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Review: Partial Splenic Embolization Outcome on Liver Cirrhosis with Esophageal Varices

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Abstract

Introduction. Liver cirrhosis may be followed by complications such as esophageal varices for 30 days mortality rate up to 15-20%. Partial splenic embolism (PSE) or partial splenic embolization has been developed as a safe and effective alternative therapy for managing bleeding in esophageal varices. This study aims to determine the outcome of PSE in patients with liver cirrhosis with esophageal varices.
Method. In this review, the literature search proceeded on three online databases (Cochrane Library, MEDLINE (PubMed), and ScienceDirect) according to PRISMA protocol. Through selections, six articles were included, and all were the reports.
Results. Of six reports, three were focused on liver function tests, and the other three were focused on bleeding varices. All were comparing before and after embolization.
Conclusion. There is a significant difference in serum cholinesterase and a decreasing incidence of varices bleeding before and after PSE treatment. However, there was no significant difference in serum albumin before and after PSE.

Keywords: partial splenic embolization, liver cirrhosis, esophageal varices

Introduction

Liver cirrhosis is a common disease, with 112 million cases worldwide.[1] In Indonesia, liver cirrhosis developed in 21.1-46.9% of patients with a history of Hepatitis B and 38.6-73.9% of those with Hepatitis C.[2] The liver pathology designated with fibrosis and the formation of regenerative nodules.[3] Fibrosis is triggered by stellate cell activity, developing an abundance extracellular matrix in the space of Disse.[2] In turn, such pathology leads to the transformation and capillarization of the portal system. This condition leads to increased intrahepatic resistance that may retain portal blood flow, resulting in portal hypertension and complications, such as esophageal varices.[2]

Esophageal varices are the second most common complication of liver cirrhosis, with clinical manifestations of melena and hematemesis.[4] Bleeding esophageal varices have a high mortality rate, with 15-20% 30-day mortality.[5] Decreased liver function and esophageal varices bleeding are detrimental to the patient, and both are the management targets for liver cirrhosis patients with esophageal varices.[6]
Management of esophageal varices comprised of pharmacologic and nonpharmacologic approaches.[2] Some options commonly used in esophageal varices cases are endoscopic sclerotherapy, varices ligation, and trans jugular intrahepatic portosystemic shunt (TIPS).[6] However, both sclerotherapy and ligation do not treat the etiology of varicose vein, while TIPS is known to cause portal hypoperfusion and decrease liver function.[6]

Partial splenic embolization (PSE) is a relatively new method to be safe and effective for managing bleeding esophageal varices.[7] Embolization rate of 30-70% effectively reduces splenic parenchymal size, resulting in reduced portal blood flow and reduced incidence of bleeding due to esophageal varices.[7] Although PSE showed positive results, there are still complications related to PSE, such as splenic abscess, sepsis, and pneumonia.[8] However, the outcome of PSE remains unclear; thus, we reviewed this option.

Methods

The literature searching was carried out in online databases, i.e., Cochrane Library, MEDLINE (PubMed), and ScienceDirect, using keywords: "partial splenic embolization", "embolization rate 30-70%", "adult", "cirrhosis", "esophageal varices", "outcome", "liver function test", and "bleeding rate". Literature selection was performed according to inclusion and exclusion criteria. A meta-analysis, systematic review, randomized controlled trial, cohort study, case report, 2) Subjects with liver cirrhosis with esophageal varices who underwent PSE, 3) Studies on subjects who have previously experienced esophageal variceal bleeding, 4) English written, 5) No year limit for publication period, and 6) Available in full text. The exclusion criteria were the correspondence, editorial, or commentary. Selected articles were appraised critically for the study's validity, level of importance, and applicability. The level of evidence is determined according to the Oxford CEBM level of evidence 2011. All selected studies were case series reports; thus, they were appraised using the Joanna Briggs Institute, Faculty of Health and Medical Sciences, University of Adelaide, South Australia, Checklist for Case Series Studies form. The literature search proceeded according to the PRISMA (Figure 1).

Results

Through a literature search following PRISMA protocol (figure 1), six articles were included after screening, and all were the reports. Of six reports, three were focused on liver function tests, and the other three were focused on bleeding varices. All were comparing before and after embolization.

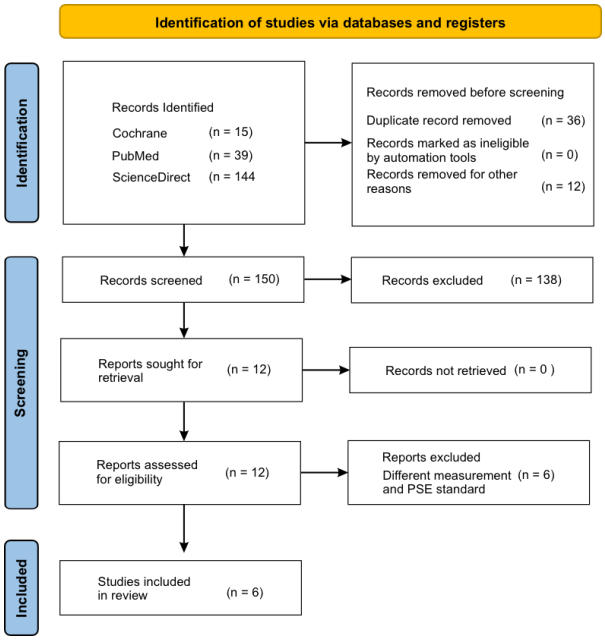

Figure 1. A literature search following PRISMA protocol found six eligible records.

Table 1 Summary of studies that meet the eligibility criteria

No	Author (year)	Samples	Study design	Intervention	Outcome	Results	Level of evidence
1	El-Gamal (2015)[9]	19 liver cirrhosis patients, 10 of which with esophageal varices	Case series report	Partial splenic embolization (PSE) with 50-70% splenic parenchymal embolization rate	Liver function test (albumin & cholinesterase) before, two months, and six months after the procedure	There was a significant increase in serum cholinesterase levels from 49.1±17.3 (IU/l) before PSE to 88±13.7 (IU/l) two months after PSE and 147±11.7 (IU/l) six months after PSE. PSE ($p < 0.001$) There was no significant change in the serum albumin level two and six months after the procedure	4
2	Hayashi (2013)[10]	Seventy–one liver cirrhosis patients, twelve of which with esophageal varices	Case series report	PSE with a 70% splenic parenchymal embolization rate	Liver function test (albumin & cholinesterase) before and one year after the procedure	There was a significant increase in serum albumin level from 3.40 ± 0.48 (g/dl) before PSE to 3.53 ± 0.47 (g/dl) one year after PSE ($p < 0.01$) There was a significant increase in serum cholinesterase level from 77 ± 26 (U/l) before PSE to 100 ± 50 (U/l) one year after PSE ($p < 0.001$)	4
3	Zhu (2009)[11]	Sixty-two liver cirrhosis patients, forty-seven of which with esophageal varices	Case series report	PSE with 50-70% splenic parenchymal embolization rate	Liver function test (albumin) before and after the procedure	There is no significant change in serum albumin values before and after the procedure in the short or long term	4
4	Pålsson (2003)[12]	Twenty-six patients, nineteen of which are diagnosed with liver cirrhosis. Esophageal varices bleeding is found in 24 of 25 patients.	Case series report	PSE with 30-40% splenic parenchymal embolization rate	Incidence of esophageal varices bleeding before and after the procedure	Bleeding incidence decreased significantly from a mean of 4.3 ± 2.9 before PSE to 1.1 ± 1.3 after the procedure ($p < 0.001$)	4
5	Sangro (1993)[13]	Forty patients, twenty–five of which are diagnosed with liver cirrhosis. Esophageal varices bleeding is found in 39 of 40 patients.	Case series report	PSE with 40-60% splenic parenchymal embolization rate	After the procedure incidence of esophageal varices bleeding	There is no incidence of esophageal variceal bleeding within 30 days after the procedure	4
6	Alwmark (1982)[14]	Twenty–five patients, nineteen of which are diagnosed with liver cirrhosis. Esophageal varices bleeding history (at least once) is found in 24 of 25 patients.	Case series report	PSE with 30-40% splenic parenchymal embolization rate	Incidence of esophageal varices bleeding before and after the procedure	Bleeding incidence decreased from an average of 2.12 episodes per year to 0.4 episodes per year after the procedure	4

Table 2. Summary of serum albumin and cholinesterase level before and after PSE

No	Author (year)	Serum albumin		Serum cholinesterase	
		Before PSE	After PSE	Before PSE	After PSE
1	El-Gamal 2015[9]	3.01±1.2 (IU/l)	Two months after PSE 2.99±0.8 (IU/L) Six months after PSE 3.31±0.13 (IU/L) (p <0.001)	49.1±17.3 (IU/l)	Two months after PSE 88±13.7 (IU/L) Six months after PSE 147±11.7 (IU/L) (p <0.001)
2	Hayashi 2013[10]	3.40 ± 0.48 (g/dl)	One year after PSE 3.53 ± 0.47 (g/dL) (p <0.01)	77 ± 26 (U/l)	One year after PSE 100 ± 50 (U/L) (p <0.001)
3	Zhu, 2009[11]	-	No significant changes in serum albumin in both short– and long-term follow up after PSE	-	-

Table 3. Bleeding incidence before and after PSE

No	Author (year)	Bleeding	
		Before PSE	After PSE
1	Pålsson, 2003[12]	Mean of 4.3 ± 2.9	Incidence decreased significantly to 1.1 ± 1.3, (p <0.001)
2	Sangro, 1993[13]	-	No incidence of esophageal varices bleeding in 30-day after PSE
3	Alwmark, 1982[14]	Mean of 2.12 episodes per year	Bleeding incidence decreased to 0.4 episodes per year

Discussion

Liver function tests (such as serum albumin and cholinesterase) are essential in liver cirrhosis complicated with esophageal varices. Kato et al. reported that PSE might improve liver function by lowering blood flow in the portal vein.[15] It will trigger compensation, namely increased flow in the hepatic artery, mesenteric artery, and mesenteric vein.[16] The change in circulation pattern increased nutrient-rich blood flow to the liver and improved liver function.[16]

Serum cholinesterase level reflects the liver's capability to synthesize protein, meaning that PSE could increase liver function.[9] In his study, El-Gamal found that the serum cholinesterase was significantly improved in the second follow-up (p <0.05), with the mean before PSE 49.1±17.3, two weeks after PSE increased to 88±13.7, and six months after PSE to 147±11.7. In addition, splenic volume after PSE showed a significant reduction in two weeks assessments using CT scan (p <0.001), with a splenic ablation rate of 53%-67% and nonsignificant change after six months of CT (p >0.05).

Meanwhile, Hayashi et al. found that PSE induces a sizeable increase in serum albumin and cholinesterase levels, reflecting the liver's ability to synthesize protein and lipid.[10] They found serum cholinesterase level was significantly improved from 77 ± 26 (U/l) before PSE to 100 ± 50 (U/l) (130 ± 65% of the pretreatment cholinesterase level) at one year after PSE (p < 0.001). In patients with preoperative splenic volume >600 mL (n = 25), serum albumin and cholinesterase were significantly improved from 3.46 ± 0.44 (g/dL) and 80 ± 25 (U/L) to 3.70 ± 0.52 (g/dL) and 121 ± 59 (U/L) one year after PSE (p = 0.009 and p <0.001, respectively). Then, in patients with infarcted splenic volume >450 mL (n = 23), serum albumin and cholinesterase were significantly improved one year after PSE compared with the pretreatment level (p = 0.016 and p <0.001). While liver transplant is the only effective management for patients with liver cirrhosis in the meantime, PSE could act as an alternative therapy for those without an available donor or limited financial capability.[10]

Zhu et al. showed a contrasting result, where there is no significant difference observed in both short-term and long-term liver function parameters.[11] This study was conducted on sixty-two consecutive patients with hypersplenism in cirrhosis who received partial splenic embolization. The patients were divided into three groups based on splenic infarction rate after partial splenic embolization: more than 70% in group A (n = 12), 50–70% in group B (n = 34), and less than 50% in group C (n = 16). The outcomes of this study were leukocyte and platelet levels, liver function parameters, and red blood cells after PSE. The results showed that after partial splenic embolization, the short- and long-term outcomes of leukocyte and platelet counts showed significant differences among the three groups (p < 0.001). In groups A and B, the leukocyte and platelet count after partial remained splenic embolization significantly higher than those before partial splenic embolization for two weeks to five years (p <0.05). In addition, there was no significant difference in liver function parameters, and red blood cell counts. However, Zhu also stated that only 54.8% of patients reached the 50-70% embolization rate, possibly affecting the result.[11] There was also difficulty controlling particle quantity for embolization, resulting in an embolization level of >70%, a risk factor for liver function decrease.[11]

These three studies were followed by other studies, such as Wang et al. and Lee et al., which showed that patients treated with PSE had significant differences. Their study focused on the outcome of a liver function, i.e., serum glutamic oxaloacetic transaminase (SGOT) and serum glutamic pyruvic transaminase (SGPT). They found that treatment with PSE differed significantly, with SGPT values decreasing considerably in all patients after two weeks of embolization. The improvement of SGPT values remains persisted until one year after PSE. In addition, three of four subjects (75%) with Child-Pugh grade B progressed to grade A two months after PSE. Wang et al., who assessed the outcomes, found that the incidence of variceal bleeding and overall survival found that PSE showed efficacy in preventing variceal recurrence, variceal bleeding, and prolonged overall survival.[18,19]
Another study by Palsson et al. focused on the bleeding incidence. Their study enrolled twenty-six severely ill patients who have been treated with a graded PSE a total of 52 times, mainly due to bleeding esophageal varices and thrombocytopenia. They found that the frequency of bleeding episodes from esophageal varices was significantly reduced from a mean of 4.3±2.9 and a median of 3.5 (1–11) before PSE to 1.1±1.3 and a median of 1.0 (0–4) after PSE (p <0.001). The mechanism remains undefined. Still, hepatic vein pressure decrease, portal vein pressure decrease, portal vein blood flow, and increased platelet are thought to reduce bleeding incidence.[12] In addition, other parameters as the outcomes in this study were platelet count levels and liver parameters (bilirubin, aspartate aminotransferase/AST, alanine aminotransfer–ase/ALT, and alkaline phosphatase/ALP). They found no significant

changes in liver parameters bilirubin, AST, or ALT. ALP showed a slight increase from mean of 7.2±5.9 (before treatment) to 9.2±6.7 (after treatment) during long-term follow-up (p = 0.009).[12] Sangro et al. also found no incidence of esophageal varices bleeding in the first 30 days after PSE.[13] Alwmark et al. found that the yearly bleeding incidence rate is decreased from 2.12 before PSE to 0.4 after PSE.[14]

Apart from esophageal varices in patients with chronic or recurrent bleeding, PSE might be indicated in some conditions such as hypersplenism and thrombocytopenia.[17] These two entities might be found in conjunction with liver cirrhosis and esophageal varices.[17] Zhu et al. showed that 34 liver cirrhosis with esophageal varices were thrombocytopenic, two of which were at a severe level (platelet count <20.000/mm^3).[11] Sangro et al. showed that 14 patients with esophageal varices were thrombocytopenic. Meanwhile, the other four studies concluded that each of their patients had both hypersplenism and thrombocytopenia.[13]

Despite the advantage, PSE complications include post-embolization syndrome (e.g., fever, abdominal pain, nausea, vomiting, loss of appetite), pneumonia, atelectasis, pleural effusion, splenic abscess, and renal failure and liver function impairment.[9] El Gamal et al. showed that post-embolization syndrome is the most common complication emerging after PSE. Fortunately, those symptoms might be managed conservatively.[9] Alwmark et al. found that 60% of patients complained of mild fevers lasting two to five days after PSE. 20% of post-PSE patients also complained of abdominal pain in the left hypochondriac area, which resolved with analgesics.[14] Apart from those two complications, pleural effusion (with or without atelectasis) might also be found in 50% of the patients.[14] In addition, no subjects complained, and most of the effusion was resolved in two weeks.[14] These results are consistent with a study by Lee et al., which also found that there were complications, namely fever in 10 (100%), pain in 8 (80%), and ascites in 1 (10%) of patients. Ascites occurred in the high embolization group.[18] Pålsson's study reporting 80% of patients experienced post-embolization syndromes such as fever and abdominal pain without severe complications.[12] Sangro and Zhu also reported similar complications. Zhu also reported six patients with severe complications instead.[11,13] Four patients complained of pleural effusion and massive ascites, while the other two patients complained of splenic abscess and portal vein thrombosis.[11] Severe complications in Zhu's study are caused by an embolization rate that exceeded 70% of his study.[11]

Conclusions

Partial splenic embolization (PSE) improves cholinesterase levels even though there is no significant change in serum albumin and decreases bleeding in cirrhosis with esophageal varices

Disclosure

Authors declare no conflict of interest

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