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Nonspecific cardiac morphofunctional syndromes in patients with coronary artery disease

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Summary

Objective

To state the concept and classification of nonspecific cardiac morphofunctional syndromes in patients with coronary artery disease (CAD) using the analysis of major comparative cross-sectional studies' results.

Material and methods

Data of "Register of coronary angiography procedures" – electronic database including results of of 20.402 consecutive patients' clinical profiles.

Results

Heart ventricles dilatation in CAD patients without myocardial infarction, functional mitral regurgitation and asymmetric left ventricular hypertrophy in stable CAD patients revealed by echocardiography characterize particular types of cardiac remodeling.

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Conclusion

These cardiac morphofunctional syndromes are often conditioned by mixed pathology and they are not always directly related to obstructive coronary atherosclerosis. We suggest calling these changes nonspecific cardiac morphofunctional syndromes.

Key words

Coronary artery disease, echocardiography, nonspecific cardiac morphofunctional syndromes.

Introduction

Coronary artery disease (CAD) remains to be the leading cause of death in population of developed countries and West Siberian region [1]. Due to this one of the most important tasks of modern cardiology is to detect and treat this disease in proper time. Nowadays it is impossible to imagine CAD diagnostics without echocardiography (EchoCG). Traditionally this technique is used for detection of frank and hidden coronary insufficiency, myocardial infarction (MI) and its complications: left ventricle (LV) thrombosis and aneurism, mitral valve chords rupture, LV wall rupture, cardiac tamponade, ischemic cardiomyopathy. At the same time, coronary atherosclerosis is related to several less obvious or non-specific syndromes, the meaning of which is not yet fully understood.

CAD prognosis and survivability are mostly determined by the degree of myocardial remodeling. Post-infarction remodeling is actively studied, though less is known about myocardial remodeling in patients with CAD without the history of MI. Compensatory myocardial remodeling, including the reduction of its contractility can be caused not only by post-infarction changes but also by chronic hypoperfusion of its segments [2]. Taking it into account, it becomes very relevant to search the factors promoting cardiac remodeling in patients with CAD without MI, and to identify its connection with localization, coronary vessels involvement and the type of coronary circulation.

Many studies are dedicated to such form of myocardial remodeling like its compensatory hypertrophy [3-5]. Asymmetrical LV hypertrophy is not enough investigated, its occurrence and clinical significance are not determined yet.

LV remodeling (regional or global) is the cause of mitral regurgitation (MR) development in CAD. Since MR is considered to be the factor, aggravating patients' prognosis, it is relevant to detect connections between ischemic MR and coronary stenosis localization.

The objective of this study was to analyze clinical morphofunctional parameters of patients with CAD and post-infarction cardiosclerosis (PICS) or without history of MI, to identify factors related with cardiac ventricles dilatation, asymmetrical LV hypertrophy, ischemic MR, and to create the conception and classification of non-specific cardiac morphofunctional syndromes in CAD.

Materials and methods

In this study we used the data of "Register of coronary angiography procedures" – electronic database including results of full clinical and instrumental examination of all consecutive patients who underwent coronary angiography in Tyumen Cardiology Research Center starting from 1991 [6]. By the end of the study (July 2015) the Register contained data about 20402 patients. Patients' selection was performed according with the task of each study's part that required its own inclusion criteria. All patients gave written informed consent about the use of their examination data for a scientific study. The protocols of this study were approved by local Ethic Committee. We evaluated demographic, height and weight characteristics, quantified body surface area and body mass index, estimated coronary atherosclerosis risk factors – smoking, arterial hypertension. diabetes mellitus, dyslipidemia, family history. thyroid function, MI history, CAD duration, concomitant diseases. angina pectoris functional class (FC) according with the Canadian Cardiovascular Society grading, and grade of circulation insufficiency according with the NYHA (New York Heart Association) classification. All patients underwent EchoCG in standard views using ultrasound scanners Imagepoint NX, Agilente Technologies – Phillips; Vivid 3, 4, 7, 9 Systems, Vingmed-General Electric – Horten and multi-frequency sensors in the range of 2.5-5.0 MHz. Selective coronary angiography was made according with the technique described by Judkins (1967) using «Diagnost ARC A», «Poly Diagnost C», «Integris Allura» – Phillips angiography equipment. Statistical analysis of the results was performed using STATISTICA (StatSoft, versions 6.1-8.0) и SPSS 17.0 software. We used Kolmogorov-Smirnov test to evaluate normality of data. Statistical significance of results was estimated using Student's t-test or Mann-Whitney U-test, depending on data distribution.

"Probabilistic" calculator of "Statistica" software was used for comparison of two relative frequencies inside one group or two unconnected groups. x^2 test and two-sided Fisher's test were used for comparison of discrete variables. Pearson's correlation coefficient (parametric) and Spearman's correlation coefficient (non-parametric) were used for investigation of correlation between variables. P-value <0.05 was considered statistically significant for all tests. Logistic regression with estimation of relative risk and 95% confidence interval (CI) was used for evaluation of variables' role in formation of outcome.

Results and discussion

Analysis of several comparative single-stage studies allowed formulating the concept of cardiac morphofunctional syndromes in CAD. According to this concept, typical CAD syndromes, having well-known diagnostic value, characterizing common forms of myocardial remodeling and directly related to coronary lesions localization and extension, are supposed to be considered specific. Syndromes, characterizing particular, atypical cardiac remodeling forms in CAD, frequently caused by mixed pathology and not always directly related to the factor of coronary stenosis are suggested to be called non-specific.

Identification of factors related to LV dilatation in patients with CAD without MI

2443 patients with CAD without MI have been selected from the Register, 50 patients had LV dilatation (LV end diastolic diameter >60 mm) and 1992 without LV dilatiation. Patients with intermediate values of LV diameter were not included in the study in order to achieve more precise group separation. LV dilatation was detected in 2.5% of patients. Patients with dilated LV had lower LV ejection fraction comparing with the patients with normal LV dimensions: 41.9±10.3% vs 60.7±4.9% (p=0.001), they had higher frequency of LV impaired function: 77.8% vs 2.2% (p<0.001), and higher class (III) of heart failure: 3 4.1 vs 20.5% (p<0.001), whereas high values of angina pectoris FC and multivascular coronary lesions were less frequent: 39.5% vs 55.8% (p=0.033); 24.5% vs 37.7% (p=0.050), respectively. Multivariate analysis demonstrated that the presence of one coronary artery lesions reduced LV dilatation risk in patients with CAD without MI by 57% [7]. Therefore, coronary stenosis was not the leading factor of LV dilatation pathogenesis in these patients, and it allowed us considering this morphofunctional syndrome as non-specific one.

Identification of factors associated with right ventricle (RV) dilatation

1362 patients with Q-wave MI, including 99 patients with RV dilatation and 1263 without it, and 1209 patients with CAD without MI and history of MI, 75 of them with RV dilatation and 1134 without RV dilatation, were selected from the Register. Transversal diastolic diameter ⩽ 26 mm measured in parasternal position was considered normal [8]. In order to achieve more precise division into groups, we included patients with RV diameter ⩾ 30 mm into the group of patients with enlarged RV. Patients with slightly enlarged RV (>26 mm and <30 mm) were excluded from the study. RV dilatation frequency in patients with CAD and PICS and in patients with CAD without MI was 7.3% and 6.2%, respectively. In both groups of patients RV dilatation was not related to localization and extension of coronary lesions, but correlated with parameters characterizing morphofunctional condition of LV [9, 10]. Lack of correlation between RV dilatation and coronary arteries' lesions and its negative correlation with angina pectoris severity indicate possible non-ischemic nature of RV dilatation in patients with CAD without MI, therefore, allowing considering this morphofunctional syndrome as a non-specific one.

Identification of factors related to LV asymmetric hypertrophy

2469 patients with chronic CAD and LV hypertrophy (myocardial mass index > 115g/m^2 for males and >95 g/m^2 for females), 297 of them had asymmetric LV hypertrophy and 2172 had symmetric LV hypertrophy. Ratio between interventricular septum thickness and LV posterior wall thickness ⩾ 1.3 was considered as the criterion of asymmetric hypertrophy. LV asymmetric hypertrophy was detected in 5.8% of patients with chronic CAD. It was related to EchoCG signs of PICS (odds ratio (OR)=2.29; 95% CI 1.64-3.20), LV systolic dysfunction (OR=2.26; 95% CI 1.54-3.30), and cardiac rhythm abnormalities (OR=1.43; 95% CI 1.01-2.00), increased end-diastolic LV and RV dimensions (OR=0.88; 95% CI 0.84-0.91 and OR=1.08; 95 % CI 1.03–1.13,respectively), enlarged aortic root diameter (OR=1.07; 95% CI 1.02-1.11), and increased LV myocardial mass (OR=1.01; 95% CI 1.009-1.014). Therefore, asymmetric LV hypertrophy is related to more evident CAD clinical manifestations that allowed estimating this cardiac syndrome as a non-specific one. Independent correlation with right coronary artery stenosis (OR=1.08; 95% CI 1.02-2.15) demonstrates possible positive

effect of myocardial revascularization in these patients [11].

Identification of factors related to significant functional MR

We selected 1570 patients with CAD and PICS, 403 of them had MR grade ⩾2 and 1167 patients had no MR,between them 765 males (139 with MR grade ⩾2 and 626 without MR) and 137 females (53 with MR grade ⩾2 and 84 without MR). We also selected 1238 patients with CD without MI history: 76 patients with MR grade ⩾2, and 1162 without MR, between them 1067 males (66 with MR grade ⩾2 and 1001 without MR) and 203 females (20 with MR grade ⩾2 and 183 without MR). Since MR severity has direct correlation with CAD patient prognosis, in this study we included patients with hemodynamically significant MR (MR grade ⩾2, regurgitant volume ⩾ 30 ml) [12]. We did not include patients with heart valvular disease, mild MR, since it is often considered to be physiological, and patients with acute CAD, because MR in these patients is often reversible [13].

There are two mechanisms of MR development in CAD: the first one is related to global pathological remodeling of LV (LV dilatation with dilatation of annulus fibrosus of mitral valve); the second one is explained by myocardium regional lesions and displacement of one of papillary muscles. In both cases MR is caused by insufficient closure of mitral valve cusps. Male patients with PICS typically had MR development mechanism based on regional myocardial lesions with right coronary artery involvement (OR 2.14; 95% CI 1.18-3.87), and global myocardium remodeling with LV dilatation and heart failure FC as the causes of MR were more frequent in female patients (OR 1.64; 95% CI 1.24-2.17 and OR 4.426; CI 1.40-12.88, respectively) [14].

In patients with CAD without MI and PICS MR was related to cardiac rhythm and conduction abnormalities, higher left atrial size index and lower LV ejection fraction [15, 16]. Lack of correlation with coronary angiography parameters demonstrated low significance of coronary stenosis in MR development in this group of patients. MR features in patients with CAD mentioned above allow considering this morphofunctional syndrome as a non-specific one.

Conclusion

One of the main conclusions following cardiac remodeling study in patients with CAD without MI is the possibility of non-ischemic factor influence on the development of ventricular dilatation and ischemic MR. It is necessary to take into account the possibility of such influence and detect etiological factor associated with ischemia in proper time, correcting, if necessary, treatment strategy.

Mentioned above results allowed to develop the classification of specific and non-specific cardiac morphofunctional syndromes associated with CAD (Table 1).

Table 1. **Cardiac morphofunctional syndromes in patients with CAD**

Specific	Non-specific
I. Ischemic cascade markers: 1) LV diastolic dysfunction 2) LV systolic dysfunction - regional (asynergy types: hypokinesis, akinesis, dyskinesis) - global II. MI and its complications: - papillary muscle or tendinous chords rupture - pericarditis - LV aneurism - LV thrombosis - free myocardial wall rupture with pseudoaneurism formation or cardiac tamponade - interventricular septum rupture	I. LV dilatation in the absence of MI II. RV dilatation in patients with and without MI III. LV asymmetric hypertrophy IV. Ischemic MR

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