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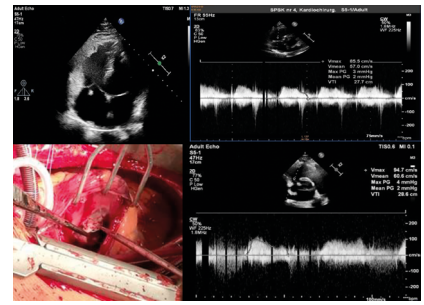

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Concordance between coronary computed tomography angiography and coronary angiography in assessing the significance of coronary artery stenosis in patients with multivessel coronary artery disease

Zgodność pomiędzy tomografią komputerową tętnic wieńcowych a koronarografią w ocenie istotności zwężeń tętnic wieńcowych u pacjentów z wielonaczyniową chorobą wieńcową

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Abstract

Introduction. Coronary artery disease (CAD) is one of the most common cardiovascular problems in Poland and worldwide. In the case of multivessel coronary artery disease (MVD), the matter of further management and treatment is even more complicated. The non-invasive diagnostic methods are commonly used in the initial diagnostics of CAD. The following study aimed to perform a comparative analysis of the results of coronary computed tomography angiography (CCTA) and coronary angiography in relation to the demographic and clinical variables in patients with MVD.

Material and methods. The study was performed on 106 patients with MVD hospitalised in the Cardiology Department of the Central Clinical Hospital in Lodz. The available results of CCTA and coronary angiography were analysed and compared with regard to the significance of coronary artery stenosis in both examinations. Demographic and clinical characteristics of the analysed group of patients were also performed.

Results. The vast majority of the participants were male (n = 69.8%). The average age of the patients was 69.42 ± 8.28 years. Coronary artery disease risk factors were highly prevalent in the study population. The overall concordance in the assessment of the significance of coronary artery stenosis by coronary computed tomography angiography compared with coronary angiography was 73% (κ = 0.47). The highest concordance in the assessment was noted for the left main coronary artery 78% (κ = 0.5) and the lowest for the circumflex branch 69% (κ = 0.34).

Conclusions. In patients with MVD, there is a moderate concordance between the description of the significance of coronary artery stenosis in CCTA compared to coronary angiography. Coronary computed tomography angiography as a non-invasive imaging is one of the methods in the initial diagnostics of a suspected CAD. The risk factors of CAD are widespread and represent a significant problem in the analysed patient population.

Key words: multivessel coronary artery disease, coronary computed tomography angiography, coronary artery angiography

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Introduction

Cardiovascular diseases (CVD) are the most common cause of death, contributing to almost one-third of all deaths around the world [1]. In 2030, according to projections, CVD would cause more than 23 million deaths worldwide [2]. Among these diseases, ischaemic heart disease (IHD) remains the most common cause of death. IHD is estimated to affect 1,655 out of every 100 000 people, amounting to more than 120 million people worldwide [3]. In the vast majority of cases, coronary artery disease (CAD) is caused by a narrowing of the coronary arteries by atherosclerotic plaques.

In the case of significant atherosclerotic involvement of more than one coronary artery or left main coronary artery, one can speak of multivessel coronary artery disease (MVD). Patients with MVD have an increased risk of acute coronary syndromes and sudden cardiac death [4].

To date, many recognised risk factors of CAD have been identified, including an increased low-density lipoprotein (LDL) cholesterol fraction, decreased high-density lipoprotein cholesterol fraction, increased triglycerides, smoking and comorbidities such as hypertension, impaired glucose tolerance or diabetes and atherosclerosis of other arteries. In addition, male gender, older age, genetic predisposition and excessive body weight together with insufficient physical activity contribute to an increased risk of the disease [5].

A number of diagnostic methods are available to help determine the degree of myocardial ischaemia, and thus the approximate degree of stenosis in individual coronary arteries. Non-invasive imaging is an increasingly important option in the diagnostics of IHD, compared to the invasive method — coronary angiography, which was widely used not so long ago [6].

Material and methods

Study design and population

We have conducted a retrospective study of patients with diagnosed MVD and stable angina. One hundred and six participants were enrolled during the period 2020–2022, after hospitalisation in the Cardiology Department of the Central Clinical Hospital in Lodz. Eligible patients were aged 18 years or older, with a diagnosis of CAD according to the European Society of Cardiology Guidelines [7].

The findings of coronary computed tomography angiography (CCTA) and invasive coronary angiography (ICA) in patients with MVD were analysed and the results of the significance of coronary artery stenosis in both imaging methods were compared.

Coronary computed tomography angiography was performed on an outpatient basis in various computed tomography laboratories in the city of Lodz with the use of different CT scanners with a resolution of at least 64 slices. An iodine contrast agent was used in the examination. Significant stenosis of the coronary arteries was defined by the CCTA described as significant, critical, severe or > 70% of the coronary artery lumen.

Invasive coronary angiography was performed in the Cardiology Department of the Central Clinical Hospital in Lodz. Significant stenosis of the coronary arteries in ICA was defined as more than 50% in the left main coronary artery and more than 70% in the rest of the epicardial arteries. ICA was performed no more than 12 months after the CCTA in the same patient.

Exclusion criteria were defined as permanent atrial fibrillation, acute coronary syndrome or stroke within the last 3 months. The study complied with the Declaration of Helsinki and was approved by the local medical ethics committee. Written informed consent was provided by all patients before they participated in the study.

Subjects' demographic and clinical data

Patient characteristics were collected, such as age, gender, and body mass index (BMI), calculated as weight in kilograms divided by height in meters squared. Clinical information was also acquired from the medical record, such as left ventricular ejection fraction, New York Heart Association functional class, Canadian Cardiovascular Society class, the history of cigarette smoking, alcohol abuse, comorbidities: heart failure, arterial hypertension, hyperlipidaemia, diabetes mellitus type 2, chronic kidney disease, chronic obstructive pulmonary disease and blood tests such as the concentrations of haemoglobin, N-terminal pro-B-type natriuretic peptide, uric acid, LDL, high-density lipoprotein, total cholesterol, triglycerides and estimated glomerular filtration rate.

Data analysis

All the data from the study were analysed using Python SciPy (v1.10) stats library. Graphical data were presented using the matplotlib (v3.6) package. Categorical data were expressed as numbers and as a percentage of the whole study population. Left ventricular ejection fraction was expressed as a percentage of the heart failure patient group. The normal distribution of the continuous variables was assessed using the Shapiro–Wilk test and a histogram.

After the normality analysis, the continuous variables that followed the normal distribution (age and BMI) were presented by means of the standard deviation. Due to the skewed non-normal distribution of other continuous variables, they are described using the median value with lower and upper quartiles. Cohen's κ was used to determine the concordance between CCTA and ICA results in the assessment of the significance of coronary artery stenosis. The concordance between CCTA and ICA was defined as both examinations showing significant stenosis or an absence of significant stenosis in a coronary artery. In accordance with other authors' suggestions, the κ values in the range

of 0.21–0.4 were identified as a fair agreement and the values 0.41–0.6 as a moderate agreement between the diagnostic methods mentioned above [8].

Results

The study population was predominantly male (n = 69.8%). The average age of the study population was 69.42 ± 8.28 years, with a mean BMI of 27.91 ± 4.44 kg/m^2. Chronic heart failure (CHF), chronic kidney disease and diabetes mellitus type 2 were diagnosed in 52.8%, 18.9% and 35.8% of the study population, respectively.

Over 92.5% of the study participants had a history of hypertension, 100% — hyperlipidaemia, and 5.7% — chronic obstructive pulmonary disease. Patients' angina symptoms were most commonly (over 44%) classified as Canadian Cardiovascular Society class II. The detailed characteristics of the study population are presented in Table 1.

The median LDL cholesterol blood concentration was 2.26 mmol/L (1.8–3.02), N-terminal pro-B-type natriuretic peptide: 250.0 pg/mL (100.0–753.8), uric acid: 360.5 µmol/L (298.48–438.78) and estimated glomerular filtration rate was 77.8 mL/min/1.73m^2 (62.32–89.78). The remaining biochemical parameters are presented in Table 2.

The comparison of CCTA and coronary angiography results took place in 86 patients because the significance of coronary artery stenosis was not assessed in 20 patients due to an excessively high calcium score preventing the use of an iodine contrast agent.

The concordance in the assessment of the significance of coronary artery stenosis by coronary computed tomography angiography compared with coronary angiography was 73% (κ = 0.47, moderate agreement). The highest concordance in the assessment was noted for the left main coronary artery (78%, κ = 0.5, moderate agreement) and the lowest for the circumflex branch (69%, κ = 0.34, fair agreement). The detailed analysis is presented in Figure 1 and Table 3.

Table 1. Characteristics of the study group — clinical and demographic data

Age (mean, SD)	69.42, 8.28
Gender	
Men (n, %)	74 (69.8)
Women (n, %)	32 (30.2)
BMI [kg/m^2] (mean, SD)	27.91, 4.44
CCS scale	
I (n, %)	16 (15.1)
II (n, %)	47 (44.3)
III (n, %)	40 (37.8)
IV (n, %)	3 (2.8)
NYHA scale	
I (n, %)	13 (12.3)
II (n, %)	75 (70.7)
III (n, %)	17 (16.1)
IV (n, %)	1 (0.9)
HF (n, %)	56 (52.8)
HFpEF (n, % of HF)	43 (76.7)
HFmrEF (n, % of HF)	8 (14.3)
HFrEF (n, % of HF)	5 (9.0)
Smoking	
Never (n, %)	48 (45.3)
In the past (n, %)	38 (35.8)
Current (n, %)	20 (18.9)
Hypertension (n, %)	98 (92.5)
Diabetes mellitus	
Present diabetes mellitus (n, %)	38 (35.8)
Impaired fasting glucose (n, %)	3 (2.8)
Impaired glucose tolerance (n, %)	2 (2.0)
Alcohol abuse (n, %)	1 (0.9)
Dyslipidaemia (n, %)	106 (100)
CKD (n, %)	20 (18.9)
COPD (n, %)	6 (5.7)

% — a percentage of 106 patients; BMI — body mass index; CCS — Canadian Cardiovascular Society angina grade; CKD — chronic kidney disease defined as glomerular filtration rate < 60 mL/min/1.73 m^2; COPD — chronic obstructive pulmonary disease; HF – heart failure; HFmrEF — heart failure with mildly reduced ejection fraction; HFpEF — heart failure with preserved ejection fraction; HFrEF — heart failure with reduced ejection fraction; n — number of patients; NYHA — New York Heart Association Functional Classification; SD — standard deviation

Discussion

Although coronary computed tomography angiography is a very good method for coronary artery imaging, the main advantage of this test remains its high negative predictive value [9]. The exclusion of any coronary artery stenosis by CCTA has been shown to be associated with very low mortality in this group of patients (0.28%) [10]. CCTA has a high sensitivity and specificity (97.2% and 87.4%, respectively) confirmed by numerous studies. Its value increases in patients without a history of CAD (97.6% and 89.2%, respectively) and if the patient's heart rate is as close as possible to 60/minute or lower [11, 12]. The quality of this method in the assessment of coronary arteries is diminished by past interventions, such as coronary artery bypass grafting or percutaneous coronary intervention with stent implantation. Arrhythmias or fast heart rate and obesity in patients also reduce the specificity of CCTA. However, the technique of the 64-slice resolution or higher minimises these limitations [13, 14].

Table 2. Characteristics of a study group — biochemical parameters

Parameter	Median (1^{st} quartile–3^{rd} quartile)
Morphology	
RBC [mln/μL]	4.51 (4.2–4.86)
WBC [1000/μL]	7.32 (6.09–8.52)
Hgb [g/dL]	14.0 (12.8–14.78)
PLT [1000/μL]	213.0 (182.25–252.0)
Lipidogram	
Total cholesterol [mmol/L]	4.15 (3.71–4.95)
HDL [mmol/L]	1.21 (1.05–1.52)
LDL [mmol/L]	2.26 (1.8–3.02)
TG [mmol/L]	1.22 (0.93–1.85)
Others	
Sodium [mmol/L]	139.7 (138.02–140.78)
Potassium [mmol/L]	4.32 (4.12–4.56)
eGFR [mL/min/1.73m^2]	77.8 (62.32–89.78)
Creatine [μmol/L]	81.75 (72.12–97.58)
TSH [μIU/mL]	1.22 (0.73–2.1)
TnT [ng/L]	12.5 (9.0–17.0)
CK-MB mass [ng/mL]	2.8 (2.2–3.78)
NT-proBNP [pg/mL]	250.0 (100.0–753.8)
Uric acid [μmol/L]	360.5 (298.48–438.78)

CK-MB — creatine kinase-myoglobin binding; eGFR — estimated glomerular filtration rate; HDL — high-density lipoprotein; Hgb — haemoglobin; LDL — low-density lipoprotein; NT-proBNP — N-terminal pro-B-type natriuretic peptide; PLT — platelet count; RBC — red blood cells; TG — triglycerides; TnT — troponin T; TSH — thyroid-stimulating hormone; WBC — white blood cells

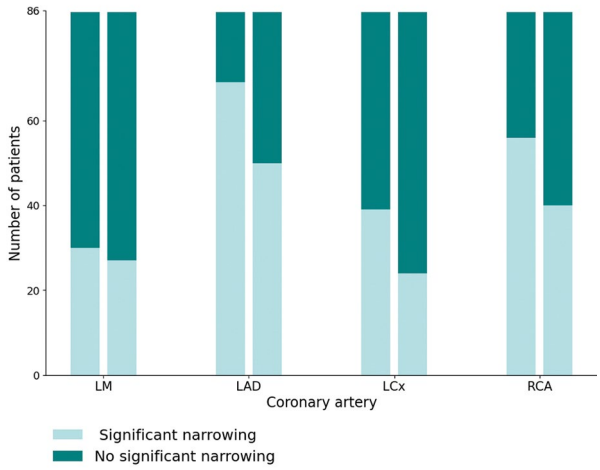

Figure 1. Comparison between coronary angiography (left bar) and coronary computed tomography angiography (right bar) in the assessment of the significant narrowing in coronary arteries; LAD — left anterior descending artery; LCx — left circumflex artery; LM — left main coronary artery; RCA — right coronary artery

Thanks to its high sensitivity and specificity, CCTA is an extremely useful method for identifying patients at high risk of cardiovascular incidents, also in the case of an asymptomatic CAD [15, 16].

Coronary angiography remains the "gold standard" for coronary artery imaging. As a diagnostic and therapeutic modality, it allows real-time visualisation of the contrast flow through the vessel and enables a percutaneous intervention to dilate the artery stenosis at the same time. In relation to CCTA, ICA is distinguished by its higher spatial and temporal resolution. Unfortunately, it is an invasive method that carries a risk of complications related to the procedure itself, such as bleeding at the insertion site (0.7%) [17] and the risk of death, myocardial infarction or stroke (0.1–0.2%) [18].

Coronary computed tomography angiography is associated with lower sensitivity and specificity in identifying patients with significant stenosis > 70% of the coronary artery lumen and for the arterial segment [19]. This discrepancy between CCTA and ICA results for the significant stenosis currently precludes the planning of coronary revascularisation using CCTA as a single imaging modality. Nevertheless, non-invasive imaging methods like coronary computed tomography angiography are increasingly likely to be the basis for future qualification for revascularisation including percutaneous coronary angioplasty and coronary artery bypass grafting in patients with MVD as demonstrated by the results of the SYNTAX III study [20].

Still, further research is needed to base future decision-making and treatment planning in MVD patients solely on non-invasive imaging i.e., CCTA, and clinical information.

Table 3. Diagnostic accuracy of coronary computed tomography angiography in coronary arteries

	LM	LAD	LCx	RCA	Total
Concordance	67 (78%)	63 (73%)	59 (69%)	62 (72%)	251 (73%)
Over-diagnosed	8 (9%)	2 (3%)	6 (7%)	4 (5%)	20 (6%)
Under-diagnosed	11 (13%)	21 (24%)	21 (24%)	20 (23%)	73 (21%)
Cohen's κ	0.50	0.40	0.34	0.45	0.47

LAD — left anterior descending artery; LCx — left circumflex artery; LM — left main coronary artery; RCA — right coronary artery

Limitations

There are several limitations to this study. This study was retrospective and involved only one centre. The CCTA examinations were performed by different laboratories and described by different radiologists, which may influence the assessment of stenosis in coronary arteries. In addition, coronary angiography was also performed by different cardiologists. It must be taken into account that CCTA is often subject to limitations due to the differences in the experience level of doctors describing the test result and the quality of the apparatus on which they were performed.

Conclusions

Coronary risk factors are widespread in patients with MVD which is an important issue and highlights the considerable work that needs to be done in educating society about the prevention of CVD. In patients with MVD, there is a moderate agreement between the description of the significance of coronary artery stenosis based on CCTA compared to ICA which rules out the eligibility of CCTA as a standalone preparation method for interventional treatment of these patients nowadays. Nevertheless, the non-invasive methods are in the process of constant perfecting and they constitute the future of cardiology, which may result in a beneficial impact on patients, for example, a reduction of complications associated with invasive procedures.

Article information

Author contributions

DK — concept author, study design, data collection, writing of the publication; OMB — writing the publication; MK — author of methods, statistical analysis; MJ — data collection, analysis and interpretation of results; MP — data collection, amending the publication; JK — data analysis, amending publications; JD — concept author, writing of publication, approval of final version of article.

Conflict of interest

The authors declare no conflict of interest.

Ethics statement

The study complied with the Declaration of Helsinki and was approved by the local medical ethics committee.

Data availability statement

Various source data from the literature describe the concordance between coronary angiography and coronary artery computed tomography. In this study, authors aimed to address the issue of concordance between computed tomography of the coronary arteries and coronarography in assessing the significance of coronary artery stenosis in patients with multivessel coronary artery disease.

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Streszczenie

Wstęp. Choroba wieńcowa jest jednym z najczęściej występujących problemów kardiologicznych zarówno w Polsce, jak i na świecie. W przypadku wielonaczyniowej choroby wieńcowej (MVD) kwestia dalszego postępowania i leczenia jest jeszcze bardziej skomplikowana. Nieinwazyjne metody obrazowania są powszechnie stosowane w diagnozowaniu choroby wieńcowej. Celem niniejszej pracy była analiza porównawcza wyników tomografii komputerowej tętnic wieńcowych (CCTA) i koronarografii w odniesieniu do zmiennych demograficznych i klinicznych u pacjentów z MVD.

Materiał i metody. Badanie przeprowadzono u 106 pacjentów z MVD hospitalizowanych w Klinice Kardiologii Centralnego Szpitala Klinicznego w Łodzi. Analizie poddano dostępne wyniki CCTA i koronarografii, porównując wyniki pod kątem istotności zwężeń w tętnicach wieńcowych w obu badaniach. Przeprowadzono również charakterystykę demograficzną oraz kliniczną analizowanej grupy pacjentów.

Wyniki. Znaczną większość pacjentów stanowili mężczyźni (n = 69,8%). Średnia wieku pacjentów wynosiła 69,42 ± ± 8,28 lat. Czynniki ryzyka choroby wieńcowej były rozpowszechnione w dużym stopniu w badanej populacji. Całościowa zgodność w ocenie istotności zwężeń w tętnicach wieńcowych w badaniu CCTA w porównaniu z koronarografią wynosiła 73% (κ = 0,47). Największa zgodność w ocenie dotyczyła pnia lewej tętnicy wieńcowej 78% (κ = 0,5), a najmniejsza — gałęzi okalającej 69% (κ = 0,34).

Wnioski. U pacjentów z MVD występuje umiarkowana zgodność pomiędzy opisem istotności zwężeń w tętnicach wieńcowych w badaniu CCTA w porównaniu do koronarografii. Tomografia komputerowa tętnic wieńcowych, jako metoda nieinwazyjna, jest jednym z narzędzi w początkowej diagnostyce przy podejrzeniu choroby wieńcowej. Czynniki ryzyka choroby wieńcowej są szeroko rozpowszechnione i stanowią istotny problem w analizowanej populacji pacjentów.

Słowa kluczowe: wielonaczyniowa choroba wieńcowa, tomografia komputerowa tętnic wieńcowych, koronarografia

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REVIEW ARTICLE

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The new face of HFpEF: systemic inflammation

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Abstract

Systemic inflammation is proposed as background of development and progres of heart failure, especially in heart failure with preserved ejection fraction (HFpEF). High-sensitivity C-reactive protein seems to be an optimal biomarker of systemic inflammation. Knowledge of systemic inflammation is important for new therapeutic fields in HFpEF with potential in inhibition of IL-1β, IL-6 or galectin-3.

Key words: HFpEF, systemic inflammation

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There has been a lot of recent progress in heart failure with preserved ejection fraction (HFpEF), leading to changes in therapeutic approaches. This is due to positive results from two major trials with sodium-glucose cotransporter 2 (SGLT2) inhibitors: EMPEROR-Preserved and DELIVER [1, 2]. These are the first studies dedicated to HF with an EF > 40% that have demonstrated clinical benefits in terms of reducing the risk of cardiovascular death and/or worsening HF (hospitalisation due to HF exacerbation, exacerbation without hospitalisation but requiring increased diuretic doses).

For many years, the distinct pathophysiology of HFpEF compared to heart failure with reduced ejection fraction (HFrEF) has been emphasised. Recent years have focused on understanding the phenomenon of systemic inflammation [3] and its significance in HFpEF. According to current knowledge in cardiology, inflammatory processes play a role in the development and progression of HF, are of particular importance in HFpEF, especially in certain subphenotypes. This was proven in the COACH (Counseling in Heart Failure) and BIOSTAT-CHF (Biology Study to Tailored Treatment in Chronic Heart Failure) studies [4, 5]. This association is likely related to a higher burden of comorbidities in HFpEF, such as diabetes, hypertension, obesity, and chronic kidney disease. The current concept indicates the involvement of systemic inflammation in myocardial remodeling in HFpEF (Paulus paradigm) with inflammation at the level of small vessels (microvascular inflammation) [6].

A promising biomarker for identifying systemic inflammation is high-sensitivity C-reactive protein (hsCRP). Measurement of CRP levels using a high-sensitivity method allows the detection of low-grade inflammatory processes with CRP levels of 2–10 mg/L. This was the focus of studies in which elevated levels of this biomarker were documented in populations with both acute and stable clinical presentations of HF (Table 1). Interleukin 6 (IL-6), which stimulates CRP production, was found to be associated with atrial fibrillation (OR 1.35; 95% CI: 1.03–1.77; p = 0.028), lower glomerular filtration rate, higher N-terminal pro-B-type natriuretic peptide, and worse exercise tolerance among 2329 patients in the BIOSTAT-CHF study [11]. Higher IL-6 levels were also associated with HFpEF (OR 1.63; 95% CI: 1.06–2.5; p = 0.027) and had predictive value for mortality (OR 1.22; 95% CI: 1.16–1.29; p < 0.001). Each doubling of IL-6 was an independent risk factor for hospitalisation for HF and cardiovascular death and all-cause mortality at 2-year follow-up (HR 1.16; 95% CI: 1.11–1.21; p < 0.001). The IL-6 signaling pathway seems to be particularly relevant for HFpEF [11].

Another important factor is the role of epicardial adipose tissue (EAT) as a direct inducer of systemic inflammation [12]. The MESA study [13], which included 6785 individuals

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Table 1. Review of selected trials evaluating inflammatory processes in heart failure

Trial name	Population	Inflammatory biomarkers
RELAX [7]	HFpEF	Elevated CRP levels in 57% of the population
TIME-CHF [8]	Elderly patients HFrEF HFpEF	Median hsCRP 6.6 mg/L 8.5 mg/L
ASCEND-HF [9]	AHF	Median hsCRP 12.6 mg/L
COACH [4]	HFrEF HFpEF	33 biomarkers from various pathophysiological pathways (inflammation, oxidative stress, remodeling, cardiac stretch, angiogenesis, atherosclerosis, and kidney function)
CANTOS [10]	Post-heart attack patients	hsCRP
BIOSTAT-CHF [5, 11]	HFrEF HFpEF	IL-6

AHF — acute heart failure; CRP — C-reactive protein; HFpEF — heart failure with preserved ejection fraction; HFrEF — heart failure with reduced ejection fraction; hsCRP — high-sensitivity C-reactive protein; IL-6 — interleukin 6

without cardiovascular diseases, revealed that the presence of epicardial adipose tissue in cardiac computed tomography was a predictor of HFpEF development (log rank $p < 0.001$) but not HFrEF (log rank $p = 0.1$) in a long-term follow-up (> 15 years).

Understanding the phenomenon of systemic inflammation is crucial for identifying new treatment options, such as inhibition of IL-1β, IL-6, or galectin-3. According to the studies conducted so far for IL-1β blockade, there was a significant 38% reduction in the risk of hospitalisation for HF and death from any cause for those patients who responded to therapy with canakinumab (documented reduction in hsCRP levels < 2 mg/L) compared to the placebo group (CANTOS trial) [10]. Currently, there is an ongoing study using the IL-6 inhibitor, ziltivekimab — a monoclonal antibody against IL-6 — in the HFpEF population [14].

However, it is still an open question what effect weight loss has on the inhibition of HF progression and the severity of systemic inflammation. This year will be the completion of two studies on semaglutide in the HFpEF population — the STEP-HFpEF and STEP-DM trials [15], which may answer this question. The STEP programme is the first to evaluate the effect of once-weekly semaglutide at a dose of 2.4 mg on symptoms, physical capacity, and functional improvement in obese HFpEF patients. A total of 1146 patients with obesity and HFpEF were randomised in the STEP-HFpEF programme [15].

In conclusion, SGLT2 inhibitors have revolutionised the approach to HF across the spectrum. Thanks to landmark trials like EMPEROR-Preserved and DELIVER, we now have therapy dedicated to patients with HF and an EF > 40% [1, 2, 16]. The published Heart Failure Association European Society of Cardiology (HFA ESC) position statement jointly with the European Heart Rhythm Association and the European Society of Hypertension on profiling patients with HFpEF to tailor therapy with a central position of SGLT2 inhibitors and diuretics in case of congestion (Figure 1), was one of the most important reports of this year's HFA ESC Congress [17]. Nonetheless, the search for HFpEF therapies — particularly considering systemic inflammation as a therapeutic target — continues.

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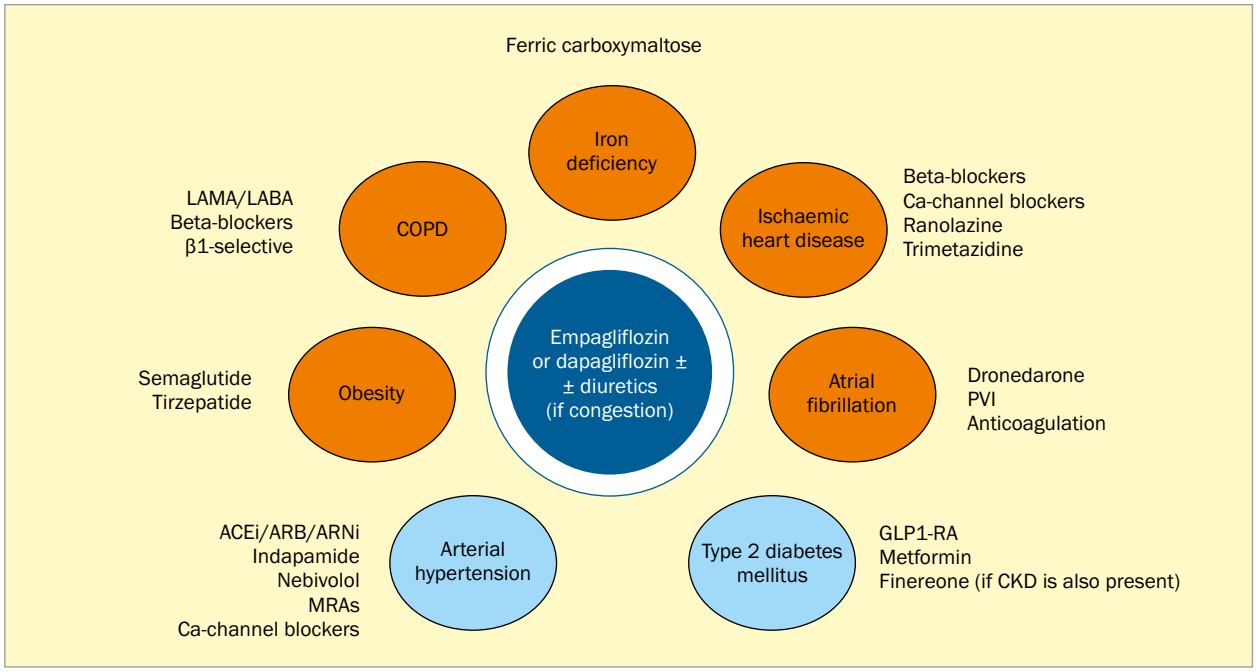

Figure 1. Profiling heart failure with preserved ejection fraction patients for personalized treatment [16]; ACEi — angiotensin-converting enzyme inhibitors; ARB — angiotensin receptor blocker; ARNi — angiotensin receptor neprilysin inhibitor; CKD — chronic kidney disease; COPD — chronic obstructive pulmonary disease; GLP1-RA — glucagon-like peptide 1 receptor agonists; LABA — long-acting β-agonist; LAMA — long-acting muscarinic receptor antagonist; MRA — mineralcorticoid receptor antagonist; PVI — pulmonary vein isolation

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Nowe oblicze HFpEF — zapalenie systemowe

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Artykuł jest tłumaczeniem pracy: Lelonek M. The new face of HFpEF: systemic inflammation. 2023; 18(4): 161–164.
DOI: 10.5603/fc.96384. Należy cytować wersję pierwotną

Streszczenie

Procesy zapalne biorą udział w powstawaniu i progresji niewydolności serca. Ostatnie lata koncentrują się na zrozumieniu zjawiska zapalenia systemowego (*systemic inflammation*) i jego znaczenia w niewydolności serca z zachowaną frakcją wyrzutową lewej komory (HFpEF). Wydaje się, że dobrym biomarkerem dla identyfikacji *systemic inflammation* jest białko C-reaktywne badane metodą wysoko czułą (hsCRP). Poznanie zjawiska *systemic inflammation* jest istotne dla nowych możliwości leczenia HFpEF w aspekcie potencjalnych celów terapeutycznych z inhibicją IL-1β, IL-6 czy galektyny-3.

Słowa kluczowe: HFpEF, zapalenie systemowe

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W temacie niewydolności serca z zachowaną frakcją wyrzutową (HFpEF, *heart failure with preserved ejection fraction*) dzieje się w ostatnim czasie bardzo dużo. Ulega zmianie podejście terapeutyczne. Jest to związane z pozytywnymi wynikami 2 dużych badań dotyczących inhibitorów kotransportera sodowo-glukozowego 2 (SGLT2i, *sodium-glucose cotransporter 2 inhibitors*) — EMPEROR-Preserved i DELIVER [1, 2]. Są to pierwsze badania dedykowane niewydolności serca z frakcją wyrzutową > 40%, które udokumentowały korzyści kliniczne w postaci redukcji ryzyka zgonu z powodów sercowo-naczyniowych i/lub progresji niewydolności serca (hospitalizacja z powodu zaostrzenia HF, zaostrzenie bez konieczności hospitalizacji, ale wymagające zwiększenia dawek leków moczopędnych).

Od wielu lat podkreśla się odmienności w patofizjologii HFpEF w porównaniu z niewydolnością serca z obniżoną frakcją wyrzutową (HFrEF, *heart failure with reduced ejection fraction*). Badania wykonywane w ostatnich latach koncentrują się na zrozumieniu zjawiska *systemic inflammation* [3] i jego znaczenia w HFpEF. Na obecnym etapie wiedzy kardiologicznej wiemy, że procesy zapalne biorą udział w powstawaniu i progresji niewydolności serca (HF, *heart failure*), a szczególne znaczenie mają w HFpEF, zwłaszcza w pewnych subfenotypach. Zostało to udokumentowane w badaniach COACH (*Counseling in Heart Failure*) oraz BIOSTAT-CHF (*Biology Study to Tailored Treatment in Chronic Heart Failure)* [4, 5]. Jest to najprawdopodobniej związane z większym obciążeniem chorobami współistniejącymi w HFpEF, takimi jak cukrzyca, nadciśnienie tętnicze, otyłość czy przewlekła choroba nerek. Aktualna koncepcja wskazuje na udział *systemic inflammation* w remodelingu mięśnia sercowego w HFpEF (*Paulus paradigm*) z zapaleniem na poziomie małych naczyń (*microvascular inflammation)* [6].

Wydaje się, że dobrym biomarkerem dla identyfikacji *systemic inflammation* jest białko C-reaktywne badane metodą wysoko czułą (hsCRP, *high-sensitivity C-reactive protein*). Pomiar stężenia CRP metodą wysoko czułą pozwala na wykrycie procesów zapalnych tlących się na poziomie stężeń 2–10 mg/l. Było to przedmiotem badań, w których udokumentowano podwyższone stężenia tego biomarkera zarówno w populacji z ostrym, jak i stabilnym obrazem klinicznym HF (tab. 1). Z kolei wśród 2329 chorych uwzględnionych w badaniu BIOSTAT-CHF [11], podwyższone stężenie interleukiny 6 (IL-6), która stymuluje

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Tabela 1. Przegląd wybranych badań oceniających procesy zapalne w niewydolności serca

Nazwa badania	Populacja	Biomarkery zapalne
RELAX [7]	HFpEF	CRP podwyższone u 57% populacji
TIME-CHF [8]	Starsi pacjenci HFrEF HFpEF	Mediana hsCRP 6,6 mg/l 8,5 mg/l
ASCEND-HF [9]	AHF	Mediana hsCRP 12,6 mg/l
COACH [4]	HFrEF HFpEF	33 biomarkery różnych szlaków patofizjologicznych (izapalenie, stres oxydacyjny, remodeling, *cardiac stretch*, angiogeneza, miażdżyca, funkcja nerek)
CANTOS [10]	Chorzy po zawale serca	hsCRP
BIOSTAT-CHF [5, 11]	HFrEF HFpEF	IL-6

AHF (*acute heart failure*) — ostra niewydolność serca; CRP (*C-reactive protein*) — białko C-reaktywne; HFpEF (*heart failure with preserved ejection fraction*) — niewydolność serca z zachowaną frakcją wyrzutową; HFrEF (*heart failure with reduced ejection fraction*) — niewydolność serca z obniżoną frakcją wyrzutową; hsCRP (*high-sensitivity C-reactive protein*) — CRP badane metodą wysoko czułą; IL-6 — interleukina-6

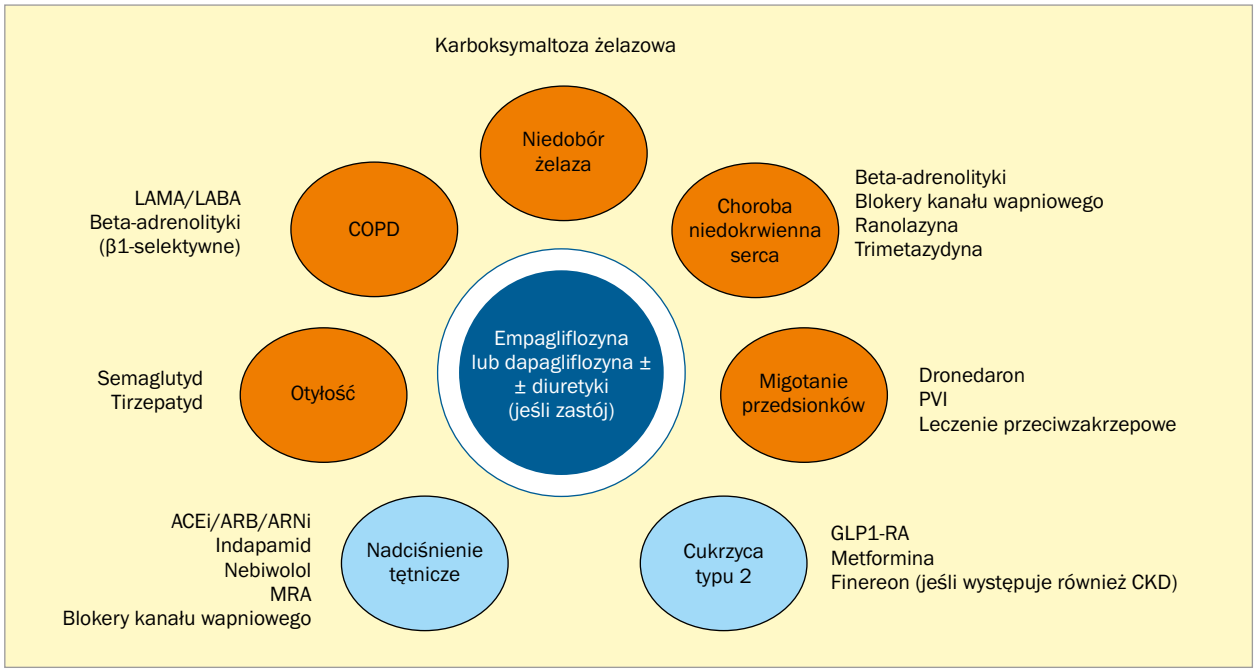
produkcję CRP, było powiązane z migotaniem przedsionków (OR 1,35; 95% CI: 1,03–1,77; p = 0,028), niższym wskaźnikiem filtracji kłębuszkowej, wyższym stężeniem N-końcowego propeptydu natriuretycznego typu B i gorszą tolerancją wysiłku. Wyższe stężenie IL-6 wiązało się z występowaniem HFpEF (OR 1,63; 95% CI: 1,06–2,5; p = 0,027) i miało znaczenie predykcyjne dla wystąpienia zgonu (OR 1,22; 95% CI: 1,16–1,29; p < 0,001). Każde podwojenie wartości IL-6 było niezależnym czynnikiem ryzyka hospitalizacji z powodu niewydolności serca oraz zgonu z powodów sercowo-naczyniowych i śmiertelności z jakiejkolwiek przyczyny w 2-letniej obserwacji (HR 1,16; 95% CI: 1,11–1,21; p < 0,001). Wydaje się, że droga sygnałowa z IL-6 może być szczególnie istotna dla HFpEF [11].

Kolejnym ważnym elementem jest rola tkanki tłuszczowej epikardialnej jako bezpośredniego czynnika indukującego rozwój *systemic inflammation* [12]. Z badania MESA [13], które objęło 6785 osób bez schorzeń sercowo-naczyniowych wiadomo, że obecność tkanki tłuszczowej epikardialnej, wykazanej w tomografii komputerowej serca, była predyktorem rozwoju w obserwacji wieloletniej (> 15 lat) HFpEF (*log rank* p < 0,001), ale nie HFrEF (*log rank* p = 0,1).

Zrozumienie zjawiska *systemic inflammation* jest istotne dla rozwoju nowych możliwości leczenia w aspekcie potencjalnych celów terapeutycznych z inhibicją IL-1β, IL-6 czy galektyny-3. W dotychczas przeprowadzonych badaniach dotyczących blokady IL-1β, u chorych, którzy odpowiedzieli na terapię canakinumabem (udokumentowana redukcja stężenia hsCRP do poziomu < 2 mg/l), odnotowano istotną (o 38%) redukcję ryzyka hospitalizacji z powodu HF i zgonu z jakiejkolwiek przyczyny w porównaniu do placebo (badanie CANTOS) [10]. Aktualnie w populacji z HFpEF prowadzone jest badanie z zastosowaniem inhibitora IL-6 — ziltiwekimabu — będącego przeciwciałem monoklonalnym przeciw IL-6 [14].

Nadal jednak otwarte pozostaje pytanie, jaki wpływ na hamowanie progresji HF oraz zaawansowanie *systemic inflammation* ma redukcja masy ciała. W tym roku zostaną zakończone 2 badania w populacji z HFpEF dotyczące semaglutydu — badanie STEP-HFpEF i STEP-DM [15] — które być może odpowiedzą na to pytanie. Program STEP jest pierwszym, który ocenia wpływ semaglutydu, podawanego raz w tygodniu w dawce 2,4 mg, na objawy, wydolność fizyczną i poprawę funkcjonowania u otyłych pacjentów z HFpEF. Łącznie w programie STEP-HFpEF zrandomizowano 1146 pacjentów z otyłością i HFpEF [15].

Na zakończenie warto podkreślić, że SGLT2i zrewolucjonizowały spojrzenie na HF. Dzięki przełomowym badaniom EMPEROR-Preserved i DELIVER po raz pierwszy mamy terapię dedykowaną pacjentom z niewydolnością serca z EF > 40% [1, 2, 16]. Opublikowane stanowisko Asocjacji Niewydolności Serca Europejskiego Towarzystwa Kardiologicznego (HFA ESC, *Heart Failure Association European Society of Cardiology*) wspólne z Europejską Asocjacją Zaburzeń Rytmu Serca oraz Europejskim Towarzystwem Nadciśnienia Tętniczego, dotyczące profilowania pacjentów z HFpEF w celu dopasowania terapii z centralną pozycją inhibitorów SGLT2 oraz diuretyków w przypadku przewodnienia (ryc. 1), stanowiło jedno z najważniejszych doniesień tegorocznego Kongresu HFA ESC [17]. Niemniej nadal trwają poszukiwania terapii HFpEF, w szczególności z uwzględnieniem *systemic inflammation* jako celu terapeutycznego.



Rycina 1. Profilowanie pacjenta z niewydolnością serca z zachowaną frakcją wyrzutową w celu ustalenia leczenia [16]; ACEi (*angiotensin-converting enzyme inhibitors*) — inhibitory konwertazy angiotensyny; ARB (*angiotensin receptor blocker*) — antagonista receptora angiotensynowego; ARNi (*angiotensin receptor neprilysin inhibitor*) — inhibitor receptora angiotensynowego i neprylizyny; CKD (*chronic kidney disease*) — przewlekła choroba nerek; COPD (*chronic obstructive pulmonary disease*) — przewlekła obturacyjna choroba płuc; GLP1-RA (*glucagon-like peptide 1 receptor agonists*) — agoniści receptora glukagonopodobnego peptydu 1; LABA (*long-acting β-agonist*) — długo działający β-agonista; LAMA (*long-acting muscarinic receptor antagonist*) — długo działający antagonista receptora muskarynowego; MRA (*mineralcorticoid receptor antagonist*) — antagonista receptora mineralokortykoidowego; PVI (*pulmonary vein isolation*) — izolacja żył płucnych

Informacje o artykule

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—

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—

Piśmiennictwo

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Tight lesion in underexpanded stent: a contemporary approach based on delayed intravascular lithotripsy

Istotna zmiana w nierozprężonym stencie — współczesne podejście oparte na opóźnionej litotrypsji wewnątrznaczyniowej

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Abstract

A patient with massive calcification of the coronary arteries and an unexpanded coronary stent is reported. Due to the persistence of Canadian Cardiovascular Society class III angina, many endovascular treatment techniques were attempted, but most of them were ineffective. Full expansion of the previously implanted stent and resolution of the lesion in the circumflex artery was finally achieved with the use of intracoronary lithotripsy. After successful treatment, the patient is under the care of a cardiology clinic and remains asymptomatic.

Key words: intravascular lithotripsy, stent, underexpanded, calcified

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Introduction

Despite the progress in percutaneous techniques in coronary artery disease treatment, underexpanded stents in calcified lesions still constitute a challenge. The risk of stent polymer exfoliation remains the contraindication for early use of intravascular lithotripsy (IVL), however, delayed optimisation with the use of IVL has become an alternative option. This valuable technique uses a balloon-mounted ultrasound source which emits sonic pressure waves. The effect of ultrasound wave propagation into the vessel wall results in fragmentation of both superficial and deep calcium deposits, even located under the stent struts, which allows better balloon and stent expansion [1]. As long as the calcified lesion remains uncovered with the stent, rotational atherectomy with increasing diameter of burrs could be effective. The use of rotational atherectomy in underexpanded stents remains an off-label procedure because of the high risk of possible complications. Intravascular lithotripsy is a modern technique dedicated to calcified coronary artery treatment. Unfocused lithotripsy energy is created at the emitters, which are contained in a fluid within a coronary artery balloon catheter. Electrical energy is delivered to the emitters, initiating the creation of steam bubbles, which expand and collapse creating sonic pressure waves. The result is microfractures in the atherosclerotic, calcified coronary artery wall, prone to further expansion during the final balloon or stent implantation.

An effective method combining initial IVL with non-compliant or very-high-pressure balloon post-dilatation should be considered in such cases when the use of in-stent

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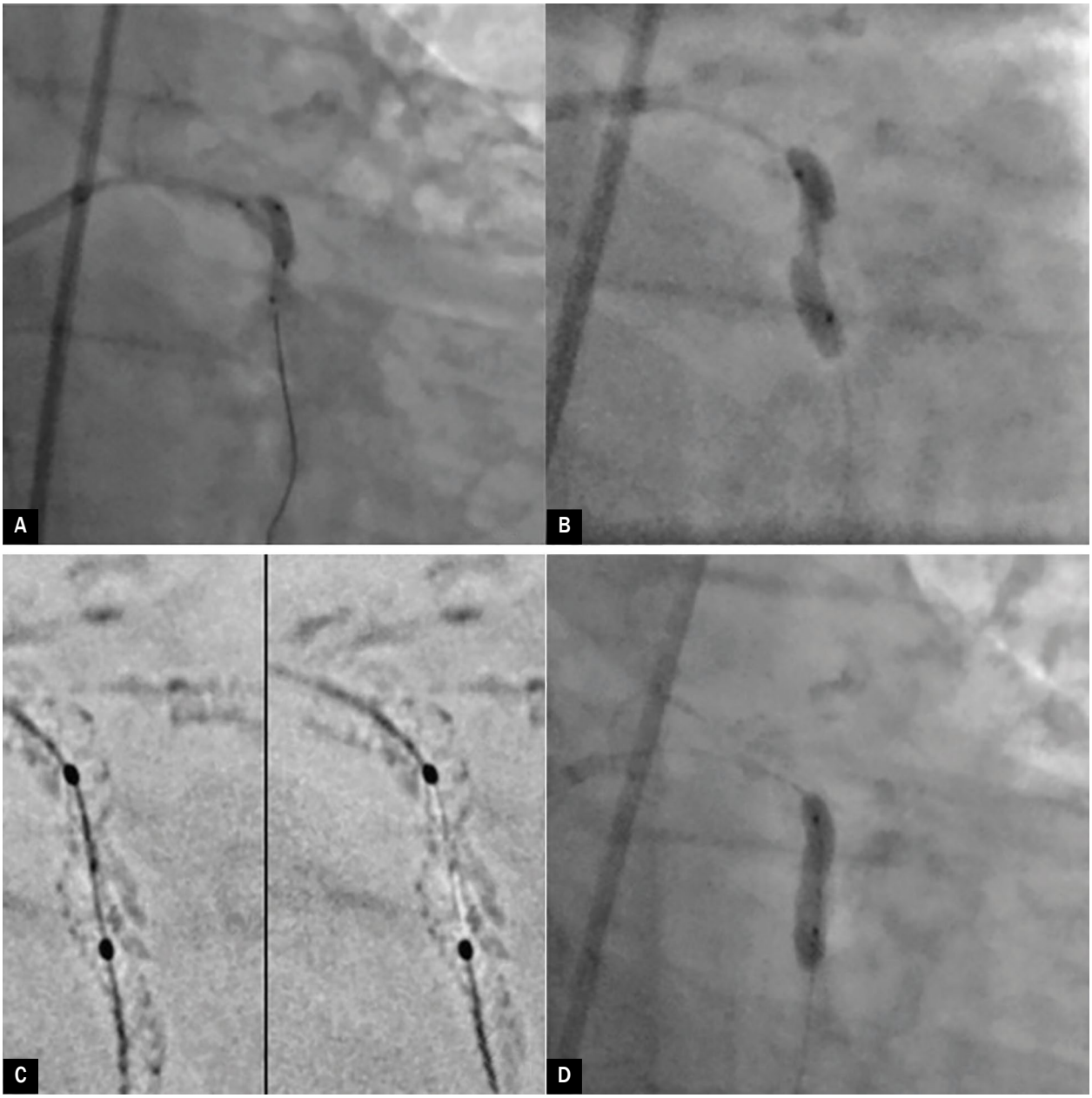

Figure 1. A. Simultaneous non-compliant 3.0 × 15 mm balloons inflation; **B.** Stent underexpansion visible in angio; **C.** Stent underexpansion visible in StentViz technique; **D.** Stent after intravascular lithotripsy and drug-coated balloon inflation

rotational atherectomy was ineffective or associated with the unacceptably high risk [2]. The aim of the publication and ongoing trial is the presentation of the clinical outcome of the contemporary approach including the IVL technique with final paclitaxel balloon inflation in tight underexpaned stent lesion.

Case report

The criteria for such a comprehensive approach met a 68-year-old diabetic patient with arterial hypertension, hyperlipidaemia and a history of stroke and myocardial infarction treated 4 months earlier with percutaneous coronary intervention in the circumflex artery. Due to persistent angina (Canadian Cardiovascular Society III class), the patient was qualified for coronary angiography, which revealed the underexpanded stent, critically narrowing the artery lumen. Then the percutaneous coronary intervention *ad hoc* was performed, with the use of various techniques even including simultaneous non-compliant (NC) 3.0 × 15 mm balloons inflation (Figure 1A). None of them was successful, because of massive calcium

deposits located under the stent structure in the 11th segment. Despite the high pressure (24 atm) and prolonged inflation of the 3.5 × 20 mm NC balloon, proper expansion was not achieved (Figure 1B). There was still dog-boning of the balloon and stent underexpansion visible in the StentViz technique (Figure 1C). The patient was clinically stable, and a second attempt with the use of IVL was scheduled in the next 2 months according to IVL producer recommendations. Another procedure was performed using a 3.0 × 12 mm IVL balloon (Shockwave Medical) which, after completing the whole lithotripsy protocol enabled a full expansion of the balloon (6 atm). Finally, the NC balloon inflation (3.5 × 15 mm, 20 atm) followed by prolonged paclitaxel-coated balloon inflation (3.5 × 20 mm, 10 atm, 90 seconds) (Figure 1D) allowed to achieve an optimal angiographic result. Nine months after successful procedure patient remains asymptomatic in ambulatory care.

Discussion

Intravascular lithotripsy constitutes a valuable complement to the available revascularization methods including rotational and orbital atherectomy, non-compliant, ultra-high-pressure, scoring or cutting balloons [3]. Underexpanded stents implanted in heavily calcified segments limit the benefits of coronary revascularization. There is still a lack of scientific data on IVL in in-stent lesions, however, sometimes lithotripsy remains the only method of treatment in the case of underexpanded stents. A hybrid approach based on IVL and non-compliant balloon, followed by drug-coated balloon inflation may be an encouraging treatment option. The final drug-coated balloon inflation allows for avoiding the implantation of another stent layer.

Moreover, it seems that full optimisation of stent expansion based on IVL can also prevent late stent thrombosis and, in such a way, may improve the patient's outcome. Obviously, there is a need for further research and more evidence on this topic.

Conclusion

The contemporary approach including delayed in-stent IVL with final paclitaxel-drug coated balloon inflation may be an encouraging and safe treatment option in underexpanded calcified in-stent lesions. There is still a lack of scientific data on IVL in in-stent lesions so further research and more evidence base data on this topic are needed. When orbital or rotational atherectomy is impossible or ineffective IVL could remain the last chance for a successful and safe method of revascularization.

Article information

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Author contributions
PW, WS, MW contributed to patient diagnosis, management, and clinical data analysis. PW wrote the manuscript draft. MW edited the manuscript. MK contributed to data analysis, interpretation, and intellectual content of critical importance to the work described. All authors had the opportunity to revise the manuscript.

Conflict of interest
The authors declare no conflict of interest.

Ethics statement
This case report was in adherence with the Declaration of Helsinki. The authors declared that written informed consent was obtained from the patient for publication of this case report and accompanying images.

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Streszczenie

W niniejszej publikacji opisano przypadek pacjenta z masywnymi zwapnieniami tętnic wieńcowych oraz nierozprężonym stentem wieńcowym. Ze względu na utrzymujące się dolegliwości dławicowe w klasie III według Kanadyjskiego Towarzystwa Kardiologicznego podjęto wiele prób leczenia wewnątrznaczyniowego, ale większość z nich okazała się nieskuteczna. Pełne rozprężenie uprzednio wszczepionego stentu oraz rezolucję zwężenia gałęzi okalającej lewej tętnicy wieńcowej udało się finalnie uzyskać z użyciem litotrypsji wewnątrzwieńcowej. Po skutecznym leczeniu pacjent znajduje się pod opieką poradni kardiologicznej i pozostaje bezobjawowy.

Słowa kluczowe: litotrypsja wewnątrznaczyniowa, stent, nierozprężony, zwapniały

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Acute tricuspid valve regurgitation in a motorcycle accident

Ostra niedomykalność zastawki trójdzielnej po wypadku motocyklowym

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Abstract

Tricuspid regurgitation is secondary in 90% of cases. We would like to present two case reports of primary tricuspid regurgitation caused by rupture of the papillary muscle as a result of traffic accidents. This series of cases presents a very rare heart injury caused by blunt chest trauma. Regular monitoring of echocardiographic parameters in the period between the stabilization of patients' condition after the accident and surgical correction of the tricuspid valve defect is an important point of patient care with severe tricuspid regurgitation.

Key words: acute tricuspid regurgitation, primary tricuspid regurgitation, heart injury

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An 18-year-old man suffered severe tricuspid regurgitation and orthopaedic injuries in a motorcycle accident. In 3 months, the patient underwent orthopaedic treatment and cardiological control to qualify for cardiac surgery. Echocardiography showed severe tricuspid regurgitation, caused by a rupture of the papillary muscle leading the tendon threads to the anterior leaflet of the tricuspid valve. The left ventricular ejection fraction was 55%, and the patient complained of exertional dyspnoea, which corresponded to New York Heart Association class II. The patient was qualified for cardiac surgery to correct the valve defect. A sternotomy and cannulation of the ascending aorta and both vena cava were performed. On the beating heart, after opening the right atrium, the tendon threads of the anterior leaflet were sutured to the muscle of the right ventricle. Edwards MC3 34 ring was sewn in for stabilization. Follow-up transoesophageal echocardiography showed insignificant, small tricuspid regurgitation. Echocardiographic control after 4 months showed no significant changes.

A 26-year-old man suffered a traffic accident as a motorcycle driver. The patient underwent type II ASD correction surgery in childhood. After the accident, the patient was hospitalized for 5 days at the Department of General Surgery due to concussion, right shoulder injuries and right lung contusion. Three days after discharge from the hospital, he went to the ER for stabbing chest pain. Echocardiography revealed significant tricuspid regurgitation and a ballot formation on the tricuspid valve. A cardiac angio-CT examination confirmed a rupture of the papillary muscle of the right ventricle. The patient was admitted to the Department of Cardiac Surgery in a semi-elective mode for surgical correction of valve defect. A surgical procedure was performed in extracorporeal circulation, including resternotomy, suturing of the torn papillary muscle of the

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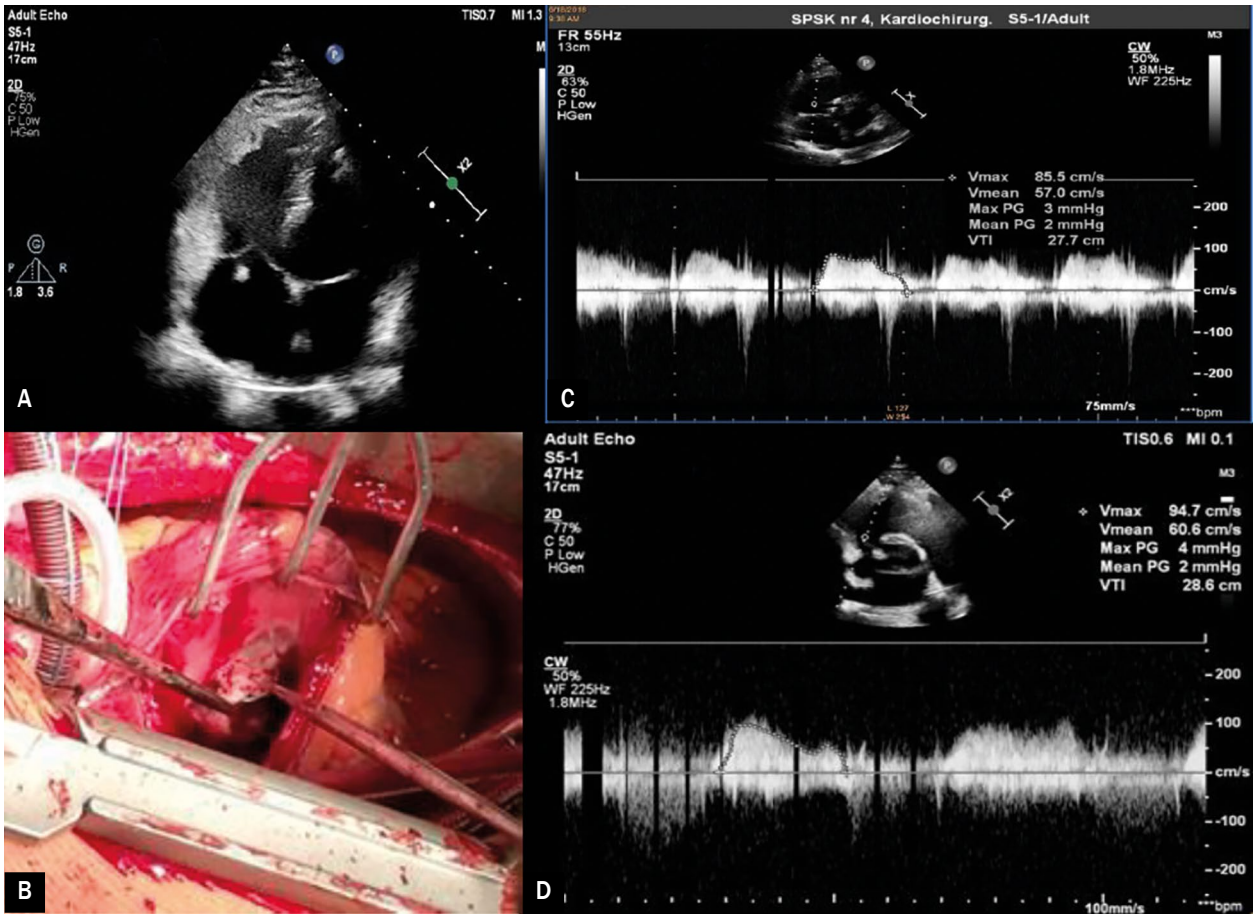

Figure 1. **A.** Fragment of the papillary muscle in the right atrium — echocardiography image; **B.** Fragment of the papillary muscle — intraoperative image; **C.** Discharge echocardiography of the first patient; **D.** Discharge echocardiography of the second patient

anterior leaflet to the right ventricular wall, and insertion of the Edwards MC3 Tricuspid Annuloplasty Ring 32. Intraoperative transoesophageal echocardiography confirmed the proper functioning of the valve after surgery. The course of hospitalization was uncomplicated.

The mechanisms responsible for such injuries in most cases are blunt force injuries [1], and car accidents are their most common cause. Typical tricuspid valve injuries include cord rupture, papillary muscle rupture, and leaflet rupture. Maisano et al. [2] reviewed 74 reported cases and found that cord rupture (n = 41, 55.4%) was the most common cause of tricuspid regurgitation. Severe tricuspid regurgitation is associated with poorer survival [3] and worsening heart failure [4]. Timely surgical treatment is essential to avoid irreversible right ventricular damage and multiple organ failure, which may be associated with increased surgical risk if interventional treatment is delayed [5].

This series of cases presents a very rare heart injury caused by blunt chest trauma. Regular monitoring of echocardiographic parameters in the period between the stabilization of patients' condition after the accident and surgical correction of the tricuspid valve defect is an important point of patient care with severe tricuspid regurgitation.

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All authors worked together on the final image of the article.

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Ethics statement
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Streszczenie

Niedomykalność zastawki trójdzielnej w 90% przypadków ma charakter wtórny. W niniejszej pracy przedstawiono dwa opisy przypadków pierwotnej niedomykalności zastawki trójdzielnej spowodowanej pęknięciem mięśnia brodawkowatego w wyniku wypadku drogowego. Ta seria przypadków przedstawia bardzo rzadki uraz serca spowodowany tępym urazem klatki piersiowej. Regularne monitorowanie parametrów echokardiograficznych w okresie między stabilizacją stanu pacjenta po wypadku a chirurgiczną korekcją wady zastawki trójdzielnej jest ważnym punktem opieki nad pacjentem z ciężką niedomykalnością trójdzielną.

Słowa kluczowe: ostra niedomykalność trójdzielna, urazowa niedomykalność trójdzielna, uraz serca

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Complex percutaneous intervention on pulmonary arteries in an adult patient with a corrected Taussig–Bing anomaly

Złożona interwencja przezskórna na tętnicach płucnych u dorosłego pacjenta ze skorygowaną anomalią Taussig–Binga

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Abstract

This study reports a case of a successful complex percutaneous intervention on pulmonary arteries in a 23-year-old adult patient with a corrected Taussig–Bing anomaly. The patient had a history of multiple surgeries, including an arterial switch operation, the Bentall procedure, and mitral valve replacement. On admission, the patient was asymptomatic, however significant stenosis of the pulmonary arteries was detected. The patient was qualified for cardiac catheterization. The complex, high-risk procedure with the implantation of three stents improved the morphology of the right pulmonary artery and consequently the function of the right ventricle. It is concluded that with the remarkable development of percutaneous techniques, more and more patients are receiving optimal, personalised treatment.

Key words: congenital heart disease, Taussig–Bing anomaly, double outlet right ventricle, percutaneous intervention, pulmonary artery stenting

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Introduction

The Taussig–Bing anomaly (TBA) is a rare congenital heart disease (CHD), a subtype of double outlet right ventricle (DORV) [1]. In TBA the aorta originates entirely from the right ventricle (RV), the pulmonary artery (PA) arises from above the non-restrictive ventricular septal defect (VSD) and there is no pulmonary-mitral fibrous continuity [2]. DORV accounts for approximately 1% of all cases of CHD and its prevalence is reported to be 0.1 per 1000 live births; TBA is the third most common type of DORV [3, 4]. The arterial switch operation (ASO) with VSD closure is the method of choice for the treatment of TBA [2]. Pulmonary arteries stenosis is a relatively frequent complication of the ASO [5, 6]. A percutaneous intervention on PA and stenting is an established method for the management of this complication [5, 6].

Case report

Patient presentation

A 23-year-old man with a corrected Taussig–Bing anomaly was admitted to the Department of Cardiology and Congenital Diseases of Adults for percutaneous intervention on the

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pulmonary arteries. He had a history of multiple surgeries. Three months after birth, he underwent pulmonary artery banding and patent ductus arteriosus ligation. One year later, he had an arterial switch operation with the LeCompte manoeuvre; the coexisting ventricular septal defect was closed with a Gore-Tex patch. At the age of 18, during a school lesson, he underwent cardiopulmonary arrest caused by ventricular fibrillation. He was first resuscitated by witnesses and then by paramedics. After the patient was discharged from the intensive care unit, he was admitted to the clinic, where significant regurgitation of neoaortic and mitral valves was found. It was decided that the patient should receive an implantable cardioverter-defibrillator for secondary prevention of sudden cardiac death before being referred to cardiac surgery. The subcutaneous implantable cardioverter-defibrillator Boston Scientific Emblem was implanted. Four years later (at the age of 22) he was finally qualified for cardiac surgery in another centre. The operation included the Bentall procedure, mitral valve replacement, and right pulmonary arterioplasty (using a bovine pericardial patch). The follow-up hospitalization in the department showed good function of the mechanical valves, but stenosis of both pulmonary arteries was detected. The patient was referred to the cardiac surgery clinic for consultation and the date of the next hospitalization in the centre was set.

On admission, the patient reported no symptoms. On physical examination, heart sounds were regular (HR 65 bpm), with mechanical valves click sounds and a systolic murmur heard best in the pulmonary valve auscultation area. His blood pressure was 102/66 mm Hg. His pharmacological treatment consisted of bisoprolol 3.75 mg/day, acenocoumarol (target INR: 2.5–3.5), potassium chloride 600 mg/day, and magnesium citrate (100 mg Mg^{2+}/day).

Initial work up

Routine laboratory tests were normal. International normalized ratio was within the therapeutic range (3.31) and N-terminal pro-B-type natriuretic peptide was not elevated (76 pg/mL).

Transthoracic echocardiography (Figure 1) showed left ventricular hypertrophy with increased left ventricular internal diameter at end-diastole and end-systole (62 and 53 mm, respectively) and left atrial enlargement (left atrium diameter — 42 mm; left atrial volume index — 64.3 mL/m^2). Dimensions of other cardiac chambers were normal. The Gore-Tex patch served as an interventricular septum (IVS), no shunt was visualised, however, this artificial IVS was dyskinetic (in the basal and mid segments). No other wall motion abnormalities were observed. Left ventricular ejection fraction was reduced to 44% — it was a consequence of abnormal IVS motion. In the aortic position, the mechanical aortic valve was observed: occluder motion was normal, the maximum pressure gradient (PG) was 12 mm Hg and

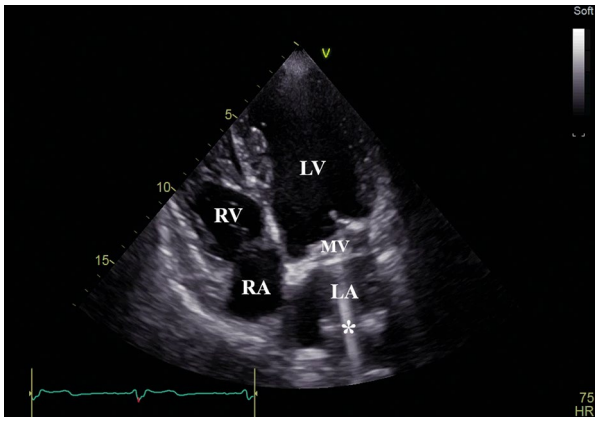

Figure 1. Transthoracic echocardiography, apical view. Visible increased left ventricular internal diameter, the mechanical mitral valve and the comet-tail artifact (marked as *); LA — left atrium; LV — left ventricle; MV — mitral valve; RA — right atrium; RV — right ventricle

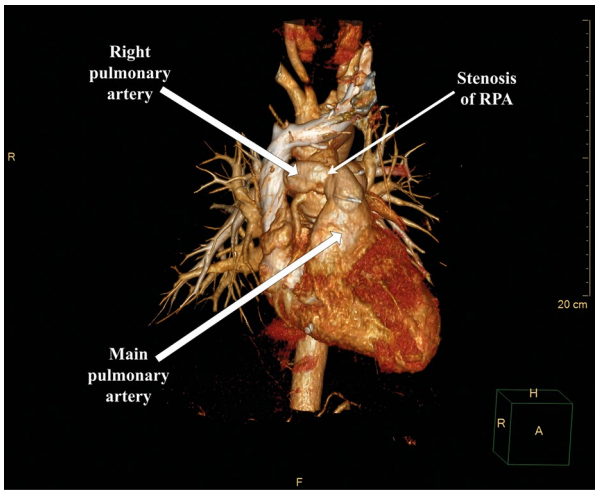

Figure 2. The computed tomography angiography with 3D reconstruction. Visible stenosis of the right pulmonary artery (RPA)

a small paravalvular leak was detected. The mechanical mitral valve was observed in the mitral position: occluder motion was normal and the maximum PG was 10 mm Hg. The tricuspid valve was normal. The PG of the pulmonary valve was 70/42 mm Hg (maximum and mean, respectively) and the peak velocity was 4.2 m/s. These measurements suggested significant stenosis of the PA. The visible part of the main PA measured 8 mm in the narrowest part. The systolic function of the RV was slightly reduced (tricuspid annular plane systolic excursion = 16 mm; peak lateral tricuspid annular systolic velocity [S'] = 8 cm/s).

The computed tomography angiography (Figure 2) showed stenosis of the entire right PA (22 × 7 mm) and proximal part of the left PA (16 × 8 mm); the main PA was 33 × 17 mm.

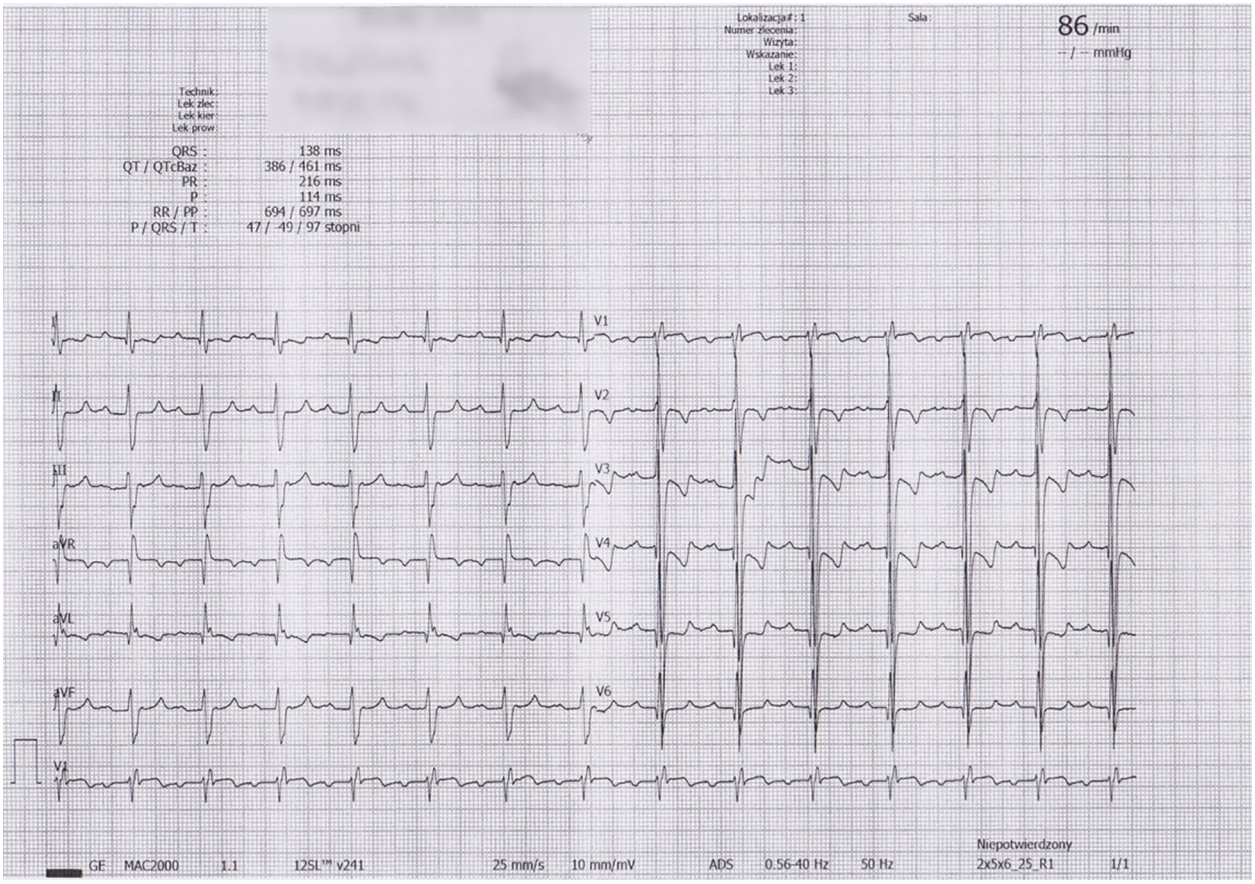

Figure 3. 12-lead electrocardiogram. Visible sinus rhythm, left axis deviation, right bundle branch block (QRS = 138 ms), left anterior hemiblock, features of left ventricular hypertrophy and 1st degree atrioventricular block (PQ = 210 ms)

The 12-lead electrocardiogram (Figure 3) showed sinus rhythm, left axis deviation, right bundle branch block (QRS = 138 ms), left anterior hemiblock, features of left ventricular hypertrophy and 1st degree atrioventricular block (PQ = 210 ms).

Diagnosis and management

The heart team, consisting of conservative cardiologists and interventional cardiologists, decided to qualify the patient for cardiac catheterization with the intention of implanting stents in the pulmonary arteries.

During catheterisation, the left pulmonary artery was measured to be 13.5 mm in the proximal segment and 16 mm in the distal segment. The proximal segment of the right pulmonary artery (RPA) was significantly stenosed with a diameter of only 4.1 mm (Figure 4 A–B). The further segment of the RPA was coiled spirally along with a bovine pericardial patch (from the right pulmonary arterioplasty); the diameter was 7.3 mm. The distal segment of the RPA was 14 mm in diameter. The pressure in the RV was about 50% of the systemic pressure (which was low at 82/43 mm Hg due to the reaction to the anaesthetics). Based on these findings, an appropriate treatment plan was implemented. The BeGraft stent 14 × 29 mm was implanted in the proximal segment of the RPA. After implantation, the pressure difference in the area of the coiled artery was still significant (20 mm Hg). The 10 × 30 mm Formula stent was implanted distally (using a 14 × 39 mm balloon-in-balloon catheter). In the control angiography, the RPA wall outline was irregular but without significant pressure differences. It was decided to implant the third stent (BeGraft 14 × × 39 mm), which connected two previously placed stents (Figure 4 C–D). At the end of the procedure, there were no significant differences in the RPA pressures and RV pressure was < 50% of systemic pressure.

Follow-up

There were no postprocedural complications and the patient was asymptomatic. Control transthoracic echocardiography showed a reduction in the maximum pulmonary valve pressure gradient to 40 mm Hg (from 70 mm Hg) and a reduction in peak velocity to 3.12 m/s (from 4.2 m/s). The function of the RV ventricle improved with tricuspid annular plane systolic excursion of 19 mm and S' of 9 cm/s (before

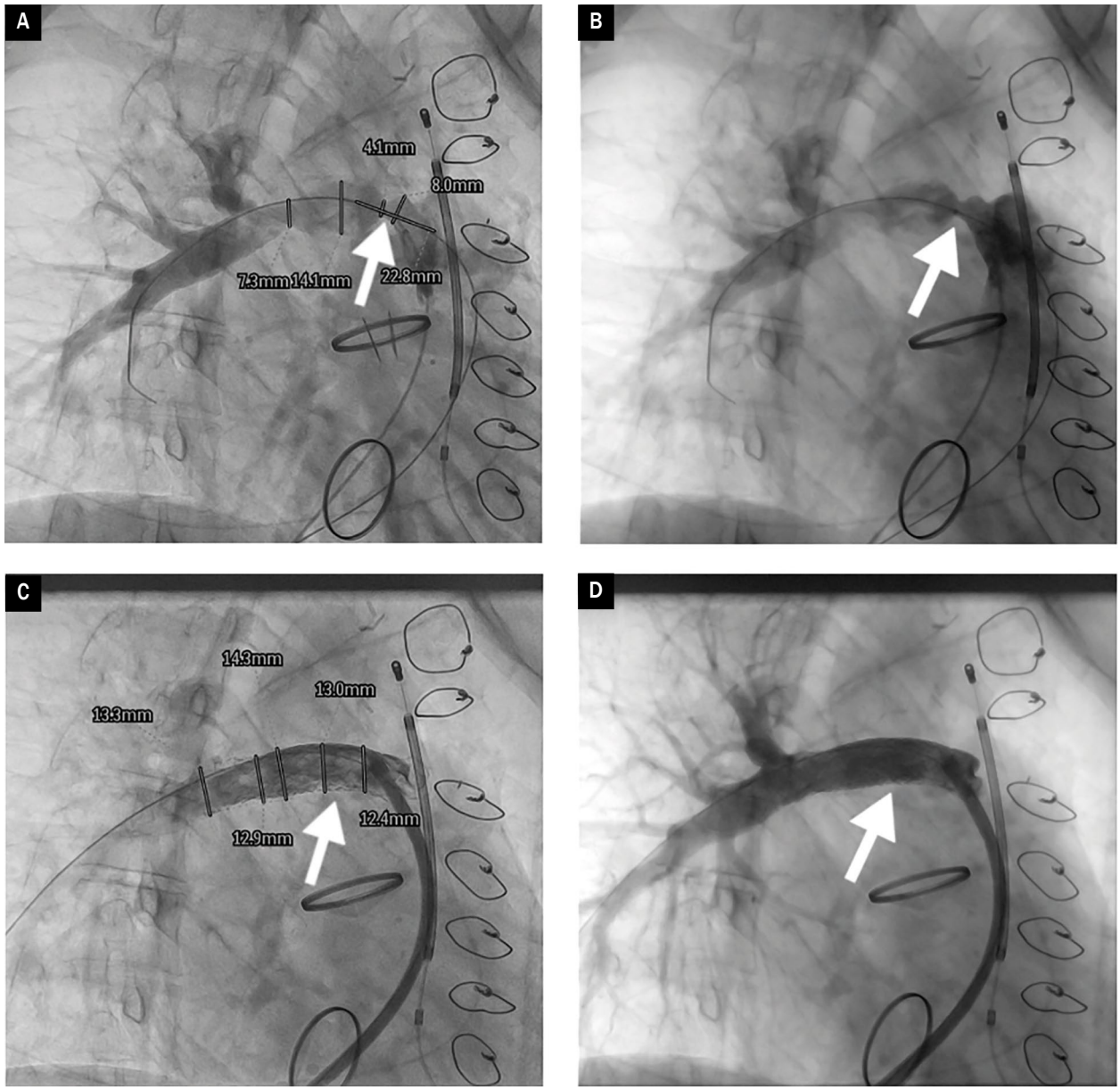

Figure 4. Pulmonary arteries angiography: **A, B.** Right pulmonary artery before stenting, the arrow points to the site of the stenosis; **C, D.** Right pulmonary artery angiography at the end of the procedure — implanted stents visible, the arrow points to the site of the former stenosis

the procedure it was 16 mm and 8 cm/s, respectively). Computed tomography angiography was performed one week after the procedure and showed three appropriately placed stents in the RPA with no evidence of mechanical damage. The postprocedural 24-hour Holter electrocardiography showed 2 supraventricular extrasystolic beats and 5 ventricular extrasystolic beats; no pauses were observed.

Eight days after the procedure, the patient was discharged from the department. His pharmacological treatment was slightly modified by reducing the dose of bisoprolol to 2.5 mg/day. He was instructed to report to the cardiology outpatient clinic at the centre in a month.

Discussion

The arterial switch operation with VSD closure is the method of choice for the treatment of TBA [2]. The operation is preferably performed early in life, using a primary one-stage approach [2]. According to the European Society of Cardiology CHD guidelines, the most common complications of the ASO include: 1) neo-aortic root dilatation, resulting in aortic regurgitation; 2) supra valvular pulmonary stenosis and pulmonary branch stenosis; 3) problems with the coronary arteries (which can cause LV dysfunction and ventricular arrhythmias); 4) acute angle of the aortic

arch arteries [5]. The LeCompte manoeuvre (frequently performed during ASO) may involve "stretching" of the pulmonary artery branches while moving the pulmonary artery bifurcation anterior to the proximal neo-ascending aorta [6]. This may predispose patients to develop branch pulmonary artery stenosis [6]. The CHD guidelines authors recommend that after ASO, stenting "should be considered for PA branch stenosis, regardless of symptoms, if > 50% diameter narrowing and right ventricular systolic pressure > 50 mm Hg and/or related reduced lung perfusion are present" [5].

In the described case, the patient underwent ASO with VSD closure in the second year of his life. The operation was complicated by significant neoaortic valve regurgitation, which was treated with a Bentall procedure. Coronary artery pathology was excluded by computed tomography angiography performed before cardiac surgery. However, the problem of PA stenosis was serious. The complex, high-risk percutaneous procedure was the only treatment option. Fortunately, it was successful in improving the morphology of the RPA and consequently the function of the RV.

Conclusions

In conclusion, the described case illustrates that with the remarkable development of percutaneous techniques, more and more patients are receiving optimal, personalised treatment for their condition. As the prevalence of CHD increases in the community, it is important to emphasise the need for specialised adult CHD centres to be available to all CHD patients. Lifelong and regular follow-up in such a centre is crucial for all patients in this group.

Article information

Author contributions

ATW — prepared the manuscript; MR, PD, TM, MM, ABD — took part in the clinical decision-making process; MR and ABD — provided medical care for patient; PD — performed the percutaneous procedure; ABD — conceived this study, reviewed and improved the manuscript.

Conflict of interest

The authors declare no conflict of interest.

Ethics statement

Patient consent has been signed and collected in accordance with the journal's patient consent policy.

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Supplementary material

Supplementary material is available at https://journals.viamedica.pl/folia_cardiologica.

Streszczenie

W niniejszej pracy przedstawiono przypadek udanej złożonej interwencji przezskórnej na tętnicach płucnych u 23-letniego pacjenta ze skorygowaną anomalią Taussig–Binga. Wada skorygowana była zabiegiem typu *arterial switch*; ponadto w wywiadzie odnotowano przebytą operację Bentalla i wymianę zastawki mitralnej. Przy przyjęciu pacjent był bezobjawowy, jednak wykryto istotne zwężenie tętnic płucnych. Pacjent został zakwalifikowany do cewnikowania serca. Złożony zabieg wysokiego ryzyka z implantacją trzech stentów poprawił morfologię prawej tętnicy płucnej, a w konsekwencji funkcję prawej komory. Podsumowując, dzięki niezwykłemu rozwojowi technik przezskórnych, coraz więcej pacjentów otrzymuje optymalne, spersonalizowane leczenie.

Słowa kluczowe: wrodzona wada serca, anomalia Taussig–Binga, dwuujściowa prawa komora, interwencja przezskórnaa stentowanie tętnicy płucnej

Folia Cardiologica 2023; 18, 4: 176–181

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HFpEF mimics: hypertrophic cardiomyopathy in light of the 2023 ACC Expert Consensus Decision Pathway on Management of Heart Failure with Preserved Ejection Fraction

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Abstract

Hypertrophic cardiomyopathy is a genetic condition which leads to myocardial hypertrophy. Main cause of death in a group of patients with this disease is sudden cardiac death. In this article we present a diagnostic path which is consistent with the American College of Cardiology Decision Pathway on Management of Heart Failure With Preserved Ejection Fraction diagnostic path. This led to diagnosis of hypertrophic cardiomyopathy and classifying it to the newly established amongst heart failure with preserved ejection fraction group — HFpEF mimics.

Key words: hypertrophic cardiomyopathy, implantable cardioverter-defibrillator, heart failure, sudden cardiac death

Folia Cardiologica 2023; 18, 4: 182–186

Introduction

Hypertrophic cardiomyopathy (HCM) is a disease with a prevalence of 0.02% to 0.23% in adults, and it has a genetic background. The European Society of Cardiology guidelines define HCM as a thickening of the left ventricular wall ≥ 15 mm detected using any imaging method, which cannot be solely explained by its increased load [1]. The pathophysiology of HCM includes not only myocardial hypertrophy but also diastolic dysfunction, mitral regurgitation, myocardial ischemia, and in some patients, left ventricular outflow tract obstruction (LVOTO). The clinical presentation of the disease can take various forms, depending on the predominant pathophysiological factor or as a result of their mutual interactions [2].

According to this year's expert statement from the American College of Cardiology regarding heart failure with preserved ejection fraction (HFpEF), HCM belongs to the newly distinguished group of HFpEF mimics. HFpEF mimics refer to patients with clinical symptoms of heart failure (HF), a left ventricular ejection fraction (LVEF) ≥ 50%, and a primary cardiac cause of HF (infiltrative cardiomyopathy, HCM, valvular heart diseases, diseases of pericardium) or non-cardiac causes of HF (kidney or liver diseases) [3].

The presented case is described in the context of the most current knowledge.

Case report

A 68-year-old female patient was admitted to the hospital due to palpitations, exertional dyspnea, and worsening exercise tolerance. According to the patient, the symptoms had been present for several months and worsened

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over the last few weeks. The patient also complained of presyncopal and syncopal episodes without any preceding warning signs.

Moreover, the patient had a history of thyroidectomy and partial resection of the left kidney due to tuberculosis.

Upon admission, the patient was classified as New York Heart Association class II patient. Physical examination revealed crackles that were audible at the lung bases during chest auscultation, and mild edema of the lower extremities up to the ankles. No other abnormalities were observed.

Chest X-ray showed an enlarged cardiac silhouette. Resting electrocardiogram (ECG) showed sinus rhythm with a heart rate of 65/min and signs of left ventricular hypertrophy (S in V3 + R in aVL > 20 mm).

Transthoracic echocardiography revealed significant asymmetric hypertrophy of the left ventricular myocardium, especially in the parabasal segments of the posterior wall and lateral wall, where thickness of the myocardium reached 18 mm in diastole. There was no increased intraventricular gradient recorded, which in the LVOT was max. 10 mm Hg, nor abnormal anterior mitral valve leaflet motion. The LVEF was preserved, however, elevated filling pressures indicative of diastolic dysfunction were observed.

Selected laboratory test results are shown in Table 1.

It was decided to prolong the Holter ECG monitoring of cardiac function. The 48-hour recording revealed sinus rhythm with an average rate of 63/min, 13 episodes of non-sustained ventricular tachycardia with a maximum rate of 145/min (Figure 1), as well as episodes of ventricular trigeminy lasting a few seconds.

A computed tomography scan of the coronary arteries performed during hospitalisation revealed mural atherosclerotic lesions.

Based on the diagnostic process, HF was diagnosed, and further imaging studies were planned. The patient was prescribed a beta-blocker titrated to heart rate, a statin, a mineralocorticoid receptor antagonist, and an SGLT2 inhibitor. Treatment for reducing uric acid levels was intensified,

Table 1. Results of selected laboratory tests

Total cholesterol	mmol/L	6.16
High-density lipoprotein	mmol/L	1.34
Non-high-density lipoprotein	mmol/L	4.82
Low-density lipoprotein	mmol/L	4.28
Triglycerides	mmol/L	1.21
Na	mmol/L	139.2
K	mmol/L	4.66
Cl	mmol/L	104.3
Glomerular filtration rate	mL/min/1.72 m^2	55.2
Creatinine	µmol/L	94.7
Urea	mmol/L	5.8
N-terminal pro-B-type natriuretic peptide	pg/mL	1778
CA125	U/mL	13
Ferritin	µg/L	18.6
Uric acid	µmol/L	417.8

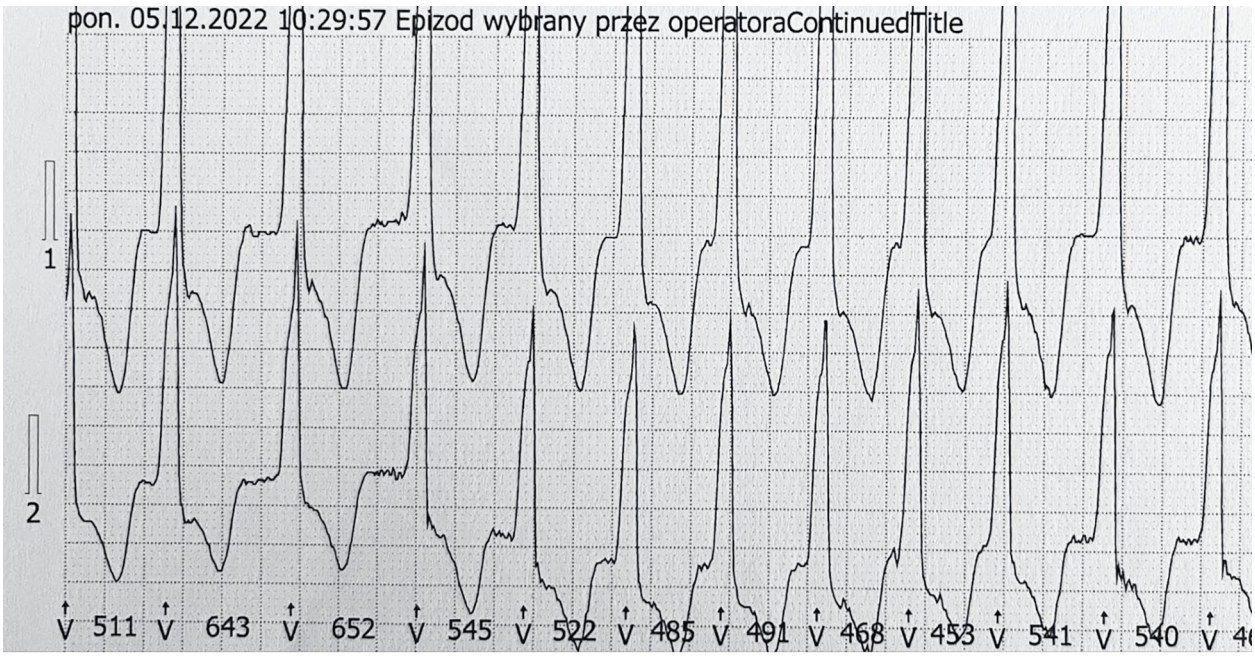

Figure 1. Ventricular tachycardia episode recorded on Holter electrocardiogram recording

and intravenous iron infusion was administered due to concurrent iron deficiency. Single-photon emission computed tomography with 3,3-diphosphono-1,2-propanodicarboxylic acid was performed to rule out amyloidosis, yielding a negative result.

Cardiac magnetic resonance (CMR) imaging was ordered to verify the findings of transthoracic echocardiography and exclude potential storage diseases that may cause myocardial hypertrophy. Myocardial thickening was observed in the basal segments of the anterior wall up to 17 mm, lateral wall up to 20 mm, and inferior wall up to 15 mm, while in the middle segments of the anterior wall, inferior wall and interventricular septum up to 13 mm. Focal and linear intramural areas of increased contrast accumulation indicative of fibrosis were present in the thickened LV segments. The assessed LVEF was 70%. Right ventricular outflow tract subvalvular obstruction resulting from concentric wall thickening was described, without RV enlargement or RV systolic dysfunction. Late gadolinium enhancement (LGE) assessed during CMR reflects the degree of myocardial fibrosis associated with life-threatening arrhythmias and sudden cardiac death (SCD). If LGE is ≥ 15% of LV mass, the patient is at high risk of SCD and implantation of a cardioverter-defibrillator is recommended [4]. However, this parameter was not evaluated in the CMR of this patient due to the lack of appropriate software.

According to the recommended diagnostic process for HFpEF by the ACC, non-cardiac causes such as kidney and liver diseases, and chronic venous insufficiency were excluded in this patient. Then, in accordance with the proposed algorithm, cardiac causes of HF belonging to the newly distinguished group of HFpEF mimics were considered, including secondary cardiomyopathies, HCM, diseases of pericardium, and valvular heart diseases. HCM without LVOTO was diagnosed based on echocardiography and CMR findings. The entire diagnostic process ultimately led to the diagnosis of HFpEF mimics (Figure 2).

The patient's family history did not indicate a history of SCD, and the patient's children were informed about the need for diagnostic evaluation for HCM. Genetic testing was not performed in this patient due to the limited availability of tests for detecting the mutations responsible for the disease.

Based on the patient's symptoms, family history, and additional test results, a 5-year risk of SCD was calculated using the European Society of Cardiology recommended SCD SCORE calculator, resulting in a score of > 6% (Table 2) (https://doc2do.com/hcm/webHCM.html). Consequently, the patient was referred to a reference center for the implantation of a cardioverter-defibrillator as primary prevention of SCD. The patient was also informed that there is no need to restrict physical activity.

Lampert et al. [5] in the observational study LIVE-HCM (Lifestyle and Exercise in Hypertrophic Cardiomyopathy) involving a group of 1660 patients with HCM or genetically predisposed to it did not observe a higher risk of death or life-threatening arrhythmias among patients engaging in intense physical activity compared to

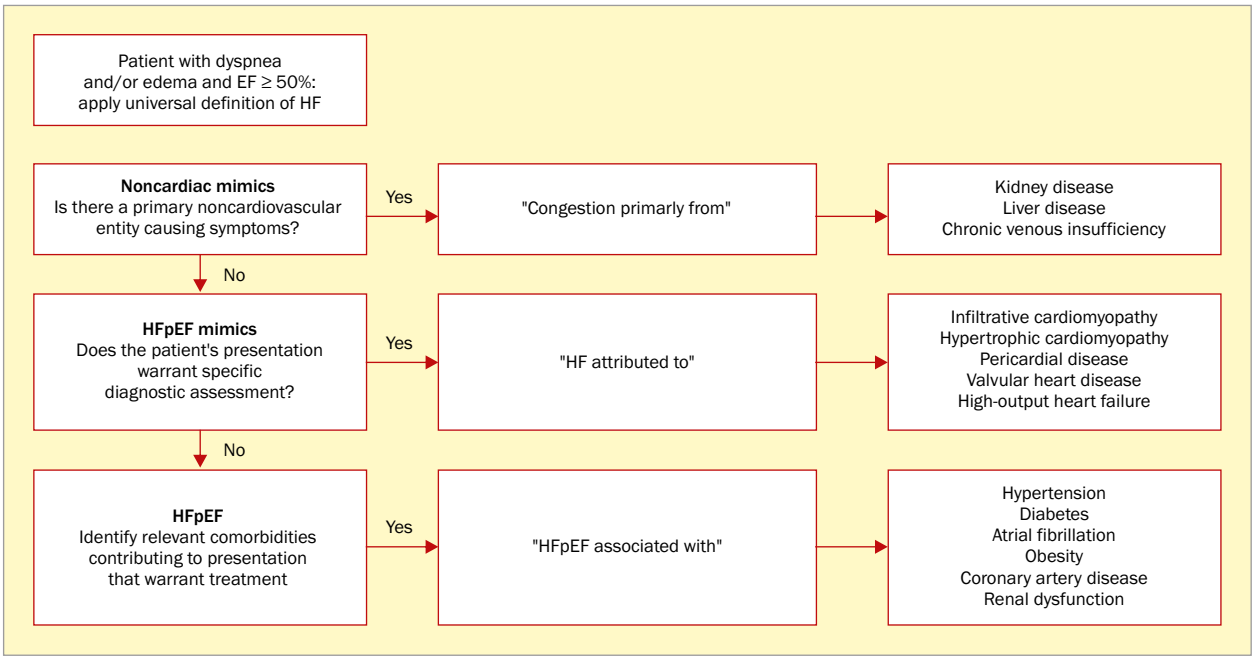

Figure 2. Diagnostic pathway for the diagnosis of HFpEF mimics — based on the 2023 ACC Expert Consensus Decision pathway on management of heart failure with preserved ejection fraction: a report of the American College of Cardiology Solution Set Oversight Committee

Table 2. Data used for calculating the sudden cardiac death (SCD) score using the recommended European Society of Cardiology (ESC) calculator

Age	68 years
Max. left ventricular wall thickness	18 mm
Left atrial dimension	46 mm
Max. gradient in the left ventricular outflow tract	10 mm Hg
Family history of SCD	No
Non-sustained ventricular tachycardia	Yes
Unexplained syncope	Yes
5-year risk of SCD	6.24%
ESC recommendation	Implantable cardioverter-defibrillator should be considered

the group of patients with moderate physical activity or a sedentary lifestyle.

Discussion

The clinical picture of HCM is diverse. The key in the diagnostic process is highly specialised imaging to determine the causes of myocardial hypertrophy and the analysis of numerous variables, such as family history, patient-reported symptoms, the presence of LVOTO, or rhythm disorders. Each of these factors will modify the therapeutic approach. The treatment of HCM is focused on reducing symptoms in patients and preventing SCD. In the case of HCM with concomitant LVOTO, pharmacotherapy will involve beta-blockers without vasodilator effect at the highest doses tolerated by the patient. In cases of intolerance to beta-blockers, verapamil or diltiazem can be considered. Additionally, disopyramide may be added to the treatment, as it contributes to reducing the pressure gradient in the LVOT through its antiarrhythmic and negative inotropic effects.

In situations where the pressure gradient in the LVOT exceeds 50 mm Hg, procedural treatment should be considered, such as Morrow procedure (ventricular septal myectomy) or alcohol (septal) ablation.

Great hopes are associated with mavacamten, a selective cardiac myosin inhibitor, which was first approved for the treatment of this form of HCM in the USA in 2022 [6].

The EXPLORER-HCM trial (mavacamten for treatment of symptomatic obstructive HCM) demonstrated improvements in exercise capacity, reduction of HF symptoms, and LVOTO in the group of patients using mavacamten compared to the placebo group [7].

On the other hand, for patients with HCM without LVOTO who are clinically symptomatic, the medications to be considered include beta-blockers, verapamil or diltiazem, and low doses of loop or thiazide diuretics. There are initial reports on the positive effects of SGLT2 inhibitors in this patient group. In a prospective study involving HCM patients taking these medications for 6 months, there was a significant improvement in LV diastolic function parameters, an increase in the 6-minute walking test distance, and a reduction in N-terminal pro-B-type natriuretic peptide levels compared to the placebo group [8].

In conclusion, the ACC consensus highlights the challenge of diagnosing HFpEF and proposes a new diagnostic algorithm enabling the diagnosis of both cardiac and non-cardiac conditions mimicking HFpEF. It identifies a new group called HFpEF mimics. Diagnosing diseases within this group, which have a different pathophysiological mechanism, allows the application of appropriate targeted therapy.

Article information

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Author contributions

KM and KM — writing; ML — writing and supervision with expertise

Conflict of interest

KM and KM declared no conflict of interest. ML — received lecture and consulting fees from AstraZeneca and Boehringer Ingelheim and were involved in clinical trials from Boehringer Ingelheim.

Ethics statement

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Funding

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Supplementary material

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HFpEF mimics — kardiomiopatia przerostowa w świetle 2023 *ACC Expert Consensus Decision Pathway on Management of Heart Failure with Preserved Ejection Fraction*

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Streszczenie

Kardiomiopatia przerostowa jest uwarunkowanym genetycznie schorzeniem prowadzącym do przerostu miokardium. Może ona przybierać różnorodny obraz kliniczny. Główną przyczyną zgonu w grupie pacjentów z tą chorobą jest nagła śmierć sercowa. W poniższym opisie przedstawiono zgodny ze stanowiskiem eksperckim *American College of Cardiology* proces diagnostyczny niewydolności serca, prowadzący do rozpoznania kardiomiopatii przerostowej oraz zakwalifikowania jej do nowo wyodrębnionej grupy *HFpEF mimics*, czyli chorób imitujących niewydolność serca z zachowaną frakcją wyrzutową lewej komory (HFpEF).

Słowa kluczowe: kardiomiopatia przerostowa, niewydolność serca, nagła śmierć sercowa, implantowalny kardiowerter-defibrylator

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Wstęp

Kardiomiopatia przerostowa (HCM, *hypertrophic cardiomyopathy)* jest schorzeniem, którego częstość występowania u osób dorosłych wynosi między 0,02 a 0,23%, a jego etiologia ma tło genetyczne. Wytyczne Europejskiego Towarzystwa Kardiologicznego (ESC, *European Society of Cardiology*) definiują HCM jako uwidocznione przy użyciu dowolnej metody obrazowania pogrubienie ściany lewej komory wynoszące ≥ 15 mm, którego nie można wytłumaczyć wyłącznie jej nadmiernym obciążeniem [1]. Patofizjologia HCM obejmuje poza przerostem mięśnia sercowego dysfunkcję rozkurczową, niedomykalność mitralną, niedokrwienie miokardium i — u części pacjentów — zwężenie drogi odpływu lewej komory (LVOTO, *left ventricle outflow tract obstruction*). Prezentacja kliniczna choroby może przybierać różne formy, w zależności od dominującego czynnika patofizjologicznego lub być wynikiem ich wzajemnego oddziaływania [2].

Zgodnie z tegorocznym stanowiskiem eksperckim Amerykańskiego Kolegium Kardiologicznego (ACC, *American College of Cardiology*) dotyczącym niewydolności serca z zachowaną frakcją wyrzutową lewej komory (HFpEF, *heart failure with preserved ejection fraction*), HCM należy do wyróżnionej po raz pierwszy grupy chorób imitujących HFpEF (*HFpEF mimics*). *HFpEF mimics* oznacza pacjentów z objawami klinicznymi niewydolności serca (HF) i frakcją wyrzutową lewej komory (LVEF, *left ventricular ejection fraction*) ≥ 50% oraz pierwotną przyczyną HF pochodzenia sercowego (kardiomiopatia naciekowa, HCM, wady zastawkowe, choroby osierdzia) lub pozasercowego (choroby nerek lub wątroby) [3].

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Opisany przypadek przedstawiono w świetle najbardziej aktualnego stanu wiedzy.

Opis przypadku

Sześćdziesięcioośmioletnia pacjentka została przyjęta na oddział z powodu uczucia napadowego kołatania serca, duszności wysiłkowej oraz pogorszenia tolerancji wysiłku. Z wywiadu uzyskanego od pacjentki wynikało, że jej objawy występowały od kilku miesięcy, a w ciągu ostatnich kilku tygodni nasiliły się. Pacjentka skarżyła się również na występowanie stanów przedomdleniowych oraz epizodów utraty przytomności bez objawów zapowiadających.

Ponadto w wywiadzie odnotowano stan po tyroidektomii oraz częściowej resekcji lewej nerki z powodu gruźlicy.

Przy przyjęciu pacjentkę zakwalifikowano do klasy II według Nowojorskiego Towarzystwa Kardiologicznego. W badaniu przedmiotowym podczas osłuchiwania klatki piersiowej słyszalne były przypodstawne trzeszczenia oraz obecne nieznaczne obrzęki kończyn dolnych do wysokości kostek. Nie zaobserwowano innych odchyleń od stanu prawidłowego.

W badaniu rentgenowskim klatki piersiowej uwidoczniono powiększenie sylwetki serca. W elektrokardiogramie (EKG) spoczynkowym rejestrowano rytm zatokowy o częstości 65/min, z cechami przerostu LV (S w V3 + R w aVL > 20 mm).

W badaniu echokardiografii przezklatkowej uwagę zwracał znacznego stopnia asymetryczny przerost mięśnia LV, zwłaszcza przypodstawnych segmentów ściany tylnej oraz bocznej, gdzie grubość mięśniówki osiągała 18 mm w rozkurczu. Nie zarejestrowano zwiększonego gradientu śródkomorowego, który w drodze odpływu lewej komory (LVOT, *left ventricle outflow tract)* wynosił maksymalnie 10 mm Hg, ani nieprawidłowego ruchu przedniego płatka zastawki mitralnej. Frakcja wyrzutowa lewej komory była zachowana, uwidoczniono natomiast świadczące o dysfunkcji rozkurczowej podwyższone ciśnienie jej napełniania.

Wyniki wybranych badań laboratoryjnych przedstawiono w tabeli 1.

Z uwagi na wysunięte podejrzenie HCM, zgodnie z wytycznymi ESC zdecydowano o wydłużeniu monitorowania czynności serca metodą Holter EKG. W trwającym 48 godzin zapisie zarejestrowano rytm zatokowy o średniej częstości 63/min, 13 epizodów nieutrwalonego częstoskurczu komorowego o maksymalnej częstości 145/min (ryc. 1), a także kilkusekundowe epizody trigemini komorowej.

Wykonane podczas hospitalizacji badanie tomografii komputerowej tętnic wieńcowych–uwidoczniło brzeżne zmiany miażdżycowe.

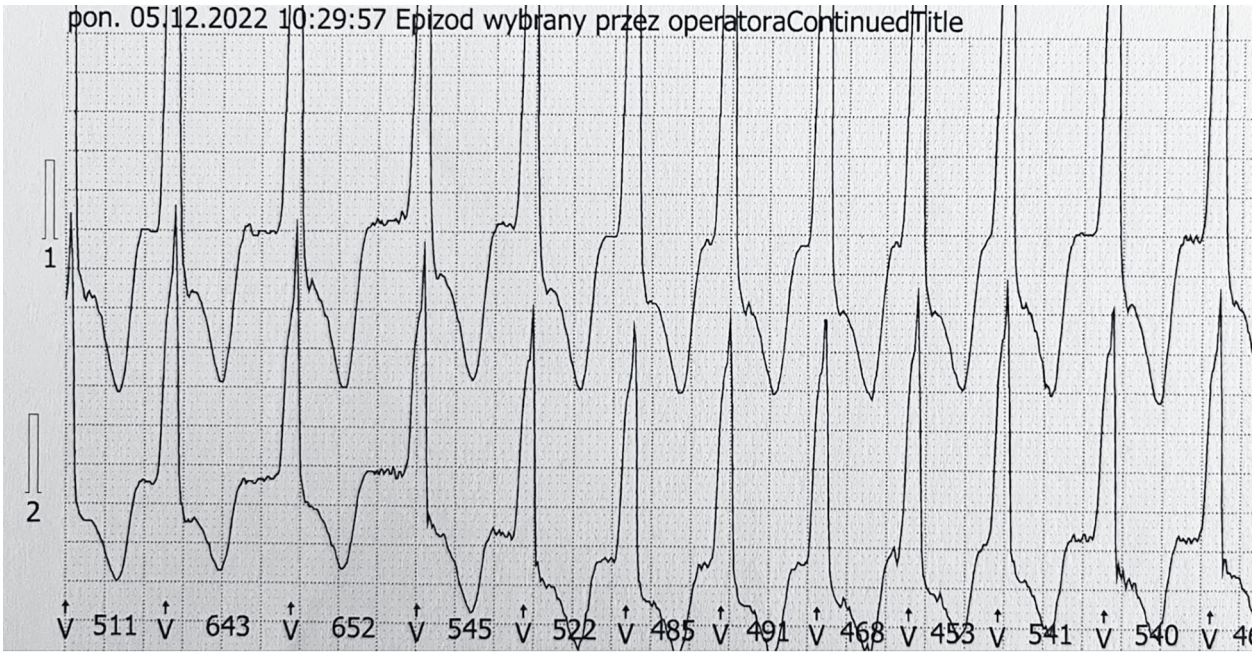
Na podstawie przeprowadzonej diagnostyki rozpoznano niewydolność serca i zaplanowano pogłębienie diagnostyki obrazowej. Włączono beta-adrenolityk w dawce dostosowanej do częstości pracy serca, statynę, antagonistę receptora mineralokortykoidowego oraz inhibitor kotransportera sodowo-glukozowego 2. Zintensyfikowano leczenie obniżające stężenie kwasu moczowego, a z powodu współistniejącego niedoboru żelaza zastosowano wlew dożylny tego pierwiastka. Wykonano również badanie tomografii emisyjnej pojedynczego fotonu z wykorzystaniem kwasu 3,3-difosfono-1,2-propanodikarboksylowego w celu wykluczenia amyloidozy, uzyskując wynik negatywny.

W celu weryfikacji obrazu uzyskanego w badaniu echokardiografii przezklatkowej oraz wykluczenia potencjalnych chorób spichrzeniowych mogących powodować przerost mięśnia sercowego zlecono wykonanie badania rezonansu magnetycznego serca (CMR, *cardiac magnetic resonance*). Pogrubienie miokardium uwidoczniono w obrębie segmentów podstawnych ściany przedniej do 17 mm, ściany bocznej do 20 mm oraz dolnej do 15 mm, natomiast w segmentach środkowych ścian przedniej, dolnej oraz przegrody międzykomorowej do 13 mm. W obrębie pogrubiałych segmentów LV zlokalizowane były śródściennie punktowe oraz linijne ogniska wzmożonego gromadzenia środka kontrastowego świadczące o wystąpieniu zwłóknienia. Oceniona podczas badania LVEF wyniosła 70%. Opisano również podzastawkowe zwężenie w drodze odpływu prawej komory wynikające z okrężnego pogrubienia ścian, bez powiększenia i zaburzeń czynności skurczowej prawej komory. Późne wzmocnienie pokontrastowe (LGE, *late gadolinium enhancement*), oceniane podczas CMR z wykorzystaniem gadolinu, odzwierciedla stopień zwłóknienia miokardium prowadzący do wystąpienia zagrażających życiu arytmii oraz nagłej śmierci sercowej (SCD,

Tabela 1. Wyniki wybranych badań laboratoryjnych

Cholesterol całkowity	mmol/l	6,16
HDL	mmol/l	1,34
Nie-HDL	mmol/l	4,82
LDL	mmol/l	4,28
Trójglicerydy	mmol/l	1,21
Na	mmol/l	139,2
K	mmol/l	4,66
Cl	mmol/l	104,3
Współczynnik przesączania kłębuszkowego	ml/min/1,72 m^2	55,2
Kreatynina	µmol/l	94,7
Mocznik	mmol/l	5,8
N-końcowy propeptyd natriuretyczny typu B	pg/ml	1778
CA125	U/ml	13
Ferrytyna	µg/l	18,6
Kwas moczowy	µmol/l	417,8

HDL (*high-density lipoprotein*) — lipoproteiny o wysokiej gęstości; LDL (*low-density lipoprotein*) — lipoproteiny o niskiej gęstości



Rycina 1. Zarejestrowany w zapisie elektrokardiograficznym metodą Holtera epizod częstoskurczu komorowego

sudden cardiac death). W przypadku kiedy wartość LGE wyniesie ≥ 15% masy LV, pacjent znajduje się w najwyższym stopniu zagrożenia SCD jest u niego implantacja kardiowertera-defibrylatora [4]. Opisany parametr nie został oceniony podczas badania CMR pacjentki z uwagi na brak odpowiedniego oprogramowania.

Zgodnie z zalecanym przez ACC procesem diagnostycznym rozpoznania HFpEF, u pacjentki wykluczono przyczyny pozasercowe, takie jak choroby nerek, wątroby, przewlekłą niewydolność żylną. Następnie, zgodnie z zaproponowanym algorytmem, rozważono kardiologiczne przyczyny niewydolności serca (HF, *heart failure*), należące do grupy *HFpEF mimics*, w tym kardiomiopatie wtórne, HCM, choroby osierdzia, wady zastawkowe. Na podstawie badania echokardiograficznego oraz CMR rozpoznano HCM bez LVOTO. Całość postępowania diagnostycznego ostatecznie pozwoliła rozpoznać *HFpEF mimics* (ryc. 2).

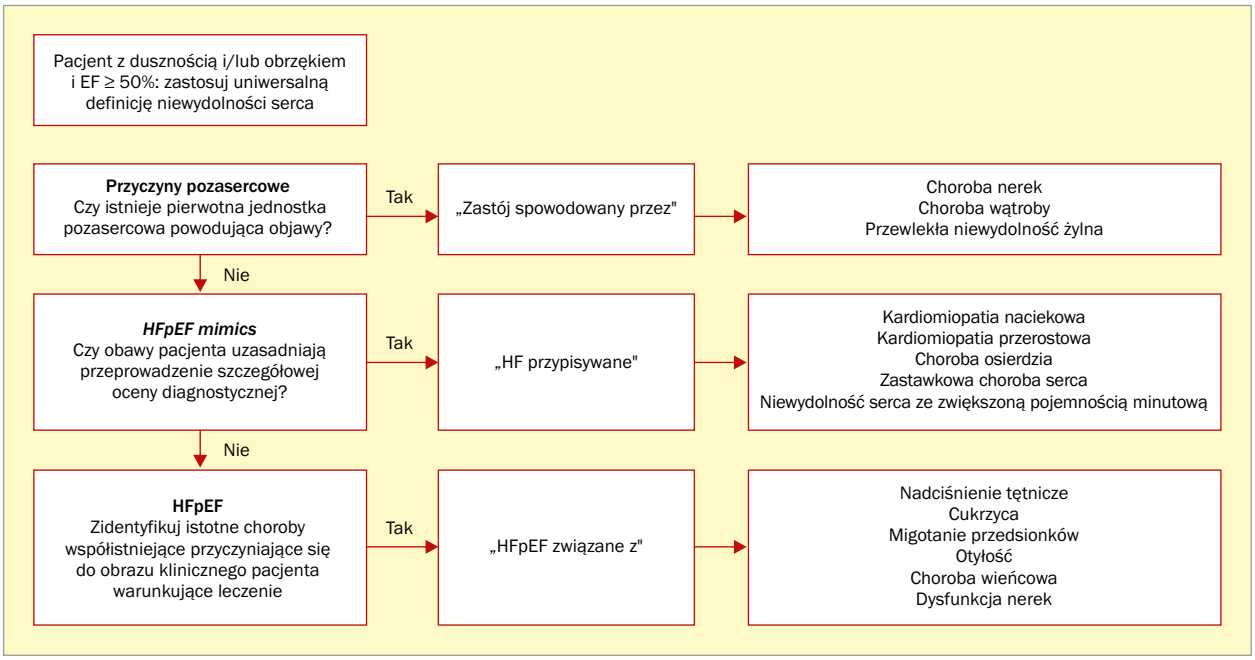
Przeprowadzony z pacjentką wywiad nie wskazywał na wystąpienie w rodzinie SCD, a dzieci pacjentki poinformowano o konieczności poddania się diagnostyce w kierunku HCM. Z powodu małej dostępności badań wykrywających mutacje odpowiedzialne za rozwój choroby, u pacjentki nie przeprowadzono badania genetycznego.

Na podstawie prezentowanych przez pacjentkę objawów, wywiadu rodzinnego oraz wyników badań dodatkowych wyliczono — używając zalecanego przez ESC kalkulatora — 5-letnie ryzyko SCD, które wyniosło > 6% (tab. 2). (https://doc2do.com/hcm/webHCM.html). Chorą skierowano do ośrodka referencyjnego w celu implantacji kardiowertera-defibrylatora w ramach prewencji pierwotnej SCD. Pacjentka została również poinformowana o braku konieczności ograniczania stopnia aktywności fizycznej.

Lampert i wsp. [5] w badaniu obserwacyjnym LIVE-HCM (*Lifestyle and Exercise in Hypertrophic Cardiomyopathy*) na grupie 1660 pacjentów z HCM lub genetycznie predysponowanych do jej wystąpienia nie zaobserwowali, aby pacjenci uprawiający intensywny wysiłek fizyczny mieli wyższe ryzyko zgonu lub zagrażających życiu zaburzeń rytmu serca w porównaniu do grupy pacjentów o umiarkowanym wysiłku fizycznym lub prowadzących siedzący tryb życia.

Dyskusja

Obraz kliniczny HCM jest różnorodny. Kluczowe w procesie diagnostycznym jest wysokospecjalistyczne obrazowanie w kierunku ustalenia przyczyn przerostu mięśnia sercowego oraz analiza licznych zmiennych, takich jak wywiad rodzinny, prezentowane przez pacjenta objawy, obecność LVOTO lub zaburzeń rytmu serca. Każdy z tych czynników modyfikować będzie proces terapeutyczny. Leczenie HCM jest ukierunkowane na zmniejszenie objawów u pacjentów oraz zapobieganie SCD. W przypadku HCM z towarzyszącym LVOTO farmakoterapia skupiać się będzie na lekach beta-adrenolitycznych niemających działania naczyniorozszerzającego w docelowo najwyższych tolerowanych przez pacjenta dawkach lub w przypadku ich nietolerancji — werapamilu bądź diltiazemu. Możliwe jest również dołączenie do leczenia disopyramidu, który poprzez swoje działanie antyarytmiczne oraz inotropowe ujemne przyczynia się do obniżenia gradientu ciśnienia w LVOT.



Rycina 2. Szlak diagnostyczny rozpoznawania HFpEF *mimics* — opracowano na podstawie *2023 ACC Expert Consensus Decision Pathway on Management of Heart Failure With Preserved Ejection Fraction: A Report of the American College of Cardiology Solution Set Oversight Committee*

Tabela 2. Dane wykorzystane do wyliczenia ryzyka nagłej śmierci sercowej (SCD, *sudden cardiac death*) przy pomocy kalkulatora zalecanego przez Europejskie Towarzystwo Kardiologiczne (ESC, *European Society of Cardiology*)

Wiek	68 lat
Max. grubość ściany lewej komory	18 mm
Wymiar lewego przedsionka	46 mm
Maks. gradient w LVOT	10 mm Hg
SCD w wywiadzie rodzinnym	Nie
Nieutrwalony częstoskurcz komorowy	Tak
Niewyjaśnione omdlenia	Tak
Ryzyko SCD w ciągu 5 lat	6,24%
Rekomendacja ESC	Należy rozważyć ICD

LVOT — droga odpływu lewej komory (*left ventricle outflow tract*); ICD (*implantable cardioverter-defibillator*) — wszczepialny kardiowerter-defibrylator

W sytuacji gdy gradient ciśnień w LVOT wynosi > 50 mm Hg, należy rozważyć leczenie zabiegowe, które obejmuje operację Morrowa, czyli miektomię przegrody międzykomorowej lub jej ablację alkoholową.

Duże nadzieje wiązane są z lekiem mawakamten — selektywnym inhibitorem miozyny sercowej, który po raz pierwszy został dopuszczony do leczenia tej postaci HCM w 2022 roku w USA [6].

W badaniu EXPLORER-HCM (*Mavacamten for treatment of symptomatic obstructive hypertrophic cardiomyopathy*) wykazano poprawę wydolności wysiłkowej, zmniejszenie objawów HF oraz LVOTO w grupie pacjentów stosujących mawakamten w porównaniu z placebo [7].

Z kolei w przypadku pacjentów z HCM bez LVOTO, u których występują objawy kliniczne, lekami wymagającymi rozważenia są: beta-adrenolityki, werapamil lub diltiazem oraz małe dawki diuretyków pętlowych lub tiazydowych. Pojawiają się także pierwsze doniesienia o korzystnym wpływie inhibitorów kotransportera sodowo-glukozowego 2 w tej grupie pacjentów. W badaniu prospektywnym, w grupie pacjentów z HCM stosujących te leki przez 6 miesięcy, uzyskano istotną poprawę parametrów funkcji rozkurczowej LV, wzrost dystansu w teście 6-minutowego marszu oraz zmniejszenie stężenia N-końcowego propeptydu natriuretycznego typu B w porównaniu z grupą placebo [8].

Podsumowując, opublikowany przez ACC konsensus zwraca uwagę na wyzwanie, jakim jest rozpoznanie HFpEF, oraz wyodrębnia nową grupę *HFpEF mimics*. Proponuje jednocześnie nowy algorytm diagnostyczny, umożliwiający diagnostykę zarówno kardiologicznych, jak i pozakardiologicznych chorób imitujących HFpEF. Choroby z tej grupy mają inny mechanizm patofizjologiczny, dlatego ich rozpoznanie daje możliwość zastosowania odpowiedniej terapii celowanej.

Informacje o artykule

Podziękowania
—

Wkład autorski
KM and KM — napisanie publikacji; ML — napisanie publikacji, nadzór merytoryczny

Konflikt interesów
KM oraz KM deklarują brak konfliktu interesów. ML — wynagrodzenie za wykłady i konsultacje od firm AstraZeneca i Boehringer Ingelheim, udział w badaniach klinicznych prowadzonych przez firmę Boehringer Ingelheim.

Oświadczenie etyczne
—

Finansowanie
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—

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Ablation of atypical atrial flutter in a patient after radiotherapy for adenocarcinoma of the right lung using the Coherent CARTOPRIME™ module of the CARTO system

Ablacja atypowego trzepotania przedsionków u pacjenta po radioterapii gruczolakoraka płuca prawego z wykorzystaniem modułu Coherent CARTOPRIME™ systemu CARTO

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Abstract

Atrial flutter (AFl) is the second most frequent persistent supraventricular arrhythmia, after atrial fibrillation (AF). In the most common type of AFl the circuit is localized in the right atrium and it is cavotricuspid isthmus dependent, what is termed typical. In atypical AFl the wave front does not go around the tricuspid annulus. It is often associated with prior cardiac surgery or ablation for AF, including linear lesions or defragmentation, where iatrogenic scar serves as the electrophysiologic substrate for reentry. The number of cases, when the circuit is related to a spontaneous low-voltage zone, in the absence of any previous atrial procedures is limited. The reasons behind it might be a significant heart disease, such as mitral valve dysfunction, impaired diastolic function or hypertension, which lead to fibrosis and functional regions of slow or no conduction (SNO, slow or no conduction zone. However, it is still not well understood how electrically silent areas occur in patients without risk factors mentioned above. We present a case report of a patient who suffered damage to the left atrial wall during radiotherapy treatment, and atypical AFl was induced on the basis of the resulting scar.

Key words: atypical atrial flutter, catheter ablation, radiotherapy, lung cancer

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Introduction

Atrial flutter (AFl) is the second most frequent persistent supraventricular arrhythmia, after atrial fibrillation (AF). In the most common type of flutter, the circuit is localized in the right atrium and it is cavotricuspid isthmus dependent, what is termed typical [1]. In atypical AFl the wave front does not go around the tricuspid annulus. It is often associated with prior cardiac surgery or ablation for AF, including linear lesions or defragmentation, where iatrogenic

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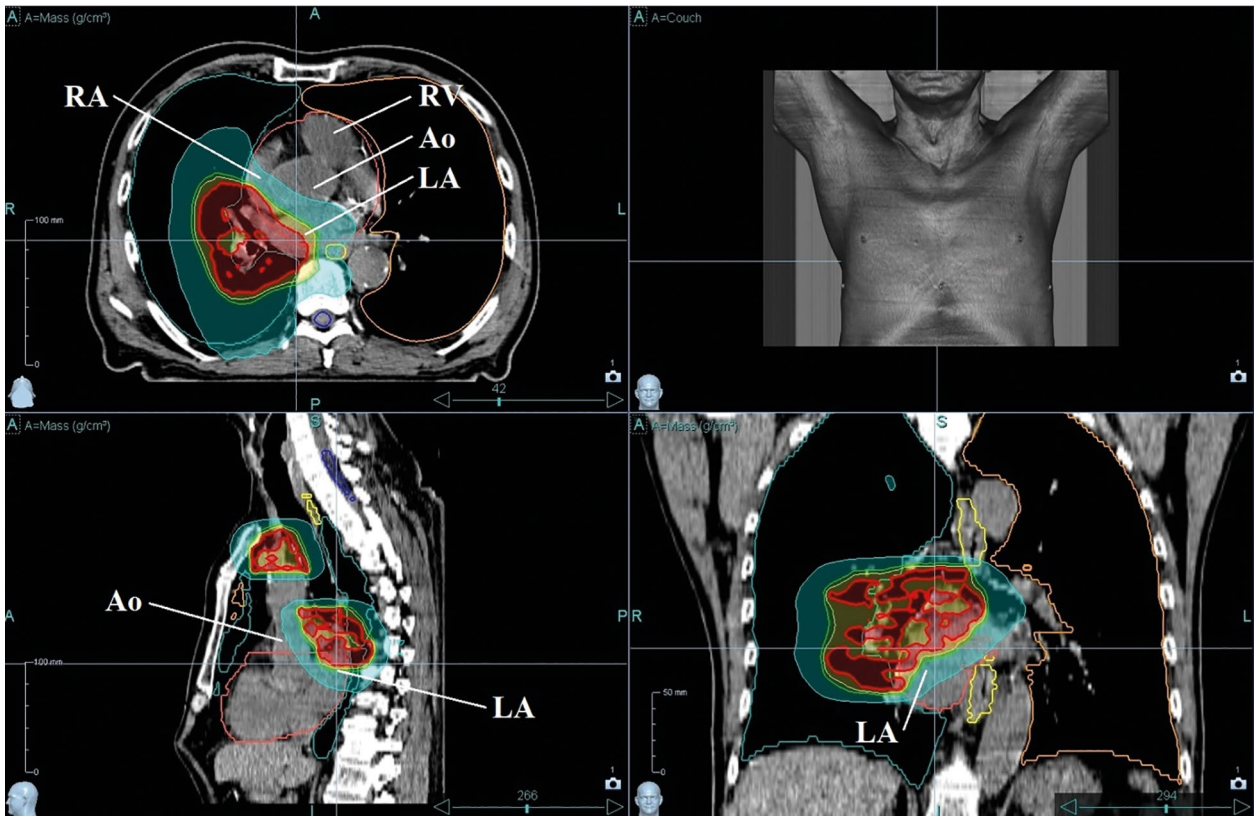

Figure 1. Radiotherapy treatment planning. Red isodose line shows volume receiving dose of 66 Gy or more (Accuray Precision® v2.0.1.1.); Ao — ascending aorta; LA — left atrium; RA — right atrium; RV — right ventricle

scar serves as the electrophysiologic substrate for reentry [1, 2]. The number of cases, when the circuit is related to a spontaneous low-voltage zone (LVZ), in the absence of any previous atrial procedures is limited [3]. The reasons behind it might be a significant heart disease, such as mitral valve dysfunction, impaired diastolic function or hypertension, which lead to fibrosis and functional regions of slow or no conduction (SNO, slow or no conduction zone) [1]. However, it is still not well understood how electrically silent areas occur in patients without risk factors mentioned above [2, 4].

Case report

A 65-year-old patient, who had undergone sequential chemo- and radiotherapy for the adenocarcinoma of the right lung with clinical stage IIIA disease (cT1bN2M0), was admitted to the Cardiology Department due to next episode of atypical AFI. In the patient's medical history, he had undergone successful electrical cardioversion for the same arrhythmia 3 months earlier. The patient had a history of coronary heart disease, having suffered an inferior wall myocardial infarction and undergone right coronary artery angioplasty with the implantation of a drug-eluting stent 12 years before, as well as having heart failure with mildly reduced ejection fraction, an abdominal aortic aneurysm, peripheral arterial disease, nicotinism, hypertension, hyperlipidemia, and hyperthyroidism during treatment. The patient had undergone bladder tumor resection 3 years prior. Patient received oncological treatment, which consisted of 5 cycles of chemotherapy (carboplatin with vinorelbine) and sequentially given radiotherapy. Irradiated volume included right lung tumor, right hilum, subcarinal and right paratracheal lymph nodes. Prescribed dose was 66 Gy in 33 fractions. Patient was treated in helical tomotherapy technique. Mean heart dose was 12.54 Gy and volume receiving more than 30 Gy was 11% (Figure 1). Patient ended radiotherapy 6 months before admission to Cardiology Department without serious adverse events. On admission to Cardiology Department, an electrocardiogram showed atypical AFI with an atrial cycle length of approximately 210ms and a ventricular rate of about 114 per minute (Figure 2). Due to the recurrence and symptoms of the patient's arrhythmia, after ruling out thrombotic material in the left atrium, he was qualified for ablation of the arrhythmia substrate. Using a 3D CARTO electroanatomic system (Biosense Webster, Inc., Diamond Bar, CA, USA) and PentaRay electrode (Biosense Webster,

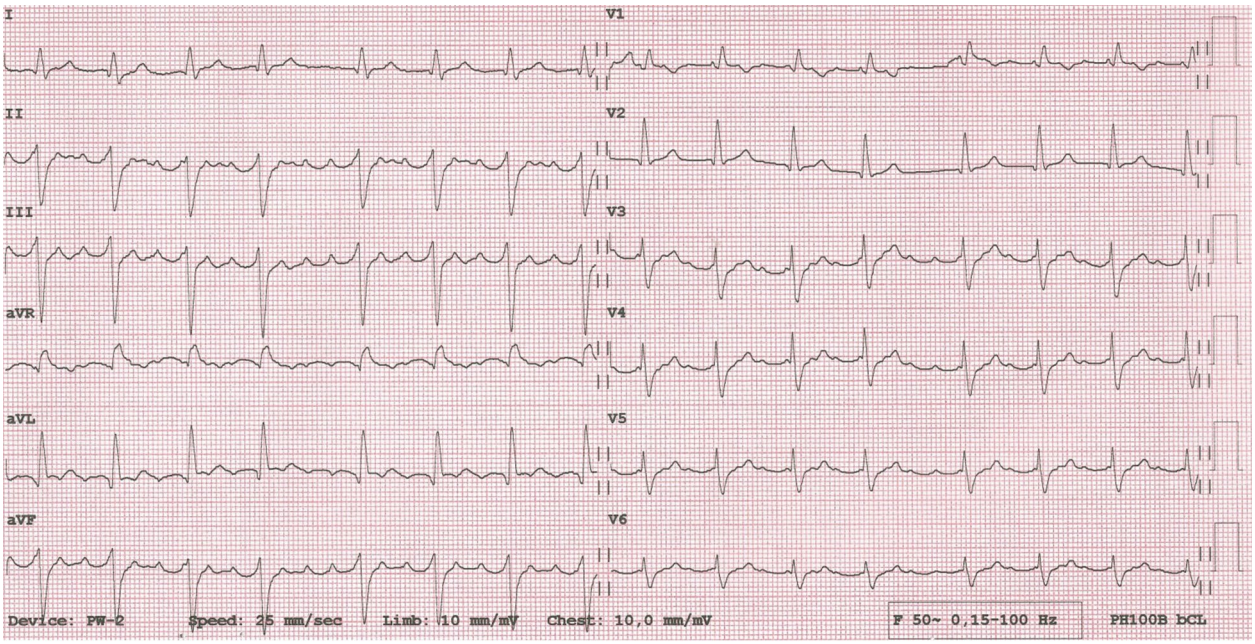

Figure 2. Electrocardiogram with atypical atrial flutter

Inc., Diamond Bar, CA, USA), the left atrium was mapped and SNO was located on the posterior wall of the atrium near the right pulmonary vein ostia. The propagation of AFI activation was then determined using the Coherent CARTOPRIME™ module of the CARTO system, and the critical isthmus of the arrhythmia was located on the roof of the left atrium near the right superior pulmonary vein ostium (Figure 3). Two applications of 40W of radiofrequency energy were then delivered to the site of the critical isthmus of the atypical AFI using a Smarttouch SF electrode (Biosense Webster, Inc., Diamond Bar, CA, USA), resulting in the termination of the arrhythmia and the restoration of sinus rhythm (Figures 4 and 5). Due to the location of the SNO near the pulmonary vein ostia and the risk of recurrence of atypical AFI, additional applications were made around the right pulmonary veins to isolate them and connect the SNO with the isolated right pulmonary veins. An electrophysiological study and aggressive atrial stimulation were then performed, but no arrhythmia was induced, so the left pulmonary veins were not isolated. No recurrence of atrial arrhythmias was observed during a 12-month follow-up observation period.

Discussion

The number of studies on radiotherapy-induced cardiotoxicity for patients with lung cancer is limited. This is mainly due to the fact that side effects of radiotherapy occur many years after treatment [5], while the 5-year survival rate for patients undergoing radio- and chemotherapy for non-small cell lung cancer is low.

The statement of the European Society of Cardiology published in 2016 on the treatment of cancer and cardiovascular toxicity states that arrhythmias occur in 16–36% of patients after radiotherapy. The problem is to determine the direct impact of radiotherapy alone on the occurrence of cardiac events. It is because of the frequent comorbidities, the direct impact of the cancer itself and additional chemotherapeutic treatment [6].

Our case report suggests the possibility of forming a low-voltage zone in the atrium due to radiotherapy. This can be a background for macro reentry arrhythmia, secondary to fibrosis caused by thoracic irradiation. Ischaemia because of artery branch occlusion, inflammation, atrial dysplasia may stand behind regional electrical conduction disturbances [7, 8]. However, AF is a more frequent occurrence in the fibrotic area [9]. In addition, a very few studies have singled out atypical AFI among episodes of arrhythmia after radiotherapy. That might be because the differentiation between atypical AFI and AF is not clear until performing intracardiac electrophysiology study.

The coexistence of coronary artery disease, hypertension, heart failure in our patient is also associated with a higher risk of AFI [1].

Radiotherapy treatment plan review revealed that significant part of planning target volume, which received full prescribed dose, was overlapping with right and posterior part of left atrium (Figure 1). High dose regions in this particular volume are potentially responsible for arrhythmia [10]. Mechanism of cardiac toxicity is complex and includes molecular, inflammatory, vascular, immunological and fibrotic mechanism [11].

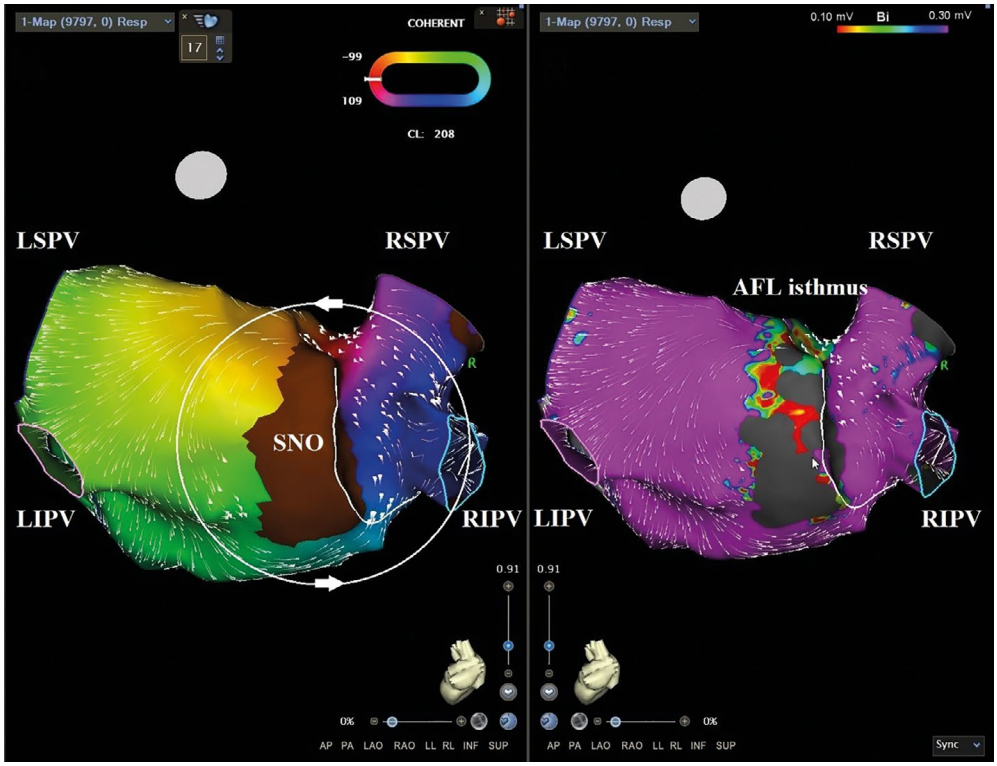

Figure 3. Electroanatomical map of the left atrium of the heart: **A.** Activation map of atypical atrial flutter with the Coherent Mapping module. Macro-reentry loop around the scar zone on the posterior wall of the left atrium near the RSPV and RIPV ostia with the critical isthmus in the roof of the left atrium at the RSPV ostium; **B.** Voltage map of left atrium; LIPV — left inferior pulmonary vein; LSPV — left superior pulmonary vein; RIPV — right inferior pulmonary vein; RSPV — right superior pulmonary vein; SNO — slow or no conduction zone

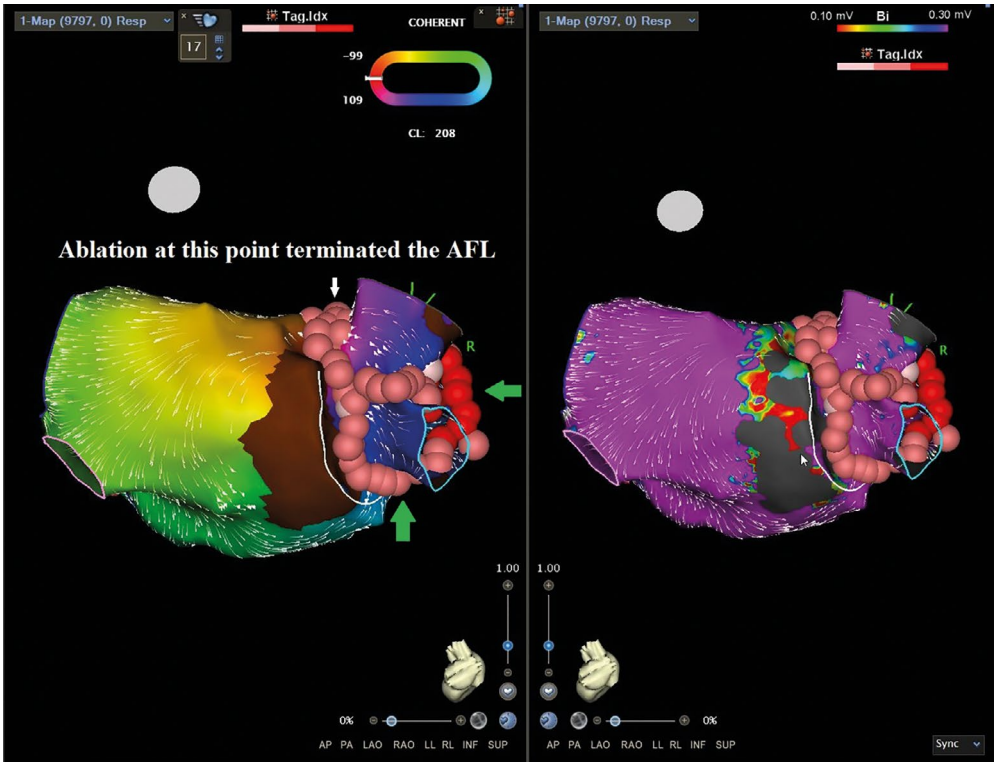

Figure 4. Radiofrequency catheter ablation points around the right pulmonary veins. The first applications performed in the critical isthmus of atypical atrial flutter (AFL) terminated arrhythmia (white arrow). Subsequent applications (green arrows) were then made to isolate the right pulmonary veins to reduce the risk of recurrence of typical AFL

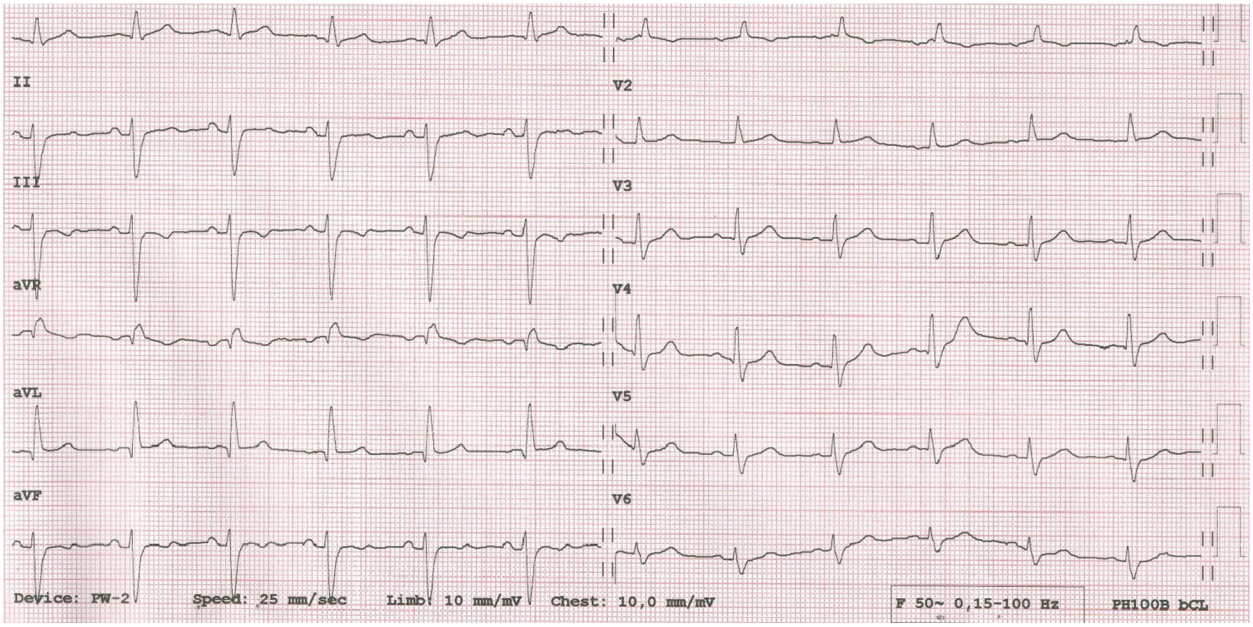

Figure 5. Sinus rhythm 72 per minute after ablation

In research of Vaidya et al. [12] it is reported that among patients with an incident of AF previously treated with radiotherapy for cancer, the frequency of concomitant AFl was higher than in the general AF population. What is more, patients treated with radiotherapy were less likely to have a history of heart failure, but had a similar rate of coronary artery disease.

Another study describing the occurrence of AFl flutter in a group of 112 patients who underwent radiotherapy for stage III non-small cell carcinoma was study by Wang et al. [13]. In this study, 26 (23.2%) patients experience a cardiac event, including 12 (8.9%) who had an arrhythmia. The study also focused on the effect of radiation dose on the rate of cardiac events. It has been shown that a mean dose above 20 Gy significantly increases the risk of cardiotoxic effects.

In a retrospective study conducted between 2010 and 2015 by Borkenhagen et al. [14] in a group of 76 patients, an association between radiation doses to individual heart structures and the appearance of cardiotoxicity was found. In this study atrial arrhythmias were found in 5 (6.6%) patients.

In a study by Dess et al. [15] in a group of 125 patients, 37 (29.6%) had cardiac events, including 11 (8.8%) arrhythmias. However, in the study group, 84% were undergoing chemotherapy and 27% had pre-existing heart disease, which may have influenced the development of myocardial conduction disturbances.

Errahmani et al. [16] conducted a study in which they assessed the occurrence of cardiac arrhythmias in breast cancer patients treated with radiotherapy with a radiation dose to the whole heart, left and right atrium, and right and left ventricle. In this study, despite the insignificant results, the authors emphasized that patients with right-sided breast cancer and irradiated right atrium may require special attention due to the risk of arrhythmias and conduction disturbances.

Hashiguchi et al. [17] demonstrated that in patients with breast cancer treated with radiotherapy, there is a tendency to a greater LVZ in the left atrium. However, the existence of LVZ did not differ significantly between the breast cancer cohort and the control group.

Article information

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Author contributions
PW — 70%; JW — 10%; MD — 10%; MM — 1%; PD — 1%; RS — 3%; BWK — 5%.

Conflict of interest
The authors declare no conflict of interest.

Ethics statement
The case report did not require approval from the Bioethics Committee. Data in the manuscript are anonymised.

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Streszczenie

Trzepotanie przedsionków (AFl) jest drugą po migotaniu przedsionków (AF) pod względem częstości występowania przetrwałą arytmią nadkomorową. W najczęstszym typie AFl obwód arytmii zlokalizowany jest w prawym przedsionku, jest zależny od cieśni trójdzielno-żylnej (CTI), a określa się go mianem typowego. W atypowym AFl obwód arytmii nie jest zależny od CTI. Atypowe AFl często związane z wcześniejszą operacją kardiochirurgiczną lub ablacją AF, w tym linijnymi zmianami lub defragmentacją, gdzie jatrogenna blizna służy jako elektrofizjologiczne podłoże do stworzenia obwodu arytmii. W praktyce klinicznej rzadko dochodzi samoistnego tworzenia stref nieskonapięciowych w ścianie przedsionków. W większości przypadków przyczyną może być choroba serca, taka jak dysfunkcja zastawki mitralnej, upośledzona funkcja rozkurczowa lub nadciśnienie tętnicze, które prowadzą do zwłóknienia i tworzenia obszarów czynnościowych o wolnym lub zerowym przewodzeniu potencjału elektrycznego. Jednakże nie jest jasne, w jaki sposób powstają strefy niskonapięciowe w ścianie przedsionków u pacjentów bez czynników ryzyka przedstawionych powyżej. W niniejszej pracy przedstawiono przypadek pacjenta, u którego doszło do uszkodzenia ściany lewego przedsionka podczas leczenia radioterapią, a na podłożu powstałej blizny doszło do indukcji atypowego AFl.

Słowa kluczowe: atypowe trzepotanie przedsionków, ablacja, radioterapia, rak płuca

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