Comparison of thermal ablative methods and myomectomy for the treatment of fibroids: a systematic review and meta-analysis

Deku Liang¹, Juan Li², DanDan Liu³, Hu Zhao⁴ and Yonghong Lin⁵

¹Department of Obstetrics and Gynecology, Chengdu Women and Children’s Central Hospital Affiliated to University of Electronic Science and Technology of China, Chengdu, China; ²Department of Interventional Radiography, Chengdu Women and Children’s Central Hospital Affiliated to University of Electronic Science and Technology of China, Chengdu, China

ABSTRACT
Objective: To examine the effectiveness and safety of thermal ablative methods and myomectomy for the treatment of uterine fibroids.

Materials and methods: We searched EMBASE, PubMed, the Cochrane Central Register of Controlled Trials, Scopus, CINAHL, ClinicalTrials.gov and Web of Science databases through April 2021. Clinical trials comparing the thermal ablative methods and myomectomy for the treatment of uterine fibroids were included.

Results: Thirteen studies including 4205 patients were eligible. The thermal ablative treatment group was associated with less major adverse events (only ultrasound guided high-intensity focused ultrasound) (RR, 0.111 [95% CI, 0.070–0.175], p = 0.0), shorter duration of hospital stays in observational studies (-0.1497 day, [95% CI, -1.593 to -0.321], p = 0.0) and in randomized controlled trials (RCTs) (-0.844 day, [95% CI, -0.1142 to -0.546], p = 0.0), higher uterine fibroid symptom (UFS) score after operation (0.252 [95% CI, 0.165–0.339], p = 0.0), transformed symptom severity (tSS) score after operation (0.515 [95% CI, 0.355–0.674], p = 0.0) and quality of life (QoL) score after operation (0.188 [95% CI, 0.093–0.283], p = 0.0) in comparison with myomectomy group. No statistically significant difference was found between the thermal ablative treatment group and myomectomy group with respect to reintervention rate and pregnancy rate.

Conclusion: The current data available demonstrate that thermal ablative methods were not inferior to myomectomy in the treatment of uterine fibroids. The findings in this study need to be further confirmed by large RCTs.

Introduction
Uterine fibroids are the most common solid pelvic tumors in women of reproductive age [1], and are often associated with symptoms including heavy menstrual bleeding, abdominal pain and pressure [2]. Prevalence varies from 50% to 77% depending on the method used for diagnosis [3]. There are many modalities for the management of symptomatic fibroids, including abdominal, laparoscopic or hysteroscopic myomectomy, hysterectomy; thermal laser, radiofrequency energy, focused ultrasound, microwave energy [4]; or interventional treatment by uterine artery embolization (UAE) [5].

For patients who prefer to preserve their fertility, uterus-sparing treatments for symptomatic fibroids are better options. In addition to myomectomy, UAE emerged as an alternative therapy during the 1990s. It has been proven to be an effective and safe treatment for women who wish to preserve their uterus [6]. However, the use of UAE in pregnant women remains controversial. A previous meta-analysis found that pregnancies in the UAE group were associated with higher rates of preterm delivery and malpresentation than those in the laparoscopic myomectomy group [7]. Thermal ablative approaches with respect to medical therapies are those which ablate pathological tissues through thermal injury, such as by using devices creating focused ultrasound, radiofrequency energy or microwave energy. These are applicable in various diseases, such as hepatocellular carcinoma, sarcoma, renal cell carcinoma and bone metastases [8–11]. Over the years, thermal ablative approaches for uterine fibroids have been developed and applied effectively [4]. When the local temperature of tissue reaches to 50–52 °C for 4–6 min, irreversible cellular damage is observed [12]. As temperature increases to 60–100 °C, coagulative necrosis occurs due to irreversible damage caused by protein coagulation [13,14]. Different thermal ablative systems for the treatment of uterine fibroids have been invented and refined...
Records identified through database searching (n = 899)

Additional records identified through other sources (n = 0)

Records after duplicates removed (n = 257)

Records screened (n = 257)

Records excluded (n = 89)
abstracts, conferences, reviews (32)

Full-text articles assessed for eligibility (n = 168)

Full-text articles excluded (n = 155)
Insufficient data (22)
Not association study (35)

Studies included in qualitative synthesis (n = 13)

Studies included in quantitative synthesis (meta-analysis) (n = 13)

**Figure 1.** PRISMA flow diagram for the meta-analysis.

**Table 1.** Basic information of all included studies used for meta-analysis.

| Study       | Year | Country | Type       | Interventions                                                                 | Age (years) | Newcastle-Ottawa scale |
|-------------|------|---------|------------|-------------------------------------------------------------------------------|-------------|------------------------|
| FL Wang     | 2013 | China   | POS        | USgHIFU treatment                                                             | 37.9 ± 5.5  | 1(S) + 2(C) + 3(O) = 6 |
|             |      |         |            | Laparoscopic myomectomy                                                       | 38.4 ± 5.0  |                        |
| Liu         | 2017 | China   | POS        | USgHIFU treatment                                                             | 41.3 ± 5.08 | 1(S) + 2(C) + 3(O) = 6 |
|             |      |         |            | Laparoscopic myomectomy                                                       | 40.93 ± 5.02|                        |
| Chen        | 2018 | China   | POS        | USgHIFU treatment                                                             | 42.59 ± 6.74| 2(S) + 1(C) + 3(O) = 6 |
|             |      |         |            | Myomectomy (open surgery, laparoscopic or transvaginal)                       | 38.74 ± 6.82|                        |
| Sasson      | 2018 | Israel  | POS        | MRgFUS treatment                                                              | 44 ± 4      | 1(S) + 2(C) + 2(O) = 5 |
|             |      |         |            | Laparoscopic or robotic assisted laparoscopic myomectomy                      | 38 ± 7      |                        |
| Brooks      | 2020 | USA     | POS        | TFA with the Sonata” system                                                   | 33.8 ± 5.23 | 1(S) + 2(C) + 3(O) = 6 |
|             |      |         |            | Myomectomy                                                                   | 34.5 ± 5.28 |                        |
| Hu          | 2020 | China   | POS        | USgHIFU treatment                                                             | 33.8 ± 5.2  | 1(S) + 2(C) + 3(O) = 6 |
|             |      |         |            | Hysteroscopic myomectomy                                                      | 33.8 ± 5.9  |                        |
| Liu         | 2020 | China   | ROS        | USgHIFU treatment                                                             | 33.8 ± 5.9  | 2(S) + 1(C) + 2(E) = 5 |
|             |      |         |            | Myomectomy (abdominal, laparoscopic or hysteroscopic)                        | 37.4 ± 6.9  |                        |
| Wang        | 2020 | China   | ROS        | USgHIFU treatment                                                             | 33.8 ± 5.9  | 2(S) + 1(C) + 2(E) = 5 |
|             |      |         |            | Laparoscopic myomectomy                                                      | 33.8 ± 5.9  |                        |
| Wu          | 2020 | China   | POS        | USgHIFU treatment                                                             | 33.8 ± 5.9  | 2(S) + 1(C) + 2(E) = 5 |
|             |      |         |            | Myomectomy (abdominal, laparoscopic or hysteroscopic)                        | 33.8 ± 5.9  |                        |
| Jiang       | 2021 | China   | ROS        | USgHIFU treatment                                                             | 33.8 ± 5.9  | 2(S) + 1(C) + 3(E) = 6 |
|             |      |         |            | Laparoscopic myomectomy                                                      | 33.8 ± 5.9  |                        |
| XY Wang     | 2013 | China   | RCT        | USgHIFU treatment                                                             | 33.8 ± 5.9  | 2(S) + 1(C) + 3(E) = 6 |
| Brucker     | 2014 | Germany | RCT        | RFVTA treatment                                                               | 33.8 ± 5.9  |                        |
|             |      |         |            | Myomectomy                                                                   | 33.8 ± 5.9  |                        |
| Rattray     | 2018 | Canada  | RCT        | Lap-RFA treatment                                                             | 33.8 ± 5.9  |                        |

C: comparability; E: exposure; Lap-RFA: laparoscopic ultrasound-guided radiofrequency ablation; MRgFUS: MR-guided focused ultrasound; O: outcome; ROS: retrospective observational study; RCT: randomized controlled trial; S: selection; RFVTA: laparoscopic radiofrequency volumetric thermal ablation; TFA: transcervical fibroid ablation; USgHIFU: ultrasound-guided high-intensity focused ultrasound.

Values are mean or mean (standard difference).
to treat the maximum amount of fibroid tissue safely, while avoiding damage to the surrounding normal uterine tissue. Some of the systems are laparoscopic radiofrequency ablation system, transcervical radiofrequency ablation system and high-intensity focused ultrasound ablation system guided by ultrasound or MRI [15–18].

As minimally invasive methods for fibroids, thermal ablative treatments are expected to provide better options for patients who want to preserve their uteri, especially those with a desire for fertility. We performed this meta-analysis to examine the effectiveness and safety of thermal ablative methods and myomectomy for the treatment of uterine fibroids.

**Methods**

The present meta-analysis was conducted based on the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines [19].

**Eligibility criteria**

Articles were included if they: (1) were comparative trials; (2) compared thermal ablative methods and myomectomy for the treatment of uterine fibroids; and (3) were published in English.

**Exclusion criteria**

Articles were excluded if they were: (1) animal experiments; (2) duplicated trials; (3) trials without comparative groups; (4) reviews; (5) comments; (6) case reports; or (7) publications not in English.

**Sources of information**

We searched EMBASE, PubMed, the Cochrane Central Register of Controlled Trials, Scopus, CINAHL, ClinicalTrials.gov and Web of Science databases for relevant trials to April 2021. Studies were identified using the following MeSH descriptors: ‘thermal’, ‘ablation’, ‘myolysis’, ‘coagulation’, ‘myomectomy’ and ‘Leiomyoma’.

**Study selection**

Two investigators performed the literature search and criteria selection independently. Retrieved articles would be included in our meta-analysis if they met the eligible criteria. Any disagreements were resolved by consensus.

**Data collection process**

Two reviewers extract data independently based on a previously designed Excel form. Reintervention rate was regarded as the primary endpoint. Secondary endpoints included major
adverse events, hospital stay, pregnancy rate, uterine fibroid symptom (UFS) score after operation, quality of life (QoL) score after operation and transformed symptom severity (tSS) score after operation. Extracted data included the first author, published time, country, study type, age of patients and type of interventions. The data form included mean (standard deviation (SD)) values and number of events. However, when only the median, median (range) or median (Q1–Q3) values were reported, the estimated mean (SD) values were attained based on the estimated formula reported [20,21].

**Table 2.** The pooled results of all meta-analysis.

| Clinical outcomes                        | No. of studies | No. of patients | Pooled results | Overall effect | Heterogeneity |
|-----------------------------------------|----------------|-----------------|----------------|---------------|---------------|
|                                         |                |                 |                | Z   | p   | I² (%) | p   |
| Reintervention rate (observational studies) | 4              | 827             | 0.760 (0.519, 1.115) | 1.40 | .160 | 22.9    | .274 |
| Reintervention rate (RCTs)              | 2              | 95              | 5.905 (0.741, 47.046) | 1.66 | .094 | 0.0     | .594 |
| Major adverse events                    | 6              | 2761            | 0.111 (0.070, 0.175) | 9.47 | .0   | 87.5    | .0   |
| Hospital stay (observational studies)   | 5              | 2404            | –1.497 (–1.593, –0.321) | 30.38 | .0   | 95.2    | .0   |
| Hospital stay (RCTs)                    | 3              | 195             | –0.844 (–1.142, –0.546) | 5.55 | .0   | 82.7    | .0   |
| Pregnancy rate                          | 2              | 1002            | 1.012 (0.933, 1.098) | 0.29 | .796 | 0.0     | .641 |
| UFS score                               | 3              | 2363            | 0.252 (0.165, 0.339) | 5.68 | .0   | 61.2    | .076 |
| QoL score                               | 2              | 2017            | 0.188 (0.093, 0.283) | 3.88 | .0   | 38.8    | .201 |
| tSS score                               | 3              | 694             | 0.515 (0.355, 0.674) | 6.33 | .0   | 96.7    | .0   |

RCT: randomized controlled trial; UFS: uterine fibroid symptom; QoL: quality of life; tSS: transformed symptom severity. Values stand risk difference (95% confidence interval), other values stand standard mean difference (95% confidence interval).

**Table 3a.** Reintervention rate (observational studies).

| Study (year) | Events | Total | Events | Total |
|--------------|--------|-------|--------|-------|
| Liu (2017)  | 1      | 99    | 0      | 67    |
| Sasson (2018)| 9      | 68    | 5      | 64    |
| Liu (2020)  | 13     | 95    | 15     | 84    |
| Wang (2020) | 24     | 235   | 21     | 115   |

**Figure 4.** Forest plot of reintervention rate for observational studies.
**Risk of bias and applicability**

The quality assessment for randomized controlled trials (RCTs) was performed via the Cochrane Collaboration tool, which incorporated six items including sequence generation, allocation concealment, blinding, incomplete outcome data, selective outcome reporting and other sources of bias. The quality assessment for observational trials was performed by the Newcastle-Ottawa scale. A score of 7–9 was defined as ‘good’, 4–6 as ‘fair’ and <4 as ‘poor’ [22].

**Summary measures**

The results were expressed as the risk ratio (RR) or mean difference, with 95% CIs. Standardized mean difference (SMD) with 95% CI was calculated for continuous values.

**Synthesis of results**

The meta-analysis was performed using STATA software version 14.0 (STATA Corporation, College Station, TX).

| Table 3b. Reintervention rate (RCTs). |
|--------------------------------------|
| Study (year) | Events | Total | Events | Total |
| Brucker (2014) | 4 | 25 | 0 | 25 |
| Rattray (2018) | 1 | 23 | 0 | 22 |

| Table 4. Major adverse events. |
|--------------------------------|
| Study (year) | Thermal ablative treatment group | Myomectomy group |
| Study (year) | Events | Total | Events | Total |
| FL Wang (2013) | 17 | 89 | 11 | 41 |
| Chen (2018) | 3 | 1353 | 60 | 586 |
| Sasson (2018) | 0 | 20 | 1 | 22 |
| Liu (2020) | 0 | 101 | 18 | 87 |
| Brooks (2020) | 0 | 44 | 3 | 44 |
| Wang (2020) | 0 | 245 | 4 | 129 |

*Figure 5. Forest plot of reintervention rate for randomized controlled trials.*
Heterogeneity was evaluated by using $\chi^2$ and $I^2$ test. Heterogeneity was assumed to be high when $p<.1$ in the $\chi^2$ test and the $I^2$ index was over 50%. A fixed-effects model was used for the meta-analysis if there was no significant heterogeneity; otherwise, a random-effects model was used. Sensitivity analyses were conducted by removing the included studies one by one if heterogeneity was significant [23]. Publication bias was illustrated using a Begg funnel plot [24]. $p$ Values less than .05 were considered statistically significant.

Results

We identified 899 trials from the selected seven databases. A total of 642 trials were excluded based on the inclusion and exclusion criteria. After reviewing the full text of the remaining 257 trials, 10 observational studies [25–34] and three RCTs [35–37] were included finally. They were then selected for subsequent meta-analysis (Figure 1). Basic information about these 13 trials is shown in Table 1.

Table 5a. Hospital stay (observational studies).

| Study (year)       | Thermal ablative treatment group | Myomectomy group |
|--------------------|----------------------------------|------------------|
|                    | n      | Mean (SD) | n     | Mean (SD) |
| FL Wang (2013)     | 89     | 2.9 (1.5) | 41    | 6.2 (2.7) |
| Liu (2017)         | 99     | 3.86 (1.62) | 67    | 7.49 (1.62) |
| Chen (2018)        | 1353   | 3.6 (3.2) | 586   | 9 (3.1)   |
| Brooks (2020)      | 44     | 0.22 (0.06) | 44    | 1.9 (2.24) |
| Hu (2020)          | 39     | 2.56 (0.98) | 42    | 3.31 (0.96) |

Figure 6. Forest plot of major adverse events.
Risk of bias and concerns regarding applicability

We assessed the three RCTs based on the Cochrane Collaboration risk-of-bias tool (Figures 2 and 3). At the same time, the 10 observational studies were assessed based on the Newcastle-Ottawa scale (Table 1).

Measured outcomes

The pooled results of all measured outcomes are summarized in Table 2.

Reintervention rate

The incidence of reintervention was recorded in four trials comparing 827 patients in observational studies (RR, 0.760 [95% CI, 0.519–1.115], p=0.160) (Table 3a and Figure 4) and two trials comparing 95 patients in RCTs (RR, 5.905 [95% CI, 0.741–47.046], p=0.094) (Table 3b and Figure 5). There were no statistical differences between the two groups.

Major adverse events

The incidence of major adverse events was reported in six trials comparing 2761 patients in observational studies, and the thermal ablative treatment group was associated with less major adverse events (only ultrasound guided high-intensity focused ultrasound) in comparison with the myomectomy group (RR, 0.111 [95% CI, 0.070–0.175], p=0.0) (Table 4 and Figure 6).
Hospital stays were reported in five trials comparing 2404 patients in observational studies (−0.1497 day, [95% CI, −1.593 to −0.321], p = .0) (Table 5a and Figure 7) and three trials comparing 195 patients in RCTs (−0.844 day, [95% CI, −0.1.142 to −0.546], p = .0) (Table 5b and Figure 8). The duration of hospital stay was shorter in the thermal ablative treatment group than that in the myomectomy group.

Pregnancy rate

Two studies with 1002 women reported the outcome of pregnancy rate. There was no significant difference between the two groups in incidence of pregnancy rate (RR, 1.012 [95% CI, 0.933–1.098] p = .796) (Table 6 and Figure 9).

Assessment of treatment outcomes

The assessment of treatment outcomes included UFS scores, QoL scores and tSS scores after operation. UFS scores and QoL scores were obtained using the UFS and QoL questionnaires [38]. Both scores ranged from 0 to 100. A higher score on the UFS questionnaire indicates more serious symptoms, and on the QoL questionnaire indicates a better QoL. The tSS score was measured using the following formula: transformed score = (raw score − 8)/32 × 100. Three trials with 2363 women compared UFS scores (0.252 [95% CI, 0.165–0.339]; p = .0) (Table 7 and Figure 10), two trials with 2017 patients compared QoL scores (0.188 [95% CI, 0.093–0.283]; p = .0) (Table 8 and Figure 11), and three trials with 694 women compared tSS scores (0.515 [95% CI, 0.355–0.674]; p = .0) (Table 9 and Figure 12). Higher UFS, tSS...
and QoL scores after operation were found in the thermal ablative treatment group than those in the myomectomy group.

**Assessment of publication bias**

The Begg funnel plot test showed that there was no publication bias for the selected trials used in the present meta-analysis ($p = .452$) (Figure 13).

**Discussion**

Uterine fibroids are common in women of reproductive age. For these patients, pharmacotherapy may not produce satisfactory results, and there is an urgent to find an optimal therapeutic option. Myomectomy has long been considered the standard treatment for symptomatic fibroids in patients who desire to preserve their fertility. Abdominal, laparoscopic or hysteroscopic myomectomies are the main surgical modalities in use. Nevertheless, thermal ablative methods have proven to be effective alternatives to traditional myomectomy. The goal of this meta-analysis was to examine the comparative efficacy and safety of thermal ablative methods and myomectomy for the treatment of uterine fibroids.

The modalities of thermal ablative treatment for uterine fibroids vary in clinical practice. The result of therapy after percutaneous magnetic resonance (MR) image-guided laser ablation was found to be comparable to hysterectomy for the management of menorrhagia caused by fibroids [39]. Berman et al. [40] reported a significant improvement in symptoms by using radiofrequency volumetric thermal ablation in patients with fibroids. Zhang et al. [41] found that fibroids could shrink by 93.1% without complications and fever,
after percutaneous microwave thermal ablation. The safety and efficacy of focused ultrasound guided by ultrasound or MRI have been confirmed for the treatment of fibroids [42,43]. In the relevant 13 studies, we included, focused ultrasound therapy was used in 10 trials, and radiofrequency therapy was used in the rest.

Ji et al. [44] showed that high-intensity focused ultrasound treatment resulted in fewer clinical complications and adverse events than treatment with mifepristone, myomectomy or hysterectomy for uterine fibroids. Wang et al. [45] reported that high-intensity focused ultrasound was associated with higher risk of reintervention and shorter duration of hospital stay than myomectomy. Lin et al. [46] found an improved QoL and low-risk of reintervention after laparoscopic radiofrequency ablation for symptomatic fibroids. Though some systematic reviews have compared the efficacy of individual thermal ablation methods with other treatments for uterine fibroids, limited data can be found comparing thermal ablative methods and myomectomy for the treatment of uterine fibroids. We believe that our study makes a significant contribution to the literature because it clarifies the advantages of the thermal ablation procedures compared to myomectomy.

In our meta-analysis, 13 trials comprising 4205 patients were included. This study compared two thermal ablation methods, focused ultrasound and radiofrequency ablation with myomectomy. There was no significant difference in the reintervention rate between the thermal ablative treatment and myomectomy group, which differs from a previous meta-analysis comparing only focused ultrasound ablation with myomectomy [45]. In addition, fewer major adverse events and shorter duration of hospital stay were found in the thermal ablative treatment group, which is consistent with the previous meta-analysis [45]. The results showed no significant differences in pregnancy rate between the thermal ablative treatment and myomectomy groups. In the

| Study (year) | Thermal ablative treatment group | Myomectomy group |
|-------------|---------------------------------|------------------|
|             | n | Mean (SD) | n | Mean (SD) |
| Chen (2018) | 1353 | 85.84 (12.12) | 586 | 83.45 (11.28) |
| Hu (2020)   | 38  | 89.7 (13.69)  | 40  | 90.91 (11.7)  |

QoL: quality of life.
procedures of thermal ablative treatment, unlike myomec-
tomy, the leiomyomas are left in situ, so the UFS and tSS 
scores after operation may be higher in the thermal ablative 
treatment group than those in the myomectomy group. 
Nevertheless, the differences in absolute scores between the 
baseline assessed pre-operatively and the endpoint of obser-
vation after operation in the ablative treatment group could 
be higher than those in the myomectomy group [26]. This 
indicates that symptoms caused by fibroids improved much 
more in the thermal ablative treatment group than in the 
myomectomy group, which could explain why the QoL score 
was higher in the ablative treatment group. However, large-
scale randomized trials are needed to validate the findings. 

Table 9. tSS scores.

| Study (year) | n   | Mean (SD) | n   | Mean (SD) |
|--------------|-----|-----------|-----|-----------|
| Liu (2020)   | 101 | 21.75 (6.99) | 87  | 11.61 (4.62) |
| Wang (2020)  | 245 | 8.07 (2.65)  | 129 | 7.67 (3.1)   |
| Sasson (2018)| 64  | 17.36 (7.28) | 68  | 15.88 (4.81) |

tSS: transformed symptom severity.

In conclusion, based on this study and available evidence, 
thermal ablative methods were found to be not inferior to 
myomectomy in the treatment of uterine fibroids. But there 
is still lack of large-scale RCTs. Those results need fur-
ther validation.
Disclosure statement
No potential conflict of interest was reported by the author(s).

Funding
The author(s) reported there is no funding associated with the work featured in this article.

References
[1] Okolo S. Incidence, aetiology and epidemiology of uterine fibroids. Best Pract Res Clin Obstet Gynaecol. 2008;22(4):571–588.
[2] Drayer SM, Catherino WH. Prevalence, morbidity, and current medical management of uterine leiomyomas. Int J Gynaecol Obstet. 2015;131(2):117–122.
[3] Lethaby A, Vollenhoven B. Fibroids (uterine myomatosis, leiomyomas). BMJ Clin Evid. 2007;2007:0814.

Figure 12. Forest plot of transformed symptom severity (tSS) scores.

Figure 13. The Begg funnel plot of major adverse events.
