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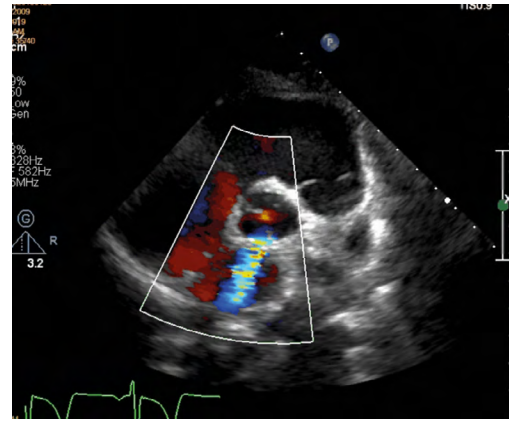

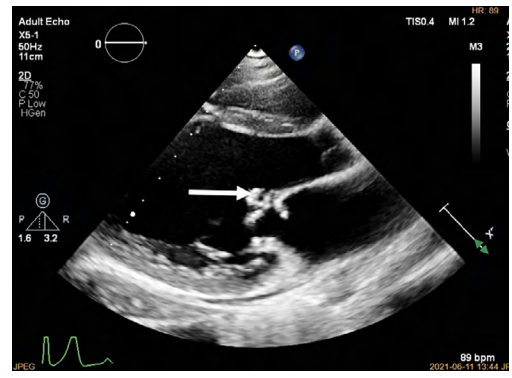

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2022, vol. 17, no. 6

Table of Contents/Spis treści

ORIGINAL ARTICLES/PRACE ORYGINALNE

REVIEW ARTICLES/PRACE POGLĄDOWE

CASE REPORTS/PRACE KAZUISTYCZNE

CARDIAC SURGERY/ KARDIOCHIRURGIA

REPORT/ SPRAWOZDANIE

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Assessment of physical activity of people employed in the IT sector during the COVID-19 pandemic

Ocena poziomu aktywności fizycznej osób zatrudnionych w sektorze IT podczas pandemii COVID-19

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Abstract

Introduction. Assessing the physical activity of IT workers during the COVID-19 pandemic can help to discern its hypothetical relationship with gender, the form of work, or other factors.

Material and methods. The study lasted from July 29, 2021 to September 14, 2021. For the assessment, a questionnaire was conducted based on the IPAQ-SF (International Physical Activity Questionnaire — Short Form) and original questions about the impact of the COVID-19 pandemic on lifestyle, including physical activity assessed on the scale –3/0/3. 363 employees of the IT sector (63 women, 300 men; average age: 29; average BMI 26.17) met the conditions for inclusion in the study.

Results. In total, 26.17% were in the insufficient group, 54% in the sufficient group and 19.83% in the high physical activity group. Overall, 51.24% estimated that the pandemic had a negative effect on their physical activity, 31.40% had no effect, and 17.36% had a positive impact.

Conclusions. IT sector employees are mostly characterized by low physical activity. Therefore, they meet the WHO guidelines for the amount of physical activity with a positive effect on health. There are no interactions in mentioned population between undertaking various types and intensities of physical activity and gender, working shifts and working methods. In future research on physical activity, it is worth considering other factors that may be behind it.

Key words: physical activity; public health; COVID-19 pandemic; lifestyle medicine

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Introduction

Restrictions introduced during the coronavirus disease 2019 (COVID-19) pandemic had a significant negative impact on lifestyle changes. On March 20, 2020, the Polish government declared an epidemic state in Poland [1] and introduced numerous restrictions to limit the spread of the COVID-19 virus: recommended self-isolation, quarantine periods, closure of sports facilities, fitness clubs, gyms and swimming pools. These restrictions resulted in a significant reduction in opportunities for physical activity [2]. Findings indicate that the changes have affected people's lifestyles

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and may have an impact on medical problems that will pose significant challenges to the healthcare system in the years to come [3, 4].

IT workers, due to the nature of their work, spend most of their time working at a computer, in a sitting position. According to the World Health Organization (WHO), a sedentary lifestyle contributes to an increased risk of type 2 diabetes, hypertension or mental health disorders, i.e.: depression, anxiety. In order to minimise the risk, extended periods of physical activity of any intensity are recommended [5]. For 18–64 year-olds, the WHO recommends 150–300 minutes of moderate- or 75–150 minutes of high-intensity activity per week.

Physical inactivity and its consequence — obesity — are modifiable risk factors for most non-communicable diseases [6]. They increase mortality and result in fewer years of disability-free life [7, 8].

This study aims to assess physical activity in IT workers during the COVID-19 pandemic and investigate if, among these individuals, there was a link between undertaking physical activity (of different types and intensities) and gender/form of work/work shift.

Material and methods

Design and selection for the study

The cross-sectional study was designed and made available online, through various social media channels (bringing together people employed in the IT sector, e.g., Facebook groups, Instagram, private companies) and e-mails (personal correspondence), approximately 1.5 years after the outbreak of the COVID-19 pandemic in Poland from July 29, 2021 to September 14, 2021. Responses were collected using the online survey application Google Sheets and processed into an Excel file for analysis. The inclusion criteria for the study was employment in the IT sector (regardless of seniority or location). Data were collected from 416 respondents and 363 of them met all the conditions of the survey. Respondents who answered "I am unable to specify" to any of the questions from the International Physical Activity Questionnaire — Short Form (IPAQ-SF) [9] were excluded. There were no other exclusion criteria. The IPAQ-SF form, in a validated Polish version, was chosen for the survey. The choice of the questionnaire was due to its simple question and answer design, sufficient to provide an initial preview of the physical activity of this group.

Population characteristics

A total of 416 IT employees took part in the survey, 363 of whom met the conditions of the survey (63 women, 300 men). The respondents ranged in age from 18 to 64 years, with a median age of 29 years. The height of the participants averaged 178.7 cm (SD = 8.14), while body weight was 47–135 kg. The mean body mass index (BMI) was 26.17 kg/m^2 (SD = 4.81) and the median was 25.35 kg/m^2. The demographic characteristics of the participants including gender, BMI category, experience, form of work during the pandemic (remote work, work at the place of employment, hybrid work) and work shift are shown in Table 1. Those declaring to work the first shift worked from morning to afternoon hours, while those declaring to work the second shift worked from afternoon to morning hours. Respondents who marked the distractor "other" did not have one work shift and worked both first and second shift over the course of a week or month.

Table 1. Demographic data and weight of respondents

Variables		Number (%)
Respondents	Participants	363 (100)
	Women	63 (17.36)
	Men	300 (82.64)
BMI	Underweight	5 (1.38)
	Normal body weight	172 (47.38)
	Overweight	115 (31.68)
	Obesity	71 (19.56)
Experience (position)	Junior	55 (15.15)
	Mid/Regular	155 (42.70)
	Senior	153 (42.15)
Work shift	First shift	312 (85.95)
	Second shift	5 (1.38)
	Other (First or second shift per week OR first or second shift per month)	40 (11.02)
	No data	6 (1.65)
Form of work	Remote work	236 (65.01)
	Work at the place of employment	32 (8.82)
	Hybrid work	95 (26.17)

Questionnaire structure

The questionnaire included a statement of voluntary participation in the survey and the objectives of the survey, as well as an anonymity and confidentiality clause. Completion and submission of the questionnaire was tantamount to informed consent to participate in the study. Sociodemographic data such as age, gender and self-reported biometric data on height and weight were collected. Respondents, given their employment in the IT sector, were asked about their experience in the industry (Junior, Mid/Regular, or Senior), the form of work during the pandemic (hybrid, remote, or at the place of employment), and their work shift. Using questions from the IPAQ-SF, physical activity (including walking time) and time spent sitting

during the day were examined. The questionnaire included additional –3/0/+3-scaled questions on respondents' subjective assessment of the impact of the pandemic on their physical activity.

IPAQ-SF

The IPAQ-SF was used for estimating the amount of time spent on physical activity during the week. This questionnaire is adapted to many populations (including Polish population). The IPAQ-SF assesses three specific types of activity: walking, moderate (sufficient) physical activity and intense physical activity. Due to the scoring protocol, data are converted to MET-minutes/week values. Metabolic equivalent (MET) is a specific metabolic equivalent and its values vary for each category of energy expenditure (3.3 MET for walking, 4 MET for moderate-intensity physical activity and 8 MET for high-intensity physical activity). In order to calculate the weekly energy expenditure (MET-minutes/ /week) for each type of physical activity, the following formula is used: weekly energy expenditure (MET-min/week) = MET × exercise duration (minutes) × frequency. The total MET-minutes/week is the sum of walking MET-min/ /week, moderate activity MET-min/week and intense activity MET-min/week. According to the scoring protocol of the IPAQ-SF, participants were categorised into three levels of physical activity: insufficient, sufficient and high.

Participants categorised as having a high level of physical activity:

— performed intense exercise (total min. 1500 MET-min/ /week) for minimum 3 days per week;
— or undertook min. 7 days of any combination of efforts of varying intensity levels exceeding 3000 MET- -min/week.

Participants in the sufficient physical activity group:

— performed min. 20 minutes of intense exercise per day for min. 3 days a week;
— or performed 30 minutes of moderate exercise (or walking) for min. 5 days a week;
— or performed any combination of physical activity (walking, moderate or intense exercise) — 600 MET-min/ /week.

Participants in the insufficient physical activity group did not undertake any activity or did not meet the criteria for a high or sufficient level.

Those with sufficient, satisfactory levels met the WHO guidelines for recommended physical activity with a positive effect on health.

The final question in the IPAQ-SF asked about daily sedentary time, obtaining it in hours and minutes.

Author questions

Respondents matched the level of perceived change resulting from the pandemic in –3/0/+3-scaled questions. Responses of –3 to –1 meant that the pandemic had a negative effect, a response of 0 meant no effect and responses of +1 to +3 meant a positive effect.

Data analysis

All statistical analyses were performed using STATISTICA 13 statistical software (StatSoft Inc., Tulsa, OK, USA). Participants were divided into subgroups (gender, form of work, work shift). Based on the mean responses and the results of the statistical tests, the direction of correlation (positive or negative) was assessed. The Mann–Whitney U test and χ^2 test were performed to verify the hypothesis of non-significance of differences between the medians and verify the correlation between type and intensity of physical activity/gender. The Kruskal–Wallis test was performed to calculate of the correlation between type and intensity of physical activity/form of work, type and intensity of physical activity/work shift. The Spearman's rank correlation coefficient test was performed to analyse the correlation between BMI and type of physical activity. The Shapiro–Wilk test was performed to assess the distribution of variables.

Results

Physical activity of respondents and time spent sitting

The average amount of time during which surveyed IT employees performed activities requiring either intense or moderate physical activity ranged from 0 to 150 minutes (median = 30 minutes) per day. The average amount of time for walking more than 10 minutes continuously ranged from 0 to 200 minutes per day (median = 29 minutes).

In the case of the IT sector on weekdays, the total time spent sitting ranged from 4 to 20 hours on weekdays, with a median of 10 hours.

After the calculation of all the respondents' physical activity values and time spent sitting, and taking into account the IPAQ-SF scoring protocol, the participants were divided into three physical activity categories: high, sufficient, insufficient, as shown in Table 2.

Table 2. Number and percentage of respondents according to high, sufficient or insufficient levels of physical activity

Level of physical activity	Number of persons	Percentage of persons
High	72	19.83%
Sufficient	196	54.00%
Insufficient	95	26.17%

Table 3. Correlations between type of physical activity and body mass index (BMI)

Variable	BMI
Engaging in activities that require intense physical activity (that cause significant acceleration of breathing and heart rate, for example, aerobics, fast running, fast cycling, digging)	p = 0.55 R Spearman = 0.031
Doing activities that require moderate physical activity (which leads to slightly faster breathing and a slightly faster heartbeat, for example, lifting lighter weights, cycling at normal pace, playing volleyball)	p = 0.588 R Spearman = –0.029
Walking min. 10 min. continuously (including strolling or walking home)	**p = 0.006*** **R Spearman = –0.144**
Sitting (including weekdays, Monday to Friday)	p = 0.33 R Spearman = 0.051

*When $p < 0.05$, the result is statistically significant

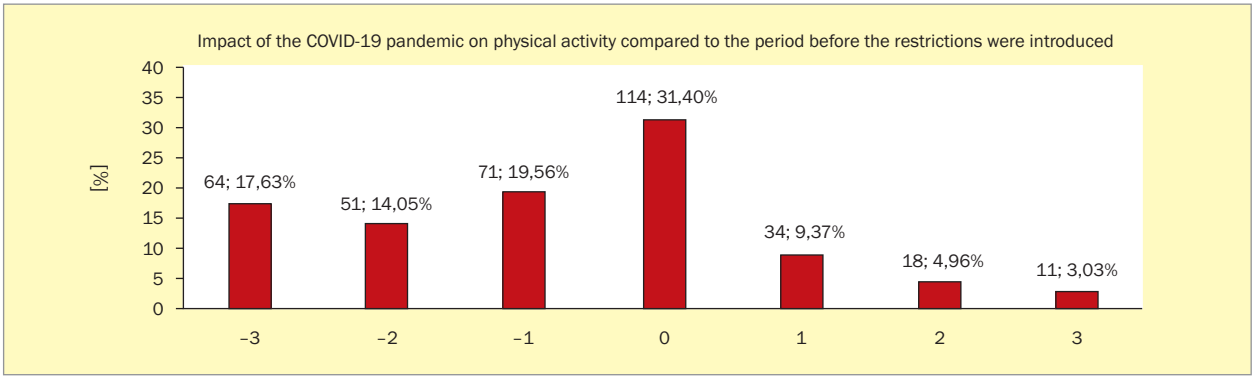

Figure 1. Responses to the question about self-reported opinion on the impact of the pandemic on physical activity (expressed in number of respondents and percentages)

Correlations

The statistical correlations obtained in the study are shown in Table 3. The only statistically significant variable is walking min. 10 minutes continuously, which correlates with a lower BMI.

Results of a question about the self-reported opinion on the impact of the COVID-19 pandemic on physical activity

The majority of respondents (51.24%) reported a reduction in physical activity due to the COVID-19 pandemic (responses ranging from –3 to –1). Less than half of respondents (31.40%) recognised its neutral impact on this area of lifestyle (response 0), while a significant minority (17.36%) noticed an increase in physical activity (responses 1 to 3). The responses are shown in Figure 1.

Discussion

A subjective lifestyle assessment of the participants revealed that the COVID-19 pandemic had a negative impact on their physical activity. More than half of respondents, 51.24%, noticed a reduction in its level due to the global situation. This may have been caused by a reduction in opportunities for physical activity (closure of sports facilities: gyms, swimming pools, fitness clubs) to which employers encourage their employees, for example, by providing them with subsidised starter packs or giving them benefits, i.e.: MultiSport cards. Other studies have also shown a negative impact of the pandemic on physical activity [10–13].

The majority of respondents worked from home (remote work) during the pandemic (65.01%), which may have been a factor in the long time spent sitting during the day. According to Hernández et al. [14] study involving remote workers, 70.1% reported a more sedentary lifestyle due to the pandemic. The change of workplace from office to home may also have affected the reduction in physical activity because some corporations allow physical activity by providing sports equipment in the office.

The participants from the IT sector, after converting the MET values and referring to the IPAQ criteria, were mostly characterised by a sufficient level of physical activity (54%). In contrast, this is due to the relatively long duration of walking rather than the duration of physical

activity undertaken. Insufficient levels of physical activity were 26.17%. Another study involving Biobank employees in the United Kingdom indicates inadequate levels of physical activity in IT workers, which was not observed in other employees [15]. While it can be assumed that the IT sector is characterised by this lifestyle, a survey conducted on office workers of Swiss organisations in Switzerland and using the same questionnaire provides different results. That survey revealed an insufficient level of physical activity at 17%; however, a significant number of respondents in that survey were women (71.10%) compared to the other surveys [16]. This suggests that there is a relationship between gender and physical activity levels, but there was no such correlation in this study. In contrast, longer walking time was found to correlate with lower BMI ($p = 0.006$), with the majority of respondents having a BMI indicating a normal body mass (47.38%) or overweight (31.68%).

No other Polish studies investigating these areas in the IT sector were noted during the material collected. This survey was conducted on employees of various IT companies, thus providing a broader and more generalised overview of the physical activity of this group.

The limitations of this survey relate, among other things, to the inadequacies of the self-reported questionnaire method used in the IPAQ-SF. Respondents gave answers based on what they were able to recall. It cannot be ruled out that the amounts of physical activity entered in this survey were indicative, i.e., they could turn out to be as much or less in reality. The respondents may also have omitted short, sporadic activities, which would also have affected the results. Responses were collected using an online questionnaire, making it impossible to verify the identity of the person who filled it in. The lack of surveys of persons with a similar lifestyle (resulting from professional work, i.e.: office work/IT sector) prior to the pandemic is another limitation, as it is thus impossible to indicate how the COVID-19 pandemic affected the physical activity of such a group.

Conclusions

This survey reveals that IT employees are mostly characterised by sufficient levels of physical activity. As such, they meet the WHO guidelines for the amount of physical activity undertaken with a positive effect on health. Moreover, neither the work shift nor gender, nor form of work are related to undertaking physical activity of different types and intensities. It can be assumed that there are other factors that determine this or, if the group of respondents had been more numerous (especially the representation of women), such relationships would have emerged. In the future, it is worth exploring this, starting by consulting experienced individuals in the IT sector and comparing physical activity levels to other non-IT office workers. The COVID-19 pandemic alone had a negative impact on the uptake of physical activity in more than 50% of the population.

Conflict of interest

None declared.

Streszczenie

Wstęp. Ocena aktywności fizycznej pracowników sektora IT podczas pandemii COVID-19 może pomóc dostrzec jej hipotetyczny związek z płcią, formą pracy czy innymi czynnikami.

Materiał i metody. Badanie trwało od 29 lipca 2021 do 14 września 2021. W celu dokonania oceny przeprowadzono ankietę opartą o IPAQ-SF (*International Physical Activity Questionnaire — Short Form*) oraz autorskie pytania dotyczące wpływu pandemii COVID-19 na styl życia, w tym aktywność fizyczną ocenianą w skali –3/0/3.Warunki włączenia do badania spełniło 363 pracowników sektora IT (63 kobiety, 300 mężczyzn, średni wiek: 29 lat, średni wskaźnik masy ciała: 26,17 kg/m^2).

Wyniki. Łącznie 26,17% badanych znajdowało się w grupie niewystarczającej, 54% w grupie dostatecznej i 19,83% w grupie wysokiej aktywności fizycznej. Oszacowano, że pandemia miała negatywny wpływ na aktywność fizyczną wśród 51,24% badanych, brak wpływu — 31,40%, a pozytywny wpływ u 17,36%.

Wnioski. Wśród badanych pracowników sektora IT, większość wykazywała niską aktywność fizyczną. W związku z tym spełniają oni warunki wytycznych Światowej Organizacji Zdrowia dotyczące podejmowanej aktywności fizycznej o pozytywnym wpływie na zdrowie. Wśród tej populacji nie dostrzeżono powiązania między podejmowaniem aktywności fizycznej różnego rodzaju i o różnej intensywności a płcią, formą pracy ani zmianą, podczas której się pracuje. W kolejnych badaniach dotyczących aktywności fizycznej warto rozważyć wzięcie pod uwagę innych czynników, które mogą to determinować.

Słowa kluczowe: aktywność fizyczna, zdrowie publiczne, pandemia COVID-19, medycyna stylu życia

Folia Cardiologica 2022; 17, 6: 323–328

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Cardiac remodeling and right ventricular function in patients with end-stage renal disease one year since maintenance hemodialysis initiation

Przebudowa serca oraz funkcja prawej komory u pacjentów ze schyłkową niewydolnością nerek rok po włączeniu hemodializoterapii

Patrycja Anna Lebioda, Katarzyna Piestrzeniewicz

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Abstract

Introduction. Due to the increasing number of patients requiring renal replacement therapy and bidirectional interactions between kidneys and heart, known as reno-cardiac syndrome, the assessment of dialysis influence on heart performance has become paramount.

Material and methods. This was a prospective study analyzing data of 22 adult patients with end-stage renal disease, referred for maintenance hemodialysis (HD) at our Dialysis Centre between January 2019 and December 2019.

Results. The median age of the patients was 59.5 (51–64) years, and 55% of the study group were females. The most common comorbidities were hypertension (86%) and diabetes (36%). At one-year follow-up, there was a significant decrease in proximal and distal right ventricular outflow tract (RVOT) dimensions ($p = 0.04$; $p = 0.007$ respectively) and in isovolumic acceleration time corrected ($p = 0.01$). As the result of the prolongation of isovolumic relaxation time corrected ($p < 0.001$) and isovolumic contraction time corrected ($p < 0.001$) a significant increase in myocardial performance index (MPI) ($p < 0.001$) was observed.

Conclusions. In patients with end-stage renal disease long-term HD negatively impacts RV function. Isovolumic acceleration and MPI measured with pulsed tissue Doppler are sensitive indicators of changes in RV function.

Key words: echocardiographic assessment, end-stage renal disease, dialysis, right ventricular function

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Introduction

End-stage renal disease (ESRD), defined as the estimated glomerular filtration rate below 15 mL/min/1.73 m^2, is a growing problem around the world due to the rising life expectancy and widespread civilization diseases leading to kidney function deterioration. Current projections indicate that by 2030 the ESRD population requiring renal replacement therapy, the most prevalent of which remains hemodialysis (HD), may reach over 5 million [1].

Cardiovascular diseases are the leading cause of death in ESRD patients. There is a strong bilateral relationship

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between renal and heart function known as a reno-cardiac syndrome. Renal failure is one of the leading comorbidities that require adequate management in the overall strategy to retard the developing heart failure [2].

Left ventricular (LV) dysfunction is an acknowledged causality factor of adverse clinical outcomes [3]. Recently the significance of right ventricular (RV) function has been highlighted [4]. Particular attention was given to dialyzed patients. Hemodialysis is associated with increased risk of pulmonary hypertension, a condition that has a negative effect on right ventricular structure and function and is recognized as a predictor of mortality in these patients [5].

Echocardiography (ECHO) is the most commonly used cardiac imaging modality competent in recognizing subclinical myocardial abnormalities of both LV and RV. There are reports showing that conventional ECHO, which is easily repetitive and widely accessible, remains accordant with novel methods like two-dimensional speckle tracking ECHO [6] or cardiac magnetic resonance (CMR) imaging [7].

The aim of the study was to investigate whether the HD implementation worsens RV function detectable by conventional echocardiographic methods. Uncovering subclinical RV myocardial abnormalities might help to identify endangered patients and therefore optimize and individualize therapy.

Material and methods

Study design and population

Out of ESRD patients referred for maintenance HD (3 times per week) at the Dialysis Station in Central Clinical Hospital in Lodz 30 consecutive patients in the period from January 2019 to December 2019 were initially selected for the prospective echocardiographic study focused on RV function. Exclusion criteria were: indication for acute HD, severe valvular disease, atrial fibrillation, severe pulmonary hypertension, LV systolic dysfunction, and poor acoustic window for ECHO.

Clinical and echocardiographic examination and blood tests were performed before HD initiation and 12 months later (11.3 ± 0.2 months). Eight patients were lost to follow-up: 6 patients have withdrawn from the study for personal or social reasons (including COVID-19 pandemic fear) and 2 patients died. Finally, data from 22 patients were analysed.

Each patient was completely informed of the purpose and procedure of the study and provided written informed consent. The study was performed in compliance with the Helsinki Declaration and with Good Clinical Practice standards and was approved by the local Bioethical Committee (RNN/135/17/KE, 11/04/2017).

Echocardiographic examination

The patients underwent transthoracic echocardiographic examinations with conventional, Doppler, and pulsed tissue Doppler imaging (TDI) using ultrasonography Vivid E95 system with S4 probe and simultaneous ECHO recording.

Transthoracic echocardiographic examinations were performed within 24 hours after completion of the second thrice-weekly HD (midweek HD). It allowed achieving optimal dry weight to avoid volume overload that might interfere with cardiac time intervals and overestimate pulmonary pressures. As the heart rate influences the duration of cardiac time intervals all the time measurements were corrected for heart rate according to the following formula: $x/\sqrt{RRinterval}$. Echocardiographic measurements were obtained by the same physician and consecutive 3-beat averaged values were reported.

Standard echocardiographic examination was performed according to the recommendations of the Working Group on Echocardiography of the Polish Cardiac Society [8]. Additionally, several RV morphology and function measurements and calculations were made according to the guidelines endorsed by the European Association of Echocardiography and the American Society of Echocardiography [9, 10]. Pulsed tissue Doppler traces at the tricuspid annulus on RV free wall were used to obtain velocities and cardiac time intervals (Figure 1). The analysed RV parameters included:

1. The RV and right atrium dimensions measured at end-diastole from a RV–focused apical 4-chamber view;
2. RV fractional area change (FAC) obtained by tracing the RV endocardial border at end-diastole and end-systole from the apical 4-chamber view;
3. Tricuspid annular plane systolic excursion (TAPSE);
4. RV systolic longitudinal myocardial tissue velocity (S');
5. RV isovolumic acceleration (IVA) calculated by dividing the peak isovolumic myocardial velocity at isovolumic contraction by the time from the onset to peak velocity measured at the lateral tricuspid annulus;
6. Cardiac time intervals:
   - isovolumic contraction time (IVCT): from the end of the a' wave to the beginning of the s' wave,
   - ejection time: from the beginning of the s' wave to the end of the s' wave,
   - isovolumic relaxation time (IVRT): from the end of the s' wave to the beginning of the e' wave.

An active myocardial relaxation plays a predominant role in RV filling pattern. IVRT duration is affected by systolic pulmonary pressure (sPAP), right atrial pressure and heart rate. Elevated sPAP delays the opening of tricuspid valve which results in prolongation of IVRT while increased right atrial pressure leads to a premature opening of the tricuspid valve and shortening of IVRT.

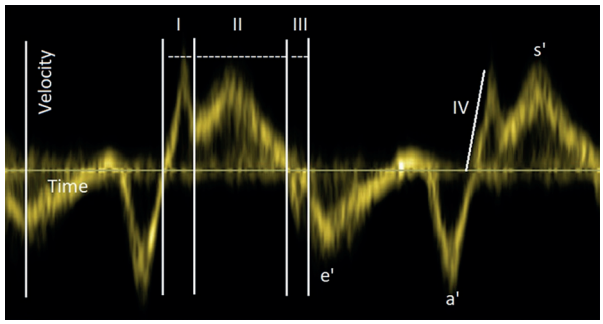

Figure 1. Velocities and cardiac time intervals obtained by pulsed tissue Doppler trace at the tricuspid annulus on the right ventricular free wall; I) isovolumic contraction time; II) ejection time; III) isovolumic relaxation time; IV) isovolumic acceleration; a' — late diastolic tricuspid annular velocity; e' — early diastolic tricuspid annular velocity; s' — peak systolic tricuspid annular velocity

7. RV myocardial performance index (MPI) — an index of global RV performance was calculated using the formula MPI = (IVCT + IVRT)/ejection time.

It is worth mentioning that echocardiographic assessment of the duration of the cardiac time intervals may be performed with the use of conventional pulse wave Doppler, however, measurements performed with pulsed wave TDI are less affected by heart rate, preload, and severity of tricuspid regurgitation and allow simultaneous measurement of both the diastolic and systolic intervals in the same cardiac cycle.

Laboratory measurements

Fasting blood samples for routine measurements including N-terminal pro-brain natriuretic peptide (NT-proBNP) were taken at baseline and at follow-up on the same day as echocardiographic examination (the day after the midweekly HD).

Statistical analysis

All the data from the study were analyzed using STATISTICA 13.3 software (TIBCO, Palo Alto, CA, USA). Qualitative data were shown as numbers, values, and percentages. In order to compare qualitative variables, Chi-squared test was performed and small samples were tested using Fisher's exact test. Continuous variables were reported as median with interquartile ranges (25–75 percentile). Normality was checked using the Shapiro-Wilk test. Comparisons between values before and after HD initiation were made with Wilcoxon signed-rank test. Statistically significant differences are graphically presented on diagrams.

Table 1. Baseline characteristics of the study group

Variable	Study group (n = 22)
Age [years]	59.50 (51–64)
Female, n (%)	12 (55)
BMI [kg/m^2]	28.84 (24.62–33.56)
Diabetes mellitus, n (%)	8 (36)
Smoking, n (%)	5 (23)
Hypertension, n (%)	19 (86)
Creatinine [μmol/L]	588.20 (469.40–731.00)
Urea [mmol/L]	18.52 (14.98–26.75)
Hb [g/dL]	11.35 (10.30–12.40)

Continuous variables are expressed as median (interquartile range [IQR]) and categorical variables as number (percentage); BMI — body mass index; Hb — hemoglobin

Results

Baseline clinical, biochemical and echocardiographic characteristics of 22 ESRD patients who have initiated the maintenance HD is presented in Table 1. RV and LV structure and function parameters at baseline and follow-up are shown in Table 2 and Table 3, respectively.

Right ventricular dimensions, systolic and diastolic function were within normal limits both at baseline and follow-up. There was a tendency to reduction in RV diameters during observation period. Significant reduction was observed with regard to the right ventricular outflow tract (RVOT) proximal and distal diameter ($p = 0.04$; $p = 0.007$, respectively) (Figure 2, Table 2) and in the value of IVA ($p = 0.01$) (Figure 3, Table 2). Significant increase in IVRTc ($p < 0.001$) and IVCTc ($p < 0.001$) and consequently in MPI ($p < 0.001$) was noted (Figure 4, Table 2). No significant changes in LV were shown at follow-up.

Discussion

There is a well-established high prevalence of cardiovascular morbidity and mortality in ESRD patients early after HD initiation [11]. Some of the potential causes are linked to changes in cardiac structure and function.

RV is designed to work in a low-pressure system and its adaptability properties are limited. It has been shown that arteriovenous fistula (AVF) for dialysis access results in the AVF-dependent volume overload that induces RV dysfunction, which affects LV function via ventricular interdependence. In HD patients the cumulative impact of AVF shunt, uremia, fluid retention, renal anemia, and inflammation affects RV performance [12]. The influence of HD

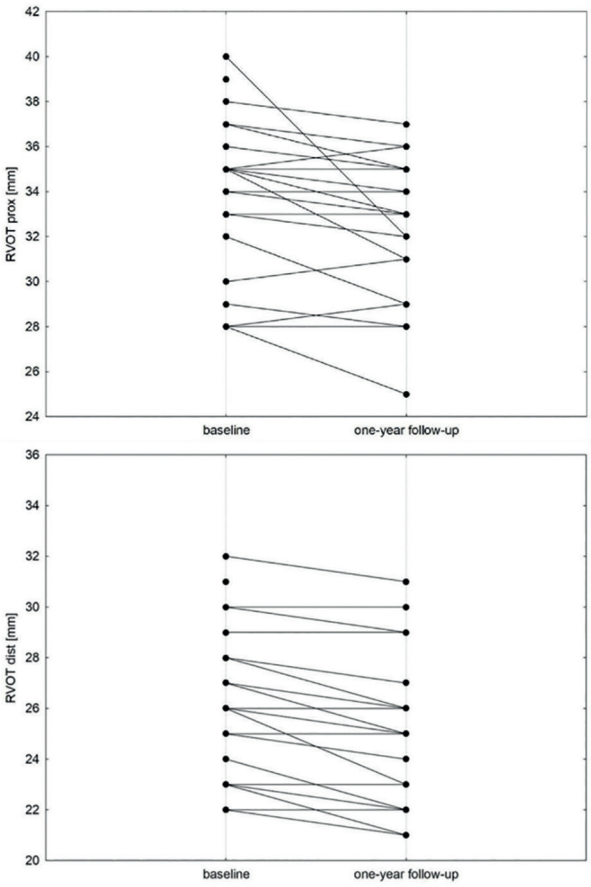

Figure 2. Right ventricular outflow tract proximal ($RVOT_{prox}$) and distal ($RVOT_{dist}$) diameter at baseline and one-year follow-up

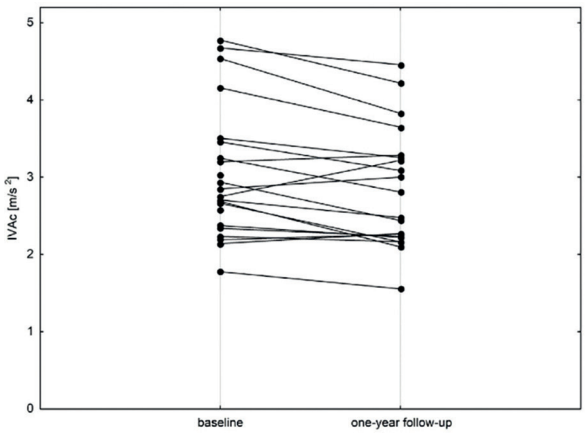

Figure 3. Isovolumic acceleration time corrected for heart rate (IVAc) at baseline and at one-year follow-up

on RV dysfunction and its contribution to increased cardiovascular events is associated with deep uncertainties and the data concerning identification of early RV malfunction indices are scarce. There are studies assessing short term changes of RV parameters e.g. TAPSE, S', FAC, MPI, before and after a single HD procedure, that show improvement of RV function associated with preload reduction [13].

In our group of patients, the proximal and distal right ventricular outflow tract (RVOT) dimensions were significantly lower at follow-up transthoracic echocardiographic examinations whereas diastolic and systolic RV area and FAC

Table 2. Right ventricular structure and function parameters at baseline and one-year follow-up

Parameter	Baseline	Follow-up	p-value
RAA [cm^2]	15.65 (13.70–17.10)	16.30 (13.20–19.00)	0.67
FAC [%]	0.47 (0.40–0.57)	0.47 (0.40–0.58)	0.99
RV_{basal} [mm]	36.00 (34.00–37.00)	35.00 (32.00–43.00)	0.24
RV_{mid} [mm]	30.00 (25.00–34.00)	27.00 (23.00–33.00)	0.82
RV_{long} [mm]	61.00 (55.00–67.00)	60.50 (54.00–69.00)	0.12
$RVOT_{prox}$ [mm]	34.00 (30.00–35.00)	32.50 (29.00–35.00)	**0.04**
$RVOT_{dist}$ [mm]	26.00 (24.00–28.00)	25.00 (23.00–27.00)	**0.007**
TR V_{max} [m/s]	2.28 (2.10–2.50)	2.30 (2.10–2.50)	0.77
SPAP [mm Hg]	24.00 (21.00–29.00)	25.00 (20.00–28.00)	0.71
IVRTc [ms]	69.29 (57.98–80.83)	82.62 (72.18–98.07)	**< 0.001**
IVCTc [ms]	67.41 (58.33–81.06)	76.08 (64.4–87.81)	**< 0.001**
ETc [ms]	317.43 (302.45–335.35)	322.91 (304.92–347.83)	0.29
MPI	0.44 (0.38–0.50)	0.49 (0.45–0.58)	**< 0.001**
IVAc [m/s^2]	2.80 (2.37–3.51)	2.69(2.24–3.29)	**0.01**
TAPSE [mm]	27.00 (25.00–30.00)	25.00 (24.00–28.00)	0.65
S' [cm/s]	14.00 (12.00–15.30)	12.75 (11.00–15.00)	0.17
AcTc [ms]	122.28 (111.26–142.49)	121.55 (112.58–137.68)	0.83

AcTc — pulmonary artery acceleration time corrected for heart rate; ETc — ejection time corrected for heart rate; FAC — fractional area change; IVAc — isovolumic myocardial acceleration corrected for heart rate; IVCTc — isovolumic contraction time corrected for heart rate; IVRTc — isovolumic relaxation time corrected for heart rate; MPI — myocardial performance index; RAA — right atrial area; RV_{basal} — right ventricular basal diameter; RV_{long} — right ventricular longitudinal diameter; RV_{mid} — right ventricular mid-cavity diameter; $RVOT_{dist}$ — distal diameter of right ventricular outflow tract; $RVOT_{prox}$ — proximal diameter of right ventricular outflow tract; S' — tricuspid annular systolic velocity; SPAP — systolic pulmonary arterial pressure; TAPSE — tricuspid annular plane systolic excursion; TR V_{max} — maximal velocity of tricuspid regurgitation

Table 3. Left ventricular structure and function parameters and NT-proBNP at baseline and one-year follow-up

Parameter	Baseline	Follow-up	p-value
EF_{LV} [%]	61.00 (56.00–65.00)	58.50 (55.00–65.00)	0.11
LVDD [mm]	51.00 (48.00–56.00)	49.50 (46.00–53.00)	0.08
TDI e'_{LV} [cm/s]	7.50 (5.60–8.00)	6.85 (4.50–8.50)	0.10
E/e'_{LV}	9.48 (6.88–12.73)	10.20 (10.20–8.82–12.36)	0.19
LAVI [mL/m^2]	36.50 (29.00–49.00)	38.50 (28.00–48.00)	0.25
D1 [mm]	51.00 (48.00–54.00)	49.00 (45.00–54.00)	0.04
D2 [mm]	50.00 (48.00–54.00)	50.00 (47.00–54.00)	0.41
D2/D1	1.00 (0.96–1.02)	1.02 (0.98–1.07)	0.64
NT-proBNP [pg/mL]	2 744.00 (926.60–10 416.00)	2 579.00 (818.40–10 950.00)	0.88

D1 — left ventricular short-axis diameter perpendicular to the septum; D2 — left ventricular short-axis diameter parallel to the septum; D2/D1 — eccentricity index; E/e'_{LV} — early mitral inflow velocity and mitral annular early diastolic velocity ratio; EF_{LV} — left ventricular ejection fraction; LAVI — left atrial volume index; LVDD — left ventricular diastolic dimension; NT-proBNP — N-terminal pro-brain natriuretic peptide; TDI e'_{LV} — tissue Doppler-derived mean early diastolic mitral annulus velocity

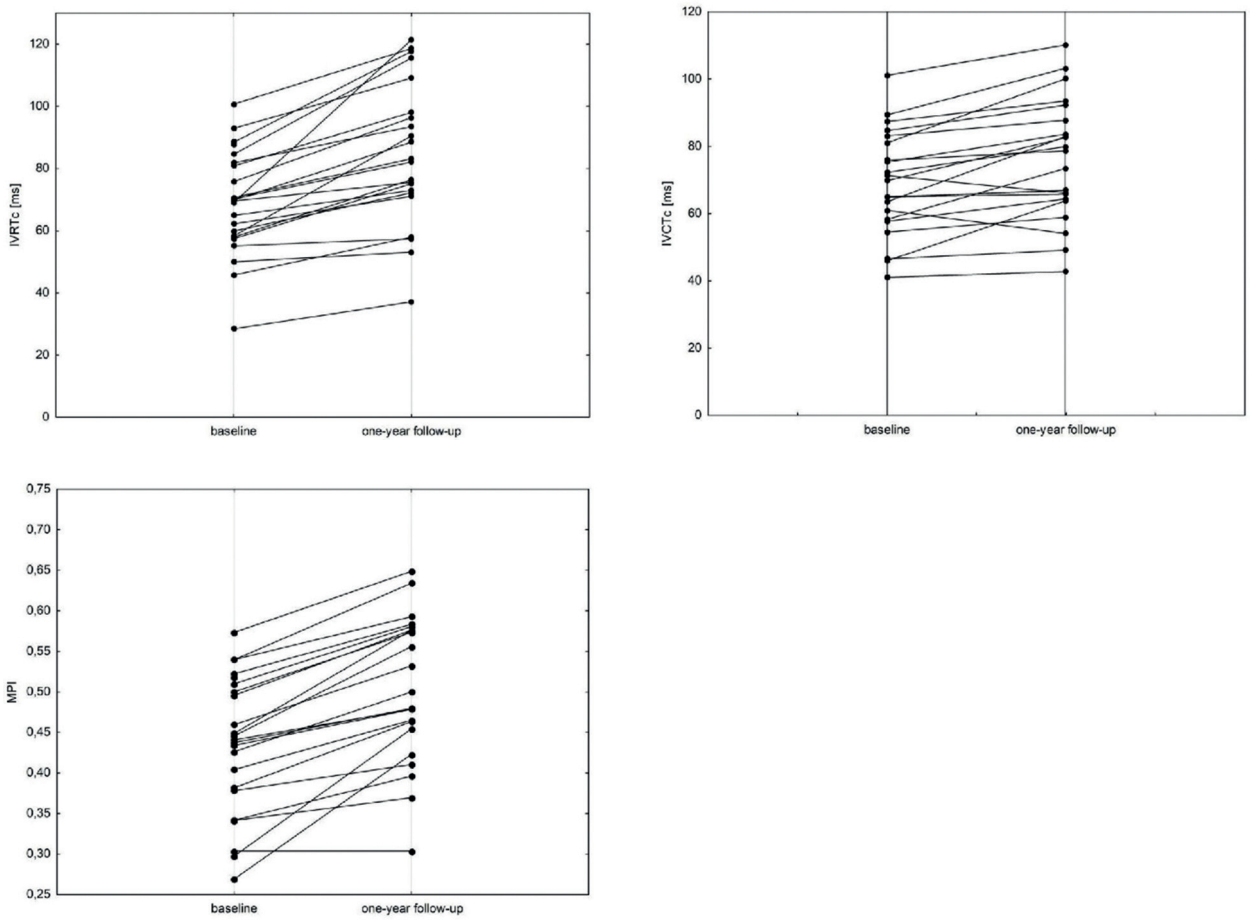

Figure 4. Isovolumic relaxation time (IVRTc), isovolumic contraction time (IVCTc) and myocardial performance index (MPI) corrected for heart rate at baseline and at one-year follow-up

did not differ significantly. However trend for a decrease in TAPSE and S' was noted suggesting a deterioration in RV longitudinal function. These results are inconsistent with the study of Tanasa et al. [6]. These authors, with the use of two-dimensional speckle tracking ECHO, revealed amelioration of RV function at 3, 6, and 12 months compared to the pre-HD values.

Despite the limitations of TAPSE and S' such as neglecting the contribution of RV radial shift and being influenced by overall heart motion, these parameters are easily reproducible, significantly related to right ventricular ejection fraction calculated (EF_{RV}) on CMR [14]. TAPSE has been shown to be related to RV FAC assessed by ECHO. FAC is a more comprehensive parameter, incorporating both the longitudinal and radial planes of RV, and is related to EF_{RV} assessed with CMR [14]. Moreover, significant relation between FAC, TAPSE, and S' with EF_{RV} assessed by three-dimensional speckle-tracking ECHO (3D STE) has been shown [15]. In patients with heart failure, TAPSE and FAC have proven prognostic value. Reduced S' at the beginning of HD was confirmed as a powerful predictor of mortality [16].

Our study showed interesting observations regarding cardiac time intervals. However, none of these parameters is recommended as a single marker of RV function or pulmonary artery pressure (PAP) due to their intrinsic limitations. At follow-up we have shown a significant increase in RV heart rate-adjusted IVRTc and IVCTc, increase in MPI and decrease in IVAc all of these suggesting impairment of RV function. Active myocardial relaxation plays an important role in RV filling pattern and prolonged IVRT is an early indicator of diastolic dysfunction. A linear relationship between IVRT and invasive measurements of systolic pulmonary artery pressure (sPAP) was described by Burstin and confirmed in multiple studies [17, 18]. MPI has an established prognostic value in pulmonary hypertension patients and correlates well with FAC [18], as well as with more advanced indices derived from CMR [19]. IVA is considered a reliable and load-independent measurement of RV contraction. It correlates with the severity of illness in conditions affecting right heart function, e.g., obstructive sleep apnea, mitral stenosis, pulmonary hypertension [20].

Initially, major attention has been focused on LV. A few studies assessing impact of HD implementation on LV function show conflicting results: deterioration of LV ejection fraction (EF_{LV}) in the CRIC study [21], worsening of LV diastolic function without changes in systolic function in the CASCADE study [22], no changes in EF_{LV} in the IDEAL study [23], while improvement of LV function was reported by Ganda et al. [24]. In our study, after one year period of maintenance HD, we observed non-significant changes in LV dimensions and EF_{LV}, but a tendency towards worsening of LV diastolic function was noted, as reflected by a decrease in early diastolic mitral annular velocity and an increase in E/e'_{LV} ratio.

We have noted a non-significant decrease in plasma NT-proBNP at one-year follow-up since HD initiation. It might seem confusing considering the revealed in this study deterioration of RV function, along with the tendency for impairment of LV function and non-significant increase in sPAP. Concerning the fact that NT-proBNP is an established marker of hypervolemia in patients undergoing HD irrespective of LV ejection fraction [25] our results may suggest a crucial role of optimized fluid status in ESRD patients on maintenance HD. A decrease in RVOT dimensions goes along with this line of thinking.

RV function analysis is a dynamically developing branch of ECHO. TDI, STE and application of three-dimensional imaging expand the possibilities of assessment of the RV complex structure and function. However, these methods require images of excellent quality and are not yet widely available in clinical practice.

The most important limitation of this study is the small sample size. It is due to the problems with including patients in the study and with follow-up visits during the time of COVID19 pandemic and the Health Care Service reorganization. Moreover, the management of several factors involved in the development of cardiovascular abnormalities such as correction of hypertension and anaemia and adequacy of delivered dialysis dose were not analysed.The results may be also affected by the selection bias because of the high mortality rate in ESRD patients.

Long-term follow-up clinical studies with the use of different imaging modalities in a large number of patients are needed to disclose the impact of maintenance HD on cardiac structure and function.

Conclusion

In patients with ESRD a long-term HD negatively impacts RV function but the relation of this process with pulmonary pressure was not revealed. IVA and MPI measured with pulsed tissue Doppler are sensitive indicators of RV function.

Conflict of interest

The authors have no conflicts of interest to declare. All co-authors have seen and agree with the contents of the manuscript and there is no financial interest to report.

Streszczenie

Wstęp. Wobec rosnącej liczby chorych wymagających leczenia nerkozastępczego oraz dwukierunkowych interakcji między nerkami a sercem, znanych jako zespół nerkowo-sercowy, ocena wpływu dializoterapii na funkcję serca stała się kluczowa.

Materiał i metody. Grupę badaną stanowiło 22 dorosłych pacjentów ze schyłkową niewydolnością nerek zakwalifikowanych do hemodializoterapii w Centrum Dializ między styczniem a grudniem 2019 roku.

Wyniki. Mediana wieku pacjentów wyniosła 59,5 roku (51–64). Kobiety stanowiły 55% badanej grupy. Najczęstszymi chorobami współistniejącymi były: nadciśnienie tętnicze (86%) oraz cukrzyca (36%). W obserwacji rocznej odnotowano istotny spadek wymiarów proksymalnego i dystalnego RVOT (odpowiednio: $p = 0,04$; $p = 0,007$) oraz istotny spadek wartości IVAc ($p = 0,01$). W konsekwencji wydłużenia IVRTc ($p < 0,001$) i IVCTc ($p < 0,001$) zaobserwowano istotny wzrost wartości MPI ($p < 0,001$).

Wnioski. U pacjentów ze schyłkową niewydolnością nerek długotrwała dializoterapia wpływa negatywnie na funkcję prawej komory. IVA oraz MPI, mierzone metodą tkankowego Dopplera pulsacyjnego, są czułymi wskaźnikami zmian w prawej komorze.

Słowa kluczowe: dializy, echokardiografia, funkcja prawej komory, schyłkowa niewydolność nerek

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REVIEW ARTICLE

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The role of multidisciplinary care for a pregnant woman with a positive cardiological history in everyday medical practice

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Abstract

Reducing maternal mortality is a global health goal of the World Health Organization. While the number of perinatal deaths from hemorrhage and infection is declining, the number of deaths related to heart disease is on the rise and is now the most important cause in Western countries. The aim of expert societies is to define contemporary, diagnostic-specific outcomes in pregnant women with heart disease.

Knowing about your cardiovascular risk during pregnancy is crucial for pre-contraceptive counseling. In the process of organizing care for a pregnant woman with cardiovascular diseases, a multidimensional approach to the problem is important, involving close cooperation between the cardiological and gynecological teams. Despite numerous publications, more studies are still needed to broaden the knowledge of cardiological care in pregnant women. The data obtained from the registers created on the initiative of the European Society of Cardiology, headed by the ROPAC register, seem promising.

Key words: pregnancy, cardiovascular diseases, perinatal care, cardiological care, ROPAC, ESC guidelines

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Introduction

Maternal conditions complicate the pregnancy in 1–4% of cases. Only limited data on the prevalence and incidence of heart diseases complicating pregnancy are still currently available [1]. Knowledge of cardiovascular risks during pregnancy and how to address them is crucial for preconception counselling [2]. As all available treatment methods affect not only the mother but also the foetus, the aim must be to optimise management from the perspective of both the mother and the child. Treatment that is beneficial to the mother may be associated with potential harm to the developing baby or, in extreme cases, treatment allowing the mother to survive may cause fetal death. On the other hand, management that protects the child may lead to suboptimal treatment outcomes for the mother. As there are no prospective or randomised studies, it seems more difficult to establish uniform rules of management for the difficult issue of the provision of care for pregnant women with a history of cardiac disease. In order to improve the current state of knowledge, further registries and prospective observational data on epidemiology and drug exposure during pregnancy are needed, provided by the European Society of Cardiology (ESC) guidelines and the Registry of Pregnancy and Cardiac Disease (ROPAC), run by the ESC and the European Surveillance of Congenital Anomalies (EUROCAT) network of registers.

Epidemiology

In Western European countries, the risk of cardiovascular disease during pregnancy has increased due to the older age of women at the time of their first pregnancy. However, this fact alone — pregnancy at a more mature age — does not explain the increased incidence of cardiovascular diseases (CVD) during pregnancy [1]. However, late pregnancies

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falling towards the end of the childbearing age (40–50 years) are statistically more likely to be associated with an increased prevalence of cardiovascular risk factors, especially diabetes, hypertension and obesity. Moreover, an increasing number of women with congenital heart defects are reaching childbearing age [3]. In Western countries, maternal heart disease is the leading cause of maternal death during pregnancy [4].

The most common cardiac condition complicating pregnancy is hypertension which occurs in 5–10% of all pregnancies. Congenital heart defects are next in line. In non-Western countries, rheumatic valvular defects predominate, representing 56–89% of all CVD during pregnancy [5].

Sources of knowledge on the management of patients with cardiovascular diseases during pregnancy

In terms of the publications on the management of cardiovascular diseases in pregnant women, the ESC guidelines occupy a special position. It is possible primarily thanks to the fact that they are among the few recommendations that still somehow escape the rules of evidence-based medicine which still prevails, especially in cardiology. For obvious ethical reasons, pregnant women have always been disqualified from participating in clinical trials, and those who are not pregnant are required to use effective contraception during the trial. Consequently, expert opinions remain the basis for almost all recommendations on this topic. The source of those opinions, apart from indirect indications obtained from animal testing, can only be the clinical experience gained in daily work with patients as well as the registers of pregnant women with a history of cardiac disease, such as ROPAC.

The first guidelines published by the ESC on pregnant women with cardiovascular diseases appeared in 2003 [1]. Those guidelines have been the foundation of knowledge in this difficult topic of pre-, peri- and postnatal care of pregnant women with a history of cardiac disease. The latest update of the ESC Guidelines on the care of pregnant women with heart diseases was published in 2018 [1]. Large amount of knowledge contained therein is based on the authors' own experience. The second component that provides a valuable source of information on the management of the analysed group of patients are the registers maintained, among others, by the ESC. The most important of those are:

ROPAC – Registry of Pregnancy and Cardiac Disease

The register was established at the initiative of the ESC in 2007 [6]. Initially, it included patients with a structural heart defect. Recruitment is currently underway for Part III of the study — female patients with aortic pathology or a genetic predisposition to its development, as well as pregnant women with at least one valve prosthesis (biological or mechanical). By the end of 2018, 5739 pregnant patients with all types of structural heart disease had been included in ROPAC. That contributed to expanding the current literature and management protocols for this type of patients as well as it allowed identification of further gaps in knowledge about this problem [6]. Aortic abnormalities are among the most common causes of heart disease-related maternal mortality [7]. In the case of valve prostheses, a high rate of complications during pregnancy are observed. The most common ones include: caesarean delivery, increased hospitalisation days during pregnancy, maternal heart failure (HF), pre-term delivery or intrauterine growth retardation [8]. For those reasons, as of February 2019, the ROPAC study is continuing with a particular focus on two types of structural heart disease: pathology within the aorta (as well as genetic predisposition to its development) and the status post replacement of at least one heart valve [9].

The partial results of the ROPAC are now published [10]. In the years 2007–2011, 1321 women were included in the study. Congenital heart defects were found in 66% of patients, valvular defects in 25%, cardiomyopathies in 7% and coronary artery disease in 2% of patients. Maternal mortality was 1% (0.007% in the normal population based on literature data). A total of 338 female patients were hospitalised during pregnancy (26%), including 133 due to HF. Caesarean section was performed in 41% of patients. Maternal and child mortality was higher in developing countries compared to developed countries. Fetal mortality was 1.7% and neonatal mortality was 0.6% [10].

The ROPAC is currently one of the most valuable sources of knowledge used for the purposes of formulating guidelines on the management of pregnant women with a positive cardiac history.

PPCM registry – PeriPartum CardioMyopathy registry

This register was created in 2016. The first results were published in 2017 [11]. This study aims to compare clinical data of patients with PPCM from ESC member countries compared to non-ESC countries. The study began in 2016 and will be continued until the number of 1000 female patients is reached. This publication aims to present preliminary results after the inclusion of the first 500 women in the study. Out of those women, 411 pregnant women from 43 countries with complete records were analysed. Pharmacological treatment initiated after pregnancy was found to be similar in both study groups, including angiotensin-converting enzyme inhibitors, angiotensin-receptor blockers, mineralocorticoid receptor antagonists. In contrast, drugs such as beta-blockers and ivabradine were used less frequently in non-ESC countries while diuretics, digoxin and bromocriptine were used more frequently

(32.6% vs. 7.1%; p < 0.001). After 1 month, persistence of HF symptoms was more common in the non-ESC group (92.3% vs. 81.3%; p < 0.001). Thromboembolic complications from the venous system, arterial emboli and cerebrovascular incidents occurred in 28 out of 411 patients (6.8%) [11]. The neonatal mortality rate was 3.1%; a detailed analysis was not included in the register. The study is part of the EURObservational Research Programme and is an initiative of the Study Group on PPCM of Herat Failure Association.

Organisation of care for women of childbearing age with cardiovascular disease — general recommendations

Preconception counselling

When providing cardiovascular care to a woman planning a pregnancy or during pregnancy, it is important to remember that it is a long-term and comprehensive process, including follow-up visits, decisions on necessary hospitalisation, tests, the inclusion of pharmacotherapy, suggestions for premature termination of pregnancy or normal termination of pregnancy, the method of termination of pregnancy — spontaneous labour or caesarean labour, breastfeeding or withholding lactation. It is crucial for the patients that the cardiologist and gynaecologist work together to develop a coherent action plan. The provision of care does not end with the childbirth; on the contrary, it must extend up to approximately six months after the birth. It is often prolonged to fulfil the planned treatment, taking advantage of the period between pregnancies.

It is clear that all women diagnosed with heart or aortic disease and planning a pregnancy need preconception counselling [12]. If there is a high risk of complications or possible contraindications to pregnancy, the risks of pregnancy and the need for careful planning should be discussed with the woman at a sufficiently young age. At the same time, it should be noted that in many cases pregnancy does not significantly increase cardiovascular risk. There is only a small group of cardiac conditions in which the pregnancy should be terminated by caesarean section (Figure 1). The minimum diagnostic tests that are necessary to estimate the risk of pregnancy in CVD women include electrocardiogram, echocardiography and cardiac diagnostic test [13]. However, in the event of aortic disorders, full imaging of this vessel by computed tomography or magnetic resonance scanning must be carried out to enable giving appropriate advice before pregnancy. Predictive factors for cardiac events in pregnant women include heart rate limit and peak oxygen uptake (in the spiroergometric test). Exercise capacity in pregnant women > 80% of maximal value is associated with successful pregnancy termination [1]. Genetic counselling should be considered in women with congenital heart disease or congenital arrhythmias, cardiomyopathy, aortic disease or genetic abnormalities associated with CVD [1].

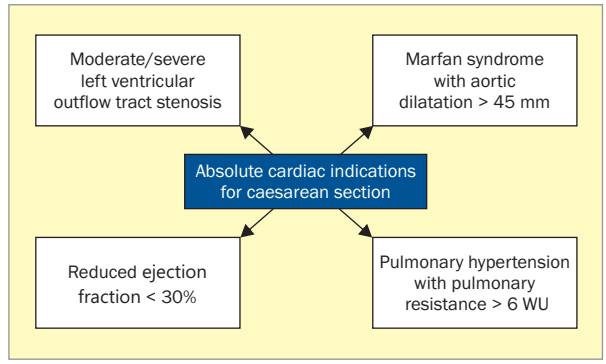

Figure 1. Absolute cardiac indications for caesarean section

Maternal cardiovascular risk assessment

In a group of patients with a suspected or positive history of CVD, it is recommended that the risk of complications be assessed and counselling be given before pregnancy. The mWHO classification (Table 1), which can be used in both the pre- and post-conceptional periods, will be helpful in this regard [14].

The risk of cardiovascular complications in pregnancy depends on the type of heart disease, ventricular and valvular function, functional class, the presence of cyanosis, pulmonary artery pressure values and other factors, including comorbidities.

The following should be considered in the risk assessment: interview findings (including functional class), arterial blood haemoglobin oxygen saturation (SaO_2), serum natriuretic peptide levels, echocardiographic assessment of ventricular and valvular function, pulmonary artery pressure and aortic dimensions, exercise capacity and the presence of arrhythmias [15].

The risk associated with a specific heart disease should be estimated based on the modified mWHO classification, although this probably performs better in populations in developed countries than in developing countries. According to this classification, heart diseases are classified into five classes (Table 2), which are associated with different risks of complications and need different management [14].

As the risk can vary over time, it should be reassessed at each pre-pregnancy visit.

Risk of obstetric and neonatal complications

Pregnant women with cardiac disease are at increased risk of obstetric complications, including preterm birth, pre-eclampsia and postpartum haemorrhage. Neonatal complications occur with a frequency of 18–30%, including a mortality rate of 1–4% [16]. Predictive factors for adverse maternal and neonatal events are shown in Table 3.

Table 1. Modified WHO (mWHO) classification of maternal cardiovascular complications

Factor	Class				
	mWHO I	mWHO II	mWHO II–III	mWHO III	mWHO IV
Risk	No appreciable increase in the risk of maternal death and at most a slight increase in the risk of other complications	A small increase in the risk of maternal death or a moderate increase in the risk of other complications	A moderate increase in the risk of maternal death or a moderate/major increase in the risk of other complications	A significant increase in the risk of maternal death or a high increase in the risk of other complications	An extremely high risk of maternal death or a high increase in the risk of other complications
Rate of cardiac events in the mother	2.5–5%	5.7–10.5%	10–19%	19–27%	40–100%
Counselling	Yes	Yes	Yes	Yes — expert advice required	Yes — pregnancy contraindicated[b]
Place of care during pregnancy and childbirth	Community hospital	Community hospital	Referral centre	Experienced obstetrics and cardiology centre	Experienced obstetrics and cardiology centre
Minimum number of visits during pregnancy	1–2	In each trimester	1 ×/2 mth	1 ×/1–2 mth	1 ×/mth

[a]Diseases that belong to particular classes — previous text; [b]In the event of a pregnancy, a possible termination should be discussed

Table 2. Classes of diagnosis according to the mWHO classification

	Class I according to mWHO	Class II according to mWHO	Class II–III according to mWHO	Class III according to mWHO	Class IV according to mWHO
Diagnosis (if the patient is otherwise in good health status and the course of the disease is uncomplicated)	Minor cardiac dysfunction(s): • pulmonary stenosis • PDA • mitral valve leaflet prolapse. Simple defect after successful repair (ASD, VSD, PDA, anomalous pulmonary venous drainage) Atrial or ventricular single ectopic beats	Uncorrected ASD or VSD Tetralogy of Fallot after corrective surgery Mostly (supraventricular) arrhythmias Turner syndrome without aortic dilatation	Slight LV dysfunction (EF > 45%) Hypertrophic cardiomyopathy Defective native valve or biological prosthesis not classified as WHO class I or IV (minor MS, moderate AS) Marfan syndrome or other HTAD without aortic dilatation Aorta < 45 mm in patients with bicuspid aortic valve Corrected aortic coarctation. AVSD	Moderate LV dysfunction (EF 30–45%) A history of PPCM without residual LV impairment Mechanical valve Systemic RV with good or slightly impaired function Fontan circulation if patient is otherwise in good health status and cardiac course is uncomplicated Uncorrected cyanotic heart defect Other complex heart defect Moderate MS Severe asymptomatic AS Moderate aortic dilatation (40–45 mm in Marfan syndrome or HTAD; 45–50 mm in patients with bicuspid aortic valve, ASI 20–25 mm/m^2 in Turner syndrome, < 50 mm in tetralogy of Fallot) Ventricular tachycardia	Pulmonary arterial hypertension Severe systemic ventricular dysfunction (EF < 30% or NYHA class III–IV) A history of PPCM with any residual LV dysfunction Severe MS Severe symptomatic AS Systemic RV with moderate to severe dysfunction Significant aortic dilatation (> 45 mm in Marfan syndrome or HTAD; > 50 mm in patients with bicuspid aortic valve, ASI > 25 mm/m^2 in Turner syndrome, > 50 mm in tetralogy of Fallot) Vascular form of Ehlers-Danlos syndrome Severe aortic (re)coarctation Fontan circulation with any complications

AS — aortic stenosis; ASD — atrial septal defect; ASI — aortic size index; AVSD — atrioventricular septal defect; EF — ejection fraction; HTAD — heritable thoracic aortic disease; LV — left ventricular; MS — mitral stenosis; NYHA — New York Heart Association; PDA — patent ductus arteriosus; PPCM — peripartum cardiomyopathy; RV — right ventricular; VSD — ventricular septal defect; WHO — World Health Organization

Table 3. Predictive factors of adverse maternal and neonatal events

Risk factors for cardiovascular events in the mother	Predictive factors of adverse neonatal events
1. past cardiac event (HF, transient cerebral ischaemia attack, stroke, arrhythmia) 2. NYHA class III/IV HF 3. left heart obstruction of blood flow (moderate or severe) 4. impaired systemic ventricular systolic function (EF < 40%) 5. impaired subpulmonary ventricular function (TAPSE amplitude < 16 mm) 6. systemic atrioventricular valve regurgitation (moderate or severe) 7. subpulmonary atrioventricular valve regurgitation (moderate or severe) 8. PAH 9. pharmacological treatment of heart disease before pregnancy 10. cyanosis (SaO_2 < 90%) 11. increased natriuretic peptide levels (NT-proBNP > 128 pg/mL at 20 weeks' gestation is a predictor of adverse events in later pregnancy) 12. history of smoking 13. mechanical valve prosthesis 14. corrected or uncorrected cyanotic heart defect	1. NYHA class III/IV HF or cyanosis at the first visit during pregnancy 2. left heart obstruction in the mother 3. smoking during pregnancy 4. SaO_2 in the mother < 90% 5. multiple pregnancy 6. taking anticoagulants during pregnancy 7. taking cardiovascular drugs before pregnancy 8. cyanotic heart defect "at giving birth" 9. mechanical valve prosthesis 10. maternal cardiac event during pregnancy 11. worsening of maternal cardiac output during pregnancy 12. abnormal uteroplacental flow on Doppler examination

EF — ejection fraction; HF — heart failure; NT-proBNP — N-terminal pro-B-type natriuretic peptide; NYHA — New York Heart Association; PAH — pulmonary arterial hypertension; TAPSE — tricuspid annular systolic displacement

Diagnosis of cardiovascular diseases in pregnancy

It is possible that some women will only be diagnosed with a cardiac condition during pregnancy. The physiological changes in the cardiovascular system that occur during pregnancy can sometimes cause symptoms that raise the suspicion of CVD (e.g., swelling), making it difficult to diagnose, for example, HF.

Diagnostic evaluation for CVD in pregnant women include:

1. medical interview and physical examination;
2. echocardiography – in case of inadequate or unexplained dyspnoea during pregnancy and/or a new pathological cardiac murmur (e.g. any diastolic murmur);
3. measurement of blood pressure using a validated device;
4. assessment of proteinuria, especially in the case of a personal or family history of hypertension or pre-eclampsia;
5. oximetry in women with congenital heart disease.

If there is an increased risk of fetal abnormalities, fetal echocardiography performed by an experienced specialist is recommended for any pregnant woman with unexplained or new cardiovascular signs and symptoms. If echocardiography is insufficient to establish a definitive diagnosis, a gadolinium-free cardiac magnetic resonance scan should be considered.

In addition, if required, the following can be done:

1. chest radiography;
2. cardiac catheterisation (only for very strict indications);
3. computed tomography (in selected women) and electrophysiological study (only for vital indications) [17].

Treatment and delivery recommendations [18]

- It is recommended that patients at high risk of complications be treated in referral centres where a multidisciplinary team of specialists is available.
- If cardiac surgery is necessary in a pregnant woman, it is advisable to administer a glucocorticosteroid to the pregnant woman between 24 and 37 week of pregnancy.
- In most cases, vaginal delivery is recommended.
- Induction of labour after the 40th completed week of pregnancy should be considered in all women with heart disease .
- In women with severe hypertension, natural labour with epidural anaesthesia should be considered.
- If the gestational age has exceeded 26 weeks, pregnancy termination should be considered before the necessary surgical intervention.
- Consideration may be given to coronary artery bypass grafting or valve surgery during pregnancy

if conservative management (including pharmacotherapy) has failed and if the mother's life is at risk or if percutaneous treatment is not available. Prophylactic antibiotic therapy during labour to prevent infective endocarditis is not recommended [18].

— In patients with severe cardiac dysfunction, full resuscitation and intensive care in the delivery room or operating theatre (intensive obstetric care room) must be provided.

These conditions include:

— anaesthetic care;
— possibility of monitoring: electrocardiogram monitoring, haemodynamic monitoring and pulse oximetry monitoring;
— full resuscitation care: drugs, intubation kit and mechanical ventilation kit, defibrillator, pacemaker and electrodes for transcutaneous and endocavitary stimulation.

Centres that are unable to provide the listed conditions of delivery should not provide obstetric care for pregnant women at risk of cardiac complications. The poor prognosis is usually related to the lack of adequate specialist care, the absence of a clear diagnosis and defined management principles. A well-prepared patient giving birth under intensive care is able to give birth successfully even with very advanced heart disease.

Conclusions

The provision of care for pregnant women with heart disease represents a major challenge in daily medical practice. When organising the management of such patients, a multidimensional approach to the problem – which involves close collaboration between the cardiology team and gynaecology team — is crucial. Despite the numerous publications, more studies are still needed to expand the knowledge of cardiac care for pregnant women. Data obtained from the Registries set up at the initiative of the ESC seem promising. These data are now the main source of knowledge for formulating recommendations on the topic of the provision of care to pregnant women with history of a cardiac disease.

Conflict of interest

None declared.

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Rola wielospecjalistycznej opieki nad ciężarną obciążoną dodatnim wywiadem kardiologicznym w codziennej praktyce lekarskiej

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Streszczenie

Zmniejszenie śmiertelności ciężarnych jest globalnym celem zdrowotnym Światowej Organizacji Zdrowia. Chociaż liczba zgonów okołoporodowych z powodu krwotoków i infekcji spada, liczba zgonów związanych z chorobami serca wzrasta i jest obecnie ich najważniejszą przyczyną w krajach zachodnich. Dążeniem towarzystw eksperckich jest określenie współczesnych, specyficznych dla diagnozy wyników u kobiet ciężarnych z chorobami serca.

Znajomość ryzyka sercowo-naczyniowego podczas ciąży ma kluczowe znaczenie dla poradnictwa prekoncepcyjnego. W procesie organizacji opieki nad ciężarną z chorobami sercowo-naczyniowymi ważne jest wielowymiarowe podejście do problemu, obejmujące ścisłą współpracę zespołu kardiologicznego i ginekologicznego. Pomimo licznych publikacji nadal potrzebne są kolejne opracowania poszerzające wiedzę na temat opieki kardiologicznej nad ciężarną. Obiecujące wydają się dane uzyskane z rejestrów utworzonych z inicjatywy Europejskiego Towarzystwa Kardiologicznego na czele z rejestrem ROPAC.

Słowa kluczowe: ciąża, choroby sercowo-naczyniowe, opieka okołoporodowa, opieka kardiologiczna, ROPAC, wytyczne ESC

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Wstęp

Choroby ze strony matki wikłają ciążę w 1–4% przypadków. Aktualnie dostępne są jedynie ograniczone dane na temat częstości występowania oraz zapadalności na choroby serca wikłające przebieg ciąży [1]. Znajomość zagrożeń związanych z układem sercowo-naczyniowym podczas ciąży oraz umiejętność ich rozwiązywania ma kluczowe znaczenie dla poradnictwa prekoncepcyjnego [2]. Ponieważ wszystkie stosowane metody leczenia wpływają nie tylko na matkę, ale również na płód, celem musi być optymalizacja postępowania z perspektywy zarówno matki, jak i dziecka. Leczenie korzystne dla matki może się wiązać z potencjalnymi szkodami dla rozwijającego się dziecka, a w skrajnych przypadkach leczenie umożliwiające przeżycie matki może być przyczyną śmierci płodu. Z drugiej strony, postępowanie chroniące dziecko może prowadzić do suboptymalnych wyników terapii u matki. Ponieważ nie ma prospektywnych lub randomizowanych badań, tym trudniejsze wydaje się ustanowienie jednolitych zasad postepowania w tym trudnym zagadnieniu, jakim jest opieka nad ciężarną z dodatnim wywiadem kardiologicznym. W celu poprawy obecnego stanu wiedzy, konieczne są kolejne rejestry i prospektywne obserwacje, danych na temat epidemiologii oraz ekspozycji

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na leki podczas ciąży dostarczają wytyczne Europejskiego Towarzystwa Kardiologicznego (ESC, *European Society of Cardiology*) i rejestr ciężarnych z chorobami serca (ROPAC, *Registry of Pregnancy and Cardiac Disease*) prowadzony przez ESC oraz sieć rejestrów *European Surveillance of Congenital Anomalies* (EUROCAT).

Epidemiologia

W krajach Europy Zachodniej ryzyko choroby sercowo-naczyniowej podczas ciąży wzrosło ze względu na dojrzalszy wiek kobiet w momencie zajścia w pierwszą ciążę. Jednakże sam fakt macierzyństwa w późniejszym czasie nie tłumaczy wzrostu częstości występowania chorób sercowo-naczyniowych (CVD, *cardiovascular disesases*) podczas ciąży [1]. Późne ciąże, przypadające pod koniec okresu rozrodczego (w wieku 40–50 lat) statystycznie częściej jednak są związane ze zwiększoną częstością występowania czynników ryzyka sercowo-naczyniowego, zwłaszcza cukrzycy, nadciśnienia tętniczego i otyłości. Ponadto wiek rozrodczy osiąga coraz większa liczba kobiet z wrodzonymi wadami serca [3]. W krajach zachodnich choroby serca matek są główną przyczyną zgonów matczynych podczas ciąży [4].

Najczęstszym schorzeniem kardiologicznym wikłającym ciążę jest nadciśnienie tętnicze występujące w przypadku 5–10% wszystkich ciąż. Kolejne miejsca zajmują wrodzone wady serca. W krajach innych niż zachodnie dominują reumatyczne wady zastawkowe stanowiące 56–89% wszystkich CVD podczas ciąży [5].

Źródła wiedzy na temat postępowania u ciężarnych pacjentek z chorobami sercowo-naczyniowymi

Wśród publikacji dotyczących postępowania w chorobach sercowo-naczyniowych u ciężarnych szczególną pozycję zajmują wytyczne ESC. Przede wszystkim dlatego, że jako jedne z nielicznych zaleceń wciąż wymykają się w pewnym sensie zasadom dominującej, zwłaszcza w kardiologii, medycyny opartej na dowodach naukowych. Z oczywistych względów etycznych kobiety w ciąży od zawsze były dyskwalifikowane z udziału w badaniach klinicznych, a od tych, które w ciąży nie są, wymaga się w czasie badania stosowania skutecznej antykoncepcji. W związku z tym bazą do prawie wszystkich zaleceń w tym temacie pozostają opinie ekspertów. Źródłem tych opinii, poza pośrednimi wskazówkami z eksperymentów na zwierzętach, może być jedynie doświadczenie kliniczne zdobywane w codziennej pracy z chorymi, a także rejestry kobiet ciężarnych z dodatnim wywiadem kardiologicznym, na przykład rejestr ROPAC.

Pierwsze wytyczne opublikowane przez ESC dotyczące ciężarnych z chorobami układu sercowo-naczyniowego ukazały się w 2003 roku [1]. Stanowiły i stanowią one fundament wiedzy w tym trudnym temacie, jakim jest opieka przed-, około- i poporodowa nad ciężarną obciążoną dodatnim wywiadem kardiologicznym. Ostatnia aktualizacja wytycznych ESC dotycząca opieki nad ciężarnymi z chorobami serca ukazała się w 2018 roku [1]. Duża część wiedzy w nich zawartej opiera się na doświadczeniu własnym autorów. Drugą komponentą stanowiącą cenne źródło informacji na temat postępowania wśród tej grupy pacjentek są rejestry prowadzone między innymi przez ESC. Do najważniejszych należą:

ROPAC (*Registry of Pregnancy and Cardiac Disease*)

Rejestr powstał z inicjatywy ESC w 2007 roku [6]. Początkowo obejmował on pacjentki ze strukturalną wadą serca. Obecnie trwa rekrutacja do III części badania — pacjentki z patologią aorty lub genetyczną predyspozycją do jej rozwoju, a także ciężarne z co najmniej jedną protezą zastawki (biologiczną lub mechaniczną). Do końca 2018 roku do ROPAC zostało włączonych 5739 pacjentek ciężarnych z wszystkimi typami strukturalnej choroby serca, co przyczyniło się do poszerzenia aktualnej literatury i protokołów postępowania u tego typu pacjentek, jak również pozwoliło zidentyfikować kolejne braki w wiedzy na temat tego problemu [6]. Nieprawidłowości aorty są jedną z najczęstszych przyczyn śmiertelności matek w związku z chorobami serca [7]. W przypadku protez zastawkowych notuje się wysoki odsetek powikłań podczas trwania ciąży — najczęściej: poród przez cięcie cesarskie, zwiększenie liczby hospitalizacji w trakcie ciąży, niewydolność serca (HF, *heart failure*) matki, przedwczesny poród czy wewnątrzmaciczne zahamowanie wzrostu [8]. Z tych powodów od lutego 2019 badanie ROPAC jest kontynuowane ze szczególnym skupieniem się na dwóch typach strukturalnej choroby serca: patologii w obrębie aorty (jak również genetycznych predyspozycji do jej rozwoju) oraz stanie po wymianie co najmniej jednej zastawki serca [9].

Opublikowane są już częściowe wyniki ROPAC [10]. W latach 2007–2011 włączono do badania 1321 kobiet. Wady wrodzone serca stwierdzono u 66% pacjentek, wady zastawkowe u 25%, kardiomiopatie u 7%, chorobę wieńcową u 2% pacjentek. Śmiertelność matek wynosiła 1% (0,007% w normalnej populacji na podstawie danych z literatury). Hospitalizowanych było 338 pacjentek w okresie ciąży (26%), z czego 133 z powodu HF. Rozwiązanie cięciem cesarskim przeprowadzono u 41% pacjentek. Śmiertelność matek i dzieci była wyższa w krajach rozwijających się w porównaniu do krajów rozwiniętych. Śmiertelność płodów wynosiła 1,7%, a noworodków 0,6% [10].

Rejestr ROPAC stanowi obecnie jedno z najcenniejszych źródeł wiedzy do formułowania wytycznych postępowania u ciężarnych z dodatnim wywiadem kardiologicznym.

Rejestr PPCM — *PeriPartum CardioMyopathy registry*

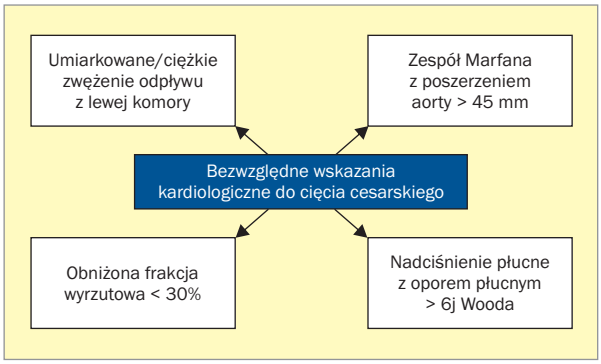
Rejestr powstał w 2016 roku. Pierwsze wyniki opublikowane zostały rok później [11]. Badanie ma na celu porównanie danych klinicznych pacjentek z PPCM z krajów zrzeszonych w ESC w porównaniu do krajów spoza ESC. Badanie rozpoczęło się w 2016 roku i trwa nadal do uzyskania 1000 pacjentek. Publikacja ma na celu przedstawienie wstępnych wyników po włączeniu do badań pierwszych 500 kobiet. Z liczby tej analizę przeprowadzono u 411 ciężarnych z 43 krajów, u których uzyskano kompletną dokumentację badania. Stwierdzono, że leczenie farmakologiczne rozpoczęte po ciąży było podobne w obu grupach badanych — obejmowało inhibitory enzymu konwertującego angiotensynę, antagonistów receptora angiotensynowego i antagonistów receptora mineralokortykoidowego. W krajach poza ESC rzadziej były stosowane takie leki, jak beta-blokery, iwabradyna, a częściej — leki moczopędne, digoksyna i bromokryptyna (32,6% *vs.* 7,1%; p < 0,001). Po miesiącu w grupie krajów spoza ESC częściej stwierdzano utrzymywanie się objawów HF (92,3% *vs.* 81,3%; p < 0,001). Powikłania zakrzepowo-zatorowe z układu żylnego, zatory tętnicze oraz incydenty mózgowo-naczyniowe wystąpiły u 28 spośród 411 pacjentek (6,8%) [11]. Śmiertelność noworodków wynosiła 3,1%, w rejestrze nie została ujęta szczegółowa analiza. Badania te są częścią *EURObservational Research Programme* (EORP) i inicjatywą *Study Group on PPCM of Heart Failure Association*.

Organizacja opieki nad kobietami w wieku rozrodczym z chorobami sercowo-naczyniowymi — zalecenia ogólne

Poradnictwo prekoncepcyjne

Podejmując się opieki kardiologicznej nad kobietą planującą ciążę lub w trakcie ciąży, należy pamiętać, że jest to proces długoterminowy i kompleksowy, obejmujący wizyty kontrolne, decyzje dotyczące koniecznej hospitalizacji, wykonania badań, włączenia farmakoterapii, sugestię odnośnie do rozwiązania ciąży wczesnego lub o czasie, sposobu rozwiązania ciąży — siłami natury lub cięciem cesarskim, karmienia piersią lub wstrzymania laktacji. Kluczowa w przypadku takich pacjentek jest współpraca kardiologa z ginekologiem w celu opracowania spójnego planu działania. Opieka nie kończy się na urodzeniu dziecka, musi obejmować okres do około 6 miesięcy po porodzie. Często jest przedłużona w celu zrealizowania zaplanowanego postępowania leczniczego, wykorzystując okres między ciążami.

Nie podlega wątpliwości, że wszystkie kobiety z rozpoznaną chorobą serca lub aorty planujące ciążę wymagają poradnictwa przed poczęciem dziecka [12]. W przypadku dużego ryzyka powikłań lub możliwych przeciwwskazań do zajścia w ciążę ryzyko związane z ciążą i konieczność jej



Rycina 1. Bezwzględne wskazania kardiologiczne do cięcia cesarskiego

starannego planowania powinno się omówić z kobietą w odpowiednio młodym wieku. Jednocześnie należy zaznaczyć, że w wielu przypadkach ciąża nie zwiększa istotnie ryzyka sercowo-naczyniowego. Istnieje jedynie niewielka grupa stanów kardiologicznych, w których ciążę należy rozwiązać poprzez cięcie cesarskie (ryc. 1). Minimalny zakres badań diagnostycznych konieczny do oszacowania ryzyka związanego z ciążą u kobiet z CVD obejmuje: elektrokardiogram, badanie echokardiograficzne i próbę wysiłkową [13]. Natomiast w przypadku schorzeń aorty, aby móc udzielić odpowiednich porad przed ciążą, trzeba przeprowadzić pełne obrazowanie tego naczynia za pomocą tomografii komputerowej lub rezonansu magnetycznego. Czynnikami predykcyjnymi zdarzeń sercowych u kobiet w ciąży są limit tętna i szczytowy wychwyt tlenu (w teście spiroergometrycznym). Wydolność wysiłkowa u ciężarnej powyżej 80% wartości maksymalnej wiąże się z pomyślnym zakończeniem ciąży [1]. U kobiet z wrodzoną wadą serca lub wrodzoną arytmią, kardiomiopatią, chorobą aorty lub nieprawidłowościami genetycznymi związanymi z CVD należy wziąć pod uwagę poradnictwo genetyczne [1].

Ocena ryzyka sercowo-naczyniowego u matki

W grupie pacjentek z podejrzeniem lub dodatnim wywiadem w kierunku CVD zaleca się ocenę ryzyka powikłań i udzielenie porady przed zajściem w ciążę. Pomocna w tej kwestii będzie klasyfikacja mWHO (*modified World Health Organization*) (tab. 1), która może być stosowana w okresie pre- i pokoncepcyjnym [14].

Ryzyko powikłań sercowo-naczyniowych w ciąży zależy od rodzaju choroby serca, czynności komór i zastawek, klasy czynnościowej, występowania sinicy, wartości ciśnień w tętnicy płucnej i innych czynników, w tym chorób współistniejących.

W ocenie ryzyka należy wziąć pod uwagę: wynik badania podmiotowego (w tym klasę czynnościową), wysycenie hemoglobiny krwi tętniczej tlenem (SaO_2), stężenia peptydów natriuretycznych w surowicy, echokardiograficzną ocenę czynności komór i zastawek, ciśnienia w tętnicy płucnej

Tabela 1. Zmodyfikowana klasyfikacja WHO (mWHO) powikłań sercowo-naczyniowych u matki [14]

Czynnik	Klasa				
	mWHO I	mWHO II	mWHO II–III	mWHO III	mWHO IV
Ryzyko	Bez uchwytnego wzrostu ryzyka zgonu matki i co najwyżej niewielki wzrost ryzyka innych powikłań	Mały wzrost ryzyka zgonu matki lub umiarkowane zwiększenie ryzyka innych powikłań	Umiarkowany wzrost ryzyka zgonu matki lub umiarkowany/duży wzrost ryzyka innych powikłań	Istotny wzrost ryzyka zgonu matki lub duży wzrost ryzyka innych powikłań	Skrajnie duże ryzyko zgonu matki lub duży wzrost ryzyka innych powikłań
Częstość zdarzeń sercowych u matki	2,5–5%	5,7–10,5%	10–19%	19–27%	40–100%
Poradnictwo	Tak	Tak	Tak	Tak — wymagana porada eksperta	Tak — ciąża przeciwwskazana[b]
Miejsce opieki w czasie ciąży i porodu	Szpital lokalny	Szpital lokalny	Szpital referencyjny	Doświadczony ośrodek położniczy i kardiologiczny	Doświadczony ośrodek położniczy i kardiologiczny
Minimalna liczba wizyt w czasie ciąży	1–2	W każdym trymestrze	1 ×/2 mies.	1 ×/1–2 mies.	1 ×/mies.

[a]Choroby należące do poszczególnych klas — p. tekst; [b]W razie ciąży należy przedyskutować jej ewentualne przerwanie

Tabela 2. Klasy rozpoznań według klasyfikacji mWHO [14]

	Klasa I wg mWHO	Klasa II wg mWHO	Klasa II–III wg mWHO	Klasa III wg mWHO	Klasa IV wg mWHO
Rozpoznanie (jeżeli poza tym pacjentka w dobrym stanie, a przebieg choroby niepowikłany)	Niewielka/-i/-ie: • stenoza płucna • przetrwały przewód tętniczy • wypadanie płatka zastawki mitralnej • prosta wada po skutecznej naprawie (ASD, VSD, przetrwały przewód tętniczy, nieprawidłowy spływ żył płucnych) • przedsionkowe lub komorowe pobudzenia ektopowe, pojedyncze	Nieskorygowany ASD lub VSD Tetralogia Fallota po operacji naprawczej Większość zaburzeń rytmu serca (nadkomorowe) Zespół Turnera bez poszerzenia aorty	Niewielkie upośledzenie czynności LV (EF > 45%) Kardiomiopatia przerostowa Wada natywnej zastawki lub protezy biologicznej niezaliczana do klasy I lub IV wg WHO (niewielka MS, umiarkowana AS) Zespół Marfana lub inna HTAD bez poszerzenia aorty Aorta < 45 mm u pacjentek z dwupłatkową zastawką aortalną Skorygowana koarktacja aorty AVSD	Umiarkowane upośledzenie czynności LV (EF 30–45%) Przebyta PPCM bez rezydualnego upośledzenia czynności LV Zastawka mechaniczna Systemowa RV z dobrą lub nieznacznie zaburzoną czynnością Krążenie Fontana, jeżeli poza tym pacjentka jest w dobrym stanie, a przebieg choroby serca — niepowikłany Nieskorygowana sinicza wada serca Inne złożone wada serca Umiarkowana MS Ciężka bezobjawowa AS Umiarkowane poszerzenie aorty (40–45 mm w zespole Marfana lub HTAD; 45–50 mm u pacjentek z dwupłatkową zastawką aortalna, ASI 20–25 mm/m^2 w zespole Turnera, < 50 mm w tetralogii Fallota) Częstoskurcz komorowy	Tętnicze nadciśnienie płucne Ciężka dysfunkcja komory systemowej (EF < 30% lub III–IV klasa wg NYHA) Przebyta PPCM z jakimkolwiek rezydualnym zaburzeniem czynności LV Ciężka MS Ciężka objawowa AS Systemowa RV z umiarkowanie lub znacznie zaburzoną czynnością Znaczne poszerzenie aorty (> 45 mm w zespole Marfana lub HTAD; > 50 mm u pacjentek z dwupłatkową zastawką aortalną, ASI > 25 mm/m^2 w zespole Turnera, > 50 mm w tetralogii Fallota) Postać naczyniowa zespołu Ehlersa-Danlosa Ciężka (re)koarktacja aorty Krążenie Fontana z dowolnymi powikłaniami

AS (*aortic stenosis*) — stenoza aortalna; ASD (*atrial septal defect*) — ubytek w przegrodzie międzyprzedsionkowej; ASI (*aortic size index*) — wskaźnik wielkości aorty; AVSD (*atrioventricular septal defect*) — ubytek przegrody przedsionkowo-komorowej; EF (*ejection fraction*) — frakcja wyrzutowa; HTAD (*heritable thoracic aortic disease*) — dziedziczna choroba aorty piersiowej; LV (*left ventricular*) — lewa komora; MS (*mitral stenosis*) — stenoza mitralna; NYHA (*New York Heart Association*) — Nowojorskie Towarzystwo Kardiologiczne; PPCM (*peripartum cardiomyopathy*) — kardiomiopatia okołoporodowa; RV (*right ventricular*) — prawa komora; VSD (*ventricular septal defect*) — ubytek w przerodzie międzykomorowej; WHO (*World Health Organization*) — Światowa Organizacja Zdrowia

Tabela 3. Czynniki predykcyjne niekorzystnych zdarzeń matki i noworodka

Czynniki ryzyka zdarzeń sercowo-naczyniowych u matki	Czynniki predykcyjne niekorzystnych zdarzeń u noworodków
1. przebyte zdarzenie sercowe (HF, napad przemijającego niedokrwienia mózgu, udar mózgu, arytmia) 2. HF w III/IV klasie NYHA 3. utrudnienie przepływu krwi w lewej części serca (umiarkowane lub ciężkie) 4. upośledzona czynność skurczowa komory systemowej (EF < 40%) 5. upośledzona czynność komory podpłucnej (amplituda skurczowego przemieszczenia pierścienia zastawki trójdzielnej < 16 mm) 6. niedomykalność zastawki przedsionkowo-komorowej komory systemowej (umiarkowana lub ciężka) 7. niedomykalność zastawki przedsionkowo-komorowej komory podpłucnej (umiarkowana lub ciężka) 8. tętnicze nadciśnienie płucne (PAH) 9. farmakologiczne leczenie choroby serca przed ciążą 10. sinica (SaO_2 <90%) 11. zwiększone stężenie peptydów natriuretycznych (NT-proBNP > 128 pg/ml w 20. tyg. ciąży jest czynnikiem predykcyjnym niekorzystnych zdarzeń w późniejszym okresie ciąży) 12. palenie tytoniu w wywiadzie 13. mechaniczna proteza zastawkowa 14. skorygowana lub nieskorygowana sinicza wada serca	1. HF w III/IV klasie NYHA lub sinica w czasie pierwszej wizyty w ciąży 2. przeszkoda w lewej części serca u matki 3. palenie tytoniu w czasie ciąży 4. SaO_2 u matki < 90% 5. ciąża wielopłodowa 6. przyjmowanie antykoagulantów w czasie ciąży 7. przyjmowanie leków kardiologicznych przed ciążą 8. sinicza wada serca „przy urodzeniu” 9. mechaniczna proteza zastawkowa 10. zdarzenie sercowe u matki w czasie ciąży 11. pogorszenie rzutu serca u matki w czasie ciąży 12. nieprawidłowy przepływ maciczno-łożyskowy w badaniu dopplerowskim

EF (*ejection fraction*) — frakcja wyrzutowa; HF (*heart failure*) — niewydolność serca; NT-proBNP (*N-terminal pro-B-type natriuretic peptide*) — N-końcowy propeptyd natriuretyczny typu B; NYHA (*New York Heart Association*) — Nowojorskie Towarzystwo Kardiologiczne

i wymiarów aorty, wydolność wysiłkową oraz występowanie zaburzeń rytmu [15].

Ryzyko związane z konkretną chorobą serca powinno się szacować na podstawie zmodyfikowanej klasyfikacji mWHO, aczkolwiek prawdopodobnie sprawdza się ona lepiej w populacjach w krajach rozwiniętych niż rozwijających się. Według tej klasyfikacji choroby serca są zakwalifikowane do 5 klas (tab. 2), które wiążą się z różnym ryzykiem powikłań i wymagają innego postępowania [14].

Z racji tego, że ryzyko może być zmienne w czasie, należy ponowić jego ocenę podczas każdej wizyty przed ciążą.

Ryzyko powikłań położniczych i noworodkowych

Ciężarne z chorobami kardiologicznymi są obciążone zwiększonym ryzykiem powikłań położniczych, w tym porodu przedwczesnego, stanu przedrzucawkowego i krwotoku w okresie poporodowym. Powikłania noworodkowe występują z częstością 18–30%, a śmiertelność wynosi 1–4% [16]. Czynniki predykcyjne niekorzystnych zdarzeń u matki i noworodka zebrano w tabeli 3.

Rozpoznanie chorób sercowo-naczyniowych w ciąży

Niewykluczone, że u części kobiet diagnoza schorzenia kardiologicznego zostanie postawiona dopiero w trakcie ciąży. Zachodzące w czasie ciąży fizjologiczne zmiany w układzie krążenia mogą niekiedy wywoływać objawy nasuwające podejrzenie CVD (np. obrzęki), co utrudnia jej rozpoznanie, na przykład HF.

Diagnostyka w kierunku CVD u ciężarnych obejmuje:

1. badanie podmiotowe i przedmiotowe;
2. badanie echokardiograficzne — w przypadku nieadekwatnej lub niewyjaśnionej duszności w czasie ciąży i/lub nowego patologicznego szmeru sercowego (m.in. każdego szmeru rozkurczowego);
3. pomiar ciśnienia tętniczego zwalidowanym aparatem;
4. ocenę białkomoczu, zwłaszcza w razie nadciśnienia tętniczego lub stanu przedrzucawkowego w wywiadzie osobniczym albo rodzinnym;
5. oksymetria u kobiet z wrodzoną wadą serca.

Jeżeli u płodu stwierdza się zwiększone ryzyko nieprawidłowości, zaleca się wykonanie echokardiografii płodowej przez doświadczonego specjalistę, a u każdej ciężarnej z niewyjaśnionymi lub nowymi objawami sercowo-naczyniowymi, podmiotowymi bądź przedmiotowymi — echokardiografii. Jeśli echokardiografia nie wystarcza do ustalenia ostatecznego rozpoznania, należy rozważyć wykonanie rezonansu magnetycznego serca bez użycia gadolinu.

Dodatkowo, w razie potrzeby można wykonać:

1. badanie radiologiczne klatki piersiowej;
2. cewnikowanie serca (jedynie z bardzo ścisłych wskazań);
3. tomografię komputerową (u wybranych kobiet) i badanie elektrofizjologiczne (tylko ze wskazań życiowych) [17].

Leczenie i zalecenia dotyczące porodu [18]

- Zaleca się, aby chore obciążone dużym ryzykiem powikłań leczyć w ośrodkach referencyjnych, gdzie dostępny jest wielodyscyplinarny zespół specjalistów.
- Jeśli u kobiety w ciąży konieczna jest operacja kardiochirurgiczna, zaleca się podawanie ciężarnej glikokortykosteroidu między 24., a 37. tygodniem ciąży.
- W większości przypadków zaleca się poród drogą pochwową.
- U wszystkich kobiet z chorobą serca należy rozważyć indukcję porodu po 40. ukończonym tygodniu ciąży.
- U kobiet z ciężkim nadciśnieniem tętniczym należy rozważyć poród drogami natury ze znieczuleniem zewnątrzoponowym.
- Jeśli wiek ciążowy przekroczył 26 tygodni, to przed konieczną interwencją chirurgiczną należy rozważyć rozwiązanie ciąży.
- Można rozważyć przeprowadzenie pomostowania aortalno-wieńcowego lub operacji zastawkowej podczas ciąży w razie nieskuteczności postępowania zachowawczego (w tym farmakoterapii) oraz w sytuacji zagrożenia życia matki lub jeśli nie ma możliwości leczenia przezskórnego. Nie zaleca się stosowania profilaktycznej antybiotykoterapii podczas porodu w celu zapobiegania infekcyjnemu zapaleniu wsierdzia [18].
- U pacjentek istotnie obciążonych kardiologicznie, muszą być spełnione warunki pełnego zabezpieczenia reanimacyjnego i intensywnego nadzoru na sali porodowej lub operacyjnej (sala intensywnej opieki położniczej). Do warunków tych należą:
- opieka anestezjologiczna;
- możliwość monitorowania: elektrokardiograficznego, hemodynamicznego i pulsoksymetrycznego;
- pełne zabezpieczenie reanimacyjne: leki, zestaw do intubacji i oddechu zastępczego, defibrylator, stymulator serca i elektrody do stymulacji przezskórnej i endokawitarnej.

Ośrodki, które nie są w stanie zapewnić wymienionych warunków porodu, nie powinny sprawować opieki położniczej nad zagrożonymi powikłaniami kardiologicznymi kobietami w ciąży. Złe rokowanie zwykle jest związane z brakiem adekwatnej opieki specjalistycznej, brakiem jednoznacznego rozpoznania i określonych zasad postępowania. Dobrze przygotowana pacjentka rodząca w warunkach intensywnego nadzoru jest w stanie pomyślnie urodzić nawet w przypadku bardzo zaawansowanej choroby serca.

Podsumowanie

Opieka nad ciężarną z chorobą serca stanowi istotne wyzwanie w codziennej praktyce lekarskiej. W procesie organizacji postępowania u takich pacjentek kluczowe jest wielowymiarowe podejście do problemu obejmujące ścisłą współpracę zespołu kardiologicznego i ginekologicznego. Pomimo licznych publikacji nadal potrzebne są kolejne opracowania poszerzające wiedzę na temat opieki kardiologicznej nad ciężarną. Obiecujące wydają się dane uzyskane z rejestrów utworzonych z inicjatywy ESC. Stanowią one obecnie główne źródło wiedzy do formułowania rekomendacji w temacie opieki nad ciężarną z dodatnim wywiadem kardiologicznym.

Konflikt interesów

Autorzy nie zgłaszają konfliktu interesów.

Piśmiennictwo

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The quality of life of patients with arterial hypertension in the bio-psycho-social dimension of health. Review of the literature

Jakość życia pacjentów z nadciśnieniem tętniczym w wymiarze bio-psycho-społecznym zdrowia. Przegląd literatury

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Abstract

Arterial hypertension (AH) is the cause of a reduction in the quality of life (QoL), influencing not only its subjective dimension, related to the deterioration of well-being but also the objective dimension, making it impossible to fulfil the current social functions and reducing the individual's ability to adapt or worsening the economic status due to the need to resign from work and social isolation. The study aims to present, based on a literature review, the QoL of patients with AH in the bio-psycho-social dimension of health. These 3 health components affect the course of the disease and at the same time determine the QoL of patients.

Key words: quality of life, hypertension, cardiology

Folia Cardiologica 2022; 17, 6: 351–355

Introduction

For many years, cardiovascular diseases have been the main cause of human health problems and even death, and their morbidity is due to many reasons [1]. Significant factors in the incidence of cardiovascular diseases, despite high blood pressure values, are also smoking, reduced physical effort, excess body weight, high cholesterol levels, diabetic diseases, unhealthy lifestyle, including unhealthy eating, stressful situations and factors. non-modifiable, genetic predisposition and environmental factors [2]. Among Poles, 9.9 million people suffered from hypertension in 2018, which accounted for 31.5% of the adult population and compared to 2013, this number increased by almost 200 000 people. The most numerous groups of patients with arterial hypertension (AH) in 2018 were women aged 65–74, among men the largest group was those aged 55–64 [3]. According to the data of the World Health Organization (WHO), today in approximately 1.28 billion adults aged 30–79 years around the world, AH was diagnosed, and 46% of these people are not aware of their disease [4].

Hypertension

Arterial hypertension remains the primary modifying factor for both cardiac and central nervous system diseases, despite the passage of time and the development of medicine [5]. Arterial hypertension is defined as measured systolic blood pressure ≥ 140 mm Hg and/or diastolic blood pressure ≥ 90 mm Hg [6]. In modern times, this disease

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Table 1. Number of hypertensive patients in the Polish population

	2013	2018
Number of hypertensive patients in Poland	9.7 mln	9.9 mln
Percent of the adult population in Poland	30.9%	31.5%

is called the disease of civilization, it is very widespread due to the progress of urbanization and globalization, as a result of which people lead unhealthy lifestyles and emerging comorbidities. The disease can sometimes "bloom" for many years practically asymptomatically, although it leads to serious health effects, e.g. stroke, ischaemic heart disease, or heart failure, the consequence of which may be death. According to available data, 8.5 million people die each year due to hypertension [7]. In selecting the appropriate treatment for hypertension, it is important to obtain the results of self-monitoring and correct blood pressure measurements at home in combination with blood pressure testing in the office. When talking about treatment, it should be borne in mind that this disease is chronic and is accompanied by treatment for the rest of the patient's life, so it is important at this point to treat the patient holistically. Most often, treatment involves taking specific, well-matched medications to maintain optimal blood pressure, which significantly extends life, but may have an impact on quality of life (QoL) [8].

Determining the quality of life in the bio-sycho-social model of health

Modern medicine is more and more often talking about assessing the QoL of a sick patient. The purpose of introducing a given concept was to obtain accurate health information, considering not only the physical health of a given person, but also various spheres of a person: mental, social, and spiritual. This methodology is often called a holistic approach to the patient. This approach allows you to gain knowledge about the multidimensional determinants of health and disease, recognizing the bio-psycho-social distinctiveness of each patient and allowing you to choose the treatment best suited to the individual needs of the patient, adopting the thesis about the uniqueness of each life. Since the QoL is a broad concept and covers a wide range of problems, from a medical point of view, researchers of the QoL of patients focus mainly on this concept, which is conditioned by the state of health [9]. The holistic health perspective is in line with the WHO's health perspective, which defines it as a state of mental, physical and social well-being, not just the absence of disease or disability. Until now, according to the biomedical concept of health, the human body was treated as a machine, and the disease was a verifiable deviation from the norm, and health was defined as the lack of disturbances in the sphere of biological human functioning and grouped the subjective states of the organism. The bio-psycho-social model of health was created from the need to look at the patient's life situation from a different perspective, considering those areas of human functioning that were so far ignored in the clinic [10].

Definition of the quality of life in disease

The concept of QoL was defined, among others, by the WHO, according to which the QoL is an individual perception by an individual of his or her life position in the cultural context and value system in which he lives, and in relation to tasks, expectations and standards determined by environmental conditions. The indicators of QoL are the ability to play the current life roles, the ability to adapt, mental well-being or functioning within given social groups [11]. In everyday medical practice, the QoL in terms of health is of great importance, considering the impact of disease and treatment on the patient's physical, mental and social functioning. Examination and assessment of the patient's QoL allow you to get to know his point of view, understand his condition, communicate with him or solve psychosocial healing problems. The aim here is to determine the effectiveness of treatment not only in terms of avoiding death, but also to assess the health and lifestyle that are relevant in chronic diseases. Testing the QoL in medical terms is the recognition of problems resulting from the disease and the treatment applied. It also seems important to define human activity in the physical, mental and social sense and to describe the patient's views on health and subjective well-being [12].

The contemporary concept of QoL was defined in the 1970s by Campbell, who proved the relationship between objective living conditions and life satisfaction [13]. Research on the QoL in medicine was first started by Rosser, who was the first to publish a method of measuring the QoL of patients. It exerted a great influence on subsequent works undertaken in this area, thus, in the following years, many definitions of QoL were created, focusing on the phenomena of health and disease [14]. Health-related (HR) QoL in 1990 defined Schipper as the functional effect of a physical, mental and social response to illness and treatment, perceived subjectively by the patient, and the assessment of the patient's life situation during the treatment period. The most important four aspects of the patient's functioning are the physical and motor skills, mental state, social and economic conditions, and somatic sensations. HRQoL allows you to look at the phenomena related to the disease in a broader aspect, both medical (e.g., testing the effectiveness of drugs) and non-medical

(functioning in the family or society). Moreover, health examinations contributed to the possibility of a better assessment of the general subjective QALY level as a measure of the QoL [15].

Factors determining the quality of life during arterial hypertension

Arterial hypertension is a significant change in a person's life, which presents a sick person with many challenges that must be dealt with. The struggle is not a short-term process but often stretches over many years or until death [16]. Improving the QoL is an integral part of the treatment of AH. Pharmacological and non-pharmacological treatment of hypertension should prevent the deterioration of the QoL of patients in the long term. Improperly selected drugs may worsen the QoL, reducing the chance of a good prognosis and effective treatment of hypertensive disease [17]. It was observed that patients who complained about complications of pharmacological treatment most often did not follow the doctor's recommendations for pharmacotherapy. And effective treatment, which would improve the QoL and alleviate the course of the disease, depends largely on compliance with the physicians' recommendations. The factors determining the patient's QoL also include material status, age, gender, socioeconomic variables of a person, housing conditions, education and many others, which contribute to QoL [18]. In some of the studies, it was shown that the above factors account for 32.7% of the variability in the quality-of-life level in patients with diagnosed hypertension [19]. And in many research studies it was concluded that in terms of the sense of well-being, a subjective assessment of health is a better determinant than an objective assessment of health. In the same studies, it was concluded that the QoL depends on clinical factors, such as blood pressure values (the higher the value, the worse the quality), overweight and organ complications, as well as the number and type of drugs used, e.g., over 4 types of drugs (all this makes the QoL deteriorate) [20]. It is also impossible not to include among these factors determining the QoL, the patient's beliefs and attitude towards his disease. In patients with long-term disease, higher levels of depression, stress, low mood, decreased energy and a higher level of social isolation are observed [21].

The quality of life of patients with arterial hypertension — a review of studies in the literature

Sawicka et al. found that the duration of the disease has an impact on the QoL of the respondents in the physical aspect, as well as the number of drugs used. The shorter the duration of the disease, the better the QoL, and the subjects who took one drug had a better QoL. The authors claim that the individual general perception of the QoL and own health is better among women and that men indicate a better QoL in terms of physical and environmental aspects [23]. The analysis of the literature shows that one of the factors having a significant impact on the QoL of people with hypertension is the level of education. According to Bień, the level of education is in a high position in the ranking of the independent factor influencing health. Hypotonic people with higher education are characterized by a higher QoL, and a low level of education is associated with higher incidence and mortality due to hypertension and a lower QoL [24]. Kocowska et al. [20] proved a significant relationship between compliance with the doctor's recommendations and the QoL. Lack of knowledge about the disease, and thus not following the doctor's recommendations, worsens the patient's QoL [20–22]. On the other hand, the results relating to the relationship between physical activity and QoL should be related to the observations of Cegła et al. [25], which conducted a study aimed at determining the impact of physical activity on the QoL of patients with confirmed AH. The analysis of the test results showed that a quarter of the patients (24,8%) with AH are not physically active and lead a passive lifestyle. Only 34% of the respondents declared that they are physically active. Therefore, it was concluded that the patients lead a less active lifestyle and that the lack of physical activity significantly deteriorates the daily functioning and QoL of patients with hypertension, and their QoL depends on the physical activity practised, its type and regularity [25, 26]. Paczkowska et al. concluded that the socio-demographic factors significantly differentiating the assessment of the QoL of the respondents included: gender, age, education, source of income, and financial situation [27]. Arterial hypertension significantly impairs the QoL of patients, regardless of sex and age, which is confirmed by many studies [27–30].

Conclusions

Arterial hypertension, as a chronic disease, affects the patient's QoL and the discomfort in the bio-psycho-social sphere in people suffering from this disease, especially in those patients who are not aware of their disease and do not have proper knowledge about its treatment. In the treatment of AH, pharmacotherapy is indicated, and often psychological support and psychoeducation.

Conflict of interest

None declared.

Streszczenie

Nadciśnienie tętnicze stanowi przyczynę obniżenia jakości życia, wywierając wpływ nie tylko na jej wymiar subiektywny, związany z pogorszeniem samopoczucia, ale również na wymiar obiektywny, uniemożliwiając pełnienie dotychczasowych funkcji społecznych i obniżając zdolność indywidualnego przystosowania się, czy też pogarszając status ekonomiczny z powodu konieczności rezygnacji z pracy zawodowej i izolacji społecznej. Celem pracy jest przedstawienie, na podstawie przeglądu literatury, jakości życia pacjentów z nadciśnieniem tętniczym w wymiarze bio-psycho-społecznym zdrowia. Powyższe trzy komponenty zdrowia wpływają na przebieg choroby, a jednocześnie warunkują jakość życia pacjentów.

Słowa kluczowe: jakość życia, nadciśnienie tętnicze, kardiologia

Folia Cardiologica 2022; 17, 6: 351–355

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The many faces of infective endocarditis

Wiele twarzy infekcyjnego zapalenia wsierdzia

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Abstract

This case report presents a history of a 55-year-old male with a history of an ascending aorta aneurysm and aortic regurgitation who underwent a David procedure, followed by implantation of a DDD pacemaker. The patient remained stable, until 4 years later he was admitted to the hospital with the suspicion of sepsis which spread to the bio-conduit and native aortic valve causing infective endocarditis. The treatment was complicated by haemorrhagic stroke and thromboembolic event. Once his condition was stabilized, he underwent yet another cardiac surgery. A few months later, he was hospitalized again and an echo revealed vegetation on the pacemaker's electrode. Ultimately the decision was made for the complete hardware removal.

Key words: infective endocarditis, cardiac device-related infective endocarditis, echocardiography, complications, HeartTeam, cardiac surgery

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Introduction

Infective endocarditis (IE), while remaining a relatively uncommon disease, still poses a serious clinical challenge in modern medicine. The incidence is estimated to range between 1.5 and 11.6 cases per 100 000 people depending on the region of the world, however studies have shown it had doubled in the last two decades in Europe with a marked 4% yearly increase [1, 2]. Despite great advances made in recent times in diagnostics and treatment, the prognosis of IE remains poor with approximately 25% in-hospital and 41% 5-year mortality rate [3, 4]. Advanced age and presence of pre-existing valvulopathies primarily concerning aortic or mitral valve or intracardiac foreign material (pacemaker electrodes, vascular prostheses) are among many of the risk factors in IE development.

Case report

A 55-year-old male with a history of an ascending aorta aneurysm, aortic regurgitation and atrial fibrillation was admitted to the Department of Cardiac Surgery for elective surgery. He underwent a David procedure, during which on cardiopulmonary bypass the graft was sutured in place, the patient's native bicuspid aortic valve was re-implanted and coronary arteries were re-attached to the aortic graft. In the early postoperative course the patient required temporary epicardial pacing. Later, the decision was made to implant a permanent DDD pacemaker.

A month after the surgery the patient presented to the emergency room with chest pain lasting over 2 weeks, worsening with body movement. On admission, he was hemodynamically stable, afebrile, with a blood pressure of

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158/93 mm Hg, with no audible murmur over the heart. Laboratory tests showed an increased serum concentration of N-terminal pro-B-type natriuretic peptide (1630 pg/mL) without elevation of the inflammatory markers. Echocardiography revealed an ejection fraction of 40% and proper functioning of the aortic conduit. Postpericardiotomy syndrome had been diagnosed and was effectively treated with ibuprofenum and colchicine.

The patient's condition remained stable, until four years later, he was admitted to the Department of Internal Medicine due to severe back pain unresponsive to medication, decreased effort tolerance and weight loss of 20 kilograms over the last 4 months. The physical examination was unremarkable. Laboratory tests revealed elevated inflammatory markers, N-terminal pro-B-type natriuretic peptide concentration, anaemia, and thrombocytopenia. Two separate blood cultures tested positive for *Streptococcus gallolyticus subspecies gallolyticus*. Vancomycin was added to the initial empirical antibiotic therapy. Suspicion of infective endocarditis was raised. Transthoracic echocardiography (TTE) showed ejection fraction of 55% and increased gradients through the aortic valve. Transoesophageal echocardiography (TOE) confirmed endocarditis, revealing oscillating masses, the biggest measuring 13 × 6mm, on the fused leaflet of the bicuspid aortic valve and significant aortic regurgitation. A few days later the patient started complaining of blurred vision in the right eye, right-sided hemianopia and dyspnoea. Head computed tomography (CT) revealed intracranial hematoma in the occipital area in the left hemisphere, indicative of a haemorrhagic stroke. Consulting neurosurgeon did not qualify the patient for surgical treatment. CT-angiography of the chest ruled out the possibility of pulmonary embolism, but showed pleural effusion. Clinically he manifested symptoms of pulmonary oedema. The patient was transferred to the Department of Cardiology for further treatment, where after a microbiology consult, vancomycin was swapped for ampicillin. His physical examination showed a systolic-diastolic murmur best heard over the aortic valve. Laboratory tests revealed elevated C-reactive protein concentration with low procalcitonin level and syderopenic anaemia. Blood and urine cultures were negative for bacterial growth. In the light of severe anaemia 2 units of red blood cells were transfused. The otolaryngologist and maxillofacial surgeon ruled out potential foci of inflammation. During the hospitalization the patient was discussed several times by the HeartTeam — cardiac surgery was postponed due to a recent haemorrhagic stroke. Given the emergence of pain in the left thigh, a Doppler ultrasound was performed, revealing patent big arterial vessels and no signs of deep vein thrombosis. Little hyperechogenic lesions obstructed a small arterial vessel within the vast lateralis muscle, which radiologists described as embolic material, most likely of valvular origin. Consulting vascular surgeon recommended further conservative treatment with acetylsalicylic acid and heparin. After another angio-CT of the head, the patient was once again discussed by the HeartTeam with the participation of a neurologist. acetylsalicylic acid and heparin were discontinued and this time the patient was finally qualified for the re-operation and referred to the Cardiac Surgery Clinic. He underwent implantation of a bio-conduit with re-implantation of the coronary vessels using the Cabrol method.

Nine months later the patient was admitted to the hospital with recurrent fever, chills, progressive weakness and severe back pain in the lumbar area. On physical examination a systolic murmur over the heart was detected. Blood tests revealed elevated inflammatory markers and signs of acute kidney injury. Blood cultures were taken and empirical antibiotic therapy was introduced. TOE showed vegetation on the pacemaker's electrode. *Enterococcus faecalis* was identified in blood samples and targeted treatment with ampicillin and ceftriaxone was implemented. Diagnosis of cardiac device-related infective endocarditis was made. Once negative blood cultures were obtained, the whole pacemaking system was removed and a temporary one was implanted. Two weeks later a permanent DDD pacemaker was re-implanted on the contralateral side. Since the source of infection had not been found, the decision was made to prescribe oral amoxicillin until the next control visit. Taking under consideration severe haemorrhagic complications in the past, no recent atrial fibrillation episodes and no thrombotic lesions in the left atrial appendage, the anticoagulation treatment was deferred until the check-up.

Discussion

To this day positive blood cultures, imaging and clinical symptoms continue to be the cornerstone of the diagnosis of infective endocarditis. The most common pathogens identified in blood cultures are staphylococci, followed by *streptococci* and *enterococci* [5]. Echocardiography remains the method of choice for diagnosis and TTE, as a non-invasive and widely available technique, should be performed immediately once IE is suspected. European Society of Cardiology recommends TOE in patients with high clinical suspicion of IE and a negative or poor-quality TTE or when a prosthetic valve or intracardiac foreign material is present [6]. TOE offers better image quality and shows higher sensitivity for the diagnosis of vegetations of approximately 85–90%, compared to 75% for TTE [6]. In cases of inconclusiveness of echocardiography additional imaging methods such as multislice CT, 18-fluorodeoxyglucose positron emission tomography/CT, and single-photon emission CT are recommended to confirm IE [7]. Despite a quick confirmation of the diagnosis and promptly administered antibiotic therapy, the patient experienced both haemorrhagic and thromboembolic complications of the disease. His condition required several HeartTeam consults to decide the right choice of

treatment. Patients with a previous history of infective endocarditis are more likely to develop another case of the disease. In such situations, the mortality rate and the incidence of serious complications are higher compared to patients with a single episode [8]. Thus, in high-risk patients certain non-specific prevention measures should be taken to minimize the probability of repeat infection. That includes frequent dental check-ups, strict cutaneous hygiene and disinfection of wounds, and rational use of antibiotics. Ultimately, the patient was diagnosed with a case of cardiac device-related infective endocarditis. Under such circumstances, by evidence-based medicine, the correct decision was made for a complete hardware removal in line with prolonged antibiotic therapy [9].

Conclusions

Infective endocarditis remains a disease with many faces, with a wide range of non-characteristic clinical manifestations and serious complications including heart failure, thromboembolic events, persisting infections, heart rhythm and conduction disorders and renal failure. Considering the benefits and risks of undertaken treatment, as well as an individual approach to the patient's status and comorbidities, are the key components of successful therapy.

Conflict of interest

The authors declare no conflict of interest.

Streszczenie

Opisany przypadek dotyczy 55-letniego mężczyzny z tętniakiem aorty wstępującej z towarzyszącą niedomykalnością zastawki aortalnej w wywiadzie. Pacjent był poddany operacji Davida z następczą implantacją stymulatora serca typu DDD. Cztery lata później rozpoznano u niego infekcyjne zapalenie wsierdzia (IZW) w obrębie wszczepionej protezy aortalnej oraz na natywnej zastawce aortalnej. Leczenie było powikłane udarem niedokrwiennym mózgu oraz epizodem zatorowo-zakrzepowym. Po stabilizacji stanu chorego, przeszedł on kolejną operację kardiochirurgiczną. Kilka miesięcy później został ponownie przyjęty do szpitala z objawami sepsy — stwierdzono obecność wegetacji na elektrodach stymulatora i rozpoznano odelektrodowe zapalenie wsierdzia. Ostatecznie podjęto decyzję o usunięciu całego układu stymulującego.

Słowa kluczowe: infekcyjne zapalenie wsierdzia, infekcyjne zapalenie wsierdzia związane z urządzeniami kardiologicznymi, echokardiografia, powikłania, HeartTeam, operacja kardiochirurgiczna

Folia Cardiologica 2022; 17, 6: 356–358

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Nickel allergy as a probable cause of complications after closing the atrial septal defect type ostium seccundum with the Amplatzer septal occluder in a 6-year-old girl

Uczulenie na nikiel jako prawdopodobna przyczyna komplikacji po zamknięciu zapinką Amplatzera ubytku w przegrodzie międzyprzedsionkowej u 6-letniej dziewczynki

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Abstract

A 6-year-old girl underwent a successful closure of a large atrial septal defects (ASD2) with an Amplatzer septal occluder (ASO). After 2 years, she required surgical removal of the implant due to a local inflammatory reaction and leakage around the occluder, closure of the ASD with an autopericardial patch and removal of the newly formed fistula between the aorta and the left atrium (Ao-LA). Fistula regeneration requiring surgical treatment was observed twice over the next two years. During this time, incidents of subfebrile body temperature with positive inflammatory markers and sterile blood cultures occurred. Interventional reclosure of the fistula was withdrawn due to its close location to the coronary artery, as well as the suspicion of an allergic reaction to nickel compounds contained in ASO, supposedly responsible for recurring complications and a very unusual course of treatment. An allergy patch test was performed, resulting positive (+++) at 96 hours. Currently, after 3 years of follow-up, there is no evidence of septal shunt or reformation of Ao-LA fistula. The patient remains asymptomatic under outpatient care, avoiding contact with nickel compounds in any form and state.

Key words: defect in the atrial septum, Amplatzer occlude, allergy to nickel, fistula

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Introduction

Atrial septal defects (ASD2) are the most common congenital heart defects [1]. In the diagnosis of ASD, the "gold standard" is transthoracic (TTE) and transoesophageal (TEE) echocardiography [2, 3]. A small ASD2 (3–4 mm) usually remains under observation, while larger ones require closure [4]. Standard management is TEE-guided transvascular closure of the defect with the use of an occluder, while surgical treatment is reserved for atypical forms [5, 6]. Recommendations after closing the defect include prophylaxis of infective endocarditis and aspirin admission

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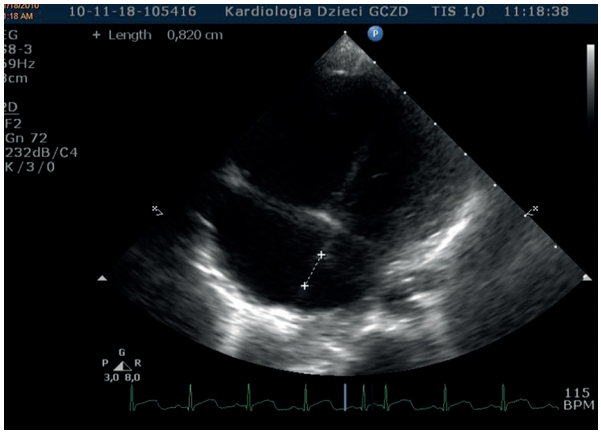

Figure 1. Transthoracic echocardiography 4-chamber view. Atrial septal defects 2 approx. 8.2 mm. The enlarged right atrium and right ventricle

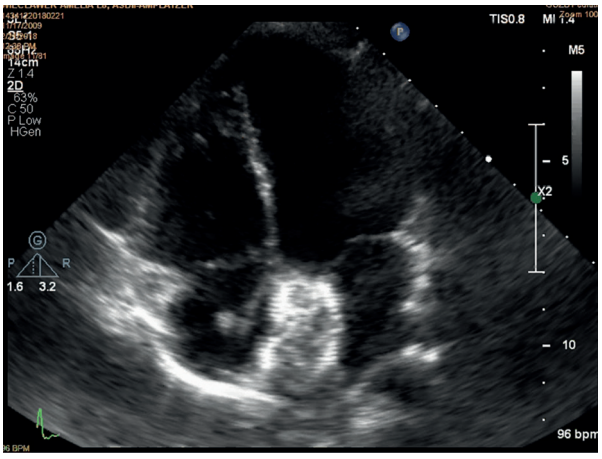

Figure 2. Transthoracic echocardiography 4-chamber view. Correctly positioned implant, No septal leakage. Significant reduction in the size of the chambers of the right heart

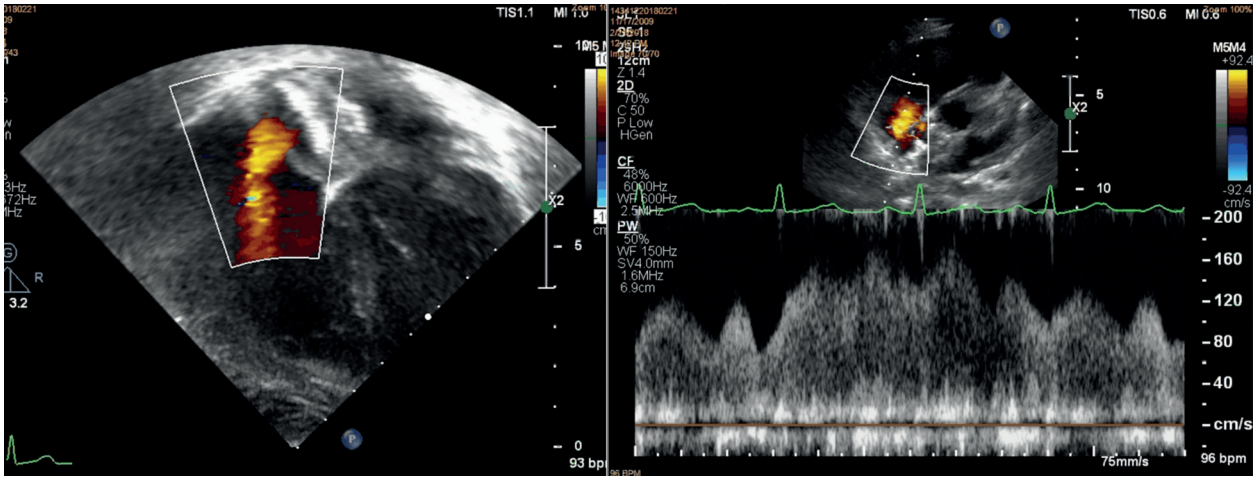

Figure 3. There is a left-to-right volume shunt around the Amplatzer occlude

over 6 months after the procedure [5, 7]. Complications after endovascular intervention are relatively rare and are estimated at 2.2–8.6% [5].

Case report

A 6-year-old girl was admitted to the pediatric cardiology department to close ASD2 diagnosed at 1 year of age. Physical examination revealed a systolic murmur at the left parasternal border and a stiffly split second heart sound. The electrocardiogram showed the right axis deviation and features of a partial right branch bundle block. Transthoracic echocardiography confirmed an ASD2, 17–20 mm in diameter with Qp:Qs = 1.9:1. The patient underwent a transvascular closure with a 19 mm Amplatzer device (Figure 1). The procedure and the early postoperative period were uneventful, the implant correct position and no residual flow was observed. An increasing leakage around the implant was found after 6 months in control TTE, along with hyperechogenic adjacent structures. After another 18 months, she was referred to the department due to fatigue, increased sweating and lack of appetite. Performed ultrasound imaging examinations (TTE, TEE) and magnetic resonance imaging exposed a correctly positioned implant and an abnormal linear structure parallel to the right atrial disc, as well as significant flow towards the right atrium (Figure 2). In addition, a fistula approximately 2 mm in diameter was visualized between the aorta and the left atrium (Ao-LA) (Figure 3). The girl underwent a cardiosurgical consult and qualified for surgical treatment (operation No. 1).

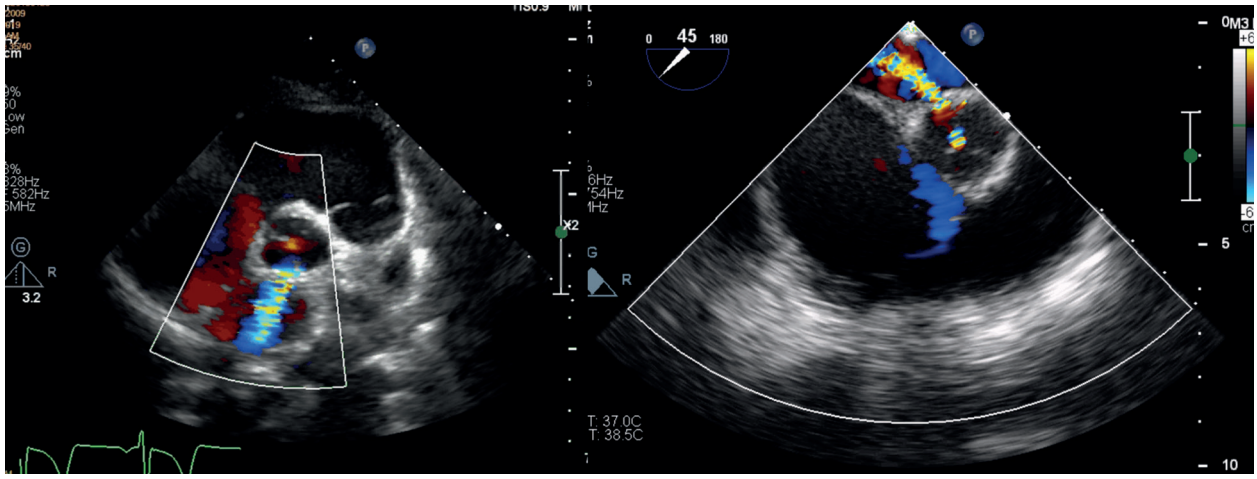

Figure 4. The fistula between the aorta and the left atrium. On the left, transthoracic echocardiography. On the right, the same image in transoesophageal echocardiography

The implant was removed, along with the adjacent cyst and fibrous tissue. The ASD was closed with an autopericardial patch and the Ao-LA shunt was ligated. After 8 days, the fistula recanalized and another operation was required to re-close the fistula (operation No. 2). The patient was discharged after several days and readmitted a month later due to fever, decreased appetite, malaise, increased fatigue and chest pain. Laboratory tests showed an increase in inflammatory markers with sterile blood cultures. Imaging revealed an Ao-LA fistula of approximately 2.5 mm. A wait-and-see attitude was adopted, with the introduction of antibiotic therapy, angiotensin-converting enzyme inhibitors, β-blockers and dehydrating drugs treatment. After 2 years, the fistula was still present, hence a decision for another reoperation was undertaken. Interventional treatment was abandoned due to the close distance of the fistula to the coronary artery. Moreover, a hypothesis of contact allergy to nickel was taken under consideration, resulting in such complications. The suspicion was later confirmed by a positive nickel allergy patch test ([+++] after 96 hours). Another operation was performed (operation no. 3) and the fistula was successfully closed. In a 3-year follow-up, no recanalization of the fistula (Figure 4) is observed. The patient remains asymptomatic under outpatient care, avoiding contact with nickel compounds in any form and state.

Discussion

The presented atypical course of ASD2 closure with the Amplatzer device indicates that allergy to nickel compounds contained in the implant may prevent effective intervention treatment. The known post-interventional complications include embolization, erosion, headaches, thrombus formation or vegetation, tachyarrhythmias, access site

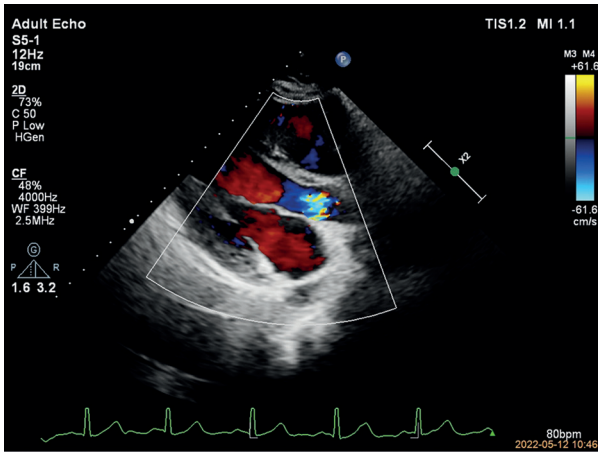

Figure 5. Transthoracic echocardiography, left ventricular long axis. Follow-up observation; no aorta and the left atrium shunt

complications, bleeding, etc. [5, 8, 9], while nickel allergy is listed last as a possible complication and the frequency of this reaction is not known [5]. The implant is covered with nitinol, which may release traces of nickel into the blood and cause an allergic reaction. In general, symptoms appear within the first few days or months and include headache, rash, fever, palpitations and shortness of breath, sometimes with pericardial effusion. If pharmacological treatment is ineffective, it may be necessary to remove the occluder [8, 9]. It is indicated that in patients with a positive family history, a nickel allergy skin test should be performed before the procedure [10]. This patient has not provided any information indicating her allergy; therefore the test was not performed. To the authors' knowledge and review of the literature, the child has not developed a reaction around the clasp with the simultaneous formation

of a self-reproducing fistula between the Ao-LA, requiring as many as three operations to close.

Conclusions

Each interventional treatment of an interatrial defect carries the risk of rare and unexpected complications, including an allergic reaction to nickel with the formation of a fistula. Surgical treatment of a fistula carries a high risk of low effectiveness.

Conflict of interest

The authors do not report any financial or personal connections with other persons or organizations that could adversely affect the content of the publication and claim the right to this publication

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Streszczenie

Sześcioletniej dziewczynce skutecznie zamknięto duży ASD2 za pomocą zapinki Amplatzera (ASO). Po 2 latach wymagane było chirurgiczne usunięcie implantu z powodu wytworzenia miejscowego odczynu i powstania przecieku wokół zapinki, zamknięcie ASD łatką z własnego osierdzia oraz usunięcie nowo powstałej przetoki pomiędzy aortą a lewym przedsionkiem (Ao-LA). W ciągu kolejnych 2 lat jeszcze dwukrotnie obserwowano samoodtwarzanie się przetoki wymagające leczenia chirurgicznego. W tym czasie pojawiały się stany gorączkowe z dodatnimi wskaźnikami zapalnymi, jednak posiewy z krwi były jałowe. Nie zdecydowano się na leczenie interwencyjne przetoki ze względu na bliską lokalizację z naczyniem wieńcowym, jak również z powodu podejrzenia reakcji uczuleniowej na związki niklu zawarte w ASO, które mogły odpowiadać za komplikacje i bardzo nietypowy przebieg leczenia. Wykonano uczuleniowy test płatkowy, który był dodatni (+++) po 96 godzinach. Aktualnie, po 3 latach obserwacji, nie stwierdza się przecieku na przegrodzie międzyprzedsionkowej ani ponownego wytworzenia przetoki Ao-LA. Dziewczynka pozostaje pod okresową kontrolą kardiologiczną i nie wykazuje żadnych niepokojących objawów, unika kontaktu ze związkami niklu, które mogą być obecne w produktach spożywczych oraz licznych przedmiotach codziennego użytku.

Słowa kluczowe: ubytek w przegrodzie międzyprzedsionkowej, zapinka Amplatzera, alergia na nikiel, przetoka

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Patient out of control: diagnostic and treatment dilemmas in Loeys-Dietz syndrome

Pacjent poza kontrolą — trudności diagnostyczne i lecznicze w zespole Loeysa-Dietza

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Abstract

Loeys-Dietz syndrome (LDS) first identified in 2005 is an aggressive congenital disorder of connective tissue characterized by multisystemic involvement (hypertelorism, and bifid/broad uvula or cleft palate). The most common features are vascular manifestations such as widespread arterial aneurysms and dissection at a young age. The diagnosis is confirmed by a molecular test and computed tomography but no specific diagnostic criteria exist. The similarity of clinical manifestations to other connective tissue disorders may be associated with poor recognition of LDS. The patient is a 20-month-old boy who was admitted to our clinic presenting circulatory failure. Tests revealed dilated ascending aorta and aortic valve regurgitation, because of which ascending aorta and aortic valve replacement was performed. Seven years later his health state deteriorated significantly. Computed tomography angiography revealed a massive aneurysm of the aortic arch (8 cm), multiple thoracic aortic aneurysms and vascular tortuosity. Based on significant clinical image LDS was diagnosed. Due to the multiplicity of aneurysms, the patient was disqualified from any further surgical treatment. LDS is characterized by an aggressive vascular course. Early diagnosis, prophylactic surgery of the aorta and pharmacological treatment are recommended in these patients as the only possibility to prolong their lives.

Key words: Loeys-Dietz syndrome, connective tissue diseases, aortic aneurysm, cardiovascular abnormalities, aortic dissection

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Introduction

Loeys-Dietz syndrome (LDS) is a rare connective tissue disorder (CTD) with autosomal dominant inheritance. 75% of cases result from de novo mutation [1]. The exact prevalence is unknown. LDS has multisystemic manifestations, considering a mainly cardiovascular system.

Case report

A 20-month-old boy was admitted to a hospital in severe general condition with the blood flow centralization. Echocardiography revealed left ventricular hypertrophy with a left ventricular ejection fraction (LVEF) of 14%. Computed tomography angiography (CTA) presented ascending aorta diameter enlarged to 3.5 cm (Figure 1), aortic arch diameter to 1.8 cm. Diagnostic cardiac catheterization revealed massive aortic valve regurgitation. Cardiac surgeons performed aortic valve replacement and supracoronary ascending aorta replacement which improved the patient's condition significantly (LVEF improved to 40%). On the 18th day after surgery, the boy was discharged with an antihypertensive drug regimen. Due to parental non-compliance, the patient did not follow treatment directions. Seven years later the boy was admitted to our clinic with features of upper respiratory tract inflammation, progressive dyspnoea and exercise intolerance. The X-ray image was inconclusive. Inflammation parameters were moderately elevated, blood culture result was negative. Empiric antibiotic therapy was initiated. Echocardiography did not show any vegetations. CTA revealed: an aortic arch aneurysm (8 cm), multiple thoracic aortic aneurysms, dilated brachiocephalic trunk (3.25 cm) (Figure 2A) and common carotid arteries, aneurysm of the right middle cerebral artery (Figure 2B). Moreover, the patient presented optic neuropathy, papilledema, dissection of a retina, intraocular inflammation and scoliosis. Based on clinical manifestation the LDS was diagnosed by two independent units. Due to the multiplicity of aneurysms Heart Team disqualified the patient from any surgical treatment. Tracheobronchial compression with atelectasis occurred as a consequence of an aortic arch aneurysm. Because of recurrent respiratory disorders demanding mechanical ventilation and repeated intubations tracheostomy was performed. Unfortunately, the patient died due to spontaneous pulmonary haemorrhage and cardiac arrest.

Due to the overlapping symptoms among Marfan-like syndromes, establishing the diagnosis of LDS may be challenging in clinical practice. Abnormal twists and turns of arteries have been considered hallmarks of LDS. However, studies have proven that tortuosity is present in many other genetically mediated arteriopathies [2]. Nevertheless, the development of quantitative methods describing arterial tortuosity such as the tortuosity index (TI) creates new possibilities to differentiate between CTD. Spinardi et al. [3] found the vertebrobasilar system (VBS) TI to be the strongest independent predictor of LDS in patients with CTD. Increased vertebral TI links with more severe dilatation of the aortic root, higher probability of cardiac surgery intervention, earlier dissection and death [4]. Another valuable tool is the newly described chalice sign, which is

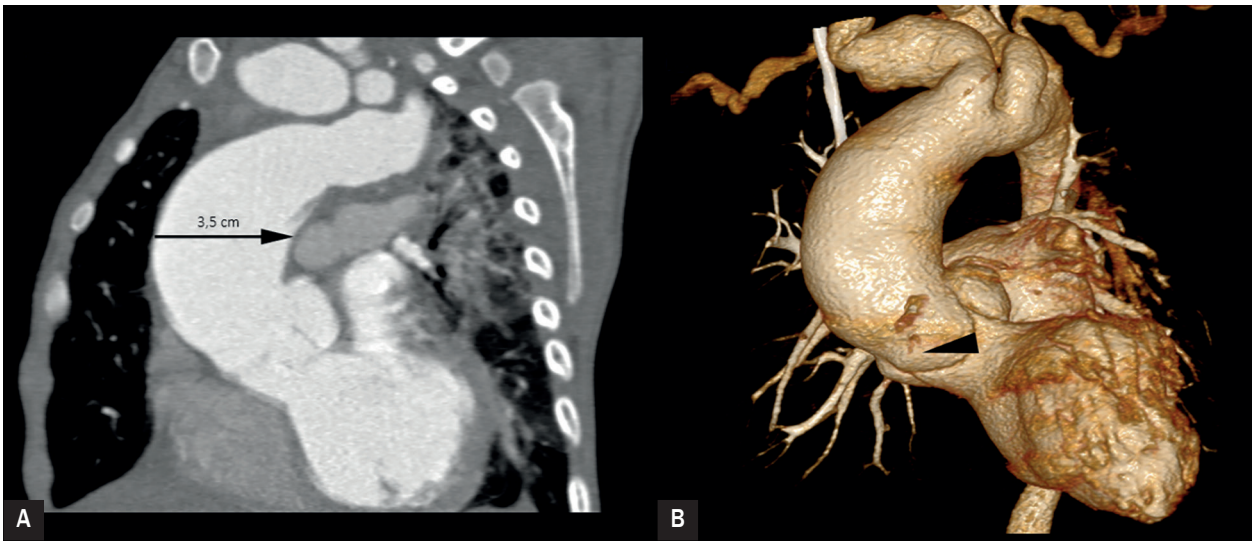

Figure 1. Multislice CT angiography of an aortic arch aneurysm in a 20-month-old boy with suspected Marfan syndrome; **A.** Sagittal CT angiogram; **B.** 3D volume rendering image show ascending aorta with a maximum diameter of 3.5 cm (arrow), a significant enlargement of the aortic root and moderately dilated three sinuses of Valsalva (arrowhead) with severe aortic regurgitation; CT — computed tomography

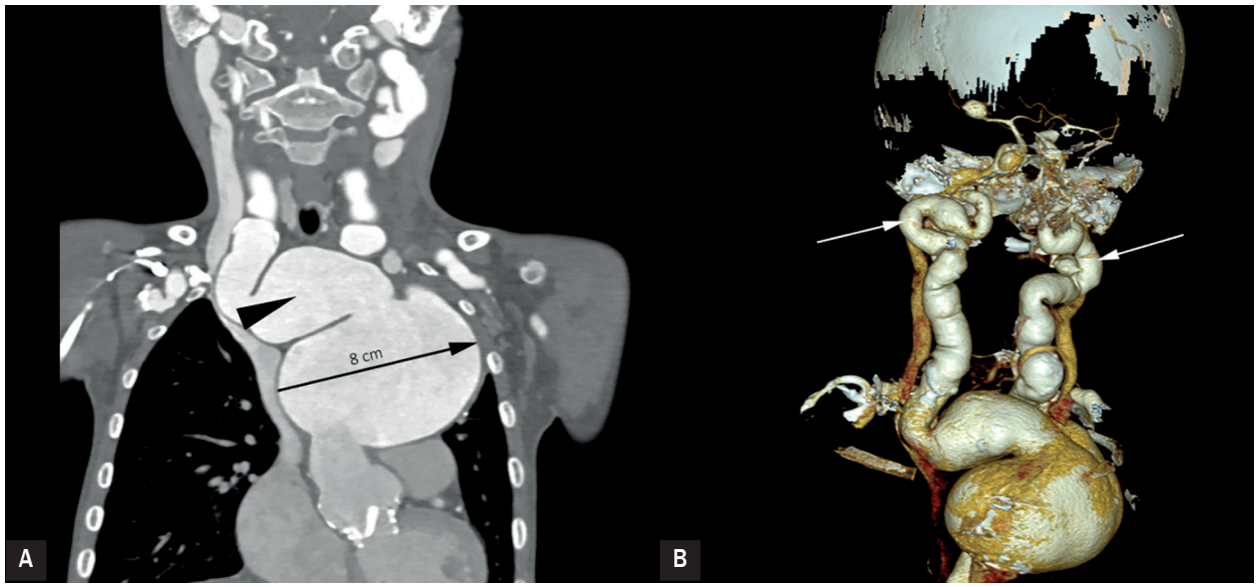

Figure 2. Multislice CT angiography of an 8-year-old boy with radiological diagnosis of Loeys-Dietz syndrome; **A.** Coronal CT angiogram shows an 8 cm aortic arch aneurysm (arrow) and dilated brachiocephalic trunk with a maximal diameter of 3.25 cm (arrowhead); **B.** 3D volume rendering image reveals markedly tortuous left and right common carotid arteries (arrows). Additional CT finding includes an aneurysm of the right middle cerebral artery (arrowhead); CT — computed tomography

defined as a carotid bifurcation angle of ≥ 80°, highly specific for LDS especially when bilateral [5].

The average life expectancy in patients with LDS is 37 years while those with vascular Ehlers–Danlos syndrome (EDS) are expected to live 48 years and patients diagnosed with Marfan syndrome and properly treated have an average lifespan of 70 years [6]. Differences are related to the known propensity toward rupture and dissection at a younger age and smaller aortic diameter in LDS [7]. The major source of early mortality is thoracic aortic dissection (67%), abdominal aortic dissection (22%) and cerebral haemorrhage (7%) [6]. A noteworthy correlation between cerebral aneurysms and extracranial arterial dissection was reported. Cerebral aneurysm found in the brain imaging screening may point out the need for careful investigation due to the higher risk of severe extracranial vascular events [8]. Conservative medication involves strict control of hypertension and reducing hemodynamic stress [9]. Most of the patients require surgical interventions. In comparison to the EDS, the fatal complication rate post-surgery is 1.7% in LDS versus 45% in EDS. All patients with LDS require annual echocardiography to control especially the aortic root. Moreover, the whole arterial tree should be assessed over aneurysms and tortuosity in magnetic resonance angiography or CTA.

Conclusion

As the LDS is characterized by the most aggressive vascular course among CTD, early diagnosis and prompt pharmacological and surgical interventions are crucial in avoiding dreadful consequences. Despite the exact criteria for diagnosing LDS are not established, we need to consider the disease when we find any LDS-related mutation in genes combined with characteristic clinical presentation: multiple arterial aneurysms, dissection or family history of the disease [10]. Future research might bring personalized gene-based management strategies.

Conflict of interest

The authors declare no conflict of interest.

Streszczenie

Zespół Loeysa-Dietza (LDS) opisany po raz pierwszy w 2005 roku jest wrodzoną wieloukładową chorobą tkanki łącznej o agresywnym przebiegu. Najczęstsze są objawy naczyniowe, takie jak rozległe tętniaki i rozwarstwienia tętnic, do których dochodzi w młodym wieku. Diagnoza stawiana jest na podstawie wyników badań molekularnych i tomografii komputerowej, jednak nadal nie istnieją specyficzne kryteria diagnostyczne. Podobieństwo objawów klinicznych do innych zaburzeń tkanki łącznej skutkuje zbyt małą rozpoznawalnością LDS. Praca przedstawia historię 20-miesięcznego chłopca przyjętego do kliniki z powodu niewydolności krążenia. Przeprowadzone badania wykazały poszerzenie aorty wstępującej i niedomykalność zastawki aortalnej, z powodu których podjęto decyzje o wymianie aorty wstępującej i zastawki aortalnej. Siedem lat po zabiegu stan zdrowia chłopca uległ znacznemu pogorszeniu. W angiografii tomografii komputerowej rozpoznano masywnego tętniaka łuku aorty (8 cm), liczne tętniaki aorty piersiowej i stwierdzono krętość naczyń. Na podstawie charakterystycznego obrazu klinicznego rozpoznano LDS. Ze względu na mnogość tętniaków pacjent został zdyskwalifikowany z dalszego leczenia operacyjnego. LDS charakteryzuje się agresywnym przebiegiem naczyniowym, więc u chorych kluczowe znaczenie mają wczesna diagnostyka, profilaktyczna operacja aorty i leczenie farmakologiczne dające jedyną możliwość przedłużenia życia.

Słowa kluczowe: zespół Loeysa-Dietza, choroby tkanki łącznej, tętniak aorty, anomalie naczyniowe, rozwarstwienie aorty

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Mitral valve vegetations in a 16-year-old girl, surgically treated with minimally invasive reconstruction

Wegetacje na zastawce dwudzielnej u 16-letniej dziewczynki leczonej chirurgicznie metodą małoinwazyjnej rekonstrukcji

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Abstract

Infective endocarditis in children is a rare complication and is most often associated with dental interventions. It may develop in course of congenital and acquired heart defects, as well as previous cardiac surgeries. The case regards a 16-year-old girl reporting significant fatigue, low-grade fever, lack of appetite with a weight loss of 5 kg, apathy, and enlargement of the spleen over six months before admission. Physical examination exposed systolic murmur in the apical region. The patient was admitted to a general paediatric ward and then, after confirming vegetation on the mitral valve, further treatment was carried out in the paediatric cardiology ward. The blood cultures revealed *Streptococcus Gordoni* infection. Intensive antibiotic treatment was initiated under the control of blood cultures, which were negative after 7 days of treatment. An interdisciplinary council meeting decided to continue the treatment. Cardiosurgical consult resulted in transferring the patient to the adult cardiosurgery ward, even though she was not of age, where a minimally invasive valve reconstruction was performed using artificial tendon threads and an artificial Carpentier–McCarthy–Adams 26 mm mitral ring. The postoperative course was uneventful and the girl was returned to the care of paediatric cardiologists. Currently, she is in good condition and is under constant control.

Key words: infective endocarditis, mitral valve, valve plasty

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Introduction

Infective endocarditis (IE) is a bacterial disease that may cause the formation of vegetations on one or more valves [1–3]. The diagnosis is based on the visualization of vegetation in echocardiography, often supplemented with computed tomography and magnetic resonance imaging [4]. Early treatment can prevent serious complications, the most dangerous of which is regurgitation and/or stenosis of one or more valves. In case of progression

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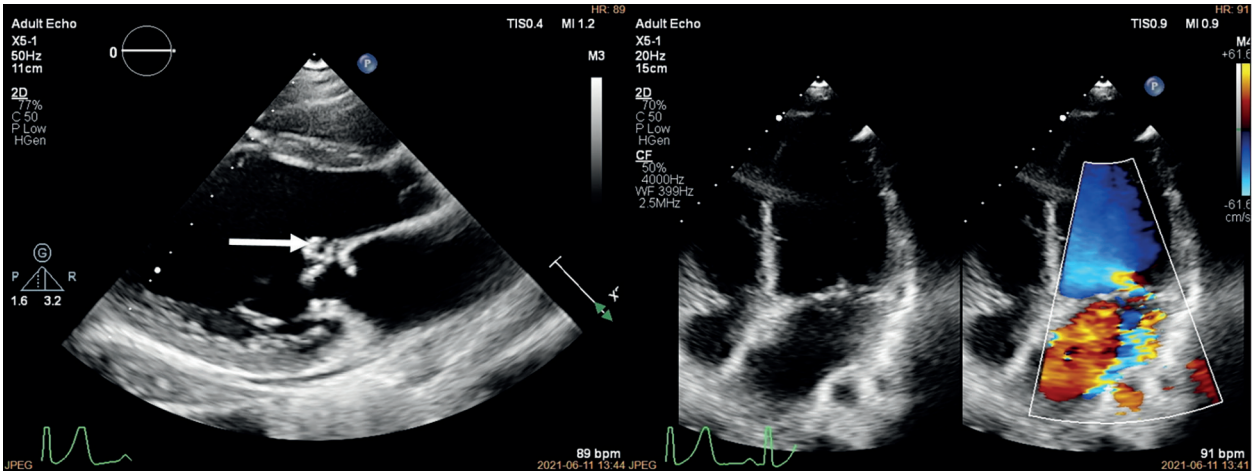

Figure 1. Echocardiographic image, left ventricular long axis. Left: on the anterior mitral valve leaflet vegetations that distort the valve (arrow). Right: massive valve regurgitation

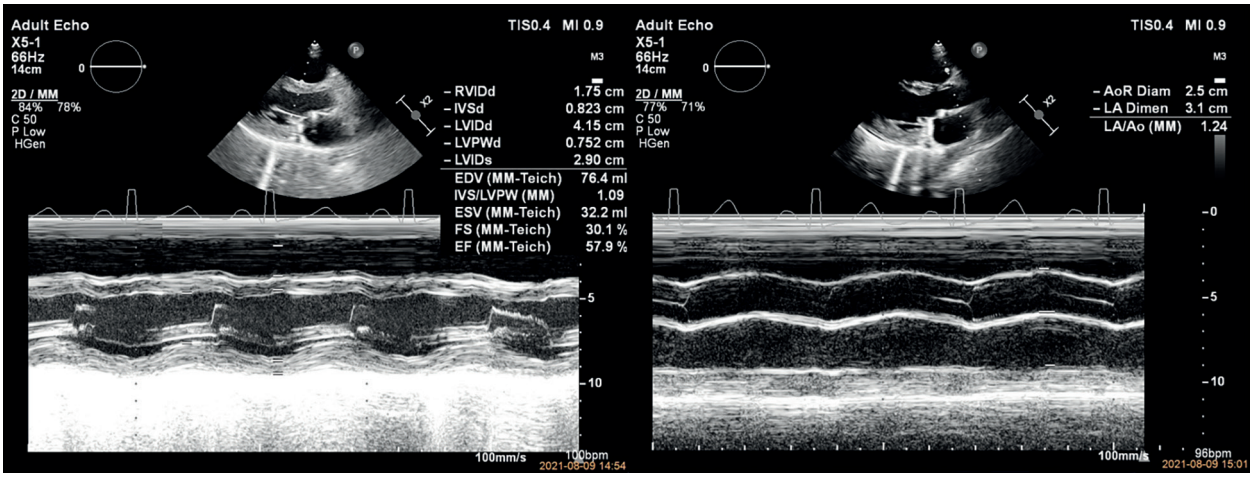

Figure 2. M-mode echocardiography. Impaired left ventricular function (ejection fraction = 57.9%) and enlarged left atrium/aorta = 1.24

surgical treatment should be considered, which should be performed by a team of highly experienced cardiac surgeons [5–7].

Case report

A 16-year-old girl was referred to the department of cardiology due to anemia, fever, fatigue, sweating, pain in the lower limbs and weight loss. Physical examination revealed a murmur in the apical region, splenomegaly, leukocytosis and increased C-reactive protein, as well as positive IgM and IgG antibodies to SARS-CoV-2. Blood cultures revealed *Streptococcus Gordoni* bacteriemia. Echocardiography showed mitral valve (MV) vegetation and a reduced left ventricular ejection fraction (Figure 1 and 2). The pharmacological therapy included cephalosporin, vancomycin, antifungal drugs, dehydrating drugs and a convertase inhibitor. After a few days, the patient's condition improved. Transoesophageal echocardiography and three-dimensional echocardiography allowed the assessment of the valve and tendon threads (Figure 3). Although the girl was a paediatric patient, the interdisciplinary council qualified her for cardiac surgery in an adult cardiosurgery ward. This was due to the fact of the superiority of experience of "adult" cardiosurgeons in treating such an abnormality. Mitral valve reconstruction was performed, using a minimally invasive method, applying artificial tendon cords and a Carpentier–McCarthy–Adams 26 mm artificial mitral ring. The intraoperative and postoperative course was uneventful. Damaged tendon threads underwent a bacteriological examination, which came out negative. Control echocardiographic examinations showed the normal function of the reconstructed

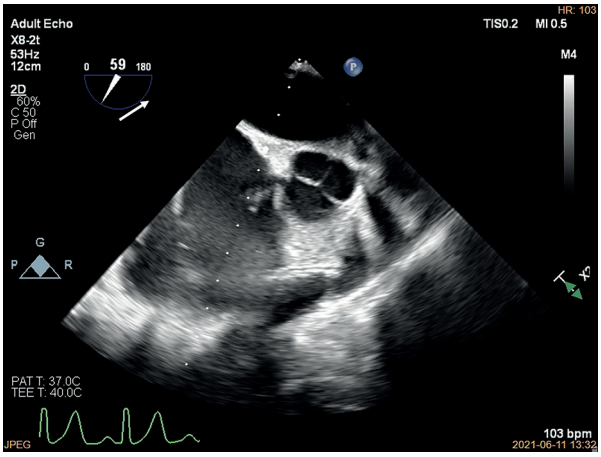

Figure 3. Transoesophageal echocardiographic image. There was no vegetation of the aortic valve (arrow), 3-leaflet aortic valve, leaflets not thickened

valve with mild regurgitation and well-preserved leaflet coaptation (Figure 4). After a week, she was referred back to the paediatric cardiology department and advised an anticoagulation warfarin treatment. Currently, the girl remains under outpatient care, in good condition, with no deviations from correct development.

Discussion

Infective endocarditis is most often of bacterial origin and is one of the most common causes of acute MV failure [1]. In some reports, the estimated annual incidence of IE is from 3 to 9 cases per 100 000 people, 40% of which are in MV [2, 3]. The appearance of chills, fatigue, low-grade fever, lack of appetite, pale skin, splenomegaly, elevated inflammatory markers and positive blood cultures should always raise the suspicion of IE. Intracardiac vegetations, as a complication of IE, are identified by echocardiography or computed tomography, sometimes supplemented with magnetic resonance imaging [3]. They are often detected incidentally. Differential diagnostics should include blood clots and tumours. The indication for surgical treatment of IE complications is an increasing regurgitation of the valve with heart failure, as well as plastic surgery or implantation of an artificial valve into the mitral field, depending on the degree of valve damage. Valvular plastic surgery can provide better long-term survival and improved heart performance compared to valve replacement [5]. The right time for patients to undergo a correction is a matter of discussion, and the current tendency is to shorten the diagnosis-surgery period [7–10]. The present patient had a problem because she was under 18 years of age. In children, the inclusion of an experienced cardiac surgeon in the treatment team is necessary to determine the optimal surgical option. The appointed team of specialists stated that the cardiosurgery department for adults will be the best place for cardiac surgery due to the much greater experience with MV reconstruction procedures in such centers compared to children's cardiac surgery centers. To the authors' knowledge, the removal of vegetation from the mitral valve in a child with simultaneous plastic surgery by minimally invasive reconstruction is the first procedure of this type performed in Poland.

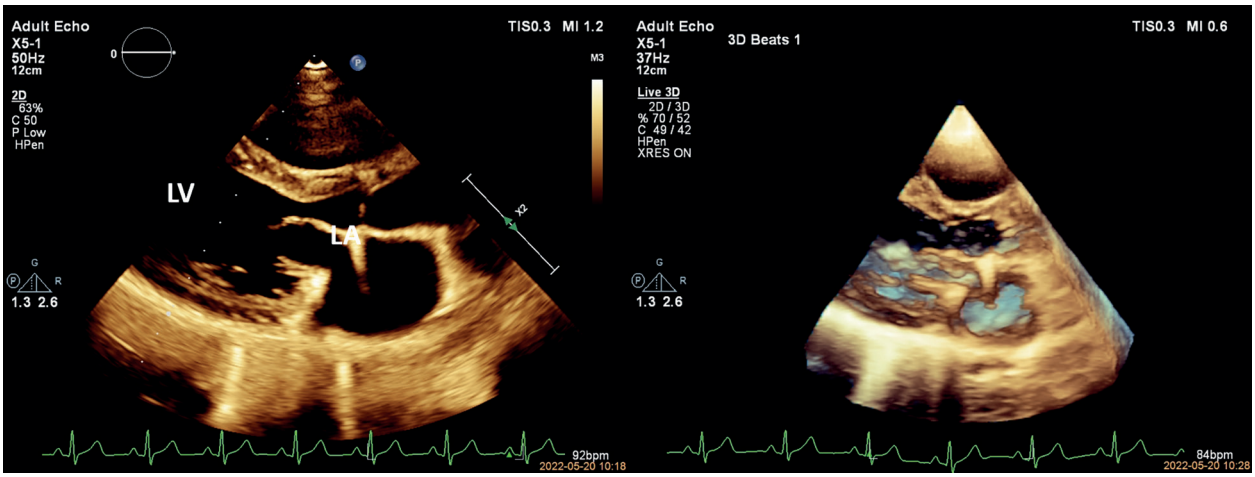

Figure 4. Image after mitral valve reconstruction. Two-dimensional echocardiography (left) and three-dimensional echocardiography (right) in the parasternal projection along the long axis of the left ventricle. Left ventricular diastolic phase. Valve leaflets open wide and flow freely into the left ventricle (LV). Enlarged left atrium (LA)

Conclusions

Clinical symptoms dominated by fatigue, low-grade fever, enlarged spleen and newly developed murmur over the heart should lead to the suspicion of IE. A damaged MV should be repaired by a highly experienced team of cardiac surgeons.

Conflict of interest

The authors do not report any financial or personal connections with other persons or organizations that could adversely affect the content of the publication and claim the right to this publication.

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Streszczenie

Infekcyjne zapalenie wsierdzia rzadko występuje u dzieci, najczęściej jest powikłaniem interwencji stomatologicznych, sprzyjają mu także wrodzone lub nabyte wady serca oraz wcześniejsze operacje kardiochirurgiczne. U 16-letniej dziewczynki od pół roku występowało znaczne osłabienie, stany podgorączkowe, spadek masy ciała o 5 kg spowodowany brakiem apetytu, apatia i powiększenie śledziony. Pojawił się także szmer skurczowy nad koniuszkiem serca. Została przyjęta na oddział ogólnopediatryczny, po stwierdzeniu wegetacji na zastawce dwudzielnej dalsze leczenie obywało się na oddziale kardiologii dziecięcej. W posiewach z krwi stwierdzono zakażenie *Streptococcus Gordoni* i włączono intensywne leczenie antybiotykami kontrolowane posiewami krwi, które po 7 dniach leczenia były ujemne. Powołano zespół specjalistów (*Endocarditis Team*), kontynuowano leczenie oraz wykonano echokardiografię przezprzełykową z oceną zmian na zastawce. Po konsultacji z kardiochirurgami zadecydowano o przeniesieniu pacjentki na oddział kardiochirurgii dla dorosłych (pomimo nieosiągnięcia wieku pełnoletniego), gdzie wykonano małoinwazyjną rekonstrukcję zastawki z użyciem sztucznych nici ścięgnistych i sztucznego pierścienia mitralnego Carpentier–McCarthy–Adams 26 mm. Przebieg pooperacyjny był niepowikłany, dziewczynkę ponownie przekazano pod opiekę kardiologów dziecięcych. Aktualnie jest w dobrym stanie i pozostaje pod stałą kontrolą lekarzy.

Słowa kluczowe: infekcyjne zapalenie wsierdzia, zastawka dwudzielna, plastyka zastawki

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Report from the European Society of Cardiology Congress 2022 in Barcelona: new discoveries in cardiovascular pharmacotherapy

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Abstract

The following paper presents an overview of the key studies presented at the European Society of Cardiology Congress 2022. The DELIVER study provided information on the efficacy of dapagliflozin independent of left ventricular ejection fraction. The ADVOR trial confirmed the beneficial effect of the inclusion of acetazolamide as a diuretic in the initial phase of acute decompensated heart failure. The REVIVED study showed no advantage of percutaneous revascularisation over optimal pharmacotherapy in stable coronary artery disease. The SECURE study demonstrated the benefit of the so-called polypill over taking each drug separately. The PANTHER meta-analysis indicated a better effect of using P2Y12 inhibitors over aspirin in chronic therapy. The ALL-HEART study revealed no benefit in treating asymptomatic hyperuricemia in patients with coronary artery disease with allopurinol. The INVICTUS trial demonstrated the superiority of vitamin K antagonists over non-vitamin K antagonist oral anticoagulants in preventing embolic complications in cases where valvular defects of rheumatic origin co-occur with atrial fibrillation.

Key words: dapagliflozin, allopurinol, percutaneous coronary revascularisation, polypill, acetazolamide

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Introduction

After a two-year hiatus due to the epidemiological situation, the European Society of Cardiology (ESC) Congress 2022 took place in a stationary format in Barcelona. As expected, it became an arena for the presentation of new data that can be applied to daily clinical practice, improve treatment outcomes in patients and accelerate their recovery. The authors of this paper have selected seven most relevant, in their opinion, recent clinical trials that are likely to have the greatest impact on the treatment of patients with heart diseases.

DELIVER (Dapagliflozin in Heart Failure with Mildly Reduced or Preserved Ejection Fraction) [1]

Sodium-glucose co-transporter 2 (SGLT-2) inhibitors are among the most recent drugs used in the treatment of heart failure (HF). Their positive effect on improving cardiac function was confirmed in the 2021 ESC guidelines for the diagnosis and treatment of acute and chronic HF as a class Ia recommendation for use in HF with reduced ejection fraction (EF). Their effectiveness in the treatment of HF with preserved and minimally reduced EF has been

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evaluated in two recent studies — EMPEROR-PRESERVED [2] and DELIVER. The latter was designed to determine the efficacy of dapagliflozin treatment in the case of HF with preserved and mildly reduced EF.

The study was participated by 6263 patients with left ventricular (LV) EF above 40% who were randomly allocated to two groups — the first received a daily dose of 10 mg of dapagliflozin in addition to full basic treatment (n = 3131) while the second was treated with a placebo (n = 3132). The primary composite endpoint included death due to cardiovascular causes and HF exacerbation. The inclusion criteria were age above 40 years, confirmed structural heart disease, LVEF above 40% and elevated natriuretic peptide levels (N-terminal prohormone of brain natriuretic peptide [NT-proBNP] > 300 pg/mL or > 600 pg/mL in patients with atrial fibrillation [AF]). The mean age of the patients was 71.7 years, 44% of the subjects were female.

The study was successful, with significantly fewer (by 18%) occurrences of a primary endpoint in patients receiving dapagliflozin. A 21% reduction in the risk of hospitalisation and urgent medical admission due to HF exacerbation was demonstrated; there was no statistically significant decrease in the number of deaths caused by cardiovascular diseases [1].

The DELIVER study is a valuable addition to the EMPEROR-PRESERVED trial [2], published a year earlier, which supplements data on the subgroup of "improved EF", i.e. HF with improved EF, and patients with HF with preserved EF and high LVEF. When correlating the data collected from both studies, it can be seen that the use of flosins is beneficial for every patient diagnosed with HF, regardless of the LVEF values. The results of these studies illustrate exactly how great of a breakthrough in the treatment of HF was the introduction of SGLT-2 inhibitors, which gained importance after the discovery of a significant improvement in cardiovascular risk indicators in diabetic patients. It is worth emphasising that meta-analyses presented at the ESC Congress confirmed the consistent protective effect of flosins across the entire spectrum of phenotypes and LVEF values in patients with HF and that these drugs are now a major element in the pharmacotherapy of patients with preserved LVEF as well.

ADVOR (Acetazolamide in Acute Decompensated Heart Failure with Volume Overload) [3]

In the case of HF, exacerbations are a frequent consequence of the disease. They are often manifested by episodes of overhydration of varying degrees, with each successive episode having an increasingly severe course and worsening the patient's prognosis. The basic drugs used in therapy are loop diuretics, which operate in the loop of Henle by inhibiting the transport of chloride and sodium. Better outcomes can be achieved by influencing diuresis with different mechanisms at the same time. The aim of the ADVOR study was to investigate whether the addition of acetazolamide — the carbonic anhydrase inhibitor and a drug that acts in the proximal convoluted tubule, i.e. in a different part of the nephron loop — would be beneficial in patients exhibiting HF exacerbation.

The inclusion criteria were hospitalisation due to exacerbated HF with clinical symptoms of overhydration, NT-proBNP > 1000 pg/mL or BNP > 250 pg/mL, and oral administration of furosemide at a dose of at least 40 mg or 20 mg of torasemide or 1 mg of bumetanide for a minimum of one month prior to randomisation. The exclusion occurred as a result of chronic use of acetazolamide or another drug having an effect on the proximal convoluted tubule (including SGLT-2 inhibitors), systolic blood pressure lower than 90 mm Hg and estimated glomerular filtration rate lower than 20 mL/min/1.73 m^2. The patients were divided into two groups: the first received an additional 500 mg acetazolamide intravenously once a day in addition to loop diuretics for three days (n = 259) and the others (n = 260) received a placebo together with loop diuretics. The mean age of the patients was 78 years. Women comprised 37.4% of participants. The primary endpoint was an effective reduction of overhydration within three days, while the secondary endpoint consisted in death from any cause or re-hospitalisation due to HF within 3 months.

The primary endpoint was achieved in 108 out of 256 (42.2%) patients receiving treatment with acetazolamide and in 79 out of 259 (30.5%) individuals from the placebo group. This represents a 46% improvement in the effective removal of excess water in patients compared to standard therapy based solely on loop diuretics. Death attributable to any cause or re-hospitalisation occurred in 76 out of 256 (29.7%) individuals receiving acetazolamide and 72 out of 259 (27.8%) patients treated with a placebo. There was no statistically significant difference between the two groups. Deterioration of renal function, hypotension and hypokalaemia were also found with similar frequency in both groups.

The ADVOR study demonstrated that the addition of a well-known diuretic — acetazolamide — to standard therapy based on loop diuretics leads to more rapid, yet equally safe, removal of excess water in patients hospitalised due to exacerbated HF, but no statistically significant difference between the incidence of death or hospital re-admission [3].

REVIVED (Percutaneous Revascularisation for Ischemic Left Ventricular Dysfunction) [4]

One of the most frequently performed cardiac procedures is coronary revascularisation. When performed on a patient

with acute coronary syndrome (ACS), it significantly increases their chances of survival. The question is whether it shows equally spectacular results when carried out in the case of stable coronary artery disease (CAD). The ISCHEMIA study revealed a lack of clear prognostic benefits for patients undergoing either percutaneous coronary intervention (PCI) or coronary artery bypass grafting. A major limitation of this trial was the exclusion of patients with a LVEF lower than 35% who could potentially benefit from revascularisation. The REVIVED study was designed to demonstrate whether PCI in patients with HF with reduced EF could improve their prognoses and increase LVEF.

The study included 700 stable patients with a LVEF lower than or equal to 35%, coronary anatomy indicating the possibility of revascularisation and confirmed myocardial viability, who were randomised into two groups — 347 patients were treated by means of PCI and optimal pharmacotherapy, while the control group (353 individuals) consisted of patients treated with pharmacotherapy alone. The primary endpoint involved death caused by any reason or hospitalisation due to HF exacerbation. The secondary endpoint consisted in the assessment of LVEF after 6 and 12 months and the evaluation of patients' quality of life.

The results of the study were surprising. During the 41-month follow-up period, the primary endpoint occurred in 129 patients (37.2%) undergoing PCI and 134 (38.0%) receiving optimal pharmacotherapy alone, with no statistically significant difference between the two groups. At 6 and 12 months, the LVEF was similar in both groups. Quality of life at 6 and 12 months indicated in favour of PCI, but after 24 months, the results in both groups levelled off. It is worth emphasising that REVIVED patients received very good pharmacological treatment, and more than 20% had previously implanted devices.

The lack of significant difference between the two treatment strategies suggests that complete percutaneous coronary revascularisation should not be pursued at all costs in stable patients with reduced EF without symptoms of CAD exacerbation. Appropriate pharmacological treatment is equally effective and additionally free of the risk associated with the procedure, which, similarly to any invasive intervention, may lead to harmful complications [4]. In the long term, successful pharmacological treatment has a comparable effect in terms of improved quality of life, consistent with the results of the earlier ORBITA trial.

SECURE (Secondary Prevention of Cardiovascular Disease in the Elderly) [5]

For quite some time, there has been a trend of combining multiple drugs in a single tablet focused on improving the outcome of preventive treatment by increasing patient cooperation. The market offers an increasing number of drug combinations designed to enhance therapeutic outcomes. But does the use of a single tablet instead of several actually help the treatment process in any meaningful way? The authors of the SECURE study sought to answer this question by evaluating the benefits of the "polypill" — a single tablet combination (100 mg acetylsalicylic acid, 2.5–10 mg ramipril and 20 or 40 mg atorvastatin) in patients characterised with high cardiovascular risk. The trial covered 2499 patients from 113 centres. Inclusion criteria consisted of a history of myocardial infarction (MI) up to 6 months prior to randomisation, age 75 years or 65 with at least one risk factor (diabetes, mild or moderate kidney disease, previous MI, coronary revascularisation or stroke). The follow-up period was 36 months.

Patients were divided into two groups — the first was treated with combination therapy (n = 1237), while the second received conventional treatment (n = 1229). The primary endpoint included death attributable to cardiovascular causes, non-fatal type 1 MI, non-fatal stroke and urgent coronary revascularisation. This occurred in 118 patients undergoing combination therapy and 156 patients in the conventional treatment group. These data represent a 24% reduction in the risk of occurrence of events classified as primary endpoints. The secondary endpoint consisting of death of cardiovascular origin, non-fatal type 1 MI or non-fatal stroke was observed in 101 individuals receiving polypills and 144 patients participating in the conventional treatment. This indicates a highly statistically significant risk reduction of 30%.

The results of the study demonstrate that combined polypill-type formulations can also be successfully applied in the secondary prevention of cardiovascular diseases. In addition to facilitating the treatment process by improving therapeutic cooperation, they also result in better long-term outcomes by extending patients' lives and helping them to remain in better health than in the case of standard therapy. The use of one-pill medication undoubtedly reduces the risk of skipping or changing any of the doses. As a result, more and more drug combinations and their mixing options are to be expected.

PANTHER (P2Y12 Inhibitors Top Aspirin for Long-term Secondary Prevention) [6]

The use of antiplatelet drugs is the foundation of pharmacotherapy in the case of chronic and ACS. Low-dose aspirin, on which dual antiplatelet therapy protocols are based, is the standard treatment. However, clinical trials have been conducted to test the feasibility of replacing acetylsalicylic acid monotherapy with P2Y12 inhibitors, particularly clopidogrel or ticagrelor.

The authors of the PANTHER meta-analysis attempted to answer the question of whether the application of P2Y12 inhibitors in chronic therapy would be as effective

and safe as the use of aspirin. The study included an analysis of data on 24 325 patients from 7 randomised trials. 12 178 individuals were receiving P2Y12 inhibitors (7545 clopidogrel and 4633 ticagrelor). The control group consisted of 12 147 aspirin users. The mean age of the patients was 64.3 years. 21.7% of the study participants were women. The group receiving P2Y12 inhibitors showed a significantly (12%) lower risk of the primary composite endpoint in the form of death due to cardiovascular causes, MI and stroke. However, no differences in overall or cardiovascular mortality were observed. It is important to emphasise that P2Y12 inhibitors entailed a 23% lower risk of MI. Similar safety was reported for both drug groups as measured by the incidence of major bleeding (1.2% vs. 1.4%) — however, only 0.4% had a history of major bleeding. Interestingly, the risk of haemorrhagic stroke and gastrointestinal bleeding was significantly higher during acetylsalicylic acid therapy.

Based on the results of the study, it can be concluded that the use of P2Y12 inhibitors in CAD will grow in importance in the future (particularly if the price decreases), and their broader clinical use should be expected. Currently, their application is limited mainly to dual antiplatelet therapy protocols for stents or ACS and in cases of aspirin intolerance, which is the basis of treatment for chronic coronary syndromes. An example of a group that may benefit from P2Y12 inhibitors are young patients after revascularisation and at high risk of gastrointestinal bleeding. However, the absolute differences in treatment outcomes are small — one out of 123 patients will avoid an incident regarded as a primary composite endpoint.

ALL-HEART (Allopurinol and Cardiovascular Outcomes in Patients with Ischemic Heart Disease) [7]

Allopurinol is a well-known and long-used xanthine oxidase inhibitor exhibiting antioxidant activity. It is used to lower uric acid concentrations in patients suffering from symptomatic gout. It has been prescribed in Poland (and nowhere else) to treat asymptomatic hyperuricaemia with a view to the hypothetical prevention of cardiovascular complications excessively often, without scientific data to recommend it. The authors of the ALL-HEART study decided to examine whether its use would improve the prognosis of patients diagnosed with ischemic heart disease.

Patients with ischemic heart disease were randomised into two groups. In the study group (n = 2853), their standard therapy was supplemented with allopurinol at a dose adjusted to the glomerular filtration rate. The control group (n = 2868) received conventional treatment. The primary endpoint was the death of cardiovascular origin, MI or stroke. This occurred in 11.0% of patients in the group treated with additional allopurinol and in 11.3% of individuals in the control group (p = 0.65). The overall mortality rate was comparable in both groups (10.1% vs. 10.6%; p = 0.77), similar to hospitalisations due to HF (2.6% vs. 3.4%; p = 0.18)

Despite the methodological limitations of the presented study, it is the only high-quality prospective trial evaluating the benefits of allopurinol outside the context of gout. It allows concluding that the use of allopurinol in patients with ischemic heart disease does not improve their prognosis in any way. In view of the above, the application of allopurinol in patients without clinical symptoms of gout is inadvisable and unjustified.

INVICTUS (Investigation Of Rheumatic AF Treatment Using Vitamin K Antagonists, Rivaroxaban or Aspirin Studies) [8]

The consequences of rheumatic heart disease affect approximately 33 million people worldwide, mostly in poorer countries. Atrial fibrillation is one of the most common complications of the classic rheumatic defect — mitral stenosis — and can also result from other types of defects. Dangerous complications of AF may consist in the blockage of peripheral arteries, including those supplying the brain, which can lead to stroke unless appropriate anticoagulants are administered.

The purpose of the INVICTUS study was to compare the efficacy of rivaroxaban and vitamin K inhibitor treatment in patients with rheumatic heart valve disease (mainly mitral stenosis) and AF. The study was participated by 4531 individuals who were randomly assigned to undergo anticoagulant treatment with rivaroxaban at a dose of 20 mg or 15 mg in the case of creatinine clearance below 50 mL//min, while the second group received vitamin K antagonists at a dose that allowed maintaining an international normalized ratio (INR) between 2.0 and 3.0 (n = 2256). The mean age of the patients was 50 years. 72% of the subjects were female. Among both groups, about 85% of individuals were diagnosed with mitral stenosis, of which about 1/4 was severe, while about 82.5% had mitral regurgitation, of which severe defect accounted for about 22%. Death, stroke, peripheral embolism and MI were identified as primary endpoints. They occurred significantly more often in persons treated with rivaroxaban (8.2%) and those receiving vitamin K antagonists (6.5%). This means that rivaroxaban entails a 25% higher risk compared to conventional treatment. No differences were observed with regard to the rate of hospitalisation due to HF failure. There were also no differences between the two groups in terms of the occurrence of major bleeding, however, the incidence of fatal bleeding was statistically significant in favour of rivaroxaban (4 vs. 15; 0.17% vs. 0.66%).

Despite the development of anticoagulant treatment, the classic vitamin K antagonists still prove to be useful

and are the only choice in specific subgroups of patients (with mechanical valve prostheses and mitral stenosis). As seen in the analysis conducted in the course of the INVICTUS trial, their application in significant valve defects of rheumatic aetiology is associated with a lower risk of stroke and cardiac death, although their significant drawback consists in the need to constantly monitor the INR index, which may be problematic for some individuals. In the case of patients who can maintain high-quality anticoagulant treatment, vitamin K antagonists should remain the treatment of first choice for co-morbid rheumatic heart disease with AF.

Conflict of interest

None declared.

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Doniesienia z kongresu *European Society of Cardiology* 2022 w Barcelonie — nowe oblicza farmakoterapii

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Streszczenie

Opracowanie zawiera przegląd najważniejszych badań zaprezentowanych w trakcie kongresu Europejskiego Towarzystwa Kardiologicznego 2022. Badanie DELIVER dostarczyło informacji o skuteczności dapagliflozyny niezależnie od frakcji wyrzutowej lewej komory. W badaniu ADVOR potwierdzono skuteczność dołączenia acetazolamidu w odwadnianiu w początkowej fazie ostrej niewydolności serca. Wyniki badania REVIVED wykazały brak przewagi przezskórnej rewaskularyzacji nad optymalną farmakoterapią w stabilnej chorobie wieńcowej. W badaniu SECURE wykazano korzyść z zastosowania tzw. *pollypill* nad osobnym przyjmowaniem każdego z leków. W metaanalizie PANTHER udowodniono lepszy efekt przyjmowania w terapii przewlekłej inhibitorów P2Y12 nad stosowaniem aspiryny. W badaniu ALL-HEART wykazano brak korzyści z leczenia bezobjawowej hiperurykemii u pacjentów z chorobą wieńcową za pomocą allopurynolu. W badaniu INVICTUS wykazano natomiast przewagę VKA nad NOAC w zapobieganiu powikłań zatorowo-zakrzepowych w przypadku współwystępowania wad zastawkowych pochodzenia reumatycznego z migotaniem przedsionków.

Słowa kluczowe: acetazolamid, allopurynol, dapagliflozyna, polypill, przezskórna rewaskularyzacja wieńcowa

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Wstęp

Po dwuletniej przerwie spowodowanej sytuacją epidemiologiczną tegoroczny kongres Europejskiego Towarzystwa Kardiologicznego odbył się w formie stacjonarnej w Barcelonie. Zgodnie z oczekiwaniami stał się areną prezentacji nowych danych, które mogą znaleźć zastosowanie w codziennej praktyce klinicznej, poprawić efekty leczenia pacjentów oraz przyspieszyć ich powrót do zdrowia. Autorzy poniższego opracowania wybrali siedem najważniejszych w ich ocenie nowych badań klinicznych, które mają szansę wpłynąć w najwyższym stopniu na proces leczenia pacjentów z chorobami serca.

DELIVER (*Dapagliflozin in Heart Failure with Mildly Reduced or Preserved Ejection Fraction*) [1]

Inhibitory kotransportera sodowo-glukozowego typu 2 (SGLT-2, *sodium-glucose co-transporter 2*) należą do najnowszych leków stosowanych w terapii niewydolności serca (HF, *heart failure*). Ich pozytywny wpływ na poprawę funkcji serca został potwierdzony w wytycznych Europejskiego Towarzystwa Kardiologicznego (ESC, *European Society of Cardiology*) 2021 dotyczących diagnostyki i leczenia ostrej i przewlekłej HF jako rekomendacja klasy Ia dla stosowania w HF z obniżoną frakcją wyrzutową (EF, *ejection fraction*).

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Ich skuteczność w leczeniu HF z zachowaną oraz minimalnie obniżoną EF została oceniona w dwóch najnowszych badaniach — EMPEROR-PRESERVED [2] i DELIVER. Założeniem badania DELIVER było określenie skuteczności leczenia dapagliflozyną w przypadku HF z zachowaną oraz łagodnie obniżoną EF.

W badaniu wzięło udział 6263 pacjentów z frakcją wyrzutową lewej komory (LVEF, *left ventricular ejection* fraction) > 40%, którzy zostali losowo przydzieleni do dwóch grup, z których pierwsza oprócz pełnego leczenia podstawowego otrzymywała dziennie 10 mg dapagliflozyny (n = 3131), natomiast druga grupa otrzymywała placebo (n = 3132). Złożony pierwszorzędowy punkt końcowy obejmował zgon z przyczyn sercowo-naczyniowych oraz zaostrzenie HF. Kryteriami włączenia były: wiek > 40 lat, potwierdzona choroba strukturalna serca, LVEF > 40% oraz podwyższony poziom peptydów natriuretycznych (NT-proBNP [*N-terminal pro-B-type natriuretic peptide*] > 300 pg/ml lub > 600 pg/ml u pacjentów z migotaniem przedsionków (AF, *atrial fibrillation*). Średni wiek pacjentów wyniósł 71,7 roku, 44% badanych stanowiły kobiety.

Badanie zakończyło się sukcesem — u pacjentów otrzymujących dapagliflozynę znamiennie rzadziej (o 18%) występował pierwszorzędowy punkt końcowy. Wykazano 21-procentową redukcję ryzyka hospitalizacji bądź pilnej wizyty lekarskiej z powodu zaostrzenia HF, bez statystycznie znamiennego zmniejszenia liczby zgonów z przyczyn sercowo-naczyniowych [1].

Badanie DELIVER stanowi cenne uzupełnienie badania EMPEROR-PRESERVED [2] opublikowanego rok wcześniej, uzupełniając dane dotyczące podgrupy *improved EF* — czyli HF z poprawą EF oraz pacjentów z HF z zachowaną EF i wysoką LVEF. Kondensując dane zebrane z obu badań, widać, że stosowanie flozyn przynosi korzyści u każdego pacjenta z HF, niezależnie od LVEF. Wyniki tych badań pokazują dokładnie, jak wielkim przełomem w leczeniu HF było wprowadzenie inhibitorów SGLT-2, których karierę w kardiologii zapoczątkowało odkrycie znacznej poprawy wskaźników ryzyka krążeniowego u pacjentów z cukrzycą. Warto podkreślić, że zaprezentowane na kongresie ESC wyniki metaanaliz potwierdziły spójny efekt ochronny flozyn w całym spektrum fenotypów i wartości LVEF u pacjentów z HF, a leki te stanowią obecnie główny element farmakoterapii pacjentów, także z zachowaną LVEF.

ADVOR (*Acetazolamide in Acute Decompensated Heart Failure with Volume Overload*) [3]

Częstymi konsekwencjami HF są jej zaostrzenia. Nierzadko przejawiają się one różnego stopnia incydentami przewodnienia, których każdy kolejny epizod ma coraz cięższy przebieg i powoduje pogorszenie rokowania u pacjenta. Podstawowymi lekami stosowanymi w terapii są diuretyki pętlowe działające w pętli Henlego poprzez hamowanie transportu jonów chlorkowych oraz sodowych. Wpływanie na diurezę poprzez równoczesne wykorzystanie różnych mechanizmów skutkuje lepszym efektem. Celem badania ADVOR było zbadanie, czy dodanie acetazolamidu będącego inhibitorem anhydrazy węglanowej — leku działającego w kanaliku krętym bliższym, czyli w innym miejscu pętli nefronu, przyniesie korzyści u pacjentów z zaostrzeniem HF.

Kryterium włączenia do badania była hospitalizacja z powodu zaostrzonej HF z wystąpieniem klinicznych objawów przewodnienia, stężenie NT-proBNP > 1000 pg/ml lub BNP > 250 pg/ml oraz doustne stosowanie ≥ 40 mg furosemidu lub 20 mg torasemidu, lub 1 mg bumetanidyny co najmniej przez miesiąc przed randomizacją. Kryterium wykluczenia stanowiło przewlekłe stosowanie acetazolamidu lub innego leku działającego w kanaliku krętym bliższym (w tym inhibitorów SGLT-2), skurczowe ciśnienie tętnicze < 90 mm Hg oraz szacowany współczynnik przesączania kłębuszkowego < 20 ml/min/1,73 m^2. Pacjentów podzielono na dwie grupy: w pierwszej (n = 259) do terapii diuretykami pętlowymi przez 3 dni włączono dodatkowo raz dziennie 500 mg acetazolamidu dożylnie, pozostali (n = 260) otrzymywali placebo łącznie z diuretykami pętlowymi. Średni wiek pacjentów to 78 lat, kobiety stanowiły 37,4%. Punktem pierwszorzędowym było skuteczne zmniejszenie przewodnienia w ciągu trzech dni, natomiast na punkt drugorzędowy składały się zgon z dowolnej przyczyny lub ponowna hospitalizacja z powodu HF w przeciągu 3 miesięcy.

Pierwszorzędowy punkt końcowy osiągnięto u 108/256 (42,2%) w grupie pacjentów leczonych z wykorzystaniem acetazolamidu oraz u 79/259 (30,5%) w grupie placebo. Oznacza to polepszenie skutecznego odwadniania pacjenta o 46% względem standardowej terapii opartej na wyłącznym stosowaniu diuretyków pętlowych. Zgon z jakiejkolwiek przyczyny lub ponowna hospitalizacja wystąpiły u 76/256 (29,7%) z grupy acetazolamidu oraz 72/259 (27,8%) z grupy placebo, bez statystycznie istotnej różnicy pomiędzy obiema grupami. Pogorszenie funkcji nerek, hipotensja oraz hipokaliemia również występowały z podobną częstością w obu grupach.

Wyniki badania ADVOR pokazały, że dołączenie od dawna znanego leku moczopędnego, acetazolamidu, do standardowej terapii opartej na diuretykach pętlowych prowadzi do szybszego, a jednocześnie równie bezpiecznego odwodnienia pacjentów hospitalizowanych z powodu zaostrzenia HF, jednak nie ma istotnej statystycznie różnicy pomiędzy wystąpieniem zgonu lub ponownej hospitalizacji [3].

REVIVED (*Percutaneous Revascularization for Ischemic Left Ventricular Dysfunction*) [4]

Jednym z najczęściej wykonywanych zabiegów kardiologicznych jest rewaskularyzacja naczyń wieńcowych.

Wykonywana w ostrym zespole wieńcowym (ACS, *acute coronary syndrome*) znacznie zwiększa szanse pacjenta na przeżycie ACS. Pytaniem pozostaje, czy wykonywana w przypadku stabilnej choroby wieńcowej wykazuje równie spektakularne efekty. W badaniu ISCHEMIA nie wykazano jednoznacznych korzyści rokowniczych dla pacjenta zarówno w przypadku zabiegu przezskórnego, jak i pomostowania tętnic wieńcowych. Poważnym ograniczeniem tego badania było wyłączenie pacjentów z LVEF < 35%, którzy potencjalnie mogliby odnieść korzyści z rewaskularyzacji. Celem badania REVIVED było wykazanie, czy przezskórna interwencja wieńcowa (PCI, *percutaneous coronary intervention*) u pacjentów z HF z obniżoną EF może przynieść poprawę rokowania oraz wzrost LVEF.

Do badania włączono 700 stabilnych pacjentów z LVEF ≤ 35%, anatomią wieńcową wskazującą na możliwość rewaskularyzacji oraz potwierdzoną żywotnością mięśnia sercowego, których zrandomizowano do dwóch grup: 347 osób leczonych z wykorzystaniem przezskórnej angioplastyki naczyń wieńcowych oraz optymalnej farmakoterapii, natomiast grupę kontrolną (353 osoby) stanowili chorzy leczeni wyłącznie farmakologicznie. Na pierwszorzędowy punkt końcowy składał się zgon z jakiejkolwiek przyczyny lub hospitalizacja spowodowana zaostrzeniem HF. Punktem drugorzędowym była ocena LVEF po 6 i 12 miesiącach oraz ocena jakości życia pacjentów.

Wyniki badania zaskakują. W ciągu 41-miesięcznej obserwacji pierwszorzędowy punkt końcowy wystąpił u 129 pacjentów (37,2%) w grupie poddanej PCI oraz u 134 (38,0%) stosujących wyłącznie optymalną farmakoterapię, bez statystycznie istotnej różnicy między obiema grupami. Funkcja wyrzutowa lewej komory była podobna u obu grup zarówno po 6, jak i po 12 miesiącach. Jakość życia po 6 i 12 miesiącach wskazywała na korzyść PCI, jednak po 24 miesiącach się zrównały. Warto podkreślić, że pacjenci REVIVED byli bardzo dobrze leczeni farmakologicznie, a ponad 20% miało wszczepione wcześniej urządzenia.

Brak istotnej różnicy pomiędzy obiema strategiami leczenia wskazuje na to, że nie należy dążyć za wszelką cenę do przezskórnej kompletnej rewaskularyzacji naczyń wieńcowych u stabilnych pacjentów z obniżoną EF bez cech zaostrzenia choroby wieńcowej. Równie skuteczne jest prawidłowe leczenie farmakologicznie, dodatkowo pozbawione jest ono ryzyka związanego z samą procedurą, która jak każdy zabieg inwazyjny może przynieść szkodliwe komplikacje [4]. Skuteczne leczenie farmakologicznie w dłuższej perspektywie daje porównywalny efekt w zakresie poprawy jakości życia, zgodnie z wynikami wcześniejszego trialu ORBITA.

SECURE (*Secondary Prevention of Cardiovascular Disease in the Elderly*) [5]

Od dłuższego czasu można zaobserwować trend łączenia wielu leków w jednej tabletce ukierunkowany na poprawę wyników terapii prewencyjnej poprzez poprawę współpracy pacjenta. Na rynku pojawia się coraz więcej połączeń lekowych mających na celu poprawę efektów leczniczych. Ale czy tak naprawdę stosowanie jednej tabletki zamiast kilku znacząco wspomaga proces leczenia? Odpowiedzi na to pytanie szukali autorzy badania SECURE, oceniając u pacjentów wysokiego ryzyka krążeniowego zalety *polypill* — jednotabletkowego połączenia substancji (100 mg kwasu acetylosalicylowego, 2,5–10 mg ramiprylu oraz 20 lub 40 mg atorwastatyny). Do badania zostało włączonych 2499 pacjentów ze 113 ośrodków. Kryterium włączenia stanowił przebyty zawał serca do 6 miesięcy przed randomizacją, a także wiek — 75 lat lub 65 lat z przynajmniej jednym czynnikiem ryzyka (cukrzyca, łagodna lub umiarkowana choroba nerek, wcześniej przebyty zawał, rewaskularyzacja wieńcowa lub udar mózgu). Średni czas obserwacji wyniósł 36 miesięcy.

Pacjentów podzielono na dwie grupy, z których pierwsza była poddana terapii opartej na preparatach łączonych (n = 1237), druga grupa była leczona w sposób klasyczny (n = 1229). Pierwszorzędowy punkt końcowy obejmował śmierć z przyczyn sercowo-naczyniowych, zawał typu 1 niezakończony zgonem, udar mózgu niezakończony zgonem oraz pilną rewaskularyzację wieńcową. Wystąpił on u 118 pacjentów leczonych z wykorzystaniem preparatów łączonych oraz u 156 pacjentów z grupy leczonej w sposób klasyczny. Dane te oznaczają 24-procentową redukcję ryzyka wystąpienia zdarzeń zakwalifikowanych do pierwszorzędowego punktu końcowego. Punkt drugorzędowy składający się ze zgonu z przyczyn sercowo-naczyniowych bądź niezakończonych zgonem zawałem serca typu 1 lub udaru mózgu niezakończonego zgonem wystąpił u 101 z grupy *polypill* oraz u 144 z grupy klasycznej. Oznacza to wysoce istotną statystycznie redukcję ryzyka o 30%.

Wyniki badania wskazują, że preparaty łączone typu *polypill* mogą być z sukcesem stosowane także w prewencji wtórnej chorób układu krążenia. Nie tylko ułatwiają proces leczenia poprzez poprawę współpracy terapeutycznej, lecz również powodują lepsze efekty odległe — wydłużenie życia pacjentów i pozostawanie w lepszym zdrowiu niż w przypadku standardowej terapii. Bez wątpienia stosowanie kilku leków w jednej tabletce zmniejsza ryzyko pominięcia lub zmian którejś z dawek. W związku z tym należy się spodziewać coraz liczniej występujących połączeń leków oraz większych możliwości połączeń.

PANTHER (*P2Y12 Inhibitors Top Aspirin for Long-term Secondary Prevention*) [6]

Stosowanie leków przeciwpłytkowych to podstawa farmakoterapii przewlekłych i ACS. Standardem postępowania jest przyjmowanie niskich dawek aspiryny (ASA, *acetylsalicylic acid*), na której opierają się także protokoły podwójnej terapii przeciwpłytkowej. Przeprowadzono jednak próby kliniczne testujące możliwość zastąpienia monoterapii ASA inhibitorami P2Y12, zwłaszcza klopidogrelem lub tikagrelorem.

Autorzy metaanalizy PANTHER próbowali znaleźć odpowiedź na pytanie, czy stosowanie w przewlekłej terapii inhibitorów P2Y12 będzie równie skuteczne i bezpieczne, co stosowanie ASA. W badaniu przeanalizowano dane dotyczące 24 325 pacjentów pochodzące z 7 badań randomizowanych. 12 178 osób przyjmowało inhibitory P2Y12 (7545 klopidogrel oraz 4633 tikagrelor), grupę kontrolną stanowiło 12 147 osób przyjmujących ASA. Średni wiek pacjentów wyniósł 64,3 roku, kobiety stanowiły 21,7% uczestników badania. W grupie pacjentów przyjmujących inhibitory P2Y12 wykazano znamienne (o 12%) mniejsze ryzyko wystąpienia pierwszorzędowego złożonego punktu końcowego, jakim był zgon z przyczyn sercowo-naczyniowych, zawał serca oraz udar mózgu. Nie zaobserwowano jednak różnic w śmiertelności ogólnej lub krążeniowej. Ważne podkreślenia jest mniejsze o 23% ryzyko wystąpienia zawału serca w przypadku stosowania inhibitorów P2Y12. Wykazano podobne bezpieczeństwo stosowania w obu grupach leków mierzone występowaniem dużych krwawień (1,2% *vs.* 1,4%) — jednak tylko u 0,4% odnotowano istotne krwawienie w wywiadzie. Co ciekawe, ryzyko udaru krwotocznego i krwawienia z przewodu pokarmowego było znamiennie wyższe podczas terapii ASA.

Patrząc na wyniki badań, można wnioskować, że w przyszłości znaczenie stosowania inhibitorów P2Y12 w chorobie wieńcowej będzie rosło (szczególnie w przypadku zmniejszenia się ceny) i należy się spodziewać szerszego wykorzystywania klinicznego. Obecnie ich zastosowanie ogranicza się do stosowania głównie w protokołach podwójnej terapii przeciwpłytkowej stentingu lub ACS oraz w przypadku nietolerancji ASA będącej podstawą leczenia przewlekłych zespołów wieńcowych. Przykładową grupą mogącą odnieść korzyść z inhibitorów P2Y12 są młodzi pacjenci po rewaskularyzacjach i wysokim ryzykiem krwawień z przewodu pokarmowego. Bezwzględne różnice w wynikach leczenia są jednak małe — uniknięcie incydentu wchodzącego w skład pierwszorzędowego złożonego punktu końcowego nastąpi u 1:123 pacjentów.

ALL-HEART (*Allopurinol and Cardiovascular Outcomes in Patients With Ischemic Heart Disease*) [7]

Allopurynol jest znanym i stosowanym od dawna inhibitorem oksydazy ksantynowej o działaniu antyoksydacyjnym, wykorzystywanym do obniżania stężenia kwasu moczowego u pacjentów cierpiących na objawową dnę moczanową. Nadmiernie często, bez danych naukowych rekomendujących takie postępowanie, bywa zalecany w naszym kraju (i nigdzie poza nim) do leczenia hiperurykemii bezobjawowej z myślą o hipotetycznej prewencji powikłań ze strony układu krążenia. Autorzy badania ALL-HEART postanowili sprawdzić, czy jego stosowanie poprawi rokowanie u pacjentów z chorobą niedokrwienną serca.

Pacjentów z chorobą niedokrwienną serca zrandomizowano do dwóch grup. W grupie badawczej (n = 2853) do standardowej terapii dołączono allopurynol w dawce dostosowanej do współczynnika filtracji kłębuszkowej. Grupa kontrolna (n = 2868) była leczona w sposób standardowy. Za pierwszorzędowy punkt końcowy przyjęto zgon z powodów sercowo-naczyniowych, zawał serca lub udar mózgu. Wystąpił on u 11% pacjentów z grupy leczonej dodatkowo allopurynolem oraz u 11,3% chorych z grupy kontrolnej (p = 0,65). Całkowita śmiertelność w obu grupach była porównywalna (10,1% *vs.* 10,6%; p = 0,77), tak samo jak hospitalizacje z powodu HF (2,6% *vs.* 3,4 %; p = 0,18).

Pomimo ograniczeń metodycznych przedstawionego badania, jest ono jedynym prospektywnym trialem wysokiej jakości oceniającym korzyści ze stosowania allopurynolu poza kontekstem dny moczanowej. Wnioski z badania są następujące: stosowanie allopurynolu u pacjentów z chorobą niedokrwienną serca w żadnym aspekcie nie poprawia ich rokowania. Wobec powyższego stosowanie allopurynolu u pacjentów bez objawów klinicznych dny moczanowej jest niewskazane i nieuzasadnione.

INVICTUS (*Investigation of Rheumatic AF Treatment Using Vitamin K Antagonists, Rivaroxaban or Aspirin Studies*) [8]

Następstwa reumatycznej choroby serca dotyczą około 33 milionów osób na całym świecie, głównie występują one w krajach biedniejszych, a AF należy do najczęściej występujących powikłań klasycznej wady reumatycznej — stenozy mitralnej, a może stanowić także powikłanie innych typów wad. Groźnymi powikłaniami AF mogą być zatory tętnic obwodowych, także tych zaopatrujących mózg, co może prowadzić do wystąpienia udaru mózgu, o ile nie zostaną zastosowane właściwe leki przeciwkrzepliwe.

Celem badania INVICTUS było porównanie skutecznością leczenia rywaroksabanem a inhibitorami witaminy K u pacjentów z chorobą reumatyczną zastawek serca (przede wszystkim stenozy mitralnej) oraz AF. W badaniu wzięło udział 4531 osób, które zostały losowo przydzielone do leczenia przeciwkrzepliwego rywaroksabanem w dawce 20 mg lub 15 mg w przypadku klirensu kreatyniny poniżej 50 ml/min, natomiast druga grupa była leczona antagonistami witaminy K w dawce pozwalającej na utrzymanie wskaźnika międzynarodowego współczynnika znormalizowanego w zakresie 2,0–3,0 (n = 2256). Średnia wieku pacjentów wyniosła 50 lat, a 72% badanych stanowiły kobiety. Wśród obu grup około 85% pacjentów miało stenozę mitralną, z czego około 1/4 stanowiło ciężkie zwężenie, natomiast około 82,5% miało niedomykalność mitralną, z czego ciężka wada stanowiła około 22% w obu grupach. Jako pierwszorzędowy punkt końcowy został określony zgon, udar mózgu, zator obwodowy lub zawał serca. Wystąpił on znamiennie częściej u 8,2% leczonych rywaroksabanem oraz u 6,5% leczonych antagonistami witaminy K. Oznacza to 25% większe ryzyko przy stosowaniu rywaroksabanu w porównaniu z klasycznym leczeniem. Nie zaobserwowano różnic w przypadku częstości hospitalizacji z powodu HF. Nie wykazano również różnic pomiędzy obiema grupami pod kątem występowania groźnych krwawień, natomiast na korzyść rywaroksabanu przemawia statystycznie istotne rzadsze występowanie krwawień zakończonych zgonem (4 *vs.* 15; 0,17% *vs.* 0,66%).

Pomimo rozwoju leczenia przeciwzakrzepowego, klasyczne leki, jakimi są antagoniści witaminy K w dalszym ciągu wykazują swoją przydatność i stanowią jedyny wybór w przypadku specyficznych podgrup pacjentów (mechaniczne protezy zastawkowe i stenoza mitralna). Jak widać w analizie przeprowadzonej w badaniu INVICTUS, stosowanie ich w istotnych wadach zastawek o etiologii reumatycznej wiąże się z mniejszym ryzykiem udaru lub zgonu sercowego, chociaż ich istotną wadą pozostaje konieczność stałego monitorowania wskaźnika międzynarodowego współczynnika znormalizowanego, co dla niektórych może być problemem. Dla pacjentów, którzy są w stanie dopilnować wysokiej jakości leczenia przeciwzakrzepowego antagoniści witaminy K powinny pozostać leczeniem pierwszego wyboru w przypadku współwystępowania reumatycznych wad serca powikłanych AF.

Konflikt interesów

Autorzy deklarują brak konfliktu interesów.

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