Emergency Medicine: Open Access
ISSN: 2165-7548

Dragusin et al., Emerg Med (Los Angel) 2016, 6:6
DOI: 10.4172/2165-7548.1000342

Review Article Open Access

Indications and Outcome of Uterine Artery Embolization (UAE) in Gynaecological Conditions: Up-to-Date and the Results of our Experience

Roxana-Cristina Drăgușin[1], Nicolae Cernea[1], Cristian Constantin[2], Dan Hertzog[2], Andrei Deaconu[2], Maria Florea[1], Lucian Zorila[1], Ciprian Patru[1], Razvan Capitanescu[1], Stefania Tudorache[1*] and Dominic-Gabriel Iliescu[1]

[1]Department of Obstetrics and Gynecology, Prenatal Diagnostic Unit, University of Medicine and Pharmacy Craiova, Emergency Clinic County Hospital, Craiova, Romania

[2]Department of Radiology, University of Medicine and Pharmacy Craiova, Emergency Clinic County Hospital, Craiova, Romania

[*]Corresponding author: Stefania Tudorache, Department of Obstetrics and Gynecology, Prenatal Diagnostic Unit, University of Medicine and Pharmacy Craiova, Emergency Clinic County Hospital, Craiova, Romania, Tel: 0040723888773, 0040251502179; E-mail: stefania.tudorache@gmail.com

Received date: October 31, 2016; **Accepted date:** November 26, 2016; **Published date:** November 29, 2016

Abstract

Introduction: The purpose of the paper is to present the safety and outcomes of uterine artery embolization (UAE) performed in patients at high risk or with active haemorrhage.

Methods: A review of the literature was performed regarding the outcome of the procedure considering the main indications and current recommendations. Also, the experience of our centre from September 2014 to September 2016 is presented.

Results: We performed a thorough search of the published literature and realized a descriptive review. The current indications are uterine fibroids, cervical neoplasia, adenomyosis, ectopic pregnancies (uterine and abdominal locations) and arterio-venous malformations. In our University Hospital, a retrospective study showed that we used the method in controlling the bleeding due to uterine fibroids, uterine ectopic pregnancies, cervical cancers and surgical high-risk dysfunctional uterine haemorrhage. All procedures were technically successful. The results of the technique were beneficial in all cases, except one case of cervical pregnancy complicated with choriocarcinoma and another case with recurrent perimenopause dysfunctional uterine bleeding in a case with multiple severe comorbid illness.

Conclusions: The availability of the procedure in settings with experienced staff in gynaecology and radiology is beneficial in selected cases.

Keywords: Uterine artery embolization; Vascular malformation; Neoplasia; Ectopic; Adenomyosis; Fibroid

Introduction

Uterine artery embolization (UAE) is a safe and efficient technique, used by interventional radiologists for more than 50 years in treatment of various gynaecologic and obstetric conditions with massive, uncontrollable haemorrhage [1]. The technique includes the selective embolization of one or both uterine artery in order to supress the uterine bleeding, to avoid surgical interventions and/or to conserve the fertile future of young women. Based on the experience of different centres in the past years, UAE proved a high rate of success, even 100% in the management of some pathologies such as arteriovenous malformations, gynaecological neoplasias, some types of ectopic pregnancies and uterine fibroids [2]. The aim of this paper is to underline the safety, but also the benefits of UAE in patients with high risk of bleeding or in patients with active massive bleeding.

Methods

A review of the literature was performed regarding the outcomes and complications of the procedure considering the main indications and current recommendations. We present the experience of our centre, the Clinic of Obstetrics and Gynaecology of Craiova Emergency County Hospital from September 2014 to September 2016, in a retrospective study of cases that benefited from UAE.

Results

The literature show the efficiency of the UAE technique in controlling genital bleeding in over 95% of arteriovenous malformation cases and gynaecological neoplasias and up to 100% in cases of abdominal or cervical ectopic pregnancy [1]. Regarding the management of uterine fibroids, it was noted a reduction of its volume in over 60% of cases at 6 months evaluation and a significant improvement of symptomatology (menorrhagia and pain) in over 82% cases.

In our experience, in the 2 years of the study, 76 patients have benefited from UAE: 47 patients with uterine fibroids, 4 patients with ectopic pregnancies (cervical, interstitial and scar pregnancy), 23 patients with cervical neoplasia, 1 patient with adenomyosis and 1 patient with premenopausal uterine dysfunctional bleeding and multiple comorbidities. In all cases the procedure was technically possible and the bleeding cessed in almost all cases, except one case of cervical ectopic pregnancy, that proved to be choriocarcinoma and the case of premenopausal uterine dysfunctional bleeding.

Discussion

Arteriovenous malformations

Uterine arteriovenous malformations (AVM) are infrequent cause for uterine bleeding, usually diagnosed in young patients with history of intermittent and abundant dysfunctional uterine bleeding during reproductive years or sporadic in postmenopausal women. There are two types of AVM: congenital or acquired. The congenital AVM are due to a defect in the formation of the primary capillary plexus during angiogenesis. The acquired AVM represent arteriovenous communications between the branches of the uterine artery and the myometrial venous plexus, usually that appears after invasive uterine interventions or at the origin of a uterine pathological process. To describe this pathology, the literature proposed different terms such as "arteriovenous fistula", "uterine arteriovenous malformation" or "arteriovenous shunt". The best way for the diagnosis of these cases will be arteriograms after exclusion of all other possible etiologies for uterine bleeding. Cases of AVM were diagnosed by the use of hysterograms, hysteroscopy (allows the visualization of the pulsations in the uterine wall and the pulsatile bleeding from the site of the malformation), Doppler ultrasound and magnetic resonance imaging. The optimal treatment for repeated intractable hemorrhage was hysterectomy, before the era of sophisticated imaging. After the 80', UAE has become an efficient and minimal invasive alternative in the management of AVM in patients that want to preserve their fertility [1,3].

In a recent study, Yoon et al. mentions that 54 patients with acquired AVM that benefited from UAE presented a primary success rate of 61% in controlling the symptoms and a secondary success rate of 91% [3]. Ghai et al. describes the proper control of uterine bleeding due to AVM in 93% cases, after UAE, but in a small lot of 15 patients [4]. Badawy et al. reports a success rate of UAE in 96% cases with a complication rate of 4% in a lot of 25 patients [1]. All studies support the utility and the benefits of UAE technique in the presence of AVM, even if sometimes the repetition of the procedure is needed in order to obtain the desired effect [5]. Regarding the future fertility, the prognosis is favorable because selective embolization avoids ovarian vascularization, therefore patients present normal menstrual cycles. Our experience with this type of pathology is still limited.

Cervical neoplasia

UAE in gynaecology was described, for the first time, in the management of genital bleeding due to pelvic neoplasia [2]. This type of bleeding can be massive, sometimes fatal and a proper haemostasis can become a major therapeutic problem even nowadays. Such local bleedings generally appear in advanced stages (III and IV) of cancer evolution, causing anaemia to the patient and excluding any possibility for the patient to undergo endocavitary radiation therapy. There have been reported multiple therapeutic options such as local application of haemostatic materials (Mohs' paste, a mixture of zinc chloride paste), surgical hypo-gastric artery ligation or UAE [6]. Studies of small lots of patients state a success rate of almost 100% of UAE in cervical neoplasia. 70% of patients present with post embolization syndrome (nausea, gluteal pain, fever) [7]. Raba et al. mention, in a recent study, that shortening of uterine arteries worsens prognosis of the haemostatic effect of their obliteration in patients with advanced cervical cancer [8]. Their gradual shortening is caused by the tumour infiltrating the parametrium, occupying the spaces running alongside the length of uterine arteries. Consequently, the reduced blood flow in uterine arteries induces a compensatory flow increase in other vessels, as well as promoting neoangiogenesis. In such situations, the share of uterine arteries in the distribution of blood to the tumour area is reduced. These theories may explain cases of UAE failure in cervical neoplasia [8].

In the 2 years of our study, 23 patients with advanced stages of cervical neoplasia have benefited from UAE for important vaginal bleeding (Figure 1). The primary rate of success of UAE was 86.9% with considerable reduction or even absence of vaginal bleeding in the 24-48 hours after procedure. The secondary success rate was 100% at 7 days post procedure. For the moment, we cannot provide more information about the success rate on the long-term, but our research is still in progress. Minor complications after UAE were present in less than 15% of cases and no major complications were reported.

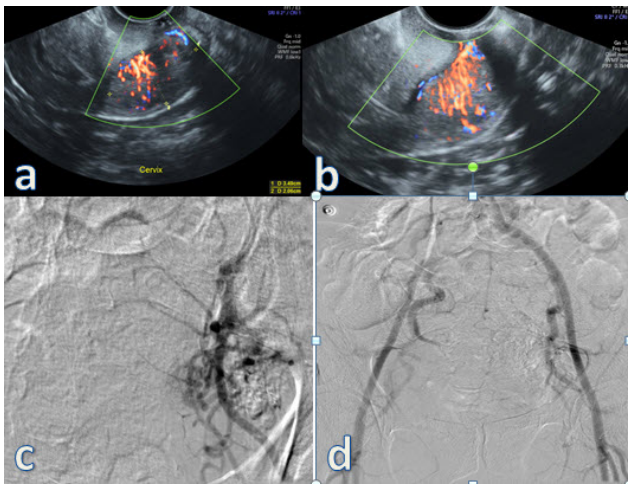

Figure 1: Bilateral UAE in cevical neoplasia (a,b) 2D and Color Doppler ultrasound image of the cervical tumor, (c) Left uterine artery selective arteriography and (d) Bilateral internal iliac selective arteriography.

Ectopic pregnancy

Ectopic pregnancy is one of the major causes of maternal mortality due to massive haemorrhage. Surgical management can be considered the best first line of treatment for tubal and ovarian pregnancies. Instead in ectopic cervical, abdominal, scar and intestitial pregnancy other therapeutic options must be taken into consideration like the use of methotrexate or UAE [1]. Ectopic abdominal pregnancy is extremely rare and is characterized by the implantation site, which could be any place in the pelvis and by associating a marked vascularization. UAE can decrease the risk of heavy bleeding after the removal of the gestational sac and placental tissue. One dilemma in the management of ectopic abdominal pregnancy is whether the placenta should be left in place or should be surgically removed at the same time as the foetus. When the placenta is firmly attached to intestines or major blood vessels, it should be left in place to reduce the risk of haemorrhage or the incidence of hysterectomy. These cases can become complicated in postoperatively with important pain, fever, infection, intestinal perforation, peritonitis, abscess and extremely rare choriocarcinoma [9,10]. The task of the angiographer is to establish all sources of blood supply to the placenta using abdominal aortography, selective celiac

arteriography, selective mesenteric angiography and selective left and right iliac arteriography. Embolization should be done usually for the vessels difficult to ligate intraoperatively [11].

Wu et al. reported a small lot of 13 cases of abdominal ectopic pregnancy that was successfully embolized in a prophylactic way or after the removal of the foetus [2]. In the 2 years of our study, we diagnosed 2 cases of abdominal ectopic pregnancies, but their clinics did not impose UAE.

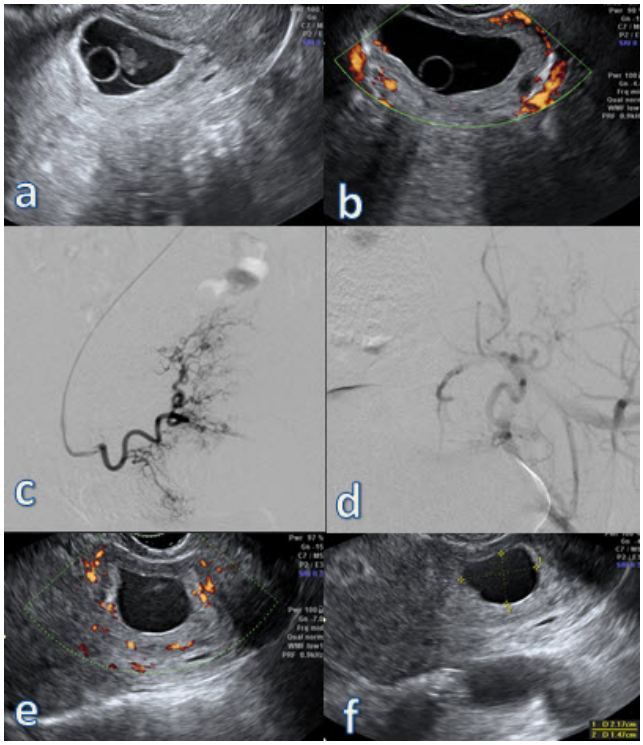

Figure 2: Bilateral selective UAE in a scar pregnancy case. (a,b) 2D and Power Doppler ultrasound images of the gestational sac located in the postcesarean scar, (c) Right uterine selective arteriography, (d) Left uterine selective arteriography and (e,f) 2D and Power Doppler ultrasound images at 72 hours post UAE that suggest the reduction of the gestatonal sac and its vascularization.

In cases of ectopic cervical pregnancies, the implantation is within the cervical canal and therefore the trophoblastic tissue is usually directly attached to the cervical tissue with important vascularization [1]. When attempting to surgically remove this type of pregnancy, there is a high risk of uncontrollable haemorrhage, which might end in hysterectomy. UAE can be extremely useful in decreasing preoperatively the blood flow in the cervical arteries allowing a safe evacuation of the pregnancy. More, recent research proposes UAE in association with systemic administration of methotrexate to increase therapeutic efficiency [12]. Potential complications of UAE in ectopic cervical pregnancy include uterine ischemia, necrosis, and subsequent amenorrhea from endometrial ischemia [13]. Wu et al. noted 15 cases of cervical ectopic pregnancies that benefited from UAE [2]. In our clinic, we used UAE in 4 cases of ectopic cervical pregnancies in order to reduce the risk of bleeding. The single case that the embolization technique did not offer the expected results proved to be a case of choriocarcinoma. The case was referred to the Oncology Clinic for specific treatment.

Caesarean scar pregnancy is a rare ectopic pregnancy, in which the embryo is implanted in the scar located at the lower segment of the uterus, characterized by a thin myometrium and a rich blood supply. The implantation and the growth of the gestational sac can cause life-threatening uterine rupture and severe haemorrhage [14]. There are 2 types of scar pregnancy: type I is characterized by the implantation and development of the gestational sac in the cervico-isthmic region or in the uterine cavity; type II is characterized by the implantation of the gestational sac in the post-caesarean section defect, with progression towards the bladder or abdominal cavity. A type II has more risks that type I. Current practice recommends a conservative management, using local administration of Methotrexate, after bilateral UAE. However, a gestational sac >5 cm and type II of scar pregnancy are prognostic factors to the failure of conservative treatment [15]. In the single case of type I scar pregnancy in our study; we used UAE followed by cervical dilatation and aspiration of the gestational sac, with favourable outcome (Figure 2).

Recently, UAE was proposed as an efficient conservative therapeutic option in the management of intestitial ectopic pregnancy, in order to preserve future fertility [16]. UAE was successfully used in our clinic in the single case of intestitial pregnancy during our 2 years study. This procedure has a double purpose: first of all to avoid a surgical intervention (young patient with a desired future fertility) and second of all, in order to prevent massive haemorrhage, if inadequate systemic response to methotrexate.

Adenomyosis

With a prevalence reported to be 10-18%, adenomyosis is a common benign uterine pathology, a non-neoplastic process where endometrial tissue proliferates into the myometrium and determines abnormal uterine bleeding and dysmenorrhoea [17]. The definitive therapeutic option for treatment of adenomyosis is currently considered hysterectomy. However, UAE can be taken into consideration as a first-line therapy for patients who want to preserve fertility or for patients that are not suitable candidates for blood transfusions or for patients with severe anaemia (before hysterectomy). UAE has no contraindication in adenomyosis management. UAE proved to be successful in 98.3% of a lot of 117 patients (with a volume reduction at 1 year in 51% cases and an improvement of symptoms in over 70% cases). In the same lot, premature menopause was observed in 1.7% of patients following UAE [18]. UAE for adenomyosis can be associated with significant complications, similar to those after UAE in uterine fibroids. Pregnancy and vaginal births are possible after UAE in adneomyosis [19].

In our study, a single patient with adenomyosis benefited from UAE with favourable results in reducing pain and vaginal bleeding. The patient had an unplanned spontaneous pregnancy after 12 months that was surgical interrupted.

Uterine fibroids

Uterine fibroids are painless benign tumours that occur in reproductive age women, in the body of the uterus and less than 5 % in the cervix. They affect about 40% of women and they are the major cause of uterine bleeding leading to anaemia. The standard line of treatment of this type of pathology is surgical excision, accomplished by laparotomy, laparoscopy or hysteroscopy [1]. The cost of treatment

of uterine fibroids represents a major economic problem. The use of drug therapy (like Gonadotropin-releasing hormone or Ulipristal acetate) has the role of decreasing the size and vascularization of the uterine fibroid, facilitating a safe surgical procedure and an improved uterine reconstruction after the excision of the tumour [4]. A minimally invasive management of a uterine fibroid includes UAE [20], percutaneous laser ablation, cryoablation, transvaginal uterine artery occlusion and magnetic resonance imaging guided focused ultrasound.

All patients who wish to be benefit from UAE for symptomatic uterine fibroids have to be examined by both the gynaecologists and radiologists; as interdisciplinary is necessary for a proper treatment and an optimal care of the patient. In 2015, a group of European researchers met in order to establish universal general recommendations regarding UAE in the management of uterine fibroids. In order to benefit from UAE, the patient should meet few conditions: a normal Pap smear in the last 12 months, a negative pregnancy test and absence of any genito-urinary inflammatory diseases, normal values of urea, creatinine, blood tests, thyroid hormones and reactive C protein. The main indication for UAE is symptomatic uterine fibroid. Relative contraindications include previous administration of Gonadotropin releasing hormone in the past 3 months, due to a high risk of uterine artery vasospasm (contraindication not valid in the case of ulipristat acetate treatment), pedicled sub-mucosal fibroids, fibroids vascularized by the ovarian artery. Absolute contraindications include malignancy, pregnancy, genito-urinary inflammatory disease, hyperthyroidism and renal failure [21].

The advantages of UAE in uterine fibroids are short hospitalization period, minimal anaesthetic and surgical trauma, no external scars and psychological benefits. The disadvantages include minor complications like puncture-associated hematomas, vomiting, hypotension, fever or secondary expulsion of the fibroid with heavy bleeding. Major complications associated with UAE are surgical management of an inguinal hematoma, persistent fever with antibiotic treatment, septic myomectomy or surgical hysterectomy for infection or massive bleeding [22]. There are reported extremely rare complications, at 5 weeks post UAE, like vesico-uterine fistula or ureter necrosis [22]. Amniotic fluid embolism is another rare complication reported in a case of a pregnant patient after UAE [23].

Several factors can be used as prognostic indicators for patients with uterine fibroids treated with UAE such as insulin-like1 growth factor (IGF1) and vascular endothelium growth factor (VEGF). The serum levels of IGF1 and VEGF are elevated prior to UAE and they decrease after the procedure, slowing increasing in 1-3 months. The growth rate of these levels is closely linked with the clinical characteristics of uterine fibroids [24]. These studies show that the reduction of the uterine fibroid after UAE is more significant in cases of large tumours. Other prognostic indicators include menopausal state, uterine fibroid location and its vascularization. A big and highly vascularized uterine fibroid will quickly reduce after embolization, but the relapse rate in the second year is high, in contrast with small and less vascularized uterine fibroids that decrease slowly, but continuously without important relapse rates [25].

Badawy et al. reported a incidence of reduction in the size of the fibroids after UAE of 20-64% (with improvement of menorrhagia over 82% and of abdominal pain and pressure over 64%) [1]. UAE is recommended in patients with fibroids with bleeding that who do not seek parenting and prefer this type of treatment instead of surgical removal. The incidence of ovarian failure was reported as high as 15% in small lots of patients. There are three hypothesis to explain this side effect. In order patients, the ovaries have lower functional reserve and thus they are more sensitive to an embolic insult. Another hypothesis was based on a reduced perfusion to the ovaries, such that a smaller embolization material can damage a large amount of tissue. Thirdly, a part of patients have reached menopause anyway during the follow-up period after UAE [21].

On long term, the efficiency of UAE in symptomatic improvement is 75% with a reduction of the uterine fibroide at 6 months of 30-60%. The minor complications rate is more elevated in cases of UAE than in cases of hysterectomy by laparotomy, in contrast major complications rate is significant higher in case of a surgical treatment than UAE [26].

In 2011, Ganguli et al. in a study of 168 patients reported 45 cases of pregnancies, respectively 26%, after UAE [27]. However, in 2012, Chang et al. supported UAE in patients who want to preserve fertility [20,28].

Nowadays, UAE is not recommended in female patients that desire to procreate due to a high risk of repeated abortion, caesarean section, postpartum bleeding and invasive placentation [23]. Follicle-stimulating hormone values are more elevated after embolization than after myomectomy, but the conception rate is clearly decreased [26]. The impact of UAE in preserving fertility in females with symptomatic uterine fibroids is not yet been cleared [20].

The follow-up of cases after UAE is the responsibility of the radiologist performing the procedure and consists in proper evaluation after a few weeks up to 3-12 months of the uterine fibroid dimensions [29]. The failure of the procedure in a short term requires careful and thorough documentation, as the absence in reduction of the uterine fibroid can diagnose a sarcoma, in which case surgical removal is necessary [30]. Most of our patients reported good results after UAE with a progressive improvement of the bleeding symptoms. Almost one quarter of patients required surgical procedures.

UAE was also proposed in menopausal women for symptomatic uterine fibroids; even if initially menopause was a contraindication (a regression of the uterine fibroid is expected in menopausal women). However this procedure proved to be efficient, with an improved symptomatology, especially in women under hormonal substitution treatment. A particular aspect is the small dimensions of the uterus in menopause and consequently of the uterine artery dimensions, that increases the technical difficulties and decreases the efficiency [31].

UAE can be used, exceptionally, before surgery in cases of high bleeding risk before myomectomy in patients that decide to preserve their uterus or in patients with contraindications for hysterectomy [32].

In our 2 years' experience, 47 patients with uterine fibroids, aged between 29-48 years old, have benefited from UAE (Figure 3). There was no report of major complications. 7 patients reported minor complications such as post embolization syndrome and minor hematomas at the puncture site. At 12 months evaluation, 28 patients presented a reduction of the uterine fibroid of more than 55% and only 5 patients presented a reduction of fewer than 15%. The almost complete absence of the symptomatology at 3 months post UAE was noted in 43 patients. 11 patients, aged between 29-38 years old, had no obstetrical history, but only 6 patients stated their desire to conceive. A single patient obtained a spontaneous pregnancy that ended at 35 weeks of gestation after giving birth by caesarean section for placenta

previa. 8 patients presented with ovarian insufficiency at 6 months post UAE, with amenorrhea, elevated values of the follicle stimulating hormone (FSH) and menopausal clinics.

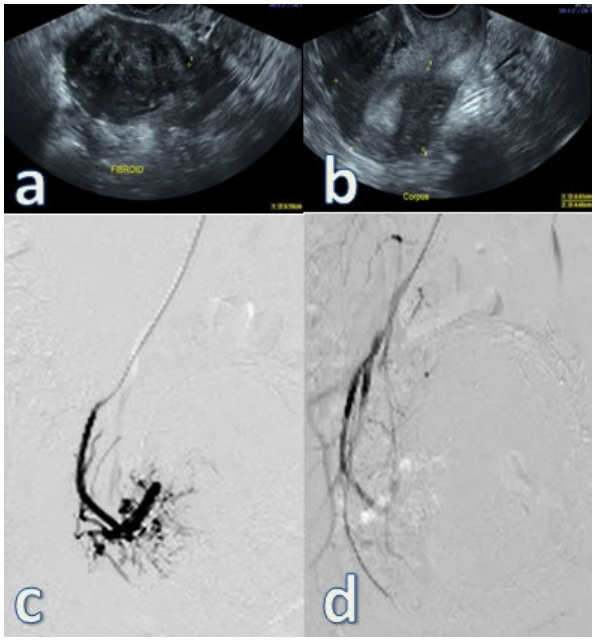

Figure 3: Bilateral UAE in uterine fibroid (a) 2D ultrasound image of the uterine fibroid, (b) 2D ultrasound image of the uterine fibroid 1 month postUAE, (c) Right uterine selective arteriography and (d) Right uterine selective arteriography after embolization.

Conclusion

Due to proven efficiency, UAE must be take into consideration in the management and prevention of gynaecological massive bleeding. Technically, the success of the procedure assumes careful selection of the cases in the hospital units that benefit from highly qualified medical employees and adequate technology. The results of using this procedure, in our clinic, are similar to the rates of success and failure reported in the literature.

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