The FEMME Trial: At Risk for Misinterpretation and “Fake News”

Sean A. Kennedy¹ · John R. Kachura¹ · Sebastian Mafeld¹

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Introduction

We would like to congratulate the authors of the FEMME trial published in the New England Journal of Medicine in July 2020 [1]. Given that this trial was published in the world’s highest impact medical journal, the reach of this study is global and its influence is potentially practice changing. The randomized controlled-trial compared uterine artery embolization (UAE) and myomectomy for fibroid treatment with a primary outcome of fibroid-related quality of life at 2 years. The trial’s conclusion, namely that women with symptomatic uterine fibroids had a better fibroid-related quality of life at 2 years than those who underwent uterine artery embolization, was quickly picked up by the media with dramatic headlines claiming, “myomectomy trumps embolization” [2]. Given that many patients and clinicians may not critically appraise the data presented, the FEMME trial may have a negative impact on public perception of UAE. A nuanced critical analysis is crucial to allow for patients to make informed decisions between myomectomy and UAE for the treatment of their fibroids.

In this trial, outcomes were excellent in both arms. The primary outcome was measured with the validated Uterine Fibroid Symptom and Quality of Life (UFS-QOL) questionnaire which ranges from 0 to 100 with a higher score representing a higher QOL [3, 4]. Myomectomy led to an improvement on this scale from 37 at baseline to 84.6 at 2 years, while UAE led to an improvement from 42.1 to 80 for the same time interval [1]. As per validation studies of UFS-QOL, this improvement was clinically meaningful for both arms with patients typically being “satisfied” and deeming the procedure to have “eliminated symptoms” with a greater than 20-point improvement [3, 4]. The mean adjusted difference in change from baseline between arms at 2 years was 8 points [1]. While this was statistically significant, the magnitude of this difference is unlikely to be clinically relevant. Both therapies led to satisfied patients with a significant improvement in symptoms.

Some of the critical data in this trial are only present in the supplementary material. We note an unusually low complete fibroid infarction rate (40%), high loss to follow-up (19%) and a lack of consistent embolization techniques among centers [1]. Another potential for bias in any trial comparing UAE with other surgical procedures is the “invasive placebo effect” whereby patients who undergo a more invasive procedure demonstrate greater placebo effects [5]. Most myomectomies in this trial were open (82%) as opposed to laparoscopic or hysteroscopic, thereby more invasive than UAE [1]. This all provides further emphasis on the importance of interpreting small relative differences between groups with caution.

✉ Sean A. Kennedy
Sean.kennedy@medportal.ca

¹ Joint Department of Medical Imaging, University Health Network, University of Toronto, Toronto, ON, Canada

Let us consider a hypothetical but plausible scenario based on data presented in this trial. A patient Googles ‘uterine-sparing’ options to manage their fibroids. They encounter news reports on the FEMME trial claiming myomectomy is superior to UAE. They consult with a gynecologist who has read the FEMME trial. Based on the gynecologist’s interpretation, only 40% of patients had complete infarction post-UAE, post-procedure complication rates were similar between arms, and the UAE arm was more likely to have additional procedures at 2 years (16% vs 7%) [1]. With these data alone, it is difficult to imagine a scenario where a patient would choose UAE! It is our sincere hope that our gynecologist colleagues understand that complete infarction is not necessarily a marker of successful treatment as many patients experience excellent clinical results with incomplete infarction. Secondly, the comparison of complication rates post-procedure should also be considered in more detail, the severity was not graded, and a 14% post-procedure infection rate seems unusually high for the UAE group.

Given the small relative difference in UFS-QOL scores between arms and multiple potential biases that could explain such differences, we feel perhaps most importantly the concluding sentence of the FEMME trial which reads: “Among women with symptomatic uterine fibroids, those who underwent myomectomy had a better fibroid-related quality of life at 2 years than those who underwent uterine-artery embolization” [1].

It would more accurately be worded as: “Among women with symptomatic uterine fibroids, both myomectomy and uterine artery embolization demonstrate significant improvement in fibroid-related quality of life at 2 years.”

Where do we go from here? The FEMME trial has cast UAE in an unfavorable light compared to myomectomy. Media have reported this accordingly. It is easy to see how patients and referring clinicians may now be less inclined to proceed with UAE given the language used in this trial. This places the onus on the global interventional radiology community to ensure public perception of UAE is not eroded. We must advocate for our patients, ensuring they are provided with fair, balanced and accurate information regarding treatment options.

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