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The possible role of abnormal uterine bleeding in cardiovascular health during perimenopausal age

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The manifestation of cardiovascular disease (CVD) in women typically occurs during menopausal transition. Abnormal uterine bleeding (AUB) in perimenopausal women could capture the disaster settings during wartime.

Aim – to study the possible pathogenic peculiarities of CVD in perimenopausal women with AUB in a frontline city.

Material and methods. The 49 perimenopausal women were enrolled in the study. The 26 women without excessive menstrual loss were included in Group I. The 23 women with AUB were involved in Group II. The variables of body mass index (BMI), menopausal Cooperman's score and anxiety and stress levels in the study groups were measured. The lipid and carbohydrate metabolism variables, C-reactive protein were detected.

Results. The data obtained showed that the variables of BMI, Cooperman's score, metabolic markers, and CRP were almost similar in the study groups. However, the level of anxiety and stress variables was significantly higher in women with AUB. The variable of BMI demonstrated weak or moderate correlation with HOMA index, blood serum insulin concentration, and CRP. The multivariate logistic regression supported the link between AUB and the Taylor scale score.

Conclusion. The increased Spielberger scale score, Taylor scale scores, and perceived stress scale score were found in perimenopausal women with AUB. The logistic regression supported the link between AUB and the anxiety Taylor scale score. The disturbed psychological status could be a valuable addition to anti-aging programs during wartime.

The research was carried out in accordance with the principles of the Declaration of Helsinki. The study protocol was approved by the Local Ethics Committee of the participating institution. The informed consent of the patient was obtained for conducting the studies.

No conflict of interests was declared by the authors.

Keywords: cardiovascular disease, menopause, abnormal uterine bleeding, wartime stress.

Можлива роль аномальних маткових кровотеч у стані серцево-судинної системи в період перименопаузи

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Прояв серцево-судинних захворювань (ССЗ) у жінок зазвичай відбувається під час менопаузального переходу. Аномальні маткові кровотечі (АМК) у жінок у перименопаузі можуть значно погіршувати якість життя під час війни.

Мета – пошук можливих патогенетичних особливостей ССЗ у жінок у перименопаузі з АМК у прифронтовому місті.

Матеріали та методи. У дослідженні взяло участь 49 жінок у перименопаузі: група I – 26 жінок без надмірних менструальних втрат, група II – 23 жінки з АМК. Вивчено такі показники, як індекс маси тіла (ІМТ), бальна оцінка за шкалою Купермана та рівень тривожності та стресу, показники ліпідного та вуглеводного обміну, С-реактивний білок (СРБ).

Результати. Такі змінні, як ІМТ, шкала Купермана, метаболічні маркери та СРБ були майже подібними в досліджуваних групах. Проте рівень тривожності та стресу був значно вищим у жінок з АМК. Показник ІМТ продемонстрував слабку або помірну кореляцію з індексом HOMA, концентрацією інсуліну в крові та СРБ. Багатовимірна логістична регресія підтвердила зв'язок між АМК та бальною оцінкою за шкалою Тейлора.

Висновок. У жінок у перименопаузі з АМК було виявлено підвищений бал за шкалою Спілбергера, шкалою Тейлора та шкалою сприйняття стресу. Логістична регресія підтвердила зв'язок між АМК та балом за шкалою тривожності Тейлора. Встановлений порушений психологічний статус жінок може бути цінним доповненням до програм боротьби зі старінням під час війни.

Дослідження проведено відповідно до принципів Гельсінської декларації. Протокол дослідження схвалено місцевим комітетом з етики закладу-учасника. На проведення досліджень отримано інформовану згоду пацієнток.

Автори не заявили про конфлікт інтересів.

Ключові слова: серцево-судинні захворювання, менопауза, аномальні маткові кровотечі, стрес воєнного часу.

Introduction

Menopause is a milestone that induces ageing and several systemic disorders. The manifestation of cardiovascular disease (CVD) in women typically occurs during a specific period of life, the menopausal transition. Arterial hypertension, tachycardia, and arrhythmia are typical of early menopausal disorders. Autonomic imbalance with dominant sympathetic regulation contributes to elevated blood pressure (BP) [11]. The fetal programming hypothesis states that low birth

weight is a risk factor for CVD and other diseases of adult life. The weak point of this hypothesis is the absence of differentiation between a small premature baby and fetal growth restriction. However, great obstetric syndromes like preeclampsia, fetal growth restriction, and stillbirth alter maternal health. The risk of arterial hypertension, coronary heart disease, and brain stroke is 9 times higher in women after preeclampsia [5,10]. The pathogenic scenario of CVD includes metabolic syndrome, chronic inflammation, atherogenic vasculopathy, endothelial malfunction, and oxidative stress [7]. Hyperandrogenicity is a trigger for diabetes mellitus type II and CVD [9]. Premenstrual syndrome is also an evident risk factor for CVD. The mechanism providing the link between premenstrual syndrome and CVD may be a malfunction of the renin-angiotensin-aldosterone system [4]. Therefore, several gestational complications, gynecological, and internal diseases could accelerate the manifestation of CVD even before menopause.

Abnormal uterine bleeding (AUB) unites a wide group of pathologies that occur at any age beginning from puberty. AUB in perimenopausal women could capture an unsolved problem transferred from reproductive age, or it may be initially developed during early ageing [13]. The consequences of AUB on overall health are well understood. The link between insulin resistance, endometrial hyperplasia, and uterine cancer is obvious. The disaster settings during wartime negatively affect the health of women. Kharkiv is a frontline city in Ukraine. Recently, the elevated level of dyslipidemia among internally displaced women of postreproductive age was found there [8]. Therefore, the increased manifestation of metabolic syndrome is a factor for CVD development. Wartime stress associated with increased sympathetic activity probably contributes to the progression of the disease [6]. The issue about the possible role of stressogenic environment on the pathogenesis of CVD in perimenopausal women has not been addressed yet.

The aim of the study is the search for the possible pathogenic peculiarities of CVD in perimenopausal women with AUB in a frontline city.

Materials and methods of the study

The cross-sectional study was carried out. The recruitment of the study was performed among patients who had visited the outpatient department for a preventive checkup or were admitted due to AUB to the gynecological department of Kharkiv Municipal Perinatal Center between 1 March 2024 and 31 May 2025. Patients were selected randomly. The technique of automated numbers was used.

The 49 perimenopausal women were enrolled in the study. The study population was divided into two groups. The 26 women without excessive menstrual loss were included in Group I. The 23 women with AUB were involved in Group II.

The eligible participants were informed about the methodology of the study, its aims, objectives, indications, and possible complications before inclusion in the study.

The exclusion criteria were preexisting medical disorders such as diabetes mellitus type I, diabetes mellitus type II, thyrotoxicosis, rheumatic disease, malignancy, etc.

Women with AUB did not have any indications for a hysterectomy. The treatment was performed via hysteroscopy. The levonorgestrel-containing intrauterine devices were inserted after hysteroscopy in all cases. The study report was compiled as per the STROBE guidelines [2].

The variables of body mass index (BMI), heart rate (HR), and BP were measured at inclusion. The menopausal Cooperman's score and psychological tests were assessed. Anxiety and stress levels in the study groups were measured using psychological diagnostic methods to assess the women's psychological and emotional state [15]. The study used these methods:

– Spielberger's scale of personal and reactive anxiety, where an indicator of up to 30 points corresponds to a low, from 31 to 44 points to a moderate, and over 45 points to a high level of anxiety;

– Taylor's anxiety measurement, where a total score of 40–50 points is considered an indicator of a very high level of anxiety; 25–40 points indicates a high level of anxiety; 15–25 points indicates an average (with a tendency to high) level; 5–15 points indicates an average (with a tendency to low) level; 0–5 points indicates a low level of anxiety;

– Perceived stress scale (PSS), where a score of more than 32 points corresponds to a high level of stress.

Biochemical studies were performed on a Cobas 6000 analyzer (Roche Diagnostics, Switzerland). The entire study population was tested for serum triglycerides (TG), total cholesterol (CHC), high-density lipoprotein cholesterol (HDL cholesterol),

Table 1

The variables of BMI, Cooperman's score, carbohydrate and lipid metabolism, CRP, AC/DC, and psychological tests

Variable, units	Menstrual function	Frequency	Mean, p	Std. deviation	Minimum	Maximum
BMI	Normal	26	29.77	4.3	25	46
	AUB	23	30.22	4.39	25	41
			p=0.7190			
Cooperman's score, points	Normal	26	26.96	9.7	11	40
	AUB	23	29.83	6.28	19	40
			p=0.2318			
HOMA index	Normal	26	3.25	1.9	0.74	7.3
	AUB	23	2.89	1.45	1.15	6.2
			p=0.4642			
Insulin, IU	Normal	26	12.91	6.47	3.46	25.44
	AUB	23	11.8	5.67	4.7	23.4
			p=0.5286			
Glucose, mmol/l	Normal	26	5.5	0.73	3.98	7.06
	AUB	23	5.7	0.77	4.65	8.47
			p=0.3557			
CRP, mg/l	Normal	26	1.92	2.09	0.3	8.02
	AUB	23	3.48	4.35	0.6	17.5
			p=0.1098			
LDL, mmol/l	Normal	26	4.03	0.95	2.56	5.7
	AUB	23	3.87	1.01	1.81	5.9
			p=0.5706			
HDL, mmol/l	Normal	26	1.59	0.38	1	2.39
	AUB	23	1.78	0.44	1.14	2.71
			p=0.1115			
VLDL, mmol/l	Normal	26	0.62	0.73	0.27	4.08
	AUB	23	0.5	0.17	0.25	1.02
			p=0.4456			
TG, mmol/l	Normal	26	1.2	0.53	0.66	2.81
	AUB	23	1.21	0.49	0.55	2.96
			p=0.9459			
TCH, mmol/l	Normal	26	6.03	1	4.28	7.59
	AUB	23	6	1.18	4.37	8.3
			p=0.9237			
AI	Normal	26	2.96	1.06	1.25	5.92
	AUB	23	2.5	0.87	0.86	4.77
			p=0.1062			
AC, ms	Normal	26	8.67	2.57	4.25	14.44
	AUB	23	8.7	3.55	4.44	17.44
			p=0.9729			
DC, ms	Normal	26	8.8	2.45	5.11	13.58
	AUB	23	8.53	3.12	4.53	17.13
			p=0.7362			
Spielberger scale score, points	Normal	26	30.15	3.08	24	36
	AUB	23	42.48	3.1	38	47
			p<0.0001			
Taylor scale score, points	Normal	26	23.88	4.96	15	38
	AUB	23	42.91	2.68	39	48
			p<0.0001			
Perceived stress scale score, points	Normal	26	20	5.77	14	37
	AUB	23	34.74	2.58	31	44
			p<0.0001			

Table 2

The linear correlation between BMI, Cooperman's score, variables of carbohydrate metabolism, CRP, AI, AC/DC, anxiety, and stress scales score

Variables	Correlation and significance	BMI	Cooperman's score	HOMA index	Insulin	Glucose	CRP	AI	AC	DC	Spielberger scale score	Taylor scale score	Perceived stress scale score
BMI	Correlation	1	0.1	**0.36**	**0.32**	0.18	**0.44**	-0.19	0.11	0.14	0.09	0.08	0.1
	p		0.515	0.012	0.025	0.224	0.002	0.2	0.442	0.33	0.527	0.601	0.513
Cooperman's score	Correlation	0.1	1	-0.05	-0.04	0.02	0.17	0.03	-0.28	-0.25	0.21	0.19	0.11
	p	.515		0.731	0.764	0.885	0.252	0.852	0.055	0.083	0.156	0.2	0.444
HOMA index	Correlation	0.36	-0.05	1	**0.95**	**0.62**	**0.49**	0.1	-0.2	-0.16	-0.03	-0.15	-0.24
	p	0.012	0.731		<0.001	<0.001	<0.001	0.479	0.173	0.273	0.831	0.317	0.103
Insulin	Correlation	**0.32**	-0.04	**0.95**	1	**0.44**	**0.5**	0.08	-0.17	-0.13	-0.03	-0.12	-0.24
	p	0.025	0.764	<0.001		0.002	<0.001	0.576	0.255	0.361	0.865	0.422	0.096
Glucose	Correlation	0.18	0.02	**0.62**	**0.44**	1	**0.28**	0.03	-0.13	-0.11	0.16	-0.03	-0.04
	p	0.224	0.885	<0.001	0.002		0.048	0.847	0.364	0.436	0.265	0.85	0.791
CRP	Correlation	**0.44**	0.17	**0.49**	**0.5**	**0.28**	1	-0.07	-0.15	-0.12	0.18	0.13	-0.05
	p	0.002	0.252	<0.001	<0.001	0.048		0.61	0.303	0.429	0.21	0.374	0.73
AI	Correlation	-0.19	0.03	0.1	0.08	0.03	-0.07	1	0.07	0.02	-0.23	-0.28	-0.23
	p	0.2	0.852	0.479	0.576	0.847	0.61		0.646	0.879	0.119	0.055	0.109
AC	Correlation	0.11	-0.28	-0.2	-0.17	-0.13	-0.15	0.07	1	**0.96**	-0.07	0.03	-0.02
	p	0.442	0.055	0.173	0.255	0.364	0.303	0.646		<0.001	0.653	0.833	0.871
DC	Correlation	0.14	-0.25	-0.16	-0.13	-0.11	-0.12	0.02	**0.96**	1	-0.06	0.04	-0.05
	p	0.33	0.083	0.273	0.361	0.436	0.429	0.879	<0.001		0.66	0.776	0.738
Spielberger scale score	Correlation	0.09	0.21	-0.03	-0.03	0.16	0.18	-0.23	-0.07	-0.06	1	**0.82**	**0.76**
	p	0.527	0.156	0.831	0.865	0.265	0.21	0.119	0.653	0.66		<0.001	<0.001
Taylor scale score	Correlation	0.08	0.19	-0.15	-0.12	-0.03	0.13	-0.28	0.03	0.04	**0.82**	1	0.77
	p	0.601	0.2	0.317	0.422	0.85	0.374	0.055	0.833	0.776	<0.001		<0.001
Perceived stress scale score	Correlation	0.1	0.11	-0.24	-0.24	-0.04	-0.05	-0.23	-0.02	-0.05	**0.76**	**0.77**	1
	p	0.513	0.444	0.103	0.096	0.791	0.73	0.109	0.871	0.738	<0.001	<0.001	

low-density lipoprotein cholesterol (LDL cholesterol), and very-low-density lipoprotein (VLDL cholesterol). The concentrations of TG and CHC were studied by the colorimetric enzymatic method, and HDL cholesterol was investigated by the colorimetric enzymatic method with pre-precipitation of LDL cholesterol and chylomicrons. The atherogenic index (AI), which reflects the ratio of atherogenic (CHD and LDL cholesterol) and antiatherogenic (HDL cholesterol) fractions of cholesterol was also calculated. The levels of glycemia and insulin on an empty stomach were detected with subsequent calculation of the HOMA index. C-reactive protein (CRP) as a marker of chronic inflammation was investigated.

The assessment of the heart rate variability (HRV) was performed. The study used the Cardiolab (KHAI-Medica Research Center, Ukraine) for the detection of AC (acceleration capacity) and DC (deceleration capacity) variables via electrocardiography.

Statistical analysis was conducted with IBM SPSS Statistics version 28.0. Armonk, NY: IBM Corp. Numeric variables were reported as means with standard deviations, while categorical data were summarized using frequencies and percentages.

Table 3

Multivariate logistic regression model with Taylor scale score

Parameter	Unstandardized Coefficients	Standardized Coefficients	Standard error	t	p	95% confidence interval for B	
Model	B	Beta				lower bound	upper bound
(Constant)	17.21		9.86	1.74	.09	-2.81	37.23
BMI	-0.06	-0.03	0.18	-0.34	.733	-0.43	0.3
Cooperman's score	0.05	0.04	0.07	0.78	.443	-0.08	0.19
HOMA index	0.86	0.14	1.32	0.65	.517	-1.82	3.55
Insulin	-0.15	-0.09	0.32	-0.46	.649	-0.81	0.51
Glucose	-1.89	-0.14	1.04	-1.81	.078	-4	0.23
CRP	0.06	0.02	0.22	0.27	.789	-0.39	0.51
AI	-0.47	-0.04	0.6	-0.77	.445	-1.69	0.76
AUB	11.14	0.54	2.72	4.09	<.001	5.61	16.67
AC	0.36	0.11	0.54	0.67	.509	-0.74	1.46
DC	-0.04	-0.01	0.59	-0.06	.949	-1.23	1.16
Spielberger scale score	0.32	0.21	0.19	1.7	.098	-0.06	0.7
Perceived stress scale score	0.27	0.23	0.14	1.95	.058	-0.01	0.55

Normality of numeric variables was evaluated using skewness and histograms. Independent sample t-tests were used to compare numeric variables that were normally distributed. Variables that were not normally distributed were analyzed using the Mann–Whitney U-test. Chi-square (or Fisher's exact test) was used to compare categorical variables. Fisher's exact test (for 2×2 tables only) was used as a significance test for qualitative data. For multivariate analyses, logistic regression analysis with an input model was used. Sample size was determined at a 95% confidence level with a 5% margin of error. A p-value below 0.05 indicated statistical significance.

The Bioethics Committee of the Kharkiv National Medical University approved the study protocol, No35.024p. All patients who met the inclusion criteria gave written informed consent to participate in the investigation.

Results

The mean age of the patients was 49.6±2.8 years in Group I and 50.2±3.6 years in Group II (p>0.05). The systolic BP was 145.4±14.6 mm Hg in Group I and 148.5±18.3 mm Hg in Group II (p>0.05). The diastolic BP was 89.6±18.1 mm Hg in Group I and 92.1±14.6 in Group II (p>0.05). The variables of HR were 80.4±19.5 and 81.6±15.8 in the same groups, respectively (p>0.05). The patients in Group II had several gynecological pathologies: endometrial hyperplasia – 7 (29.16%), small uterine myoma – 6 (24.0%), adenomyosis – 5 (20.83%), and endometrial polyps – 5 (20.83%). The data thus obtained showed that the variables of BMI, Cooperman's score, carbohydrate, lipid metabolism, CRP, and AC/DC did not differ significantly between the study groups (Table 1). However, the level of anxiety and stress variables was significantly higher in women with AUB in Group II.

The study revealed the linear correlation between several observed parameters (Table 2). The variable of BMI demonstrated weak or moderate correlation with HOMA index (r=0.36, p=0.012), insulin (r=0.32, p=025), and CRP (r=0.44, p=0.002). The moderate correlation between insulin and CRP was found (r=0.5, p<0.001). The weak positive correlation was detected in the pair: glucose vs CRP (r=0.28, p=0.048). CRP had a moderate relationship with HOMA index (r=0.49, p<0.001). However, no relationship was found between psychological tests, variables of HRV, AI, and other parameters.

The multivariate logistic regression detected the link between AUB and the Taylor scale score (Table 3). The model itself was meaningful. The different models showed a coupling between BMI and CRP (t=4.55, p<0.001), BMI and AI (t=2.24, p=0.031).

Discussion

The difference in the score by Spielberger, Taylor, and perceived stress was detected in perimenopausal women without excessive menstrual blood loss and AUB. Probably, an increased level of stress contributed to the development of AUB, or AUB itself stimulated stress-induced psychological maladaptation. The spectrum of pathologies associated with AUB and the investigations performed did not allow us to find a solution.

The psychological tests did not reveal any relationship to metabolic parameters, HRV variables, or CRP. The study did not find that AUB plays a predictive role in CVD. The differences in carbohydrate, lipid metabolism, and CRP were not detected in the perimenopausal women with or without AUB. However, the findings support a conventional point of view on the pathogenesis of CVD [14]. The relationship between carbohydrate, lipid metabolism, chronic inflammation, and BMI in perimenopausal women was found.

War ruins all hope for healthy ageing. Wartime stress was a real disaster for the population of frontline cities [3]. The level of anxiety and perceived stress was significantly higher in perimenopausal women with AUB [1]. Therefore, AUB increased the level of stress. Probably, this circumstance should be considered in the process of clinical algorithms development for safe and healthy menopause. This result cannot address the issue of the initial event in the pathogenic scenario of ageing. AUB decreased the resistance to stress.

The limitation of the study was the small number of the study population. Thus, the analysis between residents of Kharkiv and internally displaced persons was not performed. The AC/DC variables did not demonstrate any significance. Since increased activity of HRV associated with the sympathetic branch of autonomic function is known in perimenopausal women, further studies should use different parameters of HRV [1]. The prospect is multicenter research for the investigation of the role of stress in CVD and AUB.

Conclusion

The increased Spielberger scale score, Taylor scale scores, and perceived stress scale score were found in perimenopausal women with AUB. The logistic regression supported the link between AUB and the anxiety Taylor scale score. The detected peculiarities could be a valuable addition to anti-aging in war.

The further prospect is the possible implementation of the findings into health care strategies among perimenopausal women in Ukraine.

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