European Journal of Obstetrics & Gynecology and Reproductive Biology 224 (2018) 175–180

Contents lists available at ScienceDirect

European Journal of Obstetrics & Gynecology and Reproductive Biology

journal homepage: www.elsevier.com/locate/ejogrb

Full length article

Improvement in health utility after transcervical radiofrequency ablation of uterine fibroids with the sonata system: Health utility after radiofrequency ablation

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ARTICLE INFO

Article history:
Received 13 October 2017
Received in revised form 19 March 2018
Accepted 25 March 2018
Available online xxx

Keywords:
Leiomyoma
Menorrhagia
Fertility preservation
Uterine myomectomy
Quality-adjusted life years (QALYs)

ABSTRACT

Objectives: To establish the improvement in patient health utilities following treatment of symptomatic uterine fibroids with the Sonata™ System.
Study design: A prospective, single-arm trial was conducted in which 49 women in the United Kingdom, Netherlands and Mexico with fibroids were treated with transcervical, intrauterine ultrasound- guided radiofrequency ablation. The EQ-5D-3L system was utilized to collect patient health status at baseline, 3, 6, and, 12 months post-procedure. Patient-reported health states at each time point were converted into a health utility value using time-trade off methodology.
Results: In the overall cohort, patient health utility increased from a mean of 0.745 at baseline, to means of 0.838, 0.852, and 0.914 at 3 months, 6 months, and 12 months, respectively. The change from baseline at 12 months was significant. When stratified by country, the 12-month improvement in health utility remained significant for both the Mexican and Dutch cohorts.
Conclusions: Transcervical radiofrequency ablation of uterine fibroids with the Sonata System resulted in statistically significant 12-month improvements in health utility for the overall patient cohort and for the Mexican and Dutch sub-populations.

Introduction

Uterine fibroids, also known as leiomyomata, are noncancerous growths of the uterus. They can vary in size and number and often appear during childbearing years. Uterine fibroids are common; one study of women undergoing pelvic sonography found that over 80% of African-American and almost 70% of Caucasian women will have fibroids by the age of 50 [1]. Whilst the majority of uterine fibroids are asymptomatic [2], 20–50% may produce symptoms [3]; the most common symptom being abnormal uterine bleeding [4]. Fibroids may also cause pelvic pressure and pain [3]. A study of 21,746 women with symptomatic fibroids [5] found that more than half of the patients' symptoms had a negative impact on their lives. Another study found that almost a third of women with symptomatic uterine fibroids reported work absenteeism and over a third reported presenteeism (i.e., reduced work productivity) and impaired general activity [6].

Definitive treatment for uterine fibroids is hysterectomy, with or without removal of the ovaries. However, there are several treatment options for women suffering from fibroids that do not involve surgical removal of the uterus, and these include surgical removal of myomata (myomectomy); uterine artery embolization (UAE); and magnetic resonance-guided focused ultrasound (MRgFUS). With effective treatment, women who had been living with fibroid symptoms can realize improvements in health-related quality of life (HRQOL) [7].

The availability of a variety of treatment options allows women the opportunity to choose an appropriate treatment based on symptom severity, past medical history, and values and preferences (desire for fertility and for uterine preservation). A recent US study found that almost 79% of women would prefer less invasive treatments, with 51% choosing to preserve their uteri, and 43% of women under age 40 desiring fertility preservation [8].

With the goal of providing an incisionless, uterus-preserving alternative to hysterectomy and other treatment options, the Sonata® System (which received CE Mark approval) takes a transcervical approach to treating symptomatic fibroids with

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https://doi.org/10.1016/j.ejogrb.2018.03.053
0301-2115/

radiofrequency energy. Radiofrequency energy heats fibroids to a high temperature and this results in thermal fixation, coagulative necrosis and gradual reduction in fibroid volume. Fibroid ablation with the Sonata® System takes place under real-time visualization provided by an intrauterine sonography probe that is integrated within the device [9] (Fig. 1). The advantage of treatment with the Sonata® System over MRgFUS is that it takes approximately four minutes to ablate a fibroid up to 5 cm, whereas fibroid ablation with MRgFUS requires much longer ablation durations (typically 3 h in total) [10]. One advantage of the Sonata® System over UAE is that postoperative pain and symptoms are more limited and do not typically require hospital admission [11,12].

To evaluate the safety and efficacy of the Sonata® System, the Fibroid Ablation Study-EU (FAST-EU) was undertaken in Europe and Mexico. Efficacy and safety endpoints at 3, 6, and 12 months were very promising; both fibroid perfusion and fibroid volume reductions were statistically significant at 6 and 12 months compared to baseline. The detailed results were previously published in gynecologic surgical journals [11,12] In summary, mean perfused fibroid volume was reduced by 68 and 67.4% at 6 and 12 months, respectively. Similarly, mean fibroid volume was reduced by 55 and 67% at the same time intervals. The mean symptom severity score improved by more than 50% at 12 months. The number of post-procedural complications was low and these were typically minor and anticipated. There were four surgical reinterventions (8%) within 12 months.

An additional objective of the study was to obtain a descriptive profile of patient health status at baseline, 3, 6, and 12 months post treatment, to enable assessment of patient health utility and calculation of total quality-adjusted life years (QALYs) experienced by patients during the 12 months post- procedure. These data were not included in the previously published papers as these focused on traditional clinical safety and efficacy outcomes. The current paper focuses on the health utility and quality of life outcomes for women who were treated with transcervical radiofrequency ablation in the FAST-EU study.

Materials and methods

The FAST-EU study, a prospective, longitudinal, multicenter, single-arm trial, was conducted in Mexico, the United Kingdom, and the Netherlands. Given the early phase of implementation of this new technique, the chosen study design was in line with guidance on research of innovative interventions of the IDEAL collaboration (Idea, Development, Exploration, Assessment, and Long-term study) [13]. In particular, the IDEAL collaboration notes that immediate execution of comparative studies may result in the underestimation of the potential effect of a new technique.

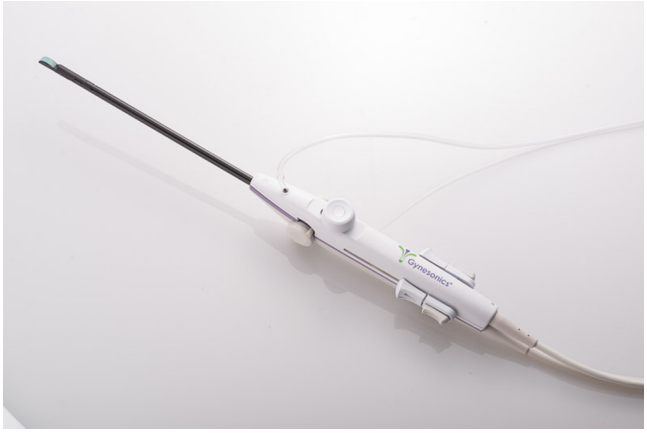

Fig. 1. Intrauterine sonography probe.

In this study, 50 consecutive women with symptomatic fibroids meeting eligibility requirements [11,12] received treatment using the Sonata® System (Gynesonics, Redwood City, CA, USA). The procedure involved transcervical, intrauterine ultrasound-guided radiofrequency ablation. The Sonata System consists of a reusable intrauterine ultrasound (IUUS) probe and a single-use disposable RFA handpiece with proprietary graphical guidance software (SMART Guide™) for fibroid targeting and ablation (Fig. 1). Through the use of the SMART Guide, each ablation with a targeted fibroid is placed to encompass as much of the fibroid as possible while keeping thermal energy within the uterine serosal margin (Fig. 2). This permits the safe and predictable delivery of RF energy to the fibroid. Treatment parameters, such as time at temperature (105° C) and power, are set by the Sonata System based on the ablation dimensions that the gynecologist has selected via the SMART Guide. The Sonata System can create a continuous range of ablation sizes up to 4.0 cm wide and up to 5.0 cm long. Multiple ablations may be created within a single fibroid and several fibroids may be treated within a single session; there is no need for staged treatment, unlike some cases of hysteroscopic myomectomy. The Sonata System is also capable of ablating a broader repertoire of fibroids than is possible with operative hysteroscopy, including intramural and selected subserous fibroids.

Patients were included in one of the participating hospitals in Mexico (one site), United Kingdom (2 sites) and The Netherlands (3 sites) between January 2011 and March 2014. Inclusion criteria included women with up to 5 fibroids of International Federation of Gynecology and Obstetrics (FIGO) types 1,2,3,4 and 2–5 (transmural) [14] with individual maximum diameter of 1–5 cm. At least one fibroid was required to indent the endometrial cavity. Patients were 28 years of age or older and not pregnant, with regular, predictable menstrual cycles and heavy menstrual bleeding for at least 3 months, with a Menstrual Pictogram score $\geq$120 and a Uterine Fibroid Symptom-Quality of Life (UFS-QOL) Symptom Severity Score (SSS) $\geq$20 for one cycle [15,16]. Exclusions included a desire for future fertility, the presence of one or more type 0 fibroids, cervical dysplasia, endometrial hyperplasia, active pelvic infection, clinically significant adenomyosis (>10% of the junctional zone measuring more than 10 mm in thickness as measured by MRI), and the presence of one or more treatable fibroids that were significantly calcified (defined as <75% fibroid enhancement by volume on contrast-enhanced MRI). MRI scans were all assessed by an independent core laboratory.

Patients were followed at 3, 6, and 12 months post-treatment. The primary study endpoint was percentage change in target fibroid perfused volume assessed at 3 months; the reduction was statistically significant at 3 months, and also at 12 months, with a nearly 70% reduction in volume ($P < 0.001$) [12]. Secondary endpoints, evaluated at 6 and 12 months, included safety outcomes, symptom severity, Health-related Quality of Life (HRQOL) and reintervention. Of note, symptom severity and HRQOL were assessed using the SSS and HRQOL subscales of the UFS −QOL questionnaire, which is a tool that has been validated in women with uterine fibroids and compared with a cohort of women without uterine fibroids [17].

While not reported previously, the EuroQol-5D-3L (EQ-5D-3L) instrument [18,19] was also utilized in FAST-EU to obtain a descriptive profile of patient health status at baseline, and at 3 months, 6 months and 12 months post-procedure.

In this study, the TTO value sets specific to the Dutch and UK populations were applied to the FAST-EU patient populations from the Netherlands and UK, respectively. As neither VAS nor TTO value sets were available for Mexico, the UK TTO value sets were also applied to the Mexican patient population (as it is the largest, most