ORIGINAL ARTICLE

Uterine-Artery Embolization or Myomectomy for Uterine Fibroids

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ABSTRACT

BACKGROUND

Uterine fibroids, the most common type of tumor among women of reproductive age, are associated with heavy menstrual bleeding, abdominal discomfort, subfertility, and a reduced quality of life. For women who wish to preserve their uterus and who have not had a response to medical treatment, myomectomy and uterine-artery embolization are therapeutic options.

METHODS

We conducted a multicenter, randomized, open-label trial to evaluate myomectomy, as compared with uterine-artery embolization, in women who had symptomatic uterine fibroids and did not want to undergo hysterectomy. Procedural options included open abdominal, laparoscopic, or hysteroscopic myomectomy. The primary outcome was fibroid-related quality of life, as assessed by the score on the health-related quality-of-life domain of the Uterine Fibroid Symptom and Quality of Life (UFS-QOL) questionnaire (scores range from 0 to 100, with higher scores indicating a better quality of life) at 2 years; adjustment was made for the baseline score.

RESULTS

A total of 254 women, recruited at 29 hospitals in the United Kingdom, were randomly assigned: 127 to the myomectomy group (of whom 105 underwent myomectomy) and 127 to the uterine-artery embolization group (of whom 98 underwent embolization). Data on the primary outcome were available for 206 women (81%). In the intention-to-treat analysis, the mean (±SD) score on the health-related quality-of-life domain of the UFS-QOL questionnaire at 2 years was 84.6±21.5 in the myomectomy group and 80.0±22.0 in the uterine-artery embolization group (mean adjusted difference with complete case analysis, 8.0 points; 95% confidence interval [CI], 1.8 to 14.1; P=0.01; mean adjusted difference with missing responses imputed, 6.5 points; 95% CI, 1.1 to 11.9). Perioperative and postoperative complications from all initial procedures, irrespective of adherence to the assigned procedure, occurred in 29% of the women in the myomectomy group and in 24% of the women in the uterine-artery embolization group.

CONCLUSIONS

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. (Funded by the National Institute for Health Research Health Technology Assessment program; FEMME Current Controlled Trials number, ISRCTN70772394.)

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The prevalence of uterine fibroids, the most common type of tumor among women of reproductive age, increases with age.[1-3] Approximately half of women with fibroids have bothersome symptoms, including heavy menstrual bleeding, abdominal pain, and pressure,[3] that negatively affect quality of life.[4,5] Submucosal fibroids and, to a lesser extent, intramural fibroids have been associated with subfertility and adverse pregnancy outcomes,[6,7] although data are inconsistent.[8]

Surgery, either myomectomy or hysterectomy, has traditionally been the primary approach for the management of symptomatic fibroids; uterine-artery embolization emerged as an alternative during the 1990s. Myomectomy involves the surgical removal of the fibroid and preservation of the uterus. Although myomectomy substantially reduces heavy bleeding, it is associated with myometrial trauma, and whether it results in improved reproductive outcomes is not known.[9]

Uterine-artery embolization, which is usually performed while the patient is under local anesthesia, involves temporary occlusion of the arteries supplying the uterus, with the use of biocompatible particles, to cause ischemic infarction of the fibroids. As compared with myomectomy, uterine-artery embolization is associated with a shorter hospital stay and an earlier return to normal activities[10,11] but also a higher likelihood of the need for additional intervention.[12] Concern regarding a possible effect on ovarian and uterine function has resulted in recommendations against the use of uterine-artery embolization in women who plan to become pregnant; however, the results of a recent meta-analysis suggested no appreciable effect on ovarian reserve.[13]

Observational studies have shown sustained improvements in quality of life, as measured with the use of the validated Uterine Fibroid Symptom and Quality of Life (UFS-QOL) questionnaire,[14-17] at 3 to 5 years after myomectomy[18] or uterine-artery embolization,[19] but long-term outcome data to directly compare these procedures are limited.[20] In two randomized trials comparing uterine-artery embolization with myomectomy[10,11,14] in which data from a total of 243 women were analyzed, myomectomy was associated with a greater improvement in quality of life and better reproductive outcomes than uterine-artery embolization; however, there was substantial attrition in one trial (the FUME [Fibroids of the Uterus: Myomectomy versus Embolization] trial),[11] and in both trials, complete follow-up occurred only through 1 year after randomization.[11,14] Two other randomized trials compared uterine-artery embolization with hysterectomy or myomectomy.[21,22] A meta-analysis that assessed rates of patient satisfaction after 2 years yielded inconclusive results, which underscores the need for more comparative evidence.[12] We conducted the FEMME trial (A Randomized Trial of Treating Fibroids with Either Embolisation or Myomectomy to Measure the Effect on Quality of Life Among Women Wishing to Avoid Hysterectomy), a multicenter, randomized trial to evaluate myomectomy, as compared with uterine-artery embolization, in women who had symptomatic uterine fibroids and did not want to undergo hysterectomy.

Methods

Trial Design and Oversight

Details of the design of the FEMME trial have been published previously.[23] The full trial protocol and statistical analysis plan are available with the full text of this article at NEJM.org.

The FEMME trial was approved by the United Kingdom National Research Ethics Service and the research department at each participating hospital. Trial oversight and monitoring were provided by a trial steering committee and by an independent data and safety monitoring committee, whose members reviewed accruing safety data during the period of recruitment. The sixth, seventh, penultimate, and last author vouch for the accuracy and completeness of the data and for the fidelity of the trial to the protocol.

Trial Participants

The participants were recruited at 29 hospitals in the United Kingdom. Women were eligible for enrollment in the trial if they were older than 18 years of age, were premenopausal, were not pregnant, and had symptomatic fibroids that could be treated with myomectomy or uterine-artery embolization. Women were excluded if they had substantial adenomyosis, had a suspected or diagnosed cancer, had recent or ongoing pelvic inflammatory disease, or had undergone a previous open abdominal myomectomy or uterine-artery embolization. All the participants provided written informed consent.

The diagnosis and characterization of uterine

fibroids involved history taking, pelvic examination, and ultrasonography, usually followed by magnetic resonance imaging (MRI) with contrast enhancement, to facilitate planning of the procedure. A gynecologist determined whether the fibroid could be treated with open abdominal or laparoscopic removal, and an interventional radiologist considered whether uterine-artery embolization was feasible. Women were eligible to participate in the trial only if they were considered to be eligible for both procedures.

TRIAL ASSIGNMENTS AND PROCEDURES

Participants were randomly assigned, in a 1:1 ratio, to undergo myomectomy or uterine-artery embolization as the primary procedure. Owing to the nature of the procedures, blinding was not considered to be feasible. Computerized randomization was performed centrally through a secure Internet facility with the use of minimization to balance the treatment-group assignments according to the longest dimension of the largest fibroid (≤7 cm vs. >7 cm), the number of fibroids (1 to 3 vs. 4 to 10 vs. >10), and whether the woman wanted to become pregnant (yes vs. no).

Bilateral selective catheterization and embolization of the uterine arteries were performed under fluoroscopic guidance. The specific embolic agent used was at the discretion of the interventional radiologist, and the end point of the embolization procedure was complete or near-complete stasis of blood flow in the uterine artery.

Myomectomy was performed by the route preferred by the operating gynecologist (open abdominal, hysteroscopic, laparoscopic, or a combination of these). A gonadotropin-releasing hormone analogue or ulipristal acetate was administered before the procedure if it was deemed by the gynecologist to be essential. Concurrent procedures such as adhesiolysis were not restricted.

OUTCOME MEASURES

The primary outcome was the score on the health-related quality-of-life domain of the UFS-QOL questionnaire (scores range from 0 to 100, with higher scores indicating a better quality of life) at 2 years after randomization. The instrument has face, construct, and discrimination validity and has been shown to be responsive to change.[15-17]

Prespecified quality-of-life secondary outcomes were the following: the score on the health-related quality-of-life domain of the UFS-QOL questionnaire at 6 months and at 1 year, the score on the symptom severity domain of the UFS-QOL questionnaire (scores range from 0 to 100, with higher scores indicating increased severity), the score on the European Quality of Life 5-Dimension 3-Level (EQ-5D-3L) questionnaire (scores range from −0.59 to 1.00, with higher scores indicating a better quality of life),[24] and the score on the EQ-5D visual analogue scale (scores range from 0 [indicating the worst possible health state] to 100 [indicating the best possible health state]).

Women estimated menstrual blood loss (the number of sanitary napkins or tampons used and the extent of soiling with blood) with the use of the pictorial blood-loss assessment chart and recorded their estimates in diary entries. Scores were then generated from the diary entries, with 0 as the lowest score (indicating no bleeding) and higher scores (no defined upper limit) indicating more bleeding. This measure was also used to generate rates of amenorrhea and of nonheavy bleeding (defined as a score <100).[25] Participants were free to choose the brand of sanitary protection they preferred and to use any pharmacologic cointerventions.

Other secondary outcomes were the occurrence of pregnancy (overall and among participants who had indicated at the time of randomization that they wanted to become pregnant), a pregnancy outcome (live birth, miscarriage, stillbirth, or termination), participant satisfaction (determined on the basis of responses to "would you have your operation again?" and "would you recommend the operation to a friend?"), the length of hospital stay, and the occurrence of additional fibroid-related procedures. Each participant-completed outcome assessment was collected at 6 months, 1 year, and 2 years after randomization. Ovarian reserve was determined on the basis of blood levels of follicle-stimulating hormone (FSH), antimüllerian hormone, and luteinizing hormone measured before myomectomy or uterine-artery embolization was performed and at 6 weeks, 6 months, and 1 year after the procedure; levels of FSH and luteinizing hormone were measured only if the blood sample was obtained on days 2 to 4 of the menstrual cycle. Adverse events were elicited during three time windows: the time from the procedure to hospital discharge, the time from discharge to the 6-month postoperative visit, and the time from the 6-month postoperative visit to

the end of the trial, during which only serious adverse events, which included adverse events that were fatal, life-threatening, or resulted in hospitalization, were reported.

STATISTICAL ANALYSIS

The original sample size was 650 participants, which would have provided the trial with 90% power (at a two-sided alpha level of 0.05) to detect a small-to-moderate difference of 8 points (0.29 of a standard deviation) in the score on the health-related quality-of-life domain of the UFS-QOL questionnaire for the comparison of myomectomy with uterine-artery embolization at 2 years; this sample size would have allowed for an approximately 20% loss of primary outcome data. The target difference between the groups was considered to be plausible on the basis of the results of the FUME trial.[11] The establishment of a validated minimally important difference is lacking with respect to UFS-QOL score,[16] as well as the secondary outcomes other than the EQ-5D score, for which a mean minimally important difference of 0.07 was derived from a review of 11 varied patient populations.[26]

Because enrollment in the trial was progressing more slowly than anticipated, and with access to individual participant UFS-QOL data from the FUME trial, the sample size target was revised to 250 participants in October 2013; at that time, 114 women had undergone randomization. A reanalysis of data from the earlier trial,[11] in which more appropriate regression methods that accounted for baseline imbalances were used, suggested that a larger difference of 12 points in the score on the health-related quality-of-life domain of the UFS-QOL questionnaire was attainable and that the pooled-group standard deviation of UFS-QOL scores was slightly lower than originally estimated. The revised sample size of 250 participants provided 90% power to detect a moderate-sized difference between the groups (0.55 of a standard deviation).

The analysis of the primary outcome was performed according to the intention-to-treat principle; the main analysis included all observed data (the complete case analysis), and a sensitivity analysis, which included data from all participants who underwent randomization, took into account any missing responses with the use of multiple imputation. A linear regression model for repeated measures[27] that included data at all time points was used to estimate least-squares mean differences between the groups (with corresponding two-sided 95% confidence intervals) in the primary outcome at 2 years. The model included participant, treatment group, baseline score, time, interaction between time and treatment group, and the minimization variables. Participants were included in the complete case analysis if they had at least one response at any of the three assessment time points. In the analysis that took missing responses into account, multiple imputation was performed with the use of the Markov chain Monte Carlo method, which assumed a joint multivariate normal distribution. The imputation model was consistent with the analysis model.[28]

For the primary outcome, a P value was generated with the use of the aforementioned linear regression model. The statistical analysis plan did not include a provision for correction for multiple comparisons when the analyses of the secondary effectiveness outcomes were performed. Therefore, the results are reported as point estimates and 95% confidence intervals, without P values. Observed data for secondary continuous outcomes were analyzed in a manner similar to that used for the primary outcome; reproductive hormone levels were log-transformed and hence are presented as the ratio of geometric means for ease of interpretation. Log-binomial regression was used to estimate relative rates and 95% confidence intervals for binary outcomes, with adjustments similar to those used in the other analyses. The widths of the confidence intervals were not adjusted for multiple comparisons, so the intervals should not be used to infer definitive treatment effects.

Several sensitivity analyses of the primary outcome were performed, including an analysis in which time was included as a continuous linear predictor, under the assumption of no interaction with treatment; an analysis in which a variable for treating hospital was added; and a per-protocol analysis that included only participants who underwent the procedure to which they had been assigned. Because some questionnaires were incomplete, we performed an additional sensitivity analysis using available subscale scores to generate an overall score.

We analyzed the treatment effect on the primary outcome in prespecified subgroups that matched the minimization variables (the size of the largest fibroid, the number of fibroids, and whether the participant wanted to become preg-

nant). The effects of these subgroups were examined by adding the variable for the interaction of subgroup with treatment group to the linear regression model. All analyses were performed with the use of SAS software, version 9.4 (SAS Institute).

RESULTS

TRIAL PARTICIPANTS

Between February 6, 2012, and May 21, 2015, a total of 254 eligible women provided consent to participate and were randomly assigned to undergo either myomectomy or uterine-artery embolization (127 women in each group). The percentage of women with available data for the primary outcome at 2 years was 81% (206 of 254 women) (Fig. 1); scores on the health-related quality-of-life domain of the UFS-QOL questionnaire were available at one or more assessment time points for 227 women (89%). Baseline characteristics of the two groups were similar, and imaging results suggested similar severity and distribution of fibroids in the two groups (Table 1). Adherence to the assigned treatment is shown in Figure 1 and in Figure S1 in the Supplementary Appendix, available at NEJM.org. Timing and other details regarding myomectomy and uterine-artery embolization are provided in Table S1. Among the initial procedures performed in the myomectomy group, 86 (82%) were open abdominal procedures.

PRIMARY OUTCOME

The mean scores on the health-related quality-of-life domain of the UFS-QOL questionnaire at 2 years were substantially higher than the baseline scores in both groups, but the magnitude of improvement was greater in the myomectomy group than in the uterine-artery embolization group (mean adjusted difference with complete case analysis, 8.0 points; 95% confidence interval [CI], 1.8 to 14.1; P=0.01; mean adjusted difference with missing responses imputed, 6.5 points; 95% CI, 1.1 to 11.9) (Table 2, Fig. 2, and Table S2). Other sensitivity analyses yielded similar results. The results of the prespecified subgroup analysis are provided in Table S3.

SECONDARY OUTCOMES

The mean score on the health-related quality-of-life domain was also higher after myomectomy than after uterine-artery embolization at both 6 months and 1 year (Table 2 and Fig. 2). The mean differences in the UFS-QOL symptom severity domain were −6.1 points (95% CI, −11.4 to −0.9), favoring myomectomy, at 6 months and −3.8 (95% CI, −9.4 to 1.8), favoring myomectomy, at 2 years, whereas menstrual bleeding scores appeared similar in the two groups (Table S4). At 2 years, the percentage of women who indicated that they would recommend a given procedure to a friend was 93% in the myomectomy group, as compared with 84% in the uterine-artery embolization group, whereas the percentages of women who indicated that they would be willing to undergo the procedure again were 78% and 74%, respectively (Table S5).

In total, 9 women (8%) in the uterine-artery embolization group and 5 women (4%) in the myomectomy group reported a pregnancy within 2 years after randomization; there were 6 live births in the uterine-artery embolization group and 4 live births in the myomectomy group. The hormonal levels did not appear to be materially different in the two groups at the majority of time points (Tables S6 and S7).

The incidence of intraoperative complications was low, with only one conversion of a myomectomy to a hysterectomy and one conversion of a laparoscopic myomectomy to an open abdominal myomectomy. At 6 months after uterine-artery embolization, 32 of 80 (40%) of the fibroids treated, for which repeat MRI was performed, were completely infarcted. The results of the intention-to-treat analysis of procedural complications are shown in Table 3, and the results of the per-protocol analysis (which included only participants who underwent the procedure to which they had been assigned) are provided in Table S8. Perioperative and postoperative complications from all initial procedures occurred in 27 of 113 women (24%) in the uterine-artery embolization group and in 34 of 118 women (29%) in the myomectomy group (relative risk, 1.2; 95% CI, 0.8 to 1.9; P=0.40). The median length of hospital stay was 2 days (interquartile range, 2 to 3) for the uterine-artery embolization group and 4 days (interquartile range, 3 to 5) for the myomectomy group. Among the 110 women in the uterine-artery embolization group and 111 women in the myomectomy group for whom data were available at 2 years, additional fibroid-related procedures were performed in 18 women (16%) and 8 women (7%), respectively (Table S9).

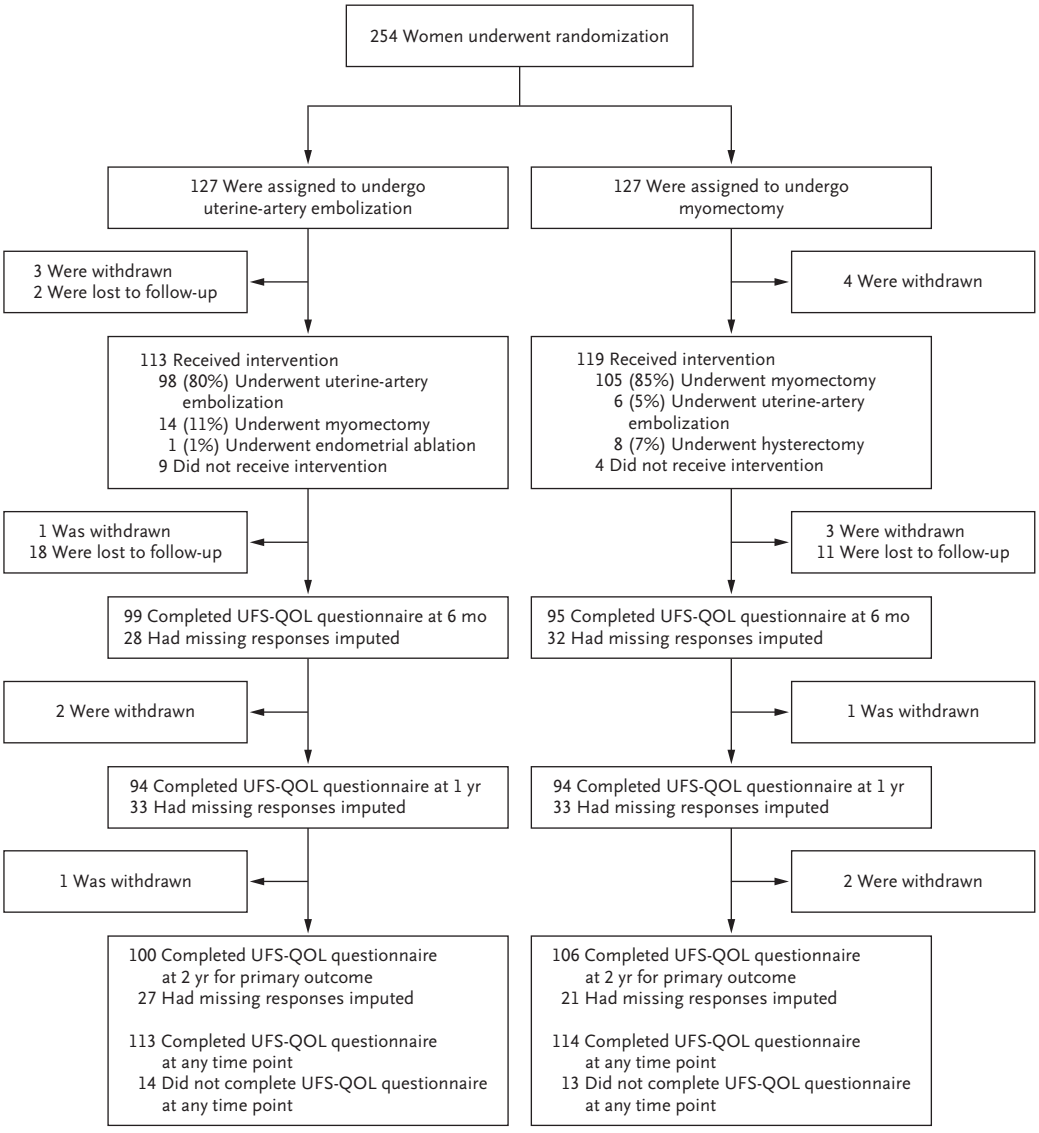


Figure 1. Randomization, Treatment, and Follow-up.

All mentions of the Uterine Fibroid Symptom and Quality of Life (UFS-QOL) questionnaire refer to the health-related quality-of-life portion of the questionnaire. Participants were deemed lost to follow-up only if they did not complete the UFS-QOL questionnaire at 2 years. Participants who did not complete the questionnaire at 6 months or at 1 year but subsequently completed the questionnaire at 2 years were not considered to be lost to follow-up.

DISCUSSION

Although improvement in participant-reported health-related quality-of-life scores was observed after both myomectomy and uterine-artery embolization at 2 years, the scores indicated a higher health-related quality of life among women assigned to undergo myomectomy. Menstrual bleeding scores appeared similar in the two groups. The overall incidence of complications associated with both procedures was low. Additional procedures were performed in 7% of the women in the myomectomy group, as compared with 16% in the uterine-artery embolization group; the median length of hospital stay was 4 days with myomectomy and 2 days with uterine-artery embolization.

The 6-to-8-point benefit, on average, in health-

Table 1. Characteristics of the Trial Participants.*

Characteristic	Uterine-Artery Embolization (N=127)	Myomectomy (N=127)
Demographic characteristics and pregnancy history		
Age — yr	40.2±6.55	42.7±6.4
Race or ethnic group — no. (%)†		
White	59 (46)	57 (45)
Black	48 (38)	54 (43)
South Asian	10 (8)	5 (4)
Mixed	6 (5)	8 (6)
Other	4 (3)	3 (2)
Body-mass index‡		
Mean	28.2±6.2	28.1±5.3
Data missing — no. (%)	8 (6)	4 (3)
Desire for pregnancy, at time of randomization — no. (%)§	61 (48)	61 (48)
Parity		
Median (IQR)	0 (0–1)	1 (0–2)
Data missing — no. (%)	2 (2)	0
Gravidity		
Median (IQR)	1 (0–2)	2 (0–3)
Data missing — no. (%)	2 (2)	0
Fibroid assessment		
Imaging used to diagnose fibroid — no. (%)¶		
Magnetic resonance imaging	89 (70)	99 (78)
Ultrasonography	36 (28)	27 (21)
Data missing	2 (2)	1 (1)
Location of largest fibroid — no. (%)		
Submucosa	6 (5)	14 (11)
Submucosa, pedunculated	1 (1)	1 (1)
Subserosa	30 (24)	21 (17)
Subserosa, pedunculated	6 (5)	5 (4)
Muscle wall‖	74 (58)	81 (64)
Other	4 (3)	0
Data missing	6 (5)	5 (4)
Longest dimension of largest fibroid§		
Distribution — no. (%)		
≤7 cm	64 (50)	64 (50)
>7 cm	63 (50)	63 (50)
Mean — cm	7.6±3.2	7.7±4.2
No. of fibroids§		
1–3 — no. (%)	84 (66)	84 (66)
4–10 — no. (%)	37 (29)	37 (29)
>10 — no. (%)	6 (5)	6 (5)
Median (IQR)	2 (1–5)	2 (1–5)

Table 1. (Continued.)

Characteristic	Uterine-Artery Embolization (N=127)	Myomectomy (N=127)
Largest fibroid volume		
Mean — cm^3	436±594	446±548
Data missing — no. (%)	3 (2)	1 (1)
Uterine volume		
Mean — cm^3	1170±1280	1240±1120
Data missing — no. (%)	9 (7)	9 (7)
Surgical and medication history		
Previous abdominal surgery — no. (%)**		
Cesarean section	12 (9)	19 (15)
Laparoscopy	19 (15)	15 (12)
Endometrial ablation	3 (2)	2 (2)
Appendectomy	8 (6)	7 (6)
Sterilization	4 (3)	5 (4)
Other	10 (8)	15 (12)
Contraceptive or hormonal treatments to control symptoms, at time of randomization — no. (%)	75 (59)	73 (57)

* Plus–minus values are means ±SD. IQR denotes interquartile range.
† Race or ethnic group was determined from hospital records.
‡ The body-mass index is the weight in kilograms divided by the square of the height in meters.
§ This variable was a minimization variable.
¶ A participant could have undergone more than one type of imaging procedure.
‖ This location is also referred to as "intramural."
** A participant could have undergone more than one type of abdominal surgery previously.

related quality-of-life scores in the myomectomy group, as compared with the uterine-artery embolization group, is consistent with a small-to-moderate standardized treatment benefit at 2 years.[29] However, the 95% confidence interval around these estimates indicates that plausible results can range from almost no benefit of myomectomy over embolization to a moderate (15-point) difference. Previous studies of these two interventions have shown similarly large improvements from baseline.[11,20] The observed between-group difference in the EQ-5D score in the current trial is consistent with the reported mean minimally important difference in that scale[26] and supports the between-group difference observed in the UFS-QOL score.

The substantially higher number of surgical reinterventions in the uterine-artery embolization group than in the myomectomy group during 2 years of follow-up may be explained in part by the lower quality of life reported in the uterine-artery embolization group. However, more hysterectomies were performed as the initial procedure in the myomectomy group than in the uterine-artery embolization group, owing either to patient preference or to clinical decision.

There were no consistent differences between the groups in the levels of biomarkers of ovarian reserve, assessed as continuous variables, even after adjustment for baseline values. Previous randomized trials, in which FSH levels were measured and varying thresholds for ovarian failure were used, also showed no convincing evidence of harm from uterine-artery embolization.[30] There were too few pregnancies in our trial to inform the effects of the procedures on fertility.

This trial was larger than previous trials that compared uterine-artery embolization with any surgery[10,11,21,22] and provides information on patient-focused outcomes. Unlike trials of previous comparisons of myomectomy and uterine-artery embolization, the current trial was a multicenter trial and did not include or exclude

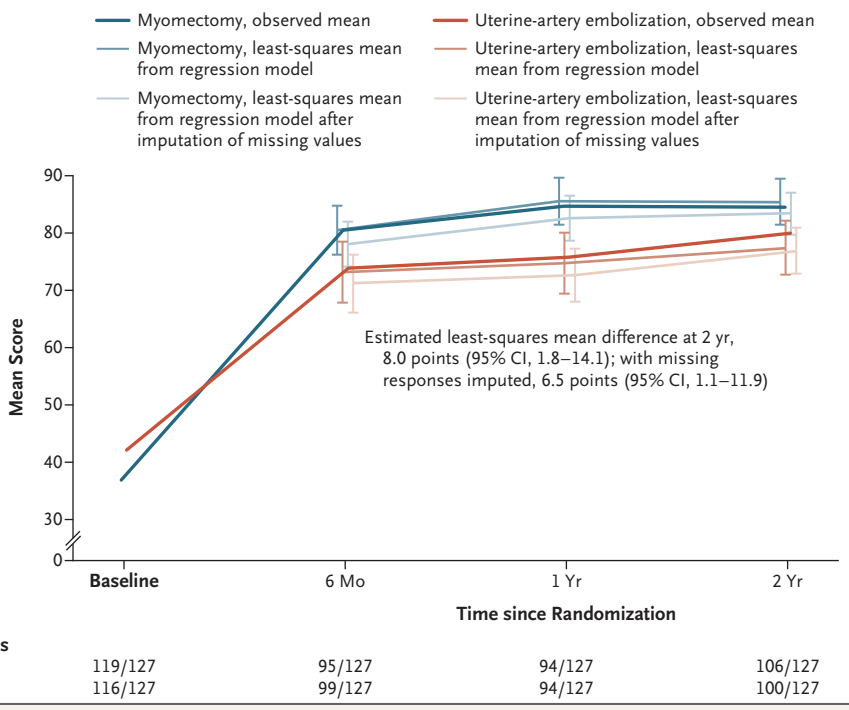
Table 2. Primary and Secondary Quality-of-Life Outcomes.*

Outcome	Uterine-Artery Embolization (N=127)	Myomectomy (N=127)	Estimated Mean Difference (95% CI)†
UFS-QOL health-related quality-of-life domain score‡			
Baseline§			
No. of participants	116	119	
Mean score	42.1±26.4	37.0±23.9	
6 mo§			
No. of participants	99	95	
Mean score	73.9±26.7	80.5±21.7	7.4 (0.5 to 14.2)
1 yr§			
No. of participants	94	94	
Mean score	75.7±26.1	84.7±22.1	10.8 (4.2 to 17.5)
2 yr, the time point of the primary outcome			
No. of participants	100	106	
Mean score	80.0±22.0	84.6±21.5	8.0 (1.8 to 14.1)
UFS-QOL symptom severity domain score¶			
Baseline			
No. of participants	122	125	
Mean score	58.5±26.0	59.4±21.0	
6 mo			
No. of participants	100	97	
Mean score	27.3±21.2	21.6±17.1	−6.1 (−11.4 to −0.9)
1 yr			
No. of participants	95	96	
Mean score	25.7±21.5	20.4±19.0	−5.4 (−11.0 to 0.2)
2 yr			
No. of participants	100	106	
Mean score	21.9±20.8	19.5±20.0	−3.8 (−9.4 to 1.8)
EQ-5D-3L score‖			
Baseline			
No. of participants	125	127	
Mean score	0.62±0.34	0.63±0.32	
6 mo			
No. of participants	100	98	
Mean score	0.77±0.30	0.85±0.17	0.09 (0.03 to 0.14)
1 yr			
No. of participants	98	98	
Mean score	0.77±0.30	0.85±0.23	0.08 (0.01 to 0.15)
2 yr			
No. of participants	99	106	
Mean score	0.80±0.29	0.88±0.20	0.07 (0.01 to 0.13)
EQ-5D visual analogue scale score**			
Baseline			
No. of participants	125	127	
Mean score	62.9±23.8	62.7±23.2	

Table 2. (Continued.)

Outcome	Uterine-Artery Embolization (N=127)	Myomectomy (N=127)	Estimated Mean Difference (95% CI)†‡
6 mo			
No. of participants	98	100	
Mean score	74.2±20.9	79.7±15.7	5.7 (1.1 to 10.3)
1 yr			
No. of participants	98	97	
Mean score	74.4±21.1	81.3±15.3	7.0 (2.1 to 11.9)
2 yr			
No. of participants	101	106	
Mean score	74.7±19.4	80.8±14.7	6.1 (1.7 to 10.6)

* Plus–minus values are means ±SD. The number of participants listed at each time point represents the total number of participants who had a fully completed questionnaire at that time point. EQ-5D denotes European Quality of Life 5-Dimension, EQ-5D-3L European Quality of Life 5-Dimension 3-Level, and UFS-QOL Uterine Fibroid Symptom and Quality of Life.
† Least-squares mean differences were estimated with the use of a regression model; estimates were adjusted for baseline value and minimization variables.
‡ Scores range from 0 to 100, with higher scores indicating a better quality of life. A mean difference of greater than zero favors myomectomy.
§ Additional participants returned partially complete questionnaires (17 participants at baseline, 6 at 6 months, and 5 at 1 year); available subscale scores were used in the sensitivity analysis.
¶ Scores range from 0 to 100, with higher scores indicating increased severity. A mean difference of less than zero favors myomectomy.
‖ Scores range from –0.59 to 1.00, with higher scores indicating a better quality of life. A mean difference of greater than zero favors myomectomy.
** Scores range from 0 (indicating the worst possible health state) to 100 (indicating the best possible health state). A mean difference of greater than zero favors myomectomy.



Observed No. of Scores				
Myomectomy	119/127	95/127	94/127	106/127
Uterine-artery embolism	116/127	99/127	94/127	100/127

Figure 2. Mean UFS-QOL Health-Related Quality-of-Life Scores over Time, According to Treatment Group.
A higher score indicates a better quality of life. I bars indicate 95% confidence intervals.

Table 3. Procedural Complications (Intention-to-Treat Analysis).

Complication	Uterine-Artery Embolization (N=127)	Myomectomy (N=127)
	no. of participants/total no. (%)	
Perioperative or predischarge complications*		
Access-artery occlusion	1/113 (1)	0
Postembolization syndrome resulting in a delay in discharge†	2/113 (2)	0
Hematoma	0	3/118 (3)
Major hemorrhage	2/113 (2)	6/118 (5)
Blood transfusion	4/113 (4)	11/118 (9)
Infection	0	5/118 (4)
Other‡	1/113 (1)	3/118 (3)
Postdischarge complications§		
Access-artery occlusion	1/109 (1)	0
Postembolization syndrome resulting in readmission	3/109 (3)	0
Hematoma	0	2/114 (2)
Infection	15/109 (14)	17/114 (15)
Other¶	10/109 (9)	8/114 (7)

* Complications occurred in 27 of 113 participants (24%) in the uterine-artery embolization group and in 34 of 118 participants (29%) in the myomectomy group (relative risk, 1.2; 95% CI, 0.8 to 1.9; P=0.40).

† Postembolization syndrome is characterized clinically by low-grade fever, pain, fatigue, nausea, and vomiting, typically within 48 hours after uterine-artery embolization, and symptoms usually resolve within a week.

‡ The complication in the uterine-artery embolization group was an episode of hypotension while the participant was in recovery after surgery. The complications in the myomectomy group were persistent oozing, resulting in ligation of the internal iliac vessels; constipation; and anesthesia awareness.

§ Postdischarge complications were recorded from the time of discharge from the hospital to 6 weeks after discharge.

¶ The complications listed here relate to 1 participant, unless otherwise specified. The complications in the uterine-artery embolization group were anemia (2 participants), sciatica, constipation, atypical cells found during the histologic examination of the fibroid, pain in the left upper thigh, fibroid expulsion, suspected infection, and readmission because of pain (2 participants). The complications in the myomectomy group were norovirus; abdominal pain; bleeding in the upper gastrointestinal tract, with *Helicobacter pylori* infection; chest pain, dyspnea, and tachycardia; a gaping wound, with leakage (2 participants); leiomyosarcoma; and constipation.

women on the basis of their intentions with regard to pregnancy. The generalizability of the findings is increased by the inclusion of multiple centers, surgeons, and interventional radiologists, as well as a substantial number of participants of African and Caribbean descent. The incidence of procedural complications was low in both groups, perhaps reflecting the expertise in the participating centers.

Our trial had some limitations. First, 19% of the participants did not return the primary outcome questionnaire at 2 years. Our analytic approach involved imputation of missing responses with the use of a recognized method but assumed that data were missing at random. Any deviation from this assumption could give rise to inconclusive results, given that the lower end of our confidence intervals around the effect estimates were close to zero. Second, a number of participants did not receive the intervention to which they were randomly assigned; however, this occurred at similar frequency in both groups, and the results were not materially different in the per-protocol analysis. Third, despite randomization, some baseline differences between the groups were noted in health-related quality of life and age. However, prespecified analyses were adjusted for the baseline health-related quality-of-life score, and a post hoc analysis with adjustment for age showed similar findings. Fourth, a substantial amount of data on FSH and luteinizing hormone levels was missing, since many blood samples were not obtained within the specified time frame. Fifth, many women declined to participate in the trial owing to having a preference for a particular treatment option. Finally, the lack of blinding may have affected the reporting of subjective outcomes.

In conclusion, this multicenter trial showed the superiority of myomectomy over uterine-artery embolization with respect to health-related quality of life. The overall incidence of perioperative and postoperative complications was similar in the two groups.

This article presents independent research commissioned by the National Institute for Health Research (NIHR). A monograph reporting the data collected in this trial has been submitted for publication in the NIHR Journals Library. Further information is available at www.journalslibrary.nihr.ac.uk/hta. The views and opinions expressed by authors in this article are those of the authors and do not necessarily reflect those of the National Health Service, the NIHR, the NIHR Central Commissioning Facility, the NIHR Evaluation, Trials and Studies Coordinating Center, the NIHR Health Technology Assessment program, or the Department of Health and Social Care.

A data sharing statement provided by the authors is available with the full text of this article at NEJM.org.

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APPENDIX

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