ABSTRACT

In this review, we assessed the short-term (3 and 6 months) and long-term (12, 24, and 36 months) symptom relief and quality of life improvement, procedure-related adverse event rate, reintervention rate, and days missed from work after laparoscopic radiofrequency ablation. Using MeSH keywords “uterine fibroid” and “ablation technique,” a systematic search was performed in PubMed, Ovid, Embase, Cochrane Library, and Clinicaltrials.gov. Studies consisting of uterine fibroid symptoms and quality of life scores were considered eligible. Both comparative and non-comparative studies were included. Using a random-effects model, a meta-analysis was performed. Eight studies with a total of 581 patients were finally included in our review. Based on validated questionnaires, quality of life improved significantly until 36 months after laparoscopic radiofrequency ablation therapy, with a maximum improvement (Health-Related Quality of Life [HRQL] questionnaire score of +41.64 [95% confidence interval (CI), 38.94–44.34] and a transformed Symptom Severity Score [tSSS] of -39.37 [95% CI, 34.70–44.04]) at 12 months after laparoscopic radiofrequency ablation. All subscales of quality of life improved significantly, and most of the changes remained stable in long-term follow-up. The overall reintervention rate was 4.39% (95% CI, 1.60%–8.45%), and the median uterine volume reduction was 69.17 cm³ (95% CI, 35.87–102.46 cm³). The overall procedure-related adverse event rate was 1.78% (95% CI, 0.62%–3.53%), and patients missed an average of 4.35 days (95% CI, 2.55–6.15 days) of work. In conclusion, laparoscopic radiofrequency ablation therapy is an efficacious way to treat small-sized and nonpedunculated symptomatic uterine fibroids, providing stable long-term symptom relief and quality of life improvement with a low risk of adverse events and reintervention and just a few days of missed work. Journal of Minimally Invasive Gynecology (2019) 26, 409–416. © 2018 AAGL. All rights reserved.

Keywords: Laparoscopic radiofrequency ablation; Meta-analysis; Quality of life; Symptomatic uterine fibroid

Uterine fibroids are the most common benign tumors of the female reproductive system, with a cumulative incidence of >70% [1,2]. Approximately 50% of uterine fibroids become symptomatic, resulting in abnormal uterine bleeding, heavy menstrual bleeding, bulk symptoms, and other complications [2]. Owing to these symptoms and the desire for uterine conservation, today more patients desire a uterine-sparing treatment for fibroids [3]. The Society of Obstetricians and Gynaecologists of Canada guideline on this topic recommends several uterine-sparing procedures, including laparoscopic radiofrequency ablation [4].

The methodology and outcomes of studies of laparoscopic radiofrequency ablation differ. Therefore, we conducted this meta-analysis to evaluate time-related postoperative uterine fibroid symptoms and quality of life in patients after laparoscopic radiofrequency ablation. In addition, subscales of quality of life, rates of adverse events and reintervention, days of work missed, and uterine volume changes were assessed to provide a more comprehensive assessment of laparoscopic radiofrequency ablation.

The authors declare that they have no conflicts of interest.

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Methods

Eligibility Criteria, Information Sources, and Search Strategy

The meta-analysis was conducted following the PRISMA guidelines [5]. We performed a systematic electronic search of PubMed, Ovid, Embase, ClinicalTrials.gov, and the Cochrane Library for journal articles published between January 2000 and March 2018 with the following MeSH key words: “uterine fibroid,” “ablation technique,” “English,” and “humans.”

Criteria for inclusion were as follows: (1) study evaluating our primary outcomes of uterine fibroid symptoms and quality of life based on a validated questionnaire, including the Health-Related Quality of Life questionnaire (HRQL), transformed Symptom Severity Score (tSSS), or EuroQoL Health Status Survey (EQ-5D); (2) intervention of laparoscopic radiofrequency ablation; (3) follow-up time of >12 months; (4) patients with no previous interventions for fibroids; (5) both comparative and noncomparative studies included; and (6) no reviews, case reports, animal studies, non-English studies, published abstracts without available full texts, or reports from meetings.

The outcomes uterine fibroid symptoms and quality of life were measured using validated questionnaires: the HRQL, tSSS, and EQ-5D. The quality of life subscales were the following 6 domains in the HRQL: “concern,” “activities,” “energy/mood,” “control,” “self-consciousness,” and “sexual function.” Those validated questionnaires are universally accepted for evaluating uterine fibroid treatment, with scores ranging from 0 to 100. When symptoms improve, HRQL, HRQL subscales, and EQ-5D scores increase, and tSSS score decreases. As for secondary outcomes, whether an adverse event was procedure-related was defined by the original authors. Reintervention was defined as repeat surgical intervention, such as hysterectomy, for symptom-related reasons. Uterine volume changes were based on ultrasound or magnetic resonance imaging findings and were calculated by the original authors. Postoperative days missed from work simply meant work days missed. Among the outcomes, reintervention and uterine volume changes showed the efficacy of a single intervention, whereas procedure-related adverse events represented the safety of the procedure. In addition, days missed from work was an index for the rest period after treatment.

Study Selection

The first 2 authors separately filtrated titles and abstracts for relevance. Full texts of related studies were accessed and evaluated for inclusion. When the first 2 authors could not reach an agreement, a third author was consulted. Moreover, to reduce the likelihood of missing potentially relevant studies, references of the selected articles were cross-checked.

Data Extraction

We extracted data representing the efficacy and safety of laparoscopic radiofrequency ablation, including primary outcomes (overall quality of life and subscale scores) and secondary outcomes (uterine volume, procedure-related adverse events, reintervention rate, and days of work missed postoperatively). Study characteristics and patients’ baseline characteristics were extracted as well.

Data for our primary outcomes at 3, 6, 12, 24, and 36 months after laparoscopic radiofrequency ablation were pooled for the meta-analysis. For the secondary outcomes, an overall analysis was performed. Some included studies were comparative, and for those studies, we assessed data only from the laparoscopic radiofrequency ablation group.

Quality Assessment

Because most of the included studies were noncomparative studies, were evaluated the quality of studies using the 11-item checklist recommended by Agency for Healthcare Research and Quality. For each of the 11 items on the checklist, a “yes” answer was scored as 1 and a “no” or “unclear” answer was scored as 0. Then quality was assessed as follows: 0–3 points, low quality; 4–7 points, moderate quality; and 8–11, high quality [6]. Data organization was done using RevMan version 5.3 (Cochrane Community, London, UK).

Data Synthesis and Analytical Methods

Data were summarized, and the meta-analysis was performed using Stata version 14.0 (StataCorp, College Station, TX). All the indices were analyzed in a random-effects model, and data were presented as mean with 95% confidence interval (CI). In addition, $I^2$ values were calculated to describe the heterogeneity among the studies, which ranged from 0% to 100% (with 25%, 50%, and 75% representing low, moderate, and high heterogeneity, respectively). When median with range and mean with standard deviation values were available in the original articles, data were transformed as described by Hozo et al [7]. Results of meta-analysis were partially converted to graphs created using Prism 6.01 (GraphPad Software, La Jolla, CA).

Results

Study and Patient Characteristics

A flow diagram of the article search process is shown in Fig 1. Among 31 potentially relevant articles screened in full text, some were excluded because they addressed transvaginal or percutaneous radiofrequency ablation [8,9], others were excluded for being published abstracts without
available full text or conference abstracts [10–12], and still others were excluded because they focused on outcomes other than uterine fibroid symptoms and quality of life after therapy [13–15].

A total of 11 studies with 749 patients met the eligibility criteria, but some studies were from the same trials [16–18]. When the data were repeated, we used the data from studies with the longer follow-up periods. Eight studies with a total of 581 patients were finally included (Table 1). Most of the studies excluded International Federation of Gynecology and Obstetrics (FIGO) type 0, 5, 6, 7, and 8 fibroids, because these types could be contraindicated [19–22]. The weighted mean patient age was 42.23 years, and mean BMI was 28.49 kg/m². The maximum mean HRQL and tSSS scores were 77.1 and 66.4, respectively, and the minimum were only 37.1 and 38.9, respectively. Among the 8 studies included, 2 studies had a score of 11 points on the AHRQ Cross-Sectional/Prevalence Study Quality checklist, 4 studies had a score of 10 points, and 2 studies had a score of 9 points.

**Primary Outcomes**

**Uterine Fibroid Symptoms and Quality of Life by Postoperative Period**

Uterine fibroid symptoms and quality of life at 3, 6, 12, 24, and 36 months after laparoscopic radiofrequency ablation were analyzed. The mean changes in HRQL and tSSS scores from baseline with 95% CIs are shown in Fig 2. HRQL scores improved by a mean of 36.70 points (95% CI, 33.60–39.79; p < .001; I² = 7.7%; 6 studies) at 3 months, by 39.00 points (95% CI, 35.38–42.62; p < .001; I² = 7.6%; 6 studies) at 6 months, by 41.64 points (95% CI, 38.94–44.34; p < .001; I² = 0.0%; 6 studies) at 12 months, by
29.21 points (95% CI, 12.44−45.98; p < .001; $I^2 = 94.5$%; 3 studies) at 24 months, and by 38.60 points (95% CI, 33.60−39.79; p < .001; 1 study) at 36 months. Similarly, tSSS scores were reduced by a mean of 33.19 points (95% CI, 30.47−35.90; p < .001; $I^2 = 0.0$%; 6 studies) at 3 months, by 37.02 points (95% CI, 32.14−41.90; p < .001; $I^2 = 44.9$%; 6 studies) at 6 months, by 39.37 points (95% CI, 34.70−44.44; p < .001; $I^2 = 89.6$%; 3 studies) at 24 months, and by 32.60 points (95% CI, 27.75−37.45; p < .001; 1 study) at 36 months. The maximum changes in both scores were seen at 12 months after treatment (Fig. 3 and 4). Only 2 studies reported EQ-5D scores, which improved by a mean of 10.17 points (95% CI, −0.11 to 20.45; p = .052; $I^2 = 88.9$%) at a weighted mean follow-up time of 34 months.

**Subscales of Quality of Life for Different Postoperative Periods**

Because the longest access to the subscales of quality of life was 24 months after treatment, a meta-analysis was performed at 3, 6, 12, and 24 months after laparoscopic radiofrequency ablation; the results are shown in Fig 5. On the one hand, the mean changes in the “activities,” “energy/mood,” “control,” and “self-consciousness” domains were significant and stable after intervention and for up to 24 months, ranging from 33.80 (95% CI, 27.69−39.91; p < .001; $I^2 = 24.1$%; 3 studies) to 36.93 (95% CI, 30.43−43.43; p < .001; $I^2 = 44.3$%; 3 studies) at 3 months, from 37.00 (95% CI, 31.91−42.09; p < .001; $I^2 = 0.0$%; 3 studies) to 40.38 (95% CI, 35.52−45.24; p < .001; $I^2 = 1.3$%; 3 studies) at 6 months, from 38.72 (95% CI, 32.13−45.30; p < .001; $I^2 = 36.0$%; 3 studies) to 42.83 (95% CI, 38.44−47.21; p < .001; $I^2 = 36.0$%; 3 studies) at 24 months.
\( I^2 = 0.0\% \); 3 studies) at 12 months, and from 39.10 (95% CI, 33.40–44.90; \( p < .001 \); 1 study) to 42.00 (95% CI, 36.30–46.70; \( p < .001 \); 1 study) at 24 months. In contrast, compared with the baseline level, the results for the “concern” and “sexual function” domains at 3, 6, 12, and 24 months were statistically significant. However, the differences among 3, 6, 12, and 24 months were not statistically significant, although the results showed fluctuations.
Secondary Outcomes

The indices for the efficacy of laparoscopic radiofrequency ablation included the overall rate of reintervention and the reduction in uterine volume. The overall rate of reintervention was 4.39% (95% CI, 1.60%–8.45%; $I^2 = 65.0%$; 7 studies), and the weighted mean duration of follow-up was 24.65 months. The uterine volume reduction was 69.17 cm$^3$ (95% CI, 35.87–102.46 cm$^3$; $p < .001$; $I^2 = 94.5%$; 2 studies) and the rate of reduction was 31.97% (95% CI, 12.98%–50.95%; $p = .001$; $I^2 = 94.5%$; 2 studies) at a 12-month follow-up.

As for indexes representing the safety and rest period of laparoscopic radiofrequency ablation, the overall procedure-related adverse event rate and days missed from work were evaluated. With a weighted mean follow-up time of 19.72 months, the overall procedure-related adverse event rate was 1.78% (95% CI, 0.62%–3.53%; $I^2 = 0.0%$; 6 studies), and patients missed an average of 4.35 days of work (95% CI, 2.55–6.15; $I^2 = 0.0%$; 5 studies) for treatment.

Discussion

Our meta-analysis summarizes the available data on time-related postoperative uterine fibroid symptoms and quality of life and subscales of quality of life improvements after laparoscopic radiofrequency ablation. We also analyzed the overall procedure-related adverse event and reintervention rate, uterine volume reduction, and days of work missed to provide a more generalized overview of laparoscopic radiofrequency ablation, because these indexes represent the safety and efficacy of a single intervention and rest period of laparoscopic radiofrequency ablation.

According to the Society of Obstetricians and Gynaecologists of Canada guideline, laparoscopic radiofrequency ablation is recommended for premenopausal women with symptomatic fibroids who wish to retain uterine[4]. During laparoscopic radiofrequency ablation, the probe is inserted into the fibroid percutaneously under laparoscopic ultrasound guidance [19,20]. The ideal patients for this approach were not defined by the guideline, but authors of the included studies mentioned ideal patient criteria. On the one hand, the ideal uterine volume is < 300 cm$^3$, and ideal fibroid diameter is < 6 cm [19–21,23]. On the other hand, pedunculated fibroids should not be treated with laparoscopic radiofrequency ablation [19,20]. In terms of contraindications, despite abdominal surgery and anesthesia contraindications, patients with pelvic malignancy history, cervical dysplasia, adenomyosis, and previous treatment of fibroids or fertility should not undergo laparoscopic radiofrequency ablation [4,19–21].

Several authors have evaluated laparoscopic radiofrequency ablation. Sandberg and Havryliuk [24,25] reviewed horizontal comparisons of uterine-sparing interventions
fibroids, including laparoscopic radiofrequency ablation, uterine artery embolization, and myomectomy, among other techniques; however, they used a single time point at 12 months after therapy and a weighted mean value to assess the efficacy of procedures. Our results can serve as an appropriate supplement. We analyzed uterine fibroid symptoms and quality of life at 3, 6, 12, 24, and 36 months after therapy, which provided global data extending from short-term to long-term follow-up. Moreover, we also provide data on safety and rest periods, by pooling procedure-related adverse events and days missed from work into meta-analysis. In addition, our present meta-analysis included more studies and patients, providing more reliable results on time-related postoperative symptom relief and quality of life improvement.

Our review indicates that the maximum improvements in uterine fibroid symptoms and quality of life occur at 12 months after laparoscopic radiofrequency ablation, with an average increase of 41.64 points in HRQL scores and an average reduction of 39.37 points in tSSS scores. These changes in HRQL and tSSS scores are considered clinically significant [26]. In addition, the changes in HRQL and tSSS scores remained stable up to 36 months after therapy, and heterogeneity among studies was low, except for the results at 24 months after therapy. The high heterogeneity at 24 months was related to the study by Kramer et al [28], who reported significantly smaller changes in HRQL scores (8.5 points; 95% CI, 1.2–17.7 points) and tSSS scores (21.0 points; 95% CI, 13.5–28.1 points). These smaller changes were possibly related to the better baseline uterine fibroid symptoms and quality of life scores in his study. Most studies suggested that patients could gain a long-term relief of symptoms, particularly for patients with severe symptoms and poor quality of life. As for subscales of quality of life, patients exhibited significant improvements from baseline in all domains up until 24 months after therapy. However, the improvements in the “concern” and “sexual function” domains were more fluctuant. This might stem from the physiological changes in perimenopausal females and the limited data for the quality of life subscales [27].

For secondary outcomes, the overall reintervention rate was only 4.39%, suggesting that the efficacy of a single intervention is sustainable. The uterine volume decreased significantly after therapy; however, the authors gave much more attention to symptom changes and quality of life changes than to uterine volume. Thus, only 2 studies with 67 patients were available for our meta-analysis, making the data insufficiently robust. In terms of safety, the overall procedure-related adverse event rate was 1.78%. Moreover, a serious adverse event like uterine perforation was reported only once [28]. The mean time to return work after therapy was 4.35 days, suggesting a short rest period after laparoscopic radiofrequency ablation.

This study has some limitations. First, because most of the studies were noncomparative, differences in study types, inclusion and exclusion criteria, and study methodology were inevitable. Second, symptoms might be related to fibroid locations [12,22]; however, not all studies classified patients by FIGO type, and so we could not analyze fibroids at different positions separately. In addition, the definition of procedure-related adverse events varied between studies; for instance, some studies regarded abdominal pain as a kind of procedure-related adverse event, whereas others did not [21,23]. Thus, related data were based partially on the subjective judgment of the authors, not on objective definitions. Furthermore, the risk of bias from loss to follow-up could be high (> 20%) in some studies with a long-term follow-up [19,29]. Moreover, owing to the high loss to follow-up, the longest follow-up among the studies was 36 months. Therefore, long-term follow-up data are still urgently needed.

In conclusion, according to our meta-analysis, laparoscopic radiofrequency ablation therapy is efficacious for small-sized and nonpedunculated symptomatic uterine fibroids. After treatment, patients will gain stable long-term symptom relief and quality of life improvement. Meanwhile, the overall risks of adverse events and reintervention are low, and patients typically miss only a few days of work.

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