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Percutaneous Transhepatic Biliary Drainage (PTBD) in Patients with nondilated Biliary system: Technical Success, Clinical Outcomes and Overall Success

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München, 12.03.2024 Sinan Deniz

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Abbreviations

BDA	Biliodigestive anastomosis
CT	Computed tomography
DAP	Dual antiplatelet
F	French
HCC	Hepatocellular cancer
HA	Hepatic artery
IR	Interventional radiology
MR	Magnetic resonance
PTBD	Percutaneous transhepatic biliary drainage
PTC	Percutaneous transhepatic cholangiography
SG	Stent-graft
SIRT	Selective internal radiotherapy
TACE	Transarterial chemoembolization
TARE	Transarterial radioembolization
US	Ultrasound

Publications

1. Percutaneous transhepatic biliary drainage (PTBD) in patients with biliary leakage: Technical and clinical outcomes. **Deniz S**, Öcal O, Wildgruber M, Ümütlü, MR, Puhr-Westerheide D, Fabritius M, Mansour N, Schulz C, Koliogiannis D, Guba M, Ricke R, Seidensticker M. Medicine (Baltimore). 2023 Sep 15; 102(37): e35213. doi: 10.1097/MD.0000000000035213.

2. Stent-graft placement for hepatic arterial bleeding: assessment of technical efficacy and clinical outcome in a tertiary care center. Öcal O, Mühlmann M, Puhr-Westerheide D, Fabritius M, **Deniz S**, Wildgruber M, D'Haese J, Werner J, Ricke J, Seidensticker M. HPB (Oxford) 2022 May; 24(5): 672-680. doi: 10.1016/j.hpb.2021.09.007.

1. Contributions

1.1 Paper I

I, Sinan Deniz, as the first author of this publication, was responsible for the conceptualization and design of the study, data collection, and analysis, as well as the interpretation, literature search, writing and submission. Co-authors were involved in statistical analysis, data acquisition, and final editing of the publication.

1.2 Paper II

I was a co-author of the second publication, where I participated in the data acquisition, interpretation of data, article review, manuscript drafting, and final editing of the manuscript.

2. Introduction

2.1 Background

Interventional radiology (IR) plays a crucial role in the management of various liver diseases, including malignancies, postoperative complications of transplant or tumor surgery, and biliary diseases [1]. The value of interventional radiology in these scenarios is multifaceted and involves minimally invasive and target-tailored procedures guided by imaging techniques, often resulting in reduced morbidity and quicker recovery compared to traditional open surgical approaches. Here is a brief overview of IR involvement in liver pathologies:

i. Primary and Secondary Liver Cancer

- *Transarterial Chemoembolization (TACE):* This transarterial technique offers a minimally-invasive treatment for intermediate-stage hepatocellular cancer (HCC) patients and liver metastases of colorectal cancer. This technique allows the delivery of chemotherapeutic agent-loaded microspheres through a microcatheter directly to the tumor via the hepatic artery, causing a focused drug delivery and vessel occlusion while minimizing systemic side effects of chemotherapy. TACE is meant to provide targeted drug delivery as well as diminish the vascular supply of the tumor, resulting in tumor shrinkage and localized control of the disease [2].

- *Radioembolization (Yttrium-90 Radioembolization):* This method involves the delivery of radioactive glass or resin microspheres directly into the tumor's feeders through a microcatheter, providing high-dose targeted radiation therapy, aka selective internal radiotherapy (SIRT) directly to liver cancers and to diverse metastatic involvements of the liver[3].

ii. Management of Postoperative Complications

- *Percutaneous drainage:* IR is instrumental in managing a huge spectrum of postoperative complications, such as fluid collections or abscesses, using imaging guidance to place the needed drainage catheters percutaneously. These can be easily performed under ultrasound, computed tomography, and fluoroscopic guidance.

- *Vascular interventions:* Hepatic arterial flow dynamics can be affected by acute thrombosis, anastomotic stenosis, or bleeding of the hepatic artery, either early or late onset. These complications have been reported to be up to 10% after pancreatic or liver surgery [4-6]. Here takes place the involvement of our second article. Although these complications have been managed surgically for a long time, due to their minimally invasive nature and lower rate of morbidity and mortality, interventional treatment options have gained popularity in managing such complications.

Acute occlusion or thrombosis of the HA is a serious complication, especially in liver transplant patients [7]. In that case, an emergency thrombolysis and/or angioplasty and, if needed, stenting of the involved arterial segment can be organ-saving [8].

In cases with HA injury, superselective embolization could be used to control bleeding while preserving the flow to the liver parenchyma. If the injury is proximal and affecting the proper or common HA, stent-graft placement can be used to exclude vascular injury from circulation. However, in challenging cases, an emergency embolization of the hepatic artery could be used as a last option, but risks related to ischemic complications of the liver have to be considered.

iii. Management of biliary diseases:

IR utilizes percutaneous transhepatic cholangiography (PTC) to visualize the biliary tree invasively by injecting percutaneously contrast agent under ultrasound guidance and fluoroscopy through a needle into the bile ducts, often followed by a catheter placement (drainage: PTBD), aiding in the diagnosis and treatment of biliary stasis, strictures or leaks. When placed, a drainage catheter can divert the produced bile away from the leak, reducing the intrahepatic biliary pressure and promoting the healing process of the injured duct. Here is the involvement of our first publication, within its specific cohort of patients.

Balloon dilatation or stent placement can be used to relieve biliary obstructions, whether caused by tumors, anastomotic strictures, or other autoimmune conditions, by promoting and preserving bile flow and preventing related complications[9].

The precision and targeted nature of these interventions contribute to their significance in the improvement of clinical patient outcomes across a wide spectrum of liver diseases.

First of all, we aimed to assess the effectiveness of biliary drainage in a specific group of patients, on the other hand, we wanted to analyze the feasibility and the success of hepatic arterial stenting in postoperative bleeding, and finally, we wanted to summarize the benefits of interventional treatment options in these two specific conditions.

2.2 Biliary Drainage

Drainage of the biliary tree involves the placement of a drain to help maintain the antegrade flow of the produced intrahepatic bile from the liver to the duodenum and/or jejunum and to alleviate symptoms and to prevent complications associated with the blocked biliary flow. Biliary drainage is often necessary in cases of bile duct obstruction, which can occur due to various conditions, such as gallstones, tumors, inflammation, and strictures.

With the increasing evidence and experience, the indications of PTBD have expanded. Few studies have reported case series with the utilization of PTBD in drainage of the non-dilated biliary tract, especially in patients with biliary leakage [10-12]. The growing number of liver surgeries have increased the number of patients referred to interventional radiology for the treatment of biliary leakage[13]. Advances in endoscopic and percutaneous drainage strategies have facilitated issues with the restoration of biliary flow. Furthermore, although endoscopic retrograde cholangiopancreatography (ERCP) has become the procedure of choice for minimally invasive treatment of many bile duct disorders, in up to 16% of cases, bile duct cannulation fails [14, 15]. Especially in patients with previous gastric or biliary tract surgery, the failure rate increases up to nine-fold [16].

The endoscopic approach necessitates a reachable Oddi sphincter with an endoscope and a cholangioscope. Due to the biliodigestive anastomosis, endoscopic biliary access could be challenging after pancreatic surgery, so a percutaneous approach is very helpful in finding and catheterizing a biliary duct. In the latter method, the catheter can be used later on to approach retrogradely and guide the endoscope for further treatments.

With the development of imaging technologies and interventional equipment, even non-dilated biliary ducts can be punctured under ultrasound guidance. This brings the possibility of dealing with an expanded pool of patients suffering from biliary leakages. This group of patients benefits from the minimally invasive means, under precise imaging guiding tools lower complication rates compared to open surgery.

2.3 Hepatic arterial stent-grafting

Clinical presentation of hepatic arterial stenosis is usually milder and occurs later than thrombosis. Technical and clinical success rates have been reported to be up to 90% after balloon angioplasty, and 1-year patency rates are around 60–80% among patients with anastomotic stenoses [17]. In patients with suboptimal results after balloon angioplasty, a metallic stent can be endovascularly deployed. The first-year patency rates amongst HA-stented liver transplantation patients are around 50% [18].

Hemorrhage arising from the branches or distal part of the hepatic artery (HA) is infrequent yet carries a potentially life-threatening complication. The causes result predominantly from postsurgical interventions, iatrogenic procedures, trauma, tumors, and pseudoaneurysms [6]. Vascular injury is mostly a consequence of postoperative pancreatic fistula after pancreatic surgery [19], where especially local infectious collections lead easily to pseudoaneurysm formation at the hepatic artery [20]. Control of the bleeding at this site is often challenging for surgeons. IR can offer, in these cases, selective coil-embolization of the pseudoaneurysm or placement of a covered stent and preservation of the flow along the hepatic artery. Both embolization and surgery for this specific issue have high mortality rates [21-23].

Another point is the dual source hepatic perfusion: The liver is perfused by the hepatic artery as well as from the portal vein. This leads to a potential flow redistribution in case of a hepatic arterial occlusion or ischemia, especially in the long term, with the advantage of portal venous perfusion preventing liver ischemia. An exception to this phenomenon is the perfusion of the biliary system, which only gets blood from the hepatic artery. Hence, preserving the arterial blood supply to the liver is crucial, especially for the biliary tree.

After the vascular access and the wire passage of the pathologic area as well as a thorough vessel measurement, a covered stent can be carefully deployed at the affected site, this excluding the pseudoaneurysm or the bleeding site. Even if statistically not powerfully significant, the patency of grafts smaller than 4 mm in diameter has been shown to be lower compared to the larger ones; this requires to be interpreted carefully along the underlying condition of the patient and the main cause of the hepatic arterial bleeding [24]. An antiplatelet regimen is being suggested with graft implantations but depending on the concern, this approach has to be tailored for each case. Since the first angioplasty performed by Charles Dotter in 1963 and the first published stent implantation in 1969, interventional radiologists have developed a common sense of treating the relevant stenotic arterial segments with stent implantation [25]. Stenting a vessel is a well-established technique in hemodynamically relevant stenoses for peripheral as well as visceral arteries. Usually, the success of angioplasty, stenting, and graft (covered stent) implantation face diverse difficulties in smaller caliper vessels.

With the advance of coronary stent and graft production, we have smaller diameter stent-grafts available for a wider spectrum of arterial segments.

2.4 Publication I

2.4.1 Methods

We retrospectively evaluated all patients who underwent ultrasound-assisted PTBD between January 2017 and December 2021 due to biliary leakage without a dilatation in biliary ducts. The cohort was evaluated for its periprocedural characteristics, medical indications, technical success (successful placement of drainage catheter), clinical success (resolved leak without additional procedures), fluoroscopy time, and procedure duration. The clinical outcomes of our study group were assessed as well.

2.4.2 Results

We identified 74 patients with a mean age of 64.1 ±15.1 years. Surgery was the most common etiology underlying the biliary leakage within 93.2% of the cases. PTBD had a technical success rate of 91.8% (68/74) and a clinical success rate of 80.8%. The mean procedure and fluoroscopy duration were 43.5 and 18.6 minutes. Age >65 years (p=0.027) and left-sided drainage (p=0.034) were significant risk factors for clinical failure. Our study has proven that PTBD is a feasible, safe, and effective treatment option in patients with biliary leakage.

2.5 Publication II

2.5.1 Methods

A retrospective analysis of patients treated with stent-graft (SG) deployment for bleeding from the hepatic artery from January 2012 to May 2020 was conducted. Besides the procedural details, risk factors of rebleeding and occlusion rates of the SGs, as well as patient mortality, were analyzed.

2.5.2 Results

Twenty-seven patients (mean age 68.8 ±10.1) were identified, and 25 of them underwent 26 stent-graft implantation procedures. Twenty-four patients had recent surgery. The technical success rate was 92.8%. Three patients (3/25) had rebleeding resulting in a clinical success rate of 88%. Intensive care need before the procedure (p=0.013) and smaller stent-graft size (<4 mm, p=0.032) were related to clinical failure. Twenty-two patients had follow-up imaging. The SG maintained its patency in 10 (45.4%) patients at the most recent imaging. A distal implantation of SG (beyond the HA bifurcation) (p=0.012) was related to occlusion with a statistical significance. The 30-day and in-hospital mortality rates after SG were 8% and 24%. In-hospital mortality was associated with the intraabdominal septic source (p=0.010) and revision surgery (p=0.001).

2.6 Discussion

The aim of this cumulative dissertation was to investigate the effectiveness of PTBD in the biliary leakage patients as well as to prove the benefits of the stent-graft placement to the hepatic artery in the setting of postoperative HA bleedings. Both of the topics embrace a relevant spectrum of procedures offered by the interventional radiology in the treatment of surgical complications of diverse liver pathologies.

The first publication being focused on biliary leakages has proven that PTBD offers a safe and effective approach in patients with postoperative biliary leakages with its high technical (91.8%) and clinical (80.8%) success rates, besides an acceptable major complication rate (4%). Various success rates in this special group of patients have been reported in the literature, varying from 25% to 90% [10, 26]. These reports contained a majority of cases with in-situ biliary drainage catheters, whereas our cohort had less than 3% patients with additional catheterization, thus proving the feasibility of biliary duct catheterization using only US as guidance. We should underline the paramount additive effect of the usage of ultrasound throughout our cohort, which provided us with a considerably shorter fluoroscopy time reported in this series of patients (18.6 min). As expected, the mean radiation dose was also lower in our cohort (6965 µGym2) compared to other groups and was not that far from the suggested dose reference level of 4300 µGym2 for percutaneous biliary interventions in patients with biliary duct dilatation [27].

The fact that the clinical success was lower among the patients older than 65 years and in cases with a left-sided liver access led us to speculate these findings as a result of the reduced regeneration capacity of patients with right hemihepatectomy as well as the diminished wound healing capacity in elderly patients.

Hepatic arterial bleeding is a rare and severe complication in the postoperative setting. Especially the rupture of a post pancreatectomy pseudoaneurysm has been shown to carry a mortality rate as high as 35-50% [28]. Surgical revision and repair remain very challenging at this site because of the underlying inflammation and potential pancreatic fluid leakages. Coiling of the pseudoaneurysm can be a method, but recent reports have proven a very high percentage of rebleed in such cases [29]. As a salvage solution, complete coiling and occlusion of the hepatic artery carries a serious risk of liver or further biliary ischemia. With the development of smaller and more flexible systems, stent-graft implantation to such segments offers a rapid solution and a faster recovery from hemorrhagic shock [23]. It is known that in long-term follow-ups, 10-25% of these stent-grafts get occluded, but are mostly asymptomatic [30]. The later the occlusion occurs, the less symptomatic the patients are. As reflected by the mortality rates of our study, the stent-grafts, despite their comparably high occlusion rates, offer compensatory time for the correction of accompanying pathologies and the development of collaterals. The distal localization of the stent-graft and the usage of multiple stent-grafts are two other factors which have been shown to be frequent amongst patients with SG occlusion; this phenomenon can be explained by the reduction of flow dynamics in the distal part of the vessels. The endothelization occurs faster in bare metal stents compared to the stent-grafts; this making the usage of dual antiplatelet regimen necessary. In our cohort, patients with DAP treatment showed a slightly better patency rate compared to the patients without antiplatelet therapy.

2.7 Limitations

The main limitations of our studies are their retrospective design and the fact that both cohorts consisted of critically ill patients of a tertiary care center, thus adding a prolonged hospital stay and increased overall morbidity and mortality, which may reflect a bias in the clinical success rates. The additional drawbacks of the second study lays on the lack of standardization of technical approach in terms of material choice, which is a common situation in such life-threatening situations. However, our cohort shows the efficacy of SG in controlling the bleeding and preserving the organ perfusion in various underlying causes, despite the foreseen risk of graft occlusion in the long term.

3. Conclusions

With the technical developments in the field of interventional radiology, many surgical complications can be managed by minimally invasive treatments, including salvage of bile leakages or managing vascular injuries of the liver.

Ultrasound-guided percutaneous transhepatic biliary drainage (PTBD) for biliary leakage demonstrates high technical and clinical success, alongside with minimal radiation exposure, brief procedural durations, and low complication rates.

Hepatic artery stent-graft placement is an effective method to treat vascular injuries presenting by bleeding or pseudoaneurysms of the hepatic artery, providing a compensatory time for the improvement of concomitant conditions and the evolution of hepatic vascular collaterals.

Both approaches offer high technical and clinical success with an acceptable safety profile.

4. Abstract

Throughout my dissertation, I aimed to assess the effectiveness, safety, and clinical outcomes of percutaneous transhepatic biliary drainage (PTBD) in a special group of patients who had non-dilated biliary systems, in the setting of postoperative management of their biliary leakages. Throughout 74 patients with a mean age of 64.1 ± 15.1 years, we found that PTBD is a safe and effective treatment option (with 91.8% vs 80.8% success rates; technical vs clinical) in patients with biliary leakage with low interventional complication rates (less than <4%).

On the other hand, hepatic arterial bleedings are rare but severe complications in patients with recent abdominal surgery, which has to be managed quickly, either interventionally or surgically. Our second study aimed to evaluate the technical and clinical outcome of stent-graft placement in the interventional treatment setting for bleeding from the hepatic artery. In 27 patients with a mean age of 68.8 ± 10.1 years a technical success rate of 92.8% was found vs a clinical success rate of 88% accompanied by a low complication rate. These results may provide the effectiveness of interventional grafting of the hepatic artery.

Both of our studies comprise the interventional salvage of two major pathologies in the postoperative management of liver pathologies.

5. Zusammenfassung

Das Ziel meiner Dissertation stellte die Evaluation von Effektivität, Sicherheit und klinischem Ergebnis der perkutanen transhepatischen Cholangiodrainage (PTCD) in einer spezifischen Patientengruppe mit postoperativem Gallenleckage dar. Bei insgesamt 74 Patienten mit einem durchschnittlichen Alter von 64,1 ± 15,1 Jahren stellten wir fest, dass die Behandlungsoption der PTCD bei Patienten mit Gallenleckage sowohl sicher als auch effektiv ist (Erfolgsraten von 91,8% vs. 80,8%; technisch vs. klinisch) bei geringen peri- und postinterventionellen Komplikationsraten (<4%).

Zudem stellen arterielle Blutungen der Leber seltene, aber schwerwiegende Komplikationen bei Patienten mit kürzlich durchgeführter abdomineller Chirurgie dar, welche sofort behandelt werden müssen. Diesbezüglich gibt es zwei Optionen, entweder interventionell oder chirurgisch. Ziel der zweiten Studie war, die technischen und klinischen Vorteile der Implantation des gecoverten Stents (aka Stent-Grafts) in der interventionellen Behandlung von Blutungen aus der A. hepatica zu evaluieren.

Unter 27 Patienten mit einem durchschnittlichen Alter von 68,8 ± 10,1 Jahren ergab sich ein technischer Erfolg von 92,8 % sowie ein klinischer Erfolg von 88 % bei einer zugleich niedrigen Komplikationsrate. Somit wurde die Effektivität des interventionellen Graftings der Arteria hepatica belegt.

Beide Studien umfassen folglich interventionelle Lösungsstrategien von zwei relevanten Pathologien im postoperativen Management von Lebererkrankungen.

Observational Study

Medicine

OPEN

Percutaneous transhepatic biliary drainage (PTBD) in patients with biliary leakage

Technical and clinical outcomes

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Abstract

The purpose of this study is to evaluate the technical and clinical outcome of percutaneous transhepatic biliary drainage (PTBD) in patients with biliary leakage. All patients who underwent ultrasound-assisted PTBD between January 2017 and December 2021 due to biliary leakage with nondilated biliary systems were retrospectively evaluated for periprocedural characteristics, medical indications, technical success (successful placement of drainage catheter), clinical success (resolved leak without additional procedures), fluoroscopy time, procedure duration, and clinical outcomes. 74 patients with a mean age of 64.1 ± 15.1 years were identified. Surgery was the most common etiology of biliary leak with 93.2% of the cases. PTBD had a 91.8% (68/74) technical success rate and an 80.8% clinical success rate. The mean procedure and fluoroscopy duration were 43.5 and 18.6 minutes. Age > 65 years (P = .027) and left-sided drainage (P = .034) were significant risk factors of clinical failure. Procedure-related major complications were 2 bleedings from the liver and 1 bleeding from an intercostal artery (major complication rate 4%). PTBD is a feasible, safe, and effective treatment option in patients with biliary leakage with low complication rates.

Abbreviations: CIRSE = Cardiovascular and interventional radiological society of Europe, CTA = Computed tomography angiography, ERCP = Endoscopic retrograde cholagiopancreaticography, INR = International normalized ratio, IV = Intravenous, NOAC = Novel oral anticoagulants, PTBD = percutaneous transhepatic biliary drainage, RV = rendezvous, SC = Subcutaneous, US = Ultrasound

Keywords: biliary leakage, biliodigestive anastomosis, hepaticojejunostomy, nondilated biliary ducts, percutaneous transhepatic biliary drainage

1. Introduction

Postoperative bile leakage is a common problem in patients with hepatobiliary or pancreatic surgeries with an incidence ranging from 0.4% to 12%.[1–3] Percutaneous transhepatic biliary drainage (PTBD) is a well-established approach for the aforementioned cohort, especially when endoscopic access through ERCP is not feasible in patients with pancreaticoduodenectomy or with Roux-en-Y anastomosis.[4–6] The percutaneous approach aims to divert the biliary outflow, thus facilitating the healing process of the leakage site.

Current surgical guidelines recommend percutaneous drainage approaches in the management of patients with failure of biliodigestive or biliobiliary anastomosis and in patients with postoperative leakages from the resection surface of the liver.[7] Since the 1970s, interventional radiology has provided a wide range of procedures to treat biliary diseases; here, the most common being interventions related to malignant biliary occlusions,[8] which are almost always associated with biliary duct dilatations. Percutaneous access to the nondilated biliary tree has always been more challenging compared with patients with obstructed bile ducts, resulting in longer procedural times and lower success rates.[9] Initial reports have shown that technical success rates drop to 25% in patients with a nondilated biliary system.[10] Furthermore, another study showed that the complication rate increased to 21% in nondilated systems, despite performing only diagnostic cholangiography without catheter placement.[11] With the development of

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All data generated or analyzed during this study are included in this published article [and its supplementary information files].

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Key Points:

1. US-guided PTBD has high success rate in patients with nondilated biliary system.
2. Major procedural complications are rare and interventionally manageable.
3. Patients >65 years and left-sided drainage have higher risk for persistent leakage.

imaging modalities and refinement in the instrumentation, the technical success rates have risen in nondilated PTBD patients up to 90%.[9,12] However, most of the patients in those cohorts had indwelling catheters either placed into the biliary system during surgery or percutaneous bilioma drainage catheters allowing to opacify intrahepatic biliary ducts. Ultrasound is recommended in PTBD procedures to guide the initial puncture, however, is not routinely used in most centers in patients with a nondilated biliary system. The cohorts mentioned above used only fluoroscopic guidance, and data on a comprehensive analysis of clinical outcomes are scarce in the literature, like the fate of biliary leakage.

In this study, we aimed to analyze the technical efficacy as well as the clinical outcome of patients with biliary leakage who received PTBD with an ultrasound-guided biliary puncture at a tertiary hepatobiliary-pancreas center.

2. Material and methods

2.1. Patients

Study approval was obtained from an institutional review board under the number 21-1148. As a retrospective study, the requirement for patient written informed consent was waived. All the PTBD procedures between 2017 and 2021 in our tertiary care center were retrospectively evaluated. Patients with dilated biliary systems (diameter of segmental bile ducts >2 mm in CT or US) have been excluded. Patient demographics, access site, periinterventional laboratory values (INR, liver function tests, bilirubin, and platelets), procedural details, including duration as well as fluoroscopy time, radiation doses and administered contrast volumes, procedure-related complications, and follow-up clinical data have been assessed using electronic patient recording system.

Seventy-four patients (45 men and 29 women, mean age 64.1 ± 15.1 years) with nondilated biliary systems were identified. All the procedures were performed by 4 interventional radiologists with an experience in biliary procedures of at least 5 years. Baseline characteristics and indications of PTBD in our patient cohort are presented in Table 1.

2.2. Technique of PTBD

Our standard preprocedural assessment included coagulation profile check, and any thrombocytopenia (<50,000/mm^3) or INR > 1.4 values have been corrected with necessary blood products and medication. All patients were monitored noninvasively during the procedures. All procedures were done in the angiography suite (Siemens Artis Zeego, Siemens Healthcare, Erlangen, Germany). All interventions were performed with local anesthesia (5 mL Lidocaine 2%) combined with mild sedoanalgesia with intravenous (iv.) midazolam (1–5 mg) and piritamide (7.5–15 mg), when possible. Patients who could not tolerate the procedure with sedoanalgesia, like intensive care unit patients, were managed with general anesthesia.

A right-sided puncture was preferred whenever feasible. A left-sided approach was used only in cases with right hemihepatectomy or clinical suspicion for left-sided biliary leakage.

Table 1

Baseline characteristics of study population.

Baseline characteristics	Number
Age (mean ± standard deviation)	64.1 ± 15.1
Gender (male)	45 (60.8%)
Surgery/ERCP/other etiologies	69/3/2
History of biliodigestive anastomosis	55 (74.3%)
Liver resection	26 (35.1%)
Pancreatic resection	20 (27.0%)
Pylorus-preserving pancreaticoduodenectomy (PPPD)	11
Whipple	9
Primary disease	
Benign	**24 (32.4%)**
Complications of biliary stone disease	7
Peptic ulcer surgery complications	5
Liver transplantation complications	3
Bariatric surgery complications	2
Pancreatitis	2
Trauma	1
Malignant	**50 (67.6%)**
Bile duct malignancies	19
Pancreatic cancer	15
Gallbladder cancer	4
Colorectal cancer metastases	3
Gastric cancer	2
Sarcomas	2
Ovarian cancer metastases	2
Duodenal cancer	2
HCC (liver transplantation)	1

ERCP = endoscopic retrograde cholangiopacreaticography; HCC = hepatocellular carcinoma.

An ultrasound-guided percutaneous puncture of a peripheral bile duct or the adjacent/neighboring region was performed with a 22 G needle of the Neff percutaneous access set (Cook Medical, Bloomington, IN, USA), followed by a gentle contrast media injection under fluoroscopy to confirm catheterization of the biliary system or repositioning if no bile duct opacified (Fig. 1A). After opacification of the biliary ducts, a guide wire (Nitrex 0,018," Medtronic, Irvine, CA, USA) was advanced and over which the sheath of the Neff set (4F) was inserted in the Seldinger method (Fig. 1B). After the exchange of the wire to a 0,035" glide-wire (Terumo, Leuven, Belgium), a 4 or 5 F Angiography catheter (mostly Cobra and Kumpe, Cordis, NJ, USA) was used to navigate the guidewire into the bowel. In challenging cases, microcatheter and microwire systems were used as complementary methods to reach the bowel. Exchange to a stiff guide wire (either 0.035" Amplatz or 0.018" V18, Boston Scientific, Natick, MA, USA) was followed by the placement of a biliary drainage catheter of 5 F to 10.2 F diameter and 25 cm to 40 cm of length (Fig. 1C). Contrast injections were done to prove and localize the leakage point. In case of failure to pass into the bowel, an external drainage catheter was placed into the biliary hilum (Fig. 2). In those cases, after the initial unsuccessful procedure, a second attempt was started on the following day A final cholangiogram was obtained to confirm the position of the drainage catheter. All cases received follow-up cholangiograms to evaluate the healing process of the bile leak, and in case of no further leakage, the drain was left for ~4 weeks; later on, the catheter was removed if indicated.

2.3. Follow-up

The *technical success* was defined as the placement of an external or internal-external drainage catheter confirmed with a final cholangiogram (including patients with a second attempt). Whereas *clinical success* was defined as healing of biliary leakage without an additional need for surgical repair,

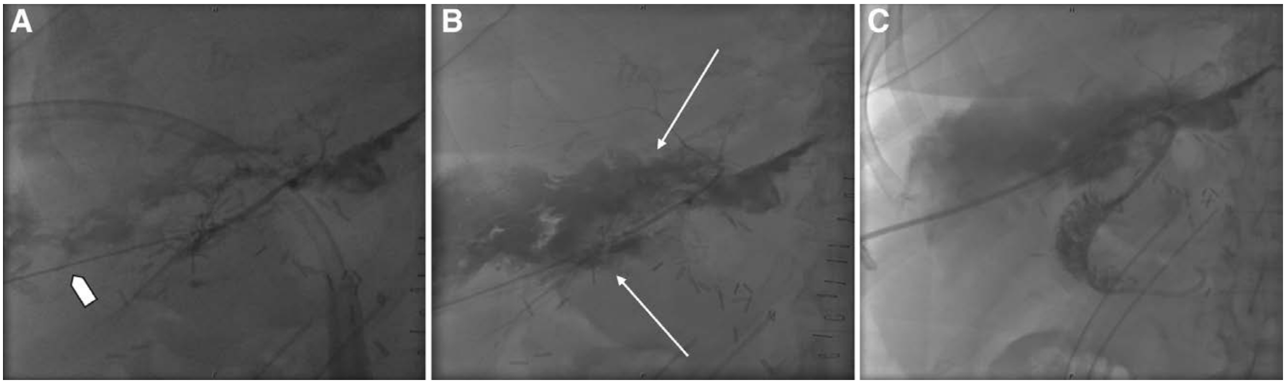

Figure 1. (A) 22 G needle stick and opacification of the nondilated biliary ducts of a 69-yr-old female patient s/p hemihepatectomy after CCC and BDA insufficiency. (B) Cholangiography through the inner sheath of the Neff set (3 F) and obvious bile leakage. (C) Placement of a 8.5-F internal-external drainage catheter and final cholangiography. BDA = biliodigestive anastomosis, CCC = cholangiocellular cancer.

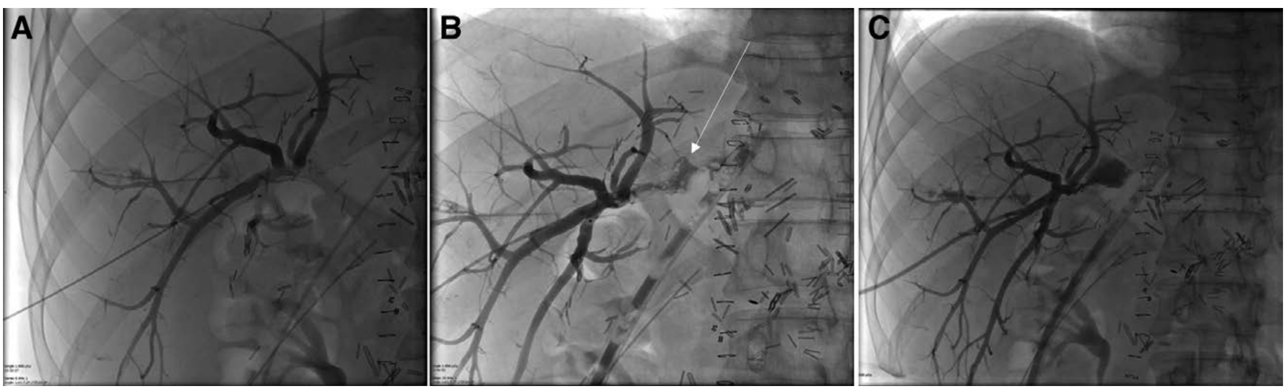

Figure 2. (A) Needle stick & opacification of the biliary system of a patient with s/p left-hemihepatectomy. (B) Biliary leakage at the BDA level. (C) Placement of a 6.3 F external drainage catheter due to passage failure through the BDA.

here meaning the successful removal of the drainage catheter within the follow-up period. Complications related to PTBD were classified according to the CIRSE classification system.[13] Major complications (from grades 2 to 6) were recorded.

2.4. Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics 23.0 (IBM, Armonk, NY). Categorical parameters were presented as number and percentage, continuous variables were presented as mean and standard deviation. Univariate analysis of the relationship between periprocedural characteristics and technical or clinical success were assessed using Chi square and t-Tests. A 2-sided P value < 0.05 was considered significant.

3. Results

In 68 of 74 patients (91.8%), PTBD placement was technically successful, including 5 patients receiving successful drainage on the second intervention. Eight patients received external drainages, and 60 received internal-external drainage catheters. In 1 patient, the external drainage was internalized in the second session. Three patients with technical failure were treated with additional ERCPs and secondary abdominal drainages, 1 patient was reoperated to correct biliodigestive anastomosis, and 2 patients were lost to the underlying disease.

Procedural characteristics were given in Table 2. Fifty-four cases (79.4%) were drained with right-sided percutaneous access, whereas 11 patients (16.1%) with left-sided access and 3 patients (4.4%) received bilateral drainages. None of the baseline parameters were correlated with technical success (Table 3).

The mean procedure duration was 43.5 ± 24.7 minutes. The average fluoroscopy time was 18.6 ± 11.9 minutes. The mean radiation dose was 6965.6 ± 8452.3 μGym². The average contrast media used was 69.8 ± 38.4 mL. The drainage catheter size varied from 5 F to 10.2 F; the most common sizes were 8 F (n:30) and 8.5 F (n:25) catheters.

Nineteen patients (25%) were not receiving any anticoagulation/antiplatelet treatment. The remaining 48 patients were receiving either prophylactic or therapeutic doses of Factor-Xa inhibition (fractionated Heparin, 0.4 IU, SC), 4 were taking antiplatelet agents because of other underlying medical diseases and 3 were on novel oral anticoagulants (NOACs). Out of 74 patients, 3 major procedure-related bleeding (4%) were diagnosed by computed tomography angiography obtained due to postinterventional hemoglobin decrease. Two patients were bleeding from the liver, and the other had bleeding from an intercostal artery. All of them were successfully managed by endovascular approach, using coils or liquid embolization. One of these patients was lost 4 days after the procedure due to the underlying multiple organ failure probably accentuated by the hemorrhagic shock. Two of these patients were under anticoagulation treatment; anticoagulation was not correlated with procedural bleeding (P > .99).

The mean follow-up period was 31.3 weeks (range 0.5–160 weeks), and the 30-day mortality of our cohort was 19% (14/74). No procedure-related mortality was encountered. In all patients, mortality resulted from underlying multiple medical conditions, mostly leading to multiple organ failure. The clinical success defined by ceased leakage and successful removal of the PTBD in the follow-up was achieved in 55 (80.8%) of 68 patients with technical success. The remaining 13 patients could not survive a catheter-free period until death due to multiple comorbidities within the follow-up period (3 days–12 weeks).

In 13 patients, a pancreatic fistula was diagnosed. Except for the patient who underwent emergent surgery due to peptic ulcer-related gastric perforation, all patients had pancreatic resections and anastomosis. Seven patients were treated with percutaneous or endoscopically placed drainage catheters, and the other 6 were operated with revision of pancreatic anastomosis. The presence of a fistula was not correlated with clinical success in our cohort (P = .446).

In patients with left-sided PTBD, the clinical success rate was significantly lower (54.5% vs 85.1%, P = .034) compared to those with right-sided PTBDs. In addition, in patients older than 65 years, the clinical success rate was significantly lower (70.2% vs 93.5%, P = .027).

4. Discussion

Our study results showed that PTBD has high technical (91.8%) and clinical (80.8%) success rates in patients with biliary leakage. In addition, the procedure has an acceptable rate of major complications (4%), and there was no procedure-related mortality in our series.

Table 2

Procedural details.

Outcomes and technical details	
Technical success rate	91.8%
Clinical success rate	80.8%
Access site (right/left/both)	79.4%/16.1%/4.4%
Fluoroscopically proven bile leakage	98.6%
Pancreatic leakage	17.3%
Major complications	3 (4%)
•Intercostal bleeding	1
•Liver bleeding	2
Mean procedure duration (minutes)	43.5
Mean fluoroscopy time (minutes)	18.6
Mean radiation dose (µGym^2)	6965.6
Administered contrast media (ml)	69.8
Mean follow-up (weeks)	31.3

In literature, various success rates have been reported in nondilated biliary interventions, being successful in 25% to 90% of the cases.[11] In 2010, Kühn et al[9] reported their experiences with PTBD in patients with a nondilated biliary system to be successful at rates of 81%. However, in 76% of the procedures, either there was an indwelling catheter, or the gallbladder was punctured to guide the initial puncture. Similarly, another study reported a technical success rate of 92% in patients with a nondilated biliary system, 46% of whom had an indwelling catheter that allows contrast injections to opacify the biliary system.[12] Similar technical success was achieved in our cohort, with only 2 patients having a supplementary technique for opacification of biliary ducts. We believe the high rate of technical success resulted from advancements in catheter and wire technologies as well as the usage of routine US guidance during the procedures.

Additionally, probably due to routine US guidance, our study (18.6 minutes) had the lowest fluoroscopy time compared to the studies mentioned above (24–42 minutes). As a result, the mean radiation dose was also lower in our cohort (6965 µGym^2) compared to other groups (18,651 µGym2) and was not that far from the suggested dose reference level of 4300 µGym^2 for percutaneous biliary interventions.[14]

We also evaluated the clinical success of the procedures in terms of healing of biliary leakage without additional surgical repair. The clinical success rate was 80.8% in our cohort, similar to the previously reported cohorts.[15,16] Most of the previous cohorts focused only on the technical outcome of these procedures; to our best knowledge, risk factors for clinical failure have not been described yet. We have found that clinical success rates were lower in patients older than 65 years, probably resulting from diminished wound healing capacity and worsened general status due to coexisting diseases. Additionally, clinical success rates were significantly lower in patients with left-sided access than in patients with right-sided access. We believe this could be the result of reduced regeneration capacity of patients with right hemihepatectomy, which was the reason in 6 of 13 patients with a left-sided approach. However, this should be interpreted cautiously, considering that this result could also originate from the low number of patients with left side access in our cohort.

The overall incidence of symptomatic biliary or pancreatic leakages after hepato-pancreato-biliary surgery has been shown to be about 3% to 10%.[17] Some of these postsurgical bile leaks could be managed with conservative treatment and drainage of intraabdominal collections.[18] However, in the long term, chronic bile leakage can lead to a worsening in quality of life and impairment of patients' metabolic status due to fluid-electrolyte depletion and fat malabsorption. Additionally, a bile leak carries the risk of visceral vascular complications due to vessel wall erosion. This is also underlined with the high mortality rate in patients with persistent leakage in our cohort. Persistent bile leakage triggers the vicious cycle of delayed anastomosis healing

Table 3

Risk factors for technical and clinical failure.

Variable	Technical success (n = 74)			Clinical success (n = 68)		
	yes	no	p value	yes	no	p value
Age (>65)	37/68	4/6	0.686	26/55	11/13	0.027
Gender (male)	42/68	4/6	>0.99	34/55	8/13	>0.99
Fluoroscopically proven bile leakage	–	–	–	53/55	13/13	>0.99
Pancreatic fistula	13/68	0/6	0.582	9/55	4/13	0.254
Access site (right)*	54/65	5/6	>0.99	46/52	8/13	0.034
Malignancy	48/68	4/6	>0.99	37/55	10/13	0.74
Liver resection	23/68	3/6	0.658	17/55	6/13	0.296
Pancreatic resection	19/68	1/6	>0.99	15/55	4/13	0.746

*3 patients received bilateral biliary drainages.

problems and related further gastrointestinal complications, which have led to multiorgan failure despite other treatment attempts.

Surgical repair can be challenging for patients with biliary leakage, especially considering adhesions due to the initial surgery. ERCP and transpapillary drainage is the first approach to be chosen, when possible but is prone to failure in 46% of the patients.[19] Additionally, ERCP can be technically challenging in patients with biliodigestive anastomosis.

Percutaneous biliary drainage, whether internal-external or just external, has become a well-accepted procedure for managing postoperative failure in biliodigestive anastomoses, the handling of the duodenal stump insufficiencies and of injuries to the extrahepatic bile ducts.[20] Biliary diversion or drainage prevents also the activation of pancreatic enzymes, reducing the risk of an additional erosion on the surgical surfaces.[21] Additionally, percutaneous biliary drainage catheters can guide endoscopic treatment in challenging cases. As stated in the paper of Albert et al,[22] ERCP can offer different solutions in the rendezvous (RV) technique with or without endoscopic ultrasound support, depending on the anatomy and the underlying cause of the biliary disease and related leakage. Here the percutaneously placed wire enables the endoscopist to grab the wire and perform the internal drainage retrogradely over the percutaneously placed instruments. There are further endoscopic techniques described in the literature for the management of challenging biliary adverse events, such as entero-enteral endoscopic bypass creation,[23] which can be used in persistent leakage.

Widely known PTBD complications are pancreatitis, hemorrhage, fistula formation between bile ducts and hepatic vessels, additional bile duct injuries, and seldomly but reported are some pneumo- or hemothorax.[24–27] Our patient group had a comparably low (4%) major complication rate, comprising 3 patients with bleeding which were successfully managed by endovascular means, and no procedure-related mortality was encountered as in the existing literature.[28] In addition, there were no cases of pneumothorax or inadvertent organ puncture as a result of ultrasound guidance.

Limitations of this study are its retrospective design and the fact that our cohort of patients mainly consisted of critically ill patients of a tertiary care center, thus adding a prolonged hospital stay and increased overall morbidity and mortality, which may have also reduced our clinical success rate. However, our study offers further evidence for PTBD performed in patients with a nondilated biliary system, especially in cases with biliary leakage and those without indwelling catheters to opacify biliary ducts.

5. Conclusion

Ultrasound-guided PTBD for biliary leakage in patients with nondilated biliary system has high technical and clinical success rates and is associated with low radiation exposure and short procedure times. Procedural complications are low as well as usually manageable through the same team.

Author contributions

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Investigation: Sinan Deniz, Christian Schulz, Max Seidensticker.
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Software: Dionysios Koliogiannis.
Supervision: Moritz Widgruber, Max Seidensticker.
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Visualization: Osman Öcal, Markus Guba.
Writing – original draft: Sinan Deniz.
Writing – review and editing: Osman Öcal, Max Seidensticker.

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ORIGINAL ARTICLE

Stent-graft placement for hepatic arterial bleeding: assessment of technical efficacy and clinical outcome in a tertiary care center

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Abstract

Background: To evaluate technical and clinical results of stent-graft (SG) placement for bleeding from the hepatic artery (HA).

Methods: All patients intended and treated with SG deployment for bleeding from the HA at single center from January 2012 to May 2020 were retrospectively identified, and procedural details, risk factors for rebleeding, SG occlusion and mortality were analyzed.

Results: Twenty-seven patients (mean age 68.8 ± 10.1) were identified, and 25 patients underwent 26 SG procedures. Twenty-four patients had recent surgery. The technical success rate was 92.8%. Three patients (3/25) had rebleeding (88% clinical success). Intensive-care need before the procedure ($p = 0.013$) and smaller stent-graft size ($\leq$4 mm, $p = 0.032$) were related to clinical failure. Twenty-two patients had follow-up imaging. The SG maintained patency in 10 (45.4%) patients at the most recent imaging. Only placement of SG distal to the HA bifurcation ($p = 0.012$) was related to occlusion. The 30-day and in-hospital mortality rate after SG was 8% and 24%. In-hospital mortality was associated with the intraabdominal septic source ($p = 0.010$) and revision surgery ($p = 0.001$).

Conclusion: Stent-grafts are effective in the emergent treatment of HA bleeding. Mortality is mainly related to the general condition of the patient, and stent-grafts offer time to treat underlying medical problems sufficiently.

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Introduction

Bleeding from hepatic artery (HA) branches is not common, but it is a potentially fatal complication of iatrogenic procedures, trauma, tumors, or hepatic artery aneurysms and seen mainly after surgery. Its incidence after pancreatic or liver surgery has been reported by up to 10%.[1–3] Vascular injury is mostly a result of postoperative pancreatic fistula after pancreatic surgery, and hemorrhagic complications are the leading cause of mortality.[4] The most common cause of extrahepatic HA pseudoaneurysm after liver transplantation are local infectious collections.[5] Management for postsurgical hemorrhage of the hepatic artery aims to control the bleeding while preserving the liver's arterial supply. Both surgical intervention and coil embolization of the hepatic artery are associated with significant morbidity and mortality.[6–8] Despite the blood inflow of the liver via the portal vein, hepatic arterial occlusion results in critical ischemia of the bile ducts. Since the initial report of stent-graft implantation into the hepatic artery,[9] several case series have demonstrated its efficacy to control bleeding from hepatic artery branches, but long term results of this technique are lacking. The objective of this study was to evaluate technical success and clinical efficacy of stent-graft implantation into the hepatic artery and identify risk factors for treatment failure, mortality, and stent-graft occlusion.

[*] These authors made equal contributions to the manuscript.

Materials and methods

Patients

This retrospective study was approved by the ethics committee of our university hospital, and informed consent was waived. The hospital electronic database was reviewed for all patients referred for embolization due to bleeding from the hepatic arterial system (from common hepatic artery to origin of segmental branches). Patients that underwent stent-graft implantation for bleeding from hepatic artery branches from January 2012 and May 2020 were identified. Patients with negative angiography were excluded. A total of 27 patients (19 men, eight women) with a mean age of 68.8 ± 10.1 (range, 53–85 years) were identified. Patient characteristics, clinical data, procedural details, and follow-up imaging results were collected.

Stent-graft procedure

Except for one patient, all patients underwent computed tomography (CT) for the evaluation of the bleeding prior to angiography. The decision of arterial access (femoral vs. upper extremity) was at the physician's discretion based on the angle between the parent artery and aorta in preprocedural CT. Celiac and superior mesenteric arteriography were performed with a 4 F catheter. After localizing the pathology and measuring the diameter and length of the diseased vessel, the indwelling sheath was exchanged with a 5–7 F long vascular sheath, based on the required introducer caliber of the stent-graft. Stent-graft size was determined considering both measurements of the vessel's diameter on angiography and prior CT images. In order to avoid undersizing of the stent-graft, the bigger measurement from these two modalities was used. If there was size discrepancy between proximal and distal landing zone of the stent-graft, the smaller stent-graft, matched to the distal part of the vessel, was intended, followed by telescopic placement the bigger stent-graft. In the case of vasospasm, 100–300 μg of nitroglycerin was injected. After crossing the diseased part with a stiff wire, GORE Viabahn (Gore & Associates, Inc., Flagstaff, AZ, USA) or Advanta (Atrium/Maquet Cardiovascular, Hudson, NH, USA) or BeGraft (Bentley InnoMed GmbH, Hechingen, Germany) or PK Papyrus covered stent (Biotronik AG, Bülach, Switzerland) covered stent-grafts were placed to the diseased vessel. If needed, a second stent-graft was deployed to cover the whole diseased section of the artery. In the case of a large side branch causing endoleak risk via collaterals, it was embolized before the stent-graft deployment.

After confirmation of the complete coverage of the bleeding site and cessation of the bleeding, all the materials removed and access site hemostasis was achieved with manual compression or closure device. There was no consistent regimen of antiplatelet therapy, and early heparinization and usage of antiplatelet therapy were decided by the operator based on the clinical situation of the patient.

Follow-up

Technical success was defined as the exclusion of the vascular pathology and cessation of the bleeding at the end of the procedure. Clinical success was defined as no further hemorrhage or additional procedure for bleeding within 30 days. Early and late complications, liver function tests, in-hospital and overall survival were recorded. All follow-up images were evaluated for stent-graft patency, liver perfusion, and collateral status in case of stent-graft occlusion.

Statistical analysis

Statistical analysis was performed with IBM SPSS Statistics 23.0 (IBM, Armonk, New York). Patient and procedure characteristics were grouped to build categorical and nominal variables, and results were presented as mean ± standard deviation, median, or percentage. Univariate analysis of the relationship between periprocedural characteristics and clinical success, stent-graft patency and in-hospital mortality was assessed with the Chi-square test. The fluoroscopy times of procedures with upper and lower extremity were compared using the non-parametric Mann–Whitney U test. A two-sided p-value <0.05 was considered statistically significant.

Results

Patients

Patient characteristics and clinical symptoms that led to an indication for angiography were listed in Table 1. Twenty-four patients had a history of surgery, including pylorus-preserving pancreaticoduodenectomy (n = 13), pancreaticoduodenectomy with Braun anastomosis (n=1), pancreas tail resection and splenectomy (n = 1), laparoscopic cholecystectomy (n = 1), hepaticojejunostomy (n = 1), right hemicolectomy with hepatoduodenal lymph node dissection (n = 1), liver transplantation (n = 1), hemihepatectomy and duodenal perforation repair (n = 1), hepatic artery anastomosis aneurysm repair (n = 1), pylorus-preserving pancreatectomy with liver resection, nephrectomy and inferior vena cava resection (n = 1), pylorus-preserving pancreatectomy with liver and bowel resection (n = 1), pylorus-preserving pancreatectomy with bowel resection and arterial reconstruction (n = 1). In other cases, bleeding was secondary to vascular erosion of primary tumor (n = 2, cholangiocarcinoma and pancreatic cancer) and ERCP with metallic stent implantation (n = 1). Twenty-four (88.8%) patients had a malignant diagnosis. Nineteen patients (70.3%) had either a post-surgical intraabdominal abscess or pancreatic fistula, while intraabdominal abscess was present in eight (29.6%) patients, pancreatic fistula in four (14.8%) patients and seven patients (25.9%) had both. Hemorrhage occurred 5–461 days (median, 19 days) after the procedure. One patient had a history of bleeding from GDA branches two days before, which was treated with coil embolization. Another patient had intermittent bleeding and underwent angiography twice, but both

Table 1 Baseline patient characteristics

Patient	Age	Gender	Disease	ICU	Etiology	PF	IAS	Surgical details	AC	PVS	Shock	Symptom	Time*
1	84	male	Pancreas ca	no	Surgery	no	no	Pancreas tail resection and splenectomy	apixaban	no	no	Abdominal pain	26
2	76	male	Pancreas ca	yes	Surgery	yes	yes	PPPD	ASA	yes	no	HB fall	13
3	82	male	IPMN	no	Surgery	yes	yes	PPPD	ASA	no	no	HB fall	19
4	56	female	CCC	no	Tumor	no	no	–	–	no	no	Hematemesis	–
5	66	male	Gallbladder stone	no	Surgery	no	no	Laparoscopic cholecystectomy	ASA	no	yes	Syncope	28
6	75	female	Ovarian cancer	no	Surgery	no	no	Right hemicolectomy with hepatoduodenal LND	enoksaparin	no	no	Bloody drainage	19
7	85	female	IPMN	no	Surgery	no	no	PPPD	–	yes	no	Hematochezia and Hb fall	24
8	64	male	Stomach cancer	no	Surgery	yes	no	Hepaticojejunostomy	–	no	no	Bloody drainage	8
9	67	male	Pancreas cancer	no	Surgery	yes	no	PPPD	–	yes	no	Abdominal pain	100
10	62	male	Pancreas cancer	no	Surgery	yes	no	PPPD	enoksaparin	no	no	Bloody drainage	25
11	53	female	Primary Biliary Sclerosis	yes	Surgery	no	no	Liver transplantation	ASA + enoksaparin	yes	no	HB fall	55
12	71	male	CCC	no	Surgery	no	no	PPPD	ASA 100	no	no	HB fall	15
13	81	male	CCC	yes	Surgery	no	yes	Hemihepatectomy and duodenal perforation repair	–	no	yes	HB fall	14
14	66	female	Gallbladder Adenocarcinoma	yes	Surgery	no	yes	PPPD with liver and bowel resection	enoksaparin	yes	yes	Bloody drainage	23
14	66	female		yes				–	heparin	yes	no	Increased_LFT	25
15	54	male	Cirrhosis	yes	Surgery	no	no	Hepatic artery anastomosis aneurysm repair	enoksaparin	no	no	Hematemesis	461
16	73	male	CCC	no	Surgery	no	yes	PD with Braun anastomosis	enoksaparin	yes	no	Abdominal pain	49
17	73	female	Leiomyosarcoma	no	Surgery	no	yes	PPPD with liver resection, nephrectomy and inferior vena cava resection	–	no	no	HB fall	40
18	73	female	Pancreas cancer	no	Tumor	no	yes	–	–	yes	no	Abdominal pain	–
19	75	male	Pancreas cancer	no	Surgery	yes	yes	PPPD	enoksaparin	no	no	HB fall	11
20	84	male	Biliary Adenocarcinoma	no	Surgery	yes	no	PPPD	–	no	no	Bloody drainage	16
21	55	male	Pancreas cancer	yes	Surgery	no	yes	PPPD	–	yes	no	HB fall	10
22	59	male	Liposarcoma	no	ERCP	no	yes	Metallic stent implantation	ASA + heparin	no	yes	Hematochezia and HB fall	5
23	80	male	Pancreas cancer	no	Surgery	yes	yes	PPPD	enoksaparin	no	no	fever	41
24	71	male	Pancreas cancer	no	Surgery - PTCD	no	yes	PPPD	enoksaparin	no	no	Hematemesis	88
25	59	male	Pancreas cancer	no	Surgery	yes	yes	PPPD	–	no	no	Bloody drainage	13
26	57	male	Pancreas NET	yes	Surgery	yes	yes	PPPD with right hemicolectomy and arterial reconstruction	no	no	yes	Hematochezia	16
27	59	female	Pancreas cancer	no	Surgery	yes	yes	PPPD	no	no	yes	Bloody drainage	9

ASA: acetylsalicylic acid, DSA: digital subtraction angiography, HB: hemoglobin, IAS: intraabdominal septic source, ICU: intensive care unit, LFT: liver function tests, LND: lymph node dissection, NET: neuroendocrine tumor, PD: pancreaticoduodenectomy, PF: pancreatic fistula, PPPD: pylorus-preserving pancreaticoduodenectomy, PVS: portal vein stenosis.
* Time between the surgery and angiography in days.

angiographies were negative, and no embolization was performed. Fifteen patients (55.5%) were receiving anticoagulation therapy, including enoxaparin (8), ASA (4), apixaban (1), ASA and enoxaparin (1), ASA and heparin (1). One patient had a second procedure due to recurrent bleeding two days after the initial stent-graft placement.

Procedural results

Technical success of stent-graft placement was achieved in 26 of 28 procedures (92.8%): Two patients did not receive stent-graft implantation. In one patient, who had pseudoaneurysm in both the common hepatic artery and splenic artery, the plan was to deploy a stent-graft to cover the pseudoaneurysm of the common hepatic artery after occlusion of the splenic artery with a vascular plug. However, during catheterization of the hepatic artery after the placement of the vascular plug, a dissection occurred, and the common hepatic artery was not filling in control angiographies. After the discussion with surgeons, the patient underwent surgical transposition of the splenic artery stump to the common hepatic artery. The other patient had pseudoaneurysms in the proper, common hepatic artery and splenic artery, and was decided to treat surgically due to plan of rest pancreatectomy. These two patients were excluded from the rest of the analysis.

Vascular access was obtained via the common femoral artery in 19 procedures, the brachial artery in five procedures, the axillary artery in one procedure. In one procedure, due to catheter instability caused by the acute angle between celiac truncus and aorta, the brachial artery was punctured in addition to the femoral artery. Pseudoaneurysm was encountered in 17, luminal irregularity (corresponding to the location of hematoma in CT) in 4, both in 2, and extravasation in 3 procedures. In 12 cases, pathology was from the common hepatic artery (CHA), from the proper hepatic artery (PHA) in 5 cases, and from the right hepatic artery (RHA) in 5 cases. There were two different foci in 3 patients (RHA & PHA, RHA & CHA, left HA & splenic artery), both of them were treated with stent-grafts (Table 2). Hepatic arterial variants were present in two patients. Both patients had replaced RHA, one with LHA injury and other one with pathology in both of replaced RHA and CHA.

One stent-graft was implanted in 12 (46.1%) procedures, two in 11 (42.3%) procedures, and three in 3 (11.5%) procedures. Self-expandable stent-grafts were used in 10 of the procedures, balloon-expandable in 11, and both in 5. A branch vessel was embolized with coils or Amplatzer vascular plug in order to prevent endoleak in 8 procedures (splenic artery, n = 3; left hepatic artery, n = 1; middle hepatic artery, n = 1; right gastric artery, n = 1; anterior sectoral branch, n = 1; segment 6 branch and gastroduodenal artery, n = 1). In one procedure, an additional duodenal branch of SMA was embolized with coils and particles. In one patient, concurrent celiac stenosis was treated with a balloon-expandable stent at the end of the procedure. Procedural complications were encountered in three (11.5%): thrombus was encountered in the lumen of the stent-graft placed into the common hepatic artery in one procedure. The flow was restored with the aspiration of the thrombi with a 5F Envoy catheter (Codman Neurovascular, Raynham, MA, USA). A stent-graft deployed into a replaced right hepatic artery occluded due to the bending proximal to the stent and treated with the deployment of another stent-graft. In the other case, after deployment of a 7-mm balloon-expandable stent-graft to treat a common hepatic artery pseudoaneurysm, extravasation was encountered at the proximal part of the stent. Another 6-mm balloon-expandable stent-graft caused the same complication at the proximal part and treated with a third 5-mm balloon-expandable stent-graft.

The median fluoroscopy time was 27.3 min (range 6.2–61), and no significant difference was observed in cases with upper or lower extremity access for median fluoroscopy time (34.8 vs. 24.2, $p = 0.136$). Eighteen patients received heparin infusion at the early post-procedural period. While twenty-three patients received acetyl-salicylic acid (ASA; six combined with clopidogrel, seven with enoxaparin, and two with both), the other two patients were anticoagulated with enoxaparin (Table 2).

Clinical success

Clinical success was achieved in 22 (88%) of 25 patients: One patient had rebleeding from hepatic artery proximal to the stent-grafts two days after the initial procedure and was treated with two additional stent-grafts. In one patient with a history of a duodenal perforation-related abscess, CT obtained five days after stent-graft implantation showed bleeding from the HA, and the patient underwent surgery after negative angiography, which revealed diffuse peritoneal bleeding due to anticoagulation. In the other patient, a small intestine bleeding was controlled surgically, and the patient underwent revision of the biliodigestive anastomosis and rest-pancreatectomy due to pancreatic fistula.

The need for intensive-care before the procedure ($p = 0.013$) and smaller stent-graft size (≤ 4 mm, $p = 0.032$) were associated with clinical failure, and there was a trend for failure in patients with shock ($p = 0.052$).

Follow-up

One patient developed median nerve compression due to failed hemostasis of brachial access and underwent hematoma evacuation six days after the procedure. One patient had an increase in liver enzymes due to hepatic arterial spasm ten days after the procedure, which was treated with prostavasin infusion for three days.

Twenty-two of 25 (88%) patients had follow-up imaging. No stent-graft migration was encountered. The stent-grafts maintained patency in 10 (45.4%) patients at the most recent imaging. Stent-graft occlusion was diagnosed with a median 22.5 (range, 1–360) days after the procedure. Stent-graft placement into distal (LHA & RHA) vessels ($p = 0.012$) was the only significant risk factor for stent occlusion (Table 3). There was a trend for occlusion in male patients ($p = 0.105$) and patients with multiple

Table 2 Procedural details and follow-up of patients with successful stent-graft implantation

Patient	DSA diagnosis	Time between CT and DSA	puncture	treated artery	Stent-graft (Size)	Fluoroscopy time (minutes)	Technical success	Postprocedural heparinization	Postprocedural Anticoagulation	Clinical success	Patency at last imaging follow-up	Imaging duration (days)*	In-hospital mortality	Last follow-up
1	PA	1 day	F	PHA	Viabahn (5/25&7/25)	27.3	yes	yes	ASA + clopidogrel + enoxaparin	Yes	Patent	9	No	11m
2	PA	6 h	F	CHA	Viabahn (7/25&8/25) & Advanta (9/32)	23.8	yes	yes	ASA	yes	Occluded	25	Yes	39d_exitus
3	PA	16 h	F	CHA	Viabahn (8/50)	10.8	yes	yes	ASA	yes	Patent	70	Yes	130d_exitus
4	PA	6 h	F	RHA	Advanta (5/18)	20.7	yes	no	ASA + clopidogrel	yes	–		No	2d
5	PA	2 h	F	RHA	Papyrus (4/20&4/15) & Viabahn (5/25)	12.3	yes	yes	ASA + clopidogrel	yes	–		No	11m
6	PA	2 h	B	CHA	Viabahn (6/25) & Papyrus (4.5/20)	30.9	yes	yes	ASA + enoxaparin	yes	Patent	270	No	9m
7	PA	3 h	F	CHA	Viabahn (6/25)	15	yes	no	ASA + clopidogrel + enoxaparin	yes	Patent	3	No	3m
8	PA	5 h	F	PHA	Viabahn (7/50&7/25)	46.5	yes	yes	ASA + enoxaparin	yes	Occluded	150	No	16m
9	PA	1 day	B	PHA	Viabahn (5/50&5/25)	38	yes	yes	ASA + enoxaparin	yes	Occluded	24	No	7m_exitus
10	LI	3 h	F	CHA	BeGraft (7/37)	48.5	yes	yes	ASA + enoxaparin	yes	Patent	300	No	10m
11	PA	16 h	F	PHA	BeGraft (4.5/24)	6.2	yes	no	ASA + enoxaparin	yes	Patent	330	No	30m_exitus
12	PA	14 h	F	CHA	Atrium (7/38&6/22&5/22)	13	yes	no	ASA + enoxaparin	yes	Occluded	45	No	4m
13	PA	–	F	PHA	Papyrus (2 × 4&20)	54.1	yes	no	ASA + clopidogrel	no	Patent	10	Yes	15d_exitus
14	PA	<1 h	F	CHA	Viabahn (5/20) & BeGraft (4/28)	27.4	yes	yes	heparin	no	Patent	2	No	2m
14	E	1 h	F & B	CHA	Viabahn (6/50&6/25)	61	yes	yes	ASA + enoxaparin	yes	Patent	7	No	2m
15	PA	13 h	F	CHA	BeGraft (2 × 4,5/18)	17	yes	no	ASA	yes	Occluded	16	No	3m
16	LI & PA	4 h	B	RHA& PHA	Papyrus (4/15&4.5/20)	53	yes	yes	ASA	yes	Occluded	390	No	20m
17	LI	21 h	B	LHA& Splenic	Papyrus (4/15)	18.5	yes	yes	ASA	yes	Occluded	360	No	13m
18	PA	4 days	A	CHA	Viabahn (2 × 7/25)	39.9	yes	no	enoxaparin	yes	–		Yes	11d_exitus
19	E	1 h	F	RHA	Papyrus (2 × 4/15)	28	yes	yes	ASA + clopidogrel	yes	Occluded	5	No	10m
20	LI	23 h	F	CHA	BeGraft (6/38)	12	yes	yes	ASA + clopidogrel	yes	Occluded	210	No	27m
21	LI & PA	1 h	B	RHA & CHA	Papyrus (2 × 4/20) & Viabahn (5/50)	31.5	yes	yes	ASA	no	Occluded	1	Yes	33d_exitus
22	PA	19 h	F	RHA	Viabahn (4/20)	33.3	yes	yes	ASA	yes	Occluded	20	No	10m_exitus

23	LI	24 h	F	CHA	Viabahn (8/50)	24.5	yes	yes	enoxaparin	yes	Patent	33	No	37d_exitus
24	PA	8 days	F	RHA	Papyrus (3,5/20&5/20)	39.4	yes	yes	ASA	yes	Occluded	3	no	2m
25	E	2 h	F	CHA	Viabahn (6/25)	10	yes	Yes	ASA + clopidogrel	yes	patent	1	no	1m

AA: axillary artery, ASA: acetylsalicylic acid, B: brachial artery, CHA: common hepatic artery, d: days, E: extravasation, FA: femoral artery, LHA: left hepatic artery, LI: luminal Irregularities, m: months, PA: pseudoaneurysm, PHA: proper hepatic artery, RHA: right hepatic artery.
* censored at the diagnosis of stent-graft occlusion.

stent-grafts (p = 0.110). Although the patency rate was higher for the stent-grafts bigger than 4 mm (80% vs. 50%), the difference was not significant (p = 0.156). Stent-graft occlusion was asymptomatic in 9 of 12 cases, maintained patency of a liver lobe artery (e.g., if just RHA was stented or in variant anatomy) was without influence on complications (p > 0.99). One of the three patients with symptomatic occlusion, occlusion was diagnosed at 7-months follow-up CT, developed liver abscesses 27 months after the procedure. Another patient, who already had liver abscess with indwelling drainage at the time of stent placement, had stent-graft occlusion three days after the placement. Three weeks later he developed another liver abscess, which was also treated successfully with CT-guided drainage. One patient died 33 days after the procedure due to hemorrhagic complications related to disseminated intravascular coagulation and multiorgan failure. His stent-graft was occluded at 25-days follow-up CT, and although this might have contributed to existing multiorgan failure, his bilirubin levels were already increased before graft occlusion. Except for this patient, in patients with stent-graft occlusion, intrahepatic arterial branches were enhancing through collaterals via either contralateral liver lobe, inferior phrenic artery or left gastric artery. Although patients with >50% stenosis (either due to thrombosis or hematoma compression) in the portal vein had higher possibility of complications (66.6% vs. 22.2%), the difference was not significant (p = 0.236).

Survival

The two patients with no stent-graft implantation (see procedural results) developed liver insufficiency and multi-organ failure due to occlusion of hepatic artery and portal vein thrombosis. Patients were lost 3 and 4 days after the angiography. The 30-days mortality rate in patients with stent-graft implantation was 2/25 (8%), and both patients died due to multi-organ failure 11 and 15 days after the procedure. Four more patients were lost due to multi-organ failure during hospitalization despite attempts to correct underlying medical conditions (in-hospital mortality rate 24%). Factors related to in-hospital mortality were intraabdominal septic source (p = 0.010) and the need for anastomosis revision surgery (p = 0.001). Of these four patients, two patients underwent revision of gastroenterostomy anastomosis, and two underwent further rest-pancreatectomy. Stent-graft occlusion was not a significant risk factor for in-hospital mortality (p > 0.99). Five of six patients, who died during the hospitalization, had CT images, and the stent was occluded in two of them.

The mean follow-up was 7.9 months (2 days- 30 months). Three patients died due to the progression of primary disease 7, 10 and 30 months after the procedure.

Discussion

Hepatic arterial hemorrhage is a rare complication of diseases affecting the liver or iatrogenic procedures but still a significant

Table 3 Risk factors for stent-graft occlusion

Stent-graft patency			
Variable	Patent	Occluded	p value
n = 22	45.4% (10)	54.5% (12)	
Malignancy	90% (9/10)	91.7% (11/12)	0.714
Etiology (surgery)	100% (10/10)	83.3% (10/12)	0.494
Gender (male)	60% (6/10)	91.7% (11/12)	0.105
Preprocedural ICU	30% (3/10)	25% (3/12)	0.583
Pancreatic fistula	40% (4/10)	41.7% (5/12)	0.639
Septic source	50% (5/10)	58.3% (7/12)	0.515
PV stenosis >50%	30% (3/10)	33.3% (4/12)	>0.99
Preprocedural anticoagulation	70% (7/10)	58.3% (7/12)	0.454
Shock	20% (2/10)	8.3% (1/12)	0.429
Pseudoaneurysm	70% (7/10)	75% (9/12)	0.583
Time from Surgery to Angiography (>30d)	20% (2/10)	41.7% (5/12)	0.268
Spasm at parent artery	40% (4/10)	58.3% (7/12)	0.335
Stented vessel (transition)	40% (4/10)	58.3% (7/12)	0.335
Treated vessel (distal)	0% (0/10)	50% (6/12)	**0.012**
Multiple stent-graft	40% (4/10)	75% (9/12)	0.110
Covered side branch	0% (0/10)	25% (3/12)	0.143
Embolized side branch	20% (2/10)	41.7% (5/12)	0.268
Heparinization	70% (7/10)	83.3% (10/12)	0.406
Dual antiplatelet	40% (4/10)	16.7% (2/12)	0.229
Procedural complications	0% (0/10)	16.7% (2/12)	0.286
Size >4 mm	80% (8/10)	50% (6/12)	0.156

ICU: intensive care unit, PV: portal vein.

determinant of survival. Patients with post-pancreatectomy bleeding have more than 6-fold increase in mortality,[10] with a mortality rate of 35–50% after the rupture of hepatic arterial pseudoaneurysms.[11] Operative management of the hepatic artery injury is associated with a high mortality rate, and bleeding sites may not be reached due to dense adhesions, inflammation, and massive bleeding.[12,13] Although coil embolization of the aneurysm sac and preserving the parent artery is an option in cases with pseudoaneurysm, the rebleeding rate has been reported up to 100%.[14] Embolization of the hepatic artery with coils has been used to control bleeding with high technical success, but despite the liver's second blood supply via the portal vein, the risk of hepatic infarction and hepatic failure is high.[7] After hepatic artery embolization rates of ischemic liver injury, and hepatic infarction or failure has been reported up to 100%.[6,8,13] Especially following major liver resection or liver transplantation, hepatic arterial embolization almost always caused re-transplantation or death.[5,13,15] Thus, hepatic failure due to embolization is intolerable and associated with high mortality.

Initial studies with stent-graft placement for hepatic arterial bleeding reported promising results.[4,16] With the technical developments, the technical success rate was 92.8% in our study, and in both of the failed cases, there was long segment vessel erosion, which led to dissection during catheterization in one case and made it too risky for perforation in the other case. Coil embolization was not attempted due to the risk of liver failure (due to accompanying partial portal vein thrombosis), and patients were scheduled for surgical reconstruction of HA. Although HA was preserved during surgery in both patients, it was eventually occluded and led to liver insufficiency induced multi-organ failure and death.

Stent-graft implantation has lower procedural time than coiling,[8] and offers immediate exclusion of the vessel pathology and rapid improvement in patients with hemorrhagic shock. In our cohort, angiographic findings were combined with preprocedural CT and the previous CT images (e.g., presurgical CTA) for selection of stent-graft size to avoid vasospasm-related undersizing, and no case of delayed migration was seen in follow-up.

Long-term occlusion rates of hepatic stent-grafts are reported between 10 and 25%, but occlusion was mostly asymptomatic, especially in delayed cases.[16–18] As reflected by our mortality rates, the stent-grafts, although accompanied by a high occlusion rate, offer time for correction of accompanying pathologies and the development of collaterals. Except for one case, in follow-up CT images of the patients with occluded stent-grafts, intrahepatic arterial branches were enhancing through collaterals. Although the stent-graft occlusion rate in our cohort (54.5%) was higher than previously reported series, we postulate that patient-related and anatomical factors explain the difference. While eight of 25 (32%) patients had a vascular injury in right or left hepatic artery in our series, which was the only significant risk factor for occlusion, this ratio was 10% and 5.8% in two other studies with stent-graft placement into hepatic artery.[16,18] Along with the small size and lower flow of distal vessels, strong intrahepatic collateralization through the other lobe may have been contributory via pressure effect. Lim et al. reported 25% partial in-stent thromboses and 42% edge stenoses, and postulated stent-graft occlusion is an ongoing process,[18] and collateral flow to may accelerate the progression from partial in-stent thrombosis to occlusion. Along with the distal location of the stent-graft, the usage of multiple stent-grafts was higher in our study than in other studies, and although it did not reach statistical significance, probably due to the low sample size, there was a tendency for stent-graft occlusion in patients with multiple stent-grafts. It was necessary for 61.5% of procedures in our cohort, either due to length of the vessel injury, or discrepancy of vessel diameter at proximal and distal to the injury, while it was between 0 and 28% in previous studies.[16,18]

The endothelization of stent-grafts is delayed compared to uncovered stents, and there is no established antiplatelet or heparinization regimen for stent-grafts placed in the visceral arteries. In our institution, post-procedural anticoagulation was at the discretion of the interventionalist based on the patient's clinical condition. Despite no statistical significance, patients receiving dual APT had higher patency (66.7% vs. 37.5%), and we recommend dual APT for six months, followed by life-long ASA in appropriate cases, as others.[8,19]

The rebleeding rate was 11.5% in 26 procedures, and smaller stent-grafts (≤4 mm) and preprocedural intensive care need were significant risk factors, which is probably the result of multiple problems and the general condition of the patients. Two patients (8%) had successful endovascular reintervention (one rebleeding and one spasm).

Although no statistical association was found in our study, hepatic stent-grafts placed after hepatobiliary surgery are prone to occlusion due to surrounding collections, which are probably the reason for initial vessel erosion, and the inflammatory response around the vessel wall continues after the deployment of stent-graft and induces thrombotic processes. Furthermore, high rate of patients with intraabdominal infection or pancreatic fistula in our cohort (70.3%), might be a reason for loss of patency due to a subclinical stent-graft infection. However, currently, no data on stent-graft infection in visceral arteries is available in the literature. The presence of intraabdominal septic source and medical condition requiring anastomosis revision were associated with in-hospital mortality. Except two patients who were lost due to multi-organ failure and DIC within 15 days after bleeding, all patients who died during hospital stay progressed to multi-organ failure despite attempts to correct medical condition surgically. None of the patients were lost due to hypovolemic shock. Therefore, stent-graft placement is an effective emergent procedure and helps to gain time to treat the underlying medical condition of the patient. 30-days and in-hospital mortality rate in our cohort were 8% and 24%, respectively, and lower than previously reported mortality rate after endovascular treatment.[19,20]

Our study has several limitations. First, it was a retrospective study with a relatively small number of patients with various diagnoses and different etiologies of bleeding. However, the history of malignancy and the etiology of bleeding had no significant correlation with clinical success, in-hospital mortality, and stent-graft patency. Lack of a standardized technical approach (self-expandable vs. balloon-expandable), post-procedural anticoagulation regimen, and follow-up imaging limit the generalizability of the results but represent the specific (stent choice, anticoagulation) condition/needs of the individual treatment. However, this article presents the experience from a high-volume tertiary center with approximately 100 cases of complex pancreatic resections annually, and it is the largest cohort of successful stent-graft implantation (25 patients) for hepatic arterial bleeding up to date. Our study underlines the efficacy of stent-graft placement to control the emergency situation as well as to gain time to control the underlying condition. The inherent risk of stent-graft occlusion is obvious and needs further research (optimal anticoagulative therapy, if doable), however, since graft occlusion usually develops over time, restoration of the medical condition is bridged, and liver failure is rare due to formation of collateral liver perfusion.

Conclusion

Treatment of hepatic arterial injury with stent-graft implantation is a promising option with high technical and clinical success rates. However, despite the need for larger cohorts, long-term patency of stent-grafts is low and associated with the location of the injury, but clinical outcome mainly depends on the general condition of the patients.

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O.Ö. and M.M. contributed equally to this work.

Conflicts of interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Jens Ricke: Grants: Bayer; Personal fees: Sirtex, Bayer. Max Seidensticker: Grants: Sirtex; Personal fees: Sirtex, Bayer.

Disclosure

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