The FEMME Trial: A Closer Look and Where We Stand

How FEMME supports UAE as an alternative to surgery for women with fibroids.

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Alongside durable symptom relief, health-related quality of life (HRQOL) has become the most important outcome measure of uterine artery embolization (UAE) for symptomatic uterine fibroids. UAE has been proven to be safe and efficacious in numerous studies over the last 2 decades. However, its place among the current spectrum of uterine-sparing treatments is an area of dispute, and existing trials often lack adequate comparison. The introduction of the Uterine Fibroid Symptom and Quality-of-Life questionnaire by Spies et al in 2002 was an important step toward the collection of meaningful patient-centric outcome data other than safety and durability, allowing the comparison of different uterus-sparing treatments.[1]

THE FEMME TRIAL

FEMME was a multicenter, randomized, open-label trial that evaluated two uterine-preserving treatments, myomectomy versus UAE, in women with symptomatic uterine fibroids who did not want to undergo a hysterectomy. The trial compared the effects of the two treatments on fibroid-related symptom changes and HRQOL in a prospective randomized controlled trial (RCT).[2]

Interventionalists around the world awaited the trial with great interest. The results were published by Manyonda et al in *The New England Journal of Medicine* in July 2020, immediately sparking criticism questioning the results, specifically referring to an unusually high rate of complications and a low rate of fibroid infarction, a known factor for clinical failures and subsequent reintervention, reported only in the UAE group.[3-6]

The conclusion that stuck and echoed from then on was that UAE was labeled to be inferior to myomectomy in treating uterine fibroids. However, that is not quite the entire story. Looking at the outcome data, although statistically significant, a four-point difference in QOL scores after 2 years of observation (taking into account lower baseline values in the myomectomy group) is not a clinically meaningful difference and should have been discussed in a broader context by the authors. Having said this, I can agree with the authors of the FEMME trial who answered the critique by saying that "women in the two groups reported a substantial improvement in QOL, but myomectomy was associated with higher scores on a fibroid-specific primary outcome" and that "these findings do not negate the proven efficacy of UAE."[7]

However, this rather balanced statement is in contrast to the apodictic conclusion of the superiority of one treatment over another in the original publication. In addition, the study revealed no substantiated difference in outcomes regarding fertility and pregnancy rates due to the lack of data. With the FEMME trial, it also becomes clear that we need a larger RCT of UAE versus myomectomy to address fertility outcomes.

CONCLUSION

Is the FEMME trial flawed? Definitely not. Instead of complaining about details of the study, we should embrace the fact that this trial again provides level 1 evidence showing the safety and efficacy of UAE. This is the bigger picture we should frame. We should put forward the argument that multiple RCTs have proven UAE to be a safe, effective alternative to surgical treatment for symptomatic uterine fibroids.[8-12]

The problem is not the quality or quantity of data regarding UAE for symptomatic fibroids but the transla-

tion into clinical practice. UAE is still marginalized in many countries and seen as a niche indication in many guidelines, despite the evidence accumulated in the last 20 years. Some think that everything has been said and studied regarding UAE for fibroids, a treatment that many interventionalists advocate as a one-size-fits-all option for women with different fibroid burden, symptomatology, personal circumstances, and expectations. I think this is the wrong approach. Despite the various treatment options available, uterine fibroid disease is and remains a challenge because we do not have comparative trials addressing specific scenarios. In other words, more evidence-based guidance allowing individualized treatment is necessary. Therefore, we should try to conduct comparative efficacy studies that address the needs of various subpopulations, improve patient selection, and ultimately lead to better, personalized care. ■

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