Review

Uterine Artery Embolization and Surgical Methods for the Treatment of Symptomatic Uterine Leiomyomas: A Systemic Review and Meta-analysis Followed by Indirect Treatment Comparison

Marcelo C.M. Fonseca, PhD, MD[1]; Rodrigo Castro, PhD, MD[1]; Marcio Machado, PhD, PharmD[2]; Tania Conte, Msc[3]; and Manoel J.B.C. Girao, PhD, MD[1]

[1]Department of Gynecology, Federal University of Sao Paulo, São Paulo, Brazil; [2]Biogen Inc, São Paulo, Brazil; and [3]Centre for Clinical Epidemiology & Evaluation, University of British Columbia, Vancouver, British Columbia, Canada

ABSTRACT

Purpose: There is significant discussion and uncertainty about the optimal management of symptomatic uterine leiomyomas (SULs). Nonsurgical procedures such as uterine artery embolization (UAE) have been developed. The goal of this study was to conduct a meta-analysis and an indirect treatment comparison to examine the comparative efficacy and safety of the surgical procedures to treat SULs compared with UAE.

Methods: MEDLINE, EMBASE, Lilacs, and the Cochrane Central Register of Controlled Trials databases were searched from inception to February 2016. Ten randomized controlled trials comparing UAE versus hysterectomy, myomectomy, and laparoscopic occlusion of the uterine arteries in patients with SUL published in a peer-reviewed journal were included. Two reviewers independently selected studies, assessed quality, and extracted data. Discrepancies were resolved through consensus.

Findings: Data from 986 patients submitted to UEA (n = 527) or surgery (n = 459) were analyzed. UAE had a lower risk of major complications (risk ratio [RR], 0.45 [95% CI, 0.22–0.95]; $P = 0.04$)and a higher risk of minor complications (RR, 1.65 [95% CI, 1.32–2.06]; $P < 0.00001$); UAE had a higher risk of re-intervention up to 2 years (RR, 3.74 [95% CI, 1.76–7.96]; $P = 0.0006$) and up to 5 years (RR, 5.01 [95% CI, 1.37–18.39]; $P = 0.02$); UAE had a similar risk of follicle-stimulating hormone levels >40 IU/L after 6 months (RR, 1.76 [95% CI, 0.24–12.95]; $P = 0.58$)and of recommending the procedure to another patient up to 5 years after treatment (RR, 1.00 [95% CI, 0.87–1.14]; $P = 0.94$). The indirect comparison between myomectomy and hysterectomy found that the 2 procedures were similar in the studied outcomes.

Implications: Compared with surgery, UAE had lower rates of major complications with an increased risk of re-intervention up to 2 and 5 years after the first procedure. UAE compared with surgery had a similar risk of ovarian failure and similar recommendation of the procedure to another patient. However, the number of trials was limited, and there was a high risk of bias in at least 2 domains. None of the trials blinded the participants and personnel or the outcome assessment. PROSPERO identifier: CRD42015026319. (*Clin Ther.* 2017;39:1438–1455) © 2017 Published by Elsevier HS Journals, Inc.

Key words: Hysterectomy, leiomyoma, meta-analysis, uterine artery embolization, uterine myomectomy.

INTRODUCTION

Women with symptomatic uterine fibroids have several treatment options that are balanced with their wish to control symptoms, to preserve the uterus, to avoid surgery, and to address childbearing desires. However, there is significant discussion and

Accepted for publication May 16, 2017.
http://dx.doi.org/10.1016/j.clinthera.2017.05.346
0149-2918/$ - see front matter

uncertainty regarding the optimal management of uterine fibroids. Treatment alternatives often involve watchful waiting and traditional and minimally invasive surgery. Among the minimally invasive procedures, there is also the laparoscopic occlusion of the uterine arteries (LOUA); nonsurgical procedures, such as uterine artery embolization (UAE), have recently been developed.

Hysterectomy and myomectomy have long track records of being performed for the treatment of fibroids over the last century; however, they are associated with significant morbidity.[1–3]

UAE presents some advantages over surgical procedures for the treatment of uterine leiomyoma such as a shorter hospital stay, lower risk of major complications, and shorter recovery time.[4] Nevertheless, it is unclear whether these benefits associated with the UAE outweigh the potential higher number of additional procedures and potential recurrence of symptoms compared with surgical procedures. We therefore conducted a meta-analysis and an indirect treatment comparison to examine the comparative efficacy and safety of the commonly used surgical procedures to treat symptomatic uterine leiomyomas compared with UAE.

MATERIALS AND METHODS

We developed a systematic review protocol, reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines,[5] and the final protocol was registered in PROSPERO (CRD42015026319).[6]

Data Sources

We conducted a systematic search of MEDLINE, EMBASE, Lilacs, the Cochrane Central Register of Controlled Trials, and ClinicalTrials.gov from inception to February 2016 to retrieve studies comparing UAE versus hysterectomy, myomectomy, and LOUA in patients with symptomatic uterine fibroids. The complete search strategies are shown in **Supplemental Appendices 1** through **5** (given in the online version at http://dx.doi.org/10.1016/j.clinthera.2017.05.346).

Study Selection

Articles were included if they: (1) included women with symptomatic fibroids; (2) compared UAE with at least 1 of the other studied procedures; (3) were classified as a randomized controlled trial (for the meta-analysis only); and (4) were published in a peer-reviewed journal. There was no language restriction.

Abstracts, letters, commentaries, secondary analyses, economic evaluations, and reviews were excluded. References from the included primary articles and excluded reviews were secondarily scrutinized searching for studies that were not found during the primary literature search.

Two independent researchers (M.C.M.F. and T.C.) performed article selection and combined the results.

Data Extraction and Synthesis

Two investigators (M.C.M.F. and T.C.) independently extracted data by using a standardized form. Discrepancies were resolved through consensus. We applied a random effects meta-analytic model in all calculations[7] and used RevMan 5.0 from the Cochrane Collaboration[8] to combine results across studies. The studies were aggregated according to the type of procedures being compared: UAE versus hysterectomy, UAE versus myomectomy, and UAE versus mixed surgeries (meaning that both procedures, hysterectomy and myomectomy, were allowed to be performed in the surgery group). The results are expressed as the risk ratio (RR) or mean difference, with 95 % CIs.

Heterogeneity was evaluated by using a Q test (χ^2 test)[9] and I^2 test.[10] Funnel plots were used to detect potential publication bias.[11] Sensitivity analysis was performed by adding studies comparing UAE versus LOUA to the model.

Indirect treatment comparison was performed according to Bucher et al.[12] The relative risk for each indirect comparison was calculated by using ITC software.[13]

Main Outcomes and Measures

The outcomes were aggregated into 4 classes: procedural, effectiveness, ovarian failure, and patient experience. The main procedural outcome was complications. Minor complications were self-limited, may require symptomatic treatment, do not have long-term implications, and do not lead to hospitalizations; major complications were serious, can be life-threatening, need treatment, may cause hospitalizations, and may have long-term implications. The main effectiveness outcome was re-intervention, which is the performance of a new procedure in addition to the initial one. It can be the same procedure that was performed initially. Re-interventions were measured in 3 time