generating ascites is reduced the effective blood volume from peripheral arterial vasodilatation (51-53). As a result, neurohumoral mechanisms and renin-angiotensin systems are activated, leading to sodium and water retention by the kidneys. The sodium and water retention manifests as ascites or edema. Increased hydrostatic pressure of portal hypertension leading to increased production, and transudation of hepatic and splanchnic lymph into the peritoneal cavity. Many literatures shows that the portal vein pressure after the shunt is significantly lower compared with the devascularization (54,55). It causes that the reduction of ascites after the shunt is more significant than those after devascularization.

Our meta-analysis revealed that the operative mortality rate of devascularization group was not significantly different from shunt group. Acute portal vein thrombus, severe infections, intraperitoneal massive hemorrhage including hemorrhage from pancreas tail vessels, splenic pedicle, or the short gastric vessels and errhysis from diaphragmatic position or spleen bed were the main reason of death. Some literatures reported that operative mortality varies between 15 and 90% depending upon the liver function (56,57). In Child-Pugh grade A operative mortality rate may be as low as 15%, but in Child-Pugh grade C, it may be as high as 90%. Treatment of underlying liver disease may reduce portal hypertension and prevent its clinical complications. Child-Pugh grade C, and failure to control early rebleeding are the variables most consistently found to predict 6-week mortality. Since most data in our studies do not include the evaluation about preoperative liver function, the correlation analysis between preoperative liver function and postoperative survival could not be performed.

Preservation of hepatocyte functions is a major determinant of long-term surgical outcome. The significant changes in some of the conventional biochemical tests on long-term follow-up may reflect late impairment of hepatocellular functions after surgical procedures (58,59). Some studies have reported that there were no difference among various surgical procedures for patients with portal hypertension in postoperative long - term survival time, our results are similar to it (19,60).

No single therapy has been rationally recognized as an ideal approach for all portal hypertension patients. The choice of therapy for these patients, then, must be based on the balance of risks between recurrent bleeding, encephalopathy, and hepatic failure (61). A shunt procedure is probably the best surgical method in extra hepatic obstruction with portal hypertension (EHPVO), for it improves survival significantly. However, in a cirrhotic with poor liver function surgery has high mortality, results in high incidence of encephalopathy and liver failure. In these patients a devascularisation procedure has lesser complications though has high rebleed rate.

Although we made these findings in this meta-analysis, there were two limitations. First, approach of devascularization including Haasab's operation, Sugiura's operation and selective pericardial devascularization. and shunt including various commonly done operations, such as portocaval shunt, proximal lienorenal shunt, distal lienorenal shunt, mesocaval shunt. However, our study was mainly based on the overall evaluation

of devascularization and shunt, and was difficult to make comments on specific procedure, which influenced the results of scientific and precise. Second, the clinical data were difficult to be completely randomized, allocated concealment, and double-blinded, so the researchers can not rule out bias in the interpretation of results.

With the advent of more high quality clinical research in the future, the limitations may be solved effectively.

Conclusions

Devascularization and shunt were widely used in treating portal hypertension with variceal hemorrhage, the two surgical procedures have different advantages and disadvantages respectively which reflected in postoperative complications and long term survival rate.

Conflicts of interest

There was no potential conflict of interest.

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