

Interventional radiology in ectopic pregnancy management

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ABSTRACT

Ectopic pregnancies especially cervical, tubal and cesarean scar pregnancies, represent obstetrical emergencies that endanger the fertility and, more important, the life of women. Interventional radiology has gained popularity over the last years in the treatment of ectopic pregnancy as combined treatment with methotrexate administration in cases of tubal pregnancy, first line treatment in cases of cesarean scar pregnancies or, more recently, as single line management in cases of cervical pregnancies with astonishing results and numerous benefits. Its primary advantage is represented by fertility preservation among young fertile women simultaneously with the avoidance of an invasive surgical method with the subsequent risks and possible complications. We present a narrative review regarding success rates of uterine artery embolization in the treatment of ectopic pregnancies.

Keywords: uterine artery embolization, methotrexate, cervical pregnancy, tubal pregnancy, cesarean scar pregnancy, conservative treatment

INTRODUCTION

Ectopic pregnancies represent extrauterine pregnancies, the vast majority are located in the fallopian tube; other locations implied are the cervix, the uterine horn, the hysterotomy or cesarean scar, ovary or the abdominal cavity (1). Regarding the incidence of ectopic pregnancy, there has been reported a range between 6 and 16% of patients who present to an emergency department with first trimester vaginal bleeding and/or pelvic pain (2). Ectopic pregnancies represent life-threatening pathologies. Due to modern methods of early diagnosis of pregnancy using transvaginal ultrasound, the maternal mortality rate has encountered a decreasing trend from 1.15 per 100,000 live births between

1980 and 1984 to 0.50 deaths per 100,000 between 2003 and 2007 (3). In contrast, cesarean scar pregnancies have an increasing tendency as the number of cesarean deliveries performed every year grows worldwide, the incidence ranging from 1/2226 to 1/1899 of pregnancies (4,5). The diagnosis of ectopic pregnancies is realized in women with amenorrhea and an atypical increasing of β -hCG serum values trends and using transvaginal ultrasound evaluation, which reveals an empty uterine cavity. The clinical picture of ectopic pregnancy includes women who present to the emergency room most frequently for vaginal bleeding or pelvic pain and sometimes lipothymia, signs of hypovolemic shock such as tachycardia, hypotension (6).

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Actual treatment of ectopic pregnancies consists in medical or radical treatment (surgical), the latter being the last treatment line in some cases and influencing primarily the woman's fertility or reproductive capacity. Interventional radiology, in well-selected cases with elevated β -hCG serum levels used as a complementary minimally invasive treatment, represents a useful tool in managing cases of ectopic pregnancies, either tubal (7), cervical (8) or cesarean scar pregnancy, having multiple advantages such as preserving the patient's fertility, reducing the surgical stress of the patient, reducing the bleeding in the management of cervical and cesarean scar pregnancies or even being cost-effective in relation to hysterectomy or salpingectomy.

CONVENTIONAL TREATMENT

There are two medical attitudes regarding the tubal pregnancy treatment: medical and surgical. The medical treatment involves Methotrexate (MTX) administration to patients who have a serum β -hCG value $\leq 5,000$ mIU/ml, are hemodynamically stable, the tubal pregnancy does not present fetal cardiac activity and consent to medical treatment (9). Contraindications for MTX administrations make the patient a candidate for surgery (the patient is hemodynamically instable, presents an intrauterine pregnancy, there are signs and symptoms of tubal pregnancy rupture or associated pathologies that are contraindications for MTX administration) as well as the patient's desire for a surgery involving a simultaneous surgical procedure (10).

Concerning cervical pregnancies, the treatment varies from systemic MTX, dilatation and curettage, MTX or potassium chloride injection in the gestational sac, uterine artery embolization to hysterectomy. Being a rare pathology, there are not clear criteria for choosing the medical or surgical treatment as shown in the case of tubal pregnancy (11).

Cesarean scar pregnancy, pathology with a rising incidence nowadays, presents its own particularities in terms of treatment. The Society for Maternal-Fetal Medicine recommends surgery treatment respectively resection or medical treatment consisting of MTX administration in association with surgical treatment (12,13). Expectant management, curettage or MTX administration as single method of treatment are not recommended due to the elevated risk of maternal morbidity and mortality (perforation, hemorrhage, development of arteriovenous malformation etc.) (14,15). The different situations of this pathology require different approaches molded on each case. Other proposed treatments include laparoscopic management (16) robotically assisted or not (17), uterine arteries ligation (18) or

transvaginal hysterotomy (19). There are protocols proposing the use of ultrasound guidance in vacuum aspiration due to the diminished amount of blood loss (20) whereas others propose curettage after a multidose regimen of MTX (21).

THE ROLE OF INTERVENTIONAL RADIOLOGY

Interventional radiology is widely used as an alternative, respectively it represents a conservative management in the gynecological sphere: uterine artery embolization (UAE) for uterine leiomyomas (22), uterine adenomyosis (23), arteriovenous malformations (24) and pelvic congestion syndrome (25). In the last years, interventional radiology has been indispensable in the management of obstetric hemorrhage: postpartum hemorrhage, abnormal placentation, abortion, as well as the therapeutic management of cervical ectopic pregnancy (CP) (26), cesarean scar pregnancy (CSP) (27) and fallopian tube ectopic pregnancy (TP) (28). We have a vast experience in the collaboration with Interventional Radiology Department of Bucharest University Emergency Hospital regarding CP (Figures 1 and 2), CSP (Figures 3-6) and TP (Figures 7 and 8) treatment. More than this, we have submitted our cases to Cesarean Scar Pregnancy Register and we published recently a proposed minimal invasive 100% success rate therapeutical protocol for first trimester diagnosed CSP (29).

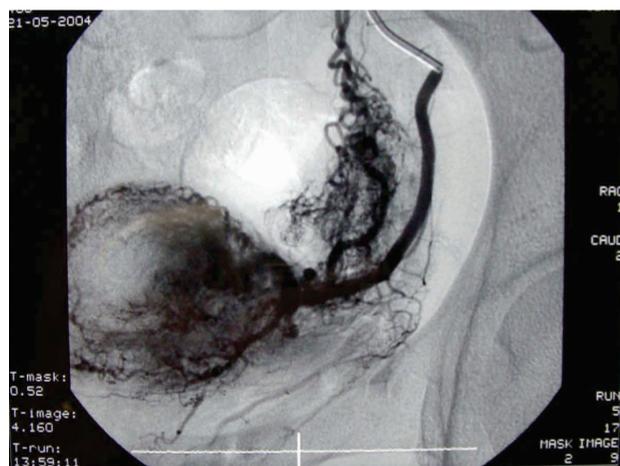


FIGURE 1. Interventional radiology image of a cervical pregnancy before UAE

UAE can be used as single method of treatment or in association with other procedures. In the vast majority of cases uterine artery embolization is used as a complementary method in the management of ectopic pregnancies to increase efficiency of the entire treatment, minimize blood loss and reduce the requirement of last line treatment- irreversible surgery, either salpingectomy or hysterectomy (26).



FIGURE 2. Interventional radiology image of a cervical pregnancy after UAE (occlusion of the uterine artery)

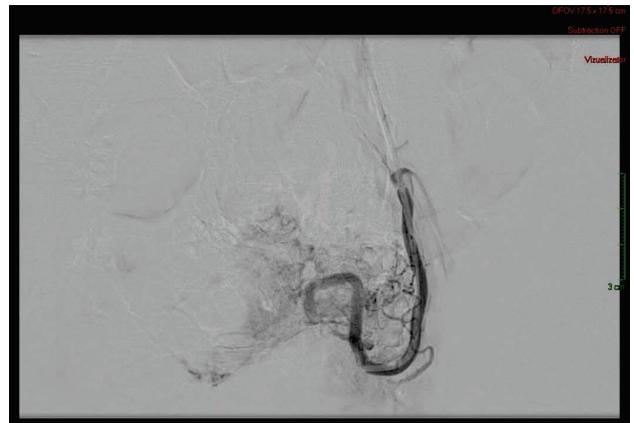


FIGURE 5. Interventional radiology image on the left side of a cesarean scar pregnancy after UAE

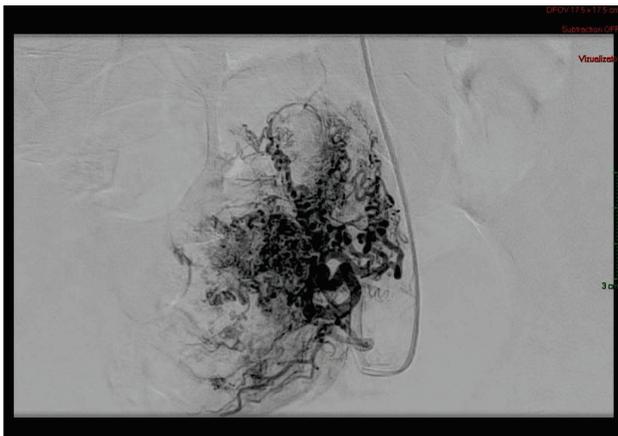


FIGURE 3. Interventional radiology image on the left side of a cesarean scar pregnancy before UAE

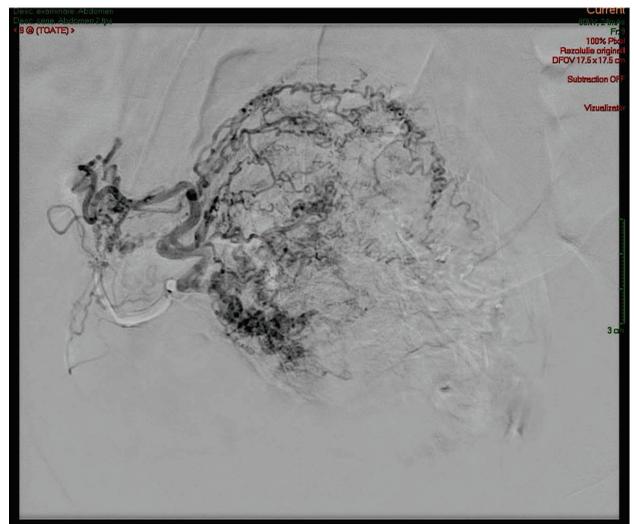


FIGURE 6. Interventional radiology image on the right side of a cesarean scar pregnancy during UAE procedure

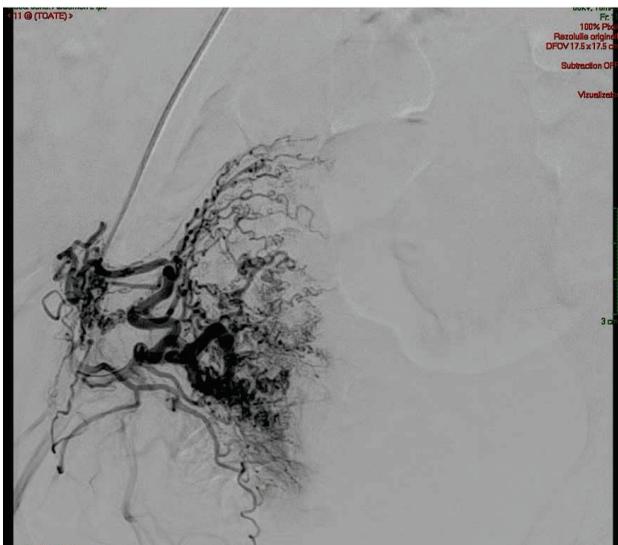


FIGURE 4. Interventional radiology image on the right side of a cesarean scar pregnancy before UAE

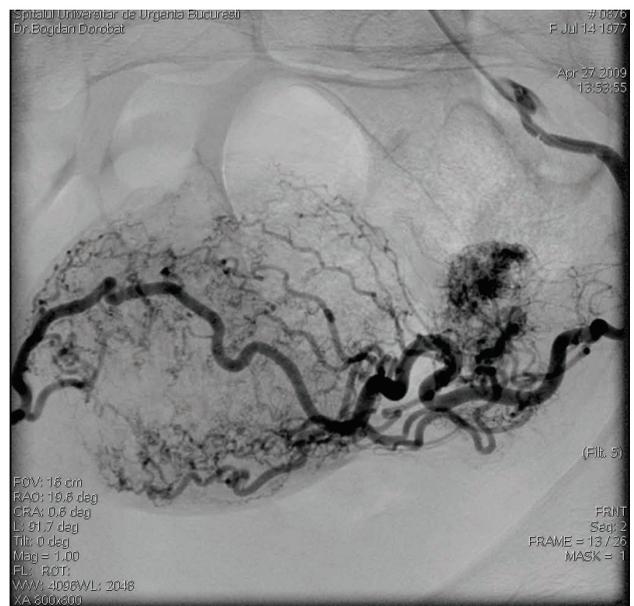


FIGURE 7. Interventional radiology image of a tubal pregnancy before UAE



FIGURE 8. Interventional radiology image of a tubal pregnancy after UAE (occlusion of the uterine artery)

METHODS

In this paper we searched the literature using PubMed and we used the terms ‘interventional radiology’ and ‘ectopic pregnancy’ to identify the conservative treatment methods for tubal, cervical and cesarean scar pregnancy. The search included articles from 2010 until November 2021. We screened the abstracts in order to select relevant studies. We included case series, retrospective studies, prospective cohort studies, randomized control study and case reports.

RESULTS

The initial search returned a total of 56 articles. We screening the articles, removed the duplicates and selected the relevant articles to our paper. Therefore, 9 articles related to the use of interventional radiology in the treatment of ectopic pregnancies were included in our review. Our review includes a total of 415 patients treated with UAE: 155 patients with CSP, 62 with CP and 198 with TP (Figures 3 and 4). The treatment success rate was between 76.9% (30) and 100% (27,31-34). The main results are presented in Table 1.

UAE in association with MTX

256 patients were treated with MTX and UAE (30,35-37) with success rates between 76.9% and 98.76%. This therapeutic management was successful in 238 patients. There were 18 patients that required additional therapies: 4 patients needed another UAE (29, 36), 6 patients needed subsequent MTX treatment (36) and 8 patients underwent surgery due to failure of treatment (36).

UAE in association with MTX and suction and curettage

4 patients (1 case of CSP and 3 cases of CP) were treated successfully using MTX administration, followed by UAE, suction and curettage (27,33). The patient with CSP was administered iv MTX with a slight decrease in the β -hCG, followed by UAE and a curettage was performed under simultaneous laparoscopic vision. The intra-operative blood loss was estimated at 50mL (27). The 3 cases of CP received a single dose of MTX: 1 patient was administered MTX intramuscular, the second patient was administered intra-arterial MTX prior to the finalization of the UAE and the third patient was given a parametrial shot of MTX simultaneously to the UAE. The curettage was performed in the first 72 hours after UAE to have a maximum benefit of the UAE (33).

UAE followed by suction and curettage

From our total of 415 patients, 133 were treated using UAE followed by curettage (31,33,34), among which Wu et al. (33) included 25 patients treated with UAE followed by hysteroscopic curettage. The success rates between 98% and 100%. One patient with CSP needed repeated suction and curettage (31); Ou et al. (31) compared the success rate of suction and curettage in cases of CSP in two groups: the first in which suction and curettage was used as single treatment and the second in which UAE was performed prior to suction and curettage. There were 4 cases of CSP in the first group in which the treatment failed: 2 patients received subsequently systematic MTX and 2 patients repeated the curettage. In the second group one patient needed a reintervention and a second curettage was performed.

UAE used as single treatment

A study by Niola et al. (32) published in 2014 included 41 cases of postpartum hemorrhage and 22 patients diagnosed with CP. The patients with CP were treated using UAE with a success rate of 100%, after which the patients were monitored using clinical and ultrasound examination at 1 month, 6 months and at 12 months 10 patients were pregnant and there were no issues during pregnancy, with an ulterior uneventful delivery.

DISCUSSION

Our research included 415 patients with ectopic pregnancy treated with UAE as single or combined treatment. From these 415 patients, in 8 cases (1.92%) treatment failed and the patients underwent radical treatment respectively surgery. In this group of 8 patients, 2 patients received treatment with MTX and UAE (35), 4 received treatment with local infusion of 5-fluorouracil, an antimetabolism

TABLE 1. Summary of the articles included in our review and main results

Article	Study type	No patients			Patients' inclusion criteria	Successful treatment rate	Reintervention rate
		CSP	CP	TP			
Kwon et al. 2017 (30)	Retrospective study	5	6	1	– high serum β -hCG level – vaginal bleeding after systemic MTX therapy	76.9%	23.1% (2 CP+1CSP) needed another UAE
Ou et al. 2020 (31)	Prospective cohort study	65	–	–	– diagnosis of CSP – unwillingness to undergo MTX therapy, or indications against it – gestational sac <5 cm – myometrial thickness <1 cm	98% (combined with suction and curettage)	2% (1 case) needed repeated suction and curettage
Niola et al. 2014 (32)	Retrospective study	–	22	–	– patients with ectopic pregnancy – follow-up of minimum 12 months	100%	–
Radajurai et al. 2021 (27)	Case report	1	–	–	– unsuccessful MTX therapy	100%	–
Hu et al. 2016 (33)	Retrospective study	–	19	–	– CP diagnosed by transvaginal color Doppler sonography – presence of villi identified in the specimens from endocervical canal curettage	100%	–
Wu et al. 2021 (34)	Retrospective study	52	–	–	– history of amenorrhea – history of C section – high β -hCG serum level – diagnosis of CSP using ultrasound examination	100%	–
Tan et al. 2014 (35)	Prospective study	–	–	162	– patients hemodynamically stable with TP	98.76%	1.23% (2 patients) needed surgery
Gao et al. 2018 (36)	Randomized control study	25	10	35	– diagnosis of EP – high serum levels of β -hCG – refused surgical resection or desire to preserve the uterus – signed the informed consent	88%	12% (6 patients needed subsequent MTX treatment and 6 needed surgery)
Elmokadem et al. 2019 (37)	Retrospective study	7	5	–	– ultrasound criteria for CSP and CP	90.9%	9.1% (1 patient needed a second UAE)

drug, and MTX followed by UAE (36) and 2 patients who received treatment with local infusion of MTX and consecutive UAE (36).

11 patients of the 415 patients included in our paper (2.65%) needed a second approach: 6 patients needed MTX administration (36), 4 patients repeated the UAE (29,36) and 1 patient required a repeated suction and curettage (31).

Uterine artery embolization, used as single or combined treatment, was successful in 396 patients from the 415 selected for our study, result a 95.42% success rate, so we can conclude that 95.42% of women receiving this treatment had their fertility saved and did not undergo surgery, resulting in the best possible outcome.

In Romania, there are medical centers which present an interventional radiology department that make possible to form multidisciplinary teams (gynecologist, interventional radiologist, anesthesiologist) with the aim to minimally invasive treat pa-

tients with ectopic pregnancies with significant results in reducing radical treatment among women of fertile age who desire to preserve their fertility or refuse surgery or have associated pathologies that might put their life at risk during surgery.

CONCLUSIONS

Uterine artery embolization has proven its utility in managing cases of ectopic pregnancies as single line treatment or combined with methotrexate administered either local, intramuscular, or intra arterial during uterine/ovarian artery embolization, associated with suction and/or curettage or with hysteroscopic curettage, thus avoiding a major surgical intervention that compromises the female fertility (hysterectomy or salpingectomy) with additional possible surgical complications, reducing the costs of medical healthcare and the surgical stress to which the patient is subjected.

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REFERENCES

- Bouyer J, Coste J, Fernandez H, Pouly JL, Job-Spira N. Sites of ectopic pregnancy: a 10 year population-based study of 1800 cases. *Hum Reprod.* 2002 Dec;17(12):3224-30.
- Murray H, Baakdah H, Bardell T, Tulandi T. Diagnosis and treatment of ectopic pregnancy. *CMAJ.* 2005 Oct 11;173(8):905-12.
- Stulberg DB, Cain L, Dahlquist IH, Lauderdale DS. Ectopic pregnancy morbidity and mortality in low-income women, 2004-2008. *Hum Reprod.* 2016 Mar;31(3):666-71.
- Osborn DA, Williams TR, Craig BM. Cesarean scar pregnancy: sonographic and magnetic resonance imaging findings, complications, and treatment. *J Ultrasound Med.* 2012;31(9):1449-56.
- Wang S, Li Y, Ma X. Lower uterine segment thickness in assessing whether cesarean scar pregnancy patients could be treated with suction curettage. *J Matern Fetal Neonatal Med.* 2020 Oct;33(19):3332-3337.
- Alkatout I, Honemeyer U, Strauss A, Tinelli A, Malvasi A, Jonat W, Mettler L, Schollmeyer T. Clinical diagnosis and treatment of ectopic pregnancy. *Obstet Gynecol Surv.* 2013 Aug;68(8):571-81.
- Committee on Practice Bulletins—Gynecology. ACOG Practice Bulletin No. 191: Tubal Ectopic Pregnancy. *Obstet Gynecol.* 2018 Feb;131(2):e65-e77.
- Hosni MM, Herath RP, Mumtaz R. Diagnostic and therapeutic dilemmas of cervical ectopic pregnancy. *Obstet Gynecol Surv.* 2014 May;69(5):261-76.
- Hajenius PJ, Mol F, Mol BW, Bossuyt PM, Ankum WM, van der Veen F. Interventions for tubal ectopic pregnancy. *Cochrane Database Syst Rev.* 2007 Jan 24;2007(1):CD000324.
- Kelly H, Harvey D, Moll S. A cautionary tale: fatal outcome of methotrexate therapy given for management of ectopic pregnancy. *Obstet Gynecol.* 2006 Feb;107(2 Pt 2):439-41.
- Mesogitis S, Pilalis A, Daskalakis G, Papanтониou N, Antsaklis A. Management of early viable cervical pregnancy. *BJOG.* 2005 Apr;112(4):409-11.
- Society for Maternal-Fetal Medicine (SMFM). Electronic address: pubs@smfm.org, Miller R, Timor-Tritsch IE, Gyamfi-Bannerman C. Society for Maternal-Fetal Medicine (SMFM) Consult Series #49: Cesarean scar pregnancy. *Am J Obstet Gynecol.* 2020 May;222(5):B2-B14.
- De Braud LV, Knez J, Mavrelos D, Thanatsis N, Jauniaux E, Jurkovic D. Risk prediction of major haemorrhage with surgical treatment of live cesarean scar pregnancies. *Eur J Obstet Gynecol Reprod Biol.* 2021 Sep;264:224-231.
- Tsakiridis I, Chatzikalogiannis I, Mamopoulos A, Dagklis T, Tsakmakidis G, Athanasiadis A, Kalogiannidis I. Cesarean scar pregnancy: A case report with surgical management after initially effective conservative treatment. *Int J Surg Case Rep.* 2019;65:238-241.
- Rivera-Rodríguez A, Jiménez-Zarazúa O, Castaldi-Bermúdez L, Vélez-Ramírez L, Coronel-Ciocca OC, Romero-Frances M, Becerra-Baeza A, Mondragón J. A case report of a misdiagnosed cesarean scar pregnancy in a hemodynamically compromised patient. *Human Pathology.* 2019;18:200344.
- Kathopoulos N, Chatzipapas I, Samartzis K, Theodora M, Lardou I, Protopapas A. Laparoscopic management of cesarean scar pregnancy: Report of two cases with video-presentation of different operative techniques and literature review. *J Gynecol Obstet Hum Reprod.* 2021 Oct;50(8):102066.
- Wang HF, Chen HH, Ting WH, Lu HF, Lin HH, Hsiao SM. Robotic or laparoscopic treatment of cesarean scar defects or cesarean scar pregnancies with a uterine sound guidance. *Taiwan J Obstet Gynecol.* 2021 Sep;60(5):821-826.
- Legris ML, Gabriele V, Host A, Akladios C, Garbin O, Lecointre L. Cesarean scar pregnancy: Two case report and therapeutic management algorithm. *J Gynecol Obstet Hum Reprod.* 2021 Apr;50(4):102056.
- OuYang Z, Xu Y, Li H, Zhong B, Zhang Q. Transvaginal hysterotomy: A novel approach for the treatment of cesarean scar pregnancy. *Taiwan J Obstet Gynecol.* 2019 Jul;58(4):460-464.
- Reid JA, Bayer LL, Edelman AB, Colwill AC. Controversies in family planning: Management of cesarean-scar ectopic pregnancy. *Contraception.* 2021 Mar;103(3):208-212.
- Naeh A, Shrim A, Shalom-Paz E, Amir M, Hallak M, Bruchim I. Cesarean scar pregnancy managed with local and systemic methotrexate: A single center case series. *Eur J Obstet Gynecol Reprod Biol.* 2019 Jul;238:138-142.
- Silberzweig JE, Powell DK, Matsumoto AH, Spies JB. Management of Uterine Fibroids: A Focus on Uterine-sparing Interventional Techniques. *Radiology.* 2016 Sep;280(3):675-92.
- Nijenhuis RJ, Smeets AJ, Morpurgo M, Boekkooi PF, Reuwer PJ, Smink M, van Rooij WJ, Lohle PN. Uterine artery embolisation for symptomatic adenomyosis with polyzene F-coated hydrogel microspheres: three-year clinical follow-up using UFS-QoL questionnaire. *Cardiovasc Intervent Radiol.* 2015 Feb;38(1):65-71.
- Lim AK, Agarwal R, Seckl MJ, Newlands ES, Barrett NK, Mitchell AW. Embolization of bleeding residual uterine vascular malformations in patients with treated gestational trophoblastic tumors. *Radiology.* 2002 Mar;222(3):640-4.
- d'Archangeau O, Maes M, De Schepper AM. The pelvic congestion syndrome: role of the "nutcracker phenomenon" and results of endovascular treatment. *JBR-BTR.* 2004 Jan-Feb;87(1):1-8.
- Gonsalves M, Belli A. The role of interventional radiology in obstetric hemorrhage. *Cardiovasc Intervent Radiol.* 2010 Oct;33(5):887-95.
- Rajadurai SM, Wong A, Brooks DM, Vance C. Combined interventional radiology and surgical management of a complex cesarean scar ectopic pregnancy. *J Med Imaging Radiat Oncol.* 2021 Oct; 65(6):728-730.
- Gong W, Li X, Ren H, Han C, Li Y, Wu Z. Superselective uterine arterial embolization combined with transcatheter intra-arterial methotrexate infusion in 40 cases with fallopian tube ectopic pregnancy. *Clin Exp Obstet Gynecol.* 2013;40(2):222-6.
- Bohiltea R, Ducu I, Mihai B, Dorobat B, Vlădăreanu EM, et al. Uterine artery embolization combined with subsequent suction evacuation as low-risk treatment for cesarean scar pregnancy. *Diagnostics.* 2021;11:2350.
- Kwon JH, Kim GM, Han K, Kim MD, Won JY, Lee DY. Safety and Efficacy of Uterine Artery Embolization in Ectopic Pregnancies Refractory to Systemic Methotrexate Treatment: A Single-Center Study. *Cardiovasc Intervent Radiol.* 2017 Sep;40(9):1351-1357.
- Ou J, Peng P, Li C, Teng L, Liu X. Assessment of the necessity of uterine artery embolization during suction and curettage for caesarean scar pregnancy: a prospective cohort study. *BMC Pregnancy Childbirth.* 2020 Jun 29;20(1):378.
- Niola R, Cavaliere C, Marcello L, Maglione F, de Ritis R, Di Pietto F, et al. Role of interventional radiology in treating obstetric haemorrhages. *Radiol Med.* 2014 Aug;119(8):607-15.
- Hu J, Tao X, Yin L, Shi Y. Successful conservative treatment of cervical pregnancy with uterine artery embolization followed by curettage: a report of 19 cases. *BJOG.* 2016 Sep;123 Suppl 3:97-102.
- Wu Y, Sun LF, Si YN, Luan XL, Gao YM. Clinical efficacy analysis of different therapeutic methods in patients with cesarean scar pregnancy. *Taiwan J Obstet Gynecol.* 2021 May;60(3):498-502.
- Tan W, Zhang J, Liu Y, Yang G, Qing T, Lin J, Wei H. Treatment of tubal pregnancy using comprehensive interventional methods. *Clin Exp Obstet Gynecol.* 2014;41(6):641-6.
- Gao J, Li X, Chen J, Gong W, Yue K, Wu Z. Uterine artery embolization combined with local infusion of methotrexate and 5- fluorouracil in treating ectopic pregnancy: A CONSORT-compliant article. *Medicine (Baltimore).* 2018 Feb;97(5):e9722.
- Elmokadem AH, Abdel-Wahab RM, El-Zayadi AA, Elrakhawy MM. Uterine Artery Embolization and Methotrexate Infusion as Sole Management for Cesarean Scar and Cervical Ectopic Pregnancies: A Single-Center Experience and Literature Review. *Can Assoc Radiol J.* 2019 Aug;70(3):307-316.