INFORMATION BRIEF (RAPID REVIEW)

MICROWAVE ABLATION FOR UTERINE FIBROIDS

Malaysian Health Technology Assessment Section (MaHTAS)
Medical Development Division
Ministry of Health Malaysia
002/2023

IPT Mark
Rapid Review
INAHTA

Malaysian Health Technology Assessment Section (MaHTAS)
Medical Development Division
Ministry of Health Malaysia
Level 4, Block E1, Precinct 1
Government Office Complex
62590, Putrajaya
Tel: 603 8883 1229

Available online via the official Ministry of Health Malaysia website: http://www.moh.gov.my

SUGGESTED CITATION: Syful Azlie MF and Izzuna MMG. Microwave ablation for uterine fibroids. Information Brief. Ministry of Health Malaysia: Malaysian Health Technology Assessment Section (MaHTAS); 2023. 6 p. Report No.: 002/2023

DISCLOSURE: The author of this report has no competing interest in this subject and the preparation of this report is entirely funded by the Ministry of Health Malaysia.

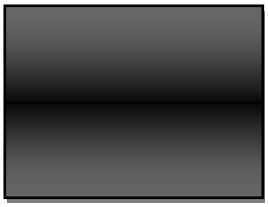
TITLE: Microwave ablation for uterine fibroids

PURPOSE

To provide brief information on the efficacy, safety, and cost-effectiveness of microwave ablation for uterine fibroids following a request from the Medical Practice Division, Ministry of Health Malaysia (MOH).

BACKGROUND

Uterine fibroids, also known as leiomyomas or myomas are the most common benign gynaecologic tumours in women of reproductive age.[1] It occurs in approximately 20% to 40% of women in this age group and about a quarter among them will have significant clinical symptoms such as dysmenorrhoea, hypermenorrhoea, abnormal uterine bleeding, secondary anaemia, pelvic pressure, and even infertility.[2] Currently, the management options are medical (hormonal and nonhormonal), nonsurgical, and surgical (myomectomy and hysterectomy).[3]



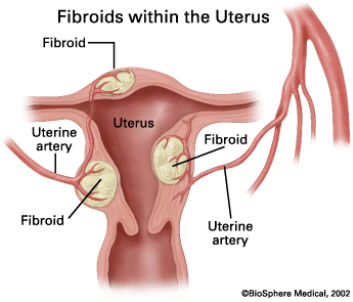


Figure 1: [redacted] ablation for uterine fibroids

There is a trend toward minimally invasive or non-invasive alternatives to conventional surgery for the treatment of uterine fibroids because these alternatives have the advantages of rapid alleviation of symptoms, fast recovery, and low risks of postoperative complications.[4] Although the most widely used minimally invasive alternative is uterine artery embolisation, the adverse effects related to it (postembolisation syndrome, risk of infection, postprocedural pain, and potential damage to the reproductive function) are causing concern.[5] To overcome the weakness of surgery and uterine artery embolisation, image-guided thermal ablation techniques (the destruction of tissue by a rapid temperature rise) have been advocated in recent years such as laser and high-intensity focused ultrasound (HIFU) ablation, radiofrequency ablation (RFA), and microwave ablation. The HIFU technique is effective and non-invasive but it is time consuming, and its indication is limited by the location, size and vascularity of the lesion.[6] However, in RFA and microwave ablation, the electrode or antenna is directly inserted into the lesions under ultrasound (US) guidance, and the generated heat

acts directly on the target tissues, overcoming the above disadvantages of HIFU.[7-8] Similar to HIFU treatment, RFA is only effective in myomas of a relatively small size (volume $\leqslant$75 cm^3) because the increasing impedance limits the further deposition of electricity into the tissue and limits the temperatures that can be achieved in the ablation zone.[9] Compared with HIFU and RFA, microwave ablation is claimed to have the following advantages: consistently higher tissue temperature, larger ablation volume, shorter operation time, less sensitivity to tissue type with more consistent results and less procedural pain because it does not rely on the conduction of electricity into the lesion, and it is not limited by impedance.[10-11] It has also been broadly used to treat solid tumours of the liver, adrenal glands, thyroid, and other organs.[12-15] However, there are limited data on microwave ablation to provide solid evidence for clinical decisions and to comprehensively evaluate the efficacy and safety of these thermal ablation therapies in the management of symptomatic uterine fibroids.

EVIDENCE SUMMARY

The systematic search found **seven** relevant articles related to microwave ablation for uterine fibroids from the scientific databases such as Medline, EBM Reviews via OVID, PubMed and from general search engines using the following search terms: *microwave ablation, thermal ablation, uterine fibroids, leiomyoma, myomas, and minimally invasive treatment.*

EFFICACY/ EFFECTIVENESS

A recent systematic review and meta-analysis (10 studies representing 671 patients) by Lu Liu et al. 2021 used Uterine Fibroid Symptom and Quality of Life (UFS-QoL) questionnaire to assess the clinical effects. Compared with baseline, the UFS scores decreased significantly (standardized mean difference [SMD] 3.37, 95% confidence interval [CI]: 2.27 to 4.47; p<0.001; reduction rate 65.9%), QoL scores increased significantly (SMD -3.12, 95% CI: -3.93 to -2.30; p<0.001; rate of increase 72.0%), and haemoglobin concentration increased significantly (SMD -2.13, 95% CI: -3.44 to -0.81; p=0.002; rate of increase 30.3%) at follow-up. The mean operation time was 34.48 minutes (95% CI: 22.82 to 46.13; p<0.001). The rate of reduction in myoma volume after microwave ablation was 85.3% (95% CI: 82.7% to 88.0%; p<0.001).[16]

Another systematic review (six articles; 541 patients with 647 fibroids) by Ierardi AM et al. 2018 also evaluated effectiveness in terms of improvement of symptoms and QoL and reduction in volume of the uterine myomas. Clinical success in terms of volume reduction rate was from 15.9% to 93.1%. This wide range of variability depends on the different time of instrumental follow-up (immediately after procedure and after six months). Studies in which clinical success was evaluated in terms of haemoglobin levels (measured before and after ablation procedures) showed an interesting improvement from 88.64 g/l to 123.21 g/l at three

months. Clinical success in terms of improvement of the QoL or health-related QoL measured using the UFS-QoL questionnaire reached normal level at 12-month or a significant improvement in scores after treatment ($p<0.05\%$). Ablation time ranging between 300 and 600 seconds. [17]

Most recently, Jonsdottira G et al. 2022 conducted a randomised controlled trial (RCT) to evaluate the efficacy, feasibility, and acceptability of microwave ablation compared to uterine artery embolisation as treatment for uterine fibroids among premenopausal women (n=17; 30-55 years). The primary outcome was volume difference of the three largest fibroids at six months post-treatment. Secondary outcomes included symptom severity score (SSS), health-related QoL, and length of hospitalisation. The study demonstrated that the volume fibroids reduction was 41.8% in the microwave ablation group compared to 62.2% in the uterine artery embolisation group ($p=0.29$). In the same way, both methods led to improvements in SSS (56.9% versus 65.2%; $p=0.88$) and in health-related QoL (45.3% versus 76.0%; $p=0.88$) without significant differences between groups. However, days of hospitalisation and sick leave were significantly fewer in the microwave ablation group ($p<0.001$ and $p=0.001$). Both methods were highly acceptable, measured as a recommendation of the method to a friend ($p=0.097$).[18]

An RCT by Lin XL et al. 2020 compared percutaneous microwave ablation and US-guided RFA for treating 133 women with symptomatic uterine adenomyosis. All patients were followed up for 12 months. Assessment endpoints included treatment time, percentage of ablated, percentage uterine regression, SSS, dysmenorrhoea scores, and adverse events. The study revealed that the mean ablation time was 16.3 ± 4.9 minutes in the microwave ablation group, which was demonstrably superior to that of the RFA group (37.5 ± 6.2 minutes). The mean percentages of ablation of uterine adenomyosis were 79.7 ± 15.1% and 79.2 ± 14.2% in the microwave ablation group and the RFA group, respectively. The percentages of regression of uterine volume also showed no marked difference between the two groups (71.7% versus 67.3%). Changes in the dysmenorrhoea scores (1.75 ± 1.13 versus 1.92 ± 0.79) and the SSSs (17.4 ± 5.0 versus 16.4 ± 4.8) after ablation were similar in the microwave ablation and RFA, and no significant difference was found between the groups.[19]

Beermann M et al. 2022 presented a long-term effect in patients treated with microwave ablation for symptomatic uterine fibroids and investigated fibroid characteristics predictive of successful treatment. A total of 16 patients underwent contrast enhanced MRI before treatment, postoperatively at 6-month and at long-term follow-up (between 16 and 36 months) to assess volumes of treated fibroids (n=42). Validated questionnaires for evaluation of uterine fibroid symptoms (UFS-QoL) and menstrual bleeding (Pictorial Bleeding Assessment Chart, PBAC) were used to assess long-term effects on symptoms. They found that most patients (82%) reported improvement up to three years after treatment. Out of 42 treated fibroids, 35 (83%) continued to shrink over time with median relative volume reduction

of 77%. For eight fibroids (19%) which showed low vascularization on the pre-treatment MRI, there was less shrinkage compared to well-vascularised fibroids (p=0.01). Most fibroids (79%) showed iso- to hyperintense T2 signal on preoperative MRI and showed a higher grade of shrinkage than hypointense fibroids (p=0.02).[20]

A retrospective observational study by Xia J et al. published in 2022 evaluated US-guided percutaneous microwave ablation for a single uterine fibroid greater than 300 cm^3. A total of 37 patients were followed up for 12 months postoperatively to assess the postoperative lesion volume reduction rate, degree of symptomatic relief, improvements in QoL, and occurrence of adverse events. Considering the results, lesion volume significantly decreased from 334.28 cm^3 (95% CI: 326.75 to 366.73) preoperatively to 52.01 cm^3 (95% CI: 46.95 to 74.69) at the 12-month follow-up (difference: 280.15 cm^3; 95% CI: 267.92 to 294.65; p<0.001). The lesion volume reduction rates at 1, 3, 6, and 12 months postoperatively were 27.30% (95% CI: 24.12 to 31.45), 52.90% (95% CI: 47.95 to 55.80), 67.90% (95% CI: 63.03 to 70.77), and 84.00% (95% CI: 80.22 to 85.94), respectively. The differences in the preoperative and postoperative UFS-QoL questionnaire scores were significant (p<0.01). The haemoglobin levels of the anaemic patients were also significantly elevated after the procedure (p<0.001).[21]

Meanwhile, Li QY et al. 2022 investigated the mid-term local treatment efficiency of US-guided percutaneous microwave ablation for uterine fibroids and the associated influencing factors. A total of 28 patients with 52 uterine fibroids who had undergone microwave ablation were retrospectively included in this study. Pre-treatment clinical characteristics, conventional ultrasound and contrast-enhanced ultrasound (CEUS) features were analysed to explore their correlation with volume reduction ratios (VRRs) of sufficient ablation (i.e., a VRR of at least 50% at the 3-month follow-up). The patients were assessed at 1-, 3-, 6-month follow-up after microwave ablation treatment and the assessment included VRR, UFS-QoL scores, clinical symptoms, and adverse events. At the 1-, 3-, 6-month follow-up, the median VRRs of uterine fibroids were 30.1%, 46.9%, and 65.8%, respectively. At the 3-month follow-up, 44.4% of fibroids obtained sufficient ablation while the remaining 55.6% obtained partial ablation (i.e., a VRR of <50%). Non-enhancing area during the early phase (i.e., within 30 seconds after injecting contrast agent) on pre-treatment CEUS was present in 22.2% uterine fibroids, which was associated with sufficient ablation at the 3-month follow-up (p<0.05). In addition, the relevant clinical symptoms of all patients were alleviated or removed. The UFS and QoL score after microwave ablation decreased significantly in comparison with those after microwave ablation (p=0.04 and p=0.057, respectively), indicating a remarkable improvement of clinical symptom and QoL.[22]

SAFETY

The procedures of microwave ablation for uterine fibroids were tolerated well and no major adverse events or complications, as those requiring further interventions and/or hospitalization was reported in the included studies. Minor complications were observed, in particular lower abdominal pain, low grade fever, and a small amount of vaginal secretion.[16-17, 21-22] By comparison, there were more adverse events in the uterine artery embolisation group (temporary menopausal symptoms that subsided after three months and patients entered menopause after the treatment at the age of 45 and 48 respectively) compared to none in the microwave ablation group.[18] Moreover, there was no significant differences in the incidence of common and severe adverse events between microwave ablation and RFA treatment.[19]

Above all, there was no retrievable information on USFDA approval or CE mark related to microwave ablation for uterine fibroids.

COST-EFFECTIVENESS

There was no retrievable evidence on the cost-effectiveness of microwave ablation for uterine fibroids. However, the price ranged from USD $5,000 to USD $6,000 per device while average ablation procedure starting from USD $35 per treatment, depending upon the patient and the case.[23-24]

CONCLUSION

Based on the above review, microwave ablation treatment resulted in significant alleviation of uterine fibroids-related symptoms and improvement in QoL, relatively short operation time, and obvious reduction in uterine fibroids volume. No major adverse events were reported, and the minor adverse events were self-limiting without any permanent adverse effects, indicating the safety of the treatment. Hence, as a minimally invasive alternative to surgical interventions, microwave ablation is a promising technique for treating uterine fibroids especially for women who want to avoid surgery. However, larger, comparative studies are still needed to better demonstrate the benefits of microwave ablation in the management of uterine fibroids.

REFERENCE

1. Bulun SE. Uterine fibroids. N Engl J Med. 2013; 369: 1344-1355
2. Donnez J, Dolmans MM. Uterine fibroid management: from the present to the future. Hum Reprod Update. 2016; 22: 665-686
3. Donnez J, Donnez O, Dolmans MM. With the advent of selective progesterone receptor modulators, what is the place of myoma surgery in current practice? Fertil Steril. 2014; 102: 640–648
4. Wang Y, Zhang S, Li C et al. Minimally invasive surgery for uterine fibroids. Ginekol Pol. 2020; 91: 149-157
5. Ierardi AM, Carnevale A, Pellegrino F et al. Uterine myomas: extravascular treatment. Semin Ultrasound CT MR. 2021; 42: 56-74
6. Arleo K, Khilnani M, Ng A et al. Features influencing patient selection for fibroid treatment with magnetic resonance-guided focused ultrasound. J Vasc Interv Radiol. 2007; 18: 681-685
7. Meng X, He G, Zhang J et al. A comparative study of fibroid ablation rates using radiofrequency or high-intensity focused ultrasound. Cardiovasc Intervent Radiol. 2010; 33: 794-799
8. Zhao W-P, Han Z-Y, Zhang J et al. A retrospective comparison of microwave ablation and high intensity focused ultrasound for treating symptomatic uterine fibroids. Eur J Radiol. 2015; 84: 413-417
9. Cho HH, Kim JH, Kim MR. Transvaginal radiofrequency thermal ablation: a day-care approach to symptomatic uterine myomas. Aust NZ J Obstet Gynaecol. 2008; 48: 296-301
10. Simon CJ, Dupuy DE, Mayo-Smith WW. Microwave ablation: principles and applications. RadioGraphics. 2005; 25(1): S69-S83
11. Hinshaw JL, Lubner MG, Ziemlewicz TJ et al. Percutaneous tumor ablation tools: microwave, radiofrequency, or cryoablation−what should you use and why? RadioGraphics. 2014; 34: 1344-1362
12. Li M, Yu X, Liang P et al. Ultrasound-guided percutaneous microwave ablation for hepatic malignancy adjacent to the gallbladder. Int J Hyperthermia. 2015; 31: 579-587
13. Ren C, Liang P, Yu XL et al. Percutaneous microwave ablation of adrenal tumours under ultrasound guidance in 33 patients with 35 tumours: A single-centre experience. Int J Hyperthermia. 2016; 32: 517-523
14. Yue W, Chen L, Wang S et al. Locoregional control of recurrent papillary thyroid carcinoma by ultrasound-guided percutaneous microwave ablation: A prospective study. Int J Hyperthermia. 2015; 31: 403-408
15. Liang P, Gao Y, Zhang H et al. Microwave ablation in the spleen for treatment of secondary hypersplenism: a preliminary study. AJR Am J Roentgenol. 2011; 196: 692-696

16. Lu Liu, Wang T, Lei B. Ultrasound-guided microwave ablation in the management of symptomatic uterine myomas: A systematic review and meta-analysis. J Minim Invasive Gynecol. 2021; 28(12): 1982-1992
17. Ierardi AM, Savasi V, Angileri SA et al. Percutaneous high frequency microwave ablation of uterine fibroids: systematic review. BioMed Res Int. 2018; 2018: 2360107
18. Jonsdottir G, Beermann M, Cronsioe A et al. Ultrasound guided microwave ablation compared to uterine artery embolisation treatment for uterine fibroids - a randomized controlled trial. Int J Hyperthermia. 2022; 39(1): 341-347
19. Lin XL, Hai N, Zhang J, et al. Comparison between microwave ablation and radiofrequency ablation for treating symptomatic uterine adenomyosis. Int J Hyperthermia. 2020; 37: 151-156
20. Beermann M, Jonsdottir G, Cronisoe A et al. Long term follow-up of uterine fibroids treated with microwave ablation: an up to 3-year observational study of volume, regrowth, and symptoms. Int J Hyperthermia. 2022; 39(1): 1158-1163
21. Xia J, Teng D, Sui G et al. Effectiveness and safety of ultrasound-guided percutaneous microwave ablation for a single uterine fibroid greater than 300 cm^3. J Minim Invasive Gynecol. 2022; S1553-4650(22)01049-4
22. Li QY, Li XL, Deng EY et al. Ultrasound-guided percutaneous microwave ablation for uterine fibroids: mid-term local treatment efficiency and associated influencing factors. Br J Radiol. 2022; 95(1137): 20220039
23. Microwave endometrial ablation cost in Malaysia. Country wise cost comparison for microwave endometrial ablation. Available at https://medigence.com/hospitals/general-surgery/microwave-endometrial-ablation/malaysia
24. Best Endometrial Ablation Hospitals and Cost in Malaysia. Available at https://www.lyfboat.com/hospitals/endometrial-ablation-hospitals-and-costs-in-malaysia/

Prepared by

Syful Azlie Md Fuzi
Biochemist
Principal Assistant Director
Health Technology Assessment Section (MaHTAS)
Medical Development Division
Ministry of Health Malaysia

Reviewed by

Dr. Roza Sarimin
Public Health Physician
Senior Principal Assistant Director
Health Technology Assessment Section (MaHTAS)
Medical Development Division
Ministry of Health Malaysia

Dr. Izzuna Mudla Mohamed Ghazali
Public Health Physician
Deputy Director
Health Technology Assessment Section (MaHTAS)
Medical Development Division
Ministry of Health Malaysia

26th January 2023