

Review

Pathophysiologic Peculiarities of Different Factors' Influence on Development and Course of IHD Complicated with Atrial Fibrillation

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Abstract

Over the last years, mortality because of cardiovascular diseases (CVD) increased significantly in Ukraine. If we speak about atrial fibrillation (AF) itself, the number of recurrent arrhythmias cases as the main cause of hospitalization of patients with AF increased at 66% over the last 20 years.

Independent development factors of AF are heart failure, aortic and mitral valve diseases, arterial hypertension, left atrial enlargement, and also obesity and obstructive sleep apnea, etc.

In 2013 A.A. Novykov from Kherson region and several other researchers proved the influence of chaotic changes of meteorofactors in cases of overt or hidden functional cardiovascular disorders (CVD) that can significantly influence its hemodynamic stability, functional ability, particularly its rhythmic activity.

The main problem in the treatment of one or another nosological entity of CVD today is not the adjustment of a medication for its treatment, but the finding of pathogenetic links in the development of the disease itself. Especially this occurs, when the patient gets several organs or systems disabled simultaneously.

Several scientists and practicing physicians are interested in the development of new approaches to diagnosis and treatment of AF in patients with ischemic heart disease (IHD) considering the peculiarities of clinical course and comorbidity. After all, the finding of complications' causes in comorbid pathology in patients with IHD will contribute to treatment optimization and prevention of other complications, especially those resulting from the anticoagulant therapy, for example when a functional liver state or metabolic processes are impaired.

Keywords

IHD; atrial fibrillation; risk factors; comorbid pathology

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The aim

The aim of the work is determination and prove of influence factors on the development and course of IHD complicated with atrial fibrillation (AF).

Background

In Ivano-Frankivsk, based on CCCH (Central City Clinical Hospital) and RCCD (Regional Cardiac Clinical Dispensary), compared to the previous year, for nowadays the number of people appealing with ischaemic stroke manifestations – has 4-fold increased, and the number of people appealing with ischaemic heart disease (IHD) complicated by the

heart rhythm disorder and their hospitalization in spring 2019, has 6-fold increased.

Results and Discussion

Atrial fibrillation occurs in 1-2% of the adult population and is one of the most widespread heart rhythm disorders. Prevalence of AF among the adult population increases with the age – from 0.5% in the age of 40-50 years up to 5-15% in the age of more than 80 years. AF occurs 1.7 times more often in males than among females. Prevalence of AF will be constantly increasing next decades, AF pandemic is foreseen, that is caused by both improved diagnostics of this arrhythmia, and the increased spread risk factors of cardiovascular and non-cardiovascular diseases, and also the tendency to the increased average life expectancy [5].

A paroxysm of AF – is the symptomatic attack that has a clearly outlined onset (palpitations, interruptions in the work of the heart, asphyxia, etc.), so it must by no means be equated with the first episode of atrial fibrillation. As practice shows, patients do not usually apply to clinicians for help after the first attack.

In 2016 there was a classification of AF clinical forms offered in European guidelines (Fig. 1) [11].

Such evaluation can influence the demand for antiarrhythmic therapy with the aim to stop and prevent AF episodes, but in no way influences approaches to the use of antithrombotic remedies.

In the basis of cardiovascular diseases, endothelial dysfunction plays a role as a subcellular factor of atherosclerosis. This dysfunction has a direct influence on the thrombogenicity, inflammatory changes, vasoreactivity, and stability of the atherosclerotic plaque and is directly related to the IHD and its complications progression [13, 17].

Structural-functional state of the myocardium is not always associated with the corresponding clinical manifestations of AF. During last years, family doctors and general physicians noticed a tendency of increasing frequency of patients with hidden, unexpressed clinical picture; especially considering the patients with comorbid pathology. As Siontis KC, Gersh BJ, Killian JM, *et al.* said in

2016, it is harder to adjust treatment schemes for these patients with each next year, especially correct antithrombotic therapy in cases of first-detected AF [6].

The results of Stewart S, Hart CL, Hole DJ, McMurray JJ study represent observations of patients with AF. 476 cases were observed: 193 patients had a classical clinical picture, 122 patients had other manifestations, and 161 patients had an asymptomatic AF [7].

Nowadays CVD morbidity rate in Ukraine reached disastrous peak values, namely 64% of all other diseases. If we are speaking about AF itself, so the amount of cases of arrhythmia relapses is the main cause of patients with AF, that increased at 66% for the last 20 years according to the results of several studies, namely – by Dziak HV, Zharinov OY in 2011, Sychov OS, Kovalenko VM, Dziak HV in 2012 [5, 7].

This state can be explained by complicity in defining complex and individual approaches to the treatment and prevention of IHD complicated with AF and comorbid pathology. [4].

Accelerated development of chronization and severity of clinical manifestations is influenced by patients' living style, as well as financial status, main risk factors, and comorbid background diseases according to Perk J, Bucker G, Gohlke H. [11].

The most significant contribution to premature mortality is made by: arterial hypertension (35.5%), hypercholesterolemia (23%), smoking (17.1%), insufficient fruit and vegetables consumption (12.9%), excessive body weight (12.5%), excessive alcohol consumption (11.9%), and hypodynamia (9%), increased body mass index that was stated by Levadskaya N, Vasylyeva LI, Kalashnykova OS in 2015, and by Vytrykhovskiy AI, Fedorov SV in 2017 [3, 15, 18].

A large-scale international study (INTERHEART) showed that the risk of CVD development was determined mainly by 6 factors in the whole world independently from a location: dyslipidemia (apo B/apo AI), smoking, arterial hypertension, abdominal obesity, psychosocial factors (stress, social isolation, depression), diabetes mellitus [1].

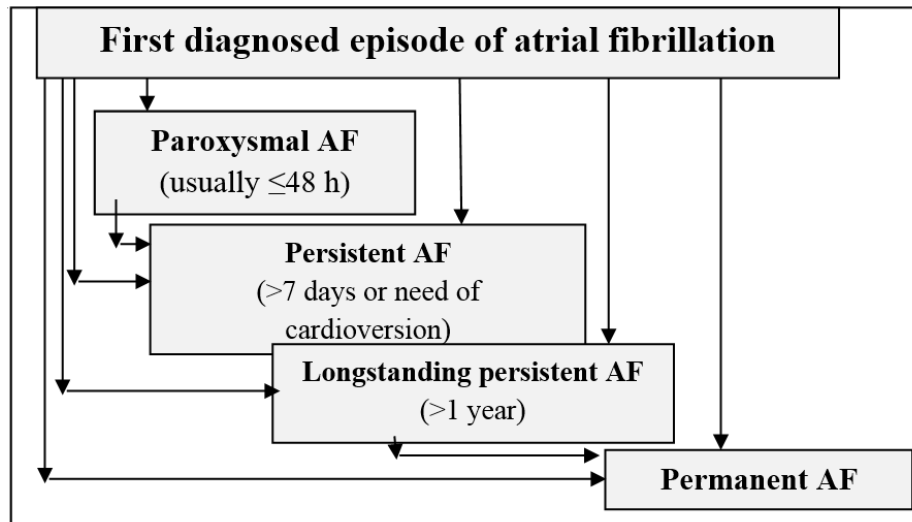


Figure 1. Classification of AF.

Estrogens decrease significantly LDL and VLDL levels, have vasodilation effect (decrease myocardial ischemia), influence positively on myocytes and vascular wall that stimulates in its turn synthesis of nitrate-nitrogen (NO) with endothelial cells [18]. It explains that fact that females are more protected from CVD complications before menopause. According to processed scientific sources – death risk from CVD among women is 56 times higher than death risk from breast cancer (this risk increases, especially in the postmenopausal period).

The main precondition of metabolic syndrome in females of the menopausal period is insulin resistance [2]. From 2006 to 2010 prominent scientists Bessesen D. G., Kushner R., Dedov I. I., Melchenko G. A. studied and confirmed in their works that "Metabolic syndrome in menopause" is characterized by abdominal obesity, AH, impaired glucose tolerance, dyslipidemia, hyperuricemia, a tendency to increased thrombosis.

The presence of triad of symptoms (hypertriglyceridemia, low HDL level, and increased LDL level) in metabolic syndrome in postmenopause raises the possibility of IHD 354-fold in females without diabetes mellitus, as it was found out by Martin S. S., Qasim A. (2008) and Drapkina O. M., Popova I. R. (2013) [3, 18].

There is an association between fatty liver dystrophy, vegetative changes, and metabolic syndrome.

H. Liu *et al.* (2014) showed a correlation between nonalcoholic fatty liver disease and natural mean squared logarithmic deviation NN after correcting for main cardiovascular risk factors. He defined also a direct correlation between metabolic syndrome and sympathetic activity index during the analysis of dynamics of heart rate variability (HRV) [10]. This was confirmed by Ukrainian researchers Hromnatska N. M., Lezhenko H. O., Rudnieva I. V., Pashkova O. Y. as well [19].

Typical clinical manifestations of vegetative disorders in patients with chronic hepatocellular system damage, particularly with fatty liver dystrophy were firstly studied by J. L. Newton in 2010. In works of prominent researchers like Long M. T., Yin X., Larson M. G., Ellinor P. T., Lubitz S. A., McManus D. D., *et al.*, there is the dependence of elevated liver enzymes influence on the increased AF risk in patients with underlying liver diseases [19].

Nowadays, the arrhythmogenic effect of steatohepatitis and NAFLD (non-alcoholic fatty liver disease) has been proved. This happens because nervous system dysfunction occurs through the influence of pro-inflammatory activation attributable to fatty liver disease. In 2014 Ballestri S., Lonardo A., Targher G., Valbusa F., Bonapace S., Bertolini L., Zenari L., Pichiri I., *et al.* demonstrated in their scientific studies correlation of chronic dysmetabolic and inflammatory liver processes, not only with

atrial fibrillation but also with other types of heart rhythm disorders.

In functional liver failure, there occurs systematic discharge of pathogenic mediators, including C-reactive protein, interleukin-6, tumor necrosis factor alpha, plasminogen-1 activator inhibitor and other cytokines that can contribute partially to development and persistence of atrial fibrillation, development of induction of atrial structural and electrical remodeling [9].

Structural-functional disorders of the heart in comorbid pathology started to be studied actively since 2001. The authors tried to study hepatic steatosis index, GGT hyperenzymemia, AST and ALT indices, to bind them with different types of cardiac remodeling that was evidence of so-called "hepatocardiac continuum" [12].

Namely, fatty tissue takes an active part in metabolic processes and produces a large amount of hormonally active substances. Its participation in metabolic processes influences metabolic processes activity in tissues of the whole body both directly and indirectly through the neuroendocrine system, while interacting with hormones of the pituitary gland, catecholamines, insulin. Cytokines have a direct influence on the regulation of character, expression, and duration of inflammation and immune response of the body [16].

At the moment, hypoadiponectinemia is considered to be an important risk factor for atherosclerosis [10]. And because in 2003, M. Kumada *et al.* found out a decrease in plasma concentration of this protein in patients with IHD, so we can reliably note that plasma adiponectin concentration is inversely proportional to body mass index – Campos G. M., Bambha K., Vittinghoff E., Rabl C., Posselt A. M., Ciofica R., *et al.* (2008), and Matsuzawa Y. (2010) proved, that low adiponectin level was an independent risk factor both for IHD, and for the fatty liver disease.

Correlation between IHD and NAFLD was studied not only in Europe; Indian scientists have also analyzed content of serum transaminases, plasminogen activator inhibitor (PAI-I), C-reactive protein, tumor necrosis factor- α in 149 patients diagnosed with IHD in 2007-2009. They made conclusions

that the revealed changes reflect anti-inflammatory status in patients with NAFLD that creates preconditions for IHD development [14].

The works of Thiruvagounder M., Khan S., Sheriff D.S. (2010) show that adiponectin has a direct action on endothelium function at the expense of endotheliocytes injury decrease and stimulation of nitric oxide supplements, as well as indirect action – through membrane-bound receptors and adapter molecules of endothelial cells [8, 19].

When we talk about cholelithiasis, chronic viral hepatitis, and patients with focal processes in the liver, then the most significant risk factors of endothelial dysfunction are hypercholesterolemia, insulin resistance and hyperinsulinemia, as well as impaired balance of nitrogen oxide and active oxygen forms.

In hepatic steatosis, a lower index of endothelium-dependent vasodilation is observed. V. S. Berezenko *et al.* (2014) proved a direct connection between NAFLD severity, impaired endothelial function and cardiovascular risk according to Villanova N., Moscatiello S., Ramilli S., Bugianesi E., Magalotti D., Vanni E., *et al.* (2005) and Berezenko V. S., Mykhayliuk K. Z., Dyba M. B. (2014). The authors noted the inverse dependence between steatosis degree and vasodilation indices.

Conclusions

1. Thus, for nowadays, there is a convincing evidence of direct influence of morphofunctional liver disorders on the structural-functional state of the heart [8].
2. A fact was also established that in comorbid course of IHD and fatty liver disease, characteristic pathologic processes are observed, which cause changes in heart rhythm variability and main structural-functional indices of the heart and vessels [19].
3. The researchers of the leading countries of the world have determined the connection of adipocytokines and resistin with functional state of the liver, however the interconnection between systemic inflammation process activity and endothelial dysfunction indices is a

prospect for further studies yet.

4. Having analyzed literature sources, it is possible to claim that fatty liver dystrophy, steatohepatosis are independent risk factors for CVD because a close connection between them and dyslipidemia and insulin resistance was proved [13, 14]. A search for common mechanisms of IHD complicated with AF development with functional liver failure remains an actual task for the modern medicine.

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