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REVIEW

Partial splenic artery embolization in cirrhotic patients

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Abstract

Splenomegaly is a common sequela of cirrhosis, and is frequently associated with decreased hematologic indices including thrombocytopenia and leukopenia. Partial splenic artery embolization (PSE) has been demonstrated to effectively increase hematologic indices in cirrhotic patients with splenomegaly. This is particularly valuable amongst those cirrhotic patients who are not viable candidates for splenectomy. Although PSE was originally developed decades ago, it has recently received increased attention. Presently, PSE is being utilized to address a number of clinical concerns in the setting of cirrhosis, including: decreased hematologic indices, portal hypertension and its associated sequela, and splenic artery steal syndrome. Following PSE patients demonstrate significant increases in platelets and leukocytes. Though progressive decline of hematologic indices occur following PSE, they remain improved as compared to pre-procedural values over long-term follow-up. PSE, however, is not without risk and complications of the procedure may occur. The most common complication of PSE is post-embolization syndrome, which involves a constellation of symptoms including fever, pain, and nausea/vomiting. The rate of complications has been shown to increase as the percent of total splenic volume embolized increases. The purpose of this review is to explore the current literature in regards to PSE in cirrhotic patients and to highlight their techniques, and statistically summarize their results and associated complications.

Key words: Partial splenic embolization; Cirrhosis; Liver disease; Thrombocytopenia; Leukopenia

Core tip: Splenomegaly is a common sequela of cirrhosis, and is frequently associated with decreased hematologic indices including thrombocytopenia and leukopenia. Partial splenic artery embolization (PSE) has been demonstrated to effectively increase hematologic indices in cirrhotic patients with splenomegaly. This is particularly valuable amongst cirrhotic patients that are not viable candidates for splenectomy. Although PSE was originally developed decades ago, it has recently received increased attention. Presently, PSE is being utilized to address a number of clinical concerns in the setting of cirrhosis, including: decreased hematologic indices, portal hypertension and its associated sequela, and splenic artery steal syndrome.

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INTRODUCTION

Portal hypertension in the setting of cirrhosis commonly leads to splenomegaly[1]. Additionally, cirrhosis is frequently associated with decreased hematologic indices, including thrombocytopenia and anemia. The prevalence of leukopenia amongst cirrhotic patients is more common than in the general population, and varies from 5% to 61%[2]. The pathogenesis of each hematologic deficiency in cirrhotic patients is multi-factorial in nature. Splenic sequestration, however, serves as a common

link; and is a contributing factor in the development of thrombocytopenia, anemia, and leukopenia in cirrhotic patients[3].

Decreased hematologic indices can have significant clinical ramifications. Thrombocytopenia increases a patient's risk of spontaneous bleeding, and may preclude surgical or endovascular interventions. Leukopenia decreases the patient's ability to overcome infection, and may serve as a contraindication to the use of chemotherapies in hepatocellular carcinoma. Anemia places a patient at increased risk should bleeding occur, may prevent surgical or endovascular interventions and can leave a patient dependent on transfusions[2].

Operative splenectomy can be used to treat splenomegaly in cirrhotic patients. While splenectomy is an effective treatment of splenomegaly in the setting of cirrhosis, it is not without risk[4]. Major complications include portal vein thrombosis and sepsis[4,5]. Additionally, some cirrhotic patients may be poor surgical candidates, thus necessitating alternative approaches to splenomegaly amongst some cirrhotic patients. In 1973, Maddison performed the first splenic artery embolization. A farmer with non-alcoholic cirrhosis presented with intractable esophageal variceal bleeding which was resistant to treatment with intra-splenic arterial infusion of vasopressin. In the setting of significant prior bleeding surgical intervention was contraindicated, and Maddison[6] performed an intra-arterial embolization of the splenic artery utilizing autologous clot as the embolic agent. The patient responded well and no complications were reported at 5 mo follow-up.

Despite Maddison's[6] early success, numerous complications of total splenic artery embolization were soon discovered[7]. Complications included splenic abscess, splenic rupture, pneumonia, septicemia, and death. In response to these complications, Spigos *et al*[8] transitioned to partial splenic embolization (PSE) paired with antibiotic prophylaxis and demonstrated significantly better outcomes. Soon partial splenic embolization gained popularity and served as a therapeutic option for cirrhotic patients with hypersplenism who were poor surgical candidates.

Amin published a 2009 prospective randomized trial of 40 cirrhotic patients who presented with hypersplenism, treating half with PSE and half with splenectomy. Over the six-month follow-up period cohorts receiving splenectomy and PSE both demonstrated a significant increase in their leukocyte and platelet counts. Patients treated with PSE had slowly decreasing leukocyte and platelet levels during the follow-up period, though they remained significantly above pre-PSE levels. Of the 20 patients treated with PSE one died of myocardial infarction within one day postop, one developed splenic abscess, and one developed a portal vein thrombus. Of the 20 patients treated with splenectomy, three patients developed portal vein thrombosis. The surgical cohort had longer procedure times, longer hospitalizations, required transfusions more frequently, and reported more postprocedural pain[9].

CLINICAL APPLICATIONS AND OUTCOMES OF PSE

In 2007 Koconis *et al*[10] published a review of partial splenic artery embolization in patients with portal hypertension, thoroughly summarizing the English language literature and addressing numerous utilizations of PSE. Benefits included increased hepatic protein synthesis, increased circulating platelet and leukocyte levels, and improvements in hepatic encephalopathy. The most contemporary study noted in the Koconis *et al*[10] review was published in 2005. We performed a review of the English language literature for PSE and focused on papers from 2005 through the present. Ultimately, eight studies were identified, and have been included in our review (Table 1)[9,11-17]. In 2012, Smith *et al*[18] also published an excellent review of splenic artery embolization, which followed a similar structure.

Hematologic indices

One of the primary goals of PSE is to increase circulating platelets and leukocytes. Resultantly, serum platelet and leukocyte counts are a natural choice for measuring procedural effectiveness. Prior to exploration of the data it should be noted that Zhu *et al*[14] reported trends in laboratory values following PSE *via* a line graph without citing specific values. Consequently, reported values from Zhu *et al*[14] represent approximations. Assessment of leukocyte and platelet values following PSE demonstrates a few trends (Table 1). First, within two weeks of PSE both platelet and white blood cell values significantly increase. This was found to be consistent in all included studies. Pre-PSE platelet values ranged from 37.4-56 K/μL, and at two weeks following PSE platelet values ranged from 80-240.7 K/μL. Leukocytes also increased, with pre-PSE values ranging 2.3-4.2 K/μL and then jumping to 4.0-12.6 K/μL at two weeks. A second trend, which was uniform across every study and cohort, is the consistent decline in both leukocyte and platelet values in the months and years following PSE. Though the rate of decline varied from study to study, the presence of a decline is consistent. Finally, there is a direct relationship between the percent of spleen which is targeted *via* PSE and the magnitude of the response of circulating platelets and leukocytes. By dividing their study into cohorts based upon the percent of spleen targeted, the 2009 Zhu *et al*[14] study further demonstrated this point. Simply put, the larger the volume of targeted spleen, the greater the resultant increase in circulating leukocytes and platelets.

PSE's ability to increase platelet and leukocyte counts has produced other clinical applications. Pegylated interferon and ribavirin induces sustained virological response in 42%-82% of patients with hepatitis C, however, thrombocytopenia is an absolute contraindication to the administration of therapy[19]. Over the past decade the use of PSE to increase platelet counts has facilitated antiviral treatment in patients who would have otherwise been too thrombocytopenic. Tahara completed a retro-

Table 1 Study demographics and outcomes of partial splenic embolization

Ref.	Year	Country	Study type	Number of Pts	Length of follow-up	Mean ± SD, platelet count prior to PSE in K/μL	Mean ± SD, WBC count prior to PSE in K/μL	Indication for PSE	Extent of spleen targeted	Mean ± SD, platelet count at 2 wk in K/μL	Mean ± SD, platelet count at 1 mo in K/μL	Mean ± SD, platelet count at 1 yr in K/μL	Mean ± SD, WBC count at 2 wk in	Mean ± SD, WBC count at 1 mo in K/μL	Mean ± SD, WBC count at 1 yr in K/μL
Kim *et al*[11]	2012	South Korea	Case series report	11	6-28 mo	Not provided	Not provided	All patients S/P OLT; 6/11 w/ thrombocytopenia, 5/11 w/refractory ascites	70%-80%	Not provided	Not provided	Not provided	Not provided	Not provided	Not provided
Elmonem *et al*[12]	2010	Egypt	Case series report	23	2 yr	41.3 ± 13.0	2.3 ± 0.47	Hypersplenism in Cirrhosis w/leukopenia and thrombocytopenia, no HCC, and no SBP	50%-70%	124.3 ± 23.9	115.8 ± 18.4	94.1 ± 12.9	8.26 ± 1.54	6.53 ± 1.74	4.62 ± 1.13
Zhu *et al*[14]	2009	China	Nonrandomized prospective trial	Total 62 Group A: 12 Group B: 34 Group C: 16	5 yr	Group A: 40.2 ± 13.0 Group B: 37.4 ± 12.3 Group C: 43.6 ± 11.7	Group A: 2.42 ± 0.44 Group B: 2.54 ± 0.57 Group C: 2.64 ± 0.4	Hypersplenism in Cirrhosis, w/ thrombocytopenia or neutropenia. No SBP, no Severe Jaundice	50%-70%	Group A: 170[1] Group B: 130[1] Group C: 80[1]	Group A: 130[1] Group B: 110[1] Group C: 70[1]	Group A: 100[1] Group B: 90[1] Group C: 50[1]	Group A: 7.5[1] Group B: 6.5[1] Group C: 4.0[1]	Group A: 6.0[1] Group B: 5.5[1] Group C: 3.7[1]	Group A: 4.5[1] Group B: 4.0[1] Group C: 3.0[1]
Amin *et al*[9]	2009	Egypt	Randomized control trial	Total 40 PSE: 20 SPL: 20	6 mo	PSE: 39.7 ± 9.7 SPL: 47.2 ± 10.3	PSE: 3.3 ± 0.7 SPL: 2.8 ± 1.1	Cirrhosis w/o bone marrow disease, ischemic heart disease, renal failure, malignancy, or medical unstability	50%	PSE: 211.5 ± 36.2 SPL: 240.7 ± 52.0	Not provided	Not provided	PSE: 12.6 ± 2.6 SPL: 7.7 ± 1.9	Not provided	Not provided
Zhu *et al*[16]	2008	China	Randomized control trial	Total 60 GF: 32 PVA: 28	3 yr	GF: 47.06 ± 14.85 PVA: 44.36 ± 16.67	GF: 2.62 ± 0.67 PVA: 2.57 ± 0.63	Hypersplenism in cirrhosis w/ thrombocytopenia or neutropenia. No SBP, no HCC, no hyperbilirubinemia	50%-70%	GF: 135.4 ± 28.1 PVA: 153.4 ± 37.1	GF: 113.2 ± 17.6 PVA: 125.4 ± 23.3	GF: 95.8 ± 13.9 PVA: 106.2 ± 17.2	GF: 6.6 ± 1.5 PVA: 7.5 ± 1.7	GF: 5.1 ± 0.9 PVA: 5.7 ± 1.2	GF: 4.2 ± 0.6 PVA: 4.7 ± 1.0
Hayashi *et al*[17]	2007	Japan	Nonrandomized prospective trial	42	1 yr	45 ± 11.7	2.9 ± 1.0	Thrombocytopenia caused by hypersplenism due to cirrhosis	70%-80%	Not provided	116 ± 51	103 ± 34	Not provided	Not provided	Not provided
Lee *et al*[15]	2007	China	Nonrandomized prospective trial	10	1 yr	56 ± 8.0	Not provided	Thrombocytopenia in setting of cirrhosis	20%-40%	192	Not provided	145	Not provided	Not provided	Not provided
N'Kontchou *et al*[13]	2005	France	Retrospective review	32	1-87 mo	48 ± 14	4.2 ± 1.6	Cirrhosis w/severe cytopenia/leukopenia preventing treatment or severe purpur, or painful splenomegaly	50%	Not provided	137.5 ± 77.4	Not provided	Not provided	6.5 ± 2.9	Not provided

[1]Data From Zhu *et al*[14,16] was extracted from a graph without exact values, values used are the authors closest approximations. PSE: Partial splenic artery embolization; SPL: Splenectomy; GF: Gel foam; PVA: Polyvinyl alcohol.

spective cohort study of 30 hepatitis C patients who were unable receive antiviral therapy secondary to thrombocytopenia and consequently were treated with PSE[20]. All 30 patients were able to receive therapy with pegylated interferon and ribavirin following a PSE-related increase in their platelet counts. A handful of other studies have demonstrated similar findings over the past decade[21-23].

Similar to the use of PSE to improve platelet counts prior to antiviral therapy in patients with hepatitis C, PSE has been used to increase hematologic indices to facilitate treatment of hepatocellular carcinoma. Hidaka *et al*[24] reported a 20 subject trial in which patients with multiple hepatocellular carcinoma lesions measuring less than 3 cm and platelet counts less than 80 received PSE to facilitate further treatment with radiofrequency ablation. Of the 20 patients, 18 demonstrated significant increases in prothrombin function as well as platelet counts, and ultimately were treated with radiofrequency ablation. A smaller study demonstrated PSE to be an effective preoperative therapy to increase platelet counts prior to hepatectomy[25]. Five patients received PSE prior to hepatectomy, while 23 patients received concomitant splenectomy with hepatectomy. The patients in the PSE arm received fewer blood transfusions and experienced fewer postoperative complications. Survival rates between the two arms were not significantly different.

Portal hypertension and associated sequelae

PSE has been demonstrated to improve portal hemodynamics in cirrhotic patients. PSE decreases splenic blood flow, splenic venous pressure, and portal venous pressure[26-28]. Additionally, in a trial of 7 patients with cirrhosis and hepatocellular carcinoma treated with a combination of transcatheter hepatic arterial embolization and PSE, Han *et al*[29] demonstrated a significant decrease in portal venous pressures following therapy. Interestingly, however, most studies which explored the hemodynamic effects of PSE did not demonstrate improvements in portal blood volume[26-28].

Portal venous hypertension is associated with numerous clinical manifestations. By improving portal hemodynamics, associated improvements in the sequelae of portal hypertension can be seen. Portal venous hypertension can lead to refractory ascites, and PSE has been found to decrease the incidence and magnitude of ascites[11]. Esophageal varices are also a common complication in patients with cirrhosis. Increased splenic arterial flow, splenic congestion, and portal venous pressures are all associated with an increased rupture risk of esophageal varices amongst cirrhotic patients[30,31]. By improving portal hemodynamics, PSE is associated with a decreased risk of variceal bleeding. Citing 4 studies, which included a total of 50 patients, Koconis *et al*[10] asserted that PSE decreased the annual incidence of variceal hemorrhage by 80%. Pålsson *et al*[32] performed PSE in 26 patients with history of bleeding esophageal varices and thrombocytopenia, 19 of whom had cirrhosis. The cohort demonstrated a decrease in the number of variceal bleeding episodes from 4.3 prior to treatment to 1.1 after PSE. Ohmoto conducted a study of 84 cirrhotic patients with large esophageal varices and thrombocytopenia[33]. 42 patients were treated with endoscopic variceal ligation (EVL) and 42 were treated with EVL and PSE. The combination therapy cohort demonstrated a reduced development of new varices from 88% to 67% ($P = 0.038$), decreased episodes of variceal bleeding from 34% to 17% ($P = 0.024$), and improved overall survival from 31% to 50% ($P = 0.042$). The literature also contains a case report of PSE being utilized to effectively address a 45-d decrease in hemoglobin secondary to diffuse gastric bleeding in portal hypertensive gastropathy[34].

PSE-related alterations in portal blood flow have also been shown to improve hepatic function[35]. Increased thrombopoietin, albumin, and cholinesterase levels as well as decreased alanine aminotransferase levels and total bilirubin levels have been demonstrated in cirrhotic patients following PSE[35,36]. These changes, however, are not uniform amongst all cirrhotic patients. Improved liver function following PSE is most pronounced in patients with initial splenic volumes greater than 600 cc[36]. In patients with hepatocellular carcinoma, PSE has been combined with transcatheter arterial chemoembolization (TACE) for promising results. In a comparison of patients treated with TACE and concomitant PSE *vs* TACE alone, those in the combined treatment cohort demonstrated improvements in platelet counts and hepatic reserve[37].

Splenic artery steal syndrome

Following liver transplant, approximately 5% of patients experience splenic artery steal syndrome (SASS). SASS is siphoning of arterial flow away from a transplanted liver due to a dominant splenic artery. While the hemodynamics of SASS are not completely understood, it is thought that increased resistance of the hepatic arterial bed and decreased resistance of the splenic arterial bed contribute to SASS[38]. High resistance of the hepatic arteries following liver transplant may be attributed to many causes, including a poorly compliant graft, post-operative edema, and subcapsular hematoma. Increased hepatic arterial resistance, when combined with low splenic arterial resistance due to splenomegaly, significantly increases splenic arterial flow while reflexively decreasing hepatic flow. Management of SASS may be surgical or endovascular. Surgical approaches include formation of an aortohepatic conduit or splenic arterial banding or ligation[38]. Proximal splenic artery embolization, *via* deployment of coils or an Amplatzer plug in the splenic artery immediately distal to the pancreatic and short gastric arteries, has been established as a safe and effective option in the non-surgical management of SASS[39-42].

COMPLICATIONS OF PSE

In exploring the morbidity and mortality associated with PSE, Koconis *et al*[10] reviewed 33 studies published be-

tween 1990 and 2005, and collectively representing 401 patients. In total, 15 major complications and 4 deaths were reported, for a major complication rate of 3.7% and a mortality rate of 1%. The rate of PSE-related complications consistently increased with volumes of splenic embolization near or greater than 70%[10].

PSE is not without risk, and the studies included in our review re-demonstrated many of the complications associated with the procedure (Table 2). Collectively, the studies we included demonstrate a direct relationship between the volume of spleen targeted for embolization and the severity of post-procedural complications. The 2009 Zhu *et al*[14] study further illustrated this point by subdividing patients in their study by percent of spleen targeted. The cohort receiving the greatest embolization (> 70%) also demonstrated the largest burden of complications. On the other hand, the patients with the least extensive embolization (< 50%) had the shortest hospital stays, lowest rate of embolization syndrome, and experienced no serious complications. Though not explicitly subdivided into cohorts based upon percent of spleen targeted during embolization, the 2008 Zhu *et al*[16] study also demonstrated an increased rate of complications among patients with embolization of > 70% of splenic volume. This correlates with the literature which has identified Child-Pugh class C and large splenic infarct volume as independent risk factors for complications with PSE[43]. Of the papers we included, Kim *et al*[11] had the smallest sample size, 11, and was an outlier in regards to their reported complications. Kim *et al*[11] reported 100% of their patients experienced post-embolization syndrome, but also reported zero serious complications. This was particularly surprising in that Kim *et al*[11] targeted 70%-80% of the spleen for embolization, more than any other study.

WORK-UP

Workup of a patient prior to PSE includes a thorough history and physical, routine laboratory studies, imaging, and prophylactic antibiotics and vaccinations. A basic laboratory panel including a CBC, PT/PTT, liver function tests, renal function tests, and a hepatitis panel is commonly noted[12,44,45]. While less frequently mentioned, antiplatelet antibody studies and bone marrow biopsies have also been described[8,37]. Abdominal computed tomography (CT) and ultrasound are useful to establish a splenic volume baseline and to screen for portal or splenic vein thrombosis[9,12-14,44-46]. Additionally, many authors endorse an upper gastrointestinal endoscopy in the workup prior to PSE to screen and/or treat esophageal varices[9,44,45]. Some authors, though not all, endorse the administration of pre-procedural broad spectrum antibiotics and/or vaccines. While Pneumovax 23 is the most commonly cited vaccination, the literature also makes note of H. influenza B and meningococcal vaccinations[18,46]. At our institution, broad-spectrum antibiotics are initiated just prior to PSE, and are continued for one to two weeks; additional vaccinations are not used.

TECHNIQUE

Numerous articles have described the technique of PSE, and generally concur in their description[9,12,46]. Vascular access is gained with a 5 French sheath in the femoral artery *via* the Seldinger technique. A 4 or 5 French cobra-type catheter is then utilized to isolate the celiac axis and splenic artery. Celiac and splenic angiography is performed to identify the distribution of splenic arteries, as well as document the presence of any collateral flow.

After mapping the anatomy of the celiac axis and the splenic artery, the catheter is secured at the site of embolization. Either a proximal or distal embolization may be performed. In the proximal, nonselective, approach the catheter is placed immediately distal to the origins of the pancreatic and short gastric arteries, and an embolic agent is released. Embolic agents are dispersed throughout the spleen and small, diffuse, randomized infarcts occur. In the distal, selective, approach, the catheter is advanced into a distal segmental branch of the splenic artery. The entire distal splenic segment is then embolized. Some authors believe sub-selection of the superior spleen is more likely to be associated with post procedural pneumonia and atelectasis, and therefore favor embolizing the inferior spleen; however, comparative studies have not been performed[18]. A microcatheter is preferred to secure access in the distal splenic segmental arteries. Of the contemporary studies reviewed for this paper, seven noted whether a distal or proximal approach was utilized. Six of the seven studies utilized a distal approach[12-15,44,47]. Though no randomized studies comparing distal and proximal PSE in cirrhotic patients have been completed, the majority of interventionalists report employing the distal approach. It should be noted, however, that the selection of a distal *vs* proximal approach may depend on the specific clinical scenario. Proximal embolization requires less time to accomplish and can be performed without use of microcatheter techniques. On the other hand sub-selecting distal splenic branches for embolization requires more time, but allows for greater precision in the percentage of splenic parenchyma that is targeted for embolization.

After identifying and securing the targeted vascular supply, embolization is performed. A variety of substances have been employed as embolic agents. Early descriptions of PSE mention the use of autologous clot. More contemporary approaches include gelatin sponge, polyvinyl alcohol particles (PVA), and tris-acryl gelatin microspheres. All of the above agents are typically delivered *via* a suspension containing contrast and, frequently, antibiotics. Of the studies reviewed, 14 noted the material used in embolization[9,12-18,33,44-48]. 8 of 14 used gel foam, 2 used tris-acryl gelatin microspheres, 2 used PVA particles, 1 used gelfoam and PVA particles in separate cohorts, and 1 used a combination of tris-acryl gelatin microspheres and PVA. Of the studies which reported

Table 2 Complications in partial splenic artery embolization

Ref.	Year	Country	Study type	Complication: Frequency of post embolization	Complication: Mean length of post embolization syndrome-days	Major complications: Total number	Persistant thrombocytopenia	Splenomegaly	Pleural effusion/ ascites	Variceal bleeding	Portal vein thrombosis	Bacterial peritonitis	Splenic abscess	PSE-related death	Repeat embolization required
Kim *et al*[11]	2012	South Korea	Case series report	100.00%	Not provided	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%
Elmonem *et al*[12]	2010	Egypt	Case series report	91.30%	Not provided	34.80%	4.30%	4.30%	8.70%	0.00%	4.30%	4.30%	4.30%	4.30%	4.30%
Zhu *et al*[14]	2009	China	Nonrandomized prospective trial	Total 85.5% Group A: 100% Group B: 91.2% Group C: 62.5%	Group A: 13 Group B: 7 Group C: 3	Total 14.5% Group A: 50% Group B: 8.8% Group C: 0%	Total 0% Group A: 0% Group B: 0% Group C: 0%	Total 0% Group A: 0% Group B: 0% Group C: 0%	Total 4.8% Group A: 16.6% Group B: 2.9% Group C: 0%	Total 1.6% Group A: 8.3% Group B: 0% Group C: 0%	Total 1.6% Group A: 8.3% Group B: 0% Group C: 0%	Total 1.6% Group A: 8.3% Group B: 2.9% Group C: 0%	Total 1.6% Group A: 8.3% Group B: 0% Group C: 0%	Total 1.6% Group A: 8.3% Group B: 0% Group C: 0%	Total 0% Group A: 0% Group B: 0% Group C: 0%
Amin *et al*[9]	2009	Egypt	Randomized control trial	Not provided	PSE: 2.1 (0.4) SPL: 4.3 (1.1)	PSE: 25% SPL: 25%	PSE: 0% SPL: 0%	PSE: 0% SPL: 0%	PSE: 10% SPL: 10%	PSE: 0% SPL: 0%	PSE: 5% SPL: 15%	PSE: 0% SPL: 0%	PSE: 5% SPL: 0%	PSE: 5% SPL: 0%	PSE: 0% SPL: 0%
Zhu *et al*[16]	2008	China	Randomized control trial	GF: 90.6% PVA: 100%	GF: 6.4 (3.6) PVA: 7.6 (2.8)	GF: 25.0% PVA: 21.4%	GF: 0% PVA: 0%	GF: 0% PVA: 0%	GF: 9.4% PVA: 10.7%	GF: 3.1% PVA: 3.6%	GF: 3.1% PVA: 7.1%	GF: 6.3% PVA: 0%	GF: 3.1% PVA: 0%	GF: 3.1% PVA: 0%	GF: 0% PVA: 0%
Hayashi *et al*[17]	2007	Japan	Nonrandomized prospective trial	100.00%	Not provided	11.90%	0.00%	0.00%	9.50%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%
Lee *et al*[15]	2007	China	Nonrandomized prospective trial	100.00%	Not provided	10.00%	0.00%	0.00%	10.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%
N'Kontchou *et al*[13]	2005	France	Retrospective review	78.10%	14	28.10%	3.10%	0.00%	6.30%	0.00%	6.30%	0.00%	6.30%	6.3%[1]	3.10%

[1]Both deaths in the trial were in patients with > 70% splenic embolization. PSE: Partial splenic artery embolization; SPL: Splenectomy; GF: Gel foam; PVA: Polyvinyl alcohol.

use of tris-acryl gelatin microspheres, one study reported using 500-700 μm microspheres, another reported using 300-500 μm microspheres, and the final study noted using microspheres ranging 200-1000 μm[13,14,47]. In 2008 Zhu *et al*[16] published a study comparing the results of gelfoam embolization with PVA. Ultimately, the study demonstrated a slightly greater increase in platelet and leukocyte counts with PVA as compared to gelfoam. The study, however, also demonstrated greater frequency and magnitude of post-embolization syndrome amongst patients embolized with PVA as compared to gelfoam. At this time, no specific agent has clearly been established as a superior embolic agent in PSE.

Although coils and Amplatzer plugs are more commonly used to perform proximal splenic artery embolization (SAE) in the setting of trauma, recently, a small number of studies have highlighted the effectiveness of proximal SAE among patients with portal hypertension. Though only reporting use in six patients, Quintini *et al*[49] demonstrated coil-induced proximal SAE to be a safe and effective treatment for refractory ascites in patients with previous orthotopic liver transplants. Additionally, Zhu *et al*[50] performed a retrospective review of Amplatzer plugs *vs* coiling in SAE. While the majority of the patients included in the study received SAE secondary to splenic artery steal syndrome, one eighth of the subjects were included secondary to portal hypertension.

Some authors set their initial target at embolization of 50%-70% of the splenic blood volume. Others, however, embrace a more conservative approach and will target 30%-40% of the spleen with the expectations of repeating the embolization with a higher target area (up to 70%) if clinical symptoms do not respond to initial treatment. In an attempt to avoid embolization of a greater portion of the spleen many authors report an iterative process of delivering small aliquots of embolic material, and following each aliquot with an angiogram to determine the extent of embolization. The increased number of iterations allows providers to more precisely target a specific percent of splenic

tissue, without excessively embolizing the spleen.

POST PSE CARE

The vast majority of patients experience some degree of pain, fever, and nausea/vomiting following PSE. These symptoms are collectively described as post-embolization syndrome[44]. Our review of the recent literature found that post-embolization syndrome is reported in 78.1%-100% of patients undergoing PSE (Tables 1 and 2). Patients are frequently hospitalized to receive supportive care for 24-48 h or until the post-embolization syndrome has resolved. Care is centered on antibiotic prophylaxis and pain management. Many antibiotics including amoxicillin/clavulanate, ofloxacin, phenoxymethylpenacillin, cotrimoxazole, cefoperazone, and erythromycin have been described in the literature. Post-procedural analgesia typically involves a combination of NSAIDS, scheduled morphine, and patient controlled analgesia.

Occasionally, patients experience more serious complications (Table 2). Severe complications are reported in 0%-34.8% of patients following PSE. The most common severe complication is pleural effusion and/or ascites, and can be treated with thoracentesis or paracentesis respectively. Other common morbidities include portal vein thrombosis and splenic abscess. Most practitioners advocate the use of anticoagulation in the treatment of post-PSE portal vein thrombosis, though Zhu *et al*[50] reported resolution of thrombus with watchful waiting. Presentation of splenic abscess has been reported between 10 d to 3 mo following PSE. Additionally, the majority of PSE-related deaths involve the development of a splenic abscess. Consequently, if post-procedural fever or other signs of infection develop, the threshold for ordering follow up imaging, usually with CT, should be low. Furthermore, due to the risks of splenic abscess, and the extended window in which it may develop, all PSE patients should be educated on the signs and symptoms of splenic abscess prior to the procedure and again upon discharge. Treatment of post-PSE splenic abscess includes percutaneous drainage and antibiotics, or occasionally, splenectomy. Mortality rates range from 0%-6.3% of patients undergoing PSE.

Follow up abdominal CT scan is frequently utilized in the first several weeks after PSE to confirm the percentage of infarcted splenic tissue. In the months following PSE, the spleen gradually decreases in size, but patients are usually followed clinically rather than monitoring with imaging, unless a complication is suspected.

CONCLUSION

PSE is an effective procedure in cirrhotic patients. It decreases rates of ascites and esophageal variceal bleeding while increasing hematologic indices. PSE can be an effective option for patients who are not surgical candidates and for whom splenectomy is contraindicated. In such patients, PSE may provide the necessary increase in hematologic indices to facilitate other treatments.

Still, PSE is not without its shortcomings. There are numerous morbidities associated with PSE. At the very least, almost all patients will experience post-embolization syndrome and will require post-procedural hospitalization. Several studies demonstrate major complication rates up to 15%-30% following PSE. The studies included in our review represented 260 patients, and collectively experienced a serious complication rate of 20.0% following PSE. In our study we included pleural effusions and ascites as major complications, and these accounted for 19 of the 52 complications. If we were to not include pleural effusions and ascites as major complications the average complication rate would have been 12.7%. Additionally, PSE-related mortality is consistently reported in 0%-6% of patients. The 260 patients included in our review collectively averaged a 2.3% mortality rate. In efforts to minimize PSE-related complications, targeted splenic volume for PSE ought to be below 70%. While an improvement of leukocyte and platelet counts has proven persistent, the magnitude of the increase consistently declines in the months and years following PSE.

Although PSE may not be appropriate in all cirrhotic patients, in the appropriate clinical context it is an efficacious tool which may provide clinical benefit for patients who otherwise may not be candidates for other medical and surgical interventions.

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