



Gynecological Malignancies: Bail-Out Interventional Radiology Treatments

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Interventional radiology presents nowadays a relevant role in the management of gynecological malignancies, especially in advanced stages where conventional surgery may be contraindicated.

Progression to multiorgan failure may be related to cancer disease extension or, more acutely, to concomitant infections, bleedings or thromboembolic complications. Infiltration of adjacent organs, as ureters and biliary ducts, ascites and pelvic collections often occur in advanced stages: considering the clinical fragility of these patients, percutaneous procedures are frequently applied. Regarding hemorrhagic complications, bleeding may occur into the tumor itself, due to cancer tissue erosion and vessels infiltration, or may be related to iatrogenic vascular lesions consequent to surgery, mini-invasive procedures and chemoradiotherapy; embolization represents a bail-out treatment in both acute and chronic scenarios.

Aim of this paper is to review interventional radiology procedures in patients affected by gynecological malignancies in advanced stages not suitable for surgery.

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Introduction

“Bail out” is a term taken from aviation English language (ie, an emergency exit from an aircraft via parachute) and applied in the medical environment to refer to potentially life-saving procedures in patients with advanced diseases stages.

Management of advanced gynecological malignancies is now in the domain of a multidisciplinary evaluation where Interventional Radiology (IR) occupies a prominent role.^{1,2} IR involvement extends to minimally invasive treatment of malignancy, often in combination with other modalities. IR plays also an important position in the management of complications from malignancy, which may result from malignancy itself or secondary to treatment.

Malignancy can induce dysfunction of many organs and body systems.³ Progression to multiorgan failure may occur spontaneously either through disease progression, by extension of the malignancy or more acutely through infection,

bleeding, and thromboembolic complications.⁴ Though debilitating, a significant portion of these complications are reversible, many of them by minimally invasive IR methods. Such treatment can relieve symptoms, alleviate pain, and improve operability of patients, thus having a significant positive impact on quality of life.³

Under image-guidance, IR percutaneous techniques in gynecologic bail-out treatment include fluid aspiration, drainage catheter placement, and transarterial embolization.

Patients with refractory malignant ascites, pleural effusion, postoperative fluid collections (abscess, seroma, or lymphocele) or with urinary and biliary tracts infiltrations may benefit from percutaneous aspiration of fluid collections or placement of drainage catheters^{5,6}; those with uncontrolled post-operative hemorrhages or tumour bleeding can be effectively managed with transarterial pelvic embolization both in acute and chronic setting.

Image Guidance

Ultrasonography (US) is a method of immediate imaging, easily available, ideal for quick identification of the local

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factors causing symptoms; US is able to confirm the presence of common complications, as biliary tree dilation or hydronephrosis. US represents also the image guidance of interventional procedures in the extravascular districts appreciable with this technique.

Computed tomography (CT) is readily available for total body study, for oncological follow-up and to check postprocedural results. CT angiography in the various acquisition phases is ideal in the context of emergency bleeding to confirm the diagnosis, to study vascular anatomy and plan the treatment.

Digital subtraction angiography (DSA) is applied to perform both endovascular procedures, as embolization, and catheter placement combined with US or CT.

The direct imaging visualization of IR devices permits safe maneuvers, improving efficacy, and minimizing trauma to surrounding structures.

Malignant Ascites

Malignant ascites (Fig. 1) arises from a variety of malignancies such as ovarian or endometrial cancer and has been reported to be associated with significant morbidity and deterioration in quality of life.

Approximately 60% of patients with malignant ascites are symptomatic and present with abdominal swelling, pain, nausea/vomiting, anorexia, and fatigue.⁷

Most of these patients require palliative treatment as an image-guided paracentesis: repeated outpatient paracentesis is safe and commonly performed, with consequent rapid relief of symptoms.⁸ This is particularly important in patients with bowel adhesions, omental, and peritoneal disease or loculated collections. When ascites is chronic and induces clinical discomfort, a pig-tail catheter may be positioned and left in place into the abdomen to avoid repeated punctures; usually 6-8 French catheters are used.

Postoperative Pelvic or Abdominal Fluid Collections

The incidence of pelvic abscesses is still reported to be approximately 4% in patients with gynecologic malignancy undergoing major pelvic surgery.⁹ These complications lengthen hospitalization and additional interventions with overall increased health care expenses. These patients require drainage of the infected fluid. Minimally invasive percutaneous drainage under image guidance is considered the primary method of management for the most infected abdominal or pelvic fluid collections.

Biliary Obstruction

Metastatic disease (Fig. 2a) at the hepatic hilar nodes or in the peripancreatic nodes may cause obstructive jaundice from extrinsic pressure on the proximal portions of the biliary tree; percutaneous interventions are required when less invasive endoscopic procedures fail to achieve adequate biliary decompression.

Percutaneous biliary drainage (PBD) (Fig. 2b) can be associated with major complications including sepsis, hemorrhage, and localized infective and inflammatory processes (abscess, peritonitis, cholecystitis, and pancreatitis).¹⁰

The incidence of complications is higher in oncology patients than in the general population, perhaps related to advanced malignancy and the potential presence of coexisting immunosuppression.^{10,11} The incidence of cholangitis in oncology patients undergoing PBD approaches 50%, with the same infection being observed twice as often in those with internal and external drainage than in those with external drainage alone.¹² The longer the duration of PBD the more likely the patient is to develop cholangitis.¹³ The incidence of infected bile in patients with malignant biliary obstruction is 25%-36%.¹⁴

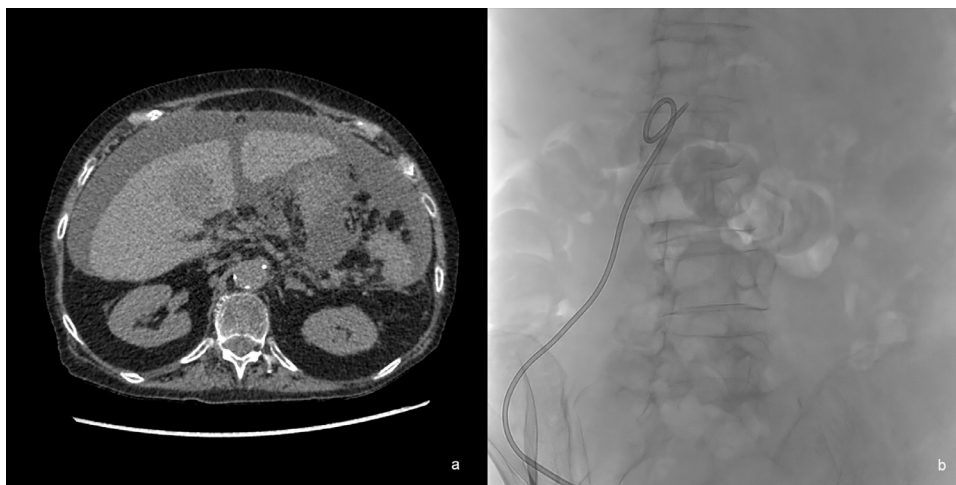


Figure 1 CT scan in axial plane showing malignant ascites from primary ovarian neoplasm with peritoneal carcinosis (a). Fluoroscopy showing peritoneal catheter drainage (b).

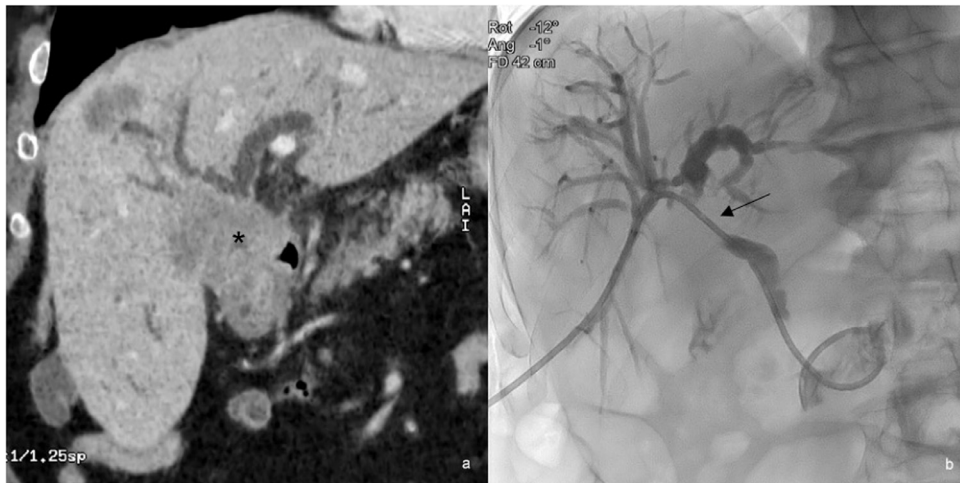


Figure 2 CT reconstruction in oblique coronal plane showing hepatic hilum metastasis (asterisk) causing biliary tree dilation and jaundice (a). Fluoroscopy shows an internal-external percutaneous biliary drainage and occlusion of the proximal segment of the biliary duct is evident as lack of contrast (b, black arrow).

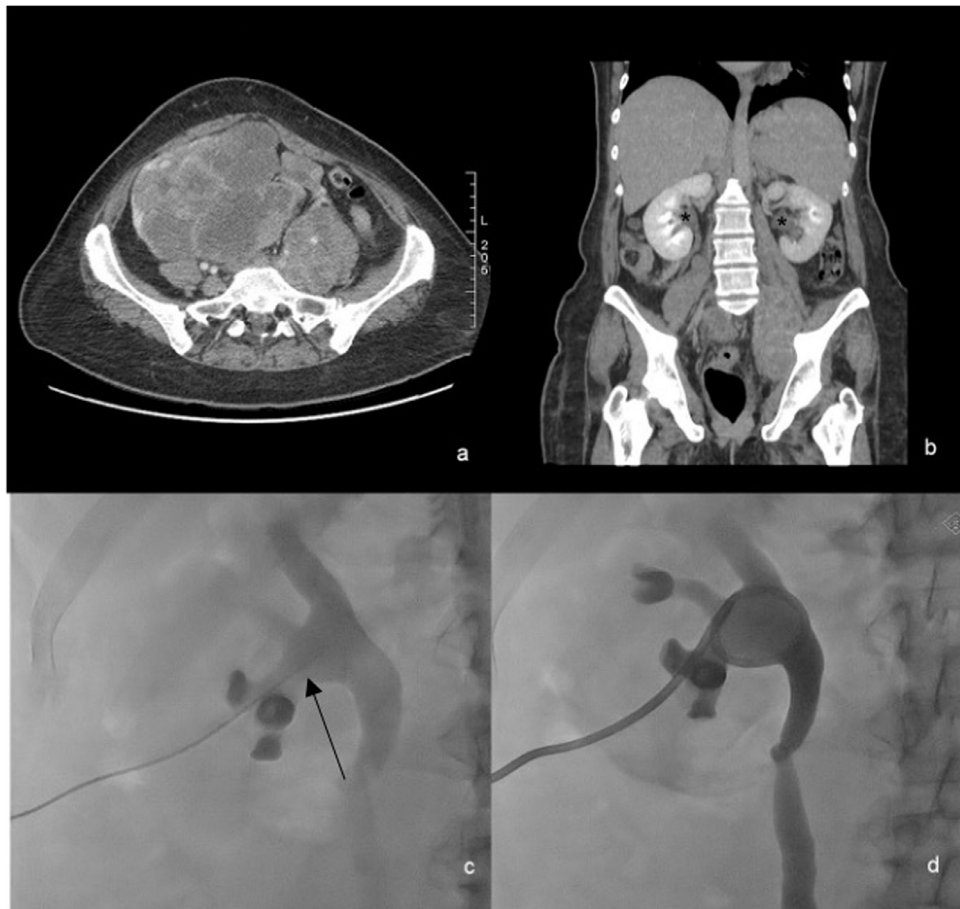


Figure 3 Axial CT scan with intravenous contrast medium shows an adnexal mass within the pelvis which causes compression on the posterior retroperitoneal structures (a). Coronal reconstruction CT scan documents the presence of bilateral hydronephrosis (b, black asterisks). Fluoroscopy in posteroanterior projection (patient landing prone) shows a 21 G Chiba needle into the lower caliceal group (c, black arrow) of the left kidney, confirmed by opacification of the urinary tract; an 8 Fr nephrostomy drainage in the pyelocaliceal cavity is shown (d).

Renal Obstruction

Malignant ureteral obstruction is an ominous sign in the cancer patient and may be due to extrinsic cancer compression, retroperitoneal adenopathy, or direct tumour invasion.¹⁵ Ureteral obstruction can be induced by a wide range of malignancies, even with gynecologic origin (Fig. 3a and b); it may be unilateral or bilateral. Percutaneous management requires urinary decompression, often by means of percutaneous nephrostomy⁶ (PCN) (Fig. 3c and d).

PCN is the most common renal intervention performed by interventional radiologists and, by providing direct access to the urinary tract, allows drainage of tract contents as well as providing access for further urologic intervention via the established route.¹⁶

Indications for PCN in the emergent setting include urinary tract sepsis, pyonephrosis, deteriorating renal function or electrolyte disturbances, such as hyperkalemia and metabolic acidosis.¹⁷ In cases of malignant ureteral obstruction, percutaneous dilatation of the stricture may be anterogradely achieved through the PCN tract: under fluoroscopic

guidance, a catheter is manipulated across the stenotic region and the lesion is progressively dilated by catheter advancement, ureteral dilator, or by inflating balloons of appropriate diameter.¹⁶ After dilatation, an internal ureteral stent, or internal-external nephron-ureteral catheter is placed to prevent restenosis.^{16,18}

Arterial Embolization

There are many, often concomitant, conditions leading to bleeding in patients with malignancy. First, malignancies themselves are a risk factor of coagulopathy: neovascularization due to growth factors, metastatic bone marrow invasion, thrombotic microangiopathy, disseminated intravascular coagulation, or macrophage activation syndrome. Furthermore, iatrogenic causes are often involved: chemotherapy causing aplasia, prevention of thromboembolic disease, post-operative pseudoaneurysms, and a fragile vascular bed following radiotherapy. Last, cancer mass may determine direct

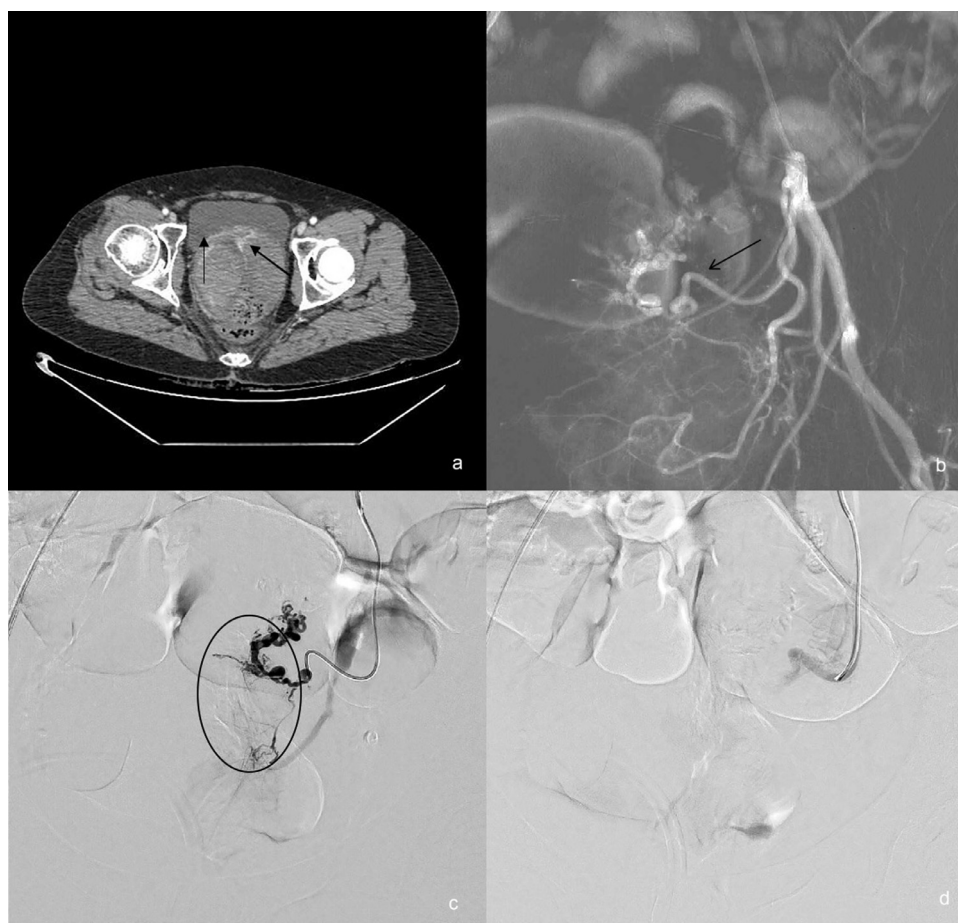


Figure 4 A 50-year-old woman with a history of pelvic pain, metrorrhagia, and drop in hemoglobin value. Contrast-enhanced CT scan demonstrates a heterogeneous mass that surround uterine cervix with multiple bleeding foci (a, black arrows). Selective left hypogastric arteriogram and roadmap showing homolateral uterine artery (b, black arrow). Superselective Digital Subtraction Angiography (DSA) of uterine artery performed with microcatheter: intra-arterial injection confirms the presence of multiple small bleeding foci and hypervascularization (c, black circle). Transcatheter arterial embolization with 300-500 μ m microspheres: final DSA control demonstrates no residual vascularity within the lesion on the left side (d).

vascular injuries. In case of hypervascularization, tumor rupture may lead to catastrophic bleeding.

Malignant tissue can erode adjacent vessels (Fig. 4a) through mechanical invasion and local inflammatory reaction; in addition, the tumor mass may obstruct venous circulation causing an increase in proximal hydrostatic pressure, resulting in varices and shunts which may finally rupture.

Transarterial catheter embolization of the internal iliac artery (Fig. 4b-d) in bleeding due to pelvic neoplasm and for preoperative devascularization was first described 40 years ago.^{19,20} During the years, endovascular embolization applications in the pelvic region have expanded including: treatment of benign diseases as myomas, prevention and control in perioperative bleeding during gynecological and obstetrics surgery,⁶ control of massive hemorrhage from pelvic tumors and trauma.²¹⁻²⁵ Gynecological tumors can present with massive vaginal bleeding; in other cases, life-threatening hemorrhages can occur as consequence of other treatment as surgery and radiotherapy. Delay in the treatment of hemorrhage can also delay the treatment of the malignancy itself; so, early and effective control of bleeding is mandatory.

Transcatheter embolization of the internal iliac arteries was described in endometrial or cervical cancers as well as in advanced uterine cancers.²⁶⁻²⁸ All experiences reported rapid control of bleeding, reduced incidence of re-bleeding and improvement in patient general conditions. Intractable hemorrhages rate has been reported to be less than 1% in a large series of gynecological oncologic patients.²⁹ The accurate assessment of the amount of vaginal blood loss is difficult and the transfusion amounts prior to arterial embolization serve only as an indicator of blood loss.

Identification of the arterial supply of a solid tumor by preoperative contrast enhanced CT facilitates devascularization of neoplastic tissue by transcatheter embolization.³⁰

Mechanical occlusion can be achieved by polyvinyl alcohol, Amplatzer occlusion devices, coils, and embospheres introduced into the tumor bed and lodged in the feeding vessel following fluoroscopic guided selective arterial catheterization.³¹⁻³³ This technique can be used alone as the primary modality of treatment, where interruption of the afferent blood supply to the tumour induces hypoxia and inhibits tumor growth; on the other hand, ablative treatments or

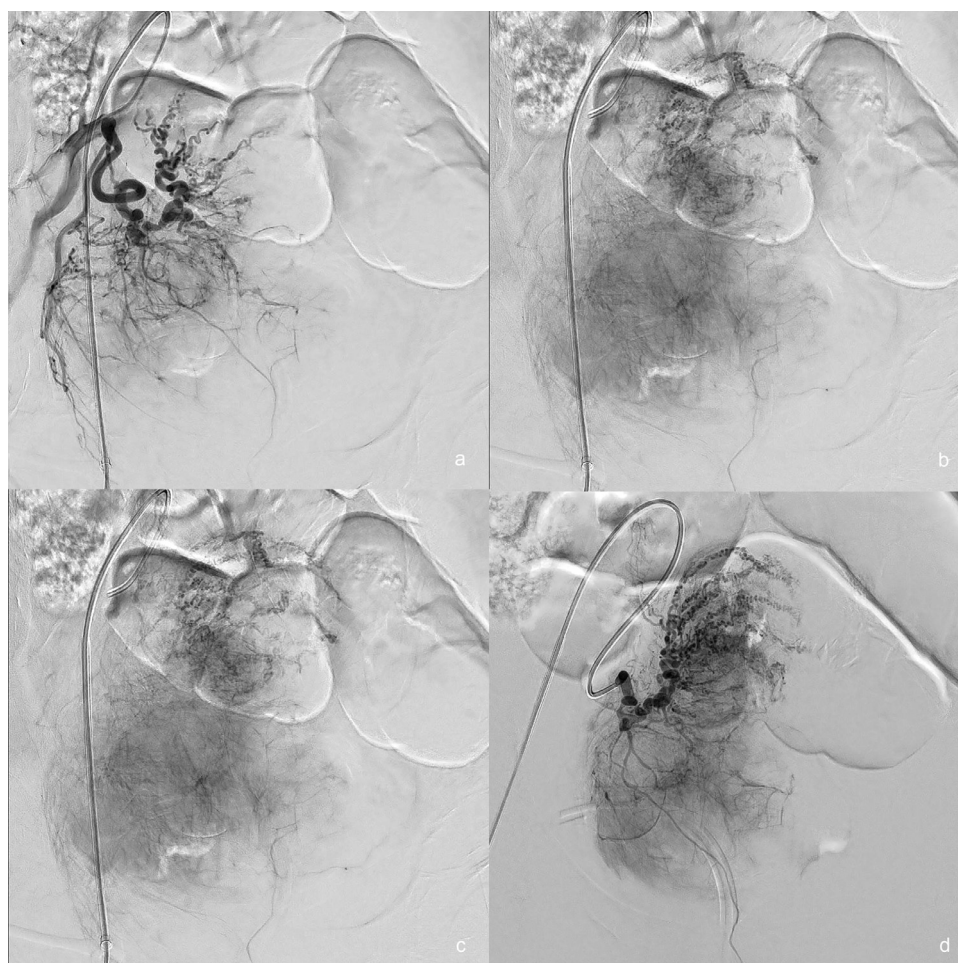


Figure 5 Same patient of Figure 4. Selective right hypogastric Digital Subtraction Angiography (DSA) showing rich hypervascularization with fine, tortuous and irregular vessels caused by structural subversion appreciable both in early (a) and delayed phases of injection (b). Selective arteriogram of distal right uterine artery: transcatheter embolization with 300-500 μm microspheres (c). DSA acquired during embolization demonstrating reduction of vascularity within the lesion (d).

conventional surgery may be applied in conjunction.³¹ In acute hemorrhagic complications of malignancies (as massive hemoptysis, hematemesis, pleural or peritoneal/retroperitoneal hemorrhages), transarterial embolization is the goal standard treatment.^{5,34} Diagnostic selective angiography at the beginning of the procedure is mandatory.

Although metrorrhagia is a common presenting feature of cervical cancer, it is extremely rare that it becomes hemodynamically threatening.⁴ Any vaginal packing should be removed during DSA to allow visualization of the bleeding point. Permanent spheres ranging 300-900 microns supplemented by absorbable gelfoam and metallic microcoils can be adopted for selective embolization (Fig. 5). The smallest spheres are first injected to occlude the capillary vessels; coils should be used to occlude distal vessel with superselective catheterization; indeed embolization of proximal vessels may

promote the development of collaterals with further bleeding. Failure to identify the site of bleeding does not preclude the embolization procedure: in these cases empiric embolization can be performed as in pelvic trauma, based on the clinical and CT findings.

The procedure should be performed by selective catheterization of the anterior division of the internal iliac artery and selective microcatheterization of the “usual suspects,” such as uterine and cervicovaginal arteries. Unless a focal vascular defect is detected, such as a pseudoaneurysm in which microcoils are appropriate, embolization is most commonly performed with gelfoam or microspheres. Embolization should always be bilateral because of the rich pelvic collateral network. Arterial bleeding can be episodic and progressing; the embolization can reduce the subsequent bleeding episodes. In the malignant setting, unlike fibroids, the arteries

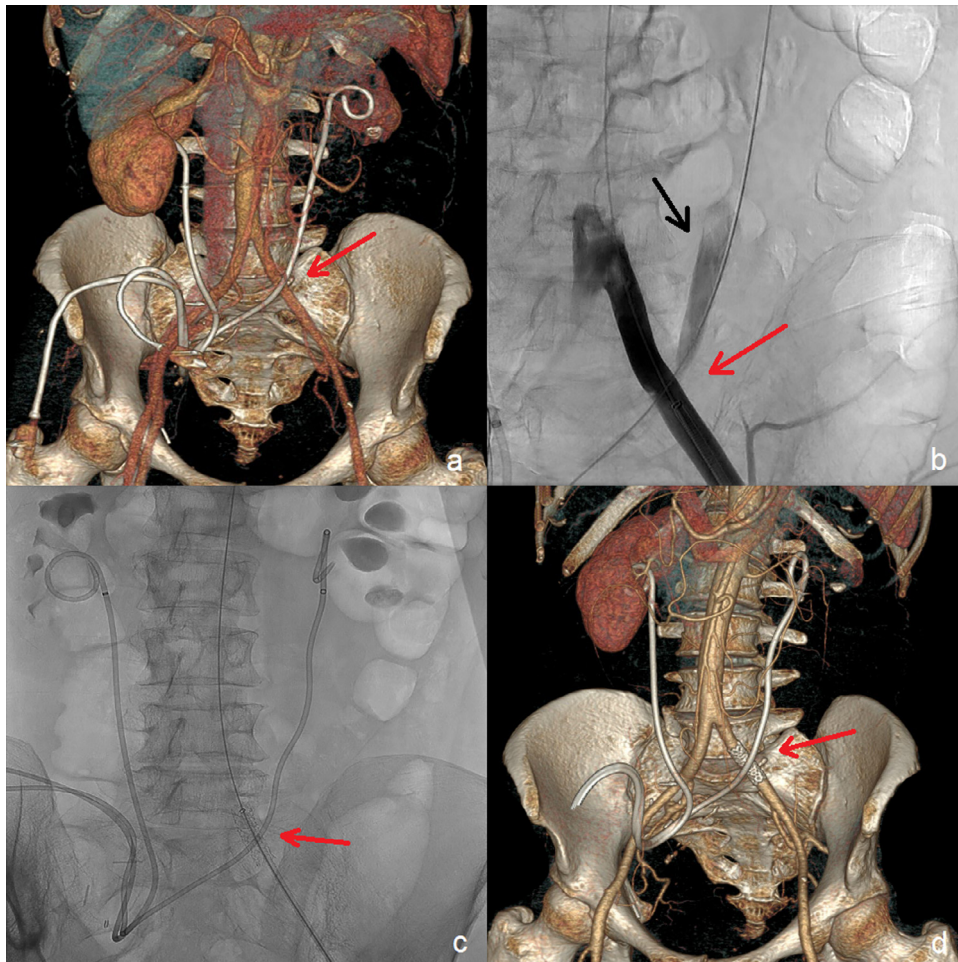


Figure 6 A 46-year-old woman with previous history of hysterectomy, cystectomy and radiotherapy with uretero-ileocutaneous fistula because of endometrial cancer. Patient carries bilateral ureteral stents. 3D CT reconstruction shows contact between left ureteral stent and left common iliac artery (a, red arrow). Patient referred to the emergency room for conspicuous bleeding from the stoma associated with pain and drop in blood pressure. Left common iliac Digital Subtraction Angiography (DSA) performed urgently after removal of the ipsilateral ureteral catheter; a safety guidewire is left in place: DSA demonstrates the simultaneous opacification of the ipsilateral ureter (b, black arrow) with contrast agent passing through the fistula created by the ureter stent (b, red arrow). Fluoroscopy shows a covered stent positioned to occlude the point of arterio-ureteral fistula (c, red arrow). Postprocedural 3D CT reconstruction demonstrates the correct positioning of the covered stent (d, red arrow). (Color version of figure is available online.)

are not usually hypertrophied. Also, prior radiation therapy can cause vascular sclerosis, degrading the arterial supply into a "lace-like" mesh. Cone-beam CT can be useful in identifying tumoral supply.²⁹

A less frequent, but potentially life-threatening, cause of lower gastrointestinal (GI) hemorrhage in the female patient is advanced pelvic neoplasm. Lower GI bleeding arising from the internal iliac artery branches is rare but clinical presentation may be quite dramatic because of the involvement of large pelvic arteries.³⁵ This may occur when there is extension of the neoplasm into adjacent rectum and sigmoid colon. In addition, hemorrhage can be the result of vessel damage from previous radiation therapy. Although transcatheter embolotherapy has a limited role in the management of most causes of lower GI bleeding, embolization techniques can be lifesaving in patients who present with massive lower GI bleeding related to an advanced pelvic malignancy. Gelfoam, polyvinyl alcohol particles, coils and covered stents have been used to occlude or exclude vessels responsible for the bleeding.³⁶⁻⁴⁰

Arterioureteric Fistula

The incidence of arterioureteric fistula is increasing and its diagnosis is probably underestimated. Risk factors are previous history of abdominal/pelvic surgery, pelvic vascular surgery, urinary shunt surgery, prolonged use of a bladder

catheter, radiotherapy or iliac vascular stents.⁴¹ By far the most common site of these fistulae is the crossover point between the iliac artery and the ureter (Fig. 6). In this area the proximity of these structures makes their walls vulnerable to inflammatory and fibrotic reactions responsible for fistula formation.⁴² Although this is a rare condition, it is important do not underlook its possible diagnosis, as the disease-specific mortality without treatment is 58% and a delay in diagnosis is a major poor prognostic indicator.^{38,40-42} The predominant symptom is hematuria and it may be either microscopic or macroscopic; it is often not particularly heavy but can be recurrent, so it may involve catastrophic bleeding. Hematuria is the only symptom in 74% of cases and is combined with lumbar pain or signs of infection in 17% and 7% of cases respectively.⁴³ The endovascular treatment in acute setting is based on positioning of a covered stent to preserve vessel flow by excluding the fistula.

Summary

Because of the expanding application of minimally invasive techniques to the management of patients affected by malignancies in advanced stages, the interventional radiologist is assuming relevant role in the multidisciplinary team that cares for these subjects. The use of both extravascular and endovascular IR techniques (Table) has greatly reduced the

Table IR Procedures With Indications and Risk Factors for Bail-Out Syndrome in Gynecological Malignancies

Procedures	Indications	Risk Factors
Imaging guided paracentesis	Symptomatic malignant ascites (abdominal swelling, pain, nausea/vomiting, anorexia, fatigue)	Bowel adhesions, omental and peritoneal disease or loculated collections
Imaging guided percutaneous drainage	Infected abdominal or pelvic fluid collections (abscesses)	Major pelvic surgery
Percutaneous biliary drainage (PBD)	- Obstructive jaundice - If endoscopy fails to achieve adequate biliary decompression	Metastatic disease at the hepatic hilar nodes or in the peripancreatic nodes
Percutaneous nephrostomy (PCN)	- Decompression of malignant ureteral obstruction unilateral or bilateral; - Urinary tract sepsis, pyonephrosis, deteriorating renal function or electrolyte disturbances	Extrinsic tumor compression, retroperitoneal adenopathy or direct tumour invasion
Percutaneous dilatation of ureteral stricture and positioning internal ureteral stent	- To treat stenosis and to prevent restenosis	Extrinsic tumor compression, retroperitoneal adenopathy or direct tumour invasion
Arterial embolization	- Massive bleeding from pelvic neoplasms (endometrial or cervical cancers); -Preoperative devascularization	- Coagulopathy related to malignancy; - Iatrogenic causes (chemotherapy, radiotherapy, postoperative pseudoaneurysms); - Hypervascularized tumor; - Mechanical vascular invasion
Occlusion of arterio-ureteric fistula	- Hematuria microscopic or macroscopic (often recurrent); - Catastrophic bleeding	- Previous history of abdominal or pelvic oncologic or vascular surgery, urinary shunt surgery; - Prolonged use of a bladder catheter; - Previous history of radiotherapy

morbidity and mortality from gynaecological cancer; certain procedures, previously requiring major surgery, can now be performed with little patient discomfort, with conscious sedation instead of general anesthesia. In these fragile patients, any bail-out intervention should be indicated considering life expectancy and quality of life.

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