Splenic artery embolization: a single center experience on the safety, efficacy, and clinical outcomes

Ron C. Gaba, Jeremy R. Katz, Ahmad Parvinian, Steven Reich, Benedictta O. Omene, Felix Y. Yap, Charles A. Owens, M. Grace Knuttinen, James T. Bui

PURPOSE
We aimed to assess the safety, efficacy, and clinical outcomes of splenic artery embolization (SAE).

MATERIALS AND METHODS
A total of 50 patients (male:female, 33:17; mean age, 49 years) who underwent 50 SAEs between 1998 and 2011 were retrospectively studied. The procedure indications included aneurysm or pseudoaneurysm (n=15), gastric variceal hemorrhage (n=15), preoperative reduction of surgical blood loss (n=9), or other (n=11). In total, 22 procedures were elective, and 28 procedures were urgent or emergent. The embolic agents included coils (n=50), gelatin sponges (n=15), and particles (n=4). The measured outcomes were the technical success of the procedure, efficacy, side effects, and the 30-day morbidity and mortality rates.

RESULTS
All embolizations were technically successful. The procedure efficacy was 90%; five patients (10%) had a recurrent hemorrhage requiring a secondary intervention. Side effects included hydrothorax (n=26, 52%), thrombocytosis (n=16, 32%), thrombocytopenia (n=13, 26%), and postembolization syndrome (n=11, 22%). Splenic infarcts occurred in 13 patients (26%). The overall and procedure-specific 30-day morbidity rates were 38% (19/50) and 14% (splenoporal thrombosis, 3/50; encapsulated bacterial infection, 1/50; splenic abscess, 1/50; femoral hematoma requiring surgery, 1/50; hydrothorax requiring drainage, 1/50). The overall and procedure-specific 30-day mortality rates were 8% (4/50) and 0%. The multivariate analysis showed that advanced patient age (P = 0.037), postprocedure thrombocytopenia (P = 0.008), postprocedure hydrothorax (P = 0.009), and the need for a secondary intervention (P = 0.004) predicted the 30-day mortality, while renal insufficiency (P < 0.0001), preprocedure hemodynamic instability (P = 0.044), and preprocedure leukocytosis (P < 0.0001) were prognostic factors for the 30-day mortality.

CONCLUSION
SAE was performed with high technical success and efficacy, but the outcomes showed nontrivial morbidity rates. Elderly patients with thrombocytopenia and hydrothorax after SAE, and patients who require secondary interventions, should be monitored for complications.

SAE procedures
The SAE procedures were performed in the interventional radiology suite using intravenous moderate sedation. Preprocedure antibiotics and the pneumococcal vaccine were not routinely provided. Patients were prepared and draped in standard sterile fashion while supine on the angiographic procedure table, and routine arterial access was gained via the right or left common femoral artery. An initial celiac arteriography...
was then performed using a 5 F visceral catheter, such as the Sos Omni Selective (AngioDynamics, Queensbury, New York, USA), SIM 1 (Cook Medical, Bloomington, Indiana, USA), or C2 (Cook Medical) catheter. Subsequent splenic arteriography was performed after switching to a 4–5 F angled glide coated catheter (Glidencath, Terumo Medical Corporation, Somerset, New Jersey, USA) or placement of a coaxial 3 F microcatheter, such as the Renegade Hi-flo catheter (Boston Scientific, Natick, Massachusetts, USA). The catheter position was confirmed using digital subtraction angiography with iohexol (Omnipaque-300, Amersham Health, Princeton, New Jersey) or injection. After selecting the appropriate catheter position for embolization, transcatheter occlusion of the splenic artery was performed using combinations of 0.018 or 0.035 metallic coils, such as the Nester and MicroNester coils (Cook Medical), an absorbable gelatin sponge (Gelfoam, Pharmacia & Upjohn, New York City, New York, USA), and particles such as Embospheres (BioSphere Medical, Rockland, Massachusetts, USA). Embolization was continued to a stasis angiographic end-point with no antegrade arterial blood flow in the proximal splenic artery. Care was taken to preserve collateral short gastric or greater pancreatic arterial supply to the spleen whenever possible. Postembolization completion arteriography was then performed. Following SAE, all catheters and vascular access devices were removed, and hemostasis was achieved at the common femoral arteriotomy with manual compression (20/50, 40%) or using a vascular closure device (9/50, 18%), such as Perclose ProGlide (Abbott Vascular, Abbott Park, Illinois, USA). The vascular sheath was left in place in eight patients (16%) for arterial blood pressure monitoring in the intensive care unit (ICU). The means of the groin hemostasis were not specified in 13 cases (26%).

**Measured outcomes and clinical follow-up**

The outcome measures of this study included the technical success of the procedure, the clinical efficacy, the adverse side effects, and the 30-day morbidity and mortality rates. Technical success was defined as immediate angiographic vessel occlusion, as demonstrated by completion angiography (12). Clinical efficacy within 30 days of embolization was assessed by the cessation of bleeding in patients presenting with hemorrhage, persistent aneurysm or pseudoaneurysm occlusion (as assessed on cross-sectional imaging or repeat angiography), appropriate reduction of the surgical blood loss (less than 150 mL) in cases of preoperative SAE, and resolution of thrombocytopenia in cases of sequestration. Rebleeding was identified by clinical signs of bleeding, such as hematemesis, coffee ground emesis, melena, or cross-sectional imaging evidence of intra-abdominal hemorrhage, accompanied by laboratory hemoglobin reduction requiring blood product transfusion.

The procedure-related complications were classified according to the Society of Interventional Radiology Standards of Practice Committee’s classification of complications (12). Morbidity was defined as the occurrence of a complication within 30 days of SAE. Complications were categorized as either procedure-specific, or directly attributable to the SAE procedure, or general, meaning that they could not be directly ascribed to the SAE procedures due to other potential origins, such as postoperative or ICU-related etiologies. Adverse side effects were distinguished from procedure-related complications and were defined as unintended but expected secondary results that did not cause harm (including asymptomatic pleural effusion, changes in the platelet level without clinical repercussions, and postembolization syndrome). An immediate postprocedure clinical follow-up was performed while the patients remained hospitalized following SAE. Outpatient clinic follow-up was performed thereafter. Patient survival was analyzed from the date of SAE until 30 days postprocedure. Patient mortality was also categorized as procedure-specific and overall in a fashion that was analogous to morbidity.

**Statistical analysis**

Descriptive statistics were used to check for erroneous entries, to assess the normality of the data, to characterize the demographic features of the study population and to evaluate the 30-day morbidity and mortality rates. Univariate and multivariate analysis of variance were used to determine the relationships between the demographic, clinical, laboratory, and procedural variables with the overall 30-day morbidity and mortality outcomes. Variables with a significance level of $P \leq 0.10$ in the univariate analysis were included in the multivariate analysis. Statistical analysis was performed using a commercially available software package (Statistical Package for Social Sciences, version 18, SPSS Inc., Chicago, Illinois, USA). $P$ values $\leq 0.05$ were considered statistically significant.

**Results**

**Patients**

A total of 50 patients were identified for retrospective investigation. The study cohort included 33 males (66%) and 17 females (34%), and the mean patient age was 49 years (range, 22–74 years). Comorbid illnesses included hypertension (n=23, 46%), hyperlipidemia (n=9, 18%), diabetes mellitus (n=14, 28%), coronary artery disease (n=7, 14%), liver cirrhosis and/or portal hypertension (n=24, 48%), renal dysfunction (n=8, 16%), pancreatitis (n=20, 40%), malignancy (n=17, 34%), and tobacco use (n=23, 46%). Both acute (n=15, 30%) and chronic (n=5, 10%) pancreatitis were present. Malignancies included pancreatic adenocarcinoma (n=11, 22%), hepatocellular carcinoma (n=4, 8%), non-small cell lung cancer (n=1, 2%), and B-cell lymphoma (n=1, 2%).

Procedure indications included splenic artery aneurysm (n=5, 10%) or pseudoaneurysm (n=10, 20%), gastric variceal hemorrhage refractory to medical therapy (n=15, 30%), preoperative reduction of surgical blood loss (n=9, 18%), splenic hemorrhage (e.g., splenic trauma, postoperative subcapsular bleeding, bleeding into pancreatic pseudocyst) (n=10, 20%), and hypersplenism (n=1, 2%). In total, 34 (68%) of cases were performed for bleeding indications. Preoperative SAE was performed as an adjunct to surgery to limit the operative blood loss. Of the nine patients who underwent preoperative SAE, eight had subsequent splenectomies and one had a subsequent splenorenal shunt. Postoperative hemorrhage occurred in one patient who had undergone Whipple resection for pancreatic adenocarcinoma complicated by postsurgical splenic artery bleeding; this patient underwent embolization of the iatrogenic vessel injury on postoperative
Figure 1. a–d. A 47-year-old man with asymptomatic incidental splenic artery aneurysm. A contrast enhanced abdominal CT scan (a) reveals a 3.2-cm splenic artery aneurysm (arrowheads). A subsequent selective splenic arteriogram (b) confirms the presence of an aneurysm. Elective embolization (c) was successfully performed using distal and proximal occlusion with metallic coils followed by a gelatin sponge. A one-month postprocedure contrast enhanced CT scan (d) shows aneurysm thrombosis (arrowheads) and demonstrates a concurrent partial splenic infarction (arrows).

day four. A total of seven patients (14%) were asymptomatic, while 43 patients (86%) were symptomatic. In total, 16 procedures (32%) were performed electively, 22 procedures (44%) were pursued urgently, and 12 procedures (24%) were performed emergently. Cases that required prompt medical attention without an immediate threat to health were considered urgent, while cases necessitating immediate medical action to maintain well being were deemed emergent. In total, 30 patients (60%) required ICU monitoring immediately pre- or postprocedure. A total of seven patients (14%) demonstrated hemodynamic instability, defined as the lowest recorded supine mean arterial blood pressure $\left(\text{MAP}=\frac{2}{3}\times\text{diastolic blood pressure}+\frac{1}{3}\times\text{systolic blood pressure}\right)$ within 24 hours prior to SAE less than or equal to 65 mmHg. A total of five patients (10%) required transfusion of more than six units of packed red blood cells within 24 hours prior to SAE.

SAE procedures
All SAE procedures were technically successful (Figs. 1–3). The embolic agents included combinations of metallic coils (n=50, 100%), gelatin sponge (n=15, 30%), and particles (n=4, 8%). The procedure efficacy was 90%; five patients (10%) had recurrent hemorrhage requiring repeat embolization (n=2) or surgery (n=3). Of the five rebleeding patients, the indication for the initial SAE was splenic trauma in four (80%) and pseudoaneurysm in one (20%). Two patients underwent repeat embolization: one patient rebled from a recanalized pseudoaneurysm 22 days after the initial SAE and was successfully coil embolized again with no 30-day adverse event or rebleeding; another patient with splenic trauma rebled 11 days after the initial SAE
and was successfully treated with repeat embolization without any complications or recurrent hemorrhage at 30 days. Including these repeat SAEs, the cumulative procedure efficacy was 47/52 (91%). Of the patients that underwent SAE for treatment of gastric variceal hemorrhage refractory to medical therapy, none (0%) suffered recurrent hemorrhage within 30 days. The mean length of hospital stay was 19 days (range, 1–118 days).

Clinical outcomes

Adverse side effects included left-sided hydrothorax (n=26, 52%), thrombocytopenia (n=16, 32%), thrombocytopenia (n=13, 26%), and postembolization syndrome (n=11, 22%). Splenic infarcts occurred in 13 patients (26%). The overall and procedure-specific 30-day morbidity rates were 38% (19/50) and 14% (7/50). Procedure-specific major complications included splenoporal venous thrombosis (n=3, 6%), infection with encapsulated bacteria (n=1, 2%), splenic abscess (n=1, 2%), femoral hematoma requiring surgery (n=1, 2%), and hydrothorax requiring a chest tube (n=1, 2%). Additional morbidity, not directly attributable to the SAE procedures, included infection with non-encapsulated bacterial organisms in ICU patients (n=5, 10%), infection with encapsulated bacteria following operative splenectomy (n=1, 2%), venous thromboembolism following splenectomy (n=1, 2%), and gastric fundal erosion by pancreatic cancer resulting in clinical evidence of bleeding (n=1, 2%). Death occurred in four patients (8%). In the patients who received elective SAE, procedure-specific major complications occurred in two patients (13%) and consisted of splenoporal venous thrombosis (n=1) and femoral hematoma requiring surgery (n=1, 6%).

On univariate analysis, advanced patient age (54 vs. 45 years, \( P = 0.024 \)), a bleeding indication for the procedures...
Splenic artery embolization

- 84% vs. 58%, \( P = 0.089 \), the need for ICU monitoring immediately pre- or postprocedure (79% vs. 48%, \( P = 0.055 \)), renal insufficiency with elevated creatinine (1.2 vs. 0.9 mg/dL, \( P = 0.091 \)), the occurrence of postembolization syndrome (37% vs. 13%, \( P = 0.048 \)), preprocedure leukocytosis (12.4 vs. 8.3 \( \times 10^3/\text{mL}, \ P = 0.051 \)), postprocedure thrombocytopenia (200 vs. 97 \( \times 10^3/\text{mL}, \ P = 0.002 \)), postprocedure hydrothorax (79% vs. 36%, \( P = 0.005 \)), and the need for a second intervention (32% vs. 0%, \( P = 0.006 \)) were risk factors for the occurrence of overall 30-day morbidity. Multivariate analysis confirmed advanced patient age (\( P = 0.037 \)), postprocedure thrombocytopenia (\( P = 0.008 \)), postprocedure hydrothorax (\( P = 0.009 \)), and the need for a second intervention (\( P = 0.004 \)) to be significant prognostic factors for overall 30-day morbidity.

Overall and procedure-specific 30-day mortality rates were 8% (4/50) and 0%. The mortality rate for elective SAE procedures was 0%. On univariate analysis, renal insufficiency with elevated creatinine (2.2 vs. 0.9 mg/dL, \( P < 0.0001 \)), preprocedure hemodynamic instability (50% vs. 11%, \( P = 0.031 \)), preprocedure leukocytosis (21.4 vs. 8.9 \( \times 10^3/\text{mL}, \ P < 0.0001 \)), postprocedure thrombocytopenia (60 vs. 169 \( \times 10^3/\text{mL}, \ P = 0.076 \)), and a low maximum postprocedure platelet count (156 vs. 451 \( \times 10^3/\text{mL}, \ P = 0.047 \)) were risk factors for overall 30-day mortality. Multivariate analysis confirmed renal insufficiency (\( P < 0.0001 \)), preprocedure hemodynamic instability (\( P = 0.044 \)), and preprocedure leukocytosis (\( P < 0.0001 \)) to be significant prognostic factors for overall 30-day mortality.

**Discussion**

SAE was introduced in 1973 as a non-surgical treatment for variceal hemorrhage and hypersplenism (13). Though limited in its early days by serious complications and high mortality, the procedure has since benefited from advances in the available technology and from improvements to the protocol. In particular, an emphasis on the principles described by Spigos et al. (14), including limited volume embolization, sterile technique, antibiotic coverage, and adequate analgesia, has led to improved outcomes and widespread utilization in a variety of settings (1). The published efficacy rates are high; a recent meta-analysis of SAE in the non-operative management of blunt splenic trauma found an overall failure rate of 15.7% (15), while success in the treatment of splenic arterial aneurysms and pseudoaneurysms is approximately 90% (16–18). In patients with portal hypertension and hypersplenism, SAE has been shown to produce significant and sustained improvements in both liver function and hematologic indices, as well as an 80% reduction in annual bleeding episodes in patients with recurrent variceal hemorrhage (5).

The results of the current study compare favorably to other series and
recommended success thresholds (12). Our retrospective analysis of 50 patients undergoing SAE for a variety of distinct indications revealed a high degree of technical success (100%) and short-term procedural efficacy (90%). Only five patients required further treatment due to rebleeding within 30 days. Of those, four had initially presented with splenic hemorrhage, a situation in which treatment failure due to rebleeding is not uncommon (19, 20). SAE showed particular promise in the fifteen patients who were treated for variceal hemorrhage, none of whom suffered recurrent bleeding at 30 days. This result corroborates the findings of prior analyses (5) and supports the utility of SAE in controlling hemorrhage in patients with isolated gastric varices or in individuals that cannot undergo transjugular intrahepatic portosystemic shunt placement for treatment of variceal hemorrhage.

While our results confirm the documented efficacy of SAE, we observed a suboptimal overall morbidity profile that warrants consideration. The overall morbidity rate of 38% exceeds the threshold recommended by Society of Interventional Radiology for SAE complications (12), but it is likely reflective of the high-risk nature of our patient cohort. In the current study, 86% of patients were symptomatic on presentation, 60% required ICU monitoring immediately pre- or postprocedure, and 60% of the procedures were performed on an urgent or emergent basis, all of which are factors that increase the risk for negative clinical outcomes. Furthermore, approximately half of the study cohort had comorbid liver cirrhosis and pre-existing pancreatitis, while about one-third had underlying malignancy. These represent confounding conditions that may limit the physiologic reserve for tolerance of a bleeding insult and may impede postprocedure recovery. It should be noted that the procedure-specific morbidity rate in our study (16%) was in line with previous complication rates, approximated at 8%–22% (12), and the procedure-specific morbidity in patients undergoing elective SAE was 13% (although one of two total complications in the elective cohort was an arterial access complication independent of SAE). Adverse outcomes in our series included known events, such as abscess, infection, clinically significant hydrothorax, and splenoportal venous thrombosis. The latter is thought to be due to portal venous stasis and derangement in platelet storage (21). Interestingly, only one of three patients with splenoportal venous thrombosis had reactive thrombocytosis after SAE, while the other two were thrombocytopenic. Similar to the overall morbidity, we propose that the overall 30-day mortality rate of 8% in our study can be attributed to the presence of significant comorbidities among the study group, as well as the attendant hazards of surgery, the ICU, and prolonged hospitalization. It should be noted that the direct procedure-related mortality in our cohort was 0%, and no patients undergoing elective SAE died. Among the four patients who died, all were in the ICU, two (50%) were hemodynamically unstable, and two (50%) required transfusion of more than six units of packed red blood cells, highlighting the tenuous preprocedure clinical state of these patients.

Commonly observed adverse side effects in our study included postembolization syndrome (22%), the self-limited constellation of fever, leukocytosis, and abdominal pain, as well as thrombocytopenia (26%), thrombocytosis (32%), and hydrothorax (52%). These findings occur with such frequency that they may well be considered expected side effects rather than complications. They are generally without clinical consequence, although in this study thrombocytopenia was associated with the occurrence of subsequent morbidity.

A relatively low rate of splenic infarction (26%) occurred in our cohort. We believe that this is related to the preservation of collateral circulation in most cases due to the predominant use of coil embolization (employed in 100% of cases) rather than particle embolization (applied in only 8% of cases) in our series. Coil embolization of the main splenic artery allows for conservation of the collateral splenic circulation via the short gastro or greater pancreatic arterial supply, which may potentially limit the degree of splenic infarction. In contrast, splenic infarction is associated primarily with distal embolization techniques (20), and the use of particles results in distal splenic arterial occlusion beyond arterial collateral arcades and increases the risk for parenchymal devascularization. Notably, the risk of clinically significant complications increases when the splenic infarction volume exceeds 70% (22), and the extent of the infarction can be minimized by limiting the volume of embolization (23). Though typically asymptomatic, potential sequelae of excessive splenic infarction include splenic abscess and infection with encapsulated bacteria (1). Notably, prophylactic vaccination after SAE is not routine and was not consistently applied in this study. In contrast to operative splenectomy, which entails a 1%–2% lifetime risk of sepsis, the effect of embolization on splenic immune function remains poorly characterized (24). In the context of splenic injury, one study of 24 patients indicated a preserved immune response to Haemophilus influenzae and Streptococcus pneumoniae 26 months after proximal SAE, with Howell-Jolly bodies present in only 8.3% (25). Another investigation followed 34 patients for an average of 4.4 years and found no evidence of splenic insufficiency as indicated by a lack of Howell-Jolly bodies in the peripheral blood (26). Several other series compared SAE patients to healthy controls and did not identify significant differences in various immunologic parameters (27, 28). Only one study found no difference between SAE and splenectomy with respect to measures of anti-pneumococcal antibodies (29). Although data from large prospective studies are lacking, the available evidence suggests that prophylactic vaccination after SAE may be unnecessary. However, the high mortality of potential splenic compromise and the low risks associated with vaccination leave room for clinical discretion.

To date, few data exist relating prognostic factors to the clinical outcomes of SAE. Advanced age has been associated with major complications in patients with splenic trauma (30), while a large infarction volume and Child-Pugh class C disease are risk factors for complications in the setting of hypersplenism (31, 32). In the current study, multivariate analysis confirmed advanced age as a risk factor and also identified postprocedural thrombocytopenia, postprocedural hydrothorax, and the need for secondary interventions as significant predictors of 30-day morbidity. The overall mortality was predicted by renal insufficiency, preprocedure hemodynamic instability,
and preprocedure leukocytosis. These clinical or laboratory signs should alert clinicians to the potential for complications and the need for close patient monitoring. It must be noted that SAE is commonly performed in urgent or emergent settings and often after other treatment modalities have failed; patient selection will therefore rarely be ideal. These prognostic factors may serve as a valuable tool in the identification of high-risk cases and as a guide for patient counseling regarding the potential for adverse outcomes. The decision to proceed with SAE should be made on an individual basis after careful assessment of the risks and benefits.

There were several important limitations to this study. First, this study was retrospective and nonrandomized in nature, and it is subject to the inherent weaknesses of nonprospective studies. Second, our investigation was conducted at a single institution. Third, very minor technical differences in the SAE procedures were present among patients in the study groups. Fourth, some patients underwent operative spleectomy during the 30-day post-procedure period, which may influence comparison with the remainder of the study cohort.

In summary, SAE is an effective intervention for treating a variety of medical conditions. While elective SAE is safe and is associated with low morbidity and mortality rates, urgent or emergent SAE may be associated with nontrivial morbidity, and the risk of complications is increased by advanced age, postprocedure thrombocytopenia or hydrothorax, and the need for secondary interventions. The presence of these factors should prompt close observation and guide clinical care. Postembolization immunocompetence and the role of prophylactic vaccination require further investigation.

Conflict of interest disclosure

The authors declared no conflicts of interest.

References


