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**Review Article** 

## Minimally Invasive Management of Uterine Fibroids - Role of Transvaginal Radiofrequency Ablation

## Karin Louise Andersson<sup>1\*</sup>, Elisa Wu<sup>2</sup>, Claudia Consoli<sup>1</sup>, Valeria Dubini<sup>1</sup>, Felice Petraglia<sup>2</sup> and Alberto Mattei<sup>1</sup>

<sup>1</sup>Department of Women and Child Health, Azienda Sanitaria Toscana Centro, Florence, Italy

<sup>2</sup>Department of Experimental, Clinical and Biomedical Sciences, Careggi University Hospital, University of Florence, Florence, Italy

## Abstract

Minimally invasive approaches in management of common gynecological pathologies such as uterine fibroids are of outmost importance to offer fertility preservation and cost-effective solutions. Transvaginal radiofrequency ablation in day surgery setting offers an efficient volume reduction solution with improvement of fibroid related symptoms in patients undergoing accurate pre-operative selection. Radiofrequency ablation represents a useful tool along with conventional surgical and non-surgical techniques in tailoring fibroid treatments.

**Keywords:** Minimally invasive surgery; Transvaginal radiofrequency ablation; Uterine fibroids

## Introduction

Recent years have brought a drastic change in approaching benign gynecological disease in general putting emphasis of the symptomatic profile and reproductive needs rather than radicality in lesion removal. Women postponing their reproductive programs within the same time frame that coincides with peak incidence peak of fibroids represents a complex challenge for ob/gyn of today. Management of uterine fibroids in women today needs to offer an extensive evaluation of numerous aspects that include previous obstetric history, future

\*Corresponding author: Karin Louise Andersson, Department of Women and Child Health, Azienda Sanitaria Toscana Centro, Florence, Italy, Tel: +39 3291631167; E-mail: karinlouise.andersson@uslcentro.toscana.it

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reproductive desire and overall symptomatology (bleeding pattern and anemia, compression symptoms and pain related symptoms).

Radiofrequency Thermal Ablation (RFA) is an outpatient, minimally invasive technique for conservative treatment of symptomatic fibroids representing a promising alternative to standard surgical myomectomy. Its application in gynecology is refining regarding procedure protocol and patient selection. Data on efficacy is promising while reproducibility aspects and associated complications are matter of lack of standardization in current literature [1]. Radiofrequency thermal ablation generates thermal effects (60°C-80°C) in the lesion tissue causing tissue cells apoptosis by thermal coagulation, formation of vascular thrombosis from biological thermal effect in the blood vessels supplying the fibroid, causing ischemic necrosis and atrophy along with inactivation of the estrogen and progesterone receptors within the fibroid preventing hormonal-dependent tumor proliferation [2].

Different technique accesses are available, including percutaneous, laparoscopic, hysteroscopic and transcervical/transvaginal approach [3]. All the different accesses can be performed as a single surgical step or combined with each other when the position of the fibroids intended for treatment allows the use of the same need-electrode through different routes [4]. The overall advantages of myolysis in respect to surgical resection include reduced morbidity (operating time, blood loss, and length of hospital stay), preservation of the endometrial cavity, real-time imaging guidance, and the feasibility of outpatient procedure [1].

## **Transvaginal Radiofrequency Ablation (TRFA)**

Transvaginal Radiofrequency Ablation (TRFA) is the most recent technique for radiofrequency myolysis using the transvaginal approach. While several studies have demonstrated the safety and efficacy of myolysis through laparoscopic route, there is yet less experience using transvaginal approach [3], although it is considered a safe and fast procedure with a short recovery period. It is effective on dimensional reduction of fibroid volume and correction of metrorrhagia [5-8]. So far, five prospective studies have been published describing application of TRFA in symptomatic uterine fibroids. Mean initial fibroid volume ranged from 18.3 cm<sup>3</sup> (SD 9.5) to 304.6 (SD 229.1), while post-operative mean volume ranged from 11.34 (SD 8.94) to 79.1 (SD 81.7). Fibroid reduction rate was calculated to range from 60% to 83% in 12 months period follow up, except for one study in which follow up was 18 months [3].

In a systematic review published by Arnreiter et al., in 2021, 10 studies using transcervical approach with Sonata System showed a reduction in total fibroid volume of 63.2% and a reduction in perfused fibroid volume of 64.5% at 12 months follow up, accompanied by improvements in symptoms and quality of life. Reintervention rate varied from 0.7% to 11.8% at 12 months. Forty-seven percent of the patients experienced mild adverse events such as dysmenorrhea, abnormal uterine bleeding, pelvic pain, urinary tract infections, fibroid expulsion/sloughing, nausea/vomiting, fluike symptoms, and other

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nongynecological symptoms such as constipation. Only four adverse events requiring inpatient treatment, including one case of deep vein thrombosis [9]. TRFA is preferable to other minimally invasive techniques such as cryotherapy or HIFU, because of its reliability, lower cost and shorter operating time [10]. It is also preferable to laparoscopic myomectomy due to reduced median blood loss (20 mL versus 35 mL), and the ability to treat a higher percentage of fibroids. Rey et al., conducted a prospective observational study and described a sample of population of women (n=205) with symptomatic FIGO type 2-3 uterine submucosal or intramural cavity-distorting fibroids, advising against utilization of TRFA fibroids of a volume larger than 500 cm<sup>3</sup>, considering the possibility of incomplete myolysis. A volume of < = 39 cm<sup>3</sup> was indicated optimal with an expected volume reduction of 80% and disappearance in half of the cases [3].

The SAGE Registry is an ongoing large study collecting data on transcervical procedures and will generate up to 2500 patient-years of outcome data along 5 years follow up. Preliminary results from the first 160 treated patients suggest broad applicability and favorable safety profile [11].

#### Pre-operative work up considerations

Accurate node description and ultrasound mapping is of outmost importance for patient selection to avoid possible complications, treatment planning and follow up. Volume calculation applying the ellipsoid formula V= $\pi/6$  x lenght x width x height as well baseline hemoglobin is useful to estimate symptoms improvement and treatment efficacy. Myolysis does not allow histological confirmation of leiomyoma compared to other traditional techniques and the role of presurgical biopsy has been addressed. As limitations in terms of sensitivity and specificity to exclude focal malignant alterations are noted pre-surgical fibroid biopsy should not be considered a standard management able to exclude enrolment of fibroids of dubious nature [12,13]. Treatment with RFA can also create challenges in histological distinction of leiomyosarcoma and benign leiomyoma due to presence of coagulative necrosis and increased mitotic index due to tissue regeneration after thermal treatment [14]. The Authors of this paper stress the fact that the pre operative work up in terms of identifying typical nodes eligible for treatment should be rigorous and restricted in order to not promote ablative treatment in cases of controversy imaging criteria in typical fibroid diagnosis as well as patient's clinical history indicating doubtful disease origin. In literature a case of misdiagnosis of leiomyosarcoma after thermal ablation has been reported [15] why this issue represents a far-off critical aspect in regards to patient selection and inclusion.

#### Technique efficacy outcome

Radiofrequency ablation has been shown to offer targeted treatment of fibroids, with lesion size reduction, improvement of symptoms and quality of life while maintaining a safe profile with few complications and low reintervention rates. Volume and diameter of the fibroids were significantly reduced by -49.00% and -24.35%, -50.52% and 31,87%, -90.20% and - 55,70 % respectively at 12-, 24- and 36-months post-intervention (p < 0.001). After laparoscopic radiofrequency ablation, overall uterine volume reduction was 69.17 cm<sup>3</sup> (95% CI 35.87-102.46) at 12 months [4,16]. Compared to UAE and magnetic resonance - guided focus ultrasound treatment (HiFU), RFA was shown to have significantly greater reduction in mean fibroid volume [17]. • Page 2 of 4 •

Reduction in volume is paired with symptoms reduction. Significant improvement in symptoms for all bleeding-related variables (total days of bleeding, days of heavy bleeding, subjective reduction in bleeding) at 2, 6 and 12 months of follow-up was demonstrated in transvaginal RFA, which also achieved a mean relative reduction in fibroid volume of more from 72% to more than 80% at 12 months' follow-up, depending on initial size of the lesions [18]. Studies showed similar improvement in symptoms after myomectomy and RFA. Based on validated questionnaires, quality of life improved significantly until 36 months after laparoscopic radiofrequency ablation therapy with a maximum improvement at 12 months of 41.64 [95% CI 38.94-44.34] in Health-Related Quality of Life questionnaire score [HRQL], a reduction of 39.37 [95% CI 34.70-44.04] in transformed Symptom Severity Score [tSSS] and by a percentage change of UFS-QOL Symptom Severity scores to -71.80% after 3 years with vaginal FRA [6,14,17]. TRFA is normally performed in outpatient setting and is associated with mild-moderate pain and limited use of analgesics (mean of 3.8 days after discharge) [3,18].

In the first comparative study evaluating myomectomy and RF with the Sonata system (CHOICES study) by Brooks et al, all stratified results for procedure costs, resource utilization and perioperative patient outcomes favors TFA over myomectomy, including operating room time, length of stay, sub-procedure costs regarding anesthesia, laboratory, pathology, pharmacy and facility procedure-related costs [13]. Also Chudnoff et al., reported in their prospective trial a significant reduction in leiomyoma symptoms with no device-related adverse events and a low surgical reintervention rate through 12 month using same approach [12]. Overall need for reintervention rate due to persistent metrorrhagia ranged from 4.39% to 16.3%, including hysteroscopic removal of free intracavitary fibroids (1.46%), hysterectomy, hysteroscopic myomectomy and endometrial ablation [4]. Low reintervention rate suggests that single intervention could be sustainable [16] and rates are comparable with ranges seen with myomectomy and UAE [19].

### Prognostic factors for treatment success

Current data suggest that RFA is a promising minimally invasive option for conservative fibroid management, however not all patients are ideal candidates for the approach. Accurate pre-operative evaluation is fundamental for reaching optimal myolysis and standardization of patient selection criteria still have to be refined as well as recommendations of women with future pregnancy wish, although, these patients may benefit the most from minimally invasive treatments [19]. For instance, pedunculated myomas (International Federation of Gynecology and Obstetrics FIGO type 7) are excluded along with giant fibroids [19].

In a case series of 59 patients treated with transvaginal RFA, in patients older than 40 years a faster and greater fibroid volume reduction was observed, compared to younger women (77.6% versus 59.7%). This could hypothetically be related to age-related differences in histological composition of the fibroid and the different hormonal milieu. In addition, larger fibroids showed a larger final volume: every 1-mL increase in initial fibroid volume was associated with a 0.12-mL increase in final volume and fibroids larger than 36.5 mL before treatment showed a mean reduction in volume at 12 months' follow up of 65% vs 85.6% of smaller fibroids [18].

However, RFA, regardless of the access route or the fibroid type or position, turned out to be effective in the long term when the major Citation: Andersson KL, Wu E, Consoli C, Dubini V, Petraglia F, et al. (2024) Minimally Invasive Management of Uterine Fibroids - Role of Transvaginal Radiofrequency Ablation. J Reprod Med Gynecol Obstet 9: 163.

fibroid to be ablated is no larger than 5 cm in diameter: the mean diameter of the dominant fibroid in the patients who required reoperation resulted greater than that of the successes [4]. In addition, the degree of fibroid vascularization could condition the myolysis result, while final volume didn't' significantly depended on type of fibroid (intramural or submucosal) [4].

### **Fertility outcome**

Current data on pregnancy outcome after RFA treatment are scant since RFA device approved by FDA are not yet endorsed for women with fertility desire and original clinical trials excluded this category from their study population. However, more and more case reports and small size prospective studies are showing promising results.

Polin et al., conducted a systematic review of the literature to summarize the available data on pregnancy outcome after laparoscopic or transcervical RFA of uterine fibroids. The literature selected consisted of ten publications, including two clinical trials for a total of 923 patients (550 patients underwent laparoscopic RFA and the other 364 transcervical RFA). Fifty pregnancies occurred, of which 40 after laparoscopic RFA and 10 after transcervical RFA. Among 50 pregnancies, 88% were full-term pregnancies (n=44), among which there are no reported cases of uterine rupture, uterine window, invasive placentation (i.e. placenta accrete), placenta abruption or fetal growth restriction. To note, there was one case of uncomplicated placenta previa and one case of delayed postpartum hemorrhage which required blood transfusion due to vaginal expulsion of a large degenerated fibroid. The fibroid was disrupted at the time of uterine closure during caesarian section [19].

The mean number of fibroids treated was between 1 and 3 and the size varied from 0.9 cm up to 12.5 cm. Average age at ablation was calculated at 37 years. Great variability was found in the interval time between RFA and pregnancy, which ranged from 3-5 to 33 months, with a mean value of 16 months [19]. Spontaneous abortion occurred in 12% of the cases (n =6); this rate placed in the lower range of the risk considered for the general obstetric population (11 to 22%) [20]. Several transcervical procedures, including hysteroscopic myomectomy, dilation and curettage, endometrial ablation can cause intrauterine adhesions formation that could cause detrimental effect on menstrual cycle, successful conception rate and spontaneous abortion; indeed, acquired uterine malformations, including adhesions or Asherman's syndrome, have been found prevalent in women that suffered pregnancy loss, although the clinical relevance is unclear [21]. In the context of the OPEN clinical trial on transcervical uterine fibroid ablation with the Sonata system (copyright), Bongers et al., compared baseline and post-ablation hysteroscopy in 37 patients and determined that RFA didn't promote intrauterine adhesiogenesis, since RF energy is targeted to fibroids beneath the endometrium without involving significant areas of endometrium [22].

More than 50% of the women had uncomplicated vaginal births with a smaller proportion of patients having cesarean delivery, even though the indication was not always specified. Standard myomectomy has always risen concerns about risk for uterine rupture due to damage to uterine wall integrity: in current literature, overall uterine rupture rate after myomectomy during labor is 0.47% and 1.52% before labor [23]. Uterine rupture is a rare but significant complication during pregnancy and labor and accurate risk rate after RFA is still to be defined due to the scarce population studied in literature.

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Limitations to these studies concern the small study population, the lack of standardized patient selection and potential bias due to limited information regarding history of infertility and attempts to conceive of these women in most publications, except for Christoffel et al., in their 36 pregnancies report after RFA, in which five women conceived more than once and four underwent Assisted Reproductive Technology (ART) [24].

#### **Procedure-related complications**

TRFA is reported to be associated with very low intra-operative and peri-operative, including 30-day readmission rate [13]. Nonspecific procedure-related are anesthesiologic complications and procedure related complications are estimated to be 1.78% of the cases and include infection (3.2%), [4] intestinal heat injury requiring surgery (1.69%) [18] and vaginal discharge (15%). Pelvic organs thermal injury including intestine and bladder is a rare but serious complication: ablative energy spread to surrounding intestinal loops, especially after laparoscopic RFA, can lead to rectouterine fistula, intestinal necrosis, and need for demolitive surgery [25-27].

#### Conclusion

Minimally invasive management of fiborids guaranteeing fertility preservation and cost effective solutions are of far-off relevance today. Transvaginal radiofrequency ablation represents a safe and efficient volume reduction technique that offers a safe approach in day-surgery setting reducing overall cost related to hospitalization and conventional surgery.

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