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Intercurrent illnesses in patients with multivalvular heart disease

Choroby współwystępujące u osób z kombinowaną wadą zastawkową serca

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Abstract

Introduction. Multivalvular heart disease has either a congenital or an acquired aetiology (*e.g.* rheumatic fever, atherosclerosis, calcification of the valves, remodelling and dilatation of ventricles). The basis of valvular degeneration is failure of endothelial tissue. The consequence of a long-standing heart defect is progressive heart failure (HF). The aim of this study was to underline the fact that HF and atrial fibrillation are frequently related to combined valvular disease.

Material and methods. The study involved documentation of 109 patients with a compound heart defect treated from 2006 to 2016. Other factors which were considered in the statistical calculation were: HF classified according to the New York Heart Association scale, presence of cardiac infarction, diabetes, macrophage activation syndrome, obesity, circulatory arrest, dyspnoea, chest pain, fatigability, unconsciousness, dizziness and performed cardioversion.

Results. HF was diagnosed in 65 cases (59.5%). 55 patients with diagnosed HF who were simultaneously suffering from mixed valvular heart disease had no other diseases of the cardiovascular system. There was no correlation between HF and heart infarct or coronary arterial disease. We found no dependency between the grade of HF (defined as NYHA classes II, III and IV) and diabetes mellitus etc.

Conclusions. The risk for the development of these diseases in the research group was much higher than in the general population. It is essential to pay special attention to the concomitance of HF, atrial fibrillation and valvular diseases.

Key words: mixed valvular disease, heart failure, atrial fibrillation

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Introduction

Mixed valvular heart disease refers to coexisting valvular stenosis and regurgitation. Combined valvular disease is the name given to describe any disease process involving two or more of the four heart valves. In practice, combined heart disease is called multivalvular disease (MVD). One of the most frequent of the acquired aetiologies of MVD is rheumatic fever.

Moreover, there is steadily rising occurrence of degenerative disease associated with atherosclerosis (a rise associated with rising life expectancy), and this is yet another reason for valvular damage occurrence. Aortic valve degeneration and mitral annular calcification are common changes associated with the ageing process. Remodelling and dilatation of the right and left ventricles (triggered by myocardial infarction or myocarditis) are significant factors of secondary or functional valvular regurgitation [1].

Broadly speaking, we can divide the factors influencing the degeneration of heart valves into: 1) genetic factors

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Table 1. New York Heart Association (NYHA) functional classifications

NYHA class	Characteristic
I	Average physical activity does not cause undue symptoms (breathlessness, palpitations or fatigue)
II	Ordinary physical activity results in undue symptoms (breathlessness, palpitations or fatigue)
III	Marked limitation of physical activity. Symptoms do not occur at rest, but less than ordinary physical activity results in undue breathlessness, palpitations or fatigue
IV	Patient is unable to carry on physical activity without discomfort. Symptoms can occur at rest. Physical activity results in increased discomfort

(homozygous familial hypercholesterolemia); 2) clinical factors (arterial hypertension, diabetes mellitus, smoking, obesity); 3) biochemical factors (higher levels of lipoprotein A, total cholesterol, low-density lipoprotein (LDL)-cholesterol, lower levels of high-density lipoprotein (HDL)-cholesterol, higher concentrations of calcium, creatinine and C-reactive protein in blood tests); and 4) demographic factors (age, sex).

The basis of valvular degeneration is failure of endothelial tissue. As a result of endothelium discontinuation, lipids, lipoproteins and proteins are deposited. Infiltrates consisting of inflammatory cells are formed (macrophages, T-lymphocytes, foam cells), fibrosis and calcification. Furthermore, new cardiovascular risk factors are not without significance. These include a high level of C-reactive protein, fibrinogen, interleukin 6, lipoprotein A, homocysteine, matrix metalloproteinase, and lipoprotein-associated phospholipase A2 (Lp-PLA2). Intima-media thickness and resting heart rate > 70–80/min may also affect endothelial tissue. These factors contribute to both atherosclerosis and degenerative lesions. The sole method of treating aortic stenosis is surgery [2, 3].

The consequence of a long-standing heart defect is progressive heart failure (HF). At present, the most frequent HF aetiologies in Poland (and Europe in general) are coronary arterial disease and hypertension [4]. HF is a condition in which the heart cannot keep up with tissue's demands for oxygen. That demand can be fulfilled only by increased filling pressure [5]. We can divide HF into right-sided or right ventricular (RV) heart failure and left-sided or left ventricular (LV) HF. The following are the symptoms of RV heart failure: swelling of feet, ankles or sacral region in recumbent patients, nocturia, pleural effusion, ascites, hepatomegaly (and also liver atrophy when the HF is of long standing), high jugular venous pressure, and Kussmaul's sign. The signs of LV HF are: dyspnoea, cough and symptoms during auscultation of lungs (crackles or rattling) [6].

When symptoms develop suddenly, a chest X-ray must be taken followed by echocardiography. When symptoms develop slowly, meaning that ambulatory care is possible, we can make an electrocardiography (ECG) or check the natriuretic peptide level, and with reference to these results decide whether echocardiography is required. Patients at high risk of HF must receive immediate echocardiography [7].

HF is classified according to the severity of the symptoms. The most commonly used classification system is that of the New York Heart Association (NYHA). The classifications are set out in Table 1 [8]. In advanced HF (NYHA class IV), roughly half of patients die within 12 months [9]. The most frequent reason for heart failure with reduced ejection fraction (HFrEF) is ischaemic heart disease. Other causes include uncontrolled hypertension, valvular heart disease and cardiomyopathies. Heart failure with correct ejection fraction is usually caused by hypertension with left ventricle hypertrophy or ischaemic heart disease, diabetes, hypertrophic or restrictive cardiomyopathy, constrictive pericarditis. HF risk factors include female sex, advanced age, and being overweight [9].

The aim of this study was to underline the importance of paying special attention to the fact that HF and atrial fibrillation (AF) are frequently related to MVD.

Materials and methods

Our study is based on the documentation of 109 cases recorded in the Clinic of Cardiology. The research involved 68 female and 39 male patients with a compound heart defect treated in the Clinic of Cardiology in Lublin from 2006 to 2016. Inclusion criteria were age 18 years or over, and a compound heart defect (*i.e.* defect of two or more valves). Exclusion criteria were: age under 18; defect of one valve; absence of any heart defect; or a case not recorded in the Clinic of Cardiology in Lublin.

Other factors which were considered in the statistical calculation were HF classified in the NYHA scale, presence of cardiac infarction, diabetes, macrophage activation syndrome (MAS), obesity, circulatory arrest, dyspnoea, chest pain, fatigability, unconsciousness, dizziness and performed cardioversion.

Statistical analysis

The occurrence of these diseases in the examined group was characterised in terms of numbers and percentages. In order to prove the relevance of two nominal variables

the χ^2 test was used. Statistical evaluation of results was carried out using STATISTICA v.20 (StatSoft, Poland).

Results

All patients with multivalvular heart disease were treated at the Department of Cardiology from 2006 to 2016. Women accounted for 62.4% of the whole group (N = 68), with men the remaining 35.8% (N = 39). The average age of the group was 68.8 years (the oldest patient was 96, the youngest 41, standard deviation was 13.7092).

In the group of patients with combined valvular disease, the following accompanying diseases were reported: 14 suffered from myocardial infarction (MI); there were nine ST-elevation myocardial infarction (STEMI) cases (8.3% of all patients) and five non-ST-elevation myocardial infarction (NSTEMI) cases (4.6% of all cases). More than one MI occurred in one patient. 37 patients suffered from coronary artery disease (CAD) (33.9% of all cases). One patient had type 1 diabetes and 20 patients had type 2 diabetes. In one case, steroid-induced diabetes was noted and one patient had impaired fasting glucose (IFG). 66 patients were diagnosed with HF classified as class II, III or IV on the NYHA scale. The most common valvular defect was mitral regurgitation (MR): 10 cases of grade 1+, 53 cases of grade 2+, 30 cases of grade 3+, and five cases of grade 4+. 85 patients had tricuspid regurgitation (TR): 21 cases of grade 1+, 36 cases of grade 2+, 28 cases of grade 3+, and one case of grade 4+. 84 patients were diagnosed with aortic regurgitation (AR): 24 cases of grade 1+, 41 cases of grade 2+, 14 cases of grade 3+, and five cases of grade 4+. 49 patients had aortic valve stenosis. Mitral valve stenosis was diagnosed in 21 cases. 14 patients had pulmonary valve regurgitation (PR): 11 cases of grade 1+, two cases of grade 2+, and one case of grade 3+.

In the group of 109 patients with multivalvular heart disease, HF was diagnosed in 65 cases (59.5%). One in four patients suffered from Grade II HF according to the NYHA scale (N = 28, 25.7%), one in five from grade III HF (N = 21, 19.3%), and one in six from Grade IV HF (N = 16, 14.7%). Myocardial infarction occurred in 15 cases (13.8%), while coronary artery disease occurred in 37 cases (33.9%). Arterial hypertension (AH) was diagnosed in 62 patients (56.9%), AF also in 62 cases (56.9%), and pulmonary hypertension in 16 cases (14.7%). Every sixth patient had an implanted pacemaker (N = 17, 15.6%), and one patient had an implantable cardioverter-defibrillator (ICD): see Table 1.

Precise characteristics of the study group are set out in Table 2.

There were no statistically significant differences in the frequency of occurrence of intercurrent illnesses such as myocardial infarction, coronary artery disease, diabetes mellitus, pulmonary hypertension, arterial hypertension, aortic aneurysm and AF in the group of patients suffering only from multivalvular heart disease, or in the group of patients with both multivalvular heart disease and HF: see Table 3.

It is clear that 55 patients with diagnosed HF who were simultaneously suffering from mixed valvular heart disease had no other diseases of the cardiovascular system. These clinical results are statistically significant ($p < 0.05$, Cramér's $V = 0.653$).

Discussion

Chronic heart failure occurs in 1–2% of the adult population in developed countries. In addition, more than 10% of people over the age of 70 suffer from chronic heart failure [10]. In Poland it is reported that 600,000–700,000 patients have HF. Moreover, every fifth person will develop HF during their lifespan [11].

The results of our paper show that patients with combined valvular disease have HF more frequently than other patients (60.55% of the examined patients had HF). In Europe, the most frequent cause of HF in patients under 75 is myocardial infarction. In patients over 75 it is hypertension. Other risk factors are myocardial hypertrophy, myocardial cell loss and fibrosis, cardiomyopathies, myocarditis, valvular diseases and arrhythmias [5]. HF usually caries an adverse prognosis, and the five-year survival rate is worse than in the case of many neoplasms [11]. The diagnosis algorithm for HF is shown in Figure 1 [12]. The treatment is based on angiotensin-converting-enzyme inhibitors or (in the case of side effects like a cough) on angiotensin receptor blockers. Furthermore, β-blockers and diuretics such as spironolactone can be applied. The next group of medications are cardiac glycosides and vasodilators. In late stage HF, catecholamines are used (dobutamine and a new inotrope called levosimendan). In the case of coexisting respiratory insufficiency, assisted respiration should be applied (patients with saturation < 90% must receive oxygen therapy, and continuous positive airway pressure (CPAP), bilevel positive airway pressure (BiPAP) ventilation or mechanical ventilation are permissible). Patients with saturation > 90% do not require oxygen therapy [7, 12, 13].

The other most frequent medical condition in the examined group was AF which accounted for 56.88% of the group. As a comparison, in the USA, AF has been diagnosed in 0.7% of the whole population [14, 15], and just over 2% of the adult population [16]. We would like to emphasise that in this research AF was usually the only disease (except for valvular disease) which can lead to HF. Patients with other diseases are classified in Table 2. Atrial fibrillation frequently occurs with valvular heart disease. Statistically, in a case of severe mitral valve stenosis, the frequency of coexisting AF stands at 10% in patients under the age of 30, and is higher in the case of older patients. AF is diagnosed frequently in conjunction with an advanced

Table 2. Characteristics of study group

		Frequency	Percentage [%]
Heart failure	No	44	40.4
	Yes	65	59.6
NYHA class	not applicable	44	40.4
	II	28	25.7
	III	21	19.3
	IV	16	14.7
Myocardial infarction (MI)	No	94	86.2
	Yes	15	13.8
Type of myocardial infarction	not applicable	94	86.2
	STEMI	9	8.3
	NSTEMI	5	4.6
	> 1 MI	1	0.9
Coronary artery disease	No	72	66.1
	Yes	37	33.9
Diabetes mellitus (DM)	No	86	78.9
	Type 1	1	0.9
	Type 2	20	18.3
	Steroid-induced diabetes	1	0.9
	Impaired fasting glucose (IFG)	1	0.9
Pulmonary hypertension		16	14.7
Arterial hypertension		62	56.9
Aortic aneurysm		8	7.3
MAS		4	3.7
Lipid disorders		6	5.5
Cardiac arrest		5	4.6
Rheumatic heart disease		1	0.9
Atrial fibrillation		62	56.9
Pacemaker		17	15.6
Cardioverter-defibrillator		1	0.9

HYHA — New York Heart Association; STEMI — ST-elevation myocardial infarction; NSTEMI — non-ST-elevation myocardial infarction, MI — myocardial infarction; MAS — macrophage activation syndrome

stage of aortic valve diseases or with significant haemodynamic tricuspid valve insufficiency [16].

HF can cause AF, and AF can lead to HF. According to the EURObservational Research Programme: The Heart Failure (ESC-HF) Pilot Survey Pilot Survey of patients with diagnosed HF, 40% of them had AF as well. On the other hand, symptoms of HF (NYHA classes II–IV) occur in about 30% of patients with AF [16].

The treatment of AF is multistage. In short-term treatment (less than 48 h), electrolyte disorders should be corrected. The treatment of the second phase is cardioversion (pharmacological cardioversion with propafenone or electrical cardioversion with amiodarone). To prevent AF recurrence, some therapeutic drugs can be used. Dronedarone, flecainide, propafenone, or sotalol can be administered to patients with correct left ventricular function and without myocardial hypertrophy. In the case of patients with stable coronary artery disease and with no HF, dronedarone can be used. Patients with diagnosed HF can receive amiodarone. Moreover, anticoagulants should be considered (especially when the AF continues for more than 48 hours): vitamin K antagonists (VKA), or new oral anticoagulants (NOACs). If the prognosis of sinus rhythm maintenance

Table 3. Intercurrent illnesses in group of patients with only multivalvular heart disease and in group of patients with multivalvular heart disease and simultaneous heart failure

		Only multivalvular heart disease (N = 44)	Multivalvular heart disease + heart failure NYHA class II–IV (N = 65)	Statistical analysis	Level of statistical significance
Myocardial infarction	No	36 81.82%	58 89.23%	$\chi^2 = 1.192$	p = 0.55
	Yes	8 18.18%	7 10.77%		
Coronary artery disease	No	26 59.09%	46 70.77%	$\chi^2 = 0.596$	p = 0.45
	Yes	18 40.91%	19 29.23%		
Diabetes mellitus	No	35 79.55%	51 78.46%	$\chi^2 = 0.019$	p = 0.99
	Yes	9 20.45%	14 21.54%		
Pulmonary hypertension	No	37 84.09%	56 86.15%	$\chi^2 = 0.090$	p = 0.96
	Yes	7 15.91%	9 13.85%		
Arterial hypertension	No	17 38.64%	30 46.15%	$\chi^2 = 0.605$	p = 0.74
	Yes	27 61.36%	35 53.85%		
Aortic aneurysm	No	40 90.91%	61 93.85%	$\chi^2 = 0.327$	p = 0.85
	Yes	4 9.09%	4 6.15%		
Atrial fibrillation	No	19 43.2%	28 43.1%	$\chi^2 = 0.01$	p = 0.99
	Yes	25 56.8%	37 56.9%		

is poor, percutaneous and surgical ablation should be considered. In the event of chronic AF, or when the potential risk of therapy is higher than its benefits, correct ventricular rhythm should be maintained (heart rate c. 80–100/min). Beta-blockers, verapamil, diltiazem or digoxin can be used in the treatment [7, 17].

Conclusions

We wish to stress that HF and AF are frequently related to combined valvular disease. The risk for the development of these diseases in our research group was significantly higher than in the general population.

The study carried out in this paper does not prove any correlation between other diseases of the cardiovascular system and mixed valvular heart disease. Consequently, it is essential to pay special attention to concomitant HF, AF and valvular diseases.

Conflicts of interest

The authors declare no conflict of interest.

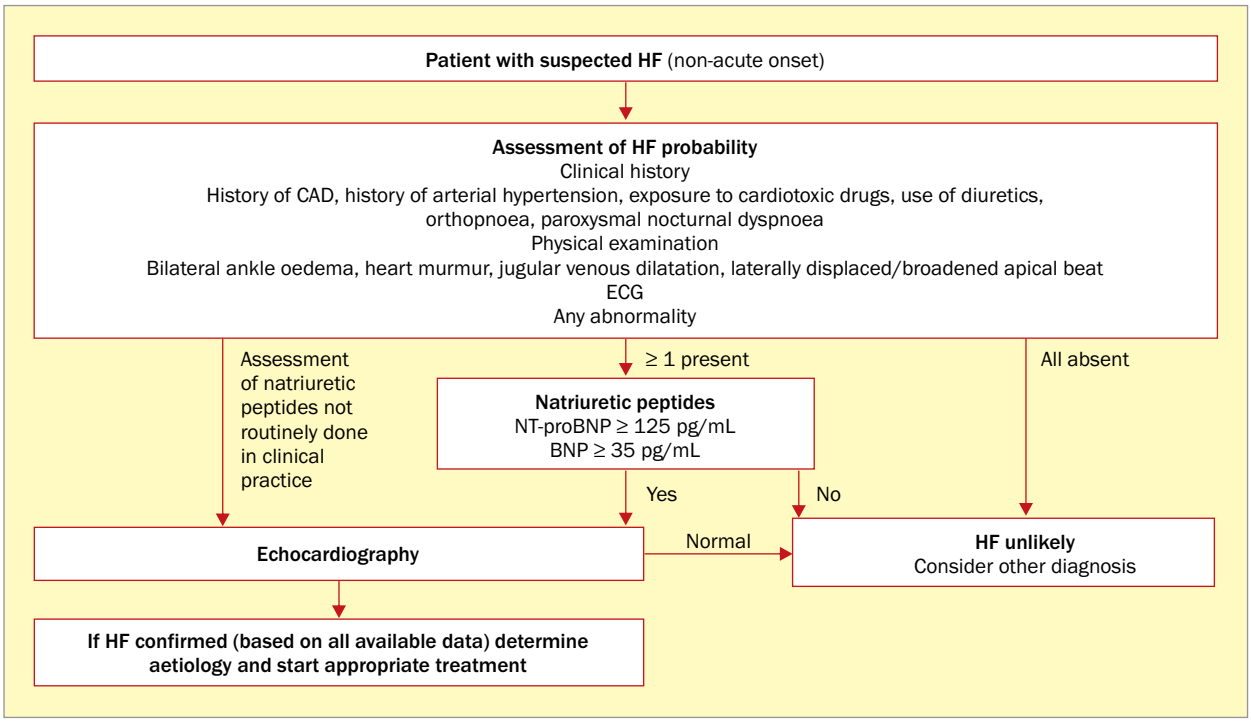

Figure 1. Diagnostic algorithm for diagnosis of HF of non-acute onset (according to [4]); HF — heart failure; CAD — coronary artery disease; ECG — electrocardiography; NT-proBNP — N-terminal pro-B-type natriuretic peptide; BNP — B-type natriuretic peptide; Normal — normal ventricular and atrial volume and function

Streszczenie

Wstęp. Wielozastawkowa wada serca może mieć etiologię wrodzoną lub nabytą (np. gorączka reumatyczna, miażdżyca tętnic, zwapnienia zastawek, przebudowa i poszerzenie komór serca). Podstawą degeneracji zastawek jest wada endotelium. Długotrwająca wada zastawek prowadzi do postępującej niewydolności serca (HF). Celem pracy było zwrócenie uwagi na fakt, że HF i migotanie przedsionków są związane z wielozastawkową wadą serca.

Materiały i metody. Niniejsza praca stanowi analizę dokumentacji 109 pacjentów leczonych z powodu złożonej wady zastawkowej w latach 2006–2016. W obliczeniach statystycznych wzięto pod uwagę również inne czynniki, takie jak: HF sklasyfikowaną według skali *New York Heart Association* (NYHA), przebyty zawał serca, cukrzycę, współwystępowanie zespołu aktywacji makrofagów (MAS), otyłość, przebyte zatrzymanie krążenia, duszność, ból w klatce piersiowej, męczliwość, zawroty głowy, przeprowadzony zabieg kardiowersji.

Wyniki. Niewydolność serca nie korelowała z wadami zastawek ($p > 0,05$) ani z zawrotami głowy ($p = 0,9$). Co więcej, nie dowiedzionno korelacji między HF a zawałem serca lub chorobą wieńcową. Autorzy nie wykazali korelacji między II a IV stopniem HF według klasyfikacji NYHA a cukrzycą.

Wnioski. Ryzyko wystąpienia tych schorzeń w badanej grupie było dużo wyższe niż w populacji ogólnej. Ważnym jest więc zwracanie szczególnej uwagi na możliwe współwystępowanie HF, migotania przedsionków i złożonej wady zastawkowej serca.

Słowa kluczowe: złożona wada zastawkowa, niewydolność serca, migotanie przedsionków

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