Maturitas 196 (2025) 108229

Contents lists available at ScienceDirect

Maturitas

journal homepage: www.elsevier.com/locate/maturitas

Original article

Impact of hysterectomy without oophorectomy on the health of postmenopausal women: Assessment of physical, psychological, and cognitive factors

Juan E. Blümel [a,*,1], Peter Chedraui [b,1], María S. Vallejo [c], Carlos Escalante [d], Gustavo Gómez-Tabares [e], Álvaro Monterrosa-Castro [f], Mónica Ñañez [g], Eliana Ojeda [h], Claudia Rey [i], Doris Rodríguez Vidal [j], Marcio A. Rodrigues [k], Carlos Salinas [l], Konstantinos Tserotasl [m], Andrés Calle [n], Maribel Dextre [o], Alejandra Elizalde [p], María T. Espinoza [q]

[a] Departamento de Medicina Interna Sur, Facultad de Medicina, Universidad de Chile, Santiago, Chile
[b] Escuela de Postgrado en Salud, Universidad Espíritu Santo, Samborondón, Ecuador
[c] Obstetricia y Ginecología, Hospital Clínico, Universidad de Chile, Santiago de Chile, Chile
[d] Departamento de Ginecología, Facultad de Medicina, Universidad de Costa Rica, Costa Rica
[e] Departamento de Ginecología, Escuela de Medicina, Facultad de Salud, Universidad del Valle, Cali, Colombia
[f] Grupo de Investigación Salud de la Mujer, Universidad de Cartagena, Cartagena, Colombia
[g] II Cátedra de Ginecología, Universidad Nacional de Córdoba, Córdoba, Argentina
[h] Departamento Académico de Medicina Humana, Universidad Andina del Cusco, Cusco, Peru
[i] Asociación Argentina para el Estudio del Climaterio, Buenos Aires, Argentina
[j] Hospital de Clínicas José de San Martín, Universidad de Buenos Aires, Buenos Aires, Argentina
[k] Department of Gynecology and Obstetrics, Federal University of Minas Gerais, Belo Horizonte, Brazil
[l] Servicio de Obstetricia y Ginecología, Hospital Ángeles, Puebla, Mexico
[m] Clínica Tserotas, Ciudad de Panamá, Panama
[n] Centro Integral de Salud Obstétrica y Femenina, Universidad Indoamérica, Academia Ecuatoriana de Medicina, Quito, Ecuador
[o] Ginecología Obstetricia, Clínica Internacional, Lima, Peru
[p] Departamento de la Mujer, Niñez y Adolescencia, Facultad de Medicina de la Universidad Nacional del Nordeste, Corrientes, Argentina
[q] Unidad de Ginecología Obstétrica, Clínica Los Ángeles, Cochabamba, Bolivia

ARTICLE INFO

Keywords:
Hysterectomy
Oophorectomy
Health
Menopausal hormone therapy
Quality of life

ABSTRACT

Objective: To determine the impact of hysterectomy without bilateral oophorectomy on the physical, psychological, and cognitive health of postmenopausal women.
Methods: This study was a sub-analysis of a cross-sectional, observational study carried out during gynecological consultations in nine Latin American countries. We collected sociodemographic and clinical data and evaluated the women's health using the EQ-5D for health status, the Menopause Rating Scale for menopausal symptoms, the 6-item Female Sexual Function Index for sexual function, the Jenkins Sleep Scale for sleep disturbances, the SARC-F for the risk of sarcopenia, and the Montreal Cognitive Assessment test for cognitive function.
Results: The sub-analysis involved 782 postmenopausal women with an average age of 56.9 years and an average body mass index of 26.5 kg/m^2. The participants had an average of 13.9 years of education, and 45.9 % of them had a university degree. The group of 104 women who had undergone hysterectomy without oophorectomy had a higher body mass index (27.5 ± 4.9 vs 26.3 ± 5.1 kg/m^2, $p < 0.03$), displayed more comorbidities (63.5 % vs 41.7 %, $p < 0.001$), worse self-perceived health (Odds ratio, OR 2.00, 95 % CI: 1.27–3.15), higher rates of severe menopausal symptoms (OR 2.39, 95 % CI: 1.51–3.77) and sleep disturbances (OR 1.75, 95 % CI: 1.10–2.79), and a higher likelihood of sarcopenia (OR 1.74, 95 % CI: 1.03–2.97) than those who had not undergone hysterectomy. No significant differences were observed regarding sexual function or cognitive performance between the

* Corresponding author at: Departamento de Medicina Sur, Facultad de Medicine, Universidad de Chile, Orquídeas 1068, Departamento 302, P.O. Box 7510258, Providencia, Santiago de Chile, Chile.
E-mail addresses: jeblumelm@gmail.com (J.E. Blümel), gustavo.gomez.tabares@correounivalle.edu.co (G. Gómez-Tabares).
[1] Juan E. Blümel and Peter Chedraui are joint first authors.

https://doi.org/10.1016/j.maturitas.2025.108229
Received 5 December 2024; Received in revised form 5 February 2025; Accepted 24 February 2025
Available online 28 February 2025

two groups. Moreover, in the six assessed health domains, menopausal hormone therapy (ever use) was found to be a protective factor, regardless of whether or not the woman had undergone a hysterectomy.
Conclusion: Women who undergo hysterectomy without oophorectomy may experience persistent physical and psychological symptoms that affect their mental health and quality of life. Menopausal hormone therapy is associated with improved health outcomes.

1. Introduction

Menopause is a crucial moment in women's life, characterized by the cessation of ovarian function and a subsequent decrease in estrogen levels. This decrease can lead to various physical and psychological changes. The natural process of menopause affects women differently and can also be influenced by surgical interventions, such as hysterectomy.

Hysterectomy is one of the most common gynecological surgeries worldwide, with over 500,000 procedures performed annually in the United States for benign conditions. The main reasons for this procedure include fibroids, endometriosis, abnormal uterine bleeding, and pelvic organ prolapse, which altogether account for about 80 % of all performed hysterectomies [1]. In the United States, the of oophorectomy at the time of a hysterectomy has consistently been between 40 and 50 % [2]. However, many women undergo a hysterectomy without oophorectomy, raising questions regarding the potential long-term health implications of this procedure among postmenopausal women.

Hysterectomy without oophorectomy preserves ovarian function, potentially resulting in a lesser impact on hormone levels and, therefore, fewer menopause-related symptoms such as hot flashes, mood changes, and the risk of chronic diseases. However, the impact of a hysterectomy alone on postmenopausal health is a topic of debate in the medical literature. Some studies suggest that ovarian preservation reduces the risk of cardiovascular disease, osteoporosis, and cognitive decline, while others suggest that the procedure may be associated with an increased risk of early menopausal symptoms, sexual dysfunction, and mental health issues [3,4].

Most studies focus on the negative effects of hysterectomy without oophorectomy immediately after surgery or in the urological field [5]. However, only a few examine its broader impact on health, as defined by the World Health Organization (WHO): a state of complete physical, mental, and social well-being, and not simply the absence of disease or infirmity. The present study aimed at assessing the impact of hysterectomy without oophorectomy on the health of postmenopausal women, using the WHO's conceptual framework of holistic well-being. We will examine various quality-of-life perspectives, particularly focusing on physical, psychological, and cognitive factors. Given the high prevalence of hysterectomies and the aging female population, our goal is to contribute to the understanding of the implications of this procedure. We hope that the information we provide can help guide clinical decisions in women's health.

2. Material and methods

2.1. Study design and participants

The present document is a sub-analysis of the REDLINC XII which was a cross-sectional and analytical investigation that collected data from January 2023 to October 2023 during general gynecological consultations in nine Latin American countries: Argentina, Bolivia, Brazil, Colombia, Costa Rica, Ecuador, Mexico, Panama, and Peru [6]. The study included women who attended routine health check-ups, who had medium or high incomes and visited private or public clinical centers.

Inclusion criteria were postmenopausal women (having experienced one year of amenorrhea) under the age of 70 who were in normal health. Women who had undergone chemotherapy or radiotherapy had a bilateral oophorectomy, or experienced menopause before the age of 42 were excluded from the study. Furthermore, women with hearing or vision impairments or those diagnosed with dementia that could impede their comprehension of the questionnaires were also excluded. Women under 42 were omitted from the analysis as the mean age at menopause in Latin America is lower than in the US and Europe [7].

2.2. Studied variables

The following data were analyzed: age (years), years of education, body mass index (BMI), number of children, having a current partner (yes/no), sexually active (at least one sexual intercourse in the last year, yes/no), smoker (yes/no), physical inactivity (defined as performing <75 min/week of intense aerobic physical activities such as running, gym workouts, tennis, etc., or <150 min/week of moderate aerobic physical activities such as fast walking, cycling, and dancing (yes/no)), postmenopausal stage was defined according to the STRAW +10 criteria (1 or more years of amenorrhea), menopausal hormone therapy (MHT) ever use (past or current use, yes/no), having comorbidities (defined as presenting one or more of the following: receiving treatment for dyslipidemia, diabetes mellitus, or hypertension; indicated as yes or no), and current use of psychotropic medications (including antidepressants, hypnotics, or anxiolytics; indicated as yes or no).

2.3. Validated tools used to assess women's health status

2.3.1. EQ-5D

This questionnaire consists of five domains: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each domain represents the increasing severity of health problems. The second part of the questionnaire includes a 20-cm visual analogue scale (VAS), ranging from ‘the worst health you can imagine’ (scored 0) to ‘the best health you can imagine’ (scored 100). Since the EQ-5D data is ordinal, the information is presented as the proportions of the population reporting level 1 (no problems), level 2 (some problems), and level 3 (extreme problems) per dimension. In general population surveys, the number of individuals reporting level 3 is small, hence studies report level 2 and level 3 as one category. Thus, the EQ-5D dimensions renders 2 levels dimensions, ‘no problems’ and ‘problems’ [8]. This questionnaire has been validated in Spanish [9] and Portuguese language [10].

2.3.2. The Menopause Rating Scale (MRS)

This tool is a validated quality of life test designed for middle-aged women. It consists of 11 items that assess menopausal symptoms, which are divided into three subscales: somatic (hot flushes, heart discomfort, sleeping problems, and muscle and joint problems), psychological (depressive mood, irritability, anxiety, and physical and mental exhaustion), and urogenital (sexual problems, bladder problems, and dryness of the vagina). Each item can be graded by the subject from 0 (not present) to 4 (1 = mild; 2 = moderate; 3 = severe; 4 = very severe). The total score for each subscale is the sum of the graded items within that subscale, and the total MRS score is the sum of the scores obtained for each subscale. For this research, the Spanish [11] and Portuguese (Brazil) language [12] versions of the MRS were used. A total MRS score of 14 points or higher indicates the presence of severe menopausal symptoms [13].

2.3.3. The 4-item Jenkins Sleep Evaluation Questionnaire [14]

This questionnaire assesses whether individuals have experienced

sleep disturbances over the past 4 weeks. The questions are related to difficulties falling asleep, waking up multiple times during the night, trouble staying asleep, and feeling tired or exhausted upon waking. Each question is rated on a Likert scale from 1 to 6 (1 = not at all, 2 = 1–3 days, 3 = 4–7 days, 4 = 8–14 days, 5 = 15–21 days, 6 = 22–28 days). In the Latin American population, a score of 12 points or higher indicates the presence of sleep disturbance [15].

2.3.4. The six item Female Sexual Function Index (FSFI-6)

This tool was originally developed in Italian [16] and later translated into Spanish to be used among middle-aged Spanish [17] and Latin American women [18]. In Brazil, surveys were conducted using the Portuguese (Brazil) language version of FSFI-6 [19]. The tool comprises six questions, each corresponding to one of the six domains of the original 19-item FSFI [20]: desire, arousal, lubrication, orgasm, satisfaction, and pain. Each question can be scored from 0 to 5, and the total FSFI-6 score indicates female sexual functioning. A score of 19 points or less suggests poorer sexual function [17].

2.3.5. The SARC-F

The risk of sarcopenia was assessed using the SARC-F tool, which is designed as a quick screening tool. This tool consists of five components: **S**trength, **A**ssistance with walking, **R**ising from a chair, **C**limbing stairs, and **F**alling (SARC-F). Participants are scored on each component from 0 to 2 points, resulting in a total score ranging from 0 to 10. A score of 4 or higher on the SARC-F indicates an increased risk of sarcopenia and poor outcomes [21]. SARC-F is an excellent test for excluding muscle function impairment and sarcopenia [22].

2.3.6. The Montreal Cognitive Assessment (MoCA) test

This tool is used to evaluate cognitive function. This screening test, developed by Nasreddine in Canada [23], can diagnose Mild Cognitive Impairment (MCI), a transitional state between normal aging and dementia, particularly Alzheimer's disease. The original version considers a score of 26 points or less as indicative of MCI. The Spanish language validation of the MoCA established a cut-off value of 21 points, which has shown a sensitivity of 71.4 % and a specificity of 74.5 % for diagnosing MCI [24]. In Brazil, the Portuguese version of the MoCA was used, with a similar cut-off value of 20 points or less [25]. In this study, a MoCA score of <21 points was used to identify individuals with MCI. An additional point is added if the individual has fewer than 12 years of education.

2.4. Statistical analysis

The statistical analysis was conducted using SPSS software, version 21.0 for Windows (SPSS Inc., Chicago, IL). Numerical variables are presented as means and standard deviations, and categorical variables are displayed as frequencies and percentages. We checked for variance homogeneity using the Levene's test ($p > 0.05$) and assessed the normality of data distribution using the Kolmogorov-Smirnov test.

The test results were used to analyze differences between numerical variables. Non-parametric data were analyzed using the Mann-Whitney *U* test, while parametric data were analyzed with the Student's *t*-test. The chi-square test was used to compare categorical data. Additionally, a logistic regression analysis was conducted to examine the relationship between each of the health issues assessed with the used validated tools and the analyzed covariates. Categorical variables were entered into each of the models as they were (tool outcomes according to their cut-off values also), while continuous variables were categorized based on their median. A stepwise procedure was used to include variables in the model, with a significance level of 10 %. To address multicollinearity in the regression analysis, the Variance Inflation Factor (VIF) was used, ensuring that all VIF values were below 10. Furthermore, interactions between variables that were statistically significant in the bivariate analysis were considered. A p value of <0.05 was considered statistically significant for all analyses.

2.5. Sample size calculation

The sample size was calculated using the MRS, instrument used to assess various health domains among the postmenopausal women. The calculation was done using StatCalc, a tool developed by the U.S. Centers for Disease Control and Prevention [26]. According to the tool, a descriptive study comparing the mean total MRS scores between two groups would require a sample size of 83 hysterectomized women and 498 controls, at a 95 % confidence level, 80 % power, and a 6:1 control-to-hysterectomy group ratio. This calculation assumes that the control group has a mean total MRS score of 12.94 ± 8.40, with an expected difference of 20 % between the groups [27].

2.6. Ethical approval

The current study received approval from the ethics committee of the Southern Metropolitan Health Service in Santiago de Chile, Chile (Memorandum 15/2023; June 22, 2022) and adheres to the Declaration of Helsinki. All participants were informed about the study, its objectives, and the tools used. Subsequently, they provided written consent to participate.

3. Results

Data of 782 postmenopausal women were included for this subanalysis (Fig. 1). Their average age was 56.9 ± 5.7 years with a mean BMI of 26.5 ± 5.1 kg/m^2. On average, they had 2.5 ± 1.8 children, with 73.8 % reporting having a partner and 69.4 % being sexually active in the past 12 months. The average attained educational was 13.9 ± 5.4 years, with 45.9 % identifying themselves as university graduates.

Characteristics of women who had undergone hysterectomy alone without oophorectomy compared to those who did not are presented in Table 1. The results show that there are no significant differences in age, number of children, having a partner, being sexually active, years of education, ever use of MHT, smoking habit, or being physically inactive between the two groups. Women who did not have a hysterectomy experienced menopause at an average age of 49.2 ± 3.6 years, while women who have had a hysterectomy underwent surgery at an average age of 44.4 ± 8.6 years. On the other hand, women who had a hysterectomy had a higher BMI compared to those who did not (27.5 ± 4.9 vs 26.3 ± 5.1 kg/m^2, $p < 0.03$), as well as a higher prevalence of comorbidities (63.5 % vs 41.7 %, $p < 0.001$).

Table 2 compares the health status (EQ-5D) of non-hysterectomized and hysterectomized women. It was observed that postmenopausal women who have had a hysterectomy experience more challenges in performing their usual activities, suffer from more pain, and having a poorer perception of their health (lower VAS score) compared to women who have not undergone a hysterectomy. When VAS score is categorized according to the median (below the median worse health perception), the rate of having a worse perception of their health was higher among women who had a hysterectomy (54.9 % vs. 38.8 %) (odds ratio [OR] 1.76, 95 % CI: 1.22–2.53). After adjusting for the covariates listed in Table 1, a logistic regression model revealed that hysterectomy was associated with a worse perception of health (OR 2.00, 95 % CI: 1.27–3.15).

In Table 3, the severity of each menopausal symptom was evaluated using the MRS. When the women were grouped by their total MRS score, it was found that 52.9 % of the women who had undergone hysterectomy experienced severe menopausal symptoms (total MRS score ≥ 14 points), compared to 29.2 % of the women who had not undergone hysterectomy (OR 2.72; 95 % CI: 1.79–4.14). The total MRS score, while higher on average in women >10 years post-hysterectomy, did not reveal statistically significant differences when compared to those who underwent hysterectomy <10 years ago (17.3 ± 11.4 vs 13.8 ± 9.3; $p <$

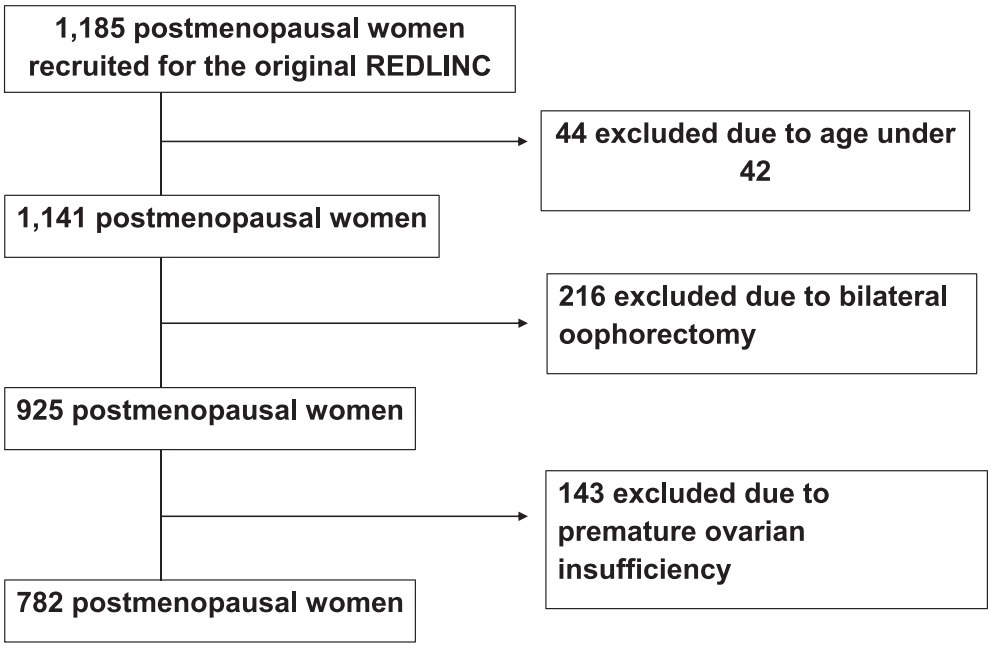

Fig. 1. Flowchart of women recruited.

Table 1
Characteristics of women according to a history of hysterectomy or not.

Characteristics	Hysterectomy		*p* value[a]
	No ($n = 678$)	Yes ($n = 104$)	
Age (years)	57.0 ± 5.7	56.6 ± 6.1	NS[1]
Body mass index (kg/m^2)	26.3 ± 5.1	27.5 ± 4.9	0.03[1]
Number of children	2.5 ± 1.9	2.4 ± 1.3	NS[1]
Has a partner	73.3 (70.0–76.6)	76.9 (68.7–85.2)	NS[2]
Sexually active	69.0 (65.5–72.5)	72.1 (63.4–80.9)	NS[2]
Educational level (years)	13.9 ± 5.5	13.8 ± 4.8	NS[1]
Age at menopause (years)	49.2 ± 3.6	–	
Age at hysterectomy (years)	–	44.4 ± 8.6	
Menopause hormone therapy (ever used)	26.0 (22.7–29.3)	31.7 (22.6–40.8)	NS[2]
Physically inactive	49.0 (45.2–52.7)	52.9 (43.1–62.6)	NS[2]
Smoker	280 (314–246)	36.5 (45.9–27.1)	NS[2]
Use of psychotropic drugs	27.4 (24.1–30.8)	36.5 (27.1–46.0)	NS[2]
Comorbidities	41.7 (38.0–45.5)	63.5 (54.1–72.9)	0.0001[2]

Data are presented as mean ± standard deviations or percentages (95 % confidence intervals).
NS, non-significant.
[a] *p* value as determined with the Student's *T* test[1] or the chi-square test[2].

Table 2
Comparison of health status (EQ-5D) between non-hysterectomized and hysterectomized women.

EQ-5D (% of any problem)	Hysterectomy		*p* value*
	No ($n = 678$)	Yes ($n = 104$)	
Mobility	14.0 (11.4–16.6)	15.4 (8.3–22.4)	NS[1]
Self-care	4.1 (2.6–5.6)	1.0 (−1.0 to −2.9)	NS[1]
Usual activities	11.5 (9.1–13.9)	20.2 (12.4–28.0)	0.013[1]
Pain/discomfort	37.9 (34.2–41.6)	55.8 (46.1–65.5)	0.001[1]
Anxiety/depression	26.8 (23.5–30.2)	28.9 (20.0–37.7)	NS[1]
VAS score[a]	77.6 ± 15.8	73.3 ± 17.4	0.013[2]
Worse health perception (%)[b]	38.8 (42.5–35.1)	54.9 (64.7–45.1)	0.002[2]

Data are presented as mean ± standard deviations or percentages (95 % confidence intervals).
NS, non-significant; CI, confidence interval.
[*] *p* value as determined with the Student's *t*-test[1] or the chi-square test[2].
[a] Lower VAS scores indicate worse health perception.
[b] VAS score below the median (score 80) defines women with worse health perception.

0.09). After adjusting for the covariates listed in Table 1 (logistic regression), it was determined that hysterectomy was associated with more severe menopausal symptoms (OR 2.39; 95 % CI: 1.51–3.77).

As shown in Table 4, women who underwent a hysterectomy experienced more sleep disturbances (Jenkins score ≥ 12 points). These disturbances were observed in 32.7 % of women who had a hysterectomy compared to 20.1 % of women who did not have a hysterectomy (OR 1.94; 95 % CI: 1.23–3.04). After adjusting for the factors listed in Table 1 using logistic regression, hysterectomy was found to be associated with a significantly increased likelihood of sleep disturbances (OR 1.75, 95 % CI: 1.10–2.79).

Regarding sexual function (Table 5), as measured by the FSFI-6, the present study found that only sexual desire was significantly lower in women who had undergone a hysterectomy. No differences were observed in other aspects of sexuality. Low sexual function (total FSFI-6 score of 19 points or lower) did not differ among groups. In a logistic regression model adjusted for covariates in Table 1, no differences in sexual function were observed between the two groups of women.

Results of the assessment with the SARC-F are presented in Table 6. Women who had a history of hysterectomy displayed higher SARC-F scores for some items, and also a higher total SARC-F scores compared to non-hysterectomized women (2.03 ± 2.05 points vs 1.48 ± 1.93, $p < 0.007$, respectively). When categorizing women according to their total SARC-F score as ≥4 points, defining a higher likelihood of sarcopenia, we found that hysterectomized women had a higher likelihood of sarcopenia compared to non-hysterectomized women (24.0 % vs. 14 %, $p = 0.02$), corresponding to an OR of 1.79 (95 % CI: 1.09–2.94). After adjusting for the factors listed in Table 1, by means of logistic regression, hysterectomy was found to be associated with a significantly increased likelihood of sarcopenia (OR 1.74, 95 % CI: 1.03–2.97).

Table 3
MRS scores (per item, subscale and total) in non-hysterectomized and hysterectomized women.

Menopause Rating Scale (Quality of Life) (Score 0 to 4, best to worst symptoms)	Hysterectomy		*p* value*
	No (n = 678)	Yes (n = 104)	
Items of the somatic subscale			
Hot flushes, sweating	1.12 ± 1.27	1.54 ± 1.31	0.002[1]
Heart discomfort, beat, heart skipping, heart racing	0.69 ± 1.00	1.03 ± 1.14	0.002[2]
Sleep problems	1.10 ± 1.25	1.61 ± 1.53	0.001[2]
Joint and muscular discomfort	1.24 ± 1.27	1.95 ± 1.46	0.001[2]
Total somatic subscale score	*4.15 ± 3.56*	*6.13 ± 4.16*	*0.001[2]*
Items of the psychological subscale			
Depressive mood	0.82 ± 1.17	1.14 ± 1.42	0.010[2]
Irritability, feeling nervous, inner tension.	1.03 ± 1.21	1.28 ± 1.34	NS[2]
Anxiety, inner restlessness, feeling panicky	0.94 ± 1.19	1.12 ± 1.27	NS[1]
Physical and mental exhaustion (fatigability)	1.30 ± 1.27	1.67 ± 1.34	0.006[1]
Total psychological subscale score	*4.74 ± 4.89*	*5.36 ± 4.40*	*NS[1]*
Items of the urogenital subscale			
Change in sexual desire, in activity and satisfaction	1.36 ± 1.32	1.66 ± 1.46	0.057[2]
Bladder problems, difficulty in urinating, incontinence	0.64 ± 1.11	1.16 ± 1.42	0.001[2]
Vaginal dryness, burning, difficulty with intercourse	1.13 ± 1.27	1.60 ± 1.50	0.004[2]
Total urogenital subscale score	*3.08 ± 2.93*	*4.45 ± 3.42*	*0.001[2]*
Total Menopause Rating Scale score	*10.74 ± 9.11*	*15.60 ± 10.52*	*0.001[1]*
Women with severe symptoms [a], % (95% CI)	**29.2 (25.8–32.6)**	**52.9 (43.1–52.6)**	**0.001[3]**

Data are presented as mean ± standard deviations or percentages (95 % confidence intervals).
NS, non-significant; CI, confidence interval.
* p value as determined with the Student's T test1, the Mann-Whitney U test2, or the chi-square test 3.
[a] MRS total score ≥ 14 points.

Table 4
Jenkins Sleep Evaluation Questionnaire scores in non-hysterectomized and hysterectomized women.

Jenkins Sleep Evaluation Questionnaire (Score 0 to 5, best to worst sleep)	Hysterectomy		*p* value*
	No (n = 678)	Yes (n = 104)	
I have trouble falling asleep	1.87 ± 1.45	2.44 ± 1.75	0.001[1]
Wake up several times per night	2.26 ± 1.68	2.74 ± 1.85	0.008[1]
Trouble staying asleep	1.85 ± 1.44	2.38 ± 1.72	0.002[1]
Wake up tired and worn out	1.97 ± 1.44	2.59 ± 1.85	0.003[1]
Total score	*7.94 ± 5.05*	*10.10 ± 5.84*	*0.001[1]*
Women with sleep disturbances [a]	**20.1 (17.0–23.1)**	**32.7 (23.5–41.9)**	**0.004[2]**

Data are presented as mean ± standard deviations or percentages (95 % confidence intervals).
CI, confidence interval.
* *p* value as determined with the Mann-Whitney *U* test[1] or the chi-square test[2].
[a] A total Jenkins score ≥ 12 points.

Cognitive function was evaluated with the MoCA tool (Table 7). In the initial analysis, it was found that 15.4 % of women who had undergone a hysterectomy had mild cognitive impairment, while 15.3 % of women without a hysterectomy had the same condition (OR: 1.00; 95 % CI 0.57–1.77). This indicates that there is virtually no difference in the prevalence of cognitive impairment between the two groups. After adjusting for various factors using a logistic regression model, no significant association was observed between hysterectomy and cognitive function. This suggests that hysterectomy does not have an important impact on cognitive performance in postmenopausal women.

In each of the binary logistic regressions conducted to evaluate the assessed health conditions, ever use of MHT emerged as a protective factor independent of other variables. Summarized in Table 8 are the ORs of the effect of MHT (ever use) obtained with each of the constructed logistic regression models, corresponding to health perception, menopausal symptoms, sleep disturbances, sexual function, the likelihood of sarcopenia, and mild cognitive impairment. MHT ever use was

Table 5
Sexual function among non-hysterectomized and hysterectomized women.

FSFI-6 (Higher score, better sexuality)	Hysterectomy		*p* value*
	No (n = 678)	Yes (n = 104)	
Sexual desire	2.34 ± 1.08	2.11 ± 1.00	0.037[1]
Sexual arousal	2.09 ± 1.47	2.11 ± 1.53	NS[1]
Lubrication	2.18 ± 1.68	2.15 ± 1.78	NS[1]
Orgasm	2.32 ± 1.78	2.29 ± 1.86	NS[1]
Satisfaction	3.30 ± 1.25	3.23 ± 1.37	NS[1]
Dyspareunia	2.58 ± 1.99	2.35 ± 1.92	NS[1]
Total FSFI-6 score	*14.80 ± 7.53*	*14.23 ± 7.86*	*NS[1]*
Women with low sexual function [a]	67.4 (63.9–70.9)	67.3 (58.1–76.5)	NS[2]

Data are presented as mean ± standard deviations or percentages (95 % confidence intervals).
* p value as determined with the Student's T test1 or the chi-square test2.
[a] Total FSFI-6 score ≤ 19 points.

Table 6
Likelihood for sarcopenia in non-hysterectomized and hysterectomized women.

SARC-F (Higher score, higher likelihood for sarcopenia)	Hysterectomy		*p* value*
	No (n = 678)	Yes (n = 104)	
Strength	0.39 ± 0.59	0.46 ± 0.62	NS[1]
Assistance in walking	0.21 ± 0.45	0.20 ± 0.43	NS[1]
Rise from a chair	0.24 ± 0.47	0.38 ± 0.58	0.015[2]
Climb stairs	0.36 ± 0.58	0.54 ± 0.61	0.001[2]
Falls	0.28 ± 0.49	0.45 ± 0.65	0.015[2]
Total SARC-F score	*1.48 ± 1.93*	*2.03 ± 2.05*	*0.007[1]*
Higher likelihood for sarcopenia [a]	**15.0 (12.4–17.7)**	**24.0 (15.7–32.4)**	**0.021[3]**

Data are presented as mean ± standard deviations or percentages (95 % confidence intervals).
* *p* value as determined with the Student's *T* test[1], the Mann-Whitney *U* test[2], or the chi-square test[3].
[a] Higher likelihood for sarcopenia total SARC-F score ≥ 4 points.

Table 7
MoCA scores: non-hysterectomized women compared to hysterectomized ones.

Domain (Score 0 to 30, worst to best cognition)	Hysterectomy		*p* value*
	No (n = 678)	Yes (n = 104)	
Short-term memory	3.62 ± 1.58	3.47 ± 1.58	NS[1]
Visuospatial construction	4.10 ± 1.11	3.71 ± 1.47	0.011[2]
Executive function	2.70 ± 0.66	2.66 ± 0.80	NS[1]
Attention and concentration	4.59 ± 1.40	4.51 ± 1.64	NS[1]
Language	2.46 ± 0.80	2.54 ± 0.79	NS[1]
Temporal and spatial orientation	5.87 ± 0.69	5.97 ± 0.17	NS[2]
Total MoCA score	*23.34 ± 3.64*	*22.87 ± 4.53*	*NS[2]*
Mild cognitive impairment [a]	**15.3 (12.6–18.1)**	**15.4 (8.3–22.4)**	**NS[3]**

Data are presented as mean ± standard deviations or percentages (95 % confidence intervals).
* *p* value as determined with the Student's *T* test[1], the Mann-Whitney *U* test[2], or the chi-square test[3].
[a] Total MoCA score < 21 points.

Table 8
Summary of the effect of MHT (ever use) on each of the evaluated health aspects of participating postmenopausal women.[a]

Questionnaire	Cut-off	OR (95 % CI)
Worse health perception (EQ-5D)	VAS score (<80 points, the median)	0.37 (0.25–0.54)
Severe menopausal symptoms (Menopause Rating Scale)	MRS total score ≥ 14 points	0.48 (0.32–071)
Sleep disturbances (Jenkins Sleep Scale)	Jenkins total score ≥ 12 points	0.63 (0.42–0.96)
Low sexual function (FSFI-6)	FSFI-6 total score ≤ 19 points	0.66 (0.46–0.93)
Risk of sarcopenia (SARC-F)	SARC-F total score ≥ 4 points	0.51 (0.30–0.86)
Cognitive impairment (MoCA)	MoCA total score < 21 points	0.24 (0.12–0.48)

Data are presented as odds ratios (OR) and their confidence intervals (CI). MHT, menopause hormone therapy.
[a] Displayed ORs represent those obtained with each of constructed logistic regression models that evaluated the various health aspects.

consistently associated with a lower probability of occurrence for all these conditions.

4. Discussion

The present study shows that having a hysterectomy without removing the ovaries may have a significant impact on women's overall health. Hysterectomized women report increased BMI and risk of sarcopenia, poorer health perceptions, and a higher rate of comorbidities, severe menopausal symptoms, and sleep disturbances, compared to those who have not undergone the procedure. However, no significant differences were observed in sexual function or cognitive performance between the two groups.

It has been suggested that undergoing a hysterectomy may affect the blood flow to the ovaries, as indicated by parameters such as peak systolic flow velocity and the pulsatility index [28]. This disruption in blood supply could result in reduced production of estradiol and progesterone after the surgery, along with a concomitant increase in FSH and LH levels, which are characteristic of ovarian failure. Our study revealed that the average age at the time of hysterectomy was 44 years (Table 1). This suggests that the surgical procedure may have accelerated hormonal changes similar to those observed during menopause. In turn, this could have accelerated the onset of the physiological and the symptomatic consequences of menopause, such as sleep disturbances, sarcopenia risk, vasomotor symptoms, and other adverse health outcomes.

The decreased levels of ovarian hormones in women who have had a hysterectomy without bilateral ovariectomy could be a significant factor in explaining our findings. Many studies have shown that estradiol is crucial in promoting the growth of new brain cells, as well as regulating neuronal activity and modulating synaptic plasticity, all of which are essential processes that maintain cognitive function [29]. In addition, estradiol affects various neurotransmitter systems, including the dopaminergic and glutamatergic systems, both of which have been implicated in the development of menopausal symptoms such as hot flashes, mood disturbances, and sleep disorders [30]. The reduction in estradiol levels after hysterectomy without ovariectomy may, therefore, harm brain function, potentially contributing to the onset or worsening of these symptoms.

The health disorders associated with a hysterectomy conserving the ovaries could be explained not only by the hormonal effects on the central nervous system but also due to other metabolic changes induced by hormonal deprivation. Many chronic diseases share common pathophysiological mechanisms and are, at least in part, different manifestations in various organs of similar molecular alterations [31]. Mitochondrial dysfunction, oxidative stress, and inflammation are inextricably linked and play a critical role in the onset and progression of non-communicable diseases. Experimental animal studies have shown that estrogen deficiency is associated with reduced antioxidant capacity and increased aortic atherosclerosis [32]. Another chronic disease, dementia, has been linked to chronic inflammation, a condition that increases after menopause [33]. However, we were unable to demonstrate that mild cognitive impairment (as assessed with the MoCA test), a predementia state, increases in women who have undergone hysterectomy without oophorectomy. This could be explained by the fact that the women in our study had an average age of 56.9 years, an age at which cognitive decline is relatively uncommon. Conversely, the risk of sarcopenia, another condition also associated with chronic inflammation, was found to be higher among the hysterectomized women. This observation may be explained by the fact that sarcopenia tends to manifest at a younger age than dementia [34].

Our study found no significant differences in sexual function between women who have had a hysterectomy and those who have not. Long time belief has been that a hysterectomy for various reasons (i.e. severe uterine bleedings, uterine fibroids, endometriosis, uterine prolapse, and malignancies of the genital tract) could have a positive impact on female sexual health, thereby improving their quality of life in this aspect [35]. However, a recent meta-analysis has concluded that a hysterectomy, regardless of the used surgical approach, does not cause a significant change in overall female sexual function [36]. These findings challenge previous expectations regarding the potential post-operative sexual benefits. However, in the previously mentioned meta-analysis, specific changes observed in certain aspects of sexual function, such as lower lubrication and the ability to achieve orgasm, were observed in women who also underwent bilateral oophorectomy. These changes may be related to the sudden decrease in sex hormones, suggesting that preserving the ovaries during surgery may be crucial in maintaining certain aspects of sexual function.

The present study found that MHT was linked to a reduced risk of health problems, regardless of whether the hysterectomy had been performed. Many studies have shown that MHT can improve the quality of life of transiting the menopause [37], reducing the risk of chronic diseases such as diabetes [38] and hypertension [39]. It is not of surprise that large-scale studies involving thousands of women have shown lower mortality rates among MHT users [40,41]. This evidence suggests that MHT may have a broader positive impact on the overall health of postmenopausal women, going beyond just alleviating menopausal symptoms.

4.1. Limitations and strengths

The current study has some limitations. Firstly, its cross-sectional design limits the ability to establish causality. Secondly, focusing on women in the late postmenopausal period may have led to inaccuracies in assessing age at menopause onset and other specific aspects of their medical history. Additionally, the study lacked detailed information on the type of ever used MHT (i.e. type of estrogen), regimens, route and duration of treatment. It is also important to note that ovarian hormone levels were not measured, unfortunately this was not part of our main objectives. Nevertheless, such data would have been relevant given the fact that as previously mentioned, hysterectomy without oophorectomy can alter ovarian hormone levels. In this context, a meta-analysis comprising 14 studies [42] demonstrated that hysterectomy negatively affects ovarian hormone levels, particularly in women over 40 years of age, corresponding to an age similar to that of the participants of our study. Another limitation, is the lack of specification regarding the type of hysterectomy performed. This may have influenced our results, as estradiol levels following hysterectomy can vary depending on the used operative approach, be it abdominal, laparoscopic, or supracervical [42].

There is a need to mention as an additional drawback the lack of clarity regarding whether some hysterectomized women might have

been using progestins. According to most clinical guidelines, the use of progestogens is primarily indicated to provide sufficient endometrial protection and is therefore not routinely recommended for hysterectomized women [43]. However, under certain conditions, such as endometriosis, the use of progestogens is advised even for hysterectomized women [44]. Consequently, some of our participants might have used progestogens in conjunction with oestrogens.

It is also important to consider that the health issues observed in women who have had a hysterectomy could be linked to pre-existing conditions. For instance, uterine fibroids, which account for around 40 % of hysterectomies in the United States, are associated with higher rates of depression (HR: 1.12; 95 % CI: 1.10–1.13) and anxiety (HR: 1.12; 95 % CI: 1.10–1.13) before surgery compared to women without fibroids [45]. Vaginal bleeding, another common indication for a hysterectomy, may also significantly impacts women's quality of life [46]. Therefore, as above mentioned, the decline in quality of life after a hysterectomy may be due to pre-existing conditions, such as vaginal bleeding and other related health issues, that were already affecting their well-being before the surgery.

One of the strengths of our study is the fact that it was conducted across multiple centers in Latin America, which helps minimize local biases. Additionally, the study used a wide range of validated questionnaires to assess both physical and psychological symptoms. These surveys were administered by clinicians with extensive clinical experience, following a standardized protocol. The used instruments have been validated in Spanish and Portuguese language and have been previously used by the authors in other studies [47,48]. Furthermore, all the tools showed high internal consistency, indicating that they reliably measure their corresponding concepts or constructs, ensuring conceptual equivalence with the original instruments [49], which is particularly important in a multinational sample.

In conclusion, many mid-aged and postmenopausal women who have undergone a hysterectomy without oophorectomy may experience various physical and psychological symptoms that can impact their health and quality of life. Our findings indicate that undergoing a hysterectomy without oophorectomy can significantly impact women's health, with potential long-term issues. This highlights the importance of providing close and ongoing follow-up care to effectively address any negative effects on the physical and emotional well-being of these patients. Furthermore, we emphasize the necessity of thorough preoperative evaluations that carefully balance the benefits and risks of the procedure. Lastly, additional research is crucial to better understand the implications of hysterectomy with ovarian conservation, especially for women with limited access to healthcare services, as this group was not represented in our study.

Contributors

Juan E. Blümel contributed to the study conception and design, statistical analysis, and text preparation and revision.

Peter Chedraui contributed to the study design, statistical analysis and text preparation and revision.

María S. Vallejo contributed to the study conception and design and text preparation and revision.

Carlos Escalante contributed to data collection and text revision.

Gustavo Gómez-Tabares contributed to data collection and text revision.

Alvaro Monterrosa-Castro contributed to data collection and text revision.

Mónica Ñañez contributed to data collection and text revision.

Eliana Ojeda contributed to data collection and text revision.

Claudia Rey contributed to data collection and text revision.

Doris Rodríguez Vidal contributed to data collection and text revision.

Marcio A. Rodrigues contributed to data collection and text revision.

Carlos Salinas contributed to data collection and text revision.

Konstantinos Tserotas contributed to data collection and text revision.

Andrés Calle contributed to data collection and text revision.

Maribel Dextre contributed to data collection and text revision.

Alejandra Elizalde contributed to data collection and text revision.

María T. Espinoza contributed to data collection and text revision.

All authors saw and approved the final version and no other person made a substantial contribution to the paper.

Ethical approval

The present study was approved by the ethics committee of the Southern Metropolitan Health Service, Santiago de Chile, Chile (Memorandum 15/2022; June 22, 2022) and complies with the Declaration of Helsinki. All participants were informed of the study, its aims and used tools, after which they provided written consent for participation.

Provenance and peer review

This article was not commissioned and was externally peer reviewed.

Funding

This research received no specific grant from funding agencies in the public, commercial, or non-for-profit sectors.

Data sharing and collaboration

There are no linked research data sets for this paper. The data of this study are not publicly available but can be requested for research collaboration projects according to ethical, privacy and legislation issues.

Declaration of competing interest

The authors declare that they have no competing interest.

References

[1] J.M. Wu, M.E. Wechter, E.J. Geller, T.V. Nguyen, A.G. Visco, Hysterectomy rates in the United States, 2003, Obstet. Gynecol. 110 (5) (2007) 1091–1095.
[2] M.R. Adelman, H.T. Sharp, Ovarian conservation vs removal at the time of benign hysterectomy, Am. J. Obstet. Gynecol. 218 (3) (2018) 269–279.
[3] Z. Wang, X. Li, D. Zhang, Impact of hysterectomy on cardiovascular disease and different subtypes: a meta-analysis, Arch. Gynecol. Obstet. 305 (5) (2022) 1255–1263.
[4] H. Hassan, I. Allen, E. Sofianopoulou, Y. Walburga, C. Turnbull, D.M. Eccles, et al., Long-term outcomes of hysterectomy with bilateral salpingo-oophorectomy: a systematic review and meta-analysis, Am. J. Obstet. Gynecol. 230 (1) (2024) 44–57.
[5] M.M. Mamik, S. Kim-Fine, L. Yang, V. Sharma, R. Gala, S. Aschkenazi, et al., Hysterectomy techniques and outcomes for benign large uteri: a systematic review, Obstet. Gynecol. 144 (1) (2024) 40–52.
[6] M.T. Espinoza, J.E. Blümel, P. Chedraui P, et al., Association between type of menopause and mild cognitive impairment: the REDLINC XII study, Maturitas 189 (2024) 108110.
[7] C. Castelo-Branco, J.E Blümel, P. Chedraui P, et al., Age at menopause in Latin America. Menopause 13 (4) (2006) 706–712.
[8] A. Szende, B. Janssen, J. Cabases (Eds.), Self-Reported Population Health: An International Perspective Based on EQ-5D, Springer, Dordrecht (NL), 2014. Available at: https://www.ncbi.nlm.nih.gov/books/NBK500356/.
[9] P. Olivares-Tirado, Calidad de Vida Relacionada a la Salud en beneficiarios de ISAPRES: Validez del cuestionario EQ-5D, Departamento de Estudios y de Salud. Ministerio de Salud, Chile, Mayo, 2006. Available at: https://www.superdesalud.gob.cl/app/uploads/2006/05/articles-3818_recurso_1.pdf.
[10] M. Santos, A.L. Monteiro, B. Santos, EQ-5D Brazilian population norms, Health Qual. Life Outcomes 19 (1) (2021) 162.
[11] P. Chedraui, W. Aguirre, L. Hidalgo, L. Fayad, Assessing menopausal symptoms among healthy middle aged women with the Menopause Rating Scale, Maturitas 57 (3) (2007) 271–278.
[12] ZEG Berlin. https://zeg-berlin.de/expertise/diagnostics-tools/menopause-rating-scale/languages/. (Accessed 22 November 2024).

[13] J.E. Blümel, E. Arteaga, J. Parra, C. Monsalve, V. Reyes, M.S. Vallejo, et al., Decision-making for the treatment of climacteric symptoms using the Menopause Rating Scale, Maturitas 111 (2018) 15–19.
[14] C.D. Jenkins, B.A. Stanton, S.J. Niemcryk, R.M Rose, A scale for the estimation of sleep problems in clinical research, J. Clin. Epidemiol. 41 (3) (1988) 313–321.
[15] D. Villarreal-Zegarra, R. Torres-Puente, S. Otazú-Alfaro, A. Al-Kassab-Córdova, J. Rey de CastroJ, E. Mezones-Holguín, Spanish version of Jenkins Sleep Scale in physicians and nurses: psychometric properties from a Peruvian nationally representative sample, J. Psychosom. Res. 157 (2022) 110759.
[16] A.M. Isidori, C. Pozza, K. Esposito, D. Giugliano, S. Morano, L. Vignozzi, et al., Development and validation of a 6-item version of the female sexual function index (FSFI) as a diagnostic tool for female sexual dysfunction, J. Sex. Med. 7 (3) (2010) 1139–1146.
[17] F.R. Pérez-López, A.M. Fernández-Alonso, M. Trabalón-Pastor, C. Vara, P. Chedraui, MenopAuse RIsk Assessment (MARIA) Research Group, Assessment of sexual function and related factors in mid-aged sexually active Spanish women with the six-item Female Sex Function Index, Menopause 19 (11) (2012) 1224–1230.
[18] P. Chedraui, F.R. Pérez-López, H. Sánchez, W. Aguirre, N. Martínez, O. Miranda, et al., Assessment of sexual function of mid-aged Ecuadorian women with the 6-item Female Sexual Function Index, Maturitas 71 (4) (2012) 407–412.
[19] Rde.C. Pacagnella, E.M. Vieira, Jr.O.M. Rodrigues, C. Souza, Adaptação transcultural do Female Sexual Function Index [Cross-cultural adaptation of the Female Sexual Function Index], Cad. Saude Publica 24 (2) (2008) 416–426.
[20] R. Rosen, C. Brown, J. Heiman, S. Leiblum, C. Meston, R. Shabsigh, et al., The Female Sexual Function Index (FSFI): a multidimensional self-report instrument for the assessment of female sexual function, J. Sex Marital Ther. 26 (2) (2000) 191–208.
[21] J.E. Morley, L. Cao, Rapid screening for sarcopenia, J. Cachexia. Sarcopenia Muscle 6 (4) (2015) 312–314.
[22] G. Bahat, O. Yilmaz, C. Kılıc, M.M Oren, M.A. Karan, Performance of SARC-F in regard to sarcopenia definitions, muscle mass and functional measures, J. Nutr. Health Aging 22 (8) (2018) 898–903.
[23] Z.S. Nasreddine, N.A. Phillips, V. Bédirian, S. Charbonneau, V. Whitehead, I. Collin, et al., The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment, J. Am. Geriatr. Soc. 53 (4) (2005) 695–699.
[24] M. Lozano-Gallego, M. Hernández-Ferrándiz, O. Turró-Gárriga, I. Pericot-Nierga, S. López-Pousa, J. Vilalta-Franch, Validación del Montreal Cognitive Assessment (Moca): test de cribado para el deterioro cognitivo leve, Datos Preliminares, Alzheimer. Real. Inves. Demenc. 43 (2009) 4–11.
[25] S. Freitas, M.R. Simões, C. Martins, M. Vilar, I. Santana, Estudos de adaptação do Montreal Cognitive Assessment (MoCA) para a população portuguesa, Avaliação. Psicológica. 9 (3) (2010) 345–357.
[26] Centers for Disease Control and Prevention, StatCalc: Statistical Calculators, Available at: https://www.cdc.gov/epiinfo/user-guide/statcalc/statcalcintro.html.
[27] J.E. Blümel, P. Chedraui, G. Baron, E. Belzares, A. Bencosme, A. Calle A, et al.; Collaborative Group for Research of the Climacteric in Latin America (REDLINC), Menopausal symptoms appear before the menopause and persist 5 years beyond: a detailed analysis of a multinational study. Climacteric 15 (6) 2012 542–551.
[28] H. Xiangying, H. Lili, S. Yifu, The effect of hysterectomy on ovarian blood supply and endocrine function, Climacteric 9 (4) (2006) 283–289.
[29] S. Sahab-Negah, V. Hajali, H.R. Moradi, A. Gorji, The impact of estradiol on neurogenesis and cognitive functions in Alzheimer's disease, Cell. Mol. Neurobiol. 40 (3) (2020) 283–299.
[30] A.L. Mize, R.H. Alper, Acute and long-term effects of 17beta-estradiol on G(i/o) coupled neurotransmitter receptor function in the female rat brain as assessed by agonist-stimulated [35S]GTPgammaS binding, Brain Res. 859 (2) (2000) 326–333.
[31] J. Camps, A. García-Heredia, Introduction: oxidation and inflammation, a molecular link between non-communicable diseases, Adv. Exp. Med. Biol. 824 (2014) 1–4.
[32] J.E. Blümel, C. Castelo-Branco, P. González, C. Moyano, M. Iturriaga, L. Videla, et al., Transdermal estrogens do not appear to modify the extent of lesional areas of aortic atherosclerosis in oophorectomized rabbits on a cholesterol-rich diet, Atherosclerosis 148 (2) (2000) 303–308.
[33] F. Yin, J. Yao, H. Sancheti, T. Feng, R.C. Melcangi, T.E. Morgan, et al., The perimenopausal aging transition in the female rat brain: decline in bioenergetic systems and synaptic plasticity, Neurobiol. Aging 36 (7) (2015) 2282–2295.
[34] J.H. Moon, J.H. Moon, K.M. Kim, S.H. Choi, S. Lim, K.S. Park, et al., Sarcopenia as a predictor of future cognitive impairment in older adults, J. Nutr. Health Aging 20 (5) (2016) 496–502.
[35] R.N. Pauls, Impact of gynecological surgery on female sexual function, Int. J. Impot. Res. 22 (2) (2010) 105–114.
[36] S.J. Dedden, M.A. Werner, J. Steinweg, B.I. Lissenberg-Witte, J.A.F. Huirne, P.M.A. J. Geomini, et al., Hysterectomy and sexual function: a systematic review and meta-analysis, J. Sex. Med. 20 (4) (2023) 447–466.
[37] H.P.G. Schneider, M. Birkhäuser, Quality of life in climacteric women, Climacteric 20 (3) (2017) 187–194.
[38] Y. Xu, J. Lin, S. Wang, J. Xiong, Q. Zhu, Combined estrogen replacement therapy on metabolic control in postmenopausal women with diabetes mellitus, Kaohsiung J. Med. Sci. 30 (7) (2014) 350–361.
[39] C.Z. Kalenga, A. Metcalfe, M. Robert, K.A. Nerenberg, J.M. MacRae, S.B. Ahmed, Association between the route of administration and formulation of estrogen therapy and hypertension risk in postmenopausal women: a prospective population-based study, Hypertension 80 (7) (2023) 1463–1473.
[40] S.H. Baik, F. Baye, C.J. McDonald, Use of menopausal hormone therapy beyond age 65 years and its effects on women's health outcomes by types, routes, and doses, Menopause 31 (5) (2024) 363–371.
[41] T.S. Mikkola, P. Tuomikoski, H. Lyytinen, P. Korhonen, F. Hoti, P. Vattulainen, et al., Estradiol-based postmenopausal hormone therapy and risk of cardiovascular and all-cause mortality, Menopause 22 (9) (2015) 976–983.
[42] Y. Huang, M. Wu, C. Wu, Q. Zhu, T. Wu, X. Zhu, et al., Effect of hysterectomy on ovarian function: a systematic review and meta-analysis, J. Ovarian Res. 16 (1) (2023) 35.
[43] N. Panay, S.B. Ang, R. Cheshire, S.R Goldstein, P. Maki, R.E. Nappi; International Menopause Society Board. Menopause and MHT in 2024: addressing the key controversies - an International Menopause Society White Paper, Climacteric 27 (5) (2024) 441–457.
[44] M.H. Moen, M. Rees, M. Brincat, T. Erel, M. Gambacciani, I. Lambrinoudaki, K. Schenck-Gustafsson K, et al.; European Menopause and Andropause Society. EMAS position statement: managing the menopause in women with a past history of endometriosis, Maturitas 67 (2010) 94–97.
[45] J.D. Wright, T.J. Herzog, J. Tsui, C.V. Ananth, S.N. Lewin, Y.S. Lu, et al., Nationwide trends in the performance of inpatient hysterectomy in the United States, Obstet. Gynecol. 122 (2 Pt 1) (2013) 233–241.
[46] R.W. Shaw, M.R. Brickley, L. Evans, M.J. Edwards, Perceptions of women on the impact of menorrhagia on their health using multi-attribute utility assessment, Br. J. Obstet. Gynaecol. 105 (11) (1998) 1155–1159.
[47] M.S. Vallejo, J.E. Blümel, A. Bencosme, A. Calle, M. Dextre, K. Díaz, et al., Factors affecting climacteric women with SARS-CoV-2 infection: a multinational Latin America study (REDLINC XI), Maturitas 165 (2022) 33–37.
[48] A. Calle, J.E. Blümel, P. Chedraui, M.S. Vallejo, A. Belardo, M. Dextre, et al., Severe menopausal symptoms linked to cognitive impairment: an exploratory study, Menopause 31 (11) (2024) 959–965.
[49] D.L. Streiner, Starting at the beginning: an introduction to coefficient alpha and internal consistency, J. Pers. Assess. 80 (1) (2003) 99–103.