Uterine artery embolization: Long term follow-up and implementation
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Introduction
INTRODUCTION

Uterine fibroids or (leiomyomas) are benign tumours in the uterine wall, which originate from the neoplastic transformation of a single smooth muscle cell of the uterus (1). The prevalence is high and has been reported up to 77%, but many of these uterine fibroids are asymptomatic (2). Symptomatic fibroids can be disabling and are associated with significant morbidity affecting approximately 20-40% of women of reproductive age (3). The most common symptom of uterine fibroids for which treatment is sought is heavy or prolonged menstrual bleeding, which may result in iron deficiency anaemia (4). When symptoms progress and pharmacotherapeutical options fail, surgical interventions like myomectomy or hysterectomy may be necessary.

During the last decade, Uterine Artery Embolization (UAE) has been studied as a minimally invasive treatment alternative to surgery in reducing symptoms of heavy menstrual bleeding (HMB) in relation with fibroids. Ravina et al first described UAE in 1995 as pre-treatment before hysterectomy/myomectomy in women with symptomatic uterine fibroids. However, many of these women no longer required a hysterectomy because their complaints were significantly reduced (5). Since then, several case-series were published which reported promising results of UAE on fibroid-related symptoms (6-9). UAE was reported to be a safe and effective alternative treatment option for surgery, although no evidence from randomized trials (RCTs) was available by then. Despite the lack of randomized data, UAE was introduced widely in daily practice in some countries. It took 7 years before four randomized studies eventually compared UAE and hysterectomy and/or myomectomy (10-14). In these trials, patients undergoing UAE showed a reduction of the length of hospital stay, quicker resumption of daily activities, more minor complications, similar major complications and satisfaction compared with surgery. Nevertheless after 2 years almost 25% of the women undergoing UAE had had a secondary hysterectomy, as shown in the Dutch EMMY (EMbolization versus hysterectoMY) trial (13). Despite these re-interventions, the health related quality of life (HRQOL) was significantly increased in both groups and this was comparable between the two interventions.

THE CLINICAL PROBLEM

Since its introduction UAE has been studied in several RCTs and its effectiveness in fibroid management in comparison to hysterectomy is clear: reduced menstrual bleeding with similar improvement in HRQOL and lower costs against a secondary hysterectomy rate of 25%. Despite this evidence, the implementation of UAE in The Netherlands is progressing
slowly. It seems that the option of UAE is not routinely being discussed with eligible patients. This can have several causes: for example the absence of knowledge on the effectiveness of UAE compared with hysterectomy or myomectomy beyond 2 years, patient’s preferences, and the availability of other (minimally invasive) alternatives. Moreover, UAE has not yet been included in the Dutch guideline on heavy menstrual bleeding.

**AIM OF THE THESIS**

The aim of this thesis was to support the implementation of UAE in the treatment of symptomatic uterine fibroids by firstly evaluating the long-term effectiveness of UAE, then by summarising the existing evidence on UAE and its alternatives and finally by including UAE in the new national guideline on the treatment of heavy menstrual bleeding.

The specific research questions of this thesis were:
1. What is the effectiveness of UAE for symptomatic uterine fibroids 5 years after intervention?
2. On the long term, are patients equally satisfied after UAE compared with surgery?
3. On the long term, are patients’ HRQOL-scores after UAE comparable to those after surgery?
4. When patients participate in a randomized trial on UAE versus hysterectomy and are allocated to the treatment that they do not prefer at baseline, how does this influence their preference (UAE or hysterectomy) afterwards and how does this affect their satisfaction and HRQOL?
5. When eligible patients decline participation in the trial (UAE or hysterectomy), but instead have a treatment of their preference outside the trial, can they expect the same improvement in HRQOL?
6. In patients undergoing UAE for symptomatic uterine fibroids, which analgesic (patient controlled analgesics or epidural analgesia) is cost-effective?
7. Apart from UAE, which other minimally invasive treatment options for symptomatic uterine fibroids are available, and what is the evidence for their clinical application?
8. Which factors are hampering or facilitating the implementation of UAE as treatment option for women with symptomatic uterine fibroids in The Netherlands?
OUTLINE OF THE THESIS

Chapter 2 describes the 5-year outcomes of UAE compared with surgery in the treatment of symptomatic uterine fibroids in the randomized EMMY trial (research question 1, 2 and 3). Chapter 3 presents the results of a systematic review and meta-analysis of the available literature, i.e. randomized trials which compared UAE and surgery in the treatment of symptomatic uterine fibroids (research question 1, 2 and 3).

Chapter 4 describes the impact of treatment preference and treatment allocation on the satisfaction and HRQOL of patients participating in a randomized trial, compared with similar patients that did not participate in the trial (research question 4 and 5).

Chapter 5 describes a decision analysis, which compared patient controlled intravenous analgesia and epidural analgesia in terms of costs and effectiveness, in patients with symptomatic uterine fibroids undergoing UAE (research question 6).

Chapter 6 gives an overview of minimally invasive treatment modalities for symptomatic uterine fibroids (research question 7).

Chapter 7 describes the results of a pilot study where we analysed those factors hampering and facilitating the implementation of UAE for symptomatic uterine fibroids in Dutch hospitals (research question 8).

Chapter 8 summarises the new Dutch guideline on heavy menstrual bleeding in Dutch.

Chapter 9 comprehends chapter 9 of the new Dutch guideline on heavy menstrual bleeding: ‘behandeling van HMB’ (in Dutch).

Chapter 10 summarises all previous chapters and discusses the findings in the context of the literature. The chapter ends with the conclusions of this thesis.

Chapter 11 provides a summary, general discussion and conclusions in Dutch.
REFERENCES


4. Fraser IS, Critchley HO, Munro MG, Broder M. Can we achieve international agreement on terminologies and definitions used to describe abnormalities of menstrual bleeding? Hum Reprod 2007;22:635-643


