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ENDOTHELIAL DYSFUNCTION IN PATIENTS WITH CARDIOVASCULAR COMPLAINTS AND ANXIETY DURING THE RUSSIAN-UKRAINIAN WAR: CASE SERIES

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ABSTRACT

Any war influences the mental and physical health of inhabitants of the country suffering from aggression. Anxiety is one of the mental disorders with increased prevalence during the war. A close relationship between anxiety and carbon dioxide concentration in the human body was revealed. There is no doubt about the pivotal role of the later in vascular tone control and the appropriate functioning of the endothelium. This paper presented case series of three female patients with similar complaints exacerbated after a stressful situation (bombing) in the period of the Russian-Ukrainian War. In addition to routine investigational methods (anamnesis taking, physical examination, electrocardiography, and transthoracic echocardiography at rest), Hamilton Anxiety Score and capnometry were used. The trend of drastically decreased end-tidal concentration of carbon dioxide and mild to severe anxiety levels was noticed. We consider there is a connection between the severity of anxiety and end-tidal concentration of carbon dioxide that indirectly reflects the possible endothelial dysfunction.

Therefore, taking into consideration patho-mechanisms and pathology data, using differential pathogenetic methods of surgical invasion and computer monitoring of post-operative period we managed to decrease mortality in severecerebro-cranial traumas to 29-30% comparing to pre computer periods 36-38 % and comparing to data of other clinics 35-45%.

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Introduction.

The impact of any war on the mental [1] and physical health [2] of people suffering from aggression, including refugees [3] cannot be overestimated. In the gamut of mental disorders anxiety takes the first place with increased prevalence in the civilian group while the war. The aggregate prevalence of anxiety, depression, and post-traumatic stress syndrome was 30.7%, 28.9%, and 23.5%, respectively [4].

There is a close relationship between anxiety, hyperventilation [5], and CO₂ concentration [6]. In patients with hyperventilation, hypocarbia was registered in two-thirds of patients [7]. The crucial role of CO₂ is defined in vascular tone regulation [8], heart contractility [9], and endothelium functioning [10].

The aim of the paper is to aware the scientific and medical community of mental disorders' explosion leading to psychosomatic consequences under any war, particularly the Russian-Ukrainian War. For this purpose, we elucidated three cases of female patients with similar cardiovascular complaints.

Materials and methods.

The current case series report presents three out-hospital female patients (42-, 15-, 39-year-old) who visited a cardiologist's office with health disorders that were exacerbated after the episode of the Kyiv bombing. We provided a precise basic questionnaire of the patients as well as a detailed physical examination according to the traditional algorithm. 12-channel electrocardiography with rhythmogram at the sweep of 50 mm/s was registered. We measured the blood pressure of the patients three times using a standardized electronic measuring instrument. Two-dimensional transthoracic echocardiography at rest (Toshiba Artida SSH-880CV) was performed according to the current protocol [11]. Among additional instrumental investigational methods was capnometry (Capnoxi Plus, THOMAS) with an end-tidal concentration of carbon dioxide measurement (EtCO₂) [12]. Besides, we assessed anxiety severity in patients with Hamilton Anxiety Scale. It takes into account 14 categories, namely anxious mood, tension, fears, insomnia, intellectual, depressed mood, somatic muscular, somatic sensory, cardiovascular, respiratory, gastrointestinal, genitourinary, autonomic symptoms, behavior at interview, each of which grades from "0" (not present) to "4" (very severe). According to the current scale, anxiety severity varies from mild (≤ 17 points), mild to moderate (18-24 points), moderate to severe (25-30), and severe (≥ 30 points) [13]. For this purpose, we used an online medical calculator [14]. The patients gave written consent to participate in observations after the explanation of the purpose and allowed to publish the results of the later with depersonalized data.

Results.

Though the patients were of different age, they had similar complaints of periodic stabbing or squeezing pain in the cardiac region without any connection with physical exertion. However, direct connection of current pain with psych-emotional stress was reported. All over above, palpitation and dyspnea while physical exertion concerned the patients.

While physical examination, no peculiarities were noticed except of overweighted state of two patients. Basic characteristics of patients are aggregated in Table 1.

Table 1. Basic characteristics of patients.

Parameter	Patient 1	Patient 2	Patient 3
Age, years	42	15	39
Sex	female	female	female
Body mass index, kg/m ²	30.1	17.1	29.8
Heart rate, bpm	77	68	75
Blood pressure, mm Hg	140/ 105	110/ 70	140/ 100
Respiratory rate, per minute	13-14	16-18	16-18

No changes were registered on ECG of the patients (Fig. 1).

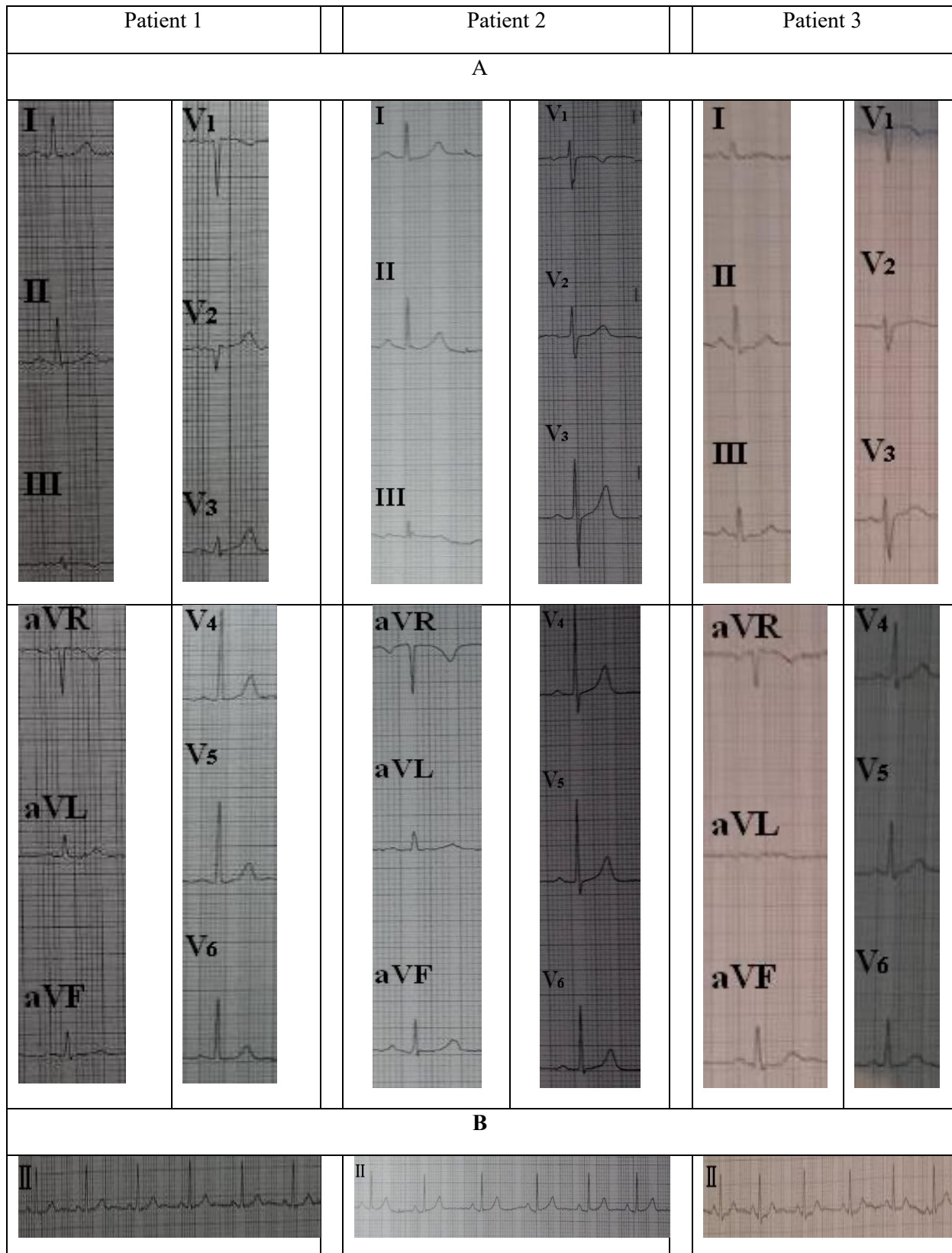


Fig. 1. ECG of the patient at rest: A – 12 leads, B - rhythmogram (10 mm/ mV, 50 mm/ s).

No pathological changes were registered while echocardiography of the patients except hemodynamically insufficient mitral valve prolapses (Table 2).

Table 2. Data of echocardiography of the patients.

Parameter	Patient 1	Patient 2	Patient 3	Reference ranges
Diameter of aorta, mm	28	21	32	20-37
Aortic valve opening, mm	18	18	22	17-25
Left atrial diameter, mm	35	31	35	20-40
Interventricular septum thickness at end diastole, mm	10	6.5	9	6-11
Left ventricular posterior wall thickness at end diastole, mm	7.9	7.1	9.1	6-11
Anterior wall of right ventricular, mm	2.8	2.3	3.5	< 5
Right ventricular dimension at end diastole, mm	26	17.8	28	9-30
Right atrial diameter, mm	35	30	35	20-40
Ejection fraction, %	61	66	72	> 55
End-diastolic volume, mL	81	77	85	51-160
End-systolic volume, mL	31	26	25	14-70
Stroke volume, mL	49	51	62	30-100
E/ A	1.1	2.0	1.2	1.5-1.6
DecTime, ms	154	154	163	160-220
Isovolumic relaxation time, ms	88	71	79	60-100
Peak velocity of diastolic flow, cm/s	82.7	112.6	73.7	62-80
Pulmonary artery systolic pressure	29.0	23.5	28.1	< 30
Mitral valve	Prolaps of anterior cuspid, regurgitation 0/+	Prolaps of anterior cuspid, regurgitation 0/+	Prolaps of anterior cuspid, regurgitation 0/+	-
Aortic valve	N	N	N	-
Tricuspid valve	regurgitation 0/+	regurgitation 0/+	regurgitation 0/+	-
Pulmonary valve	regurgitation 0/+	regurgitation 0/+	regurgitation 0/+	-

Notes: E – peak velocity of early diastolic transmitral flow (m/ s), A – peak velocity of late transmitral flow (m/ s), DecTime - deceleration time of early diastolic transmitral flow.

After routine examination further diagnoses were established, namely:

Patient 1: arterial hypertension, I stage, 1 grade, cardiovascular risk mild, metabolic cardiomyopathy? HF0-1;

Patient 2: neurovegetative dystonia, cardiac type, sinus arrhythmia, HF0;

Patient 3: arterial hypertension, I stage, 1 grade, cardiovascular risk mild. HF0-1.

Results of additional investigational methods are presented in Table 3.

Table 3. Observed parameters of the patients.

Parameter	Patient 1	Patient 2	Patient 3
Respiratory rate, per minute	13-14	16-18	16-18
EtCO ₂ , %	2.7-2.8	2.5-2.8	2.2-2.3
Hamilton anxiety rating scale, points	16	24	30

Discussion.

The anxiety of mild, moderate severity, and severe was revealed in patients 1, 2, and 3, respectively. Tachypnea was noticed in patients 2 and 3. In addition, there is an indirect correlation between RR and etCO₂. However, while comparing patients 2 and 3 with the same RR, the lower etCO₂ was registered in patient 3 with higher points according to the Hamilton anxiety rating scale. Consequently, a connection between anxiety and CO₂ concentration is based not only on hyperventilation.

In an experimental study with continuous registration of NO production in human cerebral endothelial cell cultures under hypo-, normo-, hypercapnic conditions Fathi A. R. et al. revealed the increase in NO levels in endothelial cells during hypercapnia by 36% in 8 hours in contrast to hypocapnic state with the decline in NO level by 30%. It was demonstrated the correlation between NO changes in the endothelial cells and pCO₂ [15]. Furthermore, CO₂ is a well-defined vascular tone regulator [16]. According to the above-mentioned connection of CO₂ with NO and endothelium as well as vascular tone, we hypothesized that patient 3 is characterized by the worst endothelial function with a trend toward vasospasm occurrence. It corresponds with Sara J. D. S. et al. In this research with the usage of invasive coronary reactivity testing and chart review, it was revealed that in women anxiety was significantly associated with coronary endothelial dysfunction [17]. Overall, etCO₂ in all observed patients is decreased drastically indicating the risk of life-threatening disorders manifestation [9].

Conclusions.

The level of anxiety among people living in Ukraine while the Russian-Ukrainian War, especially those who witnessed or suffered from Russian attacks, varies from mild to severe. Hypocapnia associated with anxiety is likely to worsen endothelial dysfunction and predispose to vasospasm. It can be projected that this will lead to an increase in the number of diseases, including cardiovascular group, especially non-obstructed coronary artery disease.

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Declaration of Interest Statement.

None conflict of interest is declared.

Financial Disclosure

None is declared.

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