Comparison between efficacy of partial splenic coil and particle embolization with just particle embolization in management of hypersplenism

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Purpose

The spleen is an organ found in virtually all vertebrate animals with important roles in regard to red blood cells and the immune system against infection and malignancy. It is one of the centers of activity of the Reticuloendothelial system, and can be considered analogous to a large lymphnode. It also plays important role in regulation of circulating blood volume.

Splenomegally is anatomically defined as spleen size >13 cm. S. Poulain et al classify splenomegally as:

1. Moderate splenomegally, if the greatest dimension is between 13-20 cm.
2. Severe splenomegally, if the greatest dimension is greater than 20 cm.

Splenomegally is one of the four cardinal sings of hypersplenism, the other three being cytopenia (s), normal or hyperplastic bone marrow and a response to splenectomy, hypersplenism often accompanies chronic liver disease and surgical splenectomy is the traditional treatment. However it is associated with perioperative and postoperative complications, splenic artery ligation was initially tried as a method for treating hypersplenism while preserving splenic function. Partial splenic embolization (PSE) has been proposed as an alternative to surgery. The procedure helps occlude the arterial supply of the spleen more peripherally, which results in ischemic necrosis of much of the functional spleen, followed by a decrease in splenic size and hypersplenism. It also allows preservation of adequate splenic tissue and thereby avoids the risk of overwhelming post splenectomy infection. The basic technique of therapeutic embolization involves the injection of embolic material through a catheter selectively positioned in an artery or vein in order to deliberately occlude the artery, vein or vascular bed of an organ by formation of thrombus in the blood vessels.

Beside hypersplenism, splenic arterial interventions are increasingly performed to treat various clinical conditions including, abdominal trauma, splenic hemorrhage and splenic neoplasm. PSE is also used for completion of therapeutic course of high-dose chemotherapy or immunosuppressive therapy in some patients (AIDS-cancer- hepatitis) suffering from hypersplenism induced thrombocytopenia. Another application of PSE is treating splenic artery steal syndrome and hypersplenism in liver transplant recipients. Partial splenic embolization has been associated with complications ranging from post embolization syndrome to serious complications, such as splenic abscess and septicemia. The study was conducted based on the hypothesis that it is safe and effective in the management secondary hypersplenism. We used two embolizing materials metal coils polyvinyl alcohol (PVA).
**Review of articles**

**Splenic vascular anatomy:**

The splenic artery supplies the spleen and substantial portion of the stomach and pancreas (Fig 2). The splenic artery courses superior and anterior to the splenic vein, along the superior edge of the pancreas. Near the splenic hilum, the artery usually divides into superior and inferior terminal branches, and each branch further divides into four or six segmental intrasplenic branches. The superior terminal branches are usually longer than the inferior terminal branches and provides major splenic arterial supply. A superior polar artery usually arises from the distal splenic artery near the hilum, but it may originate from the superior terminal artery. The inferior polar artery usually gives rise to the left gastroepiploic artery, but the latter may also arise from distal splenic or inf. terminal artery. Numerous short gastric branches arise from the terminal splenic or left gastroepiploic artery to supply the gastric cardiac and fundus.

The splenic artery has many branches that supply the pancreatic body and tail. The first large branch is dorsal pancreatic artery and the second large branch is the greater pancreatic artery, which arises from the middle segment of the splenic artery. When embolization is planned visualization of the pancreatic arteries is essential to reduce the risk of their unintended embolization. To avoid unintentional embolization of pancreatic artery, good knowledge of the vascular anatomy of the splenic artery and its branches is required. Sindel and colleagues in their study to measure the average distance between the origin of the last pancreatic branch and the splenic hilum, concluded to avoid the risk of pancreatitis, embolic material should be delivered through a catheter whose tip is located in the distal 3.07 cm of splenic artery.

**History of splenic embolization:**

In 1973, Maddison was the first to report the use of splenic embolization in a human being. Dr Maddison successfully used autologous clot to embolize the spleen of an actively bleeding farmer who had suffered from repeated bouts of gastrointestinal hemorrhage from esophageal varices. After that several studies were done and most of them embolized a full 100% of the spleen and did not use antibiotics. Many major complications were reported including abscess, septic shock, splenic rupture, overwhelming pneumonias and death. Because of this, most authors had recommended considerable restraint in the use of procedure, in 1979, Spigas et al published an influential article that recommended a modified approach designed to minimized the morbidity and mortality associated with PSE. They suggested antibiotic prophylaxy, adequate pain control, limited volume embolization, and careful care after embolization. Despite promising results, however, splenic embolization never gained widespread popularity, this may be due to introduction of an other important therapeutic option for the treatment of the complications of portal hypertension, transjugular intrahepatic
portosystemic shunts "TIPS" in 1982, Colapinto et al published the first article documenting the use of TIPS in a human being. Splenic embolization, however, has been used for a wide range of indications besides portal hypertension. Treatment goals successfully achieved include improvement in platelet count in patients with idiopathic thrombocytopenic purpura, decrease in transfusion requirements in patients with thalassemia, control of bleeding in blunt splenic injury. Splenic embolization has been used to treat hypersplenism secondary to a wide range of disorders, including hereditary spherocytosis (12) tropical splenomegally and Gaucher disease. It has been successful in liver transplant patients or renal transplant patients who developed azathioprine-induced neutropenia. As an adjunct to surgical splenectomy, splenic embolization has been used to decrease blood loss in high risk patients undergoing open operation (6).

Andres et al recommended particle size range of 355-500 mm, as optimal sizes, because this size provides a more predictable area of infarction than larger particles, as embolization is occurring at the arteriolar level and more distally (11) Alwmark et al. recommended that particle size range should not exceed 600-800 mm in patients undergoing splenic embolization for portal hypertension and hypersplenism (12).

**Therapeutic embolization**

**Embolic materials :**

The basic technique of therapeutic embolization involve the injection of embolic material through a catheter selectively positioned in an artery or vein in order to deliberately occlude the artery, vein or vascular bed of an organ by the formation of thrombus in the blood vessels. Recently the most commonly used embolic agents include solid particulate materials, such as gelatin sponge fragments (Gelfoam) and poly vinylalcohol (PVA), mechanical devices, such as spiral metal coil, sclerosing liquids, such as ethanol.

The PVA particles are not radiopaque, and it is available in a range of sizes from 150-250, 250-600 and 600-1000mm particles. The entail coils are made of stainless steel or plantinum and are available in a range of sizes and lengths with a spiral diameter of 1-20 mm or larger. The stainless stell coils have threads of wool, silk or Dacron attached to them to increase their thrombogenicity.

**Appropriate time to embolize :**

It is important to choose the right time for splenic embolization. Many authors have noticed that results after partial splenic embolization are better if the symptoms of hypersplenisms are not too marked and the spleen is not excessively large. They suggest in patient with portal hypertension and hematological diseases (hereditary spherocytosis, beta-thalassemia major, etc) a thrombocyte count of less than $100 \cdot 10^3$ to $120 \cdot 10^3$ is
suspicious for hypersplenism (10). They think that earlier or later signs of hypersplenism will be more evident and their recommendation is to perform the PSE procedure if a patient has the above mentioned thrombocyte count. If embolization doesn’t be performed at the right moment (when the thrombocyte count is between 100´10³ and 120´10³) then the spleen size will continue to gradually increase and the patient will have a more aggressive infarction after PSE, which will then aggravate the patient's condition after the procedure. The bigger the embolized spleen, the greater the infarction (10).

The extent of embolization:

Taking the data of A. Peterion et al symptoms of hypersplenism will be corrected better if the blood supply inside the spleen is reduced by 60%-70% (10). However it is possible that the morbidity period may last longer, abdominal pain may be present more frequently, and fever may develop more, compared to embolization (25-40%). Some authors recommend performing a smaller infarction of the spleen tissue to avoid the after-effects of PSE, preferring to repeat the procedure if necessary (12). This is extremely important because the size of infarct should be approximately 60-70% of spleen tissue. Care should be taken to avoid a larger infarct than necessary. Gastroepiploic and intrapancreatic arteries also contribute to the arterial blood supply of the spleen, which means that the organ will also be supplied with blood to a certain extent. About 25% of the normal spleen volume is required to retain its immune capacity (13). The extent of embolization seems to be critical for long term efficacy of PSE. Embolization less than 50% of the splenic mass was almost always associated with a relapse of hypersplenism, in contrast, relapse did not occur among patients who had more than 50% of their spleen embolized (14).
Methods and Materials

Patient population

Shiraz Namazi hospital is the reference center for liver transplantation and the angiographic ward was the interventional center that the patients underwent embolization. Patients were selected and transferred to radiologist by gastroenterologist and transplant specialist surgeon, adult cirrhotic patients suffering from portal hypertension or its sequels (e.g., painful spleen-pancytopenia or variceal bleeding are eligible for enrollment in this study. Patients who are younger than 14 are excluded, other exclusion criteria: child pugh class C and D and portal vein thrombosis. We had two groups including 10 patients age and sex much (Group 1 and group 2). In group 1 There were 4 females and 6 males ranging from 16 to 46 y/o (mean age 32) two of these patients were Wilson disease- one was biliary cirrhosis and other seven patients were cryptogenic cirrhosis. In group 2, 5 females and 5 males, 1 had Wilson disease, 1 had primary biliary cirrhosis and rest of them were posthepatitis or cryptogenic cirrhosis.

Procedure protocol:

The risk and potential benefits of splenic embolization were explained to each patients and informed consent was given from the patients. After selection of patients, general P/E and recent lab data was obtained. Color doppler sonography of portal and splenic vein was done and finally, splenic volumetry using abdominal CT-scan without contrast was done to estimate spleen volume. Platelet count was corrected till level of 40,000 Just before intervention. Ampicillin 1gr and Gentamicin 8mg/kg were administered intravenously, strict attention to sterility (surgical scrub) was done before starting angiographic intervention. under light sedation, splenic artery was selectively catheterized from femoral artery approach. Celiac angiography and selective splenic arterial angiography were obtained in order to demonstrate the distribution of splenic arteries and collateral circulation routes and also to localize its pancreatic branches as well as measurement the splenic artery diameter to choose the coil size in group 2. Of coarse the patients with splenic artery size of more than 10 mm enrolled to group 1 because we had no coil available more than 10mm diameter (only two patients) Using microcatheter (progreat), inferior & middle splenic arteries were superselectively catheterized and 1 or 2 vial of polyvinylalcohol PVA (Denmark- cook Europe APS-USA) ranging from 300 to 500 mm mixed with a solution of 10 ml contrast material were injected under fluoroscopic guidance. During embolization small amount of contrast material were periodically injected through the catheter to monitor the flow distribution within the spleen and flow speed in the main splenic artery. In groupe 2, after PVA embolization, several coils (cook, MRoye 8mm ´935 mm ´ 8cm) were inserted in the proximal splenic artery until the flow completely stopped. Embolization was finished when an estimated 75% of
spleen was devascularized. A post embolization arteriogram was obtained to determine the extent of devascularization. After the procedure the catheter and arterial sheet discontinued and bleeding controlled by using angioseal.. After finishing intervention, the patients were admitted in ward for 2 days. NSAID and Narcotics was used to control post-embolization syndrome. Daily follow-up including physical examination, color Doppler sonography of portal and splenic vein was done for 2 days. In second day some lab data (CBC-PT & PTT, LFT, Cr) were obtained. If hospital course was not complicated, the patients were discharged under follow up observation. 1st follow up was about 1 month after intervention, which include color Doppler sonography of portal and splenic vein and CBC. Second follow up is about 3 months after procedure that include abdominal CT, and a complete lab data.
Fig. 0: Splenic angiogram shows all upper and mid branches

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**Fig. 0:** Microcatheter in upper pole branch and subsequent embolization.

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Fig. 0: Microcatheter in lower pole branch.

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Fig. 0: 70% devascularization after PVA embolization.

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**Fig. 0:** Coil embolization of the main splenic artery.

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**Fig. 0:** More coils in the main splenic artery.

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**Fig. 0:** Complete obstruction of the main splenic artery. A few pancreatic branches are seen.

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Results

-Patients grouping and follow up:

This study was conducted in 2x10 patients with a diagnosis of hypersplenism secondary to cirrhosis their mean age was 30 y/o (16-44 y/o). Partial splenic embolization was performed successfully in ten cases and it was associated with coiling in group 2 and after that the parameters were obtained in 1 week, 1 month and 3 months after intervention.

-Chronological changes in peripheral blood cell counts:

All patients except one in group 1 showed marked improvement in platelet count and leukocyte count (P<0.01). In one patient progressive decline in platelet count was noted during the third month, however the values remained significantly higher than values before PSE. (60000 versus 18,000).

-Chronological changes in liver function parameters:

In comparison with pre-PSE level of liver function parameters values, including AST, ALT, Alb- and PT in these patients, there is no significant short and long term changes after PSE.

-Side effects and complications:

Almost all of patients had problems related to post-embolization syndrome. Pain was mild in 2 patients (relieved by the third day), moderate in seven patients (abated completely by seventh day) and very severe in one patient in group 1 and one patient in group 2 that last nearly 10 days. No statistical difference was detected between two groups regarding severity of pain.

Nearly all patients experienced a mild, vague deep pain in left upper quadrant especially during changing position nearly for 2-3 months.

Fever was mild (<38°C) in 8 patient(4 patients in group 1 and 4 in group2) and moderate (38-39) in 12 patients (6 patients in group 1 and 6 in group 2 ). No serious complication (spleenic abscess, pancreatitis, portal vein thrombosis…) developed in this study, Nausea and vomiting occurred in 3patients in group 1 and 4 patients in group 2 that abated by the second day.

Discussion

Although splenectomy has been performed to treat primary and secondary hypersplenism, this procedure is associated with immunologic impairment and increased susceptibility to overwhelming bacterial infection. Splenic artery ligation was initially
tried as a method for treating hypersplenism while splenic function preserved. In recent years, splenic embolization using Gelfoam cubes, serious complications such as splenic abscess, splenic rupture and septicemia have been encountered.

Anderson et al (*) compared Gelfoam cubes and steel coils for splenic artery embolization in dogs and found that steel coils are safer while still effective in raising platelet counts. It has also been shown that surgical devascularization at the splenic helix more effectively increases the platelet count than dose ligation of the proximal splenic artery. On the basis of these findings, we performed splenic embolization by introducting steel coils and PVA particles into the splenic artery using micro catheter inferior and middle splenic arteries were selectively catheterized and PVA embolization was done. After that several coils were deposited more proximally in splenic artery in group 2.

In 2 patients, first coils were carried by blood flow into the intrasplenic braches of the splenic artery but no complication detected in this regard.

Platelet count increased and the duration of the complications correlated with the occurrence of splenic infarction after embolization.

PVA particles with a diameter of 300-500 mm are tinier than gelfoam particles which have a diameter of 1 mm to 2 mm and therefore can embolize the distal branches of splenic artery closer to splenic sinus than gelfoam particles. As this area has fewer collateral anastomoses among the distal splenic artery, theoretically PVA with tinier particles could achieve a more complete infarction of segmental or subsegmental splenic parenchyma than golfoam particles and PVA particles are permanent embolic material. Proximal occlusion of splenic artery only by steel coils has only a short-lasting effects on the peripheral blood counts because of the development of collaterals.

An eventual factor that affects the efficacy of PSE is the extent of embolization, as it has been confirmed that a large area of embolization in the distal branches of splenic artery is crucial to assuring long-term efficacy of PSE. When 50% or less than 50% of the spleen was embolized, hypersplenism could relapse within a short period after PSE, whereas, relapse seldom occurred among patients who had more than 50% of their spleen embolized. Results of this study show that "PSE" using PVA particles and steel coils is a safe therapy for hypersplenism in cirrhosis. It seems that simultaneous embolization by coils and PVA is a more effective procedure and more permanent than only PVA embolization most probably because of relative severe ischemia of the nonembolized parts caused by secondary coiling of the main splenic artery.

Post embolization complication has close relationship with extent of PVA embolization( not coil embolization). In our study one patient had extensive PVA embolization in group 1 (more than 70%) and she experienced sever pain that lasted about 10 days. Post embolization syndrome is mainly caused by splenic ischemia, necrosis and inflammatory effusion, which closely associated with the extent of embolization. In this research, it was the most frequent side effect, although it was usually
tolerable to the patients Nevertheless there were no difference between two groups regarding post embolization syndrome.
Conclusion

Partial splenic embolization (PSE) can be an effective therapeutic alternative to splenectomy for management of hypersplenism secondary to cirrhosis. It is a simple, rapid procedure, easily performed under local anesthesia, incurs less morbidity, and there is no need for blood transfusion. Moreover, the splenic vein is preserved for further shunt operation if required, and a portion of functional splenic tissue is left in place to safeguard against overwhelming infection. This study had some limitations: the number of patients was small, and they belonged to child class A or B only. To avoid severe, lethal complications, especially splenic abscess, it is suggested that the splenic necrosis be kept less than 70% however if infarction extent is less than 50% possibility of recurrence of cytopenia is high. In this study we showed that combined PVA and coil embolization is more effective and permanent than PVA embolization alone. We guess that we can reduce amount of PVA embolization combined with coiling with the same result as 75% PVA embolization, of coarse it is the matter of further research.
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