RADIOFREQUENCY ABLATION FOR TREATMENT OF SYMPTOMATIC UTERINE FIBROIDS

Spanish language full text link

Introducción

Uterine fibroids, also called fibroma, fibromyoma or leiomyoma, are defined as a benign tumour of muscular tissue of the wall of the uterus or womb that can cause significant symptoms such as abnormal uterine bleeding or heavy menstrual bleeding, pelvic pressure or pain, and reproductive problems. In addition, there is an increased risk of developing emotional distress, depression and anxiety. It is estimated that by the age of 49 years more than 70% of Caucasian women and 84% of African-American women have a diagnosed fibroid, symptomatic or otherwise.

The diagnosis of uterine fibroids is usually made by a directed anamnesis together with a bimanual gynaecological examination, with transvaginal ultrasound being the first-line radiological evaluation.

The therapeutic approach is based primarily on the patient's preferences, reproductive intentions, symptom burden and the size and location of the myoma. The definitive treatment is hysterectomy which represents the second most common surgery for women after caesarean section; however, it is associated with significant morbidity and mortality, as well as significant economic burden and social impact on the healthcare system. Many women may desire future fertility, to preserve the uterus and/or undergo less invasive interventions, including radiofrequency volumetric thermal ablation..

Radiofrequency ablation (RFA) consists of the application of heat inside the myoma to produce tissue necrosis. The technique is performed under sedation, in an interval of 10-30 minutes, depending on the volume to be treated. The access route is through the posterior, anterior or transcervical vaginal fundus. The devices for performing RFA combine ablation with intrauterine ultrasound and are designed for diagnosis and treatment of symptomatic uterine fibroids vaginally. The technology aims to reduce symptoms by reducing myoma volume without the need for a surgical incision.

Aims

The main objective of this evaluation report is to determine the comparative effectiveness and clinical safety of RFA via the transvaginal/transcervical route in the treatment of symptomatic uterine fibroids in women at least 18 years of age who wish to preserve the uterus vs. usual treatment.

Methods

The research question, in PICOD (Patient, Intervention, Comparator, Outcome and Study Design) format, was developed by means of a systematic review of the current literature on RFA via the transvaginal/transcervical route. The methodology used was that described in the "Guide for the preparation and adaptation of rapid health technology assessment reports" published within the Spanish Network of Health Technology Assessment Agencies (RedETS) and NHS Benefits. This document was the main source for selecting the relevant evaluation elements to be dealt with in the report, among which were: the health problem, the current situation of the technology, health variables (safety and effectiveness) and the economic and organizational aspects derived from the implementation of the evaluated technology in clinical practice.

The bibliographic search was performed in different biomedical databases such as: Cochrane library, International HTA database, INAHTA, Tripdatabase, GIN, Medline and Embase, using different descriptors (MesH, Thesaurus, etc) and free terms to make up for possible deficiencies in the indexing of some articles. The search was carried out in July 2020 and receiving weekly alerts until March 2021 with the closing of the paper. A manual search of the articles' bibliographies and a search of ongoing studies in the Clinicaltrials and EU Clinical Trials Register databases were also performed. Two authors (MCMR and PCM) carried out the study selection, data extraction and quality assessment, according to predefined selection and extraction criteria, summarizing the most relevant aspects in evidence tables.

The quality of the studies and the level of bias were assessed using the specific scales recommended for each type of study according to the "Guide for the preparation and adaptation of rapid health technology assessment reports", mentioned above. Specifically, in this work we used the AMSTAR-2 scale for systematic reviews and assessment reports and the IHE (Institute of Health Economics) scale for the assessment of evidence from case series. The evaluation of the quality of the evidence for safety and effectiveness was performed following the GRADE (Grade of Recommendations, Assessment, Development and Evaluation) methodology.

In the results, the statistics tools of the Excel program version 2016 were used to calculate the means, standard deviations and medians of the data obtained.

Results

The search retrieved a total of 347 references, of which 34 were selected for full-text review and of these a total of 5 were included (1 systematic review, 1 evaluation report, 1 primary follow-up extension study, 1 cost study and 1 ongoing study). The studies were divided according to whether entry route was transvaginal or transcervical.

Since the review and the evaluation report included almost the same studies, they were used as a source of primary studies and it was decided to update the part corresponding to each of the routes depending on the greater number of studies included, in addition to the follow-up extension study. The results of 16 studies were analysed, 8 corresponding to the transvaginal route and 8 to the transcervical route. The cost study was used to assess the economic aspects within the implementation analysis and, as new evidence, the characteristics of the study in progress were described.

The main outcome variables analysed for the results of effectiveness refer to the mean reduction of myoma volume and size, severity of symptoms, and menstrual bleeding, as well as the results of reinterventions, fertility and quality of life. As for the safety variables, all complications and adverse effects directly related to the intervention were analysed.

Transvaginal route

The 8 primary studies were all prospective studies of moderate or low quality, and mostly without a comparison group. They included 635 patients with a mean age of 41.7 years and a mean follow-up of 15 months (19-205 months). The most common diagnosis was submucous myoma (42%) followed by non-specific myoma (36.75%), the mean number of myomas per patient was 1.38±0.45 and the volume ranged from 14 to 305 cm3. Health-related quality of life presented a mean of 59.8±10.4 points (100 points maximum, better quality) and symptom severity a mean of 55±16.5 points (100 points maximum, higher severity).

Various radiofrequency devices were used, and ultrasound guidance was used in all procedures.

Safety

Overall, the evidence analysed indicates that 28.96% (181/625) of patients experienced some adverse effect [95%CI (25.3-32.6)], mostly mild. The most frequent adverse effect was vaginal spotting which disappears between the first and eighth week after the procedure and pain, which also disappears in the first week.

Effectiveness

- Size: overall, the data show a mean reduction in myoma size of 48.96%, the mean difference being statistically significant (p = 0.0000) with a [95%CI (2.2-2.4)].
- Volume: based on the data analysed, a mean reduction in mean myoma volume of 75.03% was observed, with the pre-intervention vs. postintervention difference being statistically significant (p = 0.000) with a [95%CI (81.2-92.4].
- Symptom severity: a reduction of 83.49% was observed between pre- and post-intervention values, with statistically significant differences (p = 0.0000) and [CI95%]. (41.9-44.1)].
- Reintervention: 2.7% of patients required a new reintervention, which was mainly myomectomy.
- Fertility: 5 pregnancies with healthy newborns are described.

Quality of life

Generally, medical discharge takes place on the same day of surgery within 2.5 hours on average. The studies do not reflect the time of return to work or activities of daily life. Quality of life improved significantly, showing a mean increase in the questionnaire score of 54% and statistically significant differences between pre- and post-intervention. The degree of satisfaction was very high, with the majority (88.5%) of patients reporting that they were very satisfied with the intervention.

Transcervical route

The 8 primary studies were prospective, with a moderate or high risk of bias and all were case series. A total of 234 patients were included, of which only 147 had data up to the end of follow-up. The mean age was 43 years and follow-up ranged from 24 to 36 months. The mean number of fibroids per patient was 2.1±0.8 and the volume ranged from 3.3 to 71.1 cm3. Health-related quality of life had a mean 37.3±4.2 points (100 points maximum, best quality) and symptom severity a mean 58.3±4.8 points (100 points maximum, highest severity).

In this case all of the included studies used the same device and were industry-funded.

Safety

Overall, 38.04% of patients had some adverse effect [CI95% (31.6-44.5)], mostly mild. The most frequent adverse effect was myoma detachment, which reached 30.6%. In addition, three patients had serious adverse effects: deep vein thrombosis, sterile leucorrhoea and non-specific abdominal pain requiring hospital admission.

Effectiveness

- Volume: in terms of reduction in mean fibroid volume, a reduction of 66.6% and 62.4% at 12 months is reported, statistically significant in both cases (p<0.001) (data from the FAST-EU and IDE studies included in the evaluation report).

- Symptom severity: statistically significant reductions in the symptom severity score at 12 months are reported, ranging from 50.91% to 55.47% (data from the FAST-EU and IDE studies included in the evaluation report).
- Reintervention: 2.1% of the patients required a reoperation, without knowing in this case which reintervention was the majority.
- Fertility: only one study describes this variable with a pregnant patient who successfully reached full term and gave birth to a healthy child. One study had unwillingness for fertility as a requirement in the choice of participants.

Quality of life

As in the case of the transvaginal approach, medical discharge took place on the same day of the operation, with an average waiting time of 2.5 hours. Return to normal activity took 3.3 days on average, as did return to work (3.6 days). The increase in the quality of life score was around 49%, somewhat lower compared to the transvaginal approach, and 88.2% of patients were very satisfied with the procedure.

Transvaginal vs. transcervical route

Safety

Indirect comparison of the reported safety outcomes for both routes by comparing independent sample proportions indicates that the transcervical route has a higher number of mild adverse events (38.04% vs 28.96%), with statistically significant differences, [CI95% (-0.165 to -0.016), $p < 0.01$]. In principle, both routes would be expected to provide similar results, although in theory, the transcervical route could also be expected to be safer given the need for the transvaginal route to break the uterine serosa with an electrode. Therefore, we could consider that these differences could be due to the greater number and size of fibroids in patients treated by the transcervical route.

Effectiveness

Overall and for both access routes, a 47% reduction in average volume at 3 months, a 55% reduction at 6 months and a 71% reduction at 12 months are described.

The comparison of proportions of two independent samples shows that there are no statistically significant differences in re-interventions between the two routes, [95%CI (-0.02 a 0.034) and p=0.753.]

Implementation considerations

The comparison of short-term resource utilisation of direct facility and perioperative resource costs of patients undergoing transcervical RFA versus myomectomy showed that RFA had lower total costs for both process-related and stay-related costs, and only the cost of consumables was higher. No studies were found for the transvaginal route.

Discussion

The articles included in both the systematic review and the assessment report were at risk of bias. The strength of evidence for both effectiveness and safety was rated as low for all outcomes, with most studies lacking a comparison group. Inherent limitations of this type of study are confounding factors and the use of unblinded outcomes.

Although the robustness of the results was low, in our case, the information provided by the studies was homogeneous and shows in both cases a favourable safety profile, with no intraoperative complications, very few serious adverse effects and few minor adverse effects. Reoperation rates were also low in both routes. In terms of effectiveness, both routes showed a reduction in symptom severity, fertility and improvement in the patients' quality of life.

Therefore, it should be noted that, despite the lack of comparative studies, there are alternatives in the treatment of uterine fibroids that are less invasive than the traditional surgical approach of laparotomy with hysterectomy or myomectomy.

Conclusions

The lack of comparison studies does not allow conclusions to be drawn on the benefit-risk of radiofrequency ablation with transvaginal or transcervical approach in the treatment of symptomatic uterine fibroids compared to alternative uterine-sparing procedures.

Studies without a comparator indicate that radiofrequency ablation with a transvaginal or transcervical approach for symptomatic uterine fibroids has an acceptable safety profile. In terms of efficacy, the studies without a comparator indicate that technique shows a significant reduction in myoma volume, symptom severity and vaginal bleeding, as well as an improvement in quality of life.

It is recommended that clinical practice guidelines on the management of symptomatic uterine fibroids be developed that list the available treatment alternatives and their specific indications.