Best practices in minimally invasive gynecology: making sense of the evidence

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Chapter 10

Reintervention risk and quality of life outcomes after uterine-sparing interventions for fibroids: a systematic review and meta-analysis

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Abstract

Objectives: To compare uterine-sparing treatment options for fibroids in terms of reintervention risk and quality of life.

Design: Systematic review and meta-analysis according to PRISMA guidelines.

Setting: Not applicable.

Patients: Women with uterine fibroids undergoing a uterine-sparing intervention.

Interventions: Not applicable.

Main outcome measures: 1) Reintervention risk after uterine-sparing treatment for fibroids after 12, 36 and 60 months; and 2) quality of life outcomes, based on validated questionnaires. Two separate analyses were performed for the procedures that used an abdominal approach (myomectomy, uterine artery embolization [UAE], artery ligation, high-intensity focused ultrasound [HIFU], laparoscopic radiofrequency ablation [RFA]) and for the procedures managing intracavitary fibroids (hysteroscopic approach, including hysteroscopic myomectomy and hysteroscopic RFA).

Results: There were 85 articles included for analysis, representing 17,789 women. Stratified by treatment options, reintervention risk after 60 months was 12.2% (95% confidence interval 5.2–21.2%) for myomectomy, 14.4% (9.8–19.6%) for UAE, 53.9% (47.2–60.4%) for HIFU, and 7% (4.8–9.5%) for hysteroscopy. For the other treatment options, no studies were available at 60 months. For quality of life outcomes, symptoms improved after treatment for all options. The HIFU procedure had the least favorable outcomes.

Conclusions: Despite the substantial heterogeneity of the study population, this meta-analysis provides valuable information on relative treatment efficacy of various uterine-sparing interventions for fibroids, which is relevant when counseling patients in daily practice. Furthermore, this study demonstrates that long-term data, particularly for the newest uterine-sparing interventions, are urgently needed.

Introduction

Fibroids are the most common benign tumors of the female genital tract, with a symptomatic occurrence rate of 20–40% in reproductive-age women.[1] For women requiring surgical treatment but desiring uterine conservation, myomectomy has typically been the first choice for intervention. Yet technologic advances have led to a wider range of available options, depending on the location and number of fibroids, the indication for treatment, patient preference, and technologic facilities of hospitals. Uterine artery embolization (UAE) is one of the alternatives, and this well-studied technique has been used in many countries for more than three decades.[2] Other treatment options include, among others, radiofrequency ablation (RFA), (laparoscopic) ligation, and cryoablation. Advanced techniques, such as high-intensity focused ultrasound (HIFU), also have recently emerged, and are applicable without the need for surgical intervention.

Data regarding the feasibility of these uterine-sparing treatment options vary, and limited information exists on relative efficacy. Guidelines from the American College of Obstetricians and Gynecologists,[3] the National Institute for Health and Care Excellence (United Kingdom),[4] and the Society of Obstetricians and Gynecologists of Canada[5] on this topic state that patients should be counseled about the different available treatment options but do not define a preferred intervention. The objective of the present systematic review and meta-analysis was to evaluate the relative efficacy of the various uterine-sparing options for treating fibroids. We specifically aimed to compare the different techniques in terms of reintervention risk and quality of life.

Materials and methods

Eligibility criteria, information sources, search strategy

A systematic review was conducted following the PRISMA guidelines.[6] No study protocol was available. A literature search was set up in collaboration with a clinical librarian, and original articles were identified though Pubmed, Medline, Embase, and Web of Science. The exact search terms are presented in Supplemental Appendix 1 (Supplemental Appendices 1–4 are available online at www.fertstert.org). The literature search was restricted to studies published from January 2000 through February 2017. By selecting only recent studies, we aimed to provide an overview of current treatment options. We considered randomized controlled trials (RCT) and cohort studies (both noncomparative and comparative) only. Review articles, technical reports, animal studies, non-English studies, published abstracts without a full manuscript, and reports from meetings were excluded.

Studies eligible for inclusion were studies evaluating at least one of our primary outcomes: 1) surgical reintervention risk after uterine-sparing treatment; and 2) quality of life after treatment. In addition, studies had to have a minimum follow-up time of 12 months. We defined reintervention as any additional treatment needed at least one year after treatment owing to symptomatic recurrence of fibroids. Reinterventions directly related to procedure complications were excluded, and dilation and curettage was not considered to be reintervention. Because we aimed to study the reintervention risk after a first treatment for fibroids, studies were also excluded when all women in the cohort had an earlier history of intervention for fibroids. To reliably compare the quality of life outcomes, we limited our selection to studies using the Severity Symptom Score (SSS) or the Health-Related Quality of Life questionnaire (HRQL). Both have been validated for assessment of fibroid-related symptoms.[7] The SSS and HRQL are scored from 0 to 100. When symptoms improve, the SSS score decreases whereas the HRQL score increases.

Study selection

The first two authors (E.M.S. and F.H.M.P.T.) independently screened titles and abstracts for relevance. Potentially relevant studies were obtained in full text and assessed for inclusion. In case of disagreement, a third author (F.W.J.) was consulted. The references of the selected articles were cross-checked to identify other potentially relevant studies.

Data extraction

From the included studies, we extracted data regarding primary outcomes (reintervention risk and quality of life) and baseline characteristics. Variables of interest included study characteristics (study design, type(s) of treatment, country where the study was conducted, and potential source of funding) and patient characteristics (age, body mass index [BMI], and fibroid weight).

Data were pooled for meta-analysis for our primary outcomes at 12, 36 and 60 months after intervention. For the comparative studies included, each intervention group was assessed separately. Two separate analyses were performed for procedures approaching the fibroids through the abdomen (henceforth called abdominal approach) and for procedures managing intracavitary fibroids (henceforth called hysteroscopic approach). Additional subanalyses were performed to specifically evaluate the number of women undergoing hysterectomy after initial therapy.

Assessment of risk of bias

To assess the risk of bias for each study, the following criteria were employed: 1) inclusion of consecutive patients (if it was not stated that patients were consecutively included, risk of bias was assessed as unclear); 2) rate of patients that had infertility as indication for treatment, because it may influence or limit treatment choice (<10% of the study population with infertility indication was considered to indicate low risk of bias and >20% high risk); and 3) loss to follow-up rate (<10% loss to follow-up was considered to indicate low risk of bias and >20% high risk). The template of Review Manager (version 5.1) was used for data organization.

Data synthesis and statistical analysis

Descriptive characteristics were summarized with the use of SPSS version 23.0. Continuous data were presented as range and categoric data as frequency with percentage. Meta-analysis was performed with the use of Stata (version 14, Statacorp). The reintervention risk and the difference of the means of the quality of life scores were pooled in a random effects model, and 95% confidence intervals (95% CIs) were reported. In cases where only median and range were available, instead of the mean and standard deviation, data were transformed as described by Hozo et al.[8]

Results

Study and patient characteristics

The search strategy identified 3,250 unique articles. Full texts of more than 600 articles were reviewed because the reintervention risk was usually not a primary end point in studies and therefore not explicitly mentioned in the abstract.

As demonstrated in Supplemental Figure 1 (available online at www.fertstert.org), 85 original articles were deemed eligible for inclusion in this review. Eight of the studies were randomized controlled studies[9-16] and 77 were cohort studies.[17-93] Fourteen studies, of which six were RCTs, compared two different uterine-sparing treatment options (e.g. myomectomy vs. UAE).[9;10;12-15;21;35;59;60;64;75;84,93] These studies were therefore included in two main categories. Supplemental Appendix 2 (available online) provides a summary of the characteristics of the included studies.

Fifteen studies included at least in part the same cohort of patients.[9;10;12;15;32;35;42;59;63;69;72;77;94-96] Efforts were made to ensure that data from each patient was not included more than once.

Two studies were eventually excluded because we could not correct for the overlapping study period.[95;97]

Of the included studies, 33 originated from Europe (38.8%), 23 from North America (27.0%), 22 from Asia (25.9%), four from Africa (4.7%), two from Australia (2.4%) and one from Latin America (1.2%). In 29 studies (34.1%), disclosures regarding funding were reported: in 14 studies, research had been funded by a medical device company (Biocompatibles, Biosphere Medical, Boston Scientific, Gynesonics, Halt Medical, and Insightec); the other 15 studies were funded by governmental funds, research institutes, and charity organizations.

Data regarding ten treatment options was identified: abdominal, laparoscopic or robotic myomectomy, hysteroscopic myomectomy, UAE, (laparoscopic) ligation, HIFU, laparoscopic and hysteroscopic RFA, percutaneous microwave ablation, and cryoablation. An eleventh treatment option, laparoscopic uterine artery occlusion, was described in studies,[98-100] but none of those studies met our inclusion criteria. For the analysis, the data of abdominal, laparoscopic, and robotic myomectomy were combined (henceforth called myomectomy), as were the data of laparoscopic RFA and percutaneous microwave ablation, both thermal ablations. The abdominal approach included six different interventions: myomectomy, UAE, artery ligation, HIFU, laparoscopic RFA, and cryoablation. The hysteroscopic approach consisted of hysteroscopic myomectomy and hysteroscopic RFA.

Baseline characteristics of the study population are summarized in Table 10.1. The total study population included 17,789 women. A total of 15,348 women (87.8%) had undergone an abdominal approach and 1,912 (12.2%) a hysteroscopic approach. The UAE group had the largest study population (8,244), followed by myomectomy (5,114) and hysteroscopic myomectomy (1,741). For the laparoscopic cryoablation and artery ligation procedures, one study was available for each treatment option.

The mean ages of the studied populations ranged from 29.3 to 47.9 years, the mean BMIs from 21.2 to 56.6 kg/m^2, and the mean fibroid weights from 18.8 to 538.5 grams. Because only means were available from every individual study, it was not possible to calculate if the outcome measures of these baseline characteristics were statistically different between the different treatment options.

Risk of bias of the included studies

A summary of risk of bias for the individual studies is depicted in Supplemental Appendix 3 (available online). In the myomectomy group and the hysteroscopic myomectomy group, none of the studies excluded infertility as indication of treatment. For the other treatment options, approximately one-half of the studies explicitly mentioned excluding infertility.

Table 10.1: Baseline characteristics

	Number of studies or substudies	Number of patients	Age (year)	Number of studies or substudies	BMI (kg/m^2)	Number of studies or substudies	Fibroid weight (grams)	Number of studies or substudies
Overall	96	17,489	29.3–47.9	81	21.2–56.6	24	18.8–538.5	32
Abdominal approach								
Myomectomy	20	5114	29.3–43.5	15	21.2–27.5	7	--	--
UAE	40	8244	32.3–47.0	34	23–28.4	5	59–538.5	12
Artery ligation	1	50	39.6	1	--	--	180.9	1
Laparoscopic RFA	8	652	40.0–43.6	8	22.7–30.5	5	76.8–95.0	2
(MR/US)-HIFU	17	1548	36.2–46.0	14	21.6–56.6	6	53.2–396.3	13
Laparoscopic cryoablation	1	20	46.9	1	27.6	1	75	1
TOTAL	87	15,348	29.3–47.0	74	21.2–56.6	24	53.2–538.5	29
Hysteroscopic approach								
Hysteroscopic myomectomy	6	1741	31.4–47.9	5	--	--	--	--
Hysteroscopic RFA	3	120	40.1–40.8	2	--	--	18.8–112.4	3
TOTAL	9	1912	31.4–47.9	7	--	--	18.8–112.4	3

Data are presented as range of the means (minimum-maximum).
UAE= uterine artery embolization; RFA=radiofrequency ablation.

For 'loss to follow-up', a high risk of bias was observed in all groups. This was mainly attributed to studies focusing on long-term quality of life questionnaires after treatment.

Primary outcomes

Additional figures of the data from this section are available in Supplemental Appendix 4 (available online).

Reintervention risk for the abdominal procedures

The reintervention risks for the six abdominal procedures are presented in Table 10.2. Almost all analyses demonstrated considerable statistical heterogeneity. At 12 months, the reintervention risk for these abdominal procedures varied from 0.3% (laparoscopic RFA, 95% CI 0–1.6%; I^2=0%, 6 studies) up to 15% (cryoablation, 1 study). At 36 months, the reintervention risk varied from 1.2% (myomectomy, 0–5.2%, 4 studies) to 34.7% (HIFU, 27.3–42.4%, 4 studies). At 60 months, reintervention risks were 12.2% (5.2–21.2%; I^2=95.2%; 10 studies) for myomectomy, 14.4% (9.8–19.6%; I^2=65.9%; 17 studies) for UAE, and 53.9% (47.2–60.4%; I^2=99.5%; 2 studies) for HIFU (Figure 10.1). For artery ligation, laparoscopic RFA, and cryoablation, no studies were available at 60 months.

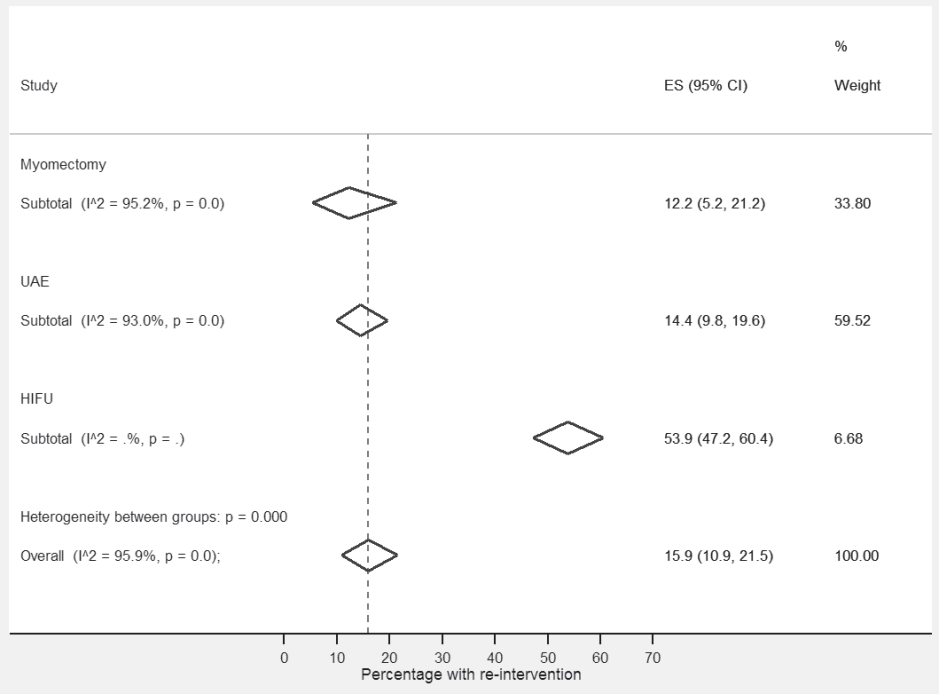

Figure 10.1: Reintervention risk 60 months after abdominal approach.

Table 10.2: Overall re-intervention risk at 12, 36 and 60 months

(%) [95% CI]	12 months	I^2	Nr of studies or substudies	36 months	I^2	Nr of studies or substudies	60 months	I^2	Nr of studies or substudies
Abdominal approach									
Myomectomy	1.1 [0.0;3.7]	89.9	8	1.2 [0;5.2]	65.9	4	12.2 [5.2;21.2]	95.2	10
UAE	3.6 [2.4;4.9]	61.9	26	7.4 [0.9;10.7]	--	3	14.4 [9.8;19.6]	65.9	17
Artery ligation	--	--	0	6	--	1	--	--	0
Laparoscopic RFA	0.3 [0.0;1.6]	0	6	10.4	--	1	--	--	0
HIFU	9.7 [4.0;17.3]	88.3	10	34.7 [27.3;42.4]	47.0	4	53.9 [47.2;60.4]	--	2
Cryoablation	15	--	1	--	--	0	--	--	0
TOTAL	**3.6 [2.5;4.8]**	**80.5**	**51**	**10.4 [4.6;18.1]**	**96.8**	**13**	**15.9 [10.9;21.5]**	**95.9**	**29**
Hysteroscopic approach									
Hysteroscopic myomectomy	6.6 [0.6;17.6]	94.0	4	3.2 [0.0;10.2]	--	3	7.0 [4.8;9.5]	--	2
Hysteroscopic RFA	11.1 [3.3;22.2]	--	3	--	--	0	--	--	0
TOTAL	**8.3 [2.7;16.0]**	**89.1**	**7**	**3.2 [0.0;10.2]**	**--**	**3**	**7.0 [4.8;9.5]**	**--**	**2**

Data are presented as percentages with 95% confidence interval [CI].
I^2 = study heterogeneity.
UAE = uterine artery embolization; RFA=radiofrequency ablation.

Subanalysis for abdominal procedures: hysterectomy as reintervention

A hysterectomy was performed 12 months after the primarily uterine-sparing abdominal intervention in 0.8% of the cases (95% CI 0.3–1.5%; I^2=66.8%; 44 studies). At 36 months, the reintervention risk for hysterectomy varied from 0.6% (myomectomy, 0–2.3%; I^2=60.2%; 4 studies) to 8.1% (laparoscopic RFA, 1 study). By 60 months, 7% (2.5–13.2%; I^2=90.6%; 8 studies) of the patients who had undergone myomectomy required a hysterectomy, compared with 9.4% after UAE (5.5–14.2%; I^2=93.6%; 15 studies). For the HIFU treatment, one study reported the reintervention risk at 60 months and noted that 8 of the 36 women (22.2%) required a hysterectomy.[59] For the other treatment options, no long-term data on hysterectomy reintervention rate were available.

Reintervention risk for hysteroscopic procedures

For the two hysteroscopic procedures, data demonstrated at 12 months a reintervention risk after hysteroscopic RFA of 11.1% (95% CI 3.3–22.2%), 3 studies), compared with 6.6% after hysteroscopic myomectomy (0.6–17.6%; I^2=94.0; 4 studies; Table 10.2). At 36 and 60 months, no data were available for hysteroscopic RFA.

Subanalysis for hysteroscopic procedures: hysterectomy as reintervention

For the reintervention risk for hysterectomy, 1.1% (95% CI 0–6.8%, 3 studies) of the patients in the hysteroscopic myomectomy group required a hysterectomy at 12 months, compared with 2% (0–5.9%, 3 studies) after hysteroscopic RFA. At 36 and 60 months, no data were available for hysteroscopic RFA.

Quality of life for abdominal procedures

For the abdominal procedures, the postoperative SSS and HRQL scores were reported in 18 and 11 studies, respectively. An overview of the outcomes is presented in Table 10.3. The mean difference of SSS between baseline and 12 months after treatment was -31.2 (95% CI -36.9–-25.5). Most mean differences of the treatment options ranged from -37 to -35, with the exception of the HIFU treatment option. The HIFU group had a mean difference of -24.5 (-90.8–-18.1; I^2=96.9%; 8 studies) and thus the least improvement of symptoms over time.

For HRQL, the mean difference in scores at 12 months was 36.1 (31.8–40.4; I^2=89.4%; 11 studies). Again, the HIFU group was associated with the least favorable outcomes, with a mean difference of 24.6 (13.4–35.8, 1 study). At 36 and 60 months, too few studies were available to pool data, but all studies showed improvement of symptoms over time or normalization of the scores after treatment.

Table 10.3: Quality of life at 12 months

(%) [95% CI]	12 months	I^2	Number of studies or substudies
Abdominal approach			
SSS scores			
Myomectomy	-37.6 [43.8;-31.4]	--	1
UAE	-35.8 [-40.6;-30.9]	82.5	4
Artery ligation	--	--	--
Laparoscopic RFA	-37 [-44.6;-29.4]	85.6	4
HIFU	-24.5 [-90.8;-18.1]	96.9	8
Laparoscopic cryoablation	-37.5 [-48.1;-26.9]	--	1
TOTAL	**-31.2 [-36.9;-25.5]**	**98.4**	**18**
HR-QL scores			
Myomectomy	39.9 [33.0;46.8]	--	1
UAE	38.9 [35.8;41.9]	35.9	3
Artery ligation	--	--	--
Laparoscopic RFA	35.1 [28.7;41.6]	79.4	5
HIFU	24.6 [13.4;35.8]	--	1
Laparoscopic cryoablation	41.3 [29.1;53.5]	--	1
TOTAL	**36.1 [31.8;40.4]**	**89.4**	**11**
Hysteroscopic approach			
SSS scores			
Hysteroscopic myomectomy	--		
Hysteroscopic RFA	-42.6 [-68.1;-17.2]	98.6	3
TOTAL	**-42.6 [-68.1;-17.2]**	**98.6**	**3**
HR-QL scores			
Hysteroscopy	--		
Hysteroscopic RFA	38.1 [22.9;53.4]	94.8	3
TOTAL	**38.1 [22.9;53.4]**	**94.8**	**3**

Data are presented as percentages with 95% confidence interval [CI].
I^2 = study heterogeneity.
UAE = uterine artery embolization; RFA=radiofrequency ablation.

Quality of life for hysteroscopic procedures

For hysteroscopic procedures, three studies of hysteroscopic RFA were analyzed (Table 10.3). All of those studies demonstrated improvement of symptoms after treatment. No data were available for quality of life after hysteroscopic myomectomy.

Discussion

Because limited evidence exists on the relative efficacy of the different uterine-sparing treatment options, choosing the best option for a patient might not always be evident. When counseling a patient about the different treatment options, long-term outcomes on reintervention risk and quality of life are, among others, important aspects to consider. In the present meta-analysis based on 85 studies, these two clinically relevant outcomes were evaluated for all available uterine-sparing treatment options for fibroids. For the treatment options with an abdominal approach (all types of myomectomy, UAE, HIFU, laparoscopic RFA, cryoablation, and artery ligation), we demonstrated that 60 months after initial therapy, myomectomy had a risk of reintervention of 12.2%, UAE 14.4%, and HIFU 54%. For the HIFU group, it is important to note that only a few studies were available on the long term. Despite the limited evidence, it is interesting to observe that the HIFU treatment option, which is one of the newest techniques, is currently associated with the least promising outcomes. The authors of the included studies suggested themselves that the high reintervention risk after HIFU might be the result of inadequate patient selection.[59;72;78] Defining the right patient population is indeed one of the key factors associated with success[2] HIFU treatment has been Food and Drug Administration (FDA) approved since 2004 for a selected patient population, and this treatment option seems attractive in terms of procedural morbidity.[78;101;102] However, the findings of this review show that this advanced technique still needs to be further evaluated, especially regarding its long-term outcomes. Obviously, this also applies to the other approaches, such as cryoablation, artery ligation, and laparoscopic RFA, that are currently lacking long-term outcomes data.

Looking specifically at myomectomy and UAE procedures, available evidence was more robust. It is important to note that confounding by indication, particularly infertility, could have influenced these reintervention risk data. Specifically for UAE, our reintervention risk was lower than in the two RCTs included in our analysis that compared UAE and surgery (myomectomy or hysterectomy) in women not desiring future pregnancy.[15;16] Those studies demonstrated after UAE a 5-year reintervention risk of 28.4–32%.[15;16] Both study groups also analyzed the costs associated with UAE compared with myomectomy or hysterectomy and concluded that the costs of UAE were substantially lower than after surgery at 12[15;103] and 24 months.[104] However at 60 months, the benefit of costs disappeared because of the increased reintervention risk.[15] As a result, studies have argued whether women undergoing embolization who were not interested in future pregnancy would not be better served by an initial definitive solution (e.g. hysterectomy).[104] On the other hand, it can also be reasoned that 70% of the women included in these studies have avoided a

more invasive procedure.[104] Although we did not perform a cost-effectiveness analysis, our findings demonstrated that <10% of the patients required a hysterectomy in the long term after UAE.

It would have been interesting in our analysis to correct for infertility as indication of treatment, but the available evidence did not allow it. Reintervention management can be expected to be different for women with future pregnancy desire compared with women without future pregnancy desire. For patients with fibroids and infertility, myomectomy is the criterion standard. Most other interventions remain a relative contraindication and have not yet been cleared by the FDA for this indication.[102;104] This was also reflected in our risk assessment of the included studies: only in the treatment group of myomectomy and hysteroscopic myomectomy were studies included that specifically enrolled patients with infertility as indication of treatment. Although successful pregnancies have been reported after embolization, it has also been associated with a higher risk of pregnancy and/or delivery complications (spontaneous abortion, malpresentation, postpartum hemorrhage, premature delivery)[105] and an increased risk of ovarian dysfunction.[106] For laparoscopic RFA and HIFU, evidence regarding pregnancy outcomes is currently poor. The safety and effectiveness of these treatments in women wishing to maintain their fertility has not been established.[107;108] For the hysteroscopic treatment options, available evidence was limited for the two procedures (hysteroscopic myomectomy and hysteroscopic RFA), especially in the long term. A systematic review has demonstrated the benefits of intracavitary fibroid removal in general for infertility treatment, but data on reintervention are currently lacking to formulate recommendations on the most favorable treatment option.[109]

Regarding quality of life after treatment (based on SSS and HRQL scores), all studies showed improvement of symptoms 12 months after therapy. Long-term outcomes were scarce for all categories although they were in line with the 12-month outcomes. Based on current evidence and with the most appropriate available questionnaires, we can conclude that in terms of quality of life, no difference was observed between the treatment options, except potentially for HIFU. That treatment option was associated in both questionnaires with the least favorable outcomes. Although the reason for this finding is unclear, it is important to realize that the necessity of reintervention probably affects quality of life and may lead to lower scores.[110] Furthermore, it is interesting to mention that one of the included RCTs evaluated quality of life in 22 patients after HIFU compared with placebo treatment.[11] They demonstrated similar symptoms reduction in the first 4 weeks, showing the potential strong impact of placebo therapy on symptom relief. However, at 12 weeks in that study, the symptoms of patients in the placebo group were significantly worse than in the treatment group.

The main limitation of the present systematic review and meta-analysis was the substantial heterogeneity observed. We are aware that patient characteristics (including age, menopause status, or indication for treatment) might influence the choice of procedure and the risk of reintervention. However, further subanalysis by patient characteristics was not possible, because most studies reported only a mean or overall percentage of their cohort, and such data presentation does not allow for further specific modifications. Because of potential confounding, we should be careful about comparing the outcomes of the different procedures with each other, and our data should not be interpreted as a comparative effectiveness analysis. Nevertheless, this meta-analysis provides insights into current reintervention risks based on a large study population. These findings can be directly applicable in daily practice for counseling patients that are often eligible for more than one treatment option. Another limitation that should be considered is that we did not evaluate the safety of the procedures (i.e., complications risk), costs, or subsequent pregnancy rates in patients desiring fertility preservation. These findings would have also been interesting to determine relative efficacy of the procedures and should be considered in future research. Strengths of this review include the description of a wide variety of treatment options with quantifiable outcomes. In addition, by focusing on reintervention risk, we evaluated only the recurrence of clinically symptomatic fibroids. We think that data on recurrence of fibroids according to periodic diagnostic follow-up may not be representative or relevant, because a proportion of patients remain asymptomatic. Moreover, a periodic follow-up could lead to unnecessary anxiety for patients and eventually extra unnecessary interventions and costs.

Over the past decades, many new uterine-sparing surgical treatments have been developed in attempts to minimize the invasiveness of the procedure and to improve women's quality of life. It is interesting to consider why some new techniques are being widely adopted while others, sometimes with promising results, never achieve widespread popularity. For example, the first publication on cryoablation dates from 1996,[111] but only one relevant article was found in our search after the year 2000.[39] In the present review almost 15% of the studies were directly sponsored by a medical devices company, and it must be considered that marketing and financial resources play a role in the success of an instrument. Sponsoring innovation is not necessarily unwarranted, but should not be ignored in terms of publication bias. Although almost all treatment options studied in this review have been approved by the FDA and appeared to be safe, it is important to keep evaluating the long-term outcomes, especially for more newly introduced treatment options. In contrast to the introduction of new drugs, techniques and de-vices may not be introduced before extensive evaluation of efficacy or safety, and the true impact of new technologies can be appreciated only over time. As a result, there is always a risk that

serious complications or suboptimal outcomes are being overlooked when the technique is not properly assessed.

Conclusion

Sixty months after initial therapy, a reintervention was necessary in 12.2% after myomectomy, in 7% after hysteroscopic myomectomy, and in 14.4% after UAE, although infertility as indication for treatment may have influenced outcomes. For HIFU, long-term results were not necessarily encouraging (54%), though based on limited evidence. For the other studied interventions, no long-term data were available at all. In terms of patient satisfaction, improvement of symptoms and quality of life was observed at 12 months after all approaches regardless of the technique applied. The HIFU treatment option showed the least improvement.

Despite the substantial heterogeneity of the study population, this meta-analysis provides valuable information on relative treatment efficacy of various uterine-sparing interventions for fibroids. Our results are important to consider when counseling patients in daily surgical practice. Furthermore, although most uterine-sparing treatment options for fibroids are FDA approved, long-term data regarding their efficacy are limited and therefore urgently needed.

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