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Intra-arterial ampicillin and gentamicin and the incidence of splenic abscesses following splenic artery embolization: A 20-year case control study☆

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ABSTRACT

Purpose: Splenic abscesses represent a major complication following splenic artery embolization. The purpose of this study was to assess the effectiveness of intra-arterial antibiotics administered during splenic artery embolization in reducing splenic abscess formation.

Materials and methods: 406 patients were screened. 313 (77.1%) patients who underwent splenic artery embolization and were > 18 years old were included. Mean age of the cohort was 58 ± 15 years (range: 18–88 years). There were 205 (65.5%) male patients and 108 (34.5%) female patients. 197 (62.9%) patients underwent embolization without intra-arterial antibiotics and 116 (37.1%) patients underwent embolization with 1 g ampicillin and 80 mg gentamicin administered in an intra-arterial fashion. Primary outcome was splenic abscess formation. Secondary outcomes included type of splenic artery embolization, embolic agent, and technical success.

Results: Partial splenic embolization was performed in 229 (73.1%) patients. Total splenic embolization was performed in 84 (26.8%) patients. Platinum coils were the most commonly used embolic agent overall (n = 178; 56.9%) followed by particulates (n = 114; 36.4%). Embolization technical success was achieved in 312 (99.7%) patients. 7 (3.6%) splenic abscesses were detected in the non-intra-arterial antibiotic group and 1 (0.9%) in the intra-arterial antibiotic cohort (P = 0.27). Coils were found to be statistically more likely to result in splenic abscesses than any other embolic agent (P = 0.03). Mean time to abscess identification was 74 days ± 120 days (range: 9–1353 days).

Conclusion: Splenic abscesses occurred more frequently in patients who did not receive intra-arterial antibiotics during splenic embolization; however, this did not reach statistical significance.

1. Introduction

Splenic artery embolization was initially reported in 1973 and was followed by the development of partial splenic embolization in 1979 [1,2]. Since its inception, splenic artery embolization has become a safe and effective intervention for the treatment of hypersplenism, splenic trauma, cirrhosis with portal hypertension, idiopathic thrombocytopenic purpura, hereditary spherocytosis, and thalassemia [3,4]. However, there are major complications that can follow splenic artery embolization including: splenic abscess formation, inadvertent splenic

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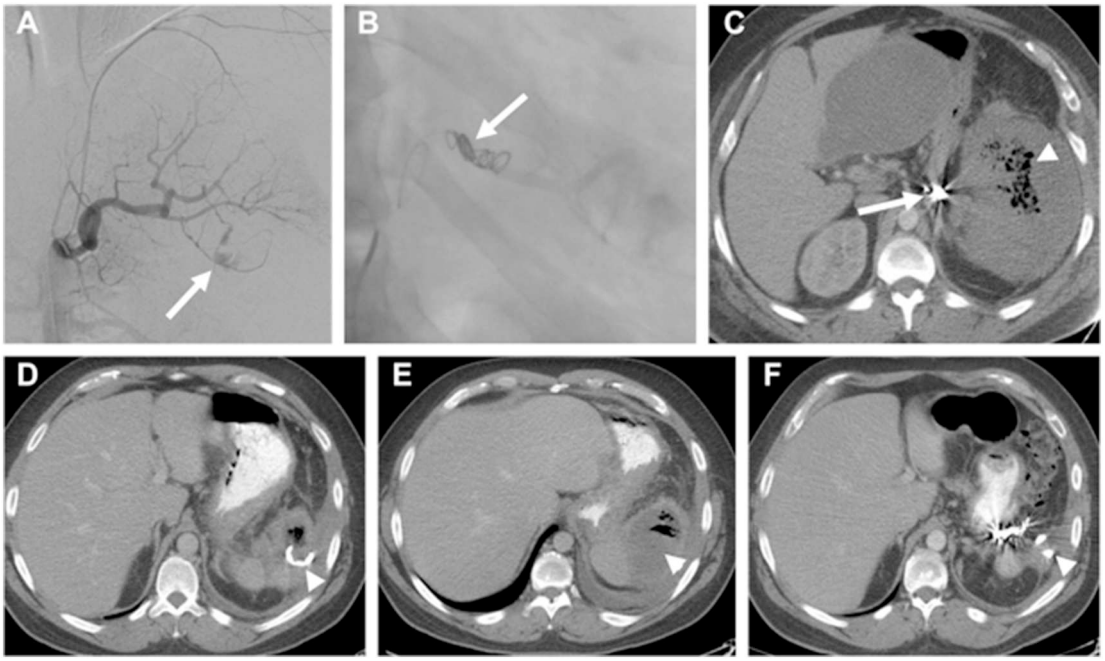

Fig. 1. 40-year-old male status post fall with splenic laceration. (A) Digital subtraction arteriography demonstrating active extravasation from the lower pole of the spleen (white arrow) as well as irregularity of interpolar branches. (B) Selective splenic artery embolization of interpolar and inferior segmental branches with 300–500 μm particles. No intra-arterial antibiotics were administered. Coil embolization of the proximal splenic artery was also performed (white arrow). (C) Axial computed tomography image demonstrating coils within the proximal splenic artery (white arrow). A large gas-containing fluid collection is seen within the splenic bed (white arrowhead). (D, E) Prolonged catheter drainage was performed. Follow-up axial computed tomography image at 93 days after drainage demonstrating a pigtail catheter (D, white arrowhead) and reduction in size of the fluid collection with residual abscess still present (E, white arrowhead). (F) Catheter exchange was performed with follow-up computed tomography at 150 days after embolization demonstrating complete decompression of the abscess (white arrowhead). The drain was subsequently removed.

infarction, contrast-induced renal insufficiency, splenic cyst development, and non-target embolization [5].

Splenic abscesses have been documented to occur in 6.8% of patients undergoing splenic artery embolization [5]. Practice guidelines have suggested that pre-procedural systemic antibiotic prophylaxis prior to splenic embolization when there is intent to infarct splenic tissue be given as this may result in significant volumes of necrotic tissue in contaminated areas [6,7]. Intra-arterial antibiotics have been recommended as a prophylactic technique during splenic embolization to reduce the rate of splenic abscess formation; however, these results are based on secondary findings from a single study of 44 patients [8].

The purpose of this study was to determine whether the incidence of splenic abscess formation following splenic embolization was effected by the addition of intra-arterial ampicillin and gentamicin to the embolic mixture.

2. Methods

2.1. Patient selection

This study was conducted with institutional review board approval and complied with the Health Insurance Portability and Accountability Act. Informed consent was not required for this retrospective study. A retrospective search of the IRAD laboratory database generated from the Electronic Medical Record Search (EMERSE; Ann Arbor, MI) was performed from December 25, 1996 to November 7, 2017 (7622 days) [9,10].

2.2. Inclusion and exclusion criteria

Using the search terms “splenic embolization” and “spleen embolization,” 406 patients were identified. 93 (22.9%) patients who did not undergo splenic artery embolization or were < 18 years old were excluded. 313 (77.1%) patients who underwent splenic artery embolization were included in the analysis.

2.3. Measured and defined variables

Age, gender, indication for splenic artery embolization, type of splenic artery embolization, embolic agent, technical success of splenic artery embolization, immediate complications, absence or presence of systemic antibiotics prior to embolization, absence or presence of intra-arterial antibiotics during embolization, absence or presence of systemic antibiotics following embolization, presence of splenic abscess on post-embolization cross-sectional imaging, and mortality were recorded. Primary outcome was splenic abscess formation. Secondary outcomes included type of splenic artery embolization, embolic agent, technical success, and follow-up duration. Type of splenic artery embolization was defined by the operator as partial (i.e., < 90% devascularization on arteriography) or total (i.e., ≥ 90% devascularization on arteriography). The initial parenchymal arteriographic blush of the spleen was calculated by assuming the spleen had a shape of a semicircle on the anteroposterior projection. The formula: Area = $\pi r^2/2$ was then applied to calculate the initial area of parenchymal blush. The percentage of devascularization was then calculated using the formula (% devascularization) = 1-(area parenchymal blush after embolization)/(initial area of parenchymal blush). Embolic agents were classified as platinum coils, particulates, gelatin foam pledgets (Gelfoam, Upjohn, Kalamazoo, MI), or microvascular plugs. Technical success was defined as successful administration of embolic agent. Immediate complications were recorded according to the Society of Interventional Radiology practice guidelines [11,12]. Intra-arterial antibiotics were 1 g ampicillin (Fresenius Kabi; Lake Zurich, IL) and 80 mg gentamicin (Fresenius Kabi; Lake Zurich, IL). Absence or presence of splenic abscess was determined based on manual review of all imaging and medical documentation in all patients.

2.4. Splenic artery embolization technique

Splenic artery embolization techniques are shown in Fig. 1. Splenic artery embolization has been described elsewhere [13–17]. All patients were seen by an attending interventional radiologist in the clinic or during inpatient consultation before the procedure. Procedures were performed with general anesthesia or moderate sedation with intravenous midazolam (Pfizer; New York City, NY) and fentanyl (Akorn; Lake Forest, IL) administered by an attending anesthesiologist or certified registered nurse anesthetist. Under ultrasound-guidance, a 5-French sheath was placed and celiac and splenic arteriography were performed. Using a 2.8-French microcatheter (Renegade Hi-Flo, Boston Scientific; Marlborough, MA), 4-French catheter, or 5-French catheter, splenic artery embolization was performed. Choice of embolic agent, including platinum coils, particulates, gelatin foam pledgets, or microvascular plugs, was based on operator preference. In cases utilizing intra-arterial antibiotics, 1 g ampicillin and 80 mg gentamicin were mixed with the embolic agents and instilled during embolization. Post-embolization arteriography was performed in all patients.

2.5. Statistical analyses

The proportions of two independent groups were compared by an approximate z-test, while the paired proportions were compared by a McNemar's test. Independence between two categorical variables was assessed by a Chi-squared test or Fischer's exact test. In order to compare the time to detect splenic abscesses, Kaplan-Meier curves were generated for each group of patients and a log-rank test was conducted. For continuous variables, two-sample *t*-tests were conducted to compare population means of two independent groups. A P-value < 0.05 was considered as statistically significant for all tests. Analyses were performed by R software version 3.2.2 (R Core Team; Vienna, Austria).

3. Results

3.1. Patient demographics

Patient demographics are shown in Table 1. The proportion of splenic aneurysm and pseudoaneurysm in the non-intra-arterial antibiotic group was significantly higher than that in the intra-arterial antibiotic group (P = 0.004 and P = 0.008, respectively). The proportion of thrombocytopenia and splenomegaly in the non-intra-arterial antibiotic group were significantly lower than those in the intra-arterial antibiotic group (P < 0.001 and P = 0.002, respectively).

197 (62.9%) patients underwent splenic embolization without intra-arterial antibiotics and 116 (37.1%) patients underwent splenic embolization with intra-arterial antibiotics.

Table 2
Type of embolization, embolic agent, and technical success rate.

	All patients		No Intra-arterial antibiotics		Intra-arterial antibiotics		P value
	n = 313		n = 197		n = 116		
Type of embolization							
Partial	229	73.1%	129	65.5%	100	86.2%	< 0.001
Total	84	26.8%	68	34.5%	16	13.8%	
Embolic agent							
Coils	178	56.9%	146	74.1%	32	27.6%	< 0.001
Particles	114	36.4%	34	17.3%	80	69.0%	< 0.001
Gelatin foam	57	18.2%	40	20.3%	17	14.7%	0.22
Vascular plug	18	5.8%	17	8.3%	1	0.9%	0.004
Glue	6	1.9%	6	3.0%	0	0.0%	0.08
Balloon occlusion	3	1.0%	2	1.0%	1	0.9%	1.0
Technical success	312	99.7%	196	99.5%	61	100.0%	1.0

Patients may have had more than one embolic agent used for embolization.

3.2. Type of embolization

Type of embolization is shown in Table 2. Partial splenic embolization was performed in 229 (73.1%) patients, with 129 (65.5%) patients in the non-intra-arterial antibiotic group and 100 (86.2%) patients in the intra-arterial antibiotic group receiving partial splenic embolization (P < 0.001). Total splenic embolization was performed in 84 (26.8%) patients overall with a higher proportion of patients in the non-intra-arterial antibiotic group (n = 68; 34.5%) undergoing total splenic embolization compared to the intra-arterial antibiotic group (n = 16; 13.8%) (P < 0.001).

3.3. Embolic agent

Embolic agent is shown in Table 2. Platinum coils were the most commonly used embolic agent overall (n = 178; 56.9%) followed by particulates (n = 114; 36.4%), gelatin foam pledgets (n = 57; 18.2%),

Table 1
Patient demographics and indication for splenic embolization.

	All patients		No intra-arterial antibiotics		Intra-arterial antibiotics		P value
	n = 313		n = 197		n = 116		
Age							
Mean ± SD	58 ± 15		59 ± 15		56 ± 16		0.73
Range	18–88		18–88		18–75		
Sex							
Male	205	65.5%	151	76.7%	54	46.6%	< 0.001
Female	108	34.5%	48	24.3%	60	51.7%	
Indication							
Splenic laceration	157	50.1%	102	51.8%	55	47.4%	0.48
Portal hypertension	69	22.0%	39	20.0%	30	26.5%	0.21
Splenic artery aneurysm	45	14.4%	37	18.8%	8	7.9%	0.004
Thrombocytopenia	37	11.8%	6	3.0%	31	26.7%	< 0.001
Pseudoaneurysm	21	6.7%	19	9.6%	2	1.7%	0.008
Splenic rupture	16	5.1%	10	5.1%	6	5.2%	1.0
Splenomegaly	11	3.5%	2	1.0%	9	7.8%	0.002
Gastrointestinal bleed	9	2.9%	6	3.0%	3	2.6%	1.0
Splenic steal	8	2.6%	7	3.6%	1	0.9%	0.27
Non-bleeding varices	4	1.3%	4	2.0%	0	0.0%	1.0
Surgical complication	3	1.0%	3	1.5%	0	0.0%	1.0

Patients may have had more than one indication for embolization.

and microvascular plugs (n = 18; 5.8%) (some patients had multiple agents used for embolization). Platinum coils were the most commonly used embolic agent in the non-intra-arterial antibiotic patients (n = 146; 74.1%) followed by Gelfoam pledgets (n = 40; 20.3%) and particulates (n = 34; 17.3%). Particulates were the most commonly used embolic agent in the intra-arterial antibiotic patients (n = 80; 69.0%) followed by coils (n = 32; 27.6%) and gelatin foam pledgets (n = 17; 14.7%). The proportion of platinum coils and vascular plugs used in the non-intra-arterial antibiotic group was significantly higher than that in the intra-arterial antibiotic group ($P < 0.001$ and $P = 0.004$, respectively). The proportion of particulates used in the non-intra-arterial antibiotic group was significantly lower than that in the intra-arterial antibiotic group ($P < 0.001$). There was; however, no significant difference in rate of utilization of gelatin foam pledgets between the two groups ($P = 0.944$).

3.4. Technical success

Technical Success is shown in Table 2. Splenic artery embolization technical success was achieved in 312/313 (99.7%) patients. Splenic artery embolization was technically successful in 116/116 (100%) of intra-arterial antibiotic patients and 196/197 (99.5%) non-intra-arterial antibiotic patients. The technical failure was secondary to inadvertent dissection of the splenic artery prior to embolization, and the patient received no embolization material. There was no significant difference in the proportions of technical successes between the two groups ($P = 1.0$).

3.5. Immediate complications

There were no immediate minor or major complications according to the Society of Interventional Radiology practice guidelines [11,12].

3.6. Systemic antibiotics

Systemic antibiotics are shown in Table 3. Overall, pre-embolization and post-embolization systemic antibiotics were given in 119/313 (38.0%) and 160/313 (51.1%) patients, respectively. In the non-intra-arterial antibiotic patients, pre-embolization and post-embolization systemic antibiotics were given in 77/197 (39.1%) and 100/197 (50.8%) patients, respectively. In the intra-arterial antibiotic patients, pre-embolization and post-embolization systemic antibiotics were given in 42/116 (36.2%) and 60/116 (51.7%) patients, respectively. There was no significant difference between the proportion of pre-embolization ($P = 0.63$) and post-embolization ($P = 0.91$) antibiotics prescribed between the two groups.

3.7. Splenic abscesses

Incidence of splenic abscess formation is shown in Table 4. Eight (2.6%) splenic abscesses were detected. Seven (3.6%) splenic abscesses were detected in the non-intra-arterial antibiotic group and 1 (0.9%) splenic abscess was detected in the intra-arterial antibiotic group. There was no significant difference between the incidence of splenic abscess formation between the two groups ($P = 0.27$). When the form of embolic agent used to perform splenic embolization was assessed, coils were found to be used either alone or in conjunction with another embolic agent in 75% of the cases that resulted in abscesses and were statistically more likely to result in abscess formation ($P = 0.03$). The one abscess reported within the intra-arterial antibiotic group was performed on a patient with thrombocytopenia and was detected following a partial embolization using embolic particles.

Overall, the mean time to abscess identification was 74 ± 120 days following initial embolization (range: 9–1353 days). The mean time to abscess identification in the non-intra-arterial antibiotics patients was 83 ± 126 days (range: 9–1353 days). The single splenic abscess identified in the intra-arterial antibiotic patient was discovered 26 days after the embolization. There was no significant difference in the Kaplan-Meier curves for detection of splenic abscesses between groups ($P = 0.253$).

3.8. Mortality

Eighteen (5.8%) patients died during the study period. The mortality rate in the non-intra-arterial antibiotic and intra-arterial antibiotic patients was 6.6% (n = 13) and 4.3% (n = 5), respectively ($P = 1.0$).

4. Discussion

Splenic abscess development is associated with a mortality rate as high as 16% [18]. Following proper antibiotic therapy with catheter or surgical drainage; however, mortality may be reduced to 5.6% [19]. Owing to the significant complications associated with splenic abscesses, proper pre-procedural, intra-procedural, and post-procedural antibiotic prophylaxis during splenic artery embolization should be considered as a method to potentially prevent abscess formation. While the use of systemic antibiotics has become standard practice during splenic artery embolization when infarction is the goal to prevent contamination by skin flora and subsequent abscess development, it has been suggested that delivering intra-arterial antibiotics during embolization may mitigate retrograde transport of enteric pathogens [7,8].

The results of the current study suggest that intra-arterial antibiotics administered during splenic artery embolization do not significantly reduce the rate of splenic abscess formation. *Masada* et al. described the rate of splenic abscess formation following splenic artery embolization with intra-arterial antibiotics [8]. Only one splenic abscess was discovered among the 44 subjects; however, prompting the investigators to compare C-reactive protein (CRP) levels as a marker for inflammation. Their analysis showed that CRP levels were significantly lower in the group which received gelatin sponge embolization in conjunction with intra-arterial antibiotics compared to those who received gelatin sponge embolization alone at two weeks post-embolization. Although CRP is a nonspecific proxy for abscess formation, these results appear to

Table 3
Use of systemic antibiotics and duration from embolization until administration of post-embolization antibiotics.

	All patients		No intra-arterial antibiotics		Intra-arterial antibiotics		P value
	n = 313		n = 197		n = 116		
Systemic antibiotics							
Pre-embolization	119	38.0%	77	39.1%	42	36.2%	0.63
Post-embolization	160	51.1%	100	50.8%	60	51.7%	0.91
Time from embolization to antibiotics (days)							
Mean ± SD	6.4 ± 15.6		8.2 ± 17.3		3.8 ± 9.1		
Median	0		0		0		
Range	0–89		0–89		0–41		

Table 4
Rate of abscess formation and duration until abscess detection.

	All patients		No intra-arterial antibiotics		Intra-arterial antibiotics		P value
	n = 313		n = 197		n = 116		
Abscess detected on cross-sectional imaging	8	2.6%	7	3.6%	1	0.9%	0.27
Time to abscess detection (days)							
Mean ± SD	74 ± 120		83 ± 126		26 ± 0		0.253
Median	25.5		25		26		
Range	9–1353		9–1353				

suggest that intra-arterial antibiotics prevent abscess formation; however these results were not supported by the current analysis.

Previously, partial splenic embolization has been shown to protect against severe infection as it preserves functional splenic tissue [4]. However, recent reports have indicated that complete splenic embolization may be associated with lower rates of splenic abscess formation when compared to partial embolization [20–22]. The present study consisted of predominantly partial splenic embolizations (73.1%), and this held especially true within the intra-arterial antibiotic group where 86.2% of the embolizations were partial in nature. If claims of previous reports hold true, the authors would expect the rate of abscess formation recorded in the current study to be higher as significantly more partial embolizations were performed. While there are major complications that may occur with both partial and total splenic embolizations, they both remain safer options for the treatment of many splenic pathologies when compared to surgical splenectomy. The morbidity of severe complications after splenectomy, including laparoscopic and open splenectomy, approach 26% [23].

There is currently no consensus on which embolic agent provides the most durable short-term therapeutic response during splenic embolization [7]. It is possible that the higher rate of platinum coil utilization in the non-intra-arterial antibiotic patients partially contributed to the increased rate of splenic abscess formation. The wedge-shaped post-procedural enhancement seen on contrast-enhanced computed tomography following segmental coil embolization may lead to increased destruction of the splenic white pulp, thereby impairing immunologic function [8]. Further research is needed to determine if partial splenic embolization with gelatin foam pledgets and particulates preserves immunological function and decreases rates of splenic abscess formation.

The selection of the proper antibiotic during splenic embolization is also debatable. The most common pathogens isolated from splenic abscesses related to splenic artery embolization include *Staphylococcus epidermis, Enterobacter cloaca,* and *Bacteroides fragilis* [24,25]. The previous study utilized the second-generation cephalosporin, flomoxef, while the current study used a combination of ampicillin and gentamicin. While no standard for intra-arterial antibiotic exists, coverage of common skin, enteric, and anaerobic pathogens should be required for adequate prophylaxis.

There are several limitations to the present study including its retrospective nature. Additionally, time to imaging follow-up was not consistent for every patient and the detection rate of splenic abscesses varies between imaging modalities [26]. A variety of indications for splenic embolization were included in this analysis; as such the difference in abscess formation may be partially related to the pathophysiologic mechanisms involved with the different diseases. Also the indications for splenic artery embolization differed between the two comparison groups. There were proportionately more patients presenting with splenic lacerations in the group which did not receive intra-arterial antibiotics and proportionately more patients presenting with portal hypertension and thrombocytopenia in the intra-arterial antibiotic group. There was also confounding between the effect of the systemic antibiotics and the intra-arterial antibiotics on prevention of splenic abscess formation.

5. Conclusion

While the incidence of splenic abscess formation was lower in patients who underwent splenic embolization with intra-arterial ampicillin and gentamicin, this observation did not reach statistical significance.

COI Statements

This study was not supported by any funding.

The authors declare that they have no conflict of interest.

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

This study was conducted with institutional review board approval and complied with the Health Insurance Portability and Accountability Act. Informed consent was not required for this study.

For this type of study consent for publication is not required.

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