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Cardiovascular Disease and Depression/Anxiety, Two Complication of Menopause Status

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Abstract

Objective: Postmenopausal women are at an increased risk of Cardiovascular Disease. We aimed to investigate whether this risk differed between individuals with a naturally occurring and other reasons for menopause within a large population-based Iranian sample.

Study design: A total number of 1763 postmenopausal women (defined by amenorrhea for more than a year, or FSH > 30-40 mIU/ml), 900 of them with a natural menopause and 863 of them with other reasons for menopause caused by (hysterectomy without oophorectomy or one side oophorectomy, hysterectomy with oophorectomy or two side oophorectomy without hysterectomy) were recruited as part of the Mashhad Stroke and Heart Atherosclerotic Disorders (MASHAD) cohort study. Biochemical and hematological risk factors were measured in all the subjects and the data were analyzed by SPSS software version 20

Results: There was a significant difference in the presence of cardiovascular disease in the natural menopause group compared with other reasons for menopause group ($p<0.05$). There was also a meaningful difference between the prevalence of depression and anxiety in the natural menopause individuals compared with other reasons for menopause group ($p<0.05$).

Discussion: High prevalence of CVD, depression and anxiety in other reasons in menopause women were observed among Mashhad urban females. It should be considered as a noticeable message. Furthermore, studies are necessary to determine different parameters between evaluating CVD, depression and anxiety among menopauses women.

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Introduction

Background

Menopause means the permanent cessation of menstruation due to loss of ovarian follicular function, which occurs at a mean age of 51 years normally. It is expected that a woman will spends almost a third of her life beyond the menopause. After the menopause, a marker of the end of a woman's reproductive life, the amount of circulating estrogen falls significantly so the symptoms and disorders related to estrogen deficiency will appear [1].

Menopause can occur before the median age of natural menopause (age 51 years) that called early menopause. It is may be occur due to medical or surgical interventions such as chemotherapy or surgical procedures such as oophorectomy[2]. Some epidemiological studies reported that women who undergo early menopause or premature menopause are under higher risk of all-causes mortalities. However, it is necessary to study more on this controversial issue [3].

Menopause can increase the risk of cardiovascular diseases (CVD) [4]. CVD is the most important cause of mortality and morbidity worldwide [5]. Over the past decades the importance of CVD among women has been increased. Therefore, researchers have investigated whether there are gender differences in CVD risk. In the past two decades the epidemiological status of CVD has changed dramatically so, that it becomes the source of disease burden in women population [6, 7].

The importance of CVD among women has been highlighted over past decade, leading researchers to investigate the impact of gender differences in CVD risk factors. In some of these studies mentioned higher CVD risk in postmenopausal women but it is not certainly clear whether menopause is an issue of aging, estrogen deficiency or both [6]. Metabolic syndrome (MetS) is used to define the risk of cardiovascular diseases including obesity, dyslipidemia, hypertension and insulin resistance [7]. Some evidence shows a link between the menopause and some components of the MetS, but results have been inconsistent. There is a hypothesis that the menopause is associated with an increase in the risk of cardiovascular disease independent of normal aging [8].

Objectives

In this study we want to explore the associations between normal and other reasons of menopause with CVD and lipid profile as a risk factor of CVD in a large population-based Iranian samples.

Materials and Methods

Population Study

In current cross-sectional study, 1556 postmenopausal women (with amenorrhea for more than a year by questioner or FSH > 30-40 mIU/ml) [9], 783 of them include of natural menopause and 773 of them consist of other reason menopause (hysterectomy without oophorectomy or one side oophorectomy, hysterectomy with oophorectomy or two side oophorectomy without hysterectomy), were recruited as part of the Mashhad Stroke and Heart Atherosclerotic Disorders (MASHAD) Study using a cluster-randomized-assigned during 2007-2008, as described previously [10]. Inclusion criteria were no known history of infectious diseases, nor a family history of stroke, myocardial infarction. Informed consent was obtained from all individuals using approved protocols by the Ethics Committee of Mashhad University of Medical Sciences [10].

Anthropometric and Biochemical Measurements

Anthropometric parameters, including height, body weight, body mass index (BMI) and hip circumference (WC and HC) were measured in all the subjected as previously described [11, 12], while systolic and diastolic blood pressures were measured by sphygmomanometers [9-11]. Lipid profile levels, including total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C) , triglyceride (TG) and fasting blood glucose (FBG) and C-reactive protein (CRP), uric acid and LFT's such as total and direct bilirubin, AST and ALT were measured by standard procedure as described previously [13, 14].

Measurements of Hematological Markers

Hematological factors, including white blood cell (WBC), red blood cell (RBC), hemoglobin (HGB), hematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), red cell distribution width (RDW), platelet count (PLT), platelet distribution width (PDW) were measured in all the subjects, as described previously [15].

Clinical Evaluation of Depression and Anxiety

Depression Inventory (BDI) and Beck Anxiety Inventory (BAI) [16, 17] were completed by all participants[18]. The BDI and BAI consist of 21 multiple-choice items, with each item having four options ranked according to severity. A score of 0 to 3 is assigned to each item and the aggregate score is calculated to determine the severity of depression and anxiety [18].

Statistical Analysis

Data were analyzed using SPSS-18 software (SPSS Inc., IL, and USA). The normality of distribution was evaluated using Kolmogorov–Smirnov test. Descriptive statistics including mean ± standard deviation was considered for normally distributed variables or median ± interquartile range for variables that were not normally distributed. For normally distributed variables, Student's t-test was applied to compare clinical and baseline demographics characteristics between groups. The Mann-Whitney U test was used for continuous variables and non-normally distributed variables. For categorical parameters, Chi-square or Fisher exact tests were used. All the analyses were two-sided and p value < 0.05 was considered as significant.

Results

Anthropometric Characteristics and the Presence of Dyslipidemia According to Menopause status

Clinical and demographic characteristics of participants are presented in table 1. Among the subjects 1763, 900 (50.3%) had a natural menopause and 863 (49.7%) subjects had other reasons for the menopause. The mean age was 54.32±3.88 and 48.12±7.06 years for natural menopause and other reasons for the menopause respectively (Table 1).

Our results demonstrated that the mean of BMI was significantly higher in other reasons of menopause than natural menopause status ($p< 0.05$). But WC was significantly lower in other reasons of menopause than natural menopause ($p< 0.05$). Also, there were not significant differences between two groups in HC, mid upper circumference, systolic and diastolic blood pressure ($p>0.05$).

According to our findings the levels of LDL, BUN, creatinine, AST were significantly higher in the natural menopause group, whereas uric acid and

Table 1. Anthropometrics and clinical characteristic according to Menopause status

	Natural menopause	Other reasons for menopause	p-value
N	900	863	
Age (years)	54.32±3.88	48.12±7.06	< 0.001
BMI (Kg/m^2)	28.0±4.8	29.4±4.9	0.007
Waist circumference (cm)	101.4±12.6	95.7±12.8	< 0.001
Hip circumference (cm)	104.87±9.89	106.04±10.63	0.2
Mid upper circumference (cm)	30.50±3.71	31.25±5.51	0.094
Systolic blood pressure (mmHg)	128.7±22.3	122.8±19.6	0.76
Diastolic blood pressure (mmHg)	81.7±11.5	79.6±11.7	0.63
FBG (mg/dl)	98.91±48.28	96.13±36.39	0.27
Uric acid (mg/dl)	4.41±1.31	4.49±1.25	0.007
Cholesterol (mg/dl)	206.99±41.38	198.05±40.02	0.9
Triglyceride (mg/dl)	127(92-179)	125(91-173)	0.9
HDL (mg/dl)	46.6±9.9	47.2±10.5	0.13
LDL (mg/dl)	127.9±37.8	112.2±39.5	<0.001
hs-CRP (mg/l)	1.98(1.18-4.19)	2.41(1.25-5.76)	0.02
BUN (mg/dl)	13.65±4.55	11.95±4.09	<0.001
Creatinine (mg/dl)	0.83±0.27	0.79±0.20	0.014
Total Bilirubin (mg/dl)	0.43±0.24	0.41±0.18	0.26
Direct Bilirubin (mg/dl)	0.29±0.14	0.26±0.12	0.076
AST (mg/dl)	25.18±16.08	22.39±10.93	0.003
ALT (mg/dl)	16.61±13.37	16.59±10.53	0.9
Depression score	14.43	15.53	0.029
Anxiety score	12.46	13.92	0.006

Data are presented as mean (SD) or inter quartile range. Using ANCOVA analyses with age included as model covariates

BMI: body mass index, FBG: fasting blood glucose, HDL: high density lipoprotein, LDL: low density lipoprotein, hs-CRP: high sensitive C reactive protein, BUN: blood urea nitrogen, AST: aspartate transaminase, ALT: alanine transaminase

hs-CRP were meaningfully lower in natural menopause group compared with the group of other reasons for the menopause ($p< 0.05$). But no statistically differences were found in HC, MC, SBP, DBP, glucose, triglyceride, HDL, total and direct bilirubin, and ALT between natural menopause groups and other reasons for menopause groups (Table 1). Moreover, depression and anxiety score in other reasons of menopause group were significantly higher than natural menopause groups.

Comparison of Hematological Parameters Between Groups

We also compared the level of different hematological parameters of the participants between natural menopause group and other reasons of menopause group. Results presented in Table 2 clearly defined that individuals with a natural menopause had a significantly higher level of MCHC and platelets than the other groups ($p<0.05$). In contrast, the level of WBC was lower in the natural menopause group ($p<0.05$) (Table 2). But there were no expressive differences between groups with regard to RBC, HCT, Hb, MCV, MCH, RDW, PDW and MPV.

Logistic regression analysis was performed to determine the odds ratio (OR) of the association between demographic, biochemical and hematological (Table 3). Results obtained from univariate analysis demonstrated that BMI, WC, LDL, BUN, creatinine, AST and MCHC are associated with menopause, but when multivariate analysis was done with entering age and all factors in table to model, BMI, WC, BUN, uric acid, AST, MCHC and platelets are an independent predictive risk factor for menopause (Table 3).

Metabolic Syndrome

In this study, we investigated metabolic syndrome in natural menopause individuals compared to other reasons of menopause groups (Table 4). Our results demonstrated that 56.5% of natural menopause groups and 43.5% of other reasons of menopause groups at the risk of metabolic syndrome. Using the Chi-square for comparison, we shows significant differences risk of metabolic syndrome between natural menopauses individuals compared to other reasons of menopause groups ($p< 0.001$). According to logistic regression, our results suggested the association of metabolic syndrome with menopause status, but when data were adjusted for age in multivariate analysis, we did not found significant differences between metabolic syndrome and menopause status (Table 5).

Diabetes

In this study, we investigated diabetes in the natural menopause individuals compared with other reasons of menopause groups (Table 4). Our results demonstrated that 60.2% of natural menopause groups and 39.8% of other reasons of menopause groups at risk of diabetes. Using the Chi-square for comparison, there were significant differences risk of diabetes between natural menopause individuals compared with other reasons of menopause group ($p<0.001$). By using logistic regression, our results suggested the association of diabetes with menopause status in univariate analysis, but when data were adjusted for age in multivariate analysis, we did not found meaningful differences between diabetes and menopause status (Table 5).

CVD

We have investigated the risk of cardiovascular disease in two groups (Table 4). Our results demonstrated that 44.1% and 55.9% of natural menopause groups and other reasons of menopause groups respectively had cardiovascular disease. (History of MI, Angina or Stroke). Using the Chi-square for comparison, we found significant differences risk of cardiovascular disease between natural menopause individuals compared with other reasons of menopause groups ($p<0.001$). By using logistic regression, our results suggested that there is an association in CVD with menopause in univariate analysis, when data were adjusted for age in multivariate analysis, our result strongly showed association between CVD and menopause (Table 5).

Depression and Anxiety

Beck Depression Inventory (BDI) and Beck Anxiety Inventory (BAI) were used for classification individuals to four groups, no (<13), mild (13-19), moderate (20-28) and severe (29-63) for depression and no (<9), mild (10-16), moderate (17-29) and severe (30-63) for anxiety. Our results showed that 21.9%, 19.7% and 10.1% of women with the other reasons of menopause had mild, moderate and severe depression, respectively (Table 4). Also, our findings showed that

Table 2. CBC markers according to Menopause status

	Natural menopause	Natural menopause	p-value
WBC	5.86±1.44	5.91±1.43	0.34
RBC	4.72±0.4	4.72±0.41	0.97
HGB	13.39±1.08	13.13±1.31	0.07
HCT	40.28±3.45	39.95±3.12	0.08
MCV	84.37±5.36	84.79±5.73	0.6
MCH	28.32±2.11	27.92±2.46	0.42
MCHC	33.15±1.25	32.87±1.4	0.001
PLT	239.78±61.26	235.30±59.16	0.004
RDW	41.57±2.98	41.36±2.88	0.094
PDW	12.87±2.03	12.94±1.93	0.46
MPV	10.09±1.07	10.14±0.92	0.27

Data are presented as mean (SD). Using ANCOVA analyses with age included as model covariates. CBC: cell blood count, WBC: Wight blood cell, RBC: red blood cell, HGB: hemoglobin, HCT: hematocrit, MCV: Mean Corpuscular Volume, MCH: Mean Corpuscular Hemoglobin, MCHC: Mean Corpuscular Hemoglobin Concentration, PLT: platelets, RDW: Red Cell Distribution Width, PDW: Platelets Distribution Width, MPW: Mean platelet volume.

Table 3. Association between demographic, biochemical and hematological parameters with menopause[#].

	Odds Ratio (95% CI)	
	Univariate	Multivariate [a]
BMI	1.027(1.008-1.047)**	1.14(1.08-1.2)***
Waist circumference	0.963(0.955-0.97)***	0.928(0.91-0.947)***
Uric acid	1.047(0.974-1.124)	1.268(1.096-1.467)**
LDL	0.991(0.988-0.993)***	0.998(0.994-1.002)
BUN	0.888(0.861-0.916)***	0.94(0.897-0.985)**
Creatinine	0.331(0.193-0.566)**	1.3(0.492-3.45)
AST	0.976(0.965-0.988)**	0.984(0.969-0.999)*
MCHC	0.819(0.76-0.88)***	0.775(0.677-0.888)***
PLT	0.999(0.997-1.0)	0.997(0.994-1)*

CI, confidence interval; a: In multivariate analysis age and all factors in table inter to model

***: p< 0.001, **: p< 0.01

logistic regression has done; dependent variable was menopause status

Table 4. Prevalence of CVD, Metabolic syndrome, Diabetes, Smoking, Depression and Anxiety in Menopause

		Natural menopause	other reasons for menopause	p-value
Metabolic syndrome	Yes	520 (56.5%)	400(43.5%)	< 0.001
	no	378 (44.9%)	465(55.1%)	
Diabetes Mellitus	Yes	212(60.2%)	143 (39.8%)	< 0.001
	No	698 (49.5%)	710 (50.5%)	
CVD	Yes	79 (44.1%)	100 (55.9%)	0.031
	No	821 (51.8%)	763 (48.2%)	
Depression	No	461 (55.0%)	410 (48.3%)	0.043
	Mild	176 (19.2%)	187 (21.9%)	
	Moderate	141 (16.5%)	166 (19.7%)	
	High	110 (9.4%)	112 (10.1%)	
Anxiety	No	412 (47.3%)	337 (39.9%)	0.01
	Mild	231 (23.8%)	222 (25.6%)	
	Moderate	173 (20.6)	217 (26%)	
	High	87 (8.3%)	99(8.5%)	

Table 5. Unadjusted and Multivariate-Adjusted Odds Ratios of disease among menopause

	Odds Ratio (95% CI)	
	Unadjusted	Multivariate adjusted [a]
Metabolic syndrome (reference: no)	0.626(0.519-0.756)***	0.932(0.752-1.14)
Diabetes (reference: no)	0.648(0.5-0.83)***	0.945(0.727-1.23)
CVD(reference: no)	1.36(0.99-1.316)**	1.85(1.31-2.6)***
Depression (reference: no)	1.53(1.272-1.86)***	1.52(1.23-1.87)***
Anxiety (reference: no)	1.51(1.255-1.822)***	1.56(1.27-1.92)***

CI, confidence interval; a: In multivariate model each disease adjusted for age.

***: p< 0.001, **: p< 0.01

35.6%, 26.0% and 8.5% of women with the other reasons of menopause had mild, moderate and severe anxiety, respectively (Table 4). Using the Chi-square for comparison, we showed significant differences in risk of anxiety between natural menopause individuals and subjects with the other reasons of the menopause ($p<0.05$).

In logistic regression, we made two groups for anxiety (no <9 or yes >10) and depression (no <13 or yes >14). According to logistic regression our results suggested that there is a strong association of anxiety and depression with menopause in univariate and multivariate analysis that adjusted by age (Table 5).

Discussion

Results interestingly shown prevalence of depression and anxiety in women with other reasons of menopause is higher than participants with a natural menopause. Many observational studies have shown that the transition to menopause is a period of increased risk of depression [23, 24]. Unpredictable hormone fluctuations plus stress, body image, sexuality, infertility, or aging; anyone or a combination of these, causes emotional distress that may result in mood swings or in more severe cases, depression. Determining the cause and extent of your "menopause blues" is very important [19]. Some study suggested concerns about the physical and social consequences of aging, or her self-esteem may be affected by a culture that values youth and reproductive capacity [20].

Results of present study showed that the prevalence of cardiovascular disease was higher in participants with other reasons of menopause compared with natural menopause women. It may be explained by other reasons of menopause which it occurs earlier than normal menopause. It has been reported that cardiovascular disease, osteoporosis, urinary incontinence and depression are just a few of many common and major complaints among midlife women, which in result affects their quality of life [22]. Recent studies showed that there is not any association between CVD risk and hysterectomy, with ovarian conservation [21]. Atsma et al., have reported that there was no significant relationship between postmenopausal status and CVD. However, it has been reported that other reasons for menopause had a modest impact on CVD [22]. Some other studies confirm our observations which indicated that premenopausal women are protected against cardiovascular morbidity and mortality and the lack of ovarian function increased the risk of CVD [23].

We also evaluated the anthropometric, biochemical and hematological indices. The BMI and uric acid were higher in the other reasons of menopause compared with natural menopause group.

The results of current study showed in spite of increased CVD in participants with the other reasons for menopause than normal menopause, they have a lower risk of diabetes and as a result, metabolic syndrome. Dørum et al. published conflict results and reported that women who had undergone bilateral oophorectomy had higher BMI and a trend towards higher blood pressure, lower HDL cholesterol, and elevated triglycerides, that all of them make the metabolic syndrome prevalence higher [24]. It seems that having an abnormal menopause can disarrange insulin hemostasis. Rosano et al., have reported that insulin resistance is significantly higher in postmenopausal women than in premenopausal women [25]. Although, we cannot identify this irregularity in current research because of no measuring the insulin resistance indices, which should be included in future studies.

It is worthy to mention that this research has some limitation. Our study was cross sectional and this was the most significant limitation of our study. However, it can help us to design a cohort study.

Conclusion

The prevalence of CVD, depression and anxiety was higher in women with other reasons of menopause than subjects with natural menopause in Iranian women. This study evaluated a wide range of disturbances and CVD risk factors in subjects with normal and other reasons for menopause for the first time. But further work is required to establish the accuracy of mentioned findings.

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Declaration of interest

None declared

References

1. Kilim SR, Chandala SR. A comparative study of lipid profile and oestradiol in pre-and post-menopausal women. Journal of clinical and diagnostic research: JCDR. 2013;7(8):1596.
2. Shuster LT, Rhodes DJ, Gostout BS, Grossardt BR, Rocca WA. Premature menopause or early menopause: long-term health consequences. Maturitas. 2010;65(2):161-6.
3. Gong D, Sun J, Zhou Y, Zou C, Fan Y. Early age at natural menopause and risk of cardiovascular and all-cause mortality: A meta-analysis of prospective observational studies. International journal of cardiology. 2016;203:115-9.
4. Farahmand M, Tehrani FR, Khomami MB, Noroozzadeh M, Azizi F. Surgical menopause versus natural menopause and cardio-metabolic disturbances: A 12-year population-based cohort study. Journal of endocrinological investigation. 2015;38(7):761-7.
5. Abdulnour J, Razmjou S, Doucet É, Boulay P, Brochu M, Rabasa-Lhoret R, et al. Influence of cardiorespiratory fitness and physical activity levels on cardiometabolic risk factors during menopause transition: A MONET study. Preventive Medicine Reports. 2016;4:277-82.
6. Anagnostis P, Stevenson JC, Crook D, Johnston DG, Godsland IF. Effects of menopause, gender and age on lipids and high-density lipoprotein cholesterol subfractions. Maturitas. 2015;81(1):62-8.
7. Rurik I, Móczár C, Buono N, Frese T, Kolesnyk P, Mahlmeister J, et al. Early and Menopausal Weight Gain and its Relationship with the Development of Diabetes and Hypertension. Experimental and Clinical Endocrinology & Diabetes. 2016.
8. Eshtiaghi R, Esteghamati A, Nakhjavani M. Menopause is an independent predictor of metabolic syndrome in Iranian women. Maturitas. 2010;65 (3):262-6.
9. Novak E, Berek JS. Berek & Novak's gynecology: Lippincott Williams & Wilkins; 2007.
10. Ghayour-Mobarhan M, Moohebati M, Esmaily H, Ebrahimi M, Parizadeh SM, Heidari-Bakavoli AR, et al. Mashhad stroke and heart atherosclerotic disorder (MASHAD) study: design, baseline characteristics and 10-year cardiovascular risk estimation. International journal of public health. 2015;60(5):561-72.
11. Zomorrodian D, Khajavi-Rad A, Avan A, Ebrahimi M, Nematy M, Azarpazhooh MR, et al. Metabolic syndrome components as markers to prognosticate the risk of developing chronic kidney disease: evidence-based study with 6492 individuals. Journal of epidemiology and community health. 2015: jech-2014-205160.
12. Emamian M, Avan A, Pasdar A, Mirhafez SR, Sadeghzadeh M, Moghadam MS, et al. The lipoprotein lipase S447X and cholesteryl ester transfer protein rs5882 polymorphisms and their relationship with lipid profile in human serum of obese individuals. Gene. 2015;558(2):195-9.
13. Mirhafez SR, Zarifian A, Ebrahimi M, Ali RF, Avan A, Tajfard M, et al. Relationship between serum cytokine and growth factor concentrations and coronary artery disease. Clinical biochemistry. 2015;48(9):575-80.
14. Mirhafez SR, Pasdar A, Avan A, Esmaily H, Moezzi A, Mohebati M, et al. Cytokine and growth factor profiling in patients with the metabolic syndrome. The British journal of nutrition. 2015;113(12): 1911-9.
15. Mardan-Nika M, Pasdar A, Jamialahmadi K, Avan A, Mohebati M, Esmaily H, et al. Association of heat shock protein70-2 (HSP70-2) gene polymorphism with obesity. Annals of human biology. 2015 (just-accepted):1-19.
16. Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. Archives of general psychiatry. 1961;4:561-71.
17. Beck AT, Epstein N, Brown G, Steer RA. An inventory for measuring clinical anxiety: psychometric properties. Journal of consulting and clinical psychology. 1988;56(6):893-7.

18. Sekita A, Arima H, Ninomiya T, Ohara T, Doi Y, Hirakawa Y, et al. Elevated depressive symptoms in metabolic syndrome in a general population of Japanese men: a cross-sectional study. BMC public health. 2013;13(1):1.
19. Nicol-Smith L. Causality, menopause, and depression: a critical review of the literature. Bmj. 1996;313(7067):1229-32.
20. Hunter MS. Depression and the menopause. BMJ: British Medical Journal. 1996;313(7067):1217.
21. Lobo RA. Surgical menopause and cardiovascular risks. Menopause. 2007;14(3):562-6.
22. Atsma F, Bartelink M-LE, Grobbee DE, van der Schouw YT. Postmenopausal status and early menopause as independent risk factors for cardiovascular disease: a meta-analysis. Menopause. 2006;13(2):265-79.
23. Mohammad K, Hashemi SMS, Farahani FKA. Age at natural menopause in Iran. Maturitas. 2004;49 (4):321-6.
24. Dørum A, Tonstad S, Liavaag AH, Michelsen TM, Hildrum B, Dahl AA. Bilateral oophorectomy before 50 years of age is significantly associated with the metabolic syndrome and Framingham risk score: a controlled, population-based study (HUNT-2). Gynecologic oncology. 2008;109(3):377-83.
25. Rosano G, Vitale C, Marazzi G, Volterrani M. Menopause and cardiovascular disease: the evidence. Climacteric. 2007;10(sup1):19-24.