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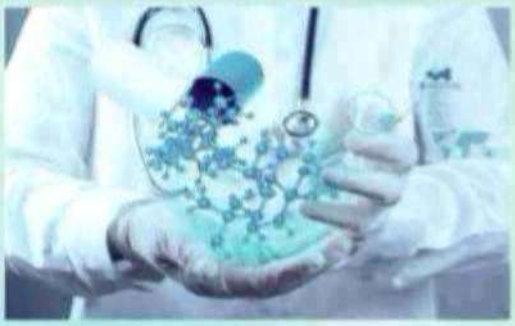

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UTERINE ARTERY EMBOLIZATION FOR UTERINE FIBROIDS AND ADENOMYOSIS IN PERIMENOPAUSAL WOMEN: EFFECTS ON ENDOTHELIAL FUNCTION, SYSTEMIC INFLAMMATION, AND CARDIOVASCULAR RISK MARKERS — AN INTERIM ANALYSIS

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✓ ***Resume***

Background. Uterine fibroids and adenomyosis are among the most prevalent benign gynecological conditions in perimenopausal women. While hysterectomy remains the definitive treatment, growing interest surrounds uterine artery embolization (UAE) as a uterus-sparing alternative. The systemic cardiovascular and endothelial effects of UAE in this population have not been fully characterized.

Objective. To evaluate the effects of bilateral UAE on endothelial function biomarkers, systemic inflammation, oxidative stress, ovarian hormone levels, and cardiac function in perimenopausal women with uterine fibroids and/or adenomyosis.

Methods. This prospective, single-arm, interim analysis includes 77 consecutive women (mean age 42.2 ± 7.8 years) who underwent bilateral UAE for symptomatic uterine fibroids and/or adenomyosis at a single tertiary center. Assessments were performed at baseline (T0), 2 months (T1), and 6 months (T2) post-procedure. Primary endpoints included changes in endothelin-1 (ET-1), nitric oxide (NO), high-sensitivity C-reactive protein (hs-CRP), interleukin-6 (IL-6), TNF-α, malondialdehyde (MDA), superoxide dismutase (SOD), estradiol, and echocardiographic parameters (GLS, E/e'). Fibroid volume reduction was assessed at 12 months (T3) in all patients.

Results. UAE produced a progressive reduction in the largest fibroid volume from 38.2 ± 35.3 cm³ at baseline to 5.4 ± 5.0 cm³ at 12 months (85.8% reduction; $p < 0.001$). Hemoglobin increased significantly from 87.3 ± 20.2 to 124.7 ± 4.5 g/L at 2 months ($p < 0.001$). Significant improvements in endothelial function were observed: ET-1 decreased from 3.76 ± 0.79 to 2.42 ± 0.56 pg/mL ($p < 0.001$) and NO increased from 30.0 ± 5.8 to 45.8 ± 8.4 µmol/L ($p < 0.001$) at 6 months. All pro-inflammatory markers declined significantly. Estradiol levels remained stable (132.5 ± 43.3 vs. 130.4 ± 43.4 pg/mL; $p = 0.75$). Metabolic parameters, GLS, and E/e' improved significantly.

Conclusions. Bilateral UAE not only achieves effective and durable reduction of fibroid burden but is associated with significant improvement in endothelial function, inflammatory, and oxidative stress markers without compromising ovarian reserve. These findings support UAE as a metabolically and cardiovascularly favorable option for perimenopausal women with uterine fibroids and/or adenomyosis.

Keywords: uterine artery embolization, uterine fibroids, adenomyosis, endothelial dysfunction, endothelin-1, nitric oxide, cardiovascular risk, perimenopause, oxidative stress, systemic inflammation

ЭМБОЛИЗАЦИЯ МАТОЧНЫХ АРТЕРИЙ ПРИ МИОМЕ МАТКИ И АДЕНОМИОЗЕ У ЖЕНЩИН В ПЕРИМЕНОПАУЗАЛЬНОМ ПЕРИОДЕ: ВЛИЯНИЕ НА ФУНКЦИЮ ЭНДОТЕЛИЯ, СИСТЕМНОЕ ВОСПАЛЕНИЕ И МАРКЕРЫ СЕРДЕЧНО-СОСУДИСТОГО РИСКА — ПРЕДВАРИТЕЛЬНЫЙ АНАЛИЗ

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✓ ***Резюме***

Введение. Миома матки и аденомиоз являются одними из наиболее распространенных доброкачественных гинекологических заболеваний у женщин в перименопаузальном периоде. Хотя гистерэктомия остается окончательным методом лечения, растет интерес к эмболизации маточных артерий (ЭМА) как к альтернативному методу, позволяющему сохранить матку. Системные сердечно-сосудистые и эндотелиальные эффекты эмболизации маточных артерий (ЭМА) в этой популяции изучены недостаточно.

Цель. Оценить влияние двусторонней ЭМА на биомаркеры эндотелиальной функции, системное воспаление, окислительный стресс, уровни гормонов яичников и функцию сердца у женщин в перименопаузе с миомой матки и/или аденомиозом.

Методы. В это проспективное, одногрупповое, промежуточное исследование включены 77 последовательно обследованных женщин (средний возраст 42,2 ± 7,8 лет), которым была проведена двусторонняя ЭМА по поводу симптоматической миомы матки и/или аденомиоза в одном третичном центре. Оценки проводились на исходном уровне (T0), через 2 месяца (T1) и через 6 месяцев (T2) после процедуры. К основным конечным точкам относились изменения уровня эндотелина-1 (ET-1), оксида азота (NO), высокочувствительного С-реактивного белка (hs-CRP), интерлейкина-6 (IL-6), TNF-α, малонового диальдегида (MDA), супероксиддисмутазы (SOD), эстрадиола и эхокардиографических параметров (GLS, E/e'). Уменьшение объема миомы оценивалось через 12 месяцев (T3) у всех пациентов.

Результаты. Эмболизация маточных артерий привела к прогрессивному уменьшению объема самой большой миомы с 38,2 ± 35,3 см³ на исходном уровне до 5,4 ± 5,0 см³ через 12 месяцев (снижение на 85,8%; p < 0,001). Уровень гемоглобина значительно увеличился с 87,3 ± 20,2 до 124,7 ± 4,5 г/л через 2 месяца (p < 0,001). Наблюдались значительные улучшения эндотелиальной функции: уровень ET-1 снизился с 3,76 ± 0,79 до 2,42 ± 0,56 пг/мл (p < 0,001), а уровень NO увеличился с 30,0 ± 5,8 до 45,8 ± 8,4 мкмоль/л (p < 0,001) через 6 месяцев. Все провоспалительные маркеры значительно снизились. Уровень эстрадиола оставался стабильным (132,5 ± 43,3 против 130,4 ± 43,4 пг/мл; p = 0,75). Метаболические параметры, GLS и E/e' значительно улучшились.

Выводы. Двусторонняя эмболизация маточных артерий не только обеспечивает эффективное и стойкое снижение количества миом, но и связана со значительным улучшением эндотелиальной функции, воспалительных маркеров и маркеров окислительного стресса без ущерба для овариального резерва. Полученные результаты подтверждают, что эмболизация маточных артерий является метаболически и сердечно-сосудисто благоприятным вариантом для женщин в перименопаузе с миомой матки и/или аденомиозом.

Ключевые слова: эмболизация маточных артерий, миома матки, аденомиоз, эндотелиальная дисфункция, эндотелин-1, оксид азота, сердечно-сосудистый риск, перименопауза, окислительный стресс, системное воспаление

MENEPOZ BO'YICHA AYOLLARDA BATAN MIBROIDLARI VA ADENOMIOZ UCHUN BATAN ARTERIYASI EMBOLIYASI: ENDOTELIAL FUNKSIYASI, TIZIMLI YALLIG'LANISH VA YURAK-QON-TOMIR XAVF BELGILARIGA TA'SIRI — ORALIQ TAHLIL

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✓ ***Rezyume***

Murakkab ma'lumot. Bachadon miomasi va adenomioz perimenopauza davridagi ayollarda eng ko'p uchraydigan benign ginekologik kasalliklar qatoriga kiradi. Gisterektomiya eng aniq davolash usuli bo'lib qolsa-da, bachadonni saqlovchi alternativa sifatida bachadon arteriyasi

embolizatsiyasiga (BAA) qiziqish ortib bormoqda. Ushbu populyatsiyada BAA ning tizimli yurak-qon tomir va endotelial ta'siri to'liq tavsiflanmagan.

Maqsad. Bachadon miomasi va/yoki adenomiozli perimenopauza davridagi ayollarda ikki tomonlama UAE ning endotelial funktsiya biomarkerlariga, tizimli yallig'lanishga, oksidlovchi stressga, tuxumdon gormonlari darajasiga va yurak faoliyatiga ta'sirini baholash.

Usullar. Ushbu istiqbolli, bir qo'lli, oraliq tahlil bitta uchinchi darajali markazda simptomatik bachadon miomasi va/yoki adenomioz uchun ikki tomonlama UAE dan o'tgan ketma-ket 77 ayolni (o'rtacha yoshi 42,2 ± 7,8 yosh) o'z ichiga oladi. Baholashlar protseduradan keyin boshlang'ich (T0), 2 oy (T1) va 6 oy (T2) da o'tkazildi. Birlamchi yakuniy nuqtalar endotelin-1 (ET-1), azot oksidi (NO), yuqori sezgirlikdagi C-reaktiv oqsil (hs-CRP), interleykin-6 (IL-6), TNF-α, malondialdegid (MDA), superoksid dismutaza (SOD), estradiol va ekokardiyografik parametrlardagi (GLS, E/e') o'zgarishlarni o'z ichiga oldi. Barcha bemorlarda mioma hajmining kamayishi 12 oydan keyin (T3) baholandi.

Natijalar. UAE eng katta mioma hajmining boshlang'ichdagi 38,2 ± 35,3 sm³ dan 12 oyda 5,4 ± 5,0 sm³ gacha progressiv ravishda kamayishini ta'minladi (85,8% pasayish; p < 0,001). Gemoglobin 2 oyda 87,3 ± 20,2 dan 124,7 ± 4,5 g/L gacha sezilarli darajada oshdi (p < 0,001). Endotelial funktsiyada sezilarli yaxshilanishlar kuzatildi: ET-1 6 oyda 3,76 ± 0,79 dan 2,42 ± 0,56 pg/ml gacha kamaydi (p < 0,001) va NO 30,0 ± 5,8 dan 45,8 ± 8,4 μmol/L gacha (p < 0,001) oshdi. Barcha yallig'lanishga qarshi markerlar sezilarli darajada kamaydi. Estradiol darajasi barqaror bo'lib qoldi (132,5 ± 43,3 va 130,4 ± 43,4 pg/ml; p = 0,75). Metabolik parametrlar, GLS va E/e' sezilarli darajada yaxshilandi.

Xulosalar. Ikki tomonlama UAE nafaqat mioma yukini samarali va uzoq muddatli kamaytirishga erishadi, balki tuxumdonlar zaxirasini buzmasdan endotelial funktsiya, yallig'lanish va oksidlovchi stress markerlarining sezilarli darajada yaxshilanishi bilan bog'liq. Ushbu topilmalar UAE ni bachadon miomasi va/yoki adenomiozli perimenopauza davridagi ayollar uchun metabolik va yurak-qon tomir jihatidan qulay variant sifatida qo'llab-quvvatlaydi.

Kalit so'zlar: bachadon arteriyasi embolizatsiyasi, bachadon miomasi, adenomioz, endotelial disfunktsiya, endotelin-1, azot oksidi, yurak-qon tomir xavfi, perimenopauza, oksidlovchi stress, tizimli yallig'lanish

Relevance

Uterine fibroids (leiomyomata uteri) and adenomyosis are the most common benign gynecological conditions in women of reproductive and perimenopausal age, with a combined prevalence exceeding 60–70% in women over 40 years. Clinically significant forms affect 25–30% of patients and are associated with substantial morbidity, including chronic pelvic pain, abnormal uterine bleeding, iron-deficiency anemia, and significant impairment of quality of life [1–3]. The perimenopausal period adds a further layer of complexity, characterized by declining estrogen levels, increasing visceral adiposity, insulin resistance, and low-grade chronic inflammation — a constellation that underpins accelerated vascular aging and rising cardiovascular risk [4, 5].

Cardiovascular disease (CVD) remains the leading cause of mortality in women, particularly after the age of 45, and mounting evidence suggests that gynecological interventions in this window may exert lasting cardiometabolic consequences [6]. Hysterectomy, even when the ovaries are preserved, has been associated with disruption of ovarian blood supply, partial estrogen deficiency, and downstream activation of the renin–angiotensin–aldosterone system (RAAS), neurohumoral pathways, and systemic inflammation — ultimately accelerating endothelial dysfunction and increasing the long-term risk of coronary artery disease, hypertension, and heart failure [10–12].

Endothelial dysfunction represents the earliest detectable vascular perturbation in the atherosclerotic continuum and can be quantified through biomarkers such as endothelin-1 (ET-1), nitric oxide (NO), and markers of systemic inflammation (hs-CRP, IL-6, TNF-α) and oxidative stress (malondialdehyde, superoxide dismutase) [7–9]. These parameters provide a window into the vascular consequences of any intervention and are increasingly recognized as relevant clinical endpoints in gynecological surgery trials.

Uterine artery embolization (UAE) has emerged as a minimally invasive, uterus-preserving alternative to hysterectomy. By selectively occluding the arterial supply to fibroids while preserving

ovarian blood flow and endocrine function, UAE is hypothesized to carry a more favorable cardiovascular and endothelial safety profile than surgical approaches [20–23]. However, prospective data specifically evaluating endothelial biomarkers, inflammatory cascades, oxidative stress parameters, and cardiac function dynamics following UAE in perimenopausal women are lacking.

The present study reports the results of an ongoing prospective interim analysis of 77 perimenopausal women who underwent bilateral UAE for symptomatic uterine fibroids and/or adenomyosis, with a comprehensive evaluation of endothelial function, systemic inflammation, oxidative stress, hormonal profile, metabolic parameters, and echocardiographic indices across a six-month follow-up period.

Purpose of the study: To evaluate the effects of bilateral uterine artery embolization on endothelial function biomarkers (ET-1 and NO), systemic inflammatory markers (hs-CRP, IL-6, TNF-α), oxidative stress indices (MDA, SOD), estradiol levels, metabolic parameters, and echocardiographic indices of cardiac function in perimenopausal women with symptomatic uterine fibroids and/or adenomyosis over a six-month follow-up period.

Materials and Methods

Study Design

This is a prospective, single-center, single-arm, pre-specified interim analysis of an ongoing observational study designed to compare UAE with hysterectomy. The present report includes exclusively the UAE cohort, as enrollment in the hysterectomy comparator group is ongoing. All procedures were performed at the Republican Specialized Scientific and Practical Medical Center of Therapy and Medical Rehabilitation, Tashkent, Uzbekistan, between March 2025 and June 2026. The study was conducted in accordance with the Declaration of Helsinki, and written informed consent was obtained from all participants.

Patient Population

Inclusion criteria were: female sex; age 25–55 years; ultrasound- and MRI-confirmed symptomatic uterine fibroids (single or multiple) and/or adenomyosis (focal, multifocal, or diffuse); clinically indicated UAE; willingness to attend scheduled follow-up visits. Exclusion criteria included: active uterine or cervical malignancy; coagulopathy or contraindication to contrast media; renal insufficiency (eGFR < 30 mL/min/1.73 m²); current use of hormone replacement therapy or immunosuppressants; active infectious or autoimmune disease; prior pelvic radiation; refusal of consent.

UAE Procedure

All UAE procedures were performed by experienced interventional radiologists via a transfemoral or transradial approach under fluoroscopic guidance. Following selective catheterization of the uterine arteries bilaterally, embolization was performed using calibrated microspheres (300–500 μm, with stepwise upscaling to 500–700 μm or 700–900 μm as required) until near-complete cessation of fibroid perfusion was achieved while preserving ovarian arterial flow. Technical success was defined as bilateral uterine artery occlusion with absence of fibroid blush on completion angiography. All patients received procedural antibiotic prophylaxis and standardized post-embolization analgesia.

Follow-Up Schedule and Outcome Assessments

Assessments were performed at four time points: baseline (T0, pre-procedure), 2 months (T1), 6 months (T2), and 12 months (T3). Imaging follow-up (pelvic ultrasound with volume measurements) was performed at all time points. Laboratory assessments were performed at T0, T1, and T2 and included: (1) Endothelial function: serum ET-1 (pg/mL) and plasma NO (μmol/L); (2) Inflammation: high-sensitivity CRP (mg/L), IL-6 (pg/mL), TNF-α (pg/mL); (3) Oxidative stress: malondialdehyde (MDA, nmol/mL), superoxide dismutase (SOD, U/mL); (4) Hormonal profile: serum estradiol (pg/mL); (5) Metabolic profile: fasting glucose (mmol/L), HOMA-IR, total cholesterol (mmol/L); (6) Full blood count including hemoglobin. Echocardiography was performed at T0 and T2 by a blinded cardiologist, with assessment of global longitudinal strain (GLS, %) and the E/e' ratio as indices of diastolic function and left ventricular mechanics.

Statistical Analysis

All continuous variables are presented as mean ± standard deviation (SD). Normality was assessed by the Shapiro–Wilk test. Changes from baseline at T1 and T2 were evaluated using paired-sample Student's t-test for normally distributed variables. A p-value < 0.05 was considered statistically

significant. No imputation was performed for missing values. All analyses were conducted in Python (SciPy v1.11). Given the single-arm design of this interim report, no between-group comparisons are presented. Confidence intervals were not computed at this stage of the ongoing study; these will be reported in the full analysis following completion of the hysterectomy cohort.

Result and discussions

Baseline Characteristics

Seventy-seven women who underwent bilateral UAE met the inclusion criteria and are included in this interim analysis. The mean age was 42.2 ± 7.8 years (range 22–53 years), reflecting the perimenopausal population at highest risk for both fibroid burden and cardiovascular co-morbidity. Mean BMI was 26.7 ± 3.5 kg/m², consistent with pre-obesity. Clinically significant comorbidities were present in a substantial minority: arterial hypertension was documented in 24.7% of patients, type 2 diabetes mellitus in 11.7%, and current smoking in 13.0%, indicating a non-trivial baseline cardiovascular risk profile. Mean systolic and diastolic blood pressures were 118.0 ± 9.8 and 78.2 ± 7.5 mmHg, respectively. Severe anemia was a prominent pre-procedural finding, with mean hemoglobin of 87.3 ± 20.2 g/L, reflecting the menorrhagia burden of the population. All procedures were technically successful bilateral UAE (Table 1).

Table 1. Baseline clinical and demographic characteristics of the UAE cohort (n = 77)

Characteristic	UAE Group (n = 77)
Age, years, mean ± SD	42.2 ± 7.8 (range 22–53)
BMI, kg/m², mean ± SD	26.7 ± 3.5
Systolic BP, mmHg, mean ± SD	118.0 ± 9.8
Diastolic BP, mmHg, mean ± SD	78.2 ± 7.5
Arterial hypertension, n (%)	19 (24.7%)
Type 2 diabetes mellitus, n (%)	9 (11.7%)
Current smoking, n (%)	10 (13.0%)
Baseline hemoglobin, g/L, mean ± SD	87.3 ± 20.2
UAE type: bilateral, n (%)	77 (100%)

UAE, uterine artery embolization; BP, blood pressure; BMI, body mass index; SD, standard deviation.

Fibroid Burden and Hemoglobin Recovery

Bilateral UAE produced a progressive, statistically significant reduction in fibroid burden across all assessment time points. The mean largest fibroid diameter decreased from 31.9 ± 22.2 mm at baseline to 14.0 ± 9.7 mm at 12 months. Correspondingly, the mean largest fibroid volume declined from 38.2 ± 35.3 cm³ at T0 to 22.9 ± 21.2 cm³ at 2 months (40.1% reduction), 13.5 ± 12.4 cm³ at 6 months (64.7% reduction), and 5.4 ± 5.0 cm³ at 12 months, representing a mean reduction of 85.8 ± 1.0% ($p < 0.001$). This degree of fibroid devascularization is consistent with published data from large UAE registries [24, 25].

Resolution of abnormal uterine bleeding was accompanied by rapid and clinically significant improvement in hemoglobin levels: mean Hb increased from 87.3 ± 20.2 g/L at baseline to 124.7 ± 4.5 g/L at 2 months ($p < 0.001$), representing a mean gain of 37.4 g/L. This prompt hematological recovery is relevant for both quality of life and cardiovascular risk, as correction of chronic anemia reduces myocardial oxygen demand and cardiac remodeling stimuli (Table 2).

Endothelial Function: ET-1 and Nitric Oxide

A key novel finding of this study is the highly significant and progressive improvement in endothelial function markers following UAE. Serum ET-1, a potent vasoconstrictor and marker of endothelial

activation, decreased from 3.76 ± 0.79 pg/mL at baseline to 3.02 ± 0.57 pg/mL at 2 months and to 2.42 ± 0.56 pg/mL at 6 months ($p < 0.001$). Concurrently, plasma NO, reflecting endothelium-derived vasodilatory capacity, increased progressively from 30.0 ± 5.8 μmol/L at T0 to 37.1 ± 7.4 μmol/L at T1 and 45.8 ± 8.4 μmol/L at T2 ($p < 0.001$). The bidirectional improvement — reduction in ET-1 and increase in NO — strongly suggests a shift from a pre-procedural state of endothelial activation and vasoconstriction toward a more favorable endothelial phenotype within 6 months of UAE.

These findings are mechanistically coherent: resolution of chronic anemia reduces cardiac output-driven shear stress abnormalities, while abatement of the fibroid-associated pro-inflammatory microenvironment reduces systemic endothelial injury. Critically, because estradiol levels remained stable (see below), this endothelial improvement cannot be attributed to hormonal fluctuations and must reflect the direct anti-inflammatory and hemodynamic consequences of UAE.

Table 2. Fibroid volume reduction and hemoglobin recovery following UAE

Parameter	Baseline (T0)	2 months (T1)	6 months (T2)	12 months (T3)
Largest fibroid diameter, mm	31.9 ± 22.2	25.4 ± 17.7	19.2 ± 13.4	14.0 ± 9.7
Largest fibroid volume, cm³	38.2 ± 35.3	22.9 ± 21.2	13.5 ± 12.4	5.4 ± 5.0*
Volume reduction (%)	—	40.1%	64.7%	85.8%*
Hemoglobin, g/L	87.3 ± 20.2	124.7 ± 4.5*	—	—

* $p < 0.001$ vs. baseline (paired t-test). — Data not assessed at this time point.

Table 3. Endothelial function, inflammatory, and oxidative stress biomarkers before and after UAE

Biomarker	Baseline (T0)	2 months (T1)	6 months (T2)	p (T0 vs T2)
Endothelial Function				
ET-1, pg/mL	3.76 ± 0.79	3.02 ± 0.57	2.42 ± 0.56	< 0.001
NO, μmol/L	30.0 ± 5.8	37.1 ± 7.4	45.8 ± 8.4	< 0.001
Inflammatory Markers				
hs-CRP, mg/L	6.61 ± 2.04	2.81 ± 1.13	1.81 ± 0.80	< 0.001
IL-6, pg/mL	9.64 ± 3.39	5.07 ± 1.79	3.24 ± 1.41	< 0.001
TNF-α, pg/mL	12.10 ± 4.49	7.73 ± 2.69	5.64 ± 2.05	< 0.001
Oxidative Stress				
MDA, nmol/mL	3.88 ± 1.22	2.76 ± 0.66	1.85 ± 0.61	< 0.001
SOD, U/mL	1122.8 ± 204.9	1403.0 ± 223.9	1611.8 ± 233.5	< 0.001

All p-values are for paired t-test comparing T0 to T2 (n = 76). ET-1, endothelin-1; NO, nitric oxide; hs-CRP, high-sensitivity C-reactive protein; IL-6, interleukin-6; TNF-α, tumor necrosis factor-alpha; MDA, malondialdehyde; SOD, superoxide dismutase.

Systemic Inflammation and Oxidative Stress

Baseline values of all inflammatory markers were elevated, consistent with the chronic low-grade inflammatory state associated with uterine fibroids, adenomyosis, and the perimenopausal period. hs-CRP decreased from 6.61 ± 2.04 mg/L at T0 to 2.81 ± 1.13 mg/L at T1 and 1.81 ± 0.80 mg/L at T2 ($p < 0.001$ for both comparisons). Notably, the greatest absolute decline occurred within the first 2 months, and values approached near-normal levels by 6 months — suggesting that the transient post-embolization inflammatory response, well-documented in the literature, resolves completely and is followed by a net anti-inflammatory effect. IL-6 declined from 9.64 ± 3.39 to 3.24 ± 1.41 pg/mL ($p < 0.001$) and TNF-α from 12.10 ± 4.49 to 5.64 ± 2.05 pg/mL ($p < 0.001$) at 6 months.

Oxidative stress indices demonstrated complementary bidirectional changes. MDA, a marker of lipid peroxidation and oxidative tissue damage, declined from 3.88 ± 1.22 nmol/mL at T0 to 1.85 ± 0.61 nmol/mL at T2 ($p < 0.001$). Conversely, SOD activity, reflecting antioxidant defense capacity, increased significantly from 1122.8 ± 204.9 U/mL at T0 to 1611.8 ± 233.5 U/mL at T2 ($p < 0.001$). The simultaneous reduction in lipid peroxidation products and upregulation of antioxidant enzyme activity indicate a shift from oxidative stress toward redox homeostasis following UAE (Table 3).

Ovarian Reserve, Metabolic Profile, and Cardiac Function

Serum estradiol levels showed no statistically significant change from baseline to 6 months (132.5 ± 43.3 vs. 130.4 ± 43.4 pg/mL; $p = 0.75$), confirming the preservation of ovarian endocrine function following bilateral UAE. This finding is of particular clinical significance: in perimenopausal women, maintaining estrogen levels is critical for endothelial protection, bone health, and neurocognitive function.

Despite estradiol stability, significant improvements were observed in the metabolic profile. Fasting glucose decreased from 6.01 ± 1.00 to 4.97 ± 0.58 mmol/L ($p < 0.001$) and HOMA-IR from 3.70 ± 0.87 to 2.49 ± 0.61 ($p < 0.001$), suggesting improved insulin sensitivity possibly mediated by the resolution of chronic inflammation (which impairs the PI3K/Akt insulin signaling pathway in endothelium). Total cholesterol also decreased significantly from 5.68 ± 0.68 to 4.08 ± 0.57 mmol/L ($p < 0.001$).

Echocardiographic reassessment at 6 months revealed significant improvement in both indices of cardiac function. GLS improved from -15.10 ± 1.75% to -19.48 ± 1.51% ($p < 0.001$), indicating enhanced left ventricular systolic mechanics; a more negative GLS reflects better global myocardial deformation. The E/e' ratio declined from 11.55 ± 2.08 to 8.81 ± 1.79 ($p < 0.001$), consistent with improvement in diastolic function and reduction in left ventricular filling pressure. These echocardiographic changes are likely multifactorial, reflecting the combined benefit of anemia correction, reduced inflammatory load, and improved metabolic parameters (Table 4).

Table 4. Hormonal, metabolic, and cardiac function parameters before and after UAE

Parameter	Baseline (T0)	6 months (T2)	p value
Hormonal Profile			
Estradiol, pg/mL	132.5 ± 43.3	130.4 ± 43.4	0.753 (NS)
Metabolic Profile			
Fasting glucose, mmol/L	6.01 ± 1.00	4.97 ± 0.58	< 0.001
HOMA-IR	3.70 ± 0.87	2.49 ± 0.61	< 0.001
Total cholesterol, mmol/L	5.68 ± 0.68	4.08 ± 0.57	< 0.001
Cardiac Function (Echocardiography)			
GLS, %	-15.10 ± 1.75	-19.48 ± 1.51	< 0.001
E/e'	11.55 ± 2.08	8.81 ± 1.79	< 0.001

NS, not significant; GLS, global longitudinal strain; HOMA-IR, homeostatic model assessment of insulin resistance. All p-values for paired t-test (n = 76).

Discussion

This interim analysis of 77 perimenopausal women who underwent bilateral UAE provides a comprehensive and clinically meaningful picture of the systemic biological effects of this procedure, extending well beyond the traditionally reported outcomes of fibroid volume reduction and symptom relief. To our knowledge, this is among the first prospective studies to simultaneously characterize the trajectory of endothelial function biomarkers, inflammatory cascades, oxidative stress, hormonal integrity, metabolic parameters, and echocardiographic indices in the UAE population.

The fibroid volume reduction observed in our cohort — 85.8% at 12 months — is at the upper end of published data. The EMMY trial (Hehenkamp et al., n = 177) demonstrated significant symptomatic relief and quality of life outcomes comparable to hysterectomy with shorter hospitalization in the UAE arm [24]. The Ontario Uterine Fibroid Embolization Trial (Pron et al., n = 538) and the FEMME trial (Manyonda et al., n = 254) confirmed high patient satisfaction and sustained fibroid burden reduction [23, 25]. The FIBROID Registry (Spies et al., n = 3,000+) reported similar rates of volume reduction across diverse clinical settings. Our results are consistent with these benchmark studies, reinforcing the technical efficacy of UAE in a Central Asian population treated at a specialized center.

The most clinically impactful findings of the present study relate to endothelial function. The simultaneous decline in ET-1 and increase in NO following UAE — both reaching statistical significance with $p < 0.001$ — indicates a substantive shift in the endothelial redox and vasoregulatory balance. ET-1 is not merely a vasoconstrictor; it is a pleiotropic mediator of vascular smooth muscle proliferation, platelet activation, and RAAS upregulation [14]. Elevated ET-1 in women with uterine fibroids likely reflects both the local hypervascular state of the fibroid myometrium and the systemic low-grade inflammation associated with anemia and chronic pain. Following fibroid devascularization and correction of anemia, the drivers of ET-1 upregulation are abruptly removed, explaining the rapid and sustained decline observed. Conversely, the increase in NO reflects restoration of endothelial NO synthase (eNOS) activity, which is inhibited by both oxidative stress (via superoxide-mediated NO scavenging) and inflammatory cytokines — both of which were significantly reduced in our cohort.

This endothelial improvement trajectory stands in sharp contrast to the established cardiovascular consequences of hysterectomy. Laughlin-Tommaso et al. demonstrated in a retrospective cohort of 2,094 women that hysterectomy with ovarian conservation was associated with a 33% increase in coronary artery disease risk and a 17% increase in hypertension over 20 years [10]. Rocca et al. reported accelerated arterial stiffening of 10–15% within the first years after hysterectomy [11], while Moorman et al. documented a 15–20% decline in estradiol within the first year post-hysterectomy despite ovarian preservation, due to disruption of utero-ovarian blood flow [12]. By contrast, our data demonstrate stable estradiol at 6 months following UAE ($p = 0.75$), corroborating findings from Spies et al. (n = 66; no significant estradiol decline in 95% of patients) [21] and Tropeano et al. (n = 83; ovarian function impairment in < 5%, predominantly in women over 45) [22]. The hormonal neutrality of UAE thus appears to be a key mediator of its favorable endothelial profile.

The reduction in systemic inflammatory markers is equally noteworthy. hs-CRP, IL-6, and TNF-α — each independently associated with endothelial dysfunction and atherosclerotic risk — all declined significantly by 6 months. This pattern aligns with the known biology of fibroid pathology: fibroids are metabolically active structures that sustain local and systemic inflammatory signaling through production of growth factors and pro-inflammatory cytokines. Their devascularization and involution following UAE effectively removes this chronic inflammatory source. Pron et al. had previously documented a transient, moderate elevation of CRP in the first days post-UAE [23]; our data show that this short-term rise is followed by a sustained anti-inflammatory effect, a distinction that is critically important for counseling patients about cardiovascular risk over the medium term.

The improvement in oxidative stress parameters — MDA reduction and SOD upregulation — also merits discussion. Chronic anemia promotes oxidative stress through mitochondrial inefficiency, hypoxia-inducible factor activation, and iron cycling with Fenton chemistry, contributing to endothelial damage independent of inflammation [16]. Correction of anemia post-UAE, combined with resolution of fibroid-associated inflammatory oxidative burden, likely explains the substantial improvement in

MDA and SOD. This oxidative stress recovery in turn supports the endothelial improvements in ET-1 and NO, since reactive oxygen species are the primary mechanism of eNOS uncoupling and NO bioavailability reduction [9].

The metabolic improvements — reduced fasting glucose, HOMA-IR, and total cholesterol — were unexpected insofar as no dietary or pharmacological intervention was made. Resolution of chronic inflammation likely plays a central role, as cytokines such as TNF-α and IL-6 directly impair insulin signaling in peripheral tissues and the liver [18]. The reduction in total cholesterol by a mean of 1.60 mmol/L over 6 months is clinically meaningful and warrants prospective confirmation, as it may partly reflect improvement in hepatic lipid metabolism secondary to reduced inflammatory burden.

The echocardiographic findings add a unique dimension to the present study. Improvement in GLS and E/e' following UAE has not previously been systematically reported. GLS is a sensitive marker of subclinical left ventricular systolic dysfunction that precedes changes in ejection fraction [19] and is impaired both by anemia (via compensatory tachycardia and increased wall stress) and by inflammatory cardiomyopathy (via cytokine-mediated myofibril disruption). The improvement in E/e', reflecting reduced left ventricular filling pressure and better diastolic compliance, is consistent with the combined effects of anemia correction, lower inflammatory and oxidative load, and improved insulin sensitivity. These cardiac benefits, observed in the absence of any cardiac-specific treatment, support the hypothesis that UAE exerts a favorable systemic cardiometabolic effect in perimenopausal women.

Several limitations of the present analysis must be acknowledged. First, this is an interim, single-arm analysis; the hysterectomy comparator group is currently being enrolled, and no direct between-group statistical comparisons are possible at this stage. All conclusions regarding superiority or non-inferiority of UAE relative to hysterectomy are based on contextualization with published literature rather than on internally controlled data from the current study. Second, the follow-up period for biomarkers is limited to 6 months, and longer-term trajectories — particularly of ET-1, NO, and cardiac parameters — remain to be established. Third, the absence of flow-mediated dilation (FMD) measurements, which represent the clinical gold standard for endothelial function assessment, is a limitation; reliance on circulating biomarkers, while informative, captures only part of the endothelial phenotype. Fourth, the single-center design at a specialized institution may limit generalizability. Fifth, potential confounders — including lifestyle changes, use of analgesics, and seasonal variation in biomarkers — were not formally controlled.

Conclusion

This prospective interim analysis demonstrates that bilateral uterine artery embolization in perimenopausal women with symptomatic uterine fibroids and/or adenomyosis produces significant and multidimensional systemic benefits extending far beyond fibroid volume reduction. At 6 months post-procedure, UAE is associated with significant improvement in endothelial function (reduction in ET-1, increase in NO), resolution of systemic inflammation (hs-CRP, IL-6, TNF-α), attenuation of oxidative stress (MDA reduction, SOD upregulation), preservation of ovarian endocrine function (stable estradiol), and improvement in metabolic and echocardiographic parameters. These findings collectively define a favorable cardiovascular and endothelial safety profile for UAE that is mechanistically coherent and clinically important for patient selection in the perimenopausal population. The full comparative analysis with the hysterectomy cohort, upon completion of enrollment, will allow definitive conclusions regarding the relative cardiovascular benefits of UAE versus surgical treatment.

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