ISSN NO. 2320-5407

Journal homepage: http://www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH

RESEARCH ARTICLE

Favorable Short-term Outcome after Partial Splenic Embolization (PSE) in Patients with Cirrhotic Liver Disease and Severe Hyperspenism

Salah El-Gamal, [1] **Yahia Z. Gad,**[1] **Osama El-Baz,**[2] **Talal Amer** [3]
Departments of Internal Medicine,[1] Clinical Pathology,[2] Radiology, [3] Mansoura University, Mansoura, Egypt

Manuscript Info

Manuscript History:

Received: 15 January 2015
Final Accepted: 22 February 2015
Published Online: March 2015

Key words:

Corresponding Author

Salah El-Gamal

Abstract

Backgroud/aims: PSE is an interventional radiological alternative to surgical splenectomy (SN) used for management of hyperplenism in cirrhotic patients and lacks the disadvantages of SN. Despite a significant prevalence of cirrhotic liver disease in Nile Delta, Egypt, sparse PSE-related local data motivated us to investigate the safety and efficacy of PSE in Egyptian cirrhotics with hypersplenism.

Patients and methods: A total of eligible 19 cirrhotic patients with severe hypersplenism were enrolled after giving well-informed consent. Patients were subjected to thorough history taking, clinical examination, laboratory, radiological evaluation and upper gastrointestinal endoscopy. Complete blood picture (CBC), serum cholinesterase level, liver biochemistry tests, serum creatinine, prothrombin time, blood and/or ascitic fluid cultures were done once before the procedure, and twice at 2 weeks, 6 months interval post-PSE

Results: the embolization technique was done successfully to all patients with a splenic ablation rate of 50-70%, confirmed at 2 wks' post procedure CT with no further repeated sessions on follow-up. PSE significantly improved platelet counts and the other studied hematological parameters. Minor complications occurred in the PSE group while major ones were significant in another age- sex-, Child class-matched SN group. No reported deaths in both groups.

Conclusions: our results revealed that PSE could safely and effectively treat cirrhotic patients with hypersplenism. Controlled splenic parenchymal ablation significantly lowers post-PSE morbidity and avoids the disadvantages of SN.

Copy Right, IJAR, 2015,. All rights reserved

INTRODUCTION

Hypersplenism is a well-known complication of portal hypertension in patients with liver cirrhosis that can result in thrombocytopenia and/ or leukocptopenia.[1] It results from increased pooling and / or destruction of the corpuscular elements of the blood by the enlarged spleen.[2] The resulting severe peripheral cytopenia may cause severe haemorrhagic episodes and / or precludes further treatment options as interferon therapy, anti-neoplastic chemotherapy or major surgery.[3-6]

There are several possible approaches to management of hypersplenism including; SN, ligation and banding of the splenic artery, percutaneous placement of a narrowed stent in the splenic artery, PSE.[7-12] SN remains for long the traditional, definitive therapy until PSE has become the first line therapy for hypersplenism in many institutions, and has been proposed as an effective alternative to SN for improving blood cell counts.[6,11-13] In addition to absent risk of overwhelming post-SN infection,[14] PSE can eliminate the splenic hyperdynamic component of portal hypertension; decrease the functional splenic mass, together with the preservation of the transhepatic portal flow.[15-18]

Despite the significant prevalence of liver cirrhosis-related hypersplenism in Egypt, PSE-related local data are still sparse. Thus, this work was designed to investigate the safety and efficacy of PSE in Egyptian patients with cirrhotic liver disease and hypersplenism.

Material and Methods

From June 2010 to June 2012, cirrhotic patients with hypersplenism, admitted from outpatient Medical and Surgical Clinics of Mansoura University Hospitals, were evaluated for possible enrolled.

We excluded patients with collagen vascular diseases, ischemic heart disease, uncontrolled diabetes mellitus, malignancy, renal insufficiency, hypocellular, or infiltrated bone marrow, spontaneous bacterial peritonitis, or marked jaundice and other features of advanced liver disease. The criteria to diagnose hypersplenism include splenomegaly, variable combinations of anemia, leucopenia and/ or thrombocytopenia, a normal or compensatory hypercellular bone marrow and significant improvement in the peripheral blood picture following SN.[19] The diagnosis of hypersplenism was made by the clinical, laboratory data, ultrasonography and bone marrow biopsy. Severe hypersplenism is defined as platelet count

$< 70x10^3/mm^3$ and/ or white cell count $< 2\ x10^3/mm^3$in patients with splenomegaly [20]

Thus, an eligible 19 cirrhotic patients with severe hypersplenism, thrombocytopenia ‹ 70,000/uL (range 55,700-67,100 /uL) with / or without neutropenia were enrolled after giving a well-informed consent. The study protocol was reviewed and approved by the local ethical committee of Mansoura Faculty of Medicine.

All selected patients were subjected to thorough history taking, clinical examination, laboratory, radiological evaluation and upper gastrointestinal endoscopy. Patients' functional hepatic reserve was scored according to the Child-Pugh system. CBC, serum cholinesterase level, liver biochemistry tests, serum creatinine, prothrombin time, blood and/or ascitic fluid cultures were done once before the procedure, and twice at 2 weeks, 6 months interval post-PSE. Enhanced abdominal CT was done just before, and 2 wks, and 6 months after the PSE procedure to assess the splenic volume.

The embolization technique was done under strict aseptic precautions with separate trays for the embolization solution and the angiographic equipment. All patients started antibiotic prophylaxis 6 hrs before the procedure and continued for 5 days thereafter. Intravenous sedation and local xylocaine 2% anaesthesia were applied to all patients. A percutaneous right common femoral artery approach with a modified Seldinger's puncture technique was used for superselective splenic artery catheterization.[21] A preliminary splenic arteriography was performed to visualize the splenic arterial distribution. Distal to the distribution of the pancreatic branches at the hilum of the spleen, the catheter is then, introduced to minimize the risk of pancreatitis. Polyvinyl alcohol sponge particles, measuring 250-355Um (Boston Scientific Corporation), was gently injected slowly, in small amounts, to one or two of the polar splenic arteries to achieve complete stasis, as visualized under fluoroscopic guidance, together with moderate slowing of the splenic blood flow.[22] Controlled embolization of 50%-70 of the splenic parenchyma is the target, once reached, the embolization procedure is terminated.[23,24,25] The extent of embolization can be assessed by observing the degree of peripheral amputation of the segmental branches by digital substraction angiography. Post-embolization angiography was done to demonstrate the non-visualized areas of the spleen due to occlusion of its arterial supply. Also, post-embolization CT scanning with contrast was done to evaluate the degree of splenic infarction and to correlate with the angiographic findings. For pain control, paracetamol or pentazocine was given to all symptomatic patients.

Based on CT images, pre-PSE splenic volume and 2 wks' post-PSE residual volume were measured and calculated on a 3.1 workstation (GE medical systems, Milwakee, WI, USA) using volumetric analysis software. The infracted splenic volume (mL) was obtained by subtracting the post-PSE residual volume from the pre-PSE splenic volume. The splenic infarction rate (%) = the splenic infracted volume/the pre-PSE splenic volume x100%.

Post-PSE complications are: a) major complications defined as complicated disease requiring surgical or interventional treatment or a prolonged postoperative hospital stay of more than 30 days, and included splenic abscess, splenic rupture, pneumonia, refractory ascites, pleural effusion, variceal bleeding, and liver failure. b) Minor complication had minimal consequences and could be tolerated by patients or treated using conservative methods, including post-embolization syndrome, abdominal fullness and loss of appetite. [26]

Post-PSE complications were recorded and compared with that of another group (n. =19) (age-, sex- and Child's class-matched) where SN with / or without devascularization and left gastric ligation, had been performed during the same study period. Supportive in-hospital care continues to all patients until they have significantly recovered from complications whether major or minor.

Statistical analyses were performed by using statistical software, (SPSS, V.15; SPSS Inc. Chicago, IL, USA). Student's *t*-test and x^2- tests were used to compare variables as appropriate. A *P* value of ≤ 0.05 was considered statistically significant.

Results

During a 2-years' study period, a total of eligible19 patients (12 males and 7 females; with an age range 39-47 year), with liver cirrhosis [Child class A (n. =16), Child class B (n. =3)] and severe hypersplenism and platelet counts ‹ 70 $x10^3/mm^3$, were enrolled. Technically, PSE has been successfully performed in all patients (n. =19) with a hospital stay of 4-6 days and no mortality in the short-term follow-up period. Patients' demographics and clinical presentations are displayed in Table 1 with dominant bleeding features.

Compared with the baseline investigations, PSE had significantly improved the platelet and total leukocyte counts at the 2wk's and 6 month's samplings while hemoglobin level gradually increased to reach a statistically significant level on the second follow up testing. Serum cholinesterase level significantly improved in the second follow-up samples ($p < 0.05$). The other blood biochemistry tests were not significantly changed. Post-PSE splenic volume showed significant reduction after 2 wks' CT scanning assessment (*P*- value < 0.001), with a splenic ablation rate of 53%-67% and non significant change after 6 month CT (*P*- value >0.05) (Table 2).

The indices of humoral immunity were within their normal range while high-sensitivity C-reactive protein (hs-CRP) was significantly decreased ($p < 0.01$) as shown in Table 3.

Regarding post-procedure complications, post-PSE ones were compared with that of another group (n. =19) (age-, sex- and Child's class- matched) where SN with / or without devascularization and left gastric ligation, had been performed during the same study period (2 years), severe complications were significant in post-SN group while post-PSE patients had more minor complications, controlled by simple analgesics, with average patients' tolerability. No procedure-related deaths were recorded (Table 3). Patients did not need further repeated PSE sessions during follow-up. Data related to blood transfusion requirements, hospital stay (days) and procedure time (min) were statistically significant in post-SN group than post-PSE one (*P*< 0.001, < 0.05, < 0.001; respectively)

Tables

Table 1: Patients' characteristics (n.=19)

Parameter	No.(%)
Gender(M/F)	12(63.16%)/7(36.84%)
Clinical presentation:	
Pallor	7(36.84%)
Easy fatigability	6 (31.85%)
Ecchymosis	9(47.37%)
Epistaxis	5(26.31%)
Recent history of haematemesis	3(15.79%)
Left hypochondrial pain	11(57.89 %)
Liver size:	
Reduced liver span/ average size	13(15.79%)/6(31.58%)
Splenomegaly:	
Mild/moderate/huge	5(26.31%)/14(73.68%)/0(0%)
Child-Pugh grading:	
A/B/C	16(84.21%)/ 3(15.79%)/0(0%)
Etiology of cirrhosis	
HCV,HBV, Both, Others	6 (31.85%)/ 5(26.31%)/3(15.79%)/ 5(26.31%)
Bone marrow biopsy:	
Hypercelluar/normocellular	15(78.94%)/4(21.04%)
GIT endoscopy:	
No varices / +ve gastroesophgeal vx	9(47.37%)/10(52.63%)

Table 2: Pre- and post-PSE laboratory and volume changes

Parameter	Pre-PSE	2 weeks post-PSE	6 months post-PSE
Platelet count ($x10^3/mm^3$)	37.18±1.99	249.11±23.98*	231.37±21.56*
Haemoglobin (gm/dL)	10.3±1.11	10.9± 1.16	12.78±1.87**
Total leucocytic count ($x10^3/ mm^3$)	3.22±0.8	11.98±3.2*	6.71±2.3**
Cholinesterase (IU/L)(28-160)	49.1±17.3	88±13.7	147±11.7**
Serum albumin (gm/dL)	3.01±1.2	2.99±0.8	3.31±0.13
Serum bilirubin (mg/dL)	1.77±0.94	2.07±1.03	1.09±0.05
Alanine aminotransferase(ALT)(IU/dL)	52.0±9	76±6	47.0±1
Aspartate aminotransferase(AST)(IU/dL)	49.0±7	54±5	45.0±2
INR	1.2±0.2	1.4±0.7	1.1 ±0.3
Splenic Volume (cm^3)	1833±98 (897-2097)	607±87* (503-989)	611±81 (507-994)

* *P*- value < 0.001
** *P*- value < 0.05

Table 3: Pre-and post-PSE immunologic changes

Parameter	Pre-PSE	6 months post-PSE
C3 (mg/dL)(86-160)	112±13	113±16
C4 (mg/dL)((17-45)	24±1.9	25±5.5
IgA (mg/dL)(110-410)	297±11	301±77
IgG (mg/dL)(870-1700)	1334±78	1399±97
IgM (mg/dL) (M:33-190, F:46-260)	111±16	121±39
Hs-CRP(ng/mL)	774±67	439±92*

**P*- value < 0.001

Table 4: Post-procedure complications

Parameter	Post-PSE (n.=19)	Post-SN (n.=19)
Major complications:		
Left sided pleural effusion and/or pneumonia	1(5.26%)	1(5.26%)
Atelectasis	1(5.26%)	2(10.53%)
Portal / mesenteric vein thrombosis	0(0 %)/0(0%)	3 (15.79%)/ 1 (5.26%)
Encephalopathy	0 (0 %)	2 (10.53%)
Ascites	2 (10.53%)	3 (15.79%)
Sepsis	0 (0%)	4 (21.04%)
Haematemesis	0 (0%)	2 (10.53 %)
High fever	1 (5.26%)	4 (21.04%)
Severe abdominal pain	0 (0%)	19 (100%)*
Minor complications:		
Nausea	17 (89.47%)*	3 (15.79%)
Vomiting	11 (47.49%) *	2 (10.53%)
Wound haematoma	1 (5.26%)	2 (10.53%)
Mild to moderate abdominal pain	19 (100%)*	0(0%)

**P*- value < 0.001

Discussion

Hypersplenism occurs in 30%-70% of patients with cirrhotic liver disease.[20] SN is the traditional treatment, but is not devoid from perioperative and post-operative complications.[13] Thus, managing cirrhotic patients with poor hepatic reserve, functions, and significant operative risks, would have urged clinicians to explore a safe, effective

and optimal strategy tackling hypersplenism-related peripheral cytopenia and their significant clinical implications.[4-6]

PSE is a new non- surgical interventional radiological method for treatment of hypersplenism secondary to portal hypertension.[27] Peripheral occlusion of the splenic arterial supply by PSE resuls in ischemic necrosis of a targeted portion of the splenic parenchymal tissue, followed by a decrease of the splenic size with subsequent improvement of hypersplenism. In cirrhotic patients, thrombocytopenia may be associated with spontaneous hemorrhagic episodes[3,28] and is generally explained by increased platelet pooling in the enlarged hyper functioning spleen,[29] impairment of platelet production from bone marrow,[30] decreased thrombopoietin production[31] and abnormalities in platelet membranes.[32]

Several studies[24,25,28,33] suggest that permanent splenic parenchymal ablation of 50-70% is associated with clinical benefits, sustained on long-term follow-up and minimal tolerable complications. On the other hand, Numata et al suggested that post-PSE induced splenic infarcts of only 30%-40% could improve hyperslenism; while 50%-60% would favorably improve the portal venous pressure.[34]
To study the effects of PSE, we enrolled eligible 19 thrombocytopenic (100%), cirrhotic patients with severe hypersplenism and presented mainly with bleeding tendency manifestations. PSE was successfully performed to all patients with the aim of controlled ablation of 50-70% of the splenic parenchyma reached and confirmed on 2 wks' follow-up CT scanning ($P < 0.001$).

Regarding post-PSE laboratory changes, a statistically significant elevation of the platelet and the leukocytic counts was observed. RBCs count showed also significant rise at the 2 wks' and 2 months' post-PSE when compared with the initial pre-PSE values (Table 2). The increased platelet count may be due to the decreasing levels of platelet-membrane associated immunoglobulin G and the reduced the sequestering splenic size; thereby decrease trapping of thrombocytes in the embolized spleen.[13] Giorgio et al suggested PSE-related direct hematopoietic activity that probably have improved the humeral splenic medullary function [35] However, the activation of the body defense mechanisms against the splenic infarct tissue may explain the observed post-PSE leukocytosis.[36]

Several studied have reported that PSE could improve the liver functional reserve[34,37,38,39] and individual liver functions [40,41]by and through immunologic mechanisms and hemodynamic changes. [42] Increased platelet-derived factors, decreased inhibitory splenic-derived factors, as TGF-B for liver regeneration could be suggested. [43] PSE decreased splenic blood flow , total portal blood flow and relatively increased superior mesenteric blood flow with subsequent decreased hepatic venous congestion and increased hepatic supply of gut-derived cytokines; all of these might contribute to hepatic functional improvement.[44-46] Despite these data, PSE did not significantly improve AST, ALT, INR, prothrombin time in our studied cirrhotic patients (n. =19). However, our findings are in accordance with some earlier reports.[43,47] Patients' selection criteria, with different Child–Pugh functional status and liver reserve are probable considerable factors. Also, different ablation parenchymal targets and sizable splenic volumes, could have variable contributions.

Serum cholinesterase level reflects the protein synthetic ability by the liver and may be affected by the lipid status. [48] Low serum cholinesterase level is associated with poor surgical outcome after liver transplantation. [49] In our work, serum cholinesterase level was significantly improved in post-PSE follow-up samples. Hayashi et al found similar finding and suggested that PSE potentially could be a therapeutic procedure, in elective cirrhotic patients, particularly those with a large preoperative splenic volume, to improve individual liver functions prior to hepatic transplantation. [48]

The normal human spleen performs several important physiological and immunological functions. [50] Previous studies[51,52] demonstrated that PSE efficiently improve hypersplenism-related manifestations and could reserve some splenic tissue reminants to maintain satisfactory immune functioning.
The spleen represents one fourth of the total lymphatic mass and has several important immunologic and critical functions as it serves as a biological filter for bacterial clearance. Also, is essential for tuftsin; a leucophilic immunoglobulin and many other antibody productions after antigenic challenge,[53,54] thus, when these functions are lost after SN, post-operative overwhelming sepsis is the cost.

In our work, the studied markers of humoral immunity were within normal limit values, at the 2 wks' and 2 months' post-PSE samples, denoting a preserved adequate functional splenic tissue with subsequent immunologic competence that would efficiently safeguard against the occurrence of post-procedure infection and would probably nullify the need for further prophylactic measures that was necessarily obligated against post-SN overwhelming sepsis. The significantly elevated hs-CRP may denote a possible underlying subclinical infection[55,56] that might have improved under the effect of in-hospital broad-spectrum antibiotic coverage.

Severe complications were reported in initial trials of PSE, where total ablation of the spleen was practiced by Maddison 1973.[18] Over-embolization of the spleen was associated with a deleterious outcome in subsequent experiences.[12] Moreover, bacterial contamination may supervene on top following massive splenic infaction, thus, adding more complications. [3,57] However, post-PSE morbidity and mortality were significantly reduced by refinement of the splenic embolization method with limited volume under aseptic technique, together with antibiotic prophylaxis. [57,.58]

In our work, avoiding the distal branch of the splenic artery, have rendered the embolization technically safe, together with controlled ablation of 50-70 % of the splenic parenchyma and thus, the procedure was completed successfully in all patients, with no reported major complications or deaths

Post-embolization syndrome (PES) is the most common side effect of PSE. [59] It is unavoidable, self-limiting, benign phenomenon that indicates local intravascular necrosis and / or extensive tissue necrosis.[37] Gut symptoms, left sided abdominal pain, fever and malaise are the components of this syndrome. PES occurred in 100% of our participants compared to 78% -100% of previously described. [60,61]

PES is the most frequent minor complication that occurred in our post-PSE patients that were controlled successfully by the conservative measures.

SN can eliminate hypersplenism-induced blood cell destruction, but the incidence of post –SN complications is 9.6-29.6% whether open or laparoscopic SN is performed. [7,62,63] In addition to increased long-term risk of post-SN septic complications. [7,63]

However, major complications were evident in our post-SN group, where severe abdominal pain was the most significant (*P*- value < 0.001). Portal/mesenteric vein thrombosis occurred in (15.79%, 5.26%) of cases. Both could be explained by the occurrence of severe post SN thrombocytosis. [64] Portal venous slowing following removal of splenic venous component after SN may contribute to portal vein thromboses; a data documented as a 20-30 % incidence in previous reports. [65-67]

Regarding the infarction rate, the extent of embolization seems to be critical in the long-term efficacy of PSE. An embolization rate of ≤ 50% of the splenic mass was almost invariably associated with relapse of hypersplenism.[68] In contrast, relapse did not occur among patients who had ›50% of the spleen embolized.[6] The recurrence of thrombocytopenia seems to be dependent on the severity of the underlying liver pathology, and on the regenerative potential of the spleen. In children, splenic regeneration is possible. [22,69] Presence of functioning splenules is an added factor for recurrent thrombocytopenia.[70] Nio et al believe that splenic regeneration in adults after PSE is quite rare, but its detailed mechanisms are still unclear. [69] With recurrence of symptoms, repeated PSE session still a possible therapeutic option.[22]

From our work, we found shorter hospital stay and procedure-related time with lesser blood transfusion requirements in PSE group than SN group. Proper perioperative antibiotic usage, controlled embolization adopted technique and the eligible non Child C class selected participants, would probably explain our positive findings.

Regarding its advantages and safety, PSE could be considered as a suitable alternative to SN and the treatment of choice for non-Class C Child cirrhotic patients with hypersplenism. .

In conclusion; our results revealed the safety, efficacy and feasibility of PSE in managing hypersplenism in cirrhotic patients. Controlled embolization with a targeted ablation rate of 50%-70% of the splenic parenchyma can be strongly advised to avoid the disadvantages of SN.

Acknowledgement:

Authors are grateful to the Surgical Department staff, Mansoura University, for their co-operation during this work.

References

1. He XH, Gu JJ, Li WT, et al. Comparison of total splenic artery embolization and partial splenic embolization for hypersplenism. World J Gasteroenterol 2012; 18(24): 3138-3144.
2. Peck-Radosavljevic M. Hypersplenism. Eur J Gasteroenterol Hepatol 2001; 13: 317-23.
3. Witte CL, Ovitt TW, Van Wyck DB, et al. Ischemic therapy in thrombocytopenia. Arch Surg 1976; 111: 1115-21.
4.Miyake Y, Ando M, Kajii E, Toyokawa T, Nakatsu M, Hirohata M. Partial splenic embolization prior to combination therapy of interferon and ribavirin in chronic heptitis C patients with thrombocytopenia. Hepatol Res 2008; 38: 980-6.
5.Kauffman CR, Mahvash A, Kopetz S, Wolff RA, Ensor J, Wallace MJ. Partial splenic embolization for cancer patients with thrombocytopenia requiring chemotherapy. Cancer 2008; 112: 2283-8.
6.Sangro B, Bibao J, Corella C, Longo J, Beloqui O, et al. Partial splenic embolization for the treatment of hypersplenism in cirrhosis. Hepatology 1993; 18: 309-14.
7. Winslow ER, Brunti LM. Perioperative outcome of laparoscopic versus splenectomy: a meta-analysis with an emphasis on complications. Surgery 2003; 134: 647-653; Discussion 654-655.
8. Nussler NC, Setimacher U, Haase R, Stange B, Heise M, Neuhaus P. Diagnosis and treatment of arterial steal syndromes in liver transplant recipients. Liver Transpl 2003; 9: 596-602.
9. Firat A, Boyvat F, Moray G, et al. Comparison of two splenic artery interventions in the treatment of hypersplenism.: primary report. Transplant Proc 2005; 37: 1094
10.Spigos DG, Jonasson O, Mozes M, Capek V. Partial splenic embolization for the treatment of hypersplenism. Am J Roentgenol 1979; 132: 777-782.
11. Yoshida H, Mamada Y, Tariai N, Tajiri T. Partial splenic embolization Hepatol Res 2008; 38: 225-233
12. N'Konichou G, Seror O, Bourcier V, Mohand D, Ajavon Y, Castera I, et al. . Partial splenic embolization in patients with cirrhosis: efficacy, tolerance and long-term outcome in 32 patients. Eur J Gasteroenterol Hepatol 2005; 27: 179-184.
13. McCormick PA, Murphy KM. Splenomegaly, hypersplenism and coagulation abnormalities in liver disease. Baillieres Clin Gasteroenterol 2000; 14: 1009.
14.Dwivedi MK, Pal RK, Dewanga L, et al. Efficacy of partial splenic embolization in the management of hypaersplenism. Indian J Radiol Imaging 2002; 12: 371.
15. Yamauchi T, Furui S, Irie T, Kusano S. Partial splenic embolization with Y shaped silicone particles. Acta Radiol 1994; 35: 335-9.
16.Zannini G, Masciariello S, Pagano G, Sangiuolo P, Zotti G, Laccarino V. Percutaneous splenic artery occlusion for portal hypertension: A new mechanical technique for hypersplenism. Arch Surg. 1983; 118: 897-900.
17. Vorobioff J, Bredfeldt JE, Groszmann RI. Hyperdunamic splanchnic circulation in portah hypertensive rat model. A primary factor for maintenance of portal hypertension Am J Physiol 1983; 244: G52-7.
18. Maddison FE. Embolic therapy in hypersplenism. Investig Radiol 1973; 8: 280-1.
19. Shah SH, Hayes PC, Allan PL, Nicoll J, Finlayson ND. Measurement of spleen size and its relation to hypersplenism and portal hemodynamics in portal hypertension due to hepatic cirrhosis. Am J Gastroenterol 1996; 91: 2580-3.
20. Liangpunsakul S, Ulmer P, Chalasani N. Predictors and implications of severe hypersplenism in patients with cirrhosis. Am J Med Sci 2003; 326: 111-6.
21.Herrero JI, Sangero B, Quiroga J, et al. Partial splenic embolization in the treatment of thrombocytopenia in renal transplantation. Transplantation 1997; 63(3): 482-4.
22. Kumpe DA, Rumack CM, Pretoriuos DH, et al. Patial splenic eembolization in children with hypersplenism. Radiology 1985; 155: 357.

23. Madoff DC, Deneys A, Wallace MJ, et al. Splenic arterial interventions: anatomy, indications, technical considerations, and potential complications. Radiographics 2005; 25 (Suppl 1): S191-211.
24. Huang JH, Gao F, Gu YK, et al. Combined treatment of hepatocellular carcinoma with partial splenic embolization and transcatheter hepatic arterial chemoembolization. World J Gasteroenterol 2007; 13(48): 6595-6597.
25- Romano M, Giojelli A, Capuano G, et al. Partial splenic embolization in patients with idiopathic portal hypertension. Eur J Radiol 2004; 49: 268.
26. He XH, Li VT, Wei-Jun Peng WJ, et al. Total embolization of the main splenic artery as a supplemental treatment modality for hypersplenism. World J Gasteroenterol 2011; 17(24): 2953-2957.

27. Xu RY, Liu B, Lin N. Therapeutic effects of endoscopic variceal ligation combined with partial splenic embolization for portal hypertension. World J Gasteroenterol 2004; 10(7): 1072-1074.

28. Zhu K, Meng J, Qian JM, et al. Partial splenic embolization for hypersplenism in cirrhosis: A long term outcome in 62 pateints. Dig and Liver Dis 2009;41: 411-416.
29. Coons JC, Barcelona RA, Freedy T, Hagerty MF. Eptifibatide-associated acute, profound thrombocytopenia. Ann Pharmacother 2005; 39: 368-372
30. Khaykin Y, Paradiso-Hardy FL, Madan M. Acute thrombocytopenia associated with Eptifibatide therapy. Can J Cardiol 2003; 19:797-801.
31. Xu RY, Liu B, Lin N. Therapeutic effects of endoscopic variceal ligation comined with partial splenic embolization for portal hypertension. World J Gasteroenterol 2004; 10: 1072-1074.
32. Curtis BR, Swyers J, Divgi A, McFarland JG, Aster RH. Thrombocytopenia after second exposure to abciximab is caused by platelets that recognize abciximab-coated
platelets. Blood 2002; 99: 2054-2059.
33. Lee CM, Leung TK, Wang HJ, et al. Evaluation of the effect of partial splenic embolization on platelet values for liver cirrhosis patients with thrombocytopenia. World J Gasteroenterol 2007; 13(4): 619-622.
34. Numata S, Akagi K, Sakino I, Ogata H, Kawadoko T, Susuki M, Nomiyama k, Tsuji H, Fujishima M. Partial splenic embolization for the treatment of liver cirrhosis with hypersplenism: assessment of clinical response and liver function. Jpn J Gasteroenterol 1997; 94: 526-531.
35. Giorgio B, Giuseppe Z, Stephano M, et al. Percutaneous splenic artery occlusion for portal hypertension. Arch Surg 1983; 118: 897-900.
36. Firat A, Boyvat F, Moray G, et al. Comparison of two splenic artery interventions in the treatment of hypersplenism.: primary report. Transplant Proc 2005; 37: 1094.
37. Murata K, Shiraki K, Takase K, et al. Long-term follow-up for patients with liver cirrhosis after partial splenic embolization. Hepatogastroenterol. 1996;43:1212-1217.
38. Hirai K, Kawazoe Y, Yamashita K, et al. Trans-catheter partial splenic embolization in patients with hypersplenism: A clinical evaluation for supportive therapy for hepatocellular carcinoma and liver cirrhosis. Hepato Gasteroenterol 1986; 33: 105-108
39. Sakata K, Hiari K, Tanikawa K, et al. A long-term investigation of transcatheter splenic arterial embolization for hypersplenism. Hepatogasteroenterol 1996; 43: 309-318.
40. Noguchi H, Hirai K, Aoki Y, et al. Changes in platelet kinetics after a partial splenic artery embolization in cirrhotic patients with hyersplenism. Heplatology 1995; 22: 1982-8.
41. Vujic I, Lauver JW. Severe complications from partial splenic embolization in patients with liver failure. Br J Radiol 1981; 54: 492-5.
42. Wang BH, Zhou LQ. Partial splenic embolization therapy for chronic idiopathic thrombocytopenic purpura in children: a report of 2 cases. Zhonghua GanZang Bing ZaZhi 2006, 8: 2.
43. Akahoshi T, Hashizume M, Tanoue K, et al. Role of the spleen in liver fibrosis in rates may be mediated by transforming growth factor-beta. J Gasteroenterol hepatol 2002; 17: 59-65.
44. Barcena R, Moreno A, Foruny JR, et al. improved graft function in liver transplanted patients after partial splenic embolization: reversal of splenic artery steal syndrome? Clin Transplant 2006; 20: 517-523.

45. Kato M, Shimohashi N, Ouchi J, et al. Partial splenic embolization facilitates completion of interferon therapy in patients with chronic HCV and hypersplenism. J Gasteroenterol 2005; 40: 1076-1079.
46.Mukaiya M, Hitata K, Yamashiro K, et al. Changes in portal hemodynamics and hepatic function after partial splenic embolization (PSE) and percutaneous transhepatic obliteration(TPO). Cancer Chemother Pharmacol 1994; 34 (Suppl): S37-41.
47. Palsson B, Hallen M, Forsherg AM, Alwmark A. Partial splenic embolization: Long-term outcome. Langenbecks Arch Surg 2003; 387: 421-426.
48. Hayashi H, Beppu T, Masuda T, et al. Large splenic volume may be a useful predictor for partial splenic embolization induced liver function improvement in cirrhotic patients . J Hepatobiliary Pancreat Sci 2014; 21: 51-57.
49. Weismuller TJ, Prokein J, Becker T, et al. Prediction of survival after liver transplantation by pre-transplant parameters. Scand J Gastroenterol. 2008; 43: 736-746.
50.Cooper MJ, Williamson RCN. Splenectomy, indications, hazards, and alternatives. Br J Surg.1984; 71: 173-80.

51.Berchtold P, Mc Millan R. Therapy for chronic idiopathic thrombocytopenic purpura in adults. Blood. 1989; 74: 2309-2317.
52. Tsiotos G, Schlinkert RT. Laparoscopic splenectomy for immune thrombocytopenic purpura. Arch Surg. 1997; 132: 642- 646.
53. Stanislawska J, Interewicz B, Maksymowicz M, et al. The response of the spleen dendritic cell-enriched population to bacterial and allogenic antigens. Ann Transplant. 2005; 10: 17-23.
54. Israel DM, Hassal E, Culhan JA, Philips RR. Partial splenic embolization in children and hypersplenism. J Pediatr. 1994; 124: 95-100.
55. Ockene IS, Matthews CF, Rifai N, Ridker PM, et al. Variability and classification accuracy of serial high-sensitivity C-reactive protein measurements in healthy adults. Clin Chem. 1991; 47: 444- 450.
56. Ridker PM. High-sensitivity C-reactive protein: potential adjunct for global risk assessmentin the primary prevention of cardiovascular disease. Circulation 2001; 103: 1813-1818.
57. Alwmark A, Begmark S, Gulstrand P. et al. Evaluation of splenic embolization in patients with portal hypertension and hypersplenism. Ann Surg. 1982; 196: 518-524.
58. Mozes MF, Spigos DG, Pollak R, et al. Partial splenic embolization: an alternative to splenectomy. Results of a prospective, randomized study. Surgery. 1984; 96: 694-701.
59. Tajiri M, Onda M, Yoshida H, et al. Long-term hematological and biochemical effects of partial splenic embolization in hepatic cirrhosis. Hepatogasteroenterology 2002; 49: 1445.
60. Nishida O, Moriyasu F, Nakamura T, et al. Interrelationship between splenic and superior mesenteric venous circulation manifested by transient splenic arterial occlusion using a balloon catheter. Hepatology 1987; 7: 442-6.
61. Zhu K, Meng X, Li Z, et al. Partial splenic arterial embolization using polyvinyl alcohol particles for hypersplenism in cirrhotics.: A prospective randomized study. Eur J Radiol 2008; 66: 100-1.
62. Watanabe Y, Horiuchi A, Yoshida M, et al. Significance of laparoscopic splenectomy in patients with hypersplenism. World J Surg. 2007; 31: 541-55.
63. Kojouri K, Vesely SK, Terrel DR, George JN. Splenectomy for adult patients with idiopathic thrombocytopenic purpura: a systematic review to assess long-term platelet count response, prediction of response and surgical complications. Blood 2004; 104: 2023-34.
64. Belli A, Rommani F, Riolo F. Thrombosis in the portal vein in the absence of hepatic disease. Surg Gynaecol Obstet 1989; 169: 46.
65. Eguchi A, Hashizume M, Kitano S, et al. High rate of portal thrombosis after splenectomy in patients oesophageal varices and idiopathic portal hypertension. Arch Surg. 1991; 26: 752.
66. Ezzat FA, Abu Elmagd KM, Aly MA, et al. Selective shunt versus non shunt surgery for management of both schistosomal and non schistosomal variceal bleeding. Ann Surg. 1990; 212: 97.
67. Abou El Hoda MF, Dawoud IE, Setein MF, et al. Postsplenectomy portal vein thrombosis: frequency and significance. Egypt J Surg. 1996; 15: 5.
68. Sakai T, Shiraki K, Inouse H, et al. Complications of partial splenic embolization in cirrhotic patients. Dig Dis Sci. 2002; 47: 388.
69. Nio M, Hayashi Y, Sano N, et al. Long-term efficacy of partial splenic embolization in children. J Pediatr Surg.2003; 38(12): 1780-1782.
70. Gibon I, Rickard KA, Badovich G, et al. Management of splenectomy failures in immune thrombocytopenic purpura: role of accessory splenectomy. Aust N Z J Med 1986; 16: 695-698.