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Original Article

Hepatic Arterioportal Fistulas: A Retrospective Analysis of 97 Cases

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Abstract

Background and Aims: Hepatic arterioportal fistulas (HAPFs) are abnormal shunts or aberrant functional connections between the portal venous and the hepatic arterial systems. Detection of HAPFs has increased with the advances in diagnostic techniques. Presence of HAPFs over a prolonged period can aggravate liver cirrhosis and further deteriorate liver function. However, the underlying causes of HAPFs and the treatment outcomes are now well characterized. This study aimed to summarize the clinical characteristics of patients with HAPFs, and to compare the outcomes of different treatment modalities. ***Methods:*** Data of 97 patients with HAPFs who were admitted to the Second Xiangya Hospital between January 2010 and January 2020 were retrospectively reviewed. Demographic information, clinical manifestations, underlying causes, treatment options, and short-term outcomes were analyzed. ***Results:*** The main cause of HAPF in our cohort was hepatocellular carcinoma (78/97, 80.41%), followed by cirrhosis (10/97, 10.31%). The main clinical manifestations were abdominal distention and abdominal pain. Treatment methods included transcatheter arterial embolization (n=63, 64.9%), surgery (n=13, 13.4%), and liver transplantation (n=2, 2.1%); nineteen (19.6%) patients received conservative treatment. Among patients who underwent transcatheter arterial embolization, polyvinyl alcohol, lipiodol combined with gelatin sponge, and spring steel ring showed comparable efficacy. ***Conclusions:*** Hepatocellular carcinoma and cirrhosis are common causes of HAPFs. Transcatheter arterial embolization is a safe and effective method for the treatment of HAPFs, and polyvinyl alcohol, lipiodol combined with gelatin sponge, and spring steel ring showed comparable efficacy in our cohort.

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Keywords: Hepatic arterioportal fistulas; Embolization; Hepatocellular carcinoma; Cirrhosis.

Abbreviations: CT, computed tomography; DSA, digital subtraction angiography; HAPFs, hepatic arterioportal fistulas; HCC, hepatocellular carcinoma; MRI, magnetic resonance imaging; PVA, polyvinyl alcohol.

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Introduction

Hepatic arterioportal fistulas (HAPFs) refer to abnormal shunts or aberrant functional connections between the portal vein and the hepatic artery.[1] HAPFs are rare entities; however, advances in diagnostic techniques have helped increase the detection rate of HAPFs. HAPFs can be congenital, although most of these lesions are acquired.[2] Common causes include hepatocellular carcinoma (HCC), cirrhosis, and iatrogenic (secondary to liver biopsy, transhepatic biliary drainage, transhepatic cholangiogram, and surgery).[3] Patients with HAPFs may be asymptomatic or can present with symptoms of portal hypertension (such as ascites, gastrointestinal bleeding, diarrhea, and congestive heart failure).[4,5] The symptoms are largely dependent on the size, location, shunt volume, and liver resistance of the fistula.[6,7] Moreover, HAPFs may impair the arterial blood perfusion in the liver, critically affecting the supply of oxygen and various nutrients to the liver, and eventually aggravating liver function.[8] Effective sealing of the fistula can reduce the portal pressure, increase blood perfusion, and hasten recovery.

The treatment modalities of HAPFs include surgery and minimally-invasive percutaneous interventions (usually transcatheter embolization). However, surgery is costly and is usually associated with major trauma and slow recovery. Conversely, transcatheter embolization offers the advantages of low morbidity, repeatability, and lower cost; therefore, it is regarded as the first-line treatment for HAPFs.[4,9–11] Various embolic agents have been used, such as lipiodol, gelatin sponge particles, spring steel coils, and polyvinyl alcohol (PVA) particles. The aim of embolization is to obliterate the fistula, improve clinical condition, and prolong survival time.[12] Embolization can be performed with a single material or a combination of materials; the type of embolic agent employed is primarily dependent on the size of the fistula. Each agent has its advantages and disadvantages, and can be chosen appropriately based on the individual circumstances. For example, lipiodol is useful in patients with poor or no blood shunt,[13–15] however, it can easily occlude small blood vessels and cause liver tissue ischemia. Therefore, it is not suitable in HCC cases with severe HAPFs.[16] PVA needs to be combined with a contrast agent and is effective in long-

term sealing, with fewer side effects. Spring steel coils are long-term embolization materials that are normally used for high-flow HAPFs; however, coils are typically used for simple shunts because in complex shunts, the coil may not reach small feeders that are difficult to access and distally located. Moreover, shunts with multiple feeders are prone to recanalization.[17,18] Gelatin sponge particles are a medium-term embolization material, which are typically resorbed within 2–4 weeks, leading to a high recanalization rate.[19]

Despite an increase in the reported cases of HAPFs, the clinical characteristics of these patients and the efficacy of the different embolization methods are not well characterized in the contemporary literature. In the present study, we sought to retrospectively summarize the characteristics of HAPFs treated in a single center and compare the efficacy of different embolization methods.

Methods

This was a retrospective, single-center study conducted at a tertiary care hospital in China. The study was approved by the ethics committee of the Second Xiangya Hospital, Central South University. Written informed consent was obtained from all subjects. The study protocols conformed to the ethical principles enshrined in the latest version of the Declaration of Helsinki. Data pertaining to consecutive patients with HAPFs who were admitted to the Second Xiangya Hospital of Central South University between January 2010 and January 2020 were retrieved from the medical records. For all patients, the diagnosis of HAPF was based on imaging examination (digital subtraction angiography (DSA), Doppler ultrasound, computed tomography (CT), or magnetic resonance imaging (MRI)). On DSA, HAPFs manifest as filling of the contrast medium in the portal vein through the fistula in the arterial phase after injection of the contrast medium. CT or MRI signs of HAPFs include early visualization of the portal vein, early enhanced visualization of the portal vein, abnormal vascular mass, and wedge-shaped or triangular hepatic segment (Fig. 1). On Doppler ultrasound, HAPFs are characterized by bidirectional, low-impedance bidirectional blood flow in the portal vein (Fig. 2).

Treatment methods

Transcatheter arterial embolization: After clearly displaying the location, size, and type of the fistula, the most appropriate embolization material and embolization method were selected to occlude the fistula. The embolic materials used were lipiodol (Guerbet Group, France, 1238 yuan per bottle), PVA (Cook Group, USA, 1450 yuan per bottle), gelatin sponge granule particle (made by our hospital, 98 yuan per piece), spring steel (Cook Group, USA, 1898 yuan per piece), or a combination of two or more materials of the above four materials. The size and number of embolic materials used depended on the size of fistula.

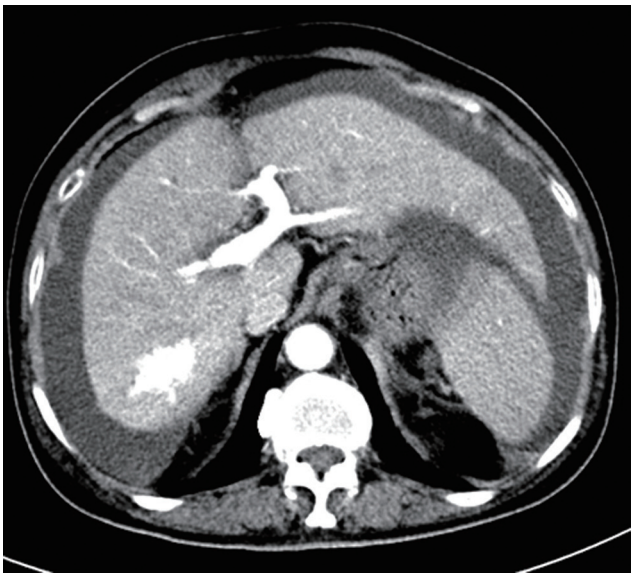

Fig. 1. Representative computed tomography findings of HAPF showing early enhancement of the portal vein in the arterial phase. HAPF, hepatic arterioportal fistula.

Surgical treatment: Some patients with liver cancer and hepatic artery fistula were treated by surgical resection of the lesion. Some patients with liver cancer were fitted with a chemotherapy pump when necessary.

Liver transplantation: Liver transplantation was performed in some patients with congenital HAPFs or liver cancer.

Assessment of treatment outcomes

Short-term efficacy of transcatheter arterial embolization

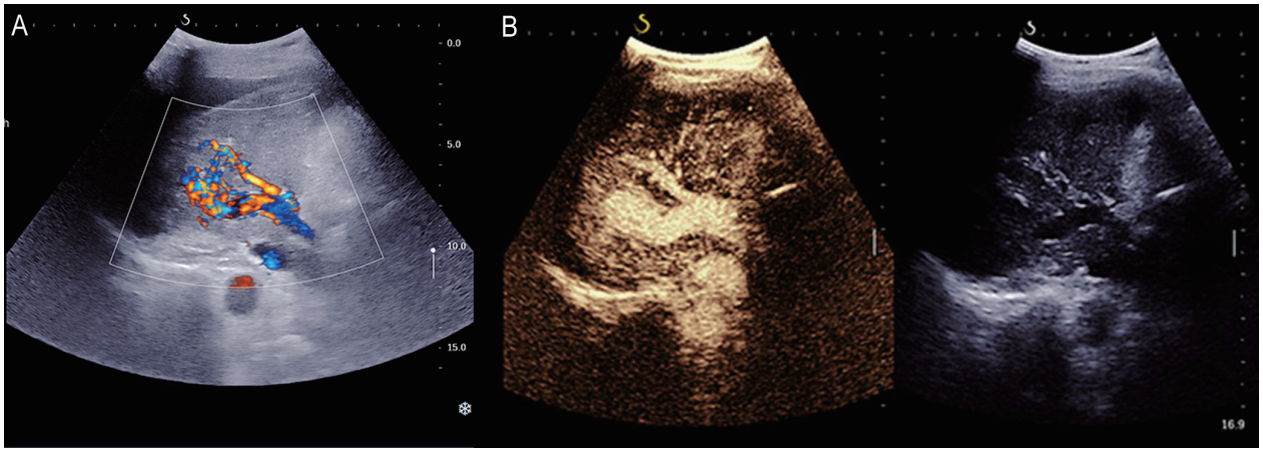

Fig. 2. Ultrasound image showing HAPFs under Doppler (A) and Sonovue contrast (B). HAPF, hepatic arterioportal fistula.

Table 1. Clinical characteristics of the study population

Clinical feature	Value
Sex, % cases (*n*)	
Male	85.57 (83)
Female	15.43 (14)
Mean age in years	52.06±13.81
Etiology, % cases (*n*)	
HCC	80.41 (78)
Cirrhosis*	10.32 (10)
Congenital	2.06 (2)
Portal spongiform transformation	2.06 (2)
Portal hypertension	2.06 (2)
Liver trauma	1.03 (1)
Unclear	2.06 (2)
HCC clinical classification, % cases (*n*)	100 (78)
Massive	41 (32)
Diffuse	35.9 (28)
Nodular	23.1 (18)
Clinical manifestations, % cases (*n*)	
Abdominal distension	42.3 (41)
Abdominal pain	40.2 (39)
Yellowish skin	3.1 (3)
Anorexia	2.1 (2)
Fatigue	2.1 (2)
Chest pain	2.1 (2)
Fever	2.1 (2)
Hematemesis and melena	1.0 (1)
Physical examination	4.0 (4)

*Nine out of the ten patients with liver cirrhosis had received medical intervention: three cases received liver biopsy, one received liver biopsy and laparoscopic cholecystectomy, two received endoscopic variceal ligation, on received endoscopic variceal ligation and transjugular intrahepatic portosystemic shunt (commonly known as TIPS), and two received cholecystectomy. There was no evidence of HAPFs before these medical interventions; therefore, it is difficult to clarify whether HAPFs were spontaneous or iatrogenic. HAPF, hepatic arterioportal fistula; HCC, hepatocellular carcinoma.

was assessed using the Child-Pugh score 3–7 days after the operation.[20] Long-term efficacy was defined as the closure of the fistula following application of the different embolization methods. Most of the HAPFs were induced by HCC; therefore, abdominal CT was used as the first-line surveillance method 1–2 months after the operation. Doppler ultrasound was also performed for patients who underwent lipiodol and/or coil treatment. Outcomes were graded as follows: (1) effective clinical closure: almost complete closure of the fistula; or (2) noneffective clinical closure: no change in the size of the fistula or aggravation of the fistula.

Statistical analysis

SPSS 21.0 software (IBM Corp., Armonk, NY, USA) was used for statistical analysis. Continuous variables were presented as the mean±standard deviation, and the matched-sample *t* test was used for between-group comparisons. The efficacy of various plugging materials in causing obliteration of the fistula was compared using the chi-squared test. Two-tailed *p* values <0.05 were considered indicative of statistically significance.

Results

A total of 97 HAPF patients were included in the analysis (mean age: 52.06±13.81years, range: 0–79); male: 83/95, 85.57%). Regarding etiology, in 80.41% (78/97) of the cases, HAPF was induced by HCC. Abdominal distension and pain were the most common clinical manifestations (Table 1), although it was sometimes difficult to determine whether the symptoms were attributable to HAPFs or the underlying diseases such as HCC and liver cirrhosis. Regarding treatment method, 63 cases (64.9%) underwent transcatheter arterial embolization, 13 cases (13.4%) underwent surgical resection, 2 cases (2.1%) received liver transplantation, and the remaining 19 cases (19.6%) received only conservative treatment (Fig. 3). All 13 patients who received surgical treatment had Barcelona Clinic Liver Cancer stage A HCC, and the tumor and the associated arteriovenous fistula were

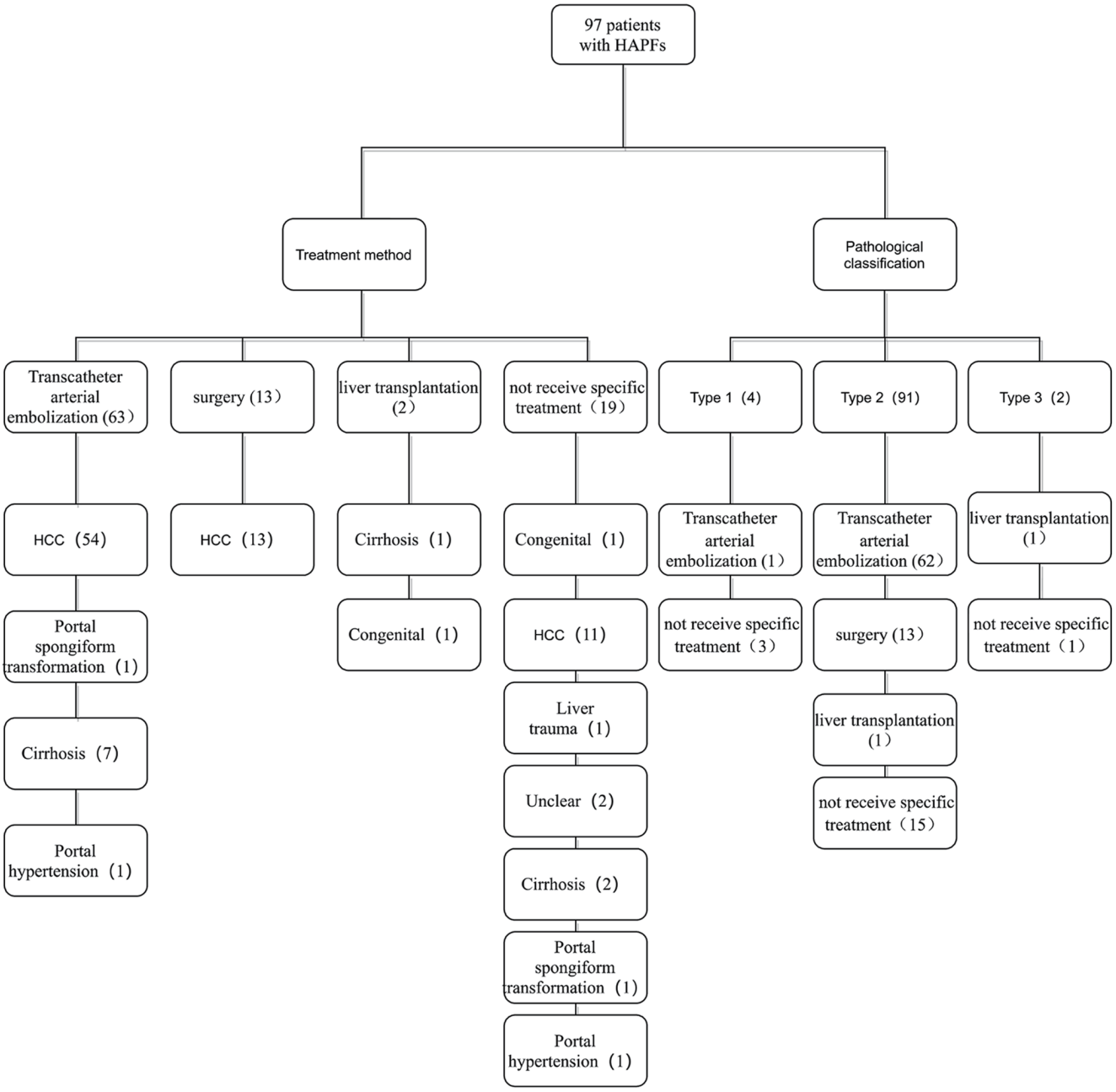

Fig. 3. Flow chart for management of the 97 cases of HAPF in the present study. HAPF, hepatic arterioportal fistula.

removed simultaneously. For the two patients who received liver transplantation, one patient had liver failure caused by chronic hepatitis B, and the other had congenital diffuse intrahepatic arteriovenous fistulas with biliary atresia. Among the 63 patients treated with transcatheter arterial embolization, 22 patients (22.7%) were treated with lipiodol embolization, 19 patients (19.5%) were treated with PVA embolization, 14 patients (14.4%) were treated with lipiodol+gelatin sponge granule particle embolization, and 8 patients (8.3%) were treated with spring steel embolization.

Among all the patients treated with transcatheter arterial embolization, discharge occurred at 3–5 days after the procedure and showed significant improvement in post-treatment liver function (assessed by Child-Pugh score) before discharge and at approximately 1 month after treatment (p=0.001; Table 2). Comparison of the outcomes revealed comparable efficacy PVA, lipiodol+gelatin sponge particles, and spring steel coils (p=0.447; Table 3). Liopiodol alone was not included in the comparison as it is not an embolic agent of choice for HAPF when used alone. Lipiodol is used in combination with other embolic agents or is used if HCC, per se, is cause of HAPF.

Discussion

HAPF was first reported approximately 50 years ago.[21] It

Table 2. Changes of liver function in patients after transcatheter arterial embolization.

Liver function status	Before therapy	3–5 days after therapy	*p* value	Before therapy	1 month after therapy*	*p* value
Child A	47	58	0.001	42	55	0.001
Child B	16	5		15	2	
Child C	0	0		0	0	

*Six patients did not undergo liver function test at 1-month follow-up; therefore, only 57 cases are included.

is defined as an abnormal intrahepatic communication between the hepatic artery and the portal venous system. HAPF is an uncommon cause of presinusoidal portal hypertension and is believed to result from increased blood flow in the portal system. Accurate diagnosis of HAPFs is challenging, as the majority of patients are asymptomatic or have nonspecific symptoms. HAPFs are sometimes incidentally detected during imaging evaluations.[1,22–24] Symptomatic HAPFs often present with complications of portal hypertension, including ascites, gastrointestinal bleeding, or heart failure.[4,5] HAPFs are usually categorized into three classes, as follows: Type 1: small peripheral intrahepatic; Type 2: large central HAPF; and Type 3: diffuse congenital intrahepatic.[22] Type 1 is usually caused by percutaneous liver biopsy. Patients are usually asymptomatic, and the HAPF typically develops thrombosis within 1 month. Close follow-up using Doppler ultrasound is recommended for these lesions. Type 2 lesions can cause portal hypertension and hepatoportal sclerosis, progressing to portal fibrosis. These fistulas require intervention to prevent the irreversible hepatic parenchymal changes. Transcatheter arterial embolization is a feasible treatment method. Type 3 is congenital HAPFs, which are usually intrahepatic and diffuse, and they cause severe portal hypertension in infancy. In the present study, 81 of the 97 patients exhibited symptoms related to portal hypertension, such as abdominal distension (41/97), abdominal pain (39/97), and gastrointestinal bleeding (1/97), although the symptoms may have also been caused by primary diseases such as HCC and cirrhosis.

Four of the 97 cases in our study were possibly Type 1, 91 cases were Type 2, and the remaining 2 were Type 3. Generally, less than 10% of HAPFs cases are congenital, usually diffuse or multiple, and most are acquired HAPFs.[4,25] Idiopathic HAPFs have also been described.[9] Common acquired causes include malignant tumors, liver cirrhosis, severe blunt or penetrating trauma, iatrogenic injury, ruptured visceral aneurysm into the portal vein, portal vein thrombosis, and Budd-Chiari syndrome.[26–28] In our cohort, the most common cause of HAPF was HCC, followed by cirrhosis, and only two patients had congenital HAPF. During HCC progression, tumors tend to infiltrate the hepatic portal vein, resulting in direct communication between the hepatic artery and portal vein, forming HAPFs.[9] Congenital HAPFs should be considered in infants who have recurrent and severe upper gastrointestinal bleeding, failure to thrive, hepatic bruit, splenomegaly or ascites. It is a rare but treatable cause of portal hypertension.[29,30] In this study, there were two children with congenital HAPFs. One was a male newborn, and the abnormality was detected *in utero* during antenatal ultrasound examination. He had a congenital arteriovenous shunt, in addition to the absence of the inferior vena cava and changes in the descending aortic arch. No special treatment was administered. The other case was a 5-year-old girl who presented with hematemesis and underwent liver transplantation after diagnosis.

Low-flow fistulas with no obvious clinical symptoms of portal hypertension do not require active intervention,[5] and periodic follow-up is recommended. In symptomatic cases, the fistula should be actively treated. Sealing of the fistula is required for the recovery of liver function. Additionally, sealing of the fistula curbs the blood shunt between the hepatic artery and the portal vein, blocking the blood supply to the tumor and starving the tumor cells of nutrients, thereby protecting normal liver tissue and reducing distant metastasis caused by HAPFs.[6,31] Both transcatheter arterial embolization and surgery are methods that can reduce portal hypertension, increase functional portal vein blood, and improve liver function.[13,31] On liver function assessment of 63 patients treated with transcatheter arterial embolization, the Child-Pugh score of 11 patients shifted from Child B to Child A 3 to 5 days after treatment, and the score of another 11 patients shifted from Child B to Child A 1 month after treatment; this indicated that transcatheter arterial embolization can help improve the liver function.

The aim of treatment of HAPFs is to achieve fistula closure. The optimum catheter position should be as close as possible to the fistula site. Currently, there is no clear consensus with respect to the choice of embolic agent; the choice should be based on the embolization properties of the agent, the angio-architecture of the shunt and its underlying mechanism.[18] Lipiodol, gelatin sponge particles, absolute ethanol, spring steel coils, PVA particles, or a combination of the above materials have been reported for embolization of the HAPFs, with acceptable results in selected patients.[32–36] However, comparison between these materials is rare. In the study by Murata *et al*.,[32] transcatheter arterial chemoembolization of HCC-associated HAPFs with corresponding portal vein occlusion showed better therapeutic efficacy, tumor response and survival outcomes compared with shunt embolization with coils and/or gelatin sponge particles. Huang *et al*.,[37] treated 97 cases of HCC-associated HAPFs with ethanol (n=64) or gelfoam (n=33); they reported higher complete occlusion rate, lower recanalization rate and better survival in the ethanol group compared to that in the gelfoam group. In the present study, we treated 63 patients with four different materials, and we

Table 3. Comparison of the outcomes of embolization of HAPFs with different embolization materials

Embolization method	Effective clinical closure	Noneffective clinical closure	Total	*p* value
Polyvinyl alcohol	18	1	19	0.447
Lipiodol+gelatin Sponge granules	12	2	14	
Spring steel	8	0	8	
Total	51	12	63	

HAPF, hepatic arterioportal fistula.

retrospectively retrieved the medical data and compared their efficacies. We found no significant difference between PVA, lipiodol+gelatin sponge, and spring steel ring. We did not compare lipiodol with the other three materials because liopiodol alone is not an embolic agent of choice for HAPF, and it is used in combination with other embolic agent or used in treatment of HCC, if HCC, per se, is the cause of HAPF.

Some limitations of our study should be acknowledged. First, this was a single-center, retrospective study with a relatively small sample size. A prospective, large-scale study is required to obtain more definitive evidence. Second, this study was conducted at a tertiary hospital, where other embolization methods such as balloon occlusion or other new materials have not been used; therefore, our results may not be generalizable to patients treated in other settings. Third, most of the HAPFs in our cohort were Type 2, and the majority were induced by HCC, which may differ from those reported in Western countries.

In conclusion, most of the HAPFs are acquired, commonly due to HCC and cirrhosis, and usually present with nonspecific symptoms such as abdominal distention and pain. The choice of embolic material should be guided by the location, size, and shunt of the fistula. The therapeutic effect of PVA and spring steel rings is acceptable but prospective, large-scale studies are warranted to obtain more definitive evidence.

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Conflict of interest

The authors have no conflict of interests related to this publication.

Author contributions

Study concept and design (YT), acquisition of data (BC, DL), analysis and interpretation of data (BC, KT, HZ, CL), drafting of the manuscript (YT, BC), critical revision of the manuscript for important intellectual content (YT, BC, DL), administrative, technical, or material support, study supervision (YT, DL).

Data sharing statement

The data used to support the findings of the study are available from the corresponding authors upon reasonable request.

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