R E V I E W

The role of interventional radiology in hepatic and renal hemorrhage embolization: single center experience and literature review

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Abstract. *Background and aim:* Intraabdominal hemorrhage secondary to liver and kidney injury is a major cause of morbidity and mortality. Endovascular arterial embolization is an established interventional radiology technique used to treat active bleeding, and its role in managing abdominal hemorrhages is growing, given the increasing trend for conservative treatment. Our study aims to retrospectively evaluate the technical and clinical results and the possible complications of arterial embolization procedures performed in emergency, in post-traumatic, iatrogenic, and pathological hepatic and renal bleedings. *Methods:* We performed a ten-year, single-center retrospective survey (from January 2010 to December 2019) of all patients treated in emergency by intra-arterial embolization of liver and kidney bleeding. Preliminary CT angiography studies were evaluated, as well as the angiographic findings. Materials used, procedural data, and clinical outcomes, including complications, were recorded. *Results:* The diagnostic angiography showed a single source of bleeding in 20 cases (66.7%), two bleeding vessels in 4 cases (13.3%), and multiple hemorrhagic sources in 6 cases (20%). All bleeding sources were successfully embolized; in 12 patients (40%), complete embolization was achieved with coils and 18 patients (60%) with hemostatic sponges. In one case, a second embolization procedure was performed for the persistence of hemodynamic instability. No major post-procedural complications were recorded. The mean procedure duration was 65.1 minutes. *Conclusions:* Based on our experience and literature data, the treatment of endovascular embolization in acute abdominal bleeding of hepatic and renal origin represents the treatment of choice, as it can provide complete therapeutic success in hemodynamically stable patients. (www.actabiomedica.it)

Key words: arterial catheter embolization, liver hemorrhage, kidney hemorrhage, interventional radiology, CT angiography

Introduction

abdominal hemorrhage is an important cause of morbidity and mortality (1-3). Since the mid-1980s, nonoperative treatment/nonoperative management (NOT/NOM) of solid organs lesions of solid organs - particularly the liver and the kidneys - in hemodynamically stable patients has been the standard care, with success rates over 90% (4-8). Operative treatment was therefore limited to patients with hemodynamic instability or signs of active hemorrhage without hemodynamic compensation. Over the past two decades, interventional radiology techniques have revolutionized the surgical approach to several pathologies (9-21), and angiographic embolization of vascular lesions of solid organs has been used as a complement to NOM, allowing hemorrhage control and further organ preservation (22-30). Together with interventional radiology procedures, the advances in diagnostic imaging scanners, especially multidetector CT, improved the diagnostic accuracy, acquisition time, and dose exposure to optimize the diagnostic and follow-up imaging management (31-43). Regarding CT technology, in recent years, dual-energy CT is gaining emerging application in the evaluation of abdominal hemorrhages thanks to the possibility of improving contrast-enhancement and reducing beam hardening artifacts, providing superior tissue characterization using virtual monoenergetic and material decomposition image processing, with an overall dose exposure reduction (44, 45).

Our study aimed to evaluate the technical and clinical results of arterial embolization procedures performed in emergency, in post-traumatic, iatrogenic, and pathological hepatic and renal bleedings, reviewing the current literature and retrospectively analyzing a series of the last ten years in a single Institution.

Institutional experience

We performed a ten-year retrospective survey (from January 2010 to December 2019) of patients with hepatic and renal bleeding treated with intra-arterial embolization in urgent conditions. All patients treated were hemodynamically stable or with clinical and laboratory signs of mild to moderate instability, responding to treatment with crystalloids and blood. The retrospective survey included 31 arterial embolization procedures in 91 patients (55 males, 36 females, mean age 56.7 years, range 38-77). Among these, 39 patients showed post-traumatic bleeding and 52 iatrogenic hemorrhages; 37 patients had hepatic bleeding, and 54 patients had renal bleeding.

Procedural evaluation and treatment technique

All patients underwent CT angiography scans using 16-320 layers multidetector scanners (Philips 4 and Toshiba Aquilion one, respectively). Delayed scans performed at 5 minutes were acquired in all cases to better document delayed contrast media extravasation.

The indication for endovascular treatment was given by the presence of parenchymal lesions between II and IV degree according to the AAST classification in patients with low hemoglobin and poor response to conservative therapy (namely, liquids, crystalloids, and concentrated red blood cells). All embolization procedures were performed in the angiography suite equipped with a biplane angiography system (Siemens Artis zee Axiom Sensis XP, Forchheim, Germany). In all cases, the approach was carried out through the common femoral artery, using 4-6F introducers (Terumo Radifocus Introducer II) and local anesthesia (10 ml of Mepivacaine 2%). Treatment always started with a preliminary angiographic study of the abdominal aorta and its main branches injecting, using a Pigtail catheter 4 or 5 F (Cordis 65 cm .035 "), 22 ml of IOMERON 400 with a flow of 20 ml/sec. In cases where the CT study indicated the bleeding site, the treatment involved the selective catheterization of vessels using the following angiographic catheters: Cobra 4F, Cordis 65 cm. 038 ", UF Cordis 4F 90 cm. 035, Sim Cordis 4F 100 cm. 038", and Terumo guide 0.035 "150-180cm.

In the presence of bleeding from small vessels, the super-selective catheterization was obtained using Microcatheter Pro great (Terumo Corporation, Tokyo, Japan) 0.025 "with micro-guide 0.021, which allowed embolization with microcoils (Boston Scientific, Interlock -35 detachable coil Natick, MA, USA) and eventually through Gelfoam-Spongostan.

We proceeded to embolize the main afferent vessel with large-caliber spirals in cases where it was impossible to catheterize the small affected vessel (Balt Extrusion, Montmorency, France). The treatment algorithm was the following: in case of bleeding from a vessel with caliber <2mm (calculated on the angiography room console), we used Gelfoam-Spongostan, while in cases of caliber >2mm, spirals were preferred. Manual compression was performed in all cases for femoral access closure. All the patients and/or family members received informed consent before the procedure. A postprocedural CT scan was performed after 48/72 hours, while hemoglobin values were monitored every 6 hours after the procedure.

Results

CT angiography examination performed before the treatment allowed identifying the bleeding origin in 72 pcs (79.1%). The diagnostic angiography showed a single source of bleeding in 60 cases (65.9%), two bleeding vessels in 12 cases (13.2%), and multiple hemorrhagic sources in the remaining 18 cases (19.7%). All bleeding vessels were successfully embolized; in 36 patients (39.6%), we performed a complete embolization of the main trunk with spirals, and in 54 patients (59.3%) the embolization was performed with hemostatic sponges (Spongostan). In one case, a second embolization procedure was performed due to the persistence of hemodynamic instability and evidence of a further bleeding focus, coming from the adrenal artery not detected during the previous angiographic examination. In no case major post-procedural complications were found. The mean duration of the embolization procedures was 65.1 minutes (min 42, max 105).

The time elapsed between the clinical and laboratory evaluation and the embolization procedure was highly variable and depended on the severity of the bleeding and the outcome of any previously conservative approach. The mean interval was 8 hours, with a range of 30 min in two hemodynamically unstable patients at 36 h in patients with progressive anemia. Three patients died during the following 30 days post-procedurally.

Literature review

Hepatic hemorrhages

The liver is among the most commonly solid organs with damages during polytrauma. The overall mortality due to hepatic trauma decreased from 70-80% in the first decades of the century to the current 10-20%, and is closely related to the injury severity, the presence of associated intra/extra-abdominal lesions, the time elapsed between the traumatic event and hospitalization, and the experience of the surgical team (25, 26, 46).

Today, up to 80-90% of closed hepatic trauma is managed in a non-operational manner, and though most studies show that the main advantage of NOM is the possibility of avoiding emergency surgery, many studies showed that NOM also allowed a real long-term survival improvement (25, 47, 48).

The success rate of NOM in closed hepatic trauma, for both pediatric and adult patients, has reached 85-100%, according to the most recent literature data. Among patients initially treated in a nonoperative manner, 10-25% develop complications related to hepatic injury, including hemobilia, biliary fistulas with the biliomas or choleperitoneum, liver necrosis/abscesses, and abdominal compartment syndrome (23, 49, 50).

Some of these complications (abdominal hypertension, bile leaks, etc.) should be considered as the "price" to be paid considering the concept of conservative management since the advantages of this option outweigh the morbidity associated with surgical treatment. Actually, few authors propose a primary role for hepatic resection in these patients (48).

Adopting non-operational management whenever possible as a standard for treatment is one of the major clinical advances in the last two decades. If urgent laparotomy becomes necessary, the currently recommended laparotomy strategy with perihepatic packing (PHP) has also shown effectiveness in significantly improving the patients' outcome (51, 52).

The embolization of the hepatic artery is increasingly used in these two situations. First, as part of the NOT when CT-angiography shows active bleeding. Secondly, when hemostasis is inadequate despite laparotomy with PHP.

Beyond initial diagnosis, preoperative diagnostic imaging examination is of utmost importance for the correct procedural indication, treatment planning, and outcome prediction (53-64). In our experience, arterial embolization has never been indicated in the absence of evident extravasation on CT images. Some authors suggest embolization as part of the NOM for patients with high-grade lesions associated with important hemoperitoneum (65). However, other studies point to the importance of documented active bleeding using CT angiography with contrast media extravasation (indication used in our study) (66, 67). If the concept of NOM with angiography and embolization is now widely accepted for patients with stable and stabilized trauma, its extension to patients with hemodynamic instability is still under discussion. In the context of primary surgical hemostasis, early postoperative angiography, with possible embolization if necessary, is increasingly used. If a nonoperative strategy is chosen initially, the need for a subsequent laparotomy/laparoscopy after interventional radiology should be considered a failure of the NOM (51, 68).

Liver lesions can be successfully treated by embolization due to the double vascularization by the hepatic artery and the portal vein. As a result, the embolization of the hepatic artery or its branches rarely causes hepatic ischemia.

Selective arteriography should be preferred to embolize the right hepatic artery due to the risk of hepatic necrosis or gallbladder; however, the incidence of specific post-embolization complications is acceptable considering the efficacy and therapeutic benefits of the procedure. In literature, hepatic lacerations type I and II show a higher success with embolization treatment, while for grade III and IV lacerations, success is lower (25, 26, 48, 65).

Gelatin sponges are among the embolizing materials used in transcatheter embolization (69). These materials are effective, inexpensive and non-toxic, but are reabsorbed over time, and the arterial flow can be restored. If complete arterial healing is achieved before the embolization material is absorbed, the restoration of arterial flow is achieved. However, in the presence of major lesions, arteriovenous fistulas, or pseudoaneurysms, the reabsorption of the material can lead to

rebleeding, requiring a second embolization or surgery (70).

Isobutyl-2-cyanoacrylate is another effective alternative for embolization. This material is also effective for an extended period, is not expensive, and has low toxicity (71, 72).

Metal coils are also considered among the best materials for arterial embolization. They can be of various sizes, they are not toxic, but they have the disadvantage of being very expensive (73, 74). Other substances less frequently used for AE are the polyvinyl alcohol particles. To increase effectiveness and reduce complications and costs, the tendency is to combine different materials. In particular, the embolization is initiated by injecting gelatin sponge or cyanoacrylate to occlude the arterial branch partially. Then, coils are positioned to completely close the vessel and stop bleeding or flow to the arteriovenous/pseudoaneurysm fistula (9, 72, 75).

A frequent cause of immediate rebleeding is reflux bleeding from a distal branch of the artery that has not been occluded. When the arterial lesion is lateral, the embolization must be proximal and distal to the bleeding, while if the lesion is terminal, it is preferable to perform the embolization as close as possible to the extravasation. High flow lateral arteriovenous fistulas can be treated by introducing a stent into the artery to block the lesion and maintain flow to the liver tissue (25, 73).

It is necessary to follow some therapeutic principles to obtain the best results and reduce the risks for the patient during embolization. Local pain due to hepatic ischemia caused by embolization is treated with analgesics. Spontaneous relief of pain occurs in about four days. Fever up to 39°C and increased liver enzymes and bilirubin are frequent after hepatic necrosis due to trauma and embolization. It should be emphasized that while 70% of the hepatic vascularization comes from the portal vein, the vascularization of the bile ducts depends almost exclusively on the arterial system. So, the embolization of the arterial branches that vascularize these ducts can cause necrosis of the wall with stenosis or leakage as complications. Fistulas of necrotic ducts can cause severe biliomas or peritonitis. These complications can be identified by ultrasound and CT and can be adequately treated with antibiotics and percutaneous drainage (76, 77).
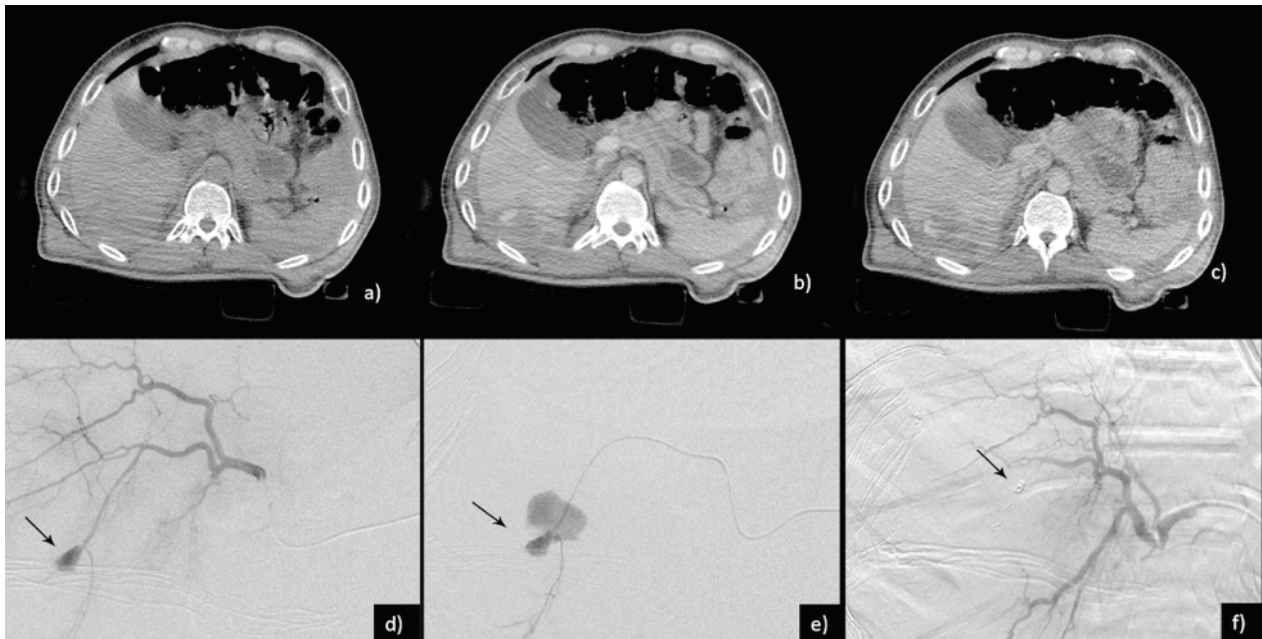
Figure 1. 31-year-old patient with road accident trauma. CT angiography (a-c) shows the presence of an extensive hepatic parenchymal laceration at the level of the VII and VI hepatic segments, with contextual active contrast blush in the arterial and venous phase. The immediate following catheter angiography (d-f) confirms the presence of active bleeding , treated by microcatheterization, injection of temporary embolizing material (Spongostan), and an embolizing coil.

In the presence of a high-flow arteriovenous fistulas, toxic sclerosing agents, such as alcohol, should not be used due to the risk of cardiopulmonary, neurological, and hematological adverse effects. On the other hand, materials with a slow embolization capacity, such as gelatin sponge and cyanoacrylate, can rarely block a high-flow fistula. In these cases, spirals are the best alternative for embolization.

Identified risk factors for these complications include high-grade injuries and the need for operational intervention in addition to the AE. Some embolized patients should be considered at greater risk for hepatic ischemia, including those with concurrent PHP or suspected portal CT lesions. Proximal AE of the main branch (lobar) or distal embolization of multiple sites probably further increases the risk as well. Although liver resections are rarely performed in emergency, the surgical option should be discussed in these situations (78, 79).

Another potential complication of embolization is the iatrogenic dissection of the celiac artery and its branches, with subsequent pseudoaneurysms formation.

Delayed vascular complications such as arteriovenous fistulas and pseudoaneurysms can occur up to 20% in hepatic trauma. AV fistulas may appear as early and intense enhancement of the portal vein and hepatic veins, while pseudoaneurysms appear as rounded focal areas of intense arterial enhancement adjacent to arterial vessels (80-82).

Kidney hemorrhages

Renal vascular lesions with bleeding occur in about 7% of penetrating traumas and 4-5% of closed abdominal traumas. Renal hemorrhage can also be caused by spontaneous renal mass failure (angiomyolipoma, renal carcinoma) and several iatrogenic procedures, including biopsy, percutaneous nephrostomy, and percutaneous lithotripsy (PCNL) (22, 83, 84). When complicated by hemorrhagic shock, renal hemorrhage requires immediate diagnosis and treatment (85, 86). Early and accurate diagnosis is the key to avoiding unnecessary nephrectomy. Ultrasonography and CT are helpful for diagnosing renal vascular lesions, but angiography remains the diagnostic
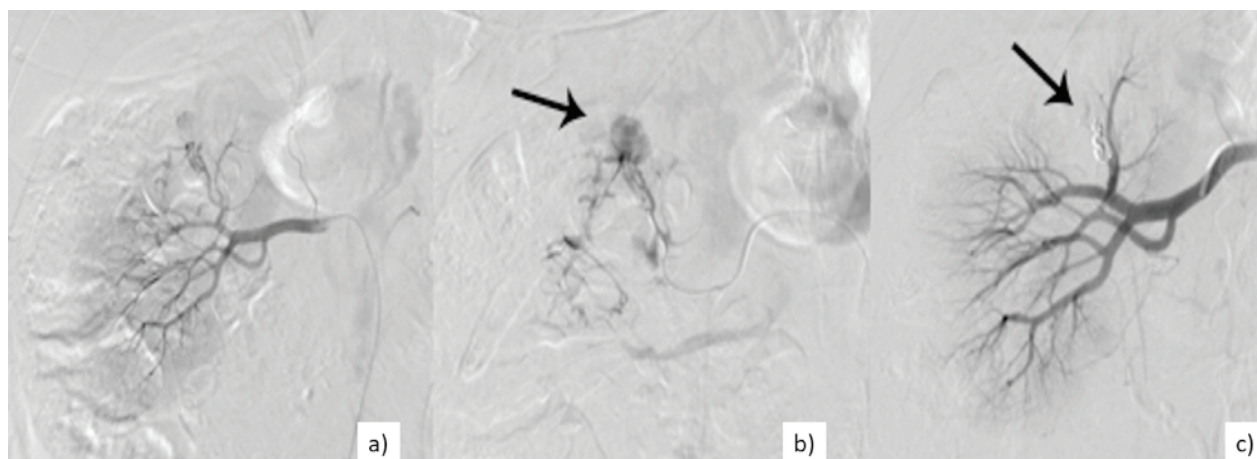
Figure 2. Renal bleeding with pseudoaneurysm - The preliminary angiographic diagnostic examination documents the presence of a pseudoaneurysm lesion of about 13 mm at the level of the upper III of the right kidney (a) with active contrast extravasation in the corresponding calyceal group and peripheral AV fistula (b). Selective microcatheterization of the branch afferent to the bleeding is performed, and two embolizing coils are released (c). The final control documents bleeding occlusion with pseudoaneurysm exclusion.

standard, as it demonstrates the lesion and offers the opportunity for endovascular treatment during the same imaging session (87-89). The criteria for angiography and embolization in patients with renal hemorrhage include persistent bleeding from a segmental renal artery with or without a parenchymal tear; condition of hemodynamic instability with grade 3-4 AAST lesions, arteriovenous fistula or pseudoaneurysm; persistent hematuria and/or rapid hemoglobin reduction (89-91).

In general, surgical repair is recommended for lesions of the main renal artery/vein and renal pelvic avulsion. According to other authors, percutaneous trans-arterial embolization can be used for all types of lesions (even major ones with pedicle avulsion) as the alternative treatment method is nephrectomy (22, 24, 92). Surgical or percutaneous treatment of renal vascular lesions is recommended in massive bleeding, renal hemorrhage persisting for more than 72 hours, or progressive deterioration of renal function. Most posttraumatic renal lesions consist of parenchymal contusions and minor superficial lacerations, which can be managed conservatively. Conservative treatment is largely ineffective in acute arterial renal bleeding and is associated with a high recurrence rate (22, 90, 93, 94).

Embolization of the renal artery is a well-established method for the treatment of massive hemorrhage or persistent hematuria. Recently, with the advancement of interventional radiographic techniques, such as improved imaging techniques, the introduction of microcatheters, and more precise embolic agents, super-selective renal artery embolization (SRAE) has emerged as an effective and minimally invasive for the diagnosis and treatment of renal hemorrhage. Endovascular management of renovascular trauma is advantageous as it is less invasive than surgery, allowing preservation of the renal parenchyma (87-89, 95).

The embolic agent should be chosen based on the type of cause of the bleeding, and the correct choice of the embolizing material is fundamental for the technical and clinical success of the procedure.

Coils are mainly used for the embolization of large renal arterial branches. The main disadvantage of spirals is that more than one spiral is usually required for adequate occlusion, increasing the procedural cost and time.

PVA is biocompatible and inert and provides rapid arterial occlusion. However, the control of PVA during injection is complex, and involuntary embolization can occur. Therefore, we reserve this alternative for difficult-to-reach injuries that cannot be superselectively catheterized.

Large trauma-related renal pseudoaneurysms and iatrogenic renal artery lesions can lead to arterial spasm, evident at angiography as a reduction in vessel

diameter. This spasm can be reversible once the stimulus is eliminated. Therefore, spirals combined with gelatin sponge are the preferred option in these cases to prevent the potential migration of spirals if used alone (22, 96-101).

Early opacification of renal veins and vena cava can be observed in the case of an arteriovenous fistula. Large PVA particles are contraindicated for patients with a renal arteriovenous fistula because they can be released into the venous circulation and lead to pulmonary embolism.

Angiography of arterial hemorrhage associated with renal tumors may show vessels within the tumor area with disorganized structure and vascularization by neovessels and collateral branches. Embolization with PVA alone or in combination with gelatin sponge is recommended for the management of tumor-related bleeding. The identification and complete embolization of all tumor-feeding arteries are essential during the embolization of acute renal bleeding associated with renal tumors. Preoperative CT angiography and angiographic examination are fundamental to outline the vascular anatomy, distribution, and presence of collateral vessels (91, 102, 103).

Another essential aspect of renal angiographic procedures is the choice of non-ionic isotonic contrast media, which should be preferred to reduce the amount of contrast medium, thus reducing the associated damage to renal function (104-106). Stent placement can also be used successfully to treat major arterial renal lesions (107).

One of the most common complications of renal arterial embolization is the post-embolization syndrome, characterized by flank pain, fever, nausea, and vomiting. Most serious complications also include non-selective embolization and spiral migration. The coaxial technique with microcatheters allows a precise localization, catheterization, and embolization of the arterial hemorrhagic branches, which reduces the loss of healthy tissue (108-110). Partial recanalization of occluded arterial branches can also lead to stenosis, with subsequent neurovascular hypertension. The incidence of renal artery dissection after catheterization was reported by up to 7.5%.

Conclusions

In conclusion, based on our experience and literature data, the treatment of endovascular embolization in acute abdominal bleeding of hepatic and renal origin represents the treatment of choice, as it can provide complete therapeutic success in hemodynamically stable patients. However, adequate clinical and therapeutic follow-up is necessary to reduce long-term mortality, especially in patients with impaired clinical conditions.

Conflict of Interest: Each author declares that he or she has no commercial associations (e.g., consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article

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