

**THIS WORK COMPLETED AT:
HANOI MEDICAL UNIVERSITY**

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The thesis will be defended at the university-level thesis assessment

council, at Hanoi Medical University.

At....., date.....month.....year 2026

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**LIST OF PUBLICATIONS
RELATED TO THE THESIS**

1. **Hoang Phuong Nguyen**, Dao LTM, Le Phuong Hoang A, et al. Prevalence of and risk factors for female sexual dysfunction in middle-aged Vietnamese women: A cross-sectional hospital-based study. *Maturitas* - Elsevier. Published 1 October 2025. DOI: [10.1016/j.maturitas.2025.108743](https://doi.org/10.1016/j.maturitas.2025.108743). PMID: 41056629. (Tập chí Q1).
2. **Nguyễn Hoàng Phương**, Nguyen Thi Tan Sinh, Hoang Thanh Van, Le Phuong Hoang Anh, Nguyen Van Anh, Do Thi Thanh Toan. Evaluation of improvements in depression, anxiety, and stress scores (DASS-21) after autologous adipose-derived mesenchymal stem cell infusion in women with sexual dysfunction. *Journal of Medical Research*. Pages 700–714, Volume 198, Issue 1 (2026). <https://doi.org/10.52852/tencyh.v198i1>.

anxiety, and stress in the early-intervention group were 8.0%, 20.0%, and 0%, respectively, lower than the corresponding proportions in the control group of 44.0%, 56.0%, and 48.0%.

▪ **Regarding quality of life (UQOL):** During the first 6 months, the total UQOL score in the intervention group gradually increased over time, whereas it tended to decline in the control group. The interaction coefficient for intervention \times assessment time was -3.45 ($p = 0.001$), indicating a statistically significant difference in the trajectory of quality of life over time between the two groups.

When the control group later received the intervention, FSFI, AMS, DASS-21, and UQOL all improved in a similar pattern, further supporting the consistency of the intervention effect.

Taken together, the findings indicate that autologous adipose-derived mesenchymal stem cell infusion is safe, well tolerated, and has the potential to improve sexual function, mental health, and quality of life in women aged 40–50 years with female sexual dysfunction at Vinmec International General Hospital. However, because this study used a wait-list control design without placebo control or blinding, the self-reported outcomes, particularly improvements in mental health, should be interpreted with caution within the study population and the 12-month follow-up period.

RECOMMENDATIONS

1. Early screening for FSD should be implemented in women aged 40–50 years, while integrating mental health assessment, particularly for depression, anxiety, and stress, in order to enable early detection and timely intervention, thereby improving quality of life.
2. Health communication and education should be strengthened to raise awareness of sexual health, reduce social stigma, and encourage women to actively discuss their concerns and seek medical support.
3. Autologous adipose-derived MSC infusion shows potential as an adjunct to hormone therapy, particularly in middle-aged women with FSD for whom hormone therapy is unsuitable or contraindicated. However, phase III double-blind clinical trials with long-term follow-up are needed to evaluate its long-term safety, efficacy, and cost-effectiveness. Future studies should also assess affordability and implementation requirements for standardized procedures before wider clinical adoption.
4. Pilot implementation of autologous adipose-derived MSC infusion should be considered at specialized women's health centers with sufficient technical capacity, in order to assess feasibility and potential applicability in clinical practice.

THESIS INTRODUCTION

1. Study justification

Female sexual dysfunction (FSD) is a health problem of both clinical and social significance, with marked effects on quality of life, mental health, and family well-being. In women aged 40 to 50 years, this period corresponds to the menopausal transition, during which hormonal, psychological, and social changes increase the risk of female sexual dysfunction.

Although female sexual dysfunction is relatively common, many women do not proactively seek medical evaluation or support because of embarrassment, limited knowledge, and the influence of cultural barriers. In Vietnam, female sexual health remains an under-researched field, and the currently available data are still limited and do not fully reflect the true burden of the condition or its related factors among middle-aged women. Current treatment approaches also have limitations in terms of efficacy and long-term safety. In this context, infusion of autologous adipose-derived mesenchymal stem cells represents a promising novel intervention because adipose tissue is an easily accessible, minimally invasive cell source that is suitable for clinical application. Results from the phase I trial at Vinmec International General Hospital showed that this therapy was safe, feasible, and initially demonstrated potential to improve sexual function and quality of life.

Therefore, we conducted the study entitled: “**Current Status of Female Sexual Dysfunction and Outcomes of Autologous Adipose-Derived Mesenchymal Stem Cell Infusion among Women Aged 40–50 Years**” with the following two objectives:

1. *Objective 1: To describe the current status of female sexual dysfunction and identify several related factors among women aged 40–50 years attending Vinmec International General Hospital in 2023–2024.*
2. *Objective 2: To evaluate the effectiveness of autologous adipose-derived mesenchymal stem cell infusion on sexual function, mental health, and quality of life in women aged 40–50 years at Vinmec International General Hospital.*

2. New contributions of the thesis

The dissertation makes four notable novel contributions. First, it provides the first systematic epidemiological data on female sexual dysfunction

among Vietnamese women aged 40 to 50 years, while also identifying associated factors through multivariable analysis with adjustment for confounding factors. These findings contribute to guiding screening, prevention, and the development of appropriate intervention programs for middle-aged women in Vietnam. Second, this is the first clinical trial in Vietnam to evaluate autologous adipose-derived mesenchymal stem cell therapy for the treatment of female sexual dysfunction. The initial findings demonstrate that the therapy is safe and effective after 12 months of follow-up. Third, the dissertation suggests the potential application of this therapy as a personalized treatment approach, particularly for middle-aged women with female sexual dysfunction who are not suitable candidates for, or have contraindications to, hormone therapy, such as those with a history of cancer. These findings also help inform the selection of participants for future studies. Fourth, the dissertation has established a feasible and scalable research framework, including the intervention process from cell preparation, infusion planning, and safety monitoring; a comprehensive set of assessment indicators covering hormonal status, psychological health, and quality of life; and a quality-assured data management system. This provides an important foundation for future interventional research in women's health care.

3. Structure of the thesis

The dissertation consists of 134 pages, including 2 pages of Introduction, 30 pages of Literature Review, 21 pages of Study Subjects and Methods, 49 pages of Results, 27 pages of Discussion, 2 pages of Conclusions, and 1 page of Recommendations. It contains 35 tables, 16 figures, and 12 charts, with 312 references.

The PhD candidate has published two articles in reputable peer-reviewed journals, including one English-language article in *Maturitas* (Q1) and one Vietnamese-language article in the *Journal of Medical Research*.

some international studies, the prevalence of anxiety was higher, whereas depression and stress were similar.

- Several factors associated with female sexual dysfunction among middle-aged women were identified, including lower educational attainment, skill-demanding occupations, lower income, staying up after midnight, no or infrequent physical activity, and lack of communication about sexual needs with the partner. Because of the cross-sectional design, these factors should be interpreted as associated factors rather than evidence of causality.

These findings indicate a substantial burden of female sexual dysfunction among middle-aged women in the study population and highlight the roles of social, economic, and cultural factors. The results provide scientific evidence to inform screening, prevention, and the development of appropriate interventions aimed at improving women's sexual health and quality of life.

2. Effectiveness of autologous adipose-derived MSC infusion on sexual function, mental health, and quality of life in women aged 40–50 years at Vinmec International General Hospital

- Autologous adipose-derived MSC infusion was safe and well tolerated in the study population. Throughout the intervention and follow-up period, no serious adverse events were recorded; adverse events were mainly mild, self-limited, and did not require specific treatment.

- During follow-up, no statistically significant differences in E2 and FSH levels were observed between the two groups. However, the clinical findings suggest that autologous adipose-derived MSC infusion has the potential to improve sexual function, mental health, and quality of life, possibly mainly through local mechanisms rather than through changes in systemic hormonal levels, as follows:

- **Regarding female sexual function (FSFI):** FSFI scores in the intervention group increased significantly in most domains as well as in the total score. After 6 months, the early intervention group improved by 6.6 points, from 19.8 to 26.4, whereas the control group showed almost no change. Improvement began to appear around month 3 and was most pronounced at month 6, with a relatively consistent pattern across the domains of female sexual function.

- **Regarding menopausal symptoms (AMS):** The therapy improved menopausal symptoms, more clearly in the early intervention group. The difference between the two groups became statistically significant from month 6 ($p = 0.014$) and was maintained through month 12 ($p = 0.001$). The degree of improvement was 69.0% in the early intervention group compared with 38.1% in the delayed intervention group. Improvement appeared earliest in urogenital symptoms at 3 months, followed by psychological symptoms at 6 months and physical symptoms at 12 months. At 6 months, the clinical response rate defined as $AMS \leq 10$ was significantly higher in the early intervention group than in the delayed intervention group (52.0% vs 12.0%; $p = 0.005$).

- **Regarding mental health (DASS-21):** Self-reported psychological symptoms assessed by DASS-21 decreased after intervention. After 6 months, the total DASS-21 score in the early-intervention group decreased by 54.6%, greater than the 16.6% reduction in the control group; the earliest difference appeared in the stress domain from month 3 ($p = 0.026$). At month 6, the proportions remaining in the pathological range for depression,

at month 6. Clinically, at month 6, the proportions of participants remaining in the pathological symptom range were lower in the intervention group than in the control group across all three domains. By month 12, when both groups had completed the intervention, DASS-21 scores had decreased to similar levels.

The improvement in DASS-21 scores in this study was likely indirectly related to improved sexual function, reduced menopausal symptoms, less discomfort during intercourse, better sleep, and improved quality of life. Although some preclinical evidence suggests that MSCs may affect biological mechanisms involved in emotional regulation, this study did not directly measure local physiological indicators, neuroinflammatory markers, or neurotrophic factors, and no mediation analysis was performed. Therefore, the main mechanism underlying the improvement in DASS-21 scores after intervention cannot yet be determined.

4.2.6. Improvement in quality of life

The study findings showed that autologous adipose-derived MSC infusion was associated with improved quality of life in women aged 40–50 years, most clearly at the 6-month time point. Before intervention, UQOL scores did not differ between the two groups; after 6 months, the intervention group had significantly higher scores across all 4 domains, namely work, health, mental health, and sexual life, and the total UQOL score was also significantly higher. Improvement was most prominent in the sexual domain, consistent with the trend of improved sexual function measured by the FSFI. Linear mixed-effects model analysis also showed that the degree of improvement over time was greater in the intervention group than in the control group; by 12 months, the difference between the two groups was no longer evident because the control group had received delayed intervention.

Compared with international studies, these findings suggest a more positive signal than some reports on HRT and cell therapy. For HRT, international studies have shown inconsistent effects on quality of life, depending on baseline symptom severity and the assessment tools used; some studies reported improvement only in a few domains such as work, mental health, and sexual life, whereas other analyses found no clear improvement in overall quality of life. For cell therapy, international evidence remains limited; some studies have reported a trend toward improvement in sexual quality of life without reaching statistical significance, and recent meta-analyses have not yet confirmed a clear effect. Therefore, the findings of this study suggest the potential of autologous adipose-derived MSCs to improve multidimensional quality of life in middle-aged women, but further randomized controlled studies with larger sample sizes are still needed to confirm efficacy.

CONCLUSION

1. Current status of FSD and some associated factors in women aged 40–50 years at Vinmec International General Hospital in 2023–2024

- The prevalence of FSD in women aged 40–50 years, assessed using the FSFI questionnaire with a cutoff score of ≤ 26.55 , was 45.1% (95% CI: 38.4%–52.0%).
- Mental health disturbances were common, with prevalences of anxiety, depression, and stress of 43.1%, 26.0%, and 31.4%, respectively. Compared with

CHAPTER 1 LITERATURE REVIEW

1.1. Definition and classification of female sexual dysfunction

Female sexual dysfunction (FSD) is defined as a persistent or recurrent disturbance in one or more domains of the sexual response cycle, including desire, arousal, orgasm, or pain during intercourse, that causes significant distress to the woman or adversely affects her relationship with her partner. According to current classification systems such as ICD-11 and DSM-5, the diagnosis is made only when symptoms have persisted for a sufficiently long period, recur over time, and are not better explained by a physical illness, another mental disorder, or the effects of medications or substances. In clinical practice, female sexual dysfunction is commonly categorized into the following major groups: low sexual desire, arousal disorder, orgasmic disorder, genito-pelvic pain/penetration disorder, and other related disorders. This approach is important for screening, diagnosis, and selection of appropriate interventions.

1.2. Epidemiology of female sexual dysfunction

FSD is a common health problem worldwide, although its prevalence varies considerably across countries, age groups, and assessment methods. In Europe, the prevalence of FSD is often reported to range from 40% to 50%, whereas in Asia, many studies have found that more than 30% of women experience at least one type of sexual dysfunction. In Vietnam, no nationwide survey has yet been conducted; however, studies in specific populations have reported a wide prevalence range, from 34.2% to 89.4%. Common manifestations include reduced sexual desire, decreased arousal, inadequate lubrication, difficulty achieving orgasm, and pain during intercourse. Overall, currently available data indicate that FSD is an important health concern, particularly among middle-aged women and women with underlying medical conditions or specific reproductive circumstances.

1.3. Causes and risk factors

FSD in middle-aged women is a multifactorial condition arising from complex interactions among biological, psychological, social, cultural, and partner-related factors. Among these, age and the menopausal transition are particularly important because they are accompanied by a decline in sex hormones, especially estrogen. Demographic factors such as educational level and marital status may also be associated with the risk of FSD.

From a biological perspective, hormonal changes in middle-aged women play a central role in the development of FSD. Reduced estrogen and androgen levels may lead to vaginal dryness, dyspareunia, decreased arousal, and reduced sexual desire. In addition, many chronic conditions, including cardiovascular disease, diabetes, metabolic disorders, autoimmune diseases, and neurological disorders, as

well as commonly used medications such as antidepressants, hormonal contraceptives, and antiandrogen agents, may impair sexual function. Gynecologic and obstetric factors, including pregnancy, childbirth, menopause, pelvic floor disorders, genital tract infections, and pelvic surgery, may also increase the risk of sexual dysfunction.

In addition, psychological and social factors have a substantial impact on women's sexual health. Depression, anxiety, chronic stress, limited communication or reluctance to discuss sexual needs with a partner, family pressures, psychological trauma, and cultural barriers may all reduce sexual desire, arousal, and sexual satisfaction. Lifestyle factors such as obesity, physical inactivity, smoking, alcohol consumption, and substance use are also associated with FSD through their effects on circulation, metabolism, hormonal balance, and mental health.

1.4. Pathophysiology of FSD in middle-aged women

The pathophysiology of FSD in middle-aged women mainly involves three major mechanisms: endocrine disturbances, neurovascular dysfunction, and chronic inflammation associated with metabolic disorders. Declining estradiol and testosterone levels during the menopausal transition and postmenopause lead to reduced genital blood flow, vaginal mucosal atrophy, decreased secretions, vaginal dryness, dyspareunia, and reduced sexual desire. At the same time, impaired neural transmission and reduced pelvic circulation limit the arousal response, while chronic inflammation and metabolic disturbances contribute to endothelial damage, reduced genital sensitivity, and worsening sexual dysfunction. These mechanisms do not act independently, but rather interact with one another, resulting in the diverse clinical manifestations observed in middle-aged women.

1.5. Instruments for assessing FSD

Because FSD is a multidimensional syndrome, the use of standardized instruments plays an important role in screening, assessing severity, and monitoring treatment outcomes. Among currently available tools, the Female Sexual Function Index (FSFI) is the most widely used. It consists of 19 items assessing 6 domains: desire, arousal, lubrication, orgasm, satisfaction, and pain during intercourse. The FSFI is easy to administer, requires only a short completion time, and has been standardized and culturally adapted for the Vietnamese population. In addition, this study used the Australasian Menopause Society symptom score sheet (AMS), to assess menopausal symptoms across 3 domains: psychological, somatic, and urogenital. The combined use of FSFI and AMS allows a relatively comprehensive assessment of sexual function and related symptoms in middle-aged women.

1.6. Interventions for improving FSD

mainly through local mechanisms such as paracrine effects, angiogenesis, and immunomodulation, thereby improving the tissue microenvironment and restoring urogenital function rather than directly altering systemic endocrine levels.

4.2.3. Changes in the Female Sexual Function Index (FSFI)

The study showed that autologous adipose-derived MSC infusion markedly improved female sexual function. After 6 months, the total FSFI score in the early-intervention group increased from 19.8 to 26.4, whereas the control group showed almost no change, and the difference between the two groups was statistically significant. Improvement began to appear from month 3, initially in lubrication, orgasm, satisfaction, and pain during intercourse; by month 6, improvement was observed across all 6 FSFI domains. Linear mixed-effects model analysis also showed that the rate of improvement over time was significantly greater in the intervention group than in the control group.

These findings indicate that the therapy had effects not only on the total FSFI score but also across multiple components of sexual function. The magnitude of improvement observed in this study was consistent with some preliminary reports on cell therapy and in line with previous phase I findings. However, current evidence remains limited because the number of clinical studies is still small and sample sizes remain modest. Therefore, larger randomized controlled trials with longer follow-up are needed to confirm the effectiveness of this therapy.

4.2.4. Changes in menopausal symptom scores (AMS)

The results showed that autologous adipose-derived MSC infusion was associated with improvement in menopausal symptoms, with greater improvement in the early-intervention group. The total AMS score decreased more in Group A than in Group B, and the between-group difference became statistically significant from month 6 and remained so through month 12. In terms of clinical significance, at month 6 the response rate defined by an AMS score ≤ 10 was 52.0% in Group A, markedly higher than 12.0% in Group B.

Analysis by domain showed that improvement did not occur simultaneously. The urogenital domain improved earliest, beginning at month 3; the psychological domain improved clearly from month 6; and the somatic domain showed clearer improvement at month 12. These findings suggest that the therapy may act through multiple mechanisms and that its effects become more apparent over the medium to long term, indicating potential utility in improving perimenopausal and menopausal symptoms in middle-aged women.

4.2.5. Changes in depression, anxiety, and stress scores (DASS-21)

The study findings showed that autologous adipose-derived MSC infusion was associated with improvement in self-reported psychological symptoms assessed by DASS-21 among women with FSD. However, the findings should be interpreted with caution because the study used a wait-list control design without placebo control or blinding. At baseline, total DASS-21 scores were comparable between the two groups. After 6 months, the intervention group showed a greater reduction than the control group across depression, anxiety, and stress. The earliest difference appeared in the stress domain from month 3 and became clearer

more likely to have FSD, possibly reflecting occupational pressure, workload, and prolonged stress.

Regarding lifestyle, staying up late and low physical activity were associated with FSD, consistent with the literature on the effects of sleep, physical activity, mental health, and sexual response. Low income may reflect financial stress and limited access to health care services. Limited communication about sexual needs with the partner was also noteworthy, indicating the influence of marital communication and sociocultural context on women's sexual health.

Because of the cross-sectional design, these factors should be interpreted as associated factors rather than evidence of causality. Some factors, such as age, BMI, number of children, mode of delivery, and contraceptive method, were not significantly associated with FSD, possibly because the study sample was relatively homogeneous.

4.2. Effectiveness of autologous adipose-derived MSC infusion on sexual function, mental health, and quality of life in women aged 40–50 years at Vinmec International General Hospital

4.2.1. Safety of autologous adipose-derived MSC infusion

The study was conducted in 50 women randomly assigned into two groups with comparable baseline characteristics in terms of age, BMI, duration of FSD, and lifestyle, indicating good baseline homogeneity. The autologous adipose-derived MSC product was culture-expanded and administered intravenously in 2 infusions 3 months apart at a dose of 1×10^6 viable cells/kg. All cell batches met quality standards, with high positivity for CD73, CD90, and CD105, negative markers below the required threshold, high cell viability, negative tests for mycoplasma, bacteria, and fungi, low endotoxin levels, and normal karyotype. These findings indicate that the cell product was stable and biologically safe before infusion.

Clinically, no serious adverse events related to the therapy were recorded. A total of 15 adverse events occurred, mostly mild; among them, 4 were considered related to the intervention, mainly post-infusion headache and pain at the infusion site. All symptoms resolved spontaneously and did not require specific treatment. These findings indicate that autologous adipose-derived MSC infusion was safe and well tolerated, consistent with the previous phase I study.

4.2.2. Changes in serum estradiol (E2) and follicle-stimulating hormone (FSH) levels

Estrogen deficiency is an important mechanism related to impaired sexual function in women during the menopausal transition; therefore, E2 and FSH were selected as evaluation indices in this study. The results showed no statistically significant differences in E2 and FSH levels between the early-intervention group and the control group at baseline and at 1, 3, 6, and 12 months after intervention. Thus, there is currently no evidence that autologous adipose-derived mesenchymal stem cell infusion markedly altered systemic endocrine indices during the follow-up period.

Although E2 and FSH did not change significantly, sexual function and quality of life improved after intervention. This finding suggests that the therapy may act

Current interventions for improving FSD include both pharmacological and nonpharmacological approaches. From a pharmacological perspective, hormone replacement therapy is effective for vasomotor symptoms, urogenital symptoms, and some manifestations of sexual dysfunction related to estrogen deficiency, although long-term use still raises concerns regarding safety. Other agents, including testosterone, flibanserin, bremelanotide, PDE5 inhibitors, topical estrogen, and lubricants, have also been studied and used to varying extents; however, their efficacy remains inconsistent, and further long-term evidence is still needed.

1.7. Autologous adipose-derived mesenchymal stem cell therapy for the treatment of FSD

Mesenchymal stem cells (MSCs) are a population of cells with proliferative, immunomodulatory, and tissue-regenerative properties. Adipose tissue is a favorable source because it is easily accessible, minimally invasive, and suitable for clinical application. Therefore, adipose-derived MSCs are considered a potential approach for improving FSD.

Preclinical studies suggest that adipose-derived MSCs may act through paracrine signaling, angiogenesis, anti-inflammatory effects, anti-apoptotic effects, and improvement of the tissue microenvironment. These mechanisms may support structural repair, improve circulation in female genital tissues, and help reduce symptoms such as vaginal dryness, dyspareunia, or perimenopause-related disturbances. Any psychological improvement, if observed, should be interpreted cautiously as an indirect result of improved genital symptoms, sleep, and quality of life, rather than evidence of a direct effect of MSCs on the central nervous system.

Clinically, evidence on MSC application in female reproductive disorders remains limited, mainly from studies with small sample sizes, short follow-up, and no control groups. Early studies in Asherman syndrome, vaginal atrophy, or primary ovarian insufficiency have reported positive signals, including symptom improvement, menstrual recovery, increased estradiol, or improved follicular activity. In Vietnam, the 2021 study by Nguyen Thanh Liem et al. showed that intravenous infusion of autologous adipose-derived MSCs in women with sex hormone deficiency was safe, feasible, and had potential to improve sexual life. However, further controlled clinical trials with standardized outcome measures are needed to confirm efficacy and safety. On this basis, the present study was conducted to evaluate the effectiveness of this therapy in women aged 40 to 50 years, while also examining the relationship between improvement in sexual function, mental health, and quality of life.

CHAPTER 2 MATERIALS AND METHODS

2.1. Study setting and duration

- The study was conducted at Vinmec Times City International General Hospital, Hanoi.

- Study duration: from October 2023 to December 2025.

2.2. Study participants

Objective 1: Women aged 40 to under 51 years who attended the Women's Health Center at Vinmec Times City International General Hospital, voluntarily agreed to participate, and had not yet reached menopause. Exclusion criteria included mental disorders, inability to complete the questionnaires independently, absence of sexual activity, complete amenorrhea for at least 12 months, or progressive cancer or ongoing cancer treatment.

Objective 2: Participants for Objective 2 were selected from the above group and additionally met endocrine and clinical criteria, including FSH \leq 29.8 IU/L, FSFI score \leq 26.55 or AMS score \geq 15, normal liver, renal, and thyroid function, no active infectious disease, and willingness to receive autologous adipose-derived mesenchymal stem cell infusion. Exclusion criteria included severe endocrine or metabolic disorders, severe systemic disease, factors interfering with the assessment of sexual activity, or current use of hormone therapy or other interventions affecting the hypothalamic-pituitary-gonadal axis.

2.3. Study design

Objective 1: Cross-sectional descriptive study.

Objective 2: Phase II randomized controlled clinical trial using a wait-list control design.

Participants were randomized in a 1:1 ratio:

- **Group A, early intervention:** infusions at T0 and T3
- **Group B, wait-list control:** observed for 6 months, then treated at T6 and T9.

Assessment time points: T0, T1, T3, T6, and T12

2.4. Sample size

Objective 1: 204 participants.

Objective 2: 50 participants, 25 in each group, calculated based on the comparison of two independent means using the change in FSFI score

2.5. Sampling method

Objective 1: Consecutive enrollment of all eligible participants during the study period.

Objective 2: Block randomization with a block size of 4 and a 1:1 allocation ratio.

2.6. Variables and data collection

Data were collected from study case report forms and standardized assessment tools:

- Female Sexual Function Index, FSFI: assessment of sexual function
- Australasian Menopause Society symptom score sheet, AMS: assessment of menopausal symptoms

The study found that the prevalence of FSD in women aged 40–50 years was 45.1% (95% CI: 38.4%–52.0%). This result falls within the range reported worldwide and is comparable to some studies from the United States, but lower than reports from China and Iran and higher than some studies from Hong Kong and Thailand. Differences among studies may be related to population characteristics, sociocultural context, measurement tools, and diagnostic cutoffs. Overall, the findings are consistent with global trends and indicate that FSD is an important health issue among middle-aged women.

In Vietnam, data on FSD remain limited and have mainly focused on specific populations such as women with depression or healthcare workers. Recent domestic studies have consistently shown that female sexual health is an issue that deserves attention; however, there is still no broadly representative evidence for middle-aged women in the community. The 45.1% prevalence of FSD found in this study indicates a substantial burden among women aged 40–50 years and provides practical evidence for the development of appropriate screening, prevention, and intervention programs to improve sexual health and overall health in Vietnamese women.

4.1.2 Mental health status: prevalence of depression, anxiety, and stress

The study found a prevalence of depression of 26.0% among women aged 40–50 years. This result is comparable to many international reports in middle-aged women and indicates that depression is an important issue during the menopausal transition. Differences across studies may be related to age, menopausal stage, underlying diseases, and assessment tools.

The prevalence of anxiety in this study was 43.1%, which is higher than some international reports. Anxiety may adversely affect sexual function through reduced arousal, reduced pleasure, and worsening of FSD. This relatively high prevalence may be related to the study sample, which consisted of women attending a hospital, many of whom were experiencing perimenopausal symptoms or other health concerns.

The prevalence of stress was 31.4%, which is comparable to that reported in some populations of middle-aged women worldwide. Prolonged stress may negatively affect sexual function through disruption of hormonal regulation, reduced arousal, and poorer quality of life.

These findings indicate that mental health problems are relatively common among women aged 40–50 years and should be routinely screened for and assessed alongside the clinical approach to care.

4.1.3 Some factors associated with FSD in women aged 40–50 years

The study identified several factors associated with FSD among women aged 40–50 years, including below-university education, skill-demanding occupations, low household income, staying up after midnight, low physical activity, and limited communication about sexual needs with the partner.

Women with below-university education were more likely to have FSD, suggesting the role of education in improving health literacy and communication about sexuality. Those engaged in skill-demanding or intellectual work were also

	months			
Total UQOL score	Before infusion	60.87 ± 16.26	68.04 ± 12.27	>0.05
	After 6 months	65.17 ± 20.49	52.04 ± 4.44	<0.001***
	After 12 months	73.78 ± 19.91	73.91 ± 10.61	>0.05

Comment: Before intervention, UQOL scores in all four domains and the total score were comparable between the two groups ($p > 0.05$). During the first 3 months, the differences between the groups were not statistically significant. At 6 months, Group A had higher scores than Group B in all four domains: work (66.71 vs. 48.71; $p < 0.001$), health (61.40 vs. 49.80; $p = 0.001$), mental health (73.00 vs. 62.00; $p = 0.005$), and sexual life (53.33 vs. 28.00; $p < 0.001$). The total UQOL score was also markedly higher in Group A (65.17 vs. 52.04; $p < 0.001$). At 12 months, when both groups had received the intervention, the differences were no longer statistically significant.

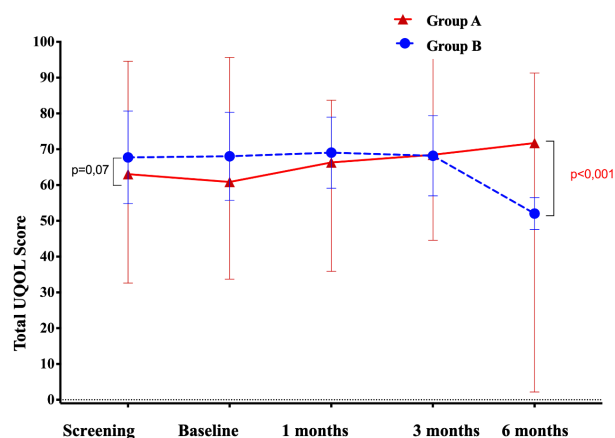


Figure 3.6. Changes in total UQOL score before and after 6 months of intervention

Linear mixed-effects model analysis showed that the trajectory of change in total UQOL score over time differed significantly between the two groups during the first 6 months of follow-up (Intervention × Time interaction: $\beta = -3.45$; $p = 0.001$). This finding indicates that quality of life improved over time to a greater extent in Group A than in Group B during the period when the control group had not yet received the intervention.

CHAPTER 4: DISCUSSION

4.1. Current status and some factors associated with FSD in women aged 40–50 years at Vinmec International General Hospital, 2023–2024

4.1.1 Prevalence of FSD

- Depression Anxiety Stress Scales 21, DASS-21: assessment of depression, anxiety, and stress
- Utian Quality of Life Scale, UQOL: assessment of quality of life
- Laboratory tests: estradiol (E2), and FSH
- Independent variables included demographic characteristics, economic factors, behavioral factors, and obstetric history.

2.7. Intervention

Autologous adipose-derived mesenchymal stem cell infusion:

- Dose: 1×10^6 cells/kg
- Route: intravenous infusion, with two infusions administered at a 3-month interval

The procedures for liposuction, cell isolation, culture, storage, quality control, and preparation of the cell product were carried out according to the protocol approved by the Ministry of Health under standard clean-room conditions. Before use, the cells were tested for sterility, viability, surface markers, and genetic stability, in compliance with quality standards of the ISCT and the Ministry of Health.

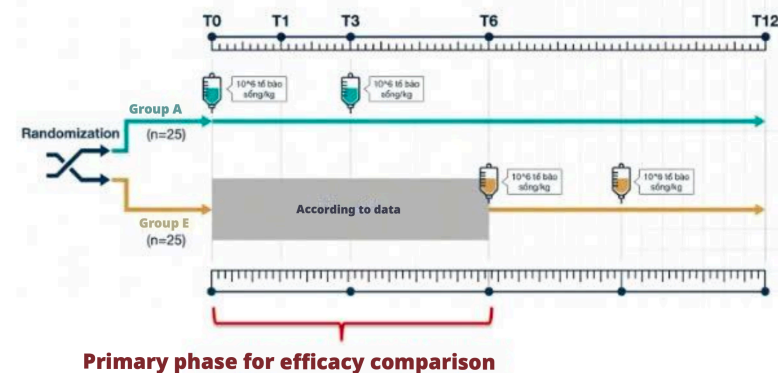


Figure 2.1. Flowchart of the phase II clinical trial intervention protocol.

2.8. Data analysis

- Data were entered and managed using REDCap software. Statistical analyses were performed using R version 4.4.0.
- Descriptive statistics included mean ± standard deviation, median with interquartile range, and frequency with percentage.
- Comparisons between groups were performed using the t - test, Mann–Whitney U test, and chi - square test, as appropriate. Multivariable logistic regression was used to identify factors associated with FSD.
- For the interventional objective, analyses included within-group and between-group comparisons, analysis of covariance with adjustment for baseline values, and linear mixed-effects models for longitudinal data.
- A p - value of less than 0.05 was considered statistically significant.

2.9. Bias and bias control

Potential sources of bias included self-administered questionnaires, the sensitive nature of the topic, and possible placebo effects. To minimize bias, the study standardized the data collection procedures, used validated instruments, provided training for the research staff, and ensured privacy during data collection.

2.10. Research ethics

The study was approved by the Vinmec–VinUni Ethics Committee under Decision No. 117/2023/CN-HĐĐĐ VMEC and by Hanoi Medical University under Certificate No. NCS2024/GCN-HMUIRB. The clinical trial was also authorized by the Ministry of Health. The study was registered at ClinicalTrials.gov with the identifier NCT06726538.

All participants provided written informed consent and had the right to withdraw from the study at any time. All data were coded and kept confidential in accordance with regulations.

	intervention (T0)	months (T12)	value#	interventi on (T6)	months (T12)	
Depression	11.5 ± 6.7	2.2 ± 3.0	<0.001	7.8 ± 4.0	2.0 ± 2.5	<0.001
Anxiety	13.9 ± 8.4	2.2 ± 2.7	<0.001	8.3 ± 4.9	2.7 ± 2.8	<0.001
Stress	17.3 ± 6.4	4.6 ± 3.0	<0.001	14.6 ± 5.7	5.0 ± 3.2	<0.001
Total DASS-21 score	42.7 ± 19.9	9.0 ± 7.9	<0.001	30.7 ± 11.7	9.7 ± 6.9	<0.001

Comment: In terms of clinical significance, at 6 months Group A had clearly lower rates of pathological-range symptoms than Group B across all three domains: depression, 8.0% vs. 44.0%; anxiety, 20.0% vs. 56.0%; and stress, 0.0% vs. 48.0%. Within-group analysis showed that after autologous adipose-derived MSC infusion, depression, anxiety, stress, and total DASS-21 scores all decreased significantly in both groups; the total score declined from 42.7 to 9.0 in Group A and from 30.7 to 9.7 in Group B.

3.2.7. Changes in quality-of-life scores (UTIAN-UQOL)

3.2.7.1. Comparison of UQOL scores between the two groups at different study time points

Table 3.8. Comparison of UQOL scores between the two groups before and after 12 months of intervention

Domain	Time point	Group A (n=25)	Group B (n=25)	p value#
Work	Before infusion	65.29 ± 17.24	69.86 ± 16.97	>0.05
	After 6 months	66.71 ± 21.86	48.71 ± 9.77	<0.001***
	After 12 months	73.71 ± 26.30	73.14 ± 14.69	>0.05
Health	Before infusion	58.20 ± 23.13	65.20 ± 17.47	>0.05
	After 6 months	61.40 ± 21.04	49.80 ± 9.07	0.001**
	After 12 months	68.60 ± 19.50	68.20 ± 17.25	>0.05
Emotional well-being	Before infusion	67.67 ± 19.52	78.00 ± 13.79	>0.05
	After 6 months	73.00 ± 22.92	62.00 ± 10.58	0.005**
	After 12 months	84.00 ± 19.20	85.83 ± 10.14	>0.05
Sexual life	Before infusion	47.67 ± 19.91	48.67 ± 19.94	>0.05
	After 6 months	53.33 ± 22.82	28.00 ± 15.00	<0.001***
	After 12	65.00 ± 22.69	62.00 ± 18.33	>0.05

Group B, although the differences did not reach statistical significance. At 6 months, the response rate in Group A increased markedly and was significantly higher than that in Group B (52.0% vs. 12.0%; $p = 0.005$), with an OR of 7.59 (95% CI: 1.64–49.86).

3.2.6. Changes in depression, anxiety, and stress scores (DASS-21)

3.2.6.1. Comparison of DASS-21 scores between the two groups at different study time points

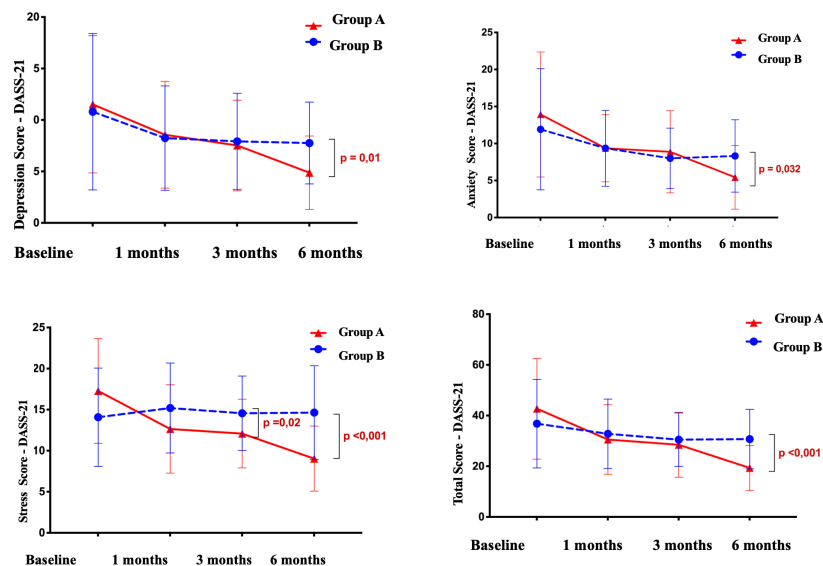


Figure 3.5. Depression, anxiety, and stress scores (DASS-21) before and after 6 months of intervention

Comment: Before intervention, depression, anxiety, stress, and total DASS-21 scores were comparable between the two groups. After 1 month, all scores decreased in both groups, but no significant between-group difference was observed. From 3 months onward, Group A began to show greater improvement in the stress domain. At 6 months, Group A had significantly lower depression, anxiety, stress, and total DASS-21 scores than Group B, with corresponding values of 4.88 vs. 7.76, 5.44 vs. 8.32, 9.04 vs. 14.6, and 19.4 vs. 30.7.

3.2.6.2. Changes in depression, anxiety, and stress scores (DASS-21) before and after intervention within each group

Table 3.7. Depression, anxiety, and stress scores (DASS-21) before and after 12 months of intervention

	Group A			Group B		
	Before	After 12	p	Before	After 6	p value#

CHAPTER 3: STUDY RESULTS

3.1. Current status and some factors associated with FSD in women aged 40–50 years

3.1.1. General characteristics of the study population

From October 2023 to June 2024, a total of 204 eligible women were enrolled in the study. The mean age of the participants was 44.4 ± 3.0 years, and the mean BMI was 22.6 ± 2.07 kg/m². Most participants were married (97.5%), lived in urban areas (91.7%), had university or postgraduate education (87.8%), and were employed (94.1%). The mean age of their partners was 47.0 ± 4.1 years, and the mean duration of marriage was 17.3 ± 4.4 years.

Regarding obstetric and gynecologic characteristics, 82.4% had one to two children; 46.0% had delivered vaginally and 40.1% by cesarean section. The most common contraceptive methods were periodic abstinence or withdrawal (37.3%), condoms (28.9%), and intrauterine devices (11.8%). Sexual intercourse frequency was mainly 3 to 8 times per month. A total of 66.7% reported little or almost no communication with their partners regarding sexual needs.

Regarding lifestyle characteristics, 40.2% reported staying up late after midnight, and the mean sleep duration was 6.87 ± 1.03 hours per night. Physical activity was limited, with only 10.3% exercising regularly. No participant reported smoking, and the prevalence of alcohol consumption was 6.9%. The proportion of households with a monthly income above 20 million VND was 68.6%.

3.1.2. Prevalence of FSD, depression, anxiety, and stress

3.1.2.1. Prevalence of FSD

Table 3.1. Prevalence of FSD according to the Female Sexual Function Index, FSFI (n = 204)

Indicator	Value n (%)
With FSD	92 (45.1%), 95% CI: 38.4% - 52.0%
FSFI domain	Mean \pm SD
Total score	25.20 \pm 5.87
Desire	4.04 \pm 1.32
Arousal	4.02 \pm 1.06
Lubrication	4.39 \pm 1.18
Orgasm	4.13 \pm 1.14
Satisfaction	4.07 \pm 1.10
Reduce pain during intercourse	4.55 \pm 1.27

Comment:

Among the 204 women assessed using the FSFI, 92 were identified as having FSD, defined as an FSFI score of 26.55 or lower, corresponding to a prevalence of 45.1% (95% CI: 38.4%–52.0%) at the time of assessment. The mean FSFI score of the overall sample was 25.20 ± 5.87 .

3.1.2.2. Prevalence of depression, anxiety, and stress

According to the DASS-21 scale, depression, anxiety, and stress were classified into normal, mild, moderate, and severe levels; the detailed distribution is presented in Figure 3.1. The prevalence rates were 26.0% for depression,

including 17.2% mild and 8.8% moderate, with no severe cases recorded; 43.1% for anxiety, including 3.4% mild, 33.8% moderate, and 5.9% severe; and 31.4% for stress, including 17.2% mild, 12.3% moderate, and 2.0% severe.

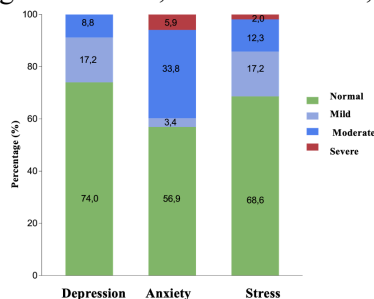


Figure 3.1. Prevalence of depression, anxiety, and stress according to the DASS-21 scale

3.1.3. Some factors associated with FSD in the study population

3.1.3.1. Multivariable analysis of factors associated with FSD

Table 3.2. Marital, lifestyle, and health behavior factors associated with FSD

Independent variable	Group	β coefficient	aOR	95% CI	p value
Educational level	Below university	1.19	3.3	1.08–10.83	0.04*
	University and postgraduate	0	1		
Occupation	Skilled/professional work	1.03	2.8	1.39–5.78	0.004**
	Homemaker/manual labor	0	1		
Monthly household income	≤ 20 million VND	1.06	2.9	1.42–6.09	0.004**
	> 20 million VND	0	1		
Staying up late after midnight	Yes, after 0:00 a.m.	0.73	2.08	1.01–4.35	0.049*
	No, before 0:00 a.m.	0	1		
Physical activity	None or rarely	0.93	2.53	1.25–5.18	0.009**
	Regular or occasional	0	1		
Communication of sexual needs with partner	No communication or avoidance	0.86	2.36	1.13–5.08	0.025*
	Moderate to open/frequent communication	0	1		

Comment: The results of the multivariable logistic regression analysis showed that several socioeconomic characteristics, lifestyle factors, and communication about sexual needs with the partner were independently associated with FSD among women aged 40 to 50 years. Specifically, women with below university education

Figure 3.2 shows that after the intervention, FSFI scores in Group A gradually increased and remained stable over time, whereas those in Group B fluctuated around baseline and did not show a clear trend toward improvement.

3.2.5. Changes in menopausal symptom scores (AMS)

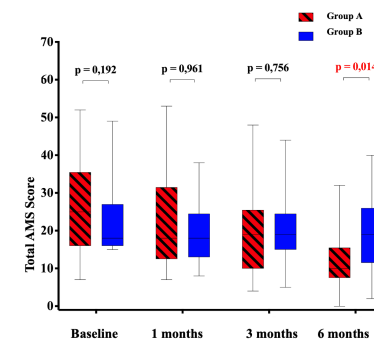


Figure 3.3. Total AMS score before and after 6 months of intervention

Comment: The total AMS score decreased over time in both groups, but the reduction was more pronounced in Group A than in Group B. Before intervention and at 1 and 3 months, the differences between the two groups were not statistically significant ($p > 0.05$). At 6 months, Group A had a significantly lower total AMS score than Group B (12.3 ± 7.17 vs. 19.0 ± 10.30 ; $p = 0.014$).

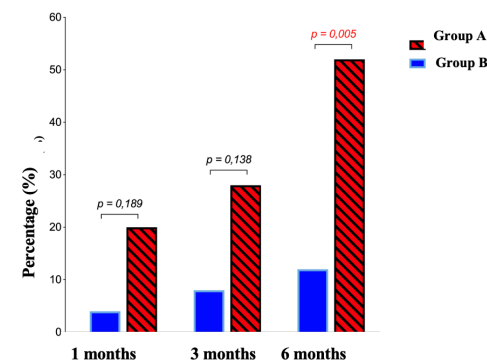


Figure 3.4. Proportion of participants responding to the intervention according to total AMS score after 6 months of treatment

Comment: To evaluate the clinical improvement of menopausal symptoms, treatment response was defined as a reduction in the total AMS score to ≤ 10 . Figure 3.4 shows that at 1 and 3 months, Group A had a higher response rate than

	After 6 months	3.72 ± 0.55	2.76 ± 0.78	<0.001***
	After 12 months	4.56 ± 0.65	3.4 ± 0.93	<0.001***
Lubrication	Before infusion	3.59 ± 1.22	3.68 ± 1.31	>0.05
	After 3 months	4.64 ± 0.83	3.53 ± 1.75	0.009**
	After 6 months	4.74 ± 0.46	3.72 ± 1.77	0.005**
	After 12 months	5.23 ± 0.48	4.99 ± 0.65	>0.05
Satisfaction	Before infusion	3.33 ± 0.92	3.44 ± 0.98	>0.05
	After 3 months	4.11 ± 0.84	3.30 ± 1.08	0.013*
	After 6 months	4.51 ± 0.47	3.30 ± 1.34	<0.001***
	After 12 months	4.75 ± 0.51	4.45 ± 0.68	0.045*
Total FSFI score	Before infusion	19.8 ± 5.36	20.1 ± 6.12	>0.05
	After 3 months	24.8 ± 3.99	19.8 ± 7.33	0.004**
	After 6 months	26.4 ± 1.72	19.9 ± 7.63	<0.001***
	After 12 months	29.5 ± 2.65	26.6 ± 3.55	0.001**

Comment: Before infusion, FSFI scores were comparable between the two groups. After 3 months, Group A had higher lubrication, satisfaction, and total FSFI scores than Group B. After 6 months, the differences became more pronounced, with desire, lubrication, satisfaction, and total FSFI scores all significantly higher in Group A than in Group B. After 12 months, scores increased in both groups; however, Group A continued to maintain higher desire, satisfaction, and total FSFI scores than Group B. Linear mixed-effects model analysis also showed that the improvement in total FSFI score over time was significantly greater in Group A than in Group B.

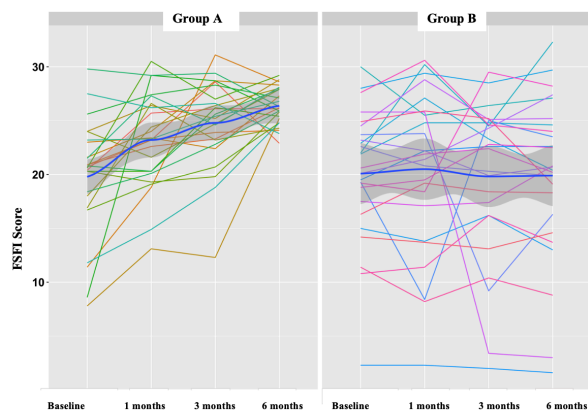


Figure 3.2. Female Sexual Function Index scores before and after 6 months of intervention

had 3.30 times higher odds of having FSD than those with university or postgraduate education (aOR = 3.30; 95% CI: 1.08–10.83; p = 0.04). Women engaged in skill-demanding occupations had 2.80 times higher odds of having FSD than homemakers or unskilled/manual workers (aOR = 2.80; 95% CI: 1.39–5.78; p = 0.004). Women with a monthly household income of ≤ 20 million VND had 2.90 times higher odds of having FSD than those with a monthly household income of > 20 million VND (aOR = 2.90; 95% CI: 1.42–6.09; p = 0.004).

Regarding lifestyle factors, women who stayed up after midnight had 2.08 times higher odds of having FSD than those who went to bed before midnight (aOR = 2.08; 95% CI: 1.01–4.35; p = 0.049). Women who did not engage in or rarely engaged in physical activity had 2.53 times higher odds of having FSD than those who engaged in physical activity occasionally or regularly (aOR = 2.53; 95% CI: 1.25–5.18; p = 0.009). In addition, women who did not communicate or avoided communicating about sexual needs with their partner had 2.36 times higher odds of having FSD than those who communicated at a moderate to open or frequent level (aOR = 2.36; 95% CI: 1.13–5.08; p = 0.025).

In summary, the factors independently associated with FSD in the multivariable model included below university education, skill-demanding occupations, monthly household income of ≤ 20 million VND, staying up after midnight, no or rare physical activity, and no communication or avoidance of communication about sexual needs with the partner.

3.2. Effectiveness of autologous adipose-derived mesenchymal stem cell infusion on sexual function, mental health, and quality of life in women aged 40–50 years at Vinmec International General Hospital

3.2.1. General characteristics of the study participants

Table 3.3. General characteristics of the study participants

Characteristic	Group A – Early intervention (N=25)	Group B – Control (N=25)	p value
	n (%) / Mean ± SD; Median [IQR]	n (%) / Mean ± SD; Median [IQR]	
Age (years)	45.3 ± 3.0	44.4 ± 3.0	> 0.05
Height (cm)	157.0 ± 4.7	157.0 ± 4.8	> 0.05
Weight (kg)	57.6 ± 6.4	55.3 ± 6.4	> 0.05
BMI (kg/m ²)	23.3 ± 2.0	22.4 ± 2.0	> 0.05
Blood group O	12 (48.0%)	6 (24.0%)	> 0.05
Blood group A	4 (16.0%)	5 (20.0%)	
Blood group B	5 (20.0%)	10 (40.0%)	

Blood group AB	4 (16.0%)	4 (16.0%)	
Screening FSH (IU/L)	7.9 ± 4.9; 6.40 [5.22–8.56]	9.1 ± 6.2; 7.82 [4.83–12.0]	> 0.05
Screening estradiol (pg/mL)	97.7 ± 119.0; 53.3 [32.0–78.0]	101.0 ± 104.0; 66.8 [37.4–123.0]	> 0.05
FSFI score	19.8 ± 5.4	20.1 ± 6.1	> 0.05

Comment:

The two study groups were comparable at baseline in terms of anthropometric characteristics, hormonal indices, and the severity of impaired sexual function, with no statistically significant differences in any comparison ($p > 0.05$).

3.2.2. Safety of autologous adipose-derived mesenchymal stem cell infusion

3.2.2.1. Characteristics of mesenchymal stem cell products isolated from adipose tissue

Table 3.4. Characteristics of adipose-derived mesenchymal stem cell products used for the treatment of FSD

Parameter	1st infusion Group A	1st infusion Group B	2nd infusion Group A	2nd infusion Group B
CD73 (%)	99.9 ± 0.2	99.9 ± 0.05	99.8 ± 0.5	99.9 ± 0.03
CD90 (%)	99.8 ± 0.2	99.9 ± 0.1	99.7 ± 0.3	99.9 ± 0.1
CD105 (%)	98.8 ± 0.97	99.3 ± 0.9	99.2 ± 0.8	99.3 ± 0.5
CD45, CD34, CD19, CD11b, HLA-DR	≤ 2%	≤ 2%	≤ 2%	≤ 2%
Cell viability (%)	97.4 ± 1.7	97.7 ± 1.7	97.6 ± 1.8	97.5 ± 1.6
Mycoplasma	Negative	Negative	Negative	Negative
Endotoxin	< 5 EU/mL	< 5 EU/mL	< 5 EU/mL	< 5 EU/mL
Bacteria and fungi	Negative	Negative	Negative	Negative
Karyotype	Normal	Normal	Normal	Normal

Comment: Following culture expansion, the autologous adipose-derived MSCs showed typical morphology, the capacity to differentiate into adipogenic, chondrogenic, and osteogenic lineages, and met quality control standards at both infusion time points. CD73, CD90, and CD105 were all positively expressed at approximately 99%, negative markers were all ≤ 2%, cell viability was high, mycoplasma, bacterial, and fungal tests were all negative, endotoxin was < 5 EU/mL, and karyotype was normal.

3.2.2.2. Number and proportion of adverse events and serious adverse events

Table 3.5. Summary of adverse events (AEs) and serious adverse events (SAEs) during the study period

Group	SAE	Related AEs	Unrelated AEs	Severity
Group A (n=25)	0	0	5	100% Grade 1
Group B (n=25)	0	4	6	90% Grade 1, 10% Grade 2
Total	0	4	11	No AEs of Grade ≥ 3 were recorded

Comment: No serious adverse events were recorded throughout the study. A total of 15 adverse events occurred, most of which were mild and all resolved completely. Of these, 4/15 adverse events were considered related to the intervention, mainly post-infusion headache or mild pain at the infusion site; none required specific medical treatment. Hematologic parameters, coagulation tests, liver function, and renal function remained generally stable over time, indicating that the preparation and infusion process of autologous adipose-derived MSCs was safe for the study participants.

3.2.3. Changes in hormonal indices (E2, FSH)

During follow-up, the median E2 and FSH levels in both groups fluctuated around baseline values. At all assessment time points, the differences in E2 and FSH concentrations between the two groups were not statistically significant ($p > 0.05$). These results indicate that there is no evidence that early intervention produced a significant change in E2 and FSH compared with delayed intervention (Figure 3.1).

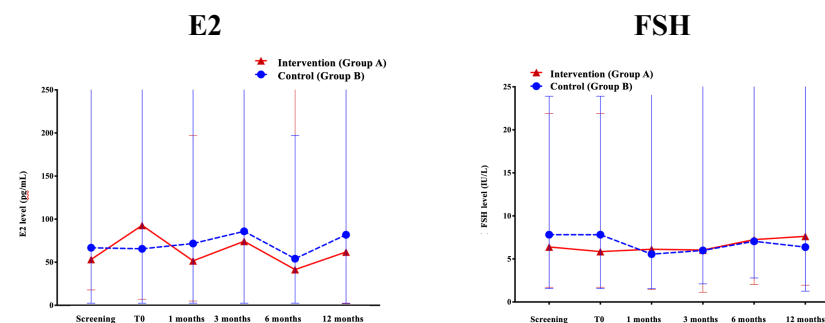


Figure 3.1. E2 and FSH hormone levels before and after 12 months of intervention

3.2.4. Changes in the Female Sexual Function Index (FSFI)

Table 3.6. Female Sexual Function Index before and after 12 months of intervention

Domain	Time point	Group A (n=25)	Group B (n=25)	p value#
Desire	Before infusion	2.76 ± 0.71	2.59 ± 0.84	>0.05
	After 3 months	3.17 ± 0.59	2.83 ± 0.77	>0.05