



Severe metrorrhagia in patients with advanced gynecologic cancer: endovascular treatment benefits in acute and chronic setting

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Received: 24 June 2019 / Accepted: 2 July 2020 / Published online: 13 July 2020
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Abstract

Purpose Interventional radiology plays an established role in the management of many conditions of the female reproductive tract. Since in benign gynecological and obstetric pathologies, as myomas and postpartum hemorrhages, uterine arteries embolization has been already evaluated, this manuscript aims to report on a single-center experience concerning the endovascular management of metrorrhagia caused by gynecological malignancies.

Materials and methods Single-center retrospective analysis of thirty patients affected by gynecologic cancer treated with endovascular embolization between January 2016 and December 2018 for acute or chronic metrorrhagia.

Results All patients were in advanced oncological stage (III or IV) with loco-regional spread of the tumor or invasion of pelvic structures, with a poor performance status. They were not suitable for surgery. On initial CT angiography, contrast media extravasation was confirmed in two patients (6.6%), while on DSA examination, tumor stain was displayed in 28 patients (93.4%). In two patients (6.6%) a pseudoaneurysm was reported.

Conclusions Endovascular treatment of metrorrhagia in oncologic patients could be a valid therapeutic alternative, especially when in elderly patients with poor clinical conditions not suitable for surgery. A bilateral and superselective embolization using non-resorbable embolic agents should be performed, except for those cases in which there is infiltration of major vessels causing pseudoaneurysms or fistulas that require embolization.

Keywords Metrorrhagia · Gynecologic cancers · Endovascular treatment · Embolization

Introduction

Interventional radiology plays an established role in the management of many conditions of the female reproductive tract because pelvic hemorrhage is one of the most common complaints of non-pregnant women acceding to the emergency department. A variety of clinical scenarios are included, ranging from obstetric and gynecologic disorders, that could result in life-threatening uterine hemorrhage unresponsive to conservative medical treatment [1]. Endovascular management of benign gynecological pathology, such as uterine myomas, has been studied extensively as well as the role of embolization for the treatment of postpartum hemorrhage [2, 3]. Aim of this manuscript is now to report on the endovascular treatment of gynecological malignancies causing metrorrhagia in acute and chronic setting.

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Materials and methods

The institutional review board approved this study. Written informed consent was obtained from all participants.

Sample

This is a single-center retrospective analysis performed on 30 women referring to an interventional radiology department from January 2016 to December 2018, because of metrorrhagia due to gynecological cancer unresponsive to conservative therapies. Ten acceded in emergency conditions due to acute vaginal hemorrhage while the others suffered from chronic bleeding.

Inclusion criteria were: vaginal bleeding unresponsive to medical therapy, inoperable gynecologic cancer, and anemia.

Exclusion criteria were all other causes of vaginal bleeding or patients suitable for surgery.

A multidisciplinary evaluation was conducted by gynecologists, oncologists, anesthesiologists and interventional radiologists: endovascular management was considered the treatment of choice.

Patients underwent to preprocedural CT using a 128-channel multidetector scanner. After basal scan, contrast-enhanced acquisitions were acquired at 30 s, 70–80 s and 180 s after intravenous injection; CT images allowed to detect active bleeding or vascular damage but also to obtain a vascular map to plan the embolization strategy.

Procedural protocol

All procedures were performed with a femoral access through a 5-Fr introducer. Based on CT findings, a diagnostic pelvic arteriogram was performed with 5-Fr diagnostic catheters to depict the origin of the main vessel supplying

the malignancy. Both hypogastric districts were examined. Then, a 2.7-Fr microcatheter was adopted to navigate into thin and tortuous vessels typical of tumoral neoangiogenesis.

Each feeder vessel refurnishing the lesion was superselectively catheterized as distal as possible and embolized, to avoid rebleeding occurrence. Permanent embolic agents, microspheres 300–500 and/or 500–700 micron, were adopted: injection was conducted until flow interruption was confirmed angiographically. Because of the bilateral arterial refurnishing of this anatomical district, embolization was always performed bilaterally to reduce the risk of rebleeding. In cases where pseudoaneurysms were diagnosed, embolization was achieved with microcoils. Final angiography was performed to exclude extra-anatomical vessels refurnishing the bleeding lesion and to verify the patency of collateral circulation.

The femoral access was closed mechanically (Femoseal or Angioseal 6 VIP, Terumo®) and with an elastic patch removed after 24 h.

Intractable hemorrhage due to malignant neoplasms presented angiographically with tumor neovascularization corresponding to vascular staining in most of the patients; bleeding related to pelvic neoplasms were typically slow and intermittent, as a result of infiltration of small tumoral vessels associated with tissue necrosis. Massive bleeding was evident only in case of large vessel involvement (Fig. 1).

Technical success was defined as disappearance of abnormal vascular pattern and/or occlusion of the targeted vessel at final arteriography.

Clinical success was considered as interruption of vaginal bleeding with improvement of hemoglobin values.

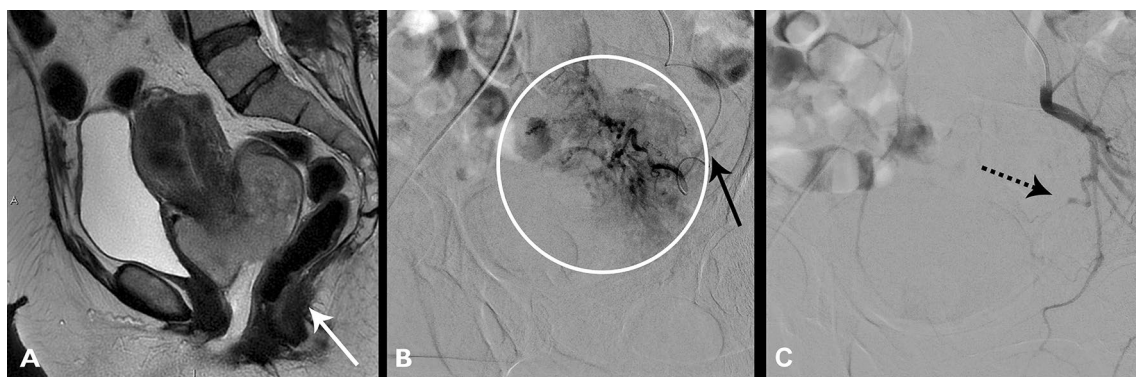


Fig. 1: 58-year-old patient hospitalized for metrorrhagia. **a** T2 sagittal MRI scan; voluminous cervical cancer mass involving vaginal fornix, not well defined from rectal wall (white arrow). **b** Diagnostic superselective DSA through a 2.7Fr microcatheter (black straight arrow)

shows an ectasic uterine artery with evidence of pathologic vascular stain in uterus body (white circle). **c** Final DSA, through diagnostic catheter after embolization, shows stop-flow in uterine artery (black dotted arrow)

Statistical analysis

Descriptive statistics were developed in the MATLAB® (MathWorks, Inc., Natick, Massachusetts, USA) environment.

Results

Thirty patients (mean age 60 years, range: 42–84) were treated with embolization of hypogastric arteries branches according to the different types of malignancies, distributed as follows: 66.6% cervical cancer, 20% endometrial cancer, 10% vulvar cancer and 3.3% ovarian cancer. According to FIGO classification system [4], patients were stratified both on the basis of the site of the primary tumor and of the involvement of the surrounding organs (Table 1). All patients were in advanced oncological stages III or IV with

Table 1 Cancer localization and FIGO classification system

Cancer localization	FIGO staging	Rate of occurrence (%)
Cervical	III-A	23
	III-B	16.6
	IV-A	23
	IV-B	3.3
	Total	66
Endometrial	III-B	3.3
	III-c	3.3
	IV-A	13.3
	Total	20
Vulvar	IIIA	10
Ovarian	III-B	3.5

loco-regional spread of the tumor or invasion of pelvic structures: Because of these characteristics associated with a poor performance status, they were not suitable for surgery; chemotherapy and/or radiotherapy had been previously performed in all patients.

On initial CT angiography, contrast media extravasation was confirmed in two patients (6.6%) where a pseudoaneurysm was diagnosed originating from the right uterine artery and from the hypogastric artery, due to massive invasion from endometrial cancer responsible for blowout syndromes (Fig. 2). In both cases, embolization was performed with microcoils.

On DSA examination, tumor stain was displayed in 28 patients (93.4%). Bilateral uterine arteries were the target in 93% of cases (28/30) because on DSA they appeared ectasic, tortuous and, moreover, neovascularity of uterus was confirmed. In 10 patients, suffering from cervical cancer, cervicovaginal branches were embolized too. In two patients with vulvar cancer, selective embolization of bilateral pudendal arteries was performed (Fig. 3).

One patient showed rebleeding after 4 days, so she underwent to a new embolization extended to further tumor's tributary arteries, even if the main cause of rebleeding was to ascribe to cancer tissue crumble.

A total of 31 endovascular procedures were technically successful in thirty patients, thus achieving 100% technical success. One patient (3.3%) required two embolization sessions.

Hemoglobin levels improved in mean from 8.5 to 10 g/dL. Twelve patients required blood transfusion before the endovascular treatment.

At 6 months follow-up, 27 patients died because of disease progression and three patients underwent radiotherapy after the embolization procedure.

No major procedure-related complications were recorded. Three minor complications occurred according

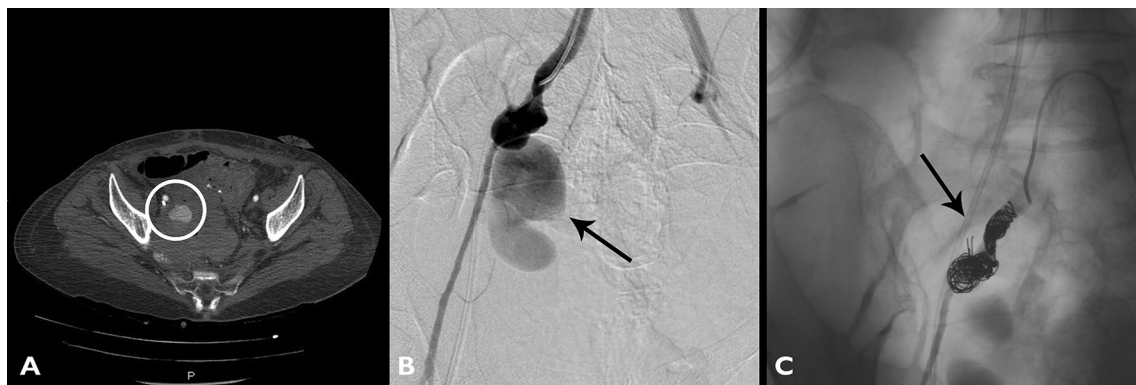


Fig. 2: 61-year-old patient hospitalized for hemorrhagic shock. **a** CT scan shows pelvic cancer mass involving right hypogastric artery and causes its erosion resulting in pseudoaneurysm. **b** Diagnostic super-

selective DSA through diagnostic 5F catheter (black straight arrow) confirms CT evidence. **c** Final DSA, through diagnostic catheter, shows that vascular exclusion of hypogastric artery occurred

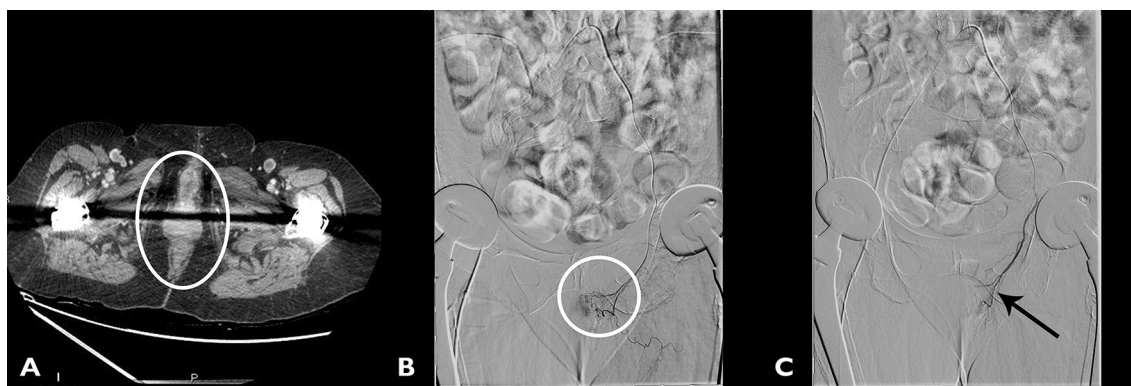


Fig. 3. 74-year-old patient hospitalized for chronic metrorrhagia. **a** CT scan shows vulvar cancer spread to perineum. **b** Diagnostic superselective DSA through a 2.7 Fr microcatheter (white circle)

shows an ectasic pudendal artery and abnormal vascularization of vulva and perineum. **c** Final DSA, through microcatheter, shows stop-flow at this level (black arrow)

Table 2 Results

Target vessel	No. patients
Bilateral uterine arteries	28
Bilateral uterin arteries and cervical branches	10
Bilateral pudendal arteries	2
Rate of complication (%)	Cirse classification
6.6 (2 patients)	Grade 2
3.3% (1 patient)	Grade 1
Rate of technical success (%)	100%

to the CIRSE (CardioVascular and Interventional Radiology Society of Europe) Standards of Practice Committee guidelines [5]: two patients experienced mild pelvic pain that disappeared after 2 days thanks to analgesic drugs (grade 2); in one patient a small pseudoaneurysm developed at the side of femoral access (grade 3) resolved with manual US-guided compression.

All results are summarized in Table 2.

Discussion

Pelvic malignancies are the most frequent cause of hemorrhage in non-pregnant women [6] and are usually managed surgically. However, in case of advanced-stage diseases, poor performance status and elevated surgical risks, conservative management may be performed with vaginal packing, transfusions, radiotherapy or chemotherapy [7]. If conservative measures fail, transcatheter arterial embolization should be considered for the management of intractable bleeding due to gynecologic malignancies [8, 9]; tumors can also invade large vessels, as external

and internal iliac arteries, producing pseudoaneurysms and causing blowout syndrome [10].

In this scenario, surgery, adjuvant radiotherapy and/or chemotherapy carry a potential risk for significant complications, particularly in elderly patients who experience age-related physiological changes and chronic diseases, which may expose them to substantial risks, morbidity, and even death during standard cancer treatments [7].

Vaginal bleeding related to pelvic cancers presents typically slow and intermittent, but persistent and poorly responsive to surgical interventions or radiotherapy [11]; it can be life-threatening in advanced uterine neoplasms and is the immediate cause of death in 6% of women with cervical cancer [12]. More massive bleeding may occur when tumors invade large vessels: the standard procedure to control massive bleeding is ligation of the internal iliac artery; however this may not be applied in patients with highly deformed pelvic anatomy because of radiotherapy, recurrence of cancerous tissue and poor general health status. Furthermore, the wide collateral blood supply to the pelvis is the reason why proximal ligation of hypogastric artery may fail to control bleeding in patients with untractable tumoral vaginal bleeding [13]. From a technical point of view, embolization can result more challenging if the patient had already undergone to surgery and/or radiotherapy because anatomic relationships are distorted and there may be atypical sources of bleeding. In spite of this, endovascular embolization, being less invasive and not requiring general anesthesia, may be indicated in these clinically frail patients.

In most cases, active bleeding within the tumor mass does not appear as contrast extravasation, but rather as an abnormal vascularization and delayed contrast stasis due to ulceration or tumoral necrosis.

After endovascular embolization, rebleeding from different bleeding foci may occur because other vessels could be

encased and invaded as tumor progresses. In those patients, re-embolization is feasible and effective while surgery is not [8].

Results from present study are in accordance with literature: bleeding was successfully managed in all patients (100%) within the first 24 h.

These data can be interpreted as achievement of both technical and clinical success: improvement of hemoglobin levels and reduction of the discomfort caused by persistent metrorrhagia. This allowed patients to continue the therapeutic protocol foreseen for their pathology.

Literature data [13–17] about the role of embolization in this scenario are scarce and mainly in form of case reports and small series. Pisco et al. [13] and Lang [16] described their experiences on patients affected by various pelvic cancers (bladder, prostate, uterus etc.) and bleeding due to radiotherapy, but not focusing on the gynecological district. Athanasoulis et al. [14] reported a case report on two patients suffering from metrorrhagia due to cervix carcinoma. Miller Jr et al. [15] focused their case-report on two patients whose pelvic bleeding was a consequence of radiotherapy for carcinoma of the cervix. Yalvac et al. [17] conducted a study on 8 patients affected by cervical cancer.

Concerning the embolic agents adopted, the choice depends on both operator experience and type of vascular lesion. When the disease is progressive, as in tumors, permanent embolics are more appropriate [18]. In this sample microspheres 300–500 or 500–700 μm were the most used embolics, associated in some cases with coils. Mechanical embolics may be less effective in patients affected by coagulopathy, so in these liquid embolics should be preferred to occlude the culprit vessel.

This study presents some limitations, first its retrospective design; however it should be considered that 90% of patients accessed in emergency conditions to the interventional radiology department; then, multiple embolics were adopted according to operator preferences and no comparison among them was available. Finally, the number of patients is small to allow definitive considerations.

In conclusion, endovascular treatment of metrorrhagia in oncologic patients is safe and effective, especially in elderly patients with poor clinical conditions not amenable to surgery; from a technical point of view, bilateral superselective embolization is mandatory. Regarding the embolic agents, microspheres seem to reduce the risk of rebleeding and penetrate more distally into the tumoral neoangiogenetic vessels. In case of large vessel involvement with pseudoaneurysms, coils should be considered.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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

Informed consent Informed consent was obtained from all individual patients included in the study.

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