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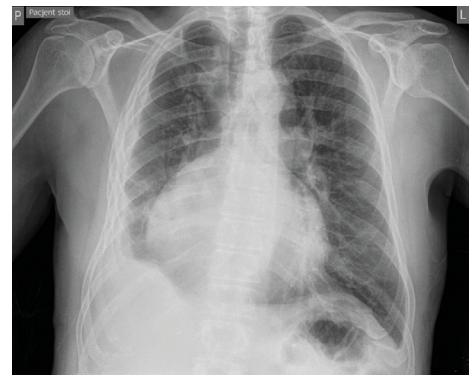

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FOLIA CARDIOLOGICA

2023, vol. 18, no. 3

Table of Contents/Spis treści

ORIGINAL ARTICLE/PRACA ORYGINALNA

YOUNG CARDIOLOGY/MŁODA KARDIOLOGIA

CASE REPORTS/PRACE KAZUISTYCZNE

Folia Cardiologica 2023
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The relationship between vitamin D serum concentration and common inflammatory biomarkers in the early postoperative period in infants with congenital heart defects operated on with extracorporeal circulation: preliminary results

Zależność pomiędzy stężeniem witaminy D w osoczu oraz rutynowymi wykładnikami stanu zapalnego we wczesnym okresie pooperacyjnym u niemowląt poddanych operacji wrodzonych wad serca z zastosowaniem krążenia pozaustrojowego — wyniki wstępne

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Abstract

Introduction. Children operated on congenital heart defects (CHD) with the use of extracorporeal circulation (ECC) experience various forms of systemic inflammatory response syndrome (SIRS) which can be measured by routine inflammatory biomarkers (C-reactive protein [CRP], procalcitonin). According to literature, vitamin D serum concentration in multiple potential ways may be related to the inflammatory response activation in the acute phase of SIRS in infants operated on CHD with the use of ECC.

Material and methods. The study group consisted of 20 infants (mean age = 7.35 months; standard deviation = 2.76) with CHD underwent cardiac surgery with the use of ECC in one cardiac unit. Serum concentration of vitamin D (in 2 forms: $25(OH)D_3$ and $1.25(OH)_2D_3$), as well as inflammatory biomarkers were measured three times: a day before surgery, on the 2nd day after the operation, and finally — in the 6th postoperative day. All participants received standard vitamin D supplementation (500 IU) orally within first week after birth as well as just after the return to oral feeding after cardiac surgery (1st postoperative day). The specimens were analysed in the local laboratory. The obtained data were analysed statistically. To asses vitamin D sufficiency the standard, recommended thresholds were used.

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Results. All patients had sufficient level of vitamin D before the surgery. Patients with any clinical sign of infection (including elevated inflammatory biomarkers) were excluded. On the 2nd postoperative day, when the peak level of CRP (median [m] = 131.59 mg/L) was observed, the $1.25(OH)_2D_3$ fell to insufficiency (m = 66.10 ng/mL). In the 6th postoperative day CRP was observed in the nearly normal ranges, while vitamin D returned to preoperative sufficiency levels.

Conclusions. The study's preliminary results show that the dynamics of early postoperative inflammatory markers level increase correlates with early postoperative serum vitamin D concentration drop below the therapeutic level. Our results eligible further studies to determine new universal protocols of preoperative, and perioperative vitamin D administration to prevent from vitamin D deficiency in children operated on for CHD in infancy.

Key words: vitamin D, systemic inflammatory response syndrome, paediatrics, paediatric cardiac surgery, congenital heart defects

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Introduction

The global development of prenatal diagnostics caused the birth prevalence of congenital heart defects (CHDs) to reach 9.410 in 1000 births between 2010 and 2017, with untreated CHD resulting in the greatest mortality during the first year of life [1, 2]. A significant proportion of these paediatric patients require one or more corrective procedures over their lifetime with the use of extracorporeal circulation (ECC). The ECC provokes the inflammatory response due to ischemic/reperfusion injury, haemodilution *etc*. [3]. Therefore, systemic inflammatory reaction syndrome (SIRS) is frequently observed in children after open heart surgery, which has been associated with both ECC and surgical trauma. The pathophysiology of SIRS involves a cytokine-mediated general capillary leakage followed by intravascular volume depletion, haemodilution, generalized oedema, circulatory compromise and altered microcirculation. Postoperative SIRS can be measured by routine biomarkers such as C-reactive protein (CRP), procalcitonin or leukocytosis [4].

Despite the powerful strategies to prevent it, SIRS increases the risk of multiple organ dysfunction syndrome and further postoperative complications. Any means of preventing or controlling these complications may improve the condition of high-risk paediatric patients, promote recovery, and decrease mortality [4, 5].

Vitamin D supplementation and control

Vitamin D is routinely measured in 2 forms: 25-hydroxy vitamin D ($25(OH)D_3$) and its active metabolite 1.25-dihydroxy vitamin D ($1.25(OH)_2D_3$). The metabolite has the highest affinity to vitamin D receptors and is mainly responsible for calcium homeostasis. Except for the mineral metabolism function, recent studies indicate that the vitamin D receptors responsible for vitamin D physiologic effects exertion are expressed in most of the body tissues providing a wide field for research on its potential in the prevention, or even treatment, in a variety of extra-skeletal conditions [6]. Nevertheless, the $25(OH)D_3$ is the compound that is optimally suited for assessing vitamin D status in most patients, due to its relatively high serum concentration and long half-life [5, 6].

Standard vitamin D supplementation recommended in the general population includes 400 IU/day from the first days of life, regardless of the way of feeding for the neonates and infants aged 0–6 months and 400–600 IU/day, depending on the daily amount of vitamin D taken with food for the infants aged 6–12 months according to the recommendations of the Polish Society of Paediatric Endocrinology and Diabetes [7]. The generally accepted thresholds for defining 'desired' vitamin D sufficiency is 75 nmol/L (30 ng/mL), with deficiency defined as below 50 nmol/L (20 ng/mL), and severe deficiency at 25 to 30 nmol/L (10–12 ng/mL) [5].

The vitamin D supplements are usually administered by the parents or tutors, who control both the way, and the frequency of supplementation. There are several vitamin D supplements available over-the-counter, including generic products, with different active constituents' concentrations. Those variable factors make monitoring of the vitamin D correct administration, dosage, and serum concentration in infants with elective cardiac surgery not easy, although it could have an impact on the postoperative pathophysiology.

Possible role of the vitamin D in cardiac surgery

The current body of knowledge supports the hypothesis that vitamin D is critical for different common conditions including autoimmune and neurological diseases, pregnancy complications, cancer as well as cardiovascular disorders and various types of infections [6]. Higher vitamin D concentrations in adult patients are associated

with significantly fewer postoperative organ dysfunctions, decreased procalcitonin levels, fewer nosocomial infections, and less frequent death and/or prolonged hospital stay [8].

Kruit et al. [9] based on a cohort study proved an inverse correlation between $25(OH)D_3$ and CRP, especially pronounced in elderly patients with inflammatory diseases. In the literature it is also strongly hypothesized that vitamin D insufficiency can be associated with increased morbidity and mortality in critically ill patients and that it may be a consequence of the critical illness itself, probably intensifying the adverse effects [10]. The analysis of the critically paediatric patients in a large multicentre intensive care unit reported a 70% vitamin D deficiency rate, suggesting the association between low vitamin level and their clinical course [11]. *In vitro* studies have suggested that vitamin D suppresses proinflammatory cytokines and increases anti-inflammatory cytokines [12].

Studies focused on adult cardiovascular patients point to vitamin D deficiency as a risk factor for acute coronary syndromes and other critical conditions associated with cardiovascular disease [13, 14].

According to case reports/series paediatric patients operated on CHD with the use of ECC often experience calcium serum level alterations and cardiogenic shock with vitamin D serum level decrease. Graham et al. [15] confirmed these observations with a secondary analysis of blood specimens (samples taken before skin incision, at the cessation of ECC and 24 hours postoperatively), reporting that 84% of neonates with CHD were vitamin D deficient postoperatively, while lower vitamin D levels were associated with increased inotropic support. Ye et al. [16] suggested that children with vitamin D deficiency before the surgery need increased postoperative inotropic support. Vitamin D supplementation in outpatient paediatric congenital heart failure (HF) showed improved cardiac function with a higher daily dose of vitamin D [17].

The current knowledge suggests that the biological role of vitamin D and the impact on heart function rely on multiple potential mechanisms such as reduced inflammation, lower risk of infections, improved cardiac function and faster postoperative recovery, which justify the need to control and finally provide its optimal serum concentration in every phase of surgical cardiac treatment.

Aim of the study

The aim of the study was the analysis of vitamin D serum concentration and common inflammatory biomarkers levels in the early postoperative period in infants with congenital heart defects operated on with the use of extracorporeal circulation.

Material and methods

Clinical data were collected prospectively from 30 consecutive paediatric patients referred for surgery to one department of paediatric cardiac surgery. All children referred for cardiac surgery with the use of ECC were carefully examined preoperatively, with regular clinical tests including serum vitamin D level tests (measured in two forms: $25(OH)D_3$ and $1.25(OH)_2D_3$). Routine preoperative exams and laboratory tests were performed. The patients referred for surgical procedures were free of any clinical or laboratory signs of infection.

Finally, after a meticulous analysis of the data obtained, the group of 20 children were enrolled on further analysis. Infants with incomplete data or additional comorbidity that could affect their clinical management were excluded from the study.

The patients were involved in the study group according to inclusion and exclusion criteria. The informed parental consent were obtained before the inclusion in the study group.

The inclusion criteria were:

- age between 30 days–12 months;
- congenital heart defects surgery with ECC in one paediatric cardiac surgery department;
- standard vitamin D3 supplementation from the first week after birth according to the recommendations of the Polish Society of Paediatric Endocrinology and Diabetes [7];
- every clinical symptom of potential infections was identified and excluded.

The exclusion criteria were:

- cardiac or gastrointestinal disease prevented feeding or drug administration before the surgery, to the day before the operation;
- confirmed or suspected William's syndrome — a genetic disorder with symptoms including cardiovascular problems and elevated blood calcium;
- born at gestational age less than 32 weeks.

The eligibility criteria were justified because infants born before 32 weeks gestational age have a significantly increased risk of nephrocalcinosis, while patients with Williams syndrome have a genetic susceptibility to hypercalcemia, and current guidelines do not recommend vitamin D supplementation [7, 18, 19].

Study group

The group consisted of 20 infants (age: 4–7 months; mean age = 7.35 months; SD = 2.76; 6 females [30%], 14 males [70%] with mean body mass 7.33 kg; SD = 1.86 kg) with CHD (Table 1) who underwent a moderate hypothermic ECC cardiac surgical correction of congenital heart defects

Table 1. Heart defects were presented, and clinical analysis and drugs were administered within the study group

Heart defects	Number (percentage)
Ventricular septal defect	10 (50)
Tetralogy of Fallot	4 (20)
Atrioventricular septal defect	3 (15)
Single ventricle	1 (5)
Atrial septal defect, pulmonary stenosis	1 (5)
Criss-cross heart, transposition of the great arteries, pulmonary stenosis	1 (5)
Clinical analysis	**Number (percentage)**
Cyanosis	7 (35) and 4 (20) patients after pulmonary artery banding
Heart failure	12 (60)
Respiratory failure	14 (70)
Genetic disorders	Down syndrome — 3 (15)
	Phenyloketonuria — 1 (5)
Other	Obesity — 1 (5)
	Urinary tract defect — 1 (5)
	Glucose intolerance — 1 (5)
	Premature infant (born 32 < and > 37 weeks gestational age) — 1 (5)
Drugs administered (preoperatively)	**Number (percentage)**
Spironolactone	7 (35)
Lisinopril	5 (25)
Propranolol	3 (15)
Acetylsalicylic acid	2 (10)
Bisoprolol	1 (5)
Levothyroxine	1 (5)

in one cardiac unit. The study group included also clinical course analysis and preoperative drug administration distinction (Table 1).

Procedure

All the cardiac surgeries with ECC were done with standard general anaesthesia. All patients received a standard perioperative institutional antibiotics prophylaxis (cefazolin). Moderate hypothermia (28–32°C) during ECC and cardiac arrest with standard single-dose antegrade cold crystalloid cardioplegia (Custodiol) was used. For deep hypothermia, a deep hypothermic circulatory arrest strategy was used, as routinely. Haematocrit values were kept above 30% during the ECC in rewarming period with continuous hemofiltration commenced in the circuit. No steroids were given routinely. The protocol of postoperative biochemical analysis was followed in every consecutive patient referred for cardiac surgery, all tests were performed in the institutional laboratory.

Blood samples were collected on the day before surgery, and on the second and sixth postoperative days as part of the routine laboratory control during the perioperative period. The samples were collected at the same time (6 AM) as a part of the morning examination panel, without the need for any additional blood collection. Serum CRP concentration was measured using a turbidimetric immunoassay (Modular Roche A PB 06-76). The normal range of CRP serum concentration was below 5 mg/L.

Vitamin D serum concentrations were measured three times: a day before surgery, on the second day after the operation and on the 6th postoperative day (PRE-OP, POD2 and POD6, respectively). All infants received a standard dose of vitamin D supplementation according to the recommendations from the first week after birth. Every patient received a standard dose of vitamin D on the first postoperative day, just after the return to oral feeding. All specimens for vitamin D analysis were collected and analysed in the local laboratory at the institution. Standard institutional thresholds for defining 25(OH)D_3 sufficiency and deficit were used compared with the sufficiency thresholds from the literature (Table 2). For 1.25$(OH)_2D_3$ status an institutional sufficiency range of 15.02–90.10 (ng/mL) was used. Clinical course analysis was also performed on every subject, with the identification of prolonged administration of catecholamines and antibiotics. The symptoms of HF, cyanosis, metabolic demands, organ insufficiency, drugs and genetic abnormalities were analysed as they can potentially cause susceptibility to vitamin D level fluctuations.

The data were simultaneously collected, while the analysis was performed after complete data collection and retrospective verification. The statistical analysis was performed after the final data collection.

Ethical considerations

The presented single-institutional prospective preliminary study was performed according to the rules and guidelines of the local Ethic Examining Committee of Human Research (Decision of Approval: NKBBN 178/2012 dated: May 14, 2012 — continuation of the ongoing study on inflammatory biomarkers) and the procedures followed the ethical standards of the Helsinki Declaration of 1975.

Table 2. The standard institutional laboratory thresholds for 25-hydroxy vitamin D (25(OH)D) sufficiency

Standard institutional 25-hydroxy vitamin D (25(OH)D) sufficiency thresholds	Range [ng/mL]	25-hydroxy vitamin D (25(OH)D) thresholds proposed by McNally et al. [5]	Range [ng/mL]
Low	20–30	Severe deficiency	10–12
Optimal	30–50	Deficiency	~ 20
High	50–100	Sufficiency	> 30
Potentially toxic	100–150		
Toxic	> 150		

Table 3. Median and mean values of serum concentration of $25(OH)D_3$ and $1.25(OH)_2D_3$ and C-reactive protein (CRP) concentration values in 3 measures: PRE-OP, POD2 and POD6

Serum concentration/day of measurement	PRE-OP	POD2	POD6
$25(OH)D_3$ [ng/mL]	Median = 36.33	Median = 27.79	Median = 35.03
	Q1 = 25.90	Q1 = 23.35	Q1 = 30.4
	Q3 = 49.15	Q3 = 31.80	Q3 = 39.3
	IQR = 23.25	IQR = 8.45	IQR = 8.9
$1.25(OH)_2D_3$ [ng/mL]	Median = 109.31	Median = 66.10	Median = 72.54
	Q1 = 57.15	Q1 = 56.22	Q1 = 55.70
	Q3 = 150	Q3 = 86.45	Q3 = 77.9
	IQR = 92.85	IQR = 30.23	IQR = 22.2
CRP [mg/L]	Mean ≤ 5	Median = 131.59	Mean ≤ 20
	Median ≤ 5	Q1 = 65,5	Median ≤ 5
		Q3 = 199	
		IQR = 133.5	

Statistical analysis methods

Statistical analysis was performed using SPSS v. 26.0 (SPSS Inc., USA). Continuous variables were presented as medians with quartiles and means with standard deviations. The data sets that did not follow a normal distribution were analysed with the nonparametric Wilcoxon test. The correlation between the data was assessed with Spearman's coefficient. Also, the coefficient of determination was set to graphically present the correlation. Statistical significance was assumed for p values of less than 0.05.

Results

All patients had a sufficient level of both $25(OH)D_3$ (median = 36.33 ng/mL [Q1 = 25.90; Q3 = 49.15; IQR = = 23.25]) and $1.25(OH)_2D_3$ (median = 109.31 ng/mL [Q1 = 57.15; Q3 = 150; IQR = 92.85]). The inflammatory biomarkers were within normal range before the surgery (Table 3, Figure 1).

In the second postoperative day the $25(OH)D_3$ serum concentration fall to severe insufficiency (median = = 27.79 ng/mL [Q1 = 23.35; Q3 = 31.80; IQR = 8.45]) and its active metabolite $1.25(OH)_2D_3$ falls significantly (median = 66.10 ng/mL [Q1 = 56.22; Q3 = 86.45; IQR = 30.23]) (Table 3, Figure 1).

In the 6th postoperative day $25(OH)D_3$ levels returned to preoperative sufficiency (median = 35.03 ng/mL [Q1 = 30.4; Q3 = 39.3; IQR = 8.9]) and $1.25(OH)_2D_3$ serum concentration significantly increased (median = 72.54 ng/mL [Q1 = 55.70; Q3 = 77.9; IQR = 22.2]) (Table 3, Figure 1).

Statistical analysis

There was a significant difference between vitamin $25(OH)D_3$ measured PRE-OP and POD2, as well as POD2 and POD6 and for $1.25(OH)_2D_3$ measured PRE-OP and POD2 (Table 4). Spearman's correlation coefficients showed a negative correlation between the CRP levels and 25-hydroxy vitamin D concentrations and between CRP levels and 1.25-dihydroxy

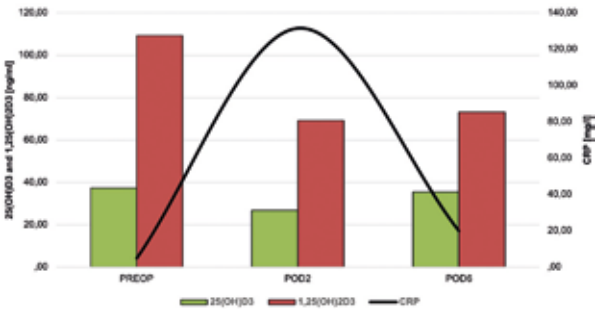

Figure 1. The median serum concentration of $25(OH)D_3$ and $1.25(OH)_2D_3$ in relationship with median C-reactive protein (CRP) values in 3 measures: PRE-OP, POD2 and POD6

vitamin D concentrations in the second postoperative day measurements (Table 5).

The p-values showed a statistically significant decrease between $25(OH)D_3$ values measured PRE-OP and POD2 and an increase in POD2 and POD6. What is more, the increase between $1.25(OH)_2D_3$ measured PRE-OP and POD2 was also statistically significant, contrary to the non-significant difference between $1.25(OH)_2D_3$ decrease between POD2 and POD3. The coefficients of determination low values show that the independent values cannot be always explained by the dependent values.

Table 4. P-values between $25(OH)D_3$ and $1.25(OH)_2D_3$ measurements in PRE-OP vs. POD2 and POD2 vs. POD6

P-values between $25(OH)D_3$ and $1.25(OH)_2D_3$ measurements in PRE-OP vs. POD2 and POD2 vs. POD6		
	PRE-OP vs. POD2	POD2 vs. POD6
$25(OH)D_3$	$p < 0.001$	$p < 0.001$
$1.25(OH)_2D_3$	$p = 0.019$	$p = 0.616$

Table 5. Spearman's correlation coefficient and coefficient of determination values

Spearman's correlation coefficient and coefficient of determination values between CRP concentration and $25(OH)D_3$ concentrations and between CRP levels and $1.25(OH)_2D_3$ in the POD2				
	$25(OH)D_3$		$1.25(OH)_2D_3$	
CRP	Spearman's correlation coefficient	Coefficient of determination	Spearman's correlation coefficient	Coefficient of determination
	–0.196	$R^2 < 0.001$	–0.226	$R^2 = 0.004$

CRP — C-reactive protein

Discussion

Our preliminary results showed significant perioperative changes in serum vitamin D levels and a negative correlation between CRP levels (commonly used as a marker of SIRS) and vitamin D levels in 20 infants undergoing cardiac surgery with ECC and receiving standard preoperative vitamin D supplementation.

Abou Zahr et al. [20] also showed a statistically significant decrease in vitamin D levels immediately and 24 hours after ECC use during paediatric cardiac surgery. The report also claims no significant change in the vitamin D binding protein in the measured probes justifying the omission of this factor in the presented preliminary report.

The presented preliminary report focused on two forms of vitamin D: 25-hydroxyvitamin D and 1.25-dihydroxy vitamin D, available in the local laboratory. The vitamin D sufficiency was determined by standard institutional thresholds which are not dedicated to, and not adjusted to paediatric patients and differ from the thresholds proposed in the literature. The generally accepted thresholds for vitamin D sufficiency differed between literature [5] and available institutional laboratories. Further studies on vitamin D serum concentration in paediatric patients should be conducted to determine adjusted thresholds and to enable better vitamin D level monitoring.

According to Boehne et. al. [4], the period between 24–72 hours is the most probable period of SIRS incidence after paediatric cardiac surgery with the use of ECC. Yet another study claims that around 20% of SIRS may happen up to 5 days after the surgery [21]. To focus on the postoperative SIRS pathophysiology, the time of the collection of blood samples for vitamin D and inflammatory biomarkers measurements was set to 2 and 6 days after the surgery. The postoperative measurements were put in comparison to preoperative, unimpaired, inflammatory patients' status. On the 6^{th} day a normalized inflammatory status was expected — confirmed by the inflammatory biomarkers. The patients that did not fulfil the inclusion criteria and developed any additional postoperative complications were excluded from the study group. On the other hand, their vitamin D status could differ from the patients included in the study, probably presenting a deeper deficiency level, which emphasizes the need to establish whether vitamin D deficiency could be associated with final clinical outcomes.

The inverse correlation between $25(OH)D_3$ and CRP had been previously studied in elderly patients with inflammatory diseases and showed a negative correlation between those [9]. The vitamin D status after cardiac surgeries with ECC in children was also compared to the albumin level as the patients' homeostasis monitoring factor, not showing any significant correlation [20].

The study group in this preliminary report was also heterogeneous. The paediatric patients with CHD have

presented with different types of CHD and concomitant disorders as the symptoms of HF, cyanosis, metabolic demands, organ insufficiency, drugs administered, genetic abnormalities etc. Although all the patients underwent cardiac surgery procedures with the use of ECC, their general condition, type and severity of surgery performed, and the time of the ECC and hypothermia applied differed. Next, the SIRS may lead to different organs disturbance, or failure altering other metabolic pathways [4]. All these factors could potentially cause susceptibility to vitamin D serum concentration fluctuations during the postoperative period and result in alterations to raw and statistical data for this preliminary report.

Furthermore, the interquartile ranges values may doubt the exact results' applicability, especially for the values of the $1.25(OH)_2D_3$ vitamin D active metabolite. The interquartile range (IQR) values for all $25(OH)D_3$ serum concentrations measured were similar, low values (IQR_{max} = 23.25 and IQR_{min} = 8.45), whereas for both $1.25(OH)_2D_3$ and CRP measurement the IQR was significantly higher ($1.25(OH)_2D_3$ IQR_{max} = 92.85; CRP IQR = 133.50) showing a notable spread of the data. The statistical analysis suggests that there may be different dynamics between $25(OH)D_3$ and $1.25(OH)_2D_3$ in the perioperative period and emphasizes the need to research a significantly larger study group to obtain more comparable results.

For the time of this preliminary study being conducted, the paediatric cardiac surgery population is supplemented with the standard doses of vitamin D recommended for the general population by the Polish Society of Paediatric Endocrinology and Diabetes. Further studies of presented relationships between the postoperative SIRS and vitamin D serum level could determine whether the perioperative vitamin D level maintenance could have a therapeutic effect and a benefit for demanding paediatric patients undergoing cardiac surgery in early infancy. And, as the clinical postoperative outcomes may in many ways depend on vitamin D status, what kind of vitamin D supplementation should be applied to paediatric cardiac surgery patients.

Limitations of the study

There are several limitations to be mentioned regarding this study. The presented report is a prospective, one-centre observational study of a small group of children referred for cardiosurgical operation in ECC without randomization. Preoperatively vitamin D was administered by parents at home, therefore one could not exclude some individual differences as an effect of suboptimal, negligent drug regimens, or even the difference in the quality of pharmacy-delivered vitamin D drops. Although the perioperative antibiotic prophylaxis algorithm was homogenous, during the observation period the range of operative trauma might differ in selected groups of patients. Therefore, the differences in values of CRP and leukocytosis in the early postoperative period might exist, although reproductive characteristics of biomarkers trends were observed. In addition, particular operative strategies at the study institution, as well as postoperative care of paediatric patients after cardiac surgery with ECC may differ from other centres. There is no doubt that further studies are needed.

Conclusions

Standard vitamin D supplementation in children with CHD referred for cardiac surgical treatment with means of surgery with ECC does not prevent perioperative serum vitamin D level drop and its potential clinical consequences.

The dynamics of early postoperative inflammatory markers level increase correlates with early postoperative serum vitamin D concentration drop below the therapeutic level.

The observation and preliminary results eligible further studies to determine new universal protocols of preoperative, and perioperative vitamin D administration to prevent vitamin D deficiency in children operated on for CHD in infancy.

Conflict of interest

None declared.

Funding

None

Streszczenie

Wstęp. Operacje kardiochirurgiczne u dzieci wykonywane z powodu wrodzonych wad serca (CHD, *congenital heart defects*) w krążeniu pozaustrojowym (ECC, *extracorporeal circulation*) prowadzą do różnych postaci zespołu ogólnoustrojowej reakcji zapalnej (SIRS, *systemic inflammatory response syndrome*) mierzonej rutynowymi biomarkerami (białko C-reaktywne [CRP, *C-reactive protein*], prokalcytonina). Stężenie witaminy D w wielu potencjalnych mechanizmach może być związane z poziomem aktywacji odpowiedzi zapalnej w ostrej fazie SIRS po ECC u operowanych niemowląt z CHD.

Materiał i metody. Badaniem objęto grupę 20 niemowląt (wiek: 4–7 miesięcy) z CHD, które poddano kardiochirurgicznej korekcji wrodzonych wad serca metodą w krążeniu pozaustrojowym w umiarkowanej hipotermii na jednym oddziale kardiochirurgicznym. Stężenie witaminy D (w dwóch postaciach: $25(OH)D_3$ i $1,25(OH)_2D_3$) oraz CRP i leukocytozy mierzono trzykrotnie: dzień przed operacją, w 2. dobie po operacji i ostatecznie — w 6. dobie pooperacyjnej. Wszystkie niemowlęta otrzymywały standardową dawkę suplementacji witaminą D (500 IU doustnie) w 1. tygodniu po urodzeniu, a także w 1. dobie pooperacyjnej tuż po powrocie do karmienia doustnego. Wszystkie próbki zostały pobrane, poddane analizie laboratoryjnej, a uzyskane dane poddano analizie statystycznej. Zastosowano standardowo przyjęte progi definiujące niedobór witaminy D.

Wyniki. Stężenie witaminy D w osoczu u wszystkich pacjentów przed operacją, jak również stężenie biomarkerów zapalnych mieściły się w zakresie normy. Jakiekolwiek objawy kliniczne potencjalnej infekcji zostały zidentyfikowane i wykluczone. W 2. dobie pooperacyjnej, kiedy obserwowano szczytowy poziom stężenia CRP, aktywny metabolit witaminy D spadł do poziomu ciężkiego niedoboru. W 6. dobie pooperacyjnej stężenie CRP było w zakresie zbliżonym do prawidłowego, a poziom witaminy D powrócił do stanu sprzed operacji.

Wnioski. Wstępne wyniki wykazały odwrotną korelację pomiędzy parametrami SIRS a poziomem witaminy D u niemowląt przy standardowej suplementacji przedoperacyjnej. Dalsze badania przedstawionych zależności mogłyby określić, czy okołooperacyjna suplementacja witaminą D może mieć efekt terapeutyczny i przynieść korzyść pacjentom pediatrycznym poddawanym zabiegom kardiochirurgicznym we wczesnym okresie niemowlęcym.

Słowa kluczowe: witamina D, zespół ogólnoustrojowej reakcji zapalnej, pediatria, kardiochirurgia dziecięca, wrodzone wady serca

Folia Cardiologica 2023; 18, 3: 99–107

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Pulmonary embolism: does SARS-CoV-2 infection affect the clinical course and prognosis?

Zatorowość płucna — czy infekcja SARS-CoV-2 wpływa na przebieg kliniczny i rokowanie?

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Lekarz Anna Żarek-Starzewska przygodę z kardiologią rozpoczęła w czasach studenckich, aktywnie działając w Studenckim Kole Naukowym przy Katedrze i Klinice Kardiologii II Wydziału Lekarskiego Warszawskiego Uniwersytetu Medycznego pod kierownictwem prof. dr hab. n. med. Marka Kucha. Obecnie jest studentką Szkoły Doktorskiej WUM, a tematyka jej badań obejmuje między innymi rolę microRNA w patogenezie oraz diagnostyce chorób sercowo-naczyniowych. Prace, których była współautorką, zostały zaprezentowane na konferencjach naukowych, takich jak EuroEcho pod patronatem Europejskiego Towarzystwa Kardiologicznego oraz *Warsaw Medical International Congress*. Do zainteresowań pozamedycznych dr Żarek-Starzewskiej należą architektura wnętrz, moda oraz muzyka rockowa.

Abstract

Introduction. Coronavirus disease 2019 (COVID-19) is a disease associated with an increased risk of thromboembolic complications up to 5 months after infection. The study aimed to assess the effect of active or recent (defined as within the past 3 months) COVID-19 on the clinical course of pulmonary embolism (PE) and patients' survival as compared to patients with pulmonary embolism without a history or active COVID-19.

Material and methods. Eighty-seven patients diagnosed with pulmonary embolism, and hospitalized from March 2020 to July 2021 were qualified for the study. The patients were divided into two groups: 1. COVID (+): patients with an active severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection confirmed by the polymerase chain reaction (PCR) or antigen test in the period no longer than 3 months before the diagnosis of PE (n = 38); 2. COVID (–): patients tested negative for SARS-CoV-2 and without typical history of infection (n = 49).

The following data were analysed: clinical data, results of computed tomography, transthoracic echocardiography, ultrasound of deep veins of lower limbs, and results of laboratory tests (D-dimer, N-terminal pro-B-type natriuretic peptide, cardiac troponin I, C-reactive protein [CRP]). For statistical analysis, Statistica version 13 was used.

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Results. Significant differences between the COVID (+) and COVID (–) groups were observed in the incidence of complete respiratory failure in 39.5% and 6.12% of patients respectively, p = 0.001 and higher in-hospital mortality 26.3% *vs.* 4.08%; p = 0.003. The Cox regression did not reveal any factor significantly associated with in-hospital mortality besides the previous diagnosis of neoplasm (hazard ratio 3.23; 95% confidence interval: 0.81; 12.95; p = 0.09).

The COVID (+) group was characterized by significantly higher levels of CRP (9.43/52.50/113.23 [mg/L] *vs.* 6.40/24.70/47.40 [mg/L]; p = 0.04).

Conclusions. Patients with COVID-19 and PE present higher mortality than patients without concurrent or recent SARS-CoV-2 infection. Further studies are warranted to identify specific factors associated with the observed higher mortality in this population.

Key words: pulmonary embolism, COVID-19, in-hospital mortality

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Introduction

Coronavirus disease 2019 (COVID-19), caused by an infection with severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) [1], besides its pulmonary manifestation, leads to hypercoagulability in many patients, which in turn becomes a significant risk factor for thrombosis, both in the venous and arterial system [2]. A nearly two-year follow-up of patients with COVID-19 infection shows that pulmonary embolism (PE) and deep vein thrombosis belong to the most common thromboembolic complications in patients with COVID-19. Their incidence is estimated at 20 to 30% in patients in a critical condition [3] and is significantly higher than in the general population (8%) [4, 5]. Whether PE increases mortality in COVID-19 patients remains unclear. Due to the high coincidence of SARS-CoV-2 infection and PE and a relatively high probability of thromboembolic complications even 5 months [6] after the COVID-19 infection, it is essential to identify specific risk factors which will enable an early diagnosis and implementation of adequate treatment to improve patient outcomes.

Objectives

The study aimed to assess the effect of active or recent (defined as within the past 3 months) COVID-19 on the clinical course of PE and patients' survival as compared to patients with PE without a history of active COVID-19. In addition, an attempt was made to identify differences between those subgroups.

Material and methods

The initial analysis included 115 consecutive patients diagnosed with pulmonary embolisms hospitalised at the cardiology department and COVID-19 departments of the hospital between March 2020 and July 2021. Twenty-eight subjects were excluded from the further assessment: 7 due to incomplete diagnostic data, 7 due to SARS-CoV-2 infection following the PE, 13 with COVID–19 defined as typical symptoms and positive antibody testing and 1 due to transfer to another hospital.

The classification of PE severity and the risk of early (30-day) mortality was based on the 2019 European Society of Cardiology Guidelines for the diagnosis and management of acute PE [7].

The patients were divided into two groups:

1. COVID (+): with an active SARS-CoV-2 infection confirmed by the polymerase chain reaction (PCR) or antigen test in the period no longer than 3 months before the diagnosis of PE,
2. COVID (–): patients with a negative PCR test for SARS-CoV-2, no typical history of infection and a negative result of antibody measurement for SARS-CoV-2.

The analysis included anthropometric, clinical, radiologic and laboratory data. The start of COVID-19 was defined as the date of positive PCR or antigen test.

The statistical analysis was performed with the use of the Statistica software, v13. The data were presented as mean (± standard deviation) in case of normally distributed variables, median (1^{st} quartile, 3^{rd} quartile) in case of non-normal distribution and count (percentages) in case of categorical variables. The Pearson χ^2 test was used for nominal variables, the Student's t-test was used for normally distributed quantitative variables and the U-Mann-Whitney test for non-normally distributed quantitative variables. Univariable Cox regression analysis was applied to determine predictive factors of in-hospital mortality.

Results

The final analysis included 87 subjects (50 men), including 38 COVID (+) patients. The mean age was 66.6 years (28–98 years). Active infection with SARS-CoV-2 was confirmed

Table 1. Comparison of clinical course, mortality, hospitalization time and biochemical parameters between COVID (+) and COVID (–) groups

Variable	COVID + group (n = 38)	COVID – group (n = 49)	p
In-hospital all-cause mortality [subjects]	10 (26.3%)	2 (4.08%)	0.003
Respiratory failure during hospitalization [subjects]	15 (39.5%)	3 (6.12%)	0.001
Age older than 65 years [subjects]	0.88/0.94/0.97	0.92/0.96/0.98	0.56
Hospitalization time [days]	6.00/10.50/16.00	3.00/6.00/10.00	0.32
Previous deep vein thrombosis [subjects]	2 (5.26%)	10 (20.4%)	0.04
Concurrent inflammatory process [subjects]	24 (63.2%)	17 (34.7%)	0.008
D-dimer 1 [ng/mL][a]	2077.5/5249.5/34502.50	2020.75/4538.00/9290.75	0.38
D-dimer max [ng/mL][b]	2353.25/5560.00/34502.50	2020.75/4538.00/9290.75	0.40
NT-proBNP 1 [pg/mL][c]	111.50/356.20/1074.50	141.00/509.40/3129.00	0.16
NT-proBNP max [pg/mL][d]	111.50/356.20/1074.50	141.00/509.40/3129.00	0.16
Troponin 1 [ng/L][e]	4.00/15.00/49.50	3.75/19.00/73.00	0.74
Troponin max [ng/L][f]	4.00/16.00/58.00	3.75/21.00/84.75	0.72
CRP [mg/L]	9.43/52.50/113.23	6.40/24.70/47.40	0.04

The data are presented as mean (± standard deviation) in case of normally distributed variables, median (1st quartile, 3rd quartile) in case of non-normal distribution and count (percentages) in case of categorical variables; [a]D-dimer 1 — D-dimer concentration in ng/ml, measured on admission to the hospital; [b]D-dimer max — maximum D-dimer concentration in ng/mL during hospitalization; [c]NT-proBNP 1 — N-terminal pro-B-type natriuretic peptide concentration in pg/mL, measured at hospital admission; [d]NT-proBNP — maximal concentration of N-terminal pro-B-type natriuretic peptide in pg/mL during hospitalization; [e]Troponin 1 — the concentration of high-sensitivity troponin I in ng/L, measured on hospital admission; [f]Troponin max — the maximum concentration of high-sensitivity troponin I in ng/L during hospitalization

in most patients with the PCR test (94.7%, n = 36). The COVID-19 infection had typical clinical symptoms in most patients (97.4%, n = 37), including fever, rhinitis, cough, muscle and joint pain. The median time from the start of COVID-19 to the diagnosis of PE was 8.5 (± 13) days. Twelve patients (13.8%) died during hospitalization. There were no significant differences in anthropometric and baseline clinical parameters, as well as typical risk factors for PE, besides age older than 65 years old in the COVID (+) group, and previous history of deep vein thrombosis, which was more frequent in the COVID (–) group. Neither were any differences observed in the baseline assessment of the PE risk and location and extension of embolic lesions (data not presented).

The clinical course differed significantly between the COVID (+) and COVID (–) groups with a higher incidence of respiratory failure and higher all-cause in-hospital mortality during hospitalisation, which was 5 times higher in the COVID (+) group than in the COVID (–) group (Table 1). However, in the Cox regression analysis, COVID-19 was not a significant predictor of death, which probably results from the limited size of the study group. The only variable significantly associated with mortality was the patient's age. The COVID (+) patients presented significantly higher values of C-reactive protein (CRP) (9.43/52.50/113.23 [mg/L] *vs.* 6.40/24.70/47.40 [mg/L]; p = 0.04). The Cox regression did not reveal any factor significantly associated with in-hospital mortality besides the previous diagnosis of neoplasm (hazard ratio 3.23; 95% confidence interval: 0.81; 12.95; p = 0.09).

Discussion

The results of this study reveal that patients with a diagnosis of pulmonary embolism and active or recent SARS-CoV-2 infection present higher in-hospital mortality than patients without a documented infection. More of them are older and without previous history of deep vein thrombosis, compared to patients without COVID-19.

Currently available literature [8, 9] leaves no doubt that SARS-CoV-2 infection significantly increases the risk of the development of PE and deep vein thrombosis in the lower limbs. Some patients were reported to develop PE even on full-dose anticoagulation [10]. However, the mortality data is not consistent. According to a study supported by the National Institute of Health of the United States, thromboembolic complications in COVID-19 patients contribute to higher mortality in this group [2], while according to other authors, the risk of death estimated based on pooled analyses among patients with COVID-19 and pulmonary embolism is similar [5] to that in patients without a diagnosed pulmonary embolism.

According to scientific reports, male sex and high body mass index are risk factors for pulmonary embolism in patients with COVID; this was not confirmed in this paper. As far as comorbidities are concerned, no specific risk factor

for the development of PE in COVID (+) patients was isolated. This finds confirmation in the available scientific literature [11]. Based on the above data the authors conclude that PE in COVID-19 is to a certain degree [12] affected by SARS-CoV-2 infection as an independent risk factor.

A concurrent inflammatory process (mainly pneumonia) and respiratory failure were observed significantly more often in the COVID-19 group than in the control group. This is correlated with an increased CRP level as well as available scientific reports, which also noticed an increase of other inflammatory parameters (white blood cells, blood platelet, fibrinogen and activated partial thromboplastin time) [12]. A lower saturation in patients with a history of COVID-19, not observed in patients with PE without a concurrent SARS-CoV-2 infection, may result from the lung involvement described in computed tomography.

We did not observe significant differences in D-dimer values between the COVID-19 (+) and COVID-19 (–) patients. However, other studies reported that the values of inflammatory parameters (CRP) and D-dimer in patients with PE and COVID-19 were significantly increased [11], therefore it requires further studies whether the measurement of these parameters may contribute to earlier diagnosis of thromboembolic complications among patients with SARS-CoV-2 or a recent history of such an infection. The consensus of the European Society of Cardiology Study Group on Biomarkers in Cardiology of the Acute Cardiovascular Care Association shows the potential usefulness of serial determination of D-dimers in COVID-19 patients in making decisions regarding diagnostic imaging for thromboembolic complications and potential modification of anticoagulant treatment [13]. Some studies indicate a prognostic value of the concentration of high-sensitivity troponin I and N-terminal pro-B-type natriuretic peptide (NT-proBNP), but the advisability of their routine determination is still under discussion [13–15] and requires further studies. An increase in the troponin level may result from numerous mechanisms unrelated to myocardial ischaemia including hypoxia, sepsis, systemic inflammation, pulmonary embolism, adrenergic hyperstimulation of the heart during cytokine storm, or myocarditis.

What seems to be clinically significant is the fact that the patients of the COVID-19 group were hospitalised longer, although their course of PE was not much more severe. This leads to a supposition that the SARS-CoV-2 infection is a risk factor for nosocomial complications contributing to prolonged hospitalisation, which may also affect the risk of death of these patients.

One of the main limitations of the study is the exclusion of patients hospitalised in the Intensive Care Unit. Thus, the results should not be extrapolated to the group of patients with severe course requiring hospitalisation at Intensive Care Unit. Typical diagnostics of pulmonary embolism were limited for epidemiological reasons. Not every patient with active SARS-CoV-2 infection received transthoracic echocardiography and ultrasound of the deep venous system. NT-proBNP was not routinely determined in all the patients but was dependent on the clinical situation. The study did not assess the mutated SARS-CoV-2 variants that can affect the clinical presentation of the disease, including, most likely, the incidence of pulmonary embolism.

Patients with COVID-19 and PE present higher mortality than patients without concurrent or recent SARS-CoV-2 infection. Further studies are warranted to identify specific factors associated with the observed higher mortality in this population.

Conflict of interest

None declared.

Streszczenie

Wstęp. Choroba koronawirusowa 2019 (COVID-19) jest związana ze zwiększonym ryzykiem powikłań zakrzepowo-zatorowych do 5 miesięcy po zakażeniu. Celem niniejszej pracy była ocena wpływu czynnego lub przebytego niedawno (w ciągu ostatnich 3 miesięcy) COVID-19 na przebieg kliniczny zatorowości płucnej (PE) i przeżycie pacjentów w porównaniu z pacjentami z zatorowością płucną bez wywiadu lub aktywnej COVID-19.

Materiały i metody. Do badania zakwalifikowano 87 pacjentów z rozpoznaniem PE, hospitalizowanych od marca 2020 do lipca 2021 roku. Pacjentów podzielono na dwie grupy: 1. COVID (+): pacjenci z czynną infekcją SARS-CoV-2 potwierdzoną łańcuchową reakcją polimerazy (PCR) lub testem antygenowym w okresie nie dłuższym niż 3 miesiące przed rozpoznaniem PE, (n = 38); 2. COVID (–): pacjenci z ujemnym wynikiem testu na SARS-CoV-2 i bez typowej historii infekcji (n = 49).

Analizie poddano dane kliniczne, wyniki tomografii komputerowej, echokardiografii przezklatkowej, USG żył głębokich kończyn dolnych, wyniki badań laboratoryjnych (D-dimer, N-końcowy fragment propeptydu natriuretycznego typu B, troponinę sercową I, białko C-reaktywne). Do analizy statystycznej wykorzystano program Statistica w wersji 13.

Wyniki. Zaobserwowano istotne różnice między grupami z COVID (+) i COVID (–) w częstości występowania całkowitej niewydolności oddechowej odpowiednio u 39,5%; 6,12% pacjentów, p = 0,001 i wyższej śmiertelności wewnątrzszpitalnej (26,3% *vs.* 4,08%; p = 0,003). Regresja Coxa nie ujawniła żadnego czynnika istotnie związanego ze śmiertelnością wewnątrzszpitalną poza wcześniejszym rozpoznaniem nowotworu (współczynnik ryzyka 3,23; 95-procentowy przedział ufności: 0,81; 12,95; p = 0,09). Grupa COVID (+) charakteryzowała się istotnie wyższymi stężeniami białka C-reaktywnego (9,43/52,50/113,23 [mg/l] *vs.* 6,40/24,70/47,40 [mg/l]; p = 0,04).

Wnioski. Wśród pacjentów z COVID-19 i PE wykazano wyższą śmiertelność niż u osób bez jednoczesnego lub niedawnego zakażenia SARS-CoV-2. Uzasadnione są dalsze badania w celu zidentyfikowania specyficznych czynników związanych z obserwowaną wyższą śmiertelnością w tej populacji.

Słowa kluczowe: zatorowość płucna, COVID-19, śmiertelność wewnątrzszpitalna

Folia Cardiologica 2023; 18, 3: 108–112

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Inappropriate prescription of a reduced dosage of NOAC in clinical practice: the results of the Polish Atrial Fibrillation (POL-AF) Registry in hospitalized patients

Niewłaściwe przepisywanie zredukowanej dawki NOAC w praktyce klinicznej — wyniki Polskiego Rejestru Migotania Przedsionków (POL-AF) u hospitalizowanych pacjentów

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Lekarz Olga Jelonek jest absolwentką Wydziału Lekarskiego Uniwersytetu Medycznego w Lublinie. Ukończyła szkolenie specjalizacyjne z kardiologii w I Klinice Kardiologii i Elektroterapii Świętokrzyskiego Centrum Kardiologii w Kielcach pod kierownictwem prof. dr hab. n. med. Beaty Wożakowskiej-Kapłon. Klinika specjalizuje się w diagnostyce i leczeniu zaburzeń rytmu serca (implantacja stymulatorów, ICD, CRT, badania elektrofizjologiczne, ablacje). W kręgu zainteresowań medycznych dr Jelonek pozostają: diagnostyka i leczenie choroby wieńcowej, terapia przeciwkrzepliwa, hipertensjologia. W wolnym czasie zajmują ją sport oraz muzyka.

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Abstract

Introduction. Prescribing non-vitamin K antagonist oral anticoagulants (NOACs) in a reduced or full dosage is important for providing patients with atrial fibrillation (AF) with efficacious and safe treatment. The study aimed to evaluate the administration frequency of reduced NOAC dosages against the guidelines and analysis of factors predisposing to such a choice in patients with AF included in the Polish Atrial Fibrillation (POL-AF) Registry.

Material and methods. The study included 1003 patients with AF treated with reduced dosages of NOACs hospitalized in ten Polish cardiology centers from January to December 2019. The criteria for appropriately reduced NOAC dosages was a dosage reduction of individual NOAC from the clinical studies, which was the basis for their registration.

Results. Among the 1003 patients who were treated with a reduced dosage of NOACs, inappropriately reduced dosages were observed in 242 patients (24.1%): in 120 patients (29.3%) treated with rivaroxaban, in 93 patients (33.8%) treated with apixaban and in 29 patients (9.1%) treated with dabigatran ($p < 0.0001$). Independent predictors of the use of inappropriately reduced dosages of NOACs were heart failure (odds ratio [OR] 1.55, confidence interval [CI]: 1.08–2.22) and hospitalization due to cardiac implantable electronic device (CIED) implantations/reimplantations (OR 2.01, CI: 1.27–3.17). Factors diminishing the chances of using inappropriately reduced dosages of NOACs were age (OR 0.98, CI: 0.97–0.998), vascular disease (OR 0.29, CI: 0.21–0.40) and creatinine clearance (CrCl) < 60 mL/min (OR 0.37, CI: 0.27–0.52).

Conclusions. In the group of patients treated with a reduced dosage of NOAC, 24.1% of patients had an inappropriately reduced dosage prescription, most frequently the patients receiving apixaban and rivaroxaban. The factor predisposing to prescribing an inappropriately reduced dosage of NOAC was heart failure and hospitalization due to CIED implantation/reimplantation. Label adherence to NOAC dosage is important to improve clinical outcomes in AF patients, and further investigation is needed to assess the best dosage of NOACs in the AF population.

Key words: atrial fibrillation, NOAC, reduced dosage, inappropriate prescription

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Introduction

Atrial fibrillation (AF) is the most common supraventricular arrhythmia. It is estimated that it can involve about 2–4% of the general population, and the prevalence of AF increases with age [1, 2]. Thromboembolic complications, stroke included, are one of the most dangerous implications of AF, and the risk of their occurrence in patients not using anticoagulant treatment is about 5% yearly [3]. Multicenter randomized clinical studies showed the efficacy and safety of non-vitamin K antagonist oral anticoagulants (NOACs) in the prevention of thromboembolic complications in patients with AF. Dabigatran (thrombin inhibitor), apixaban, and rivaroxaban (Xa factor inhibitors), which belong to this group, are characterized by predictable pharmacokinetics enabling their application without monitoring parameters of coagulation and by a lower number of interactions with pharmaceuticals different from vitamin K antagonists. These medications differ from each other in terms of dosage and indications to reduce dosages. Based on the conducted clinical studies, recommendations for choosing the appropriate NOACs dosage in patients with AF were defined. Administering NOACs in a full or reduced dosage is vital for providing patients with efficacious and safe treatment, and the choice of the dosage depends on features such as age, weight, renal impairment, or higher risk of bleeding [4–6]. However, there are some reports that indicate inappropriate administering of NOACs dosages — especially prescription of reduced dosages too frequently, which is against the guidelines. Several studies have shown a higher percentage of patients who received inappropriate reduced NOAC dosages — in Whitworth et al. [7], 33% of patients received a reduced dosage of NOAC against guidelines, and in Barra et al. [8], this percentage was even higher — 46%. An inappropriate dosage reduction of NOAC was associated with reduced effectiveness for stroke prevention without any safety benefits [9].

The study aimed to evaluate the administration frequency of NOAC dosages against the guidelines and analysis of factors predisposing to such a choice in patients with AF included in POL-AF (The Polish Atrial Fibrillation) Registry.

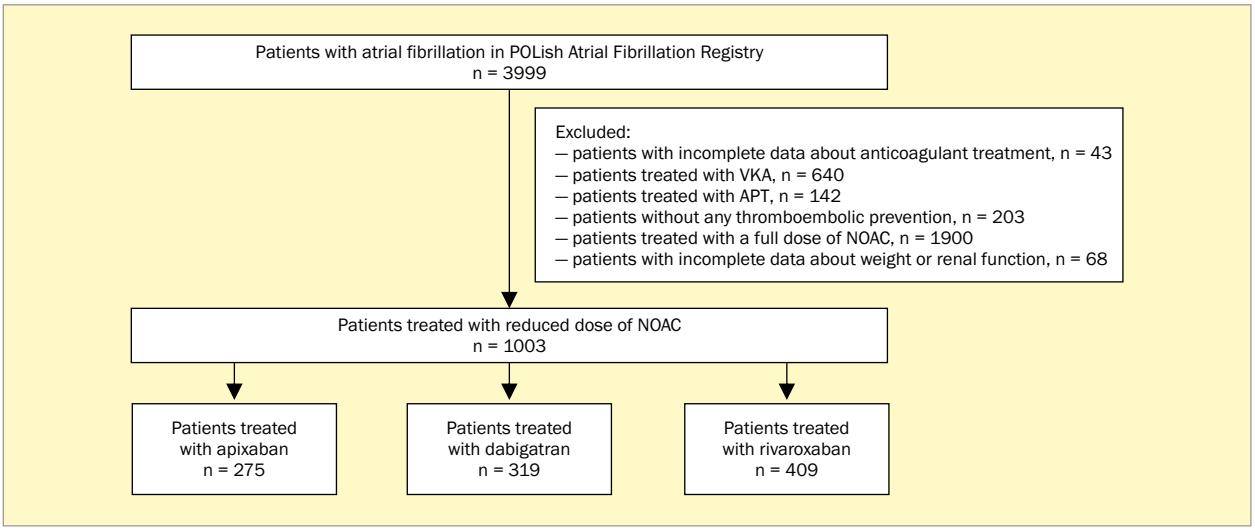

Figure 1. Flow chart of the study; APT — antiplatelet; NOAC — non-vitamin K antagonist oral anticoagulants; VKA — vitamin K antagonists

Material and methods

Study group

The Polish Atrial Fibrillation (POL-AF) Registry is a multicenter, prospective, observational study including patients with AF from ten cardiology centers — 7 academic ones, 2 regional hospitals, and one military hospital. The study was registered on clinicaltrials.gov (NCT04419012). The data was gathered from January to December 2019. The aim of the record was to obtain data concerning the clinical characteristics of patients with AF and to evaluate the undertaken steps — especially in terms of thromboembolic prophylaxis. Subsequent patients with AF, hospitalized in the centers for urgent and planned reasons — and who were over 18 years of age and suffered from arrhythmia documented with electrocardiographic examination or medical documents — were added to the record. No clear exclusion criteria were defined to gather a group well-representing Polish cardiological reality; however, patients admitted to the hospital to have ablation due to AF were not included in the record.

Based on the POL-AF record results, patients with AF treated with reduced dosages of NOACs were evaluated in the presented study. Patients receiving full NOACs doses, vitamin K antagonists, and antiplatelet therapy — i.e., those without anticoagulant treatment and with no data about weight or renal function — were excluded from the study (Figure 1).

Analyzed data

Atrial fibrillation was diagnosed based on medical records or electrocardiographic examination results upon admission to the hospital or during hospitalization. The researchers collected rudimentary data connected with demography, medical record, AF type, laboratory investigation results, and pharmacotherapy. The definitions of comorbidities are presented in *Table S1*. Creatinine clearance was achieved using the Cockroft-Gault equation. The thromboembolic risk was estimated based on the CHA_2DS_2-VASc score (congestive heart failure, hypertension, age ≥ 75 years, diabetes, stroke/transient ischemic attack, vascular disorder, age 65–74 years, sex) [10]. The risk of bleeding was defined based on the HAS-BLED score (arterial hypertension, kidney/liver failure, stroke, bleeding, labile international normalized ratio [INR], older age > 65 years, pharmaceuticals/alcohol) [11]. The study was sanctioned by the Bioethical Commission of the Swietokrzyskie Chamber of Physicians in Kielce (104/2018). The commission waived the requirement of obtaining patients' informed consent.

Appropriateness of NOAC dosage

An evaluation of the appropriateness of reduced NOAC dosage was determined based on guidelines from The European Society of Cardiology, which refer to the treatment of patients with AF, and a summary of product characteristics registered in the European Medicine Agency [1]. The criteria for the approved dosage reduction for each NOAC was as follows: dabigatran 220 mg/day for patients with creatinine clearance (CrCl) 30–50 mL/min; rivaroxaban 15 mg/day for patients with CrCl 15–49 mL/min; apixaban 5 mg/day for patients with more than two of the following: age ≥ 80 years, body weight ≤ 60 kg, or serum creatinine ≥ 1.5 mg/dL. For all NOACs, concomitant use of P-glycoprotein inhibitors was an indication of reduced dosages (*Table S2*). Inappropriate

Table S1. Definitions of comorbidities

Coronary artery disease	Previous history of angina pectoris, myocardial infarction, coronary artery bypass graft burgery, percutaneous transluminal coronary angioplasty
Peripheral arterial disease	Previous history of intermittent claudication, arterial thrombosis, percutaneous or surgical intervention in the thoracic, abdominal aorta, or lower extremity vessels
Heart failure	Characterized by typical symptoms (e.g. fatigue, breathlessness) which may be accompanied by signs (such as pulmonary crackles and peripheral oedema) caused by a structural and/or functional cardiac abnormality, resulting in a reduced cardiac output and/or elevated intracardiac pressures at rest or during stress
Hypertension	Mean arterial blood pressure values (calculated from at least two measurements made during at least two different visits to the doctor) are ≥ 140 mm Hg for systolic blood pressure and/or ≥ 90 mm Hg for diastolic blood pressure
Diabetes mellitus	The level of fasting glucose ≥ 126 mg/dL twice (each test performed on a different day) or the glucose concentration measured at any time of the day ≥ 200 mg/dL with symptoms of hyperglycaemia or at the 120th minute of the Oral Glucose Load Test, the glucose level ≥ 200 mg/dL

Table S2. Indications for NOAC dose reduction

	Reduced dose	Recommendations for dose reduction
Apixaban	2.5 mg BID	1. More than two of the following: • age ≥ 80 years • body weight ≥ 60 kg • serum creatinine ≥ 1.5 mg/dL 2. Creatinine clearance 15–29 mL/min
Dabigatran	110 mg BID	1. Creatinine clearance 30–50 mL/min 2. Concomitant use of P-glycoprotein inhibitors 3. High risk of bleeding 4. Age > 80 years or age 75–80 years
Rivaroxaban	15 mg QD	1. Creatinine clearance 15–49 mL/min

BID (*bis in die*) — twice a day; QD (*quaque die*) — once a day

reduction of the NOAC dosage was defined as fulfilling ≥ 1 criterion of dosage against the guidelines. It referred to patients with a prescribed reduced NOAC dosage, despite qualification for the full dosage ('underdosed'), and to patients with a prescribed NOAC dosage higher than the one advised or allowed ('overdosed'). According to the guidelines in force at the time the POL-AF Registry was started, NOAC dosages should be reduced when one or two antiplatelet drugs are used concomitantly; so, we considered that reducing NOAC dosages in patients taking antiplatelet drugs is the correct management.

Statistical analysis

The distribution of quantitative features (age, sex, AF type, medical record, results of laboratory investigation, pharmacotherapy) was verified with the Shapiro–Wilk test. To define the significance of the differences between the groups for particular quantitative features, the Kruskal–Wallis test was used. In the case of features for which the differences appeared to be significant, *post hoc* Dunn Bonferoni tests were also used. All the qualitative variables were coded in a zero-one system, where 0 means the lack of a particular feature and 1 means its presence. In individual NOAC groups, and later in appropriate/inappropriate dosage groups, stratum weights were calculated and the relationship between variables was estimated using a non-parametric χ^2 test. To determine the influence of chosen variables on medication dosage, a logistic regression analysis was used (the full model was presented). The effects were shown for the inappropriate dosage, whereas the appropriate dosage was the referential level. The value $p \leq 0.05$ was assumed to be

statistically significant. The data was analyzed using Statistica 13.3 software.

Results

Baseline characteristics

Among the 1003 patients treated with the reduced dose of NOACs, 409 were prescribed rivaroxaban (40.8%), 275 were prescribed apixaban (27.4%) and 319 were prescribed dabigatran (31.8%). The average age of the patients was 77.9 (± 9.4) years, patients over 74 years accounted for 68.7% of the researched population. Women accounted for 47.9% of the patients. The average result in the CHA_2DS_2-VASc score was 5.1 points, whereas, in the HAS-BLED score, it was 2.3 points. Renal impairment, defined as creatinine clearance < 60 ml/min, was diagnosed in 640 patients (63.8%). Previous bleeding, including bleeding from the digestive tract, appeared in 64 patients (6.4%) — most frequently in the group of patients treated with apixaban (28 patients, 10.2%), least frequently in patients using rivaroxaban (15 patients, 3.7%). In the studied population, the first-time episode of AF was observed in 61 patients (6.1%). Heart failure (HF) was the most frequent reason for hospital admission; it referred to 268 patients (26.7%) — most of them from the group treated with apixaban (101 patients, 36.7%). Planned reasons for hospitalization, such as electrical cardioversion and ablation of arrhythmia different from AF, were observed most often in the group treated with rivaroxaban — respectively, 67 patients (16.4%) and 21 patients (5.1%). The clinical characteristics of patients included in the study are presented in Table 1.

Assessment of the propriety of using a reduced dose of NOAC

An appropriate NOAC dosage reduction was observed in 761 patients (75.9%), and an inappropriate NOAC dosage reduction was observed in 242 patients (24.1%). An inappropriate reduced dosage was observed in 120 patients (29.3%) treated with rivaroxaban, in 93 patients (33.8%) treated with apixaban, and in 29 patients (9.1%) treated with dabigatran ($p < 0.0001$). The frequency of an appropriate and inappropriate NOAC dosage reduction in each NOAC group is shown in Table 2, while a comparison of patients treated with appropriate/inappropriate reduced NOAC dosages is shown in Table 3. Patients using inappropriately reduced NOAC dosages, in comparison to patients receiving appropriately reduced dosages, were younger (the average age was 76.9 years vs. 78.3 years, $p > 0.05$), and the proportion of women in this group was higher (51.2% vs. 46.8%, $p > 0.05$). The occurrence frequency of HF, vascular diseases, and renal impairment was lower in the group of patients treated with inappropriately reduced dosages than in the group with appropriately reduced dosages ($p < 0.05$ for all). Moreover, in this group, the number

Table 1. Clinical characteristics of patients treated with reduced dosages of NOACs

Clinical characteristic	All patients n = 1003	Patients treated with apixaban n = 275 (27.4)	Patients treated with dabigatran n = 319 (31.8)	Patients treated with rivaroxaban n = 409 (40.8)	p-value
Age, years (mean ± SD)	77.9 ± 9.4	79.6 ± 9.7	77.6 ± 9.0	77.1 ± 9.5	**< 0.003**
Age, years, n (%)					
< 65	89 (8.9)	19 (7.0)	33 (10.4)	37 (9.1)	0.336
65–74	225 (22.4)	51 (18.5)	70 (21.9)	104 (25.4)	0.103
> 74	689 (68.7)	205 (74.5)	216 (67.7)	268 (65.5)	**0.040**
Female, n (%)	480 (47.9)	136 (49.5)	147 (46.1)	197 (48.2)	0.704
Type of atrial fibrillation, n (%)					
Paroxysmal	512 (51.0)	140 (50.9)	157 (49.2)	215 (52.6)	0.668
Persistent	171 (17.0)	39 (14.2)	59 (18.5)	73 (17.8)	0.324
Permanent	320 (32.0)	96 (34.9)	103 (32.3)	121 (29.6)	0.337
Medical history, n (%)					
Hypertension	874 (87.1)	234 (85.1)	287 (90.0)	353 (86.3)	0.169
HF	729 (72.7)	211 (76.7)	222 (69.6)	296 (72.4)	0.148
CAD	633 (63.1)	181 (65.8)	202 (63.3)	250 (61.1)	0.457
Previous MI	331 (33.0)	113 (41.1)	89 (27.9)	129 (31.5)	**0.002**
PAD	189 (18.8)	58 (21.1)	58 (18.2)	73 (17.8)	0.531

→

Table 1. (cont.) Clinical characteristics of patients treated with reduced dosages of NOACs

Clinical characteristic	All patients n = 1003	Patients treated with apixaban n = 275 (27.4)	Patients treated with dabigatran n = 319 (31.8)	Patients treated with rivaroxaban n = 409 (40.8)	p-value
Vascular disease (CAD and/or PAD)	686 (68.4)	191 (69.5)	224 (70.2)	271 (66.3)	0.473
Diabetes mellitus	405 (40.4)	119 (43.3)	119 (37.3)	167 (40.8)	0.326
Previous stroke/TIA/peripheral embolism	201 (20.0)	46 (16.7)	67 (21.0)	88 (21.5)	0.337
Any previous bleeding	64 (6.4)	28 (10.2)	21 (6.6)	15 (3.7)	**0.003**
Previous gastric bleeding	46 (4.6)	22 (8.0)	13 (4.1)	11 (2.7)	**0.004**
Previous CNS bleeding	9 (0.9)	3 (1.1)	3 (0.9)	3 (0.7)	0.884
Thromboembolic risk					
CHA_2DS_2-VASc score (mean ± SD)	5.1 ± 1.5	5.2 ± 1.4	5.1 ± 1.5	5.1 ± 1.5	0.215
CHA_2DS_2-VASc score, n (%)					
= 0	3 (0.3)	1 (0.4)	0 (0.0)	2 (0.5)	0.475
= 1	3 (0.3)	0 (0.0)	3 (0.9)	0 (0.0)	**0.040**
> 1	997 (99.4)	274 (99.6)	316 (99.1)	407 (99.5)	0.617
Bleeding risk					
HAS-BLED score (mean ± SD)	2.3 ± 0.8	2.4 ± 0.9	2.2 ± 0.8	2.2 ± 0.8	**0.014**
HAS-BLED score > 2, n (%)	353 (35.2)	118 (42.9)	95 (29.8)	140 (34.2)	**0.003**
Laboratory tests					
Hemoglobin, g/dL (mean ± SD)	12.7 ± 1.8	12.2 ± 2.0	12.9 ± 1.7	12.9 ± 1.7	**< 0.001**
WBC, K/μL (mean ± SD)	8.2 ± 3.3	8.1 ± 3.2	8.2 ± 4.0	8.3 ± 2.8	0.096
Platelet count, K/μL (mean ± SD)	217.5 ± 75.3	208.6 ± 74.3	216.5 ± 70.7	224.3 ± 78.8	**0.044**
CrCl < 60 mL/min, n (%)	640 (63.8)	195 (70.9)	177 (55.5)	268 (65.5)	**< 0.0001**
Reason for hospitalization, n (%)					
Electrical cardioversion	125 (12.5)	7 (2.5)	51 (16.0)	67 (16.4)	**< 0.0001**
Planned coronarography/PCI	123 (12.3)	40 (14.5)	38 (11.9)	45 (11.0)	0.373
Planned CIED implantation/reimplantation	120 (12.0)	37 (13.5)	31 (9.7)	52 (12.7)	0.312
Acute coronary syndrome	112 (11.2)	37 (13.5)	32 (10.0)	43 (10.5)	0.360
HF	268 (26.7)	101 (36.7)	69 (21.6)	98 (24.0)	**< 0.0001**
Ablation other than AF	46 (4.6)	8 (2.9)	17 (5.3)	21 (5.1)	0.294
AF without any procedures	40 (4.0)	9 (3.3)	16 (5.0)	15 (3.7)	0.507
Other reasons for hospitalization	169 (16.8)	36 (13.1)	65 (20.4)	68 (16.6)	0.060
Concomitant treatment, n (%)					
Antiplatelets	259 (25.8)	75 (27.3)	70 (21.9)	114 (27.9)	0.157
Verapamil	4 (0.4)	1 (0.4)	2 (0.6)	1 (0.2)	0.715
Treatment before hospitalization, n (%)					
The same NOAC	773 (77.1)	144 (52.4)	272 (85.3)	357 (87.3)	**< 0.0001**
Other NOAC	43 (4.3)	37 (13.5)	5 (1.6)	1 (0.2)	**< 0.0001**
VKA	36 (3.6)	19 (6.9)	10 (3.1)	7 (1.7)	**< 0.0001**
APT	52 (5.2)	27 (9.8)	10 (3.1)	15 (3.7)	**< 0.0001**
None	99 (9.9)	48 (17.5)	22 (6.9)	29 (7.1)	**< 0.0001**

AF — atrial fibrillation; APT — antiplatelet; CAD — coronary artery disease; CHA_2DS_2-VASc — congestive heart failure, hypertension, age ≥ 75 years, diabetes, stroke/transient ischemic attack, vascular disorder, age 65–74 years, sex; CIED — cardiac implantable electronic device; CNS — central nervous system; CrCl — creatinine clearance; HAS-BLED — arterial hypertension, kidney/liver failure, stroke, bleeding, labile INR, age > 65 years, pharmaceuticals/alcohol; HF — heart failure; MI — myocardial infarction; NOAC — non vitamin K antagonist oral anticoagulants; PAD — peripheral artery disease; PCI — percutaneous coronary intervention; SD — standard deviation; TIA — transient ischaemic attack; WBC — white blood cells; VKA — vitamin K antagonist

of patients concurrently using antiplatelet treatment was lower compared to the group administered appropriately reduced dosages (0.4% vs. 33.9%, p < 0.05).

The average number of points in the CHA_2DS_2-VASc score was lower in the group with inappropriately reduced doses (4.8 vs. 5.2, p < 0.05) (Table 3). Figure 2 shows the proportion of patients treated with appropriately/inappropriately reduced dosages according to the CHA_2DS_2VASc score. Electrical cardioversion and CIED implantation/reimplantation were more frequent reasons for hospitalization among patients treated with inappropriately reduced NOAC doses (p < 0.05 for both).

Predictors of the use of inappropriately reduced dosages of NOACs

The univariate logistic regression analysis found numerous predictors of inappropriately reduced dosages of NOACs prescription (*Table S3*).

In the multivariable model, factors associated with the selection of the inappropriately reduced dosages of NOACs included the following: age, HF, vascular disease, CrCl < 60 mL/min, and hospitalization due to CIED implantations/reimplantations.

Table 4 demonstrates the predictors of the use of inappropriately reduced doses of NOACs. Independent predictors of using inappropriately reduced doses of NOACs were HF (OR 1.55, CI: 1.08–2.22) and hospitalization due to CIED implantations/reimplantations (OR 2.01, CI: 1.27–3.17). Factors diminishing chances to administer inappropriately reduced doses of NOACs were age (OR 0.98, CI: 0.97–0.998), vascular disease (OR 0.29, CI: 0.21–0.40), and CrCl < 60 mL/min (OR 0.37, CI: 0.27–0.52).

Discussion

The use of NOAC in clinical practice is becoming increasingly common; therefore, numerous international registers are being kept to assess the factors influencing the choice of anticoagulant therapy in the prevention of thromboembolic complications in patients with AF [12–14]. Despite the definite indications to reduce NOACs doses in randomized clinical studies — ARISTOTLE (Apixaban for Reduction in Stroke and Other Thromboembolic Events in Atrial Fibrillation) [4], RE-LY (Randomized Evaluation of Long-Term Anticoagulation Therapy) [5] and ROCKET-AF (Rivaroxaban once-daily, direct oral factor Xa inhibition compared with vitamin K antagonism for prevention of stroke and Embolism Trial in Atrial Fibrillation) [6] — the selection of an appropriate NOAC dosage in clinical practice still remains a huge challenge for doctors. Several studies have reported clinical outcomes according to label adherence to NOAC dosage. Using a reduced NOAC dose without any dosage-reduction criteria could lead to a below-par reduction of stroke risk [15]. Steinberg et al. [16] showed that NOAC overdosing was

Table 2. Assessment of the frequency of use of appropriately/inappropriately reduced dosages in patients treated with particular NOACs

	All patients n = 1003	Patients treated with apixaban n = 275 (27.4)	Patients treated with dabigatran n = 319 (31.8)	Patients treated with rivaroxaban n = 409 (40.8)	p-value
Appropriately reduced doses	761 (75.9)	182 (66.2)	290 (90.9)	289 (70.7)	**< 0.0001**
Inappropriately reduced doses	242 (24.1)	93 (33.8)	29 (9.1)	120 (29.3)	**< 0.0001**
• overdosed	12 (1.2)	1 (0.4)	9 (2.8)	2 (0.5)	**0.005**
• underdosed	230 (22.9)	92 (33.5)	20 (6.3)	118 (28.9)	**≤ 0.001**

Table 3. A comparison of patients treated with appropriately/inappropriately reduced dosages of NOACs

Clinical characteristics	Appropriately reduced dosages n = 761	Inappropriately reduced dosages n = 242	p-value
Age, years (mean ± SD)	78.3 ± 9.1	76.9 ± 10.3	0.157
Age, years, n (%)			
< 65	66 (8.7)	23 (9.5)	0.692
65–74	162 (21.3)	63 (26.0)	0.123
> 74	533 (70.0)	156 (64.5)	0.103
Female, n (%)	356 (46.8)	124 (51.2)	0.226

→

Table 3. (cont.) A comparison of patients treated with appropriately/inappropriately reduced dosages of NOACs

Clinical characteristics	Appropriately reduced dosages n = 761	Inappropriately reduced dosages n = 242	p-value
Type of atrial fibrillation, n (%)			
Paroxysmal	383 (50.3)	129 (53.3)	0.420
Persistent	129 (17.0)	42 (17.4)	0.884
Permanent	249 (32.7)	71 (29.3)	0.326
Medical history, n (%)			
Hypertension	668 (87.8)	206 (85.1)	0.282
HF	565 (74.2)	164 (67.8)	**0.049**
Coronary artery disease	532 (69.9)	101 (41.7)	**< 0.0001**
Previous MI	276 (36.3)	55 (22.7)	**< 0.0001**
PAD	152 (20.0)	37 (15.3)	0.105
Vascular disease (CAD and/or PAD)	570 (74.9)	116 (47.9)	**< 0.0001**
Diabetes mellitus	311 (40.9)	94 (38.8)	0.576
Previous stroke/TIA/peripheral embolism	146 (19.2)	44 (18.2)	0.729
Any previous bleeding	46 (6.0)	18 (7.4)	0.440
Previous gastric bleeding	33 (4.3)	13 (5.4)	0.502
Previous CNS bleeding	6 (0.8)	3 (1.2)	0.517
Thromboembolic risk			
CHA_2DS_2-VASc score (mean ± SD)	5.2 ± 1.5	4.8 ± 1.6	**< 0.0001**
CHA_2DS_2-VASc score, n (%)			
= 0	1 (0.1)	2 (0.8)	0.085
= 1	1 (0.1)	2 (0.8)	0.085
> 1	759 (99.8)	238 (98.2)	**0.015**
Bleeding risk			
HAS-BLED score (mean ± SD)	2.3 ± 0.8	2.3 ± 0.9	0.839
HAS-BLED score > 2, n (%)	269 (35.3)	84 (34.7)	0.856
Laboratory tests			
Hemoglobin, g/dL (mean ± SD)	12.7 ± 1.8	12.7 ± 1.9	0.349
Platelet count, K/μL (mean ± SD)	218.7 ± 77.6	213.7 ± 67.3	0.839
CrCl ml/min (mean ± SD)	50.6 ± 18.5	59.2 ± 18.3	**< 0.0001**
CrCl < 60 ml/min, n (%)	522 (68.6)	118 (48.8)	**< 0.0001**
Concomitant treatment, n (%)			
Antiplatelets	258 (33.9)	1 (0.4)	**< 0.0001**
Reason for hospitalization, n (%)			
Electrical cardioversion	81 (10.6)	44 (18.2)	**0.002**
Planned coronarography/PCI	110 (14.5)	13 (5.4)	**< 0.0001**
Planned CIED implantation/reimplantation	79 (10.4)	41 (16.9)	**0.006**
Acute coronary syndrome	110 (14.5)	2 (0.8)	**< 0.0001**
Heart failure	194 (25.5)	74 (30.6)	0.119
Ablation other than AF	31 (4.1)	15 (6.2)	0.169
AF without any procedures	28 (3.7)	12 (5.0)	0.376
Other reasons for hospitalization	128 (16.8)	41 (16.9)	0.965

AF — atrial fibrillation; CAD — coronary artery disease; CHA_2DS_2-VASc — congestive heart failure, hypertension, age ≥ 75 years, diabetes, stroke/transient ischemic attack, vascular disorder, age 65–74 years, sex; CIED — cardiac implantable electronic device; CNS — central nervous system; CrCl — creatinine clearance; HAS-BLED — arterial hypertension, kidney/liver failure, stroke, bleeding, labile INR, age > 65 years, pharmaceuticals/alcohol; HF — heart failure; MI — myocardial infarction; PAD — peripheral artery disease; PCI — percutaneous coronary intervention; SD — standard deviation; TIA — transient ischaemic attack

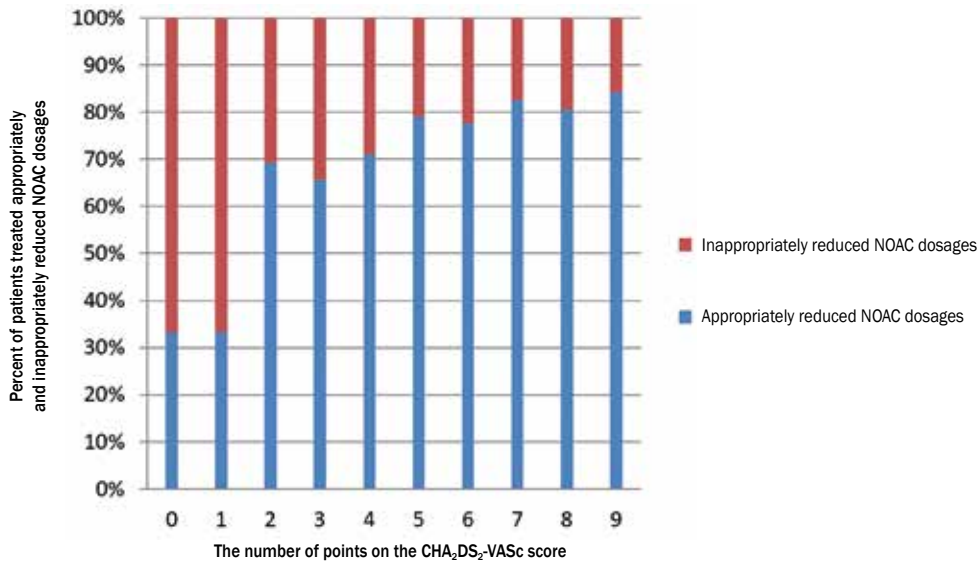

Figure 2. Prescription pattern of appropriately and inappropriately reduced non-vitamin K antagonist oral anticoagulants (NOAC) dosages based on the CHA_2DS_2-VASc score

associated with increased all-cause mortality compared to recommended doses, and underdosing was associated with increased cardiovascular hospitalization.

The presented study showed that in 24.1% of patients, inappropriately reduced NOACs dosages were used. Yu et al. [17] showed that 31% of NOAC-treated patients were undertreated. In the population of elderly patients, it was shown that 51% of them received a reduced dosage despite the lack of formal criteria for dosage reduction [18]. The proportion of patients treated with an inappropriately reduced NOAC dose in our study is higher compared to studies of other authors — reduction of a NOAC dose against the guidelines was observed in 14.4% of patients in the study of Ono et al. [19]; in 16.1% in the study of Gustafson et al. [20], whereas in the ORBIT AF II study, an inappropriate dosage reduction was observed in only 9.4% of patients [16]. The presented study is multicenter; it included hospitalized patients, administering a reduced NOAC dose despite the lack of indications defined in the guidelines could result from the presence of different from those commonly acknowledged factors substantively increasing the risk of bleeding (e.g., frailty syndrome, psycho-organic syndrome).

In the discussed study, the highest proportion of inappropriate dosage reduction referred to patients receiving rivaroxaban (29.3%) and apixaban (33.8%), which is reflected in the results of some other authors' studies. In the study of Ono et al. [19], inappropriately reduced dosages were observed in 12.8% of patients administered rivaroxaban and in 19.6% of patients treated with apixaban, whereas in the study of Gustafson et al. [20], the proportion was even higher — 47.5% and 42.5% for rivaroxaban and apixaban, respectively. One of the probable reasons for using an inappropriate dose reduction of rivaroxaban or apixaban can be an underestimation of renal function caused by different models of CrCl calculation — most laboratories present the CrCl value calculated based on MDRD (Modification of Diet in Renal Disease) formula, whereas customizing NOACs dosages in clinical studies was based on CrCl result achieved from the Cockroft–Gault equation [21, 22].

In the presented study, CrCl < 60 mL/min was shown to be a significant factor in diminishing the risk of using an inappropriate NOAC dose. It has been proven that using NOAC was associated with a reduced risk of thromboembolic and hemorrhagic complications compared to warfarin in patients with mild and moderate renal impairment [23–25]. Recent studies have also confirmed the effectiveness of reduced doses of NOAC in patients with concomitant chronic kidney disease, showing a promising benefit-risk balance in populations at high risk for cardiovascular complications [26].

In the POL-AF registry, the chance of using the inappropriately reduced NOAC dosage decreases by one percent every year. Older age was an independent factor in diminishing the risk of prescribing inappropriately reduced doses of NOACs in our study. Such conclusions were also drawn in the study of Jacobs et al. [27]; however, for the age group of ≥ 80 years — age was also a predictor of administering the appropriate reduction of doses for all researched NOACs. Interestingly enough, in the presented study, renal impairment and vascular disorder also appeared to be factors that diminished the risk of inappropriate dosage reduction. The study of Ono et al. [19] demonstrates that both older age (> 65 years), as well as renal impairment (CrCl < 60 mL/min), was independently connected with

Table S3. Factors determining the choice of inappropriately reduced dosages of NOACs: the results of univariate logistic regression analysis

Parameter	Univariate logistic regression analysis	
	OR (95% CI)	p-value
Age, years	0.99 (0.97–1.001)	0.059
< 65	1.11 (0.67–1.82)	0.692
65–74	1.30 (0.93–1.82)	0.123
> 74	0.78 (0.57–1.05)	0.103
Female	1.19 (0.89–1.60)	0.226
Paroxysmal AF	1.13 (0.84–1.51)	0.420
Persistent AF	1.03 (0.70–1.51)	0.884
Permanent AF	0.85 (0.62–1.17)	0.326
Hypertension	0.80 (0.53–1.21)	0.282
HF	**0.73 (0.53–0.99)**	**0.049**
Coronary artery disease	**0.31 (0.23–0.42)**	**< 0.0001**
Previous MI	**0.52 (0.37–0.72)**	**< 0.0001**
PAD	0.72 (0.49–1.07)	0.105
Vascular disease (CAD and/or PAD)	**0.31 (0.23–0.42)**	**< 0.0001**
Diabetes mellitus	0.92 (0.68–1.24)	0.576
Previous stroke/TIA/peripheral embolism	0.94 (0.64–1.36)	0.729
Any previous bleeding	1.25 (0.71–2.20)	0.440
Previous gastric bleeding	1.25 (0.65–2.42)	0.502
Previous CNS bleeding	1.58 (0.39–6.36)	0.517
CHA_2DS_2-VASc score	**0.83 (0.75–0.91)**	**< 0.0001**
= 0	6.33 (0.57–70.15)	0.085
= 1	6.33 (0.57–70.15)	0.085
> 1	**0.16 (0.03–0.86)**	**0.015**
HAS-BLED score	1.0 (0.84–1.19)	0.980
HAS-BLED score > 2	0.97 (0.72–1.32)	0.856
Hemoglobin (g/dL)	1.02 (0.94–1.11)	0.609
Platelet count (K/μL)	0.999 (0.997–1.001)	0.369
CrCl (mL/min)	**1.02 (1.016–1.033)**	**< 0.0001**
CrCl < 60 ml/min	**0.97 (0.72–1.32)**	**< 0.0001**
Antiplatelets	**0.008 (0.001–0.06)**	**< 0.0001**
Reason for hospitalization		
Electrical cardioversion	**1.87 (1.25–2.78)**	**0.002**
Planned coronarography/PCI	**0.34 (0.19–0.61)**	**< 0.0001**
Planned CIED implantation/reimplantation	**1.76 (1.17–2.65)**	**0.006**
Acute coronary syndrome	**0.05 (0.01–0.20)**	**< 0.0001**
HF	1.29 (0.94–1.77)	0.119
Ablation other than AF	1.56 (0.82–2.93)	0.169
AF without any procedures	1.37 (0.68–2.73)	0.376
Other reasons for hospitalization	1.01 (0.69–1.48)	0.965

AF — atrial fibrillation; CAD — coronary artery disease; CHA_2DS_2-VASc — congestive heart failure, hypertension, age ≥ 75 years, diabetes, stroke/transient ischemic attack, vascular disorder, age 65–74 years, sex; CIED — cardiac implantable electronic device; CNS — central nervous system; CrCl — creatinine clearance; HAS-BLED — arterial hypertension, kidney/liver failure, stroke, bleeding, labile INR, age > 65 years, pharmaceuticals/alcohol; HF — heart failure; MI — myocardial infarction; PAD — peripheral artery disease; PCI — percutaneous coronary intervention; TIA — transient ischaemic attack

Table 4. Factors determining the choice of inappropriately reduced dosages of non-vitamin K antagonist oral anticoagulants: the results of multivariable logistic regression analysis

Parameter	Multivariable logistic regression analysis	
	OR (95% CI)	p-value
Age	0.98 (0.97–0.998)	0.031
CrCl < 60 mL/min	0.37 (0.27–0.52)	< 0.0001
Vascular disease	0.29 (0.21–0.40)	< 0.0001
Heart failure	1.55 (1.08–2.22)	0.017
Planned CIED implantation/reimplantation	2.01 (1.27–3.17)	0.003

CI — confidence interval; CIED — cardiac implantable electronic device; CrCl — creatinine clearance; OR — odds ratio

the risk of using inappropriately reduced doses — while vascular disease was a predisposing factor for prescribing an appropriately reduced dose of NOAC. The reason for the appropriate NOAC dosage reduction in patients with vascular disorders in our study could be the simultaneous use of antiplatelet drugs. In the methodology, we assumed that reducing NOAC doses in patients taking antiplatelet drugs is the correct management — according to the guidelines in force at the time the POL-AF Registry was started, which recommend considering a NOAC dose reduction when one or two antiplatelet drugs are used concomitantly. However, guidelines from the second half of 2019 allow using full doses of NOACs with simultaneous antiplatelet therapy.

There are many potential reasons why clinicians might prescribe inappropriate NOAC doses. In the discussed study, two factors predispose to prescribing inappropriately reduced dosages of NOACs. The first of them is hospitalization due to CIED implantation/reimplantation. The probable reason for such a study result could be doctors' fear of a hematoma when administering full doses of NOACs directly after the surgery. Because the influence of hospitalization reasons on the potential of using improper decreased doses was not examined in the papers that are readily available, it is not possible to compare the acquired result with other authors' investigations.

Another factor predisposing to an inappropriate prescription of reduced dosages of NOACs in our study is HF, as in the study by Ono et al. [19]. The reason for the inappropriate reduction of NOAC dosage in patients with HF could be the fear of worsening renal function in patients concomitantly taking diuretics in the absence of proper fluid balance control. However, it should be remembered that HF is one of the factors in the CHA_2DS_2-VASc score, which measures the risk of thromboembolic complications in patients with AF and, therefore, the selection of the appropriate NOAC dosage is important to ensure effective treatment of patients.

What is important in the presented study is the risk of bleeding estimated based on the HAS-BLED score was not a significant predictive factor of using inappropriately reduced NOAC doses, just as in the studies of Ono et al. [19] and Jacobs et al. [27]. In the SAFE-NOACS study, past hemorrhagic complication was also not a factor predisposing to an inappropriate NOAC dose correction [28]. The risk of bleeding during anticoagulant treatment is higher in some of the patients; however, it should not be the reason for an inappropriate reduction of NOAC dosages because it can increase the risk of thromboembolic complications in patients.

Conclusions

In the group of hospitalized patients with AF treated with a reduced dosage of NOAC, 24.1% of them inappropriately reduced the dosage of NOAC prescription, most frequently in patients treated with apixaban and rivaroxaban. The factors predisposing to the prescription of an inappropriate reduced dosage of NOAC were HF and hospitalization due to CIED implantation/reimplantation. Age, vascular disorder and renal impairment were independent predictors lowering the risk of prescribing an inappropriate reduced dosage of NOAC.

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Conflict of interest

IGG — speaker for Bayer and Boehringer-Ingelheim; AKC — speaker for Bayer; JBednarski, AM and BWK — speaker for Bayer, Boehringer-Ingelheim and Pfizer; ATK — speaker for Boehringer-Ingelheim; MWełnicki — speaker for Bayer and Pfizer; other authors have no conflict of interest to declare.

Data availability

The data used to support the findings of this study is available from the corresponding author upon request.

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Streszczenie

Wstęp. Przepisywanie doustnych przeciwkrzepliwych leków niebędących antagonistami witaminy K (NOAC) w dawce zredukowanej lub pełnej jest istotne dla zapewnienia pacjentom z migotaniem przedsionków (AF) skutecznego i bezpiecznego leczenia. Celem badania było ocenienie częstości stosowania zredukowanych dawek NOAC w stosunku do wytycznych oraz analiza czynników predysponujących do takiego wyboru u pacjentów z AF zarejestrowanych w Polskim Rejestrze Migotania Przedsionków (POL-AF).

Materiał i metody. Badanie obejmowało 1003 pacjentów z AF leczonych zredukowanymi dawkami NOAC, hospitalizowanych w 10 polskich ośrodkach kardiologicznych od stycznia do grudnia 2019 roku. Kryterium stosowania odpowiednio zredukowanych dawek NOAC była redukcja dawki indywidualnego leku NOAC na podstawie badań klinicznych, które były podstawą ich rejestracji.

Wyniki. Spośród 1003 pacjentów leczonych zredukowanymi dawkami NOAC, nieodpowiednio zredukowane dawki zaobserwowano u 242 pacjentów (24,1%): u 120 pacjentów (29,3%) leczonych rywaroksabanem, u 93 pacjentów (33,8%) leczonych apiksabanem oraz u 29 pacjentów (9,1%) leczonych dabigatranem ($p < 0,0001$). Niezależnymi czynnikami predykcyjnymi stosowania nieodpowiednio zredukowanych dawek NOAC były: niewydolność serca (iloraz szans [OR] 1,55; przedział ufności [CI]: 1,08–2,22) oraz hospitalizacja związana z wszczepieniem/reimplantacją kardioelektronicznych urządzeń wszczepialnych (CIED) (OR 2,01; CI: 1,27–3,17). Czynnikiem zmniejszającym szanse na stosowanie nieodpowiednio zredukowanych dawek NOAC były: wiek (OR 0,98; CI: 0,97–0,998), choroba naczyniowa (OR 0,29; CI: 0,21–0,40) i klirens kreatyniny (CrCl) < 60 ml/min (OR 0,37; CI: 0,27–0,52).

Wnioski. W grupie pacjentów leczonych zredukowaną dawką NOAC, 24,1% pacjentów miało nieodpowiednio przepisane dawki, najczęściej pacjenci otrzymujący apiksaban i rywaroksaban. Czynnikami predysponującymi do przepisywania nieodpowiednio zredukowanej dawki NOAC były niewydolność serca oraz hospitalizacja związana z wszczepieniem/reimplantacją CIED. Przestrzeganie zaleceń dotyczących dawek NOAC jest istotne dla poprawy wyników klinicznych u pacjentów z AF, konieczne jest również dalsze badanie w celu oceny optymalnej dawki NOAC w populacji z AF.

Słowa kluczowe: migotanie przedsionków, NOAC, zredukowanaj dawka, niewłaściwe przepisywanie

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CASE REPORT

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Heparin-induced thrombocytopenia in a 72 years old patient with myocardial infarction without ST-segment elevation

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Abstract

The study presents a case of a 72-year-old patient who developed heparin-induced thrombocytopenia during hospitalization for non-ST elevation myocardial infarction. The coexistence of both conditions poses a significant problem regarding treatment in such patients. The authors discuss the management used and current standards of care in the course of this disease.

Key words: heparin-induced thrombocytopenia, HIT, acute coronary syndrome, NSTEMI

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Introduction

Heparin-induced thrombocytopenia is a serious complication of pharmacotherapy with the use of heparins and is associated with a hypercoagulable state, less commonly with haemorrhagic complications, and results in limitations to current therapy [1, 2]. This paper discusses the case of a 72-year-old woman who was hospitalised for a non-ST elevation myocardial infarction (NSTEMI) and developed heparin-induced thrombocytopenia (HIT) during hospitalisation.

Case report

A 72-year-old woman was admitted to the cardiology clinic for symptoms of acute coronary syndrome without ST-segment elevation. On physical examination, there were signs of stasis in the pulmonary circulation. Otherwise, there were no other lesions observed on physical examination.

On the day of admission, electrocardiography revealed a regular sinus rhythm of 88/min, intermediate axis, ST-segment depressions in I, aVL, V_2–V_6, negative T waves in I, II, aVF, V_5, V_6, pathological Q waves in III, aVF (Figure 1). Echocardiography showed severe left ventricular systolic dysfunction with left ventricular ejection fraction: 10–15%, moderate/severe mitral regurgitation (proximal isovelocity surface area: 8 mm), moderate tricuspid regurgitation (tricuspid regurgitation velocity: 3.0 m/s, maximum gradient: 35 mm Hg), enlargement of both atria, left ventricular muscle with signs of hypertrophy. Lung ultrasonography revealed B-lines over the pulmonary fields. Laboratory tests found an increase in markers of myocardial damage (dynamic increase in troponin TnT from 1141 ng/L to 1984 ng/L). Coronary angiography showed stenosis of the left anterior descending artery — approximately 50% from the ostium, as well as closure of the proximal segment after the diagonal branch, critical stenosis of the diagonal branch, closure of the proximal part of the circumflex artery

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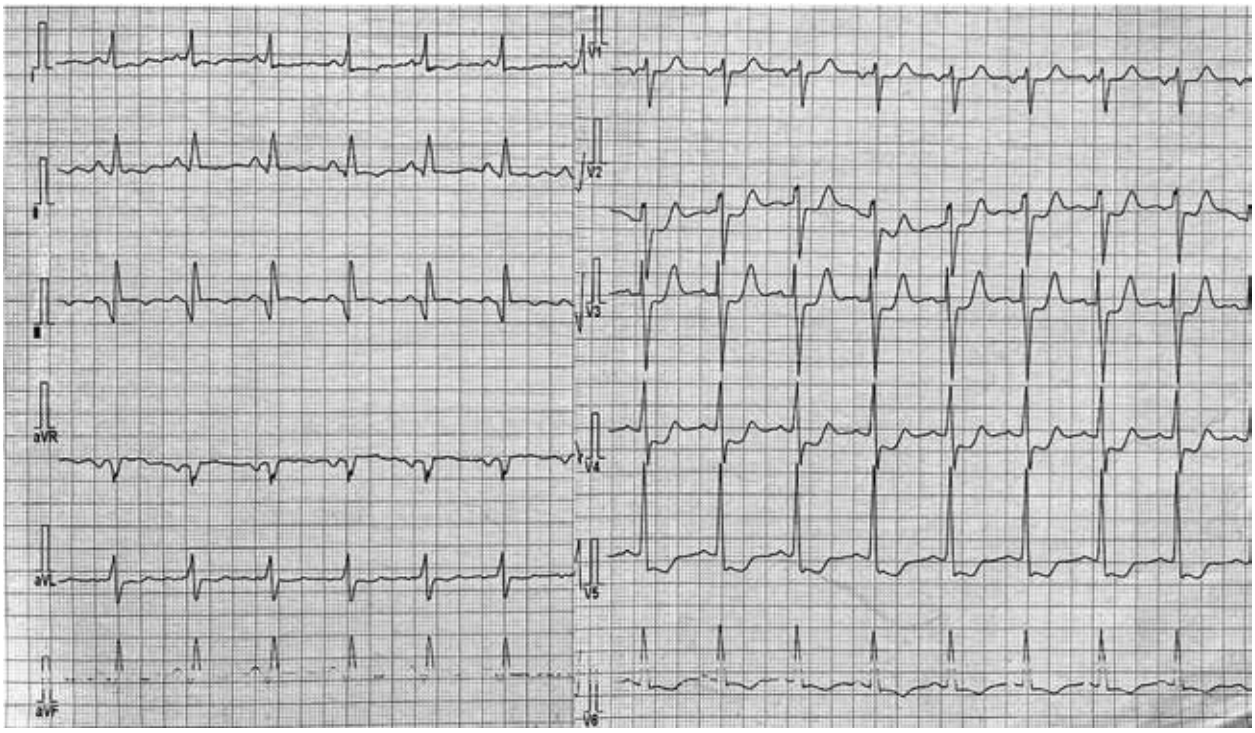

Figure 1. A 12-lead electrocardiographic recording performed on admission to hospital

(Cx) and closure of the proximal segment of the right coronary artery. A diagnosis of multivessel disease was made. The patient was consulted by a heart team and disqualified from coronary artery bypass grafting due to the very high risk of surgery (EuroScore: 11 points; EuroScore II: 7.66%), and she was qualified for palliative percutaneous coronary intervention (PCI) of the Cx.

The patient was started on pharmacotherapy including unfractionated heparin (day 1 and 2 of hospitalisation), acetylsalicylic acid, atorvastatin, furosemide, lisinopril, eplerenone, empagliflozin, and allopurinol. Clopidogrel was added to the treatment due to the high risk of bleeding (estimated using the CRUSADE Score for Post-MI Bleeding Risk). From hospital day 3, the patient received subcutaneous enoxaparin in a therapeutic dose (80 mg twice daily). On hospital day 10, low-molecular-weight heparins were discontinued and palliative PCI Cx with drug-eluting stent was performed (Figure 2). On hospital day

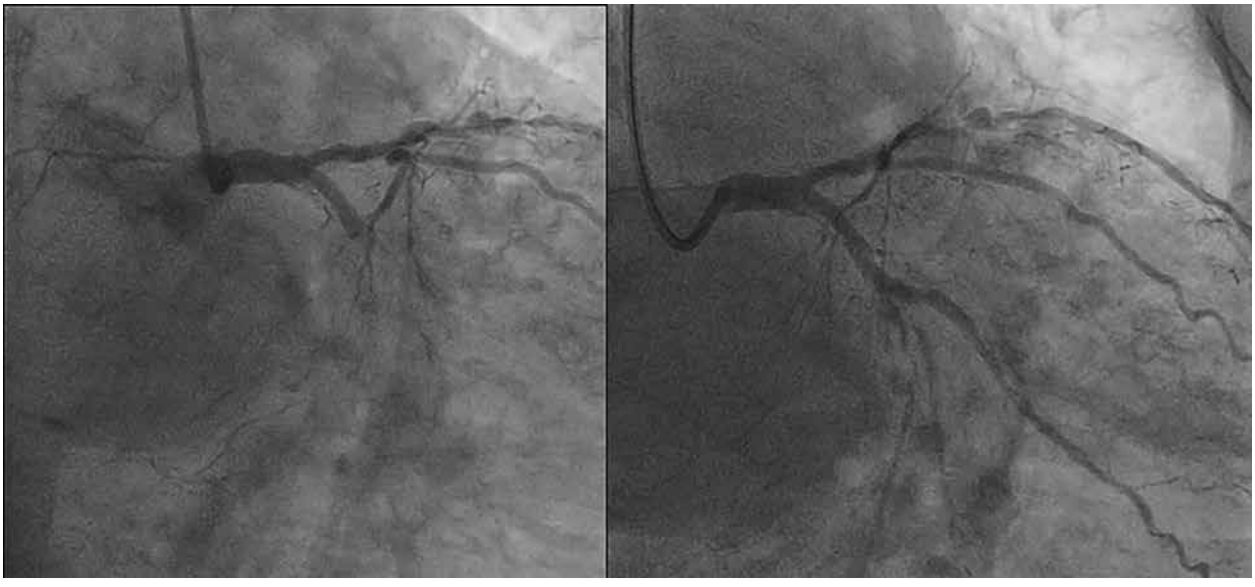

Figure 2. Angiography of the left coronary artery, right oblique view, before PCI Cx (left) and after PCI Cx (right); Cx — circumflex artery; PCI — percutaneous coronary intervention

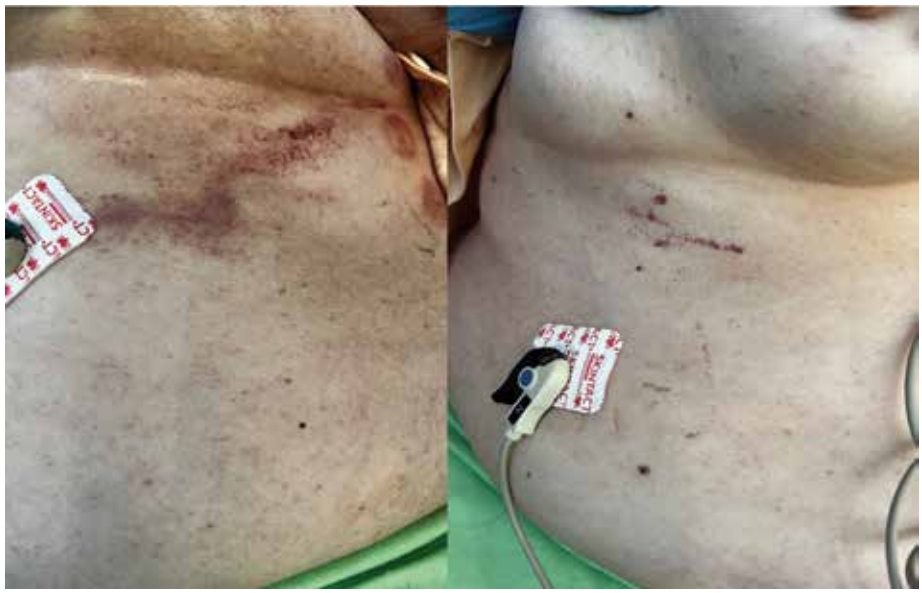

Figure 3. Haemorrhagic petechiae under both breasts

Table 1. Changes in platelet count (PLT) on subsequent hospital days compared to current patient management

Days of hospitalization	1	3	10	13	14	15	18	19	22
PLT [1000/μL]	203	226		6	3	8	36	105	177
Notes	UHF started	UHF discontinued, LMWH started	LMWH discontinued	ASA discontinued, GCS started, and PC transfused	Clopidogrel discontinued, PC transfused	PC transfused	Clopidogrel started	ASA started	

ASA — acetylsalicylic acid; GCS — glucocorticosteroids; LMWH — low molecular weight heparin; PC — platelet concentrate; UHF — unfractionated heparin

13, the patient had thrombocytopenia — platelet count (PLT) of 25 000/μL in two consecutive blood draws. The citrated platelet count was 6000/μL. Both interview and physical examination revealed no signs of bleeding or haemorrhagic diathesis in the patient. After haematology consultation, it was decided to discontinue acetylsalicylic acid, intravenous dexamethasone was started twice daily at 8 mg and 2 packs of platelet concentrate (PC) were transfused. Despite the discontinuation of heparin and the management implemented, there was a further decrease in PLT — 3000/μL, and in citrated platelet count: 4000/μL. The patient was consulted by a hematologist — treatment was modified as recommended: clopidogrel was temporarily discontinued, intravenous dexamethasone was continued twice daily, consecutively 8 and 4 mg, and 1 pack of PC was transfused daily on consecutive days.

On hospital day 15, the patient had a small number of haemorrhagic petechiae under both breasts (Figure 3). In the following days, there was a gradual increase in PLT count (Table 1). A total of 4 packs of PC were transfused to the patient. The doses of glucocorticosteroids administered were gradually reduced. When PLT increased above 30 000/μL, the patient was started on clopidogrel and then acetylsalicylic acid was restarted. The patient had no additional thrombotic or haemorrhagic episodes during her hospitalisation. On hospital day 22, the patient was discharged from the clinic in a stable condition with PLT of 177 000/μL. There were no alarming signs at the patient's one-month follow-up.

Discussion

Heparin-induced thrombocytopenia occurs in 0.1–5% of patients treated with heparins [3]. There are two types of this disease entity. Type 1 HIT has no immunological basis, the reduction in PLT is mild, usually occurs within the first 2–4 days of therapy, and there are usually no clinical sequelae. Type 2 HIT has an immunological basis and the decrease in PLT is greater (> 50%) [4]. The above diagnosis should be considered when the platelet count falls below 100 000/mL, usually 5–10 days after starting heparin treatment [5]. During the diagnostic evaluation of HIT, the determination of anti-heparin antibodies is recommended, however, this test is rarely used due to its low availability. Management of HIT includes discontinuation of heparins and implementation of alternative anticoagulant therapy. Argatroban, lepirudin, fondaparinux or non-vitamin K antagonist oral anticoagulant — preferably, rivaroxaban — are recommended [4]. In the case presented in this paper, the decrease in PLT started on hospital day 13, was rapid and worsened despite heparin withdrawal, indicating a likely immunological mechanism. Due to the very low PLT and the appearance of haemorrhagic petechiae, it was decided to transfuse PC and implement steroid therapy. An additional therapeutic challenge in the patient in question was the need for antiplatelet treatment associated with stent implantation. According to the recommendations, patients with a stent implanted in the setting of NSTEMI should receive dual antiplatelet therapy consisting of acetylsalicylic acid and P2Y12 inhibitor for up to 12 months [6]. The authors, taking into account the recommendations of the consulting haematologist, decided to discontinue antiplatelet drugs for a short period.

In the patient in question, alternative anticoagulant treatment was abandoned due to the appearance of signs of haemorrhagic diathesis in the form of petechiae. Currently, there are no detailed and clear rules for the management of the co-occurrence of acute coronary syndrome and heparin-induced thrombocytopenia. Therefore, individual decisions must be made on a case-by-case basis according to the evaluation of the clinical situation.

Conflict of interest

None declared.

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Małopłytkowość indukowana heparyną u 72-letniej chorej z zawałem serca bez uniesienia odcinka ST

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Streszczenie

W niniejszej pracy przedstawiono przypadek 72-letniej chorej, u której w trakcie hospitalizacji z powodu zawału serca bez uniesienia odcinka ST wystąpiła małopłytkowość indukowana heparyną. Współwystępowanie obu tych schorzeń stanowi istotny problem dotyczący terapii u takich chorych. Autorzy omawiają zastosowane postępowanie oraz obecne standardy postępowania w przebiegu tego schorzenia.

Słowa kluczowe: małopłytkowość indukowana heparyną, HIT, ostry zespół wieńcowy, NSTEMI

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Wstęp

Małopłytkowość indukowana heparyną jest poważnym powikłaniem farmakoterapii z wykorzystaniem heparyn, wiąże się ze stanem nadkrzepliwości, rzadziej z powikłaniami krwotocznymi oraz przekłada się na ograniczenia w dotychczas prowadzonej terapii [1, 2]. W niniejszym tekście przedstawiono opis przypadku 72-letniej pacjentki hospitalizowanej z powodu zawału serca bez uniesienia odcinka ST (NSTEMI, *non-ST elevation myocardial infarction*), u której w trakcie hospitalizacji wystąpiła małopłytkowość indukowana heparyną (HIT, *heparin induced thrombocytopenia*).

Opis przypadku

Do kliniki kardiologii z powodu objawów ostrego zespołu wieńcowego bez uniesienia odcinka ST została przyjęta 72-letnia chora. W badaniu przedmiotowym stwierdzono cechy zastoju w krążeniu płucnym. Poza tym nie zaobserwowano innych zmian w badaniu fizykalnym. W zapisie elektrokardiograficznym w dniu przyjęcia stwierdzono rytm zatokowy miarowy o częstotliwości 88/min, oś pośrednią, obniżenia odcinka ST w I, aVL, V_2–V_6, ujemne załamki T w I, II, aVF, V_5, V_6, patologiczne załamki Q w III, aVF (ryc. 1). W badaniu echokardiograficznym zobrazowano ciężką dysfunkcję skurczową lewej komory z frakcją wyrzutową lewej komory 10–15%, niedomykalność mitralną umiarkowaną/ciężką (8 mm), niedomykalność trójdzielną umiarkowaną (3,0 m/s, gradient maksymalny: 35 mm Hg), powiększenie obu przedsionków, mięsień lewej komory z cechami przerostu. W ultrasonografii płuc stwierdzono linie B nad polami płucnymi. W badaniach laboratoryjnych obserwowano wzrost stężenia markerów uszkodzenia mięśnia sercowego (dynamiczny wzrost troponiny T z 1141 ng/l do 1984 ng/l). W wykonanej

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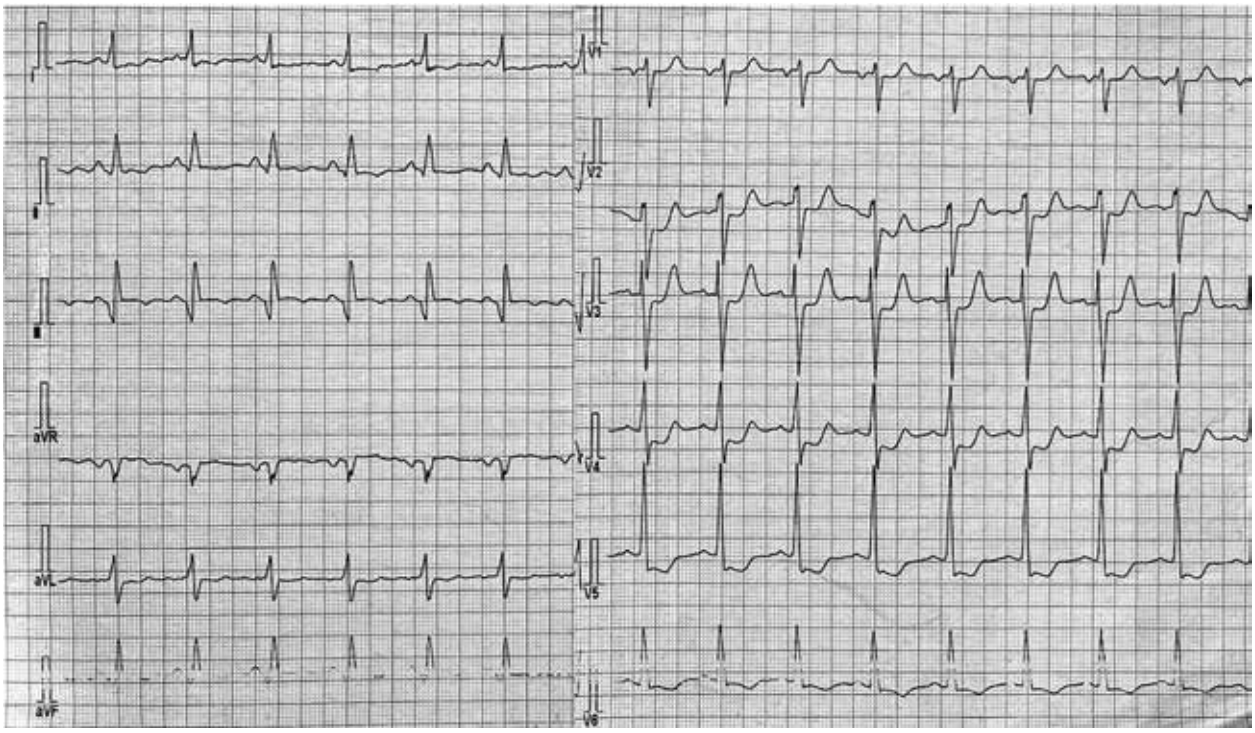
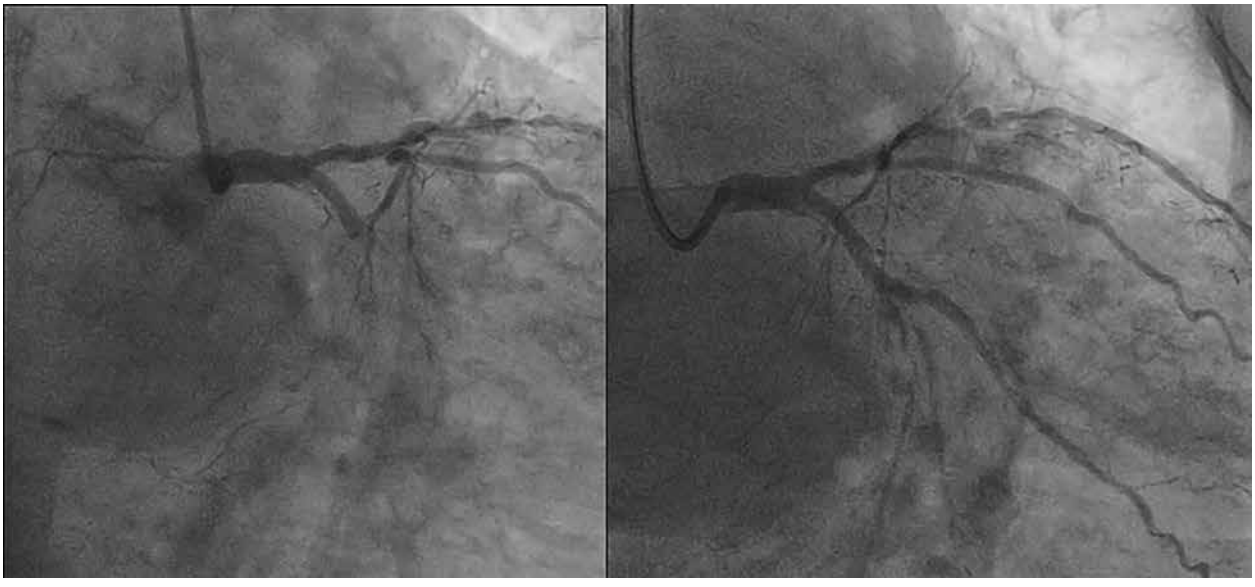


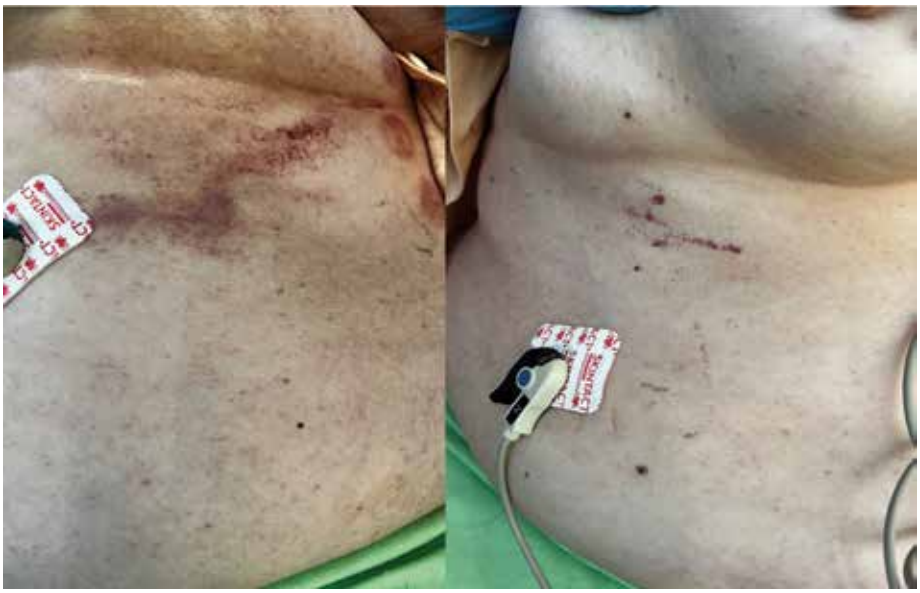
Rycina 1. Zapis elektrokardiograficzny 12-odprowadzeniowy wykonany przy przyjęciu pacjentki do szpitala

koronarografii stwierdzono w obrębie gałęzi zstępującej przedniej zwężenie około 50% od *ostium* oraz zamknięcie proksymalnego odcinka po oddaniu gałęzi diagonalnej, krytyczne zwężenie gałęzi diagonalnej, zamknięcie w części proksymalnej gałęzi okalającej (Cx, *circumflex artery*) oraz zamknięcie w proksymalnym odcinku prawej tętnicy wieńcowej. Rozpoznano chorobę wieńcową wielonaczyniową. Pacjentkę konsultowano przez kardiogrupę (*Heart Team*) i zdyskwalifikowano z pomostowania aortalno-wieńcowego ze względu na bardzo wysokie ryzyko operacji (EuroScore: 11 punktów EuroScore II: 7,66%), została jednak zakwalifikowana do paliatywnej angioplastyki wieńcowej gałęzi okalającej (PCI, *percutaneous coronary intervention*).

Chorej włączono farmakoterapię obejmującą heparynę niefrakcjonowaną (1. i 2. doba hospitalizacji), kwas acetylosalicylowy, atorwastatynę, furosemid, lisinopril,



Rycina 2. Angiografia lewej tętnicy wieńcowej, projekcja skośna prawa, przed (po lewej stronie) oraz po przezskórnej interwencji wieńcowej proksymalnej gałęzi okalającej (po prawej)



Rycina 3. Wybroczyny krwionośne pod obiema piersiami

Tabela 1. Zmiany stężenia płytek krwi w kolejnych dobach hospitalizacji w odniesieniu do aktualnego postępowania z chorą

Doba hospitalizacji	1	3	10	13	14	15	18	19	22
PLT (tys./µl)	203	226		6	3	8	36	105	177
Uwagi	Włączono UHF	Odstawiono UHF, włączono LMWH	Odstawiono LMWH	Odstawiono ASA, włączono GKS, przetoczono KKP	Odstawiono klopidogrel, przetoczono KKP	Przetoczono KKP	Włączono klopidogrel	Włączono ASA	

ASA (*acetylsalicylic acid*) — kwas acetylosalicylowy; GKS (*glucocorticosteroids*) — glikokortykosteroidy; KKP — koncentrat krwinek płytkowych; LMWH (*low molecular weight heparin*) — heparyna drobnocząsteczkowa; PLT (*platelet count*) — płytki krwi; UHF (*unfractionated heparin*) — heparyna niefrakcjonowana

eplerenon, empagliflozynę, allopurinol, do leczenia dołączono klopidogrel — ze względu na wysokie ryzyko krwawienia (oszacowane za pomocą *CRUSADE Score for Post-MI Bleeding Risk*). Od 3. dnia hospitalizacji pacjentka otrzymywała enoksaparynę w dawce terapeutycznej podskórnie (2 × dziennie po 80 mg). W 10. dobie hospitalizacji odstawiono heparyny drobnocząsteczkowe oraz wykonano paliatywną angioplastykę PCI Cx ze stentem uwalniającym lek (ryc. 2). W 13. dobie hospitalizacji u chorej w dwóch kolejnych pobraniach krwi odnotowano małopłytkowość — stężenie płytek krwi (PLT, *platelet count*): 25 tys./µl. W oznaczeniu stężenia PLT na cytrynian otrzymano wynik 6 tys./µl. U chorej nie zaobserwowano cech krwawienia ani skazy krwotocznej w badaniu podmiotowym i przedmiotowym. Po konsultacji hematologicznej zdecydowano o odstawieniu kwasu acetylosalicylowego, włączono deksametazon dożylnie 2 × dziennie po 8 mg oraz przetoczono 2 opakowania koncentratu krwinek płytkowych. Pomimo odstawienia heparyny oraz wdrożonego postępowania obserwowano dalszy spadek poziomu PLT: 3 tys./µl, w oznaczeniu płytek na cytrynian: 4 tys./µl. Chorą konsultowano hematologicznie — zgodnie z zaleceniami zmodyfikowano leczenie: czasowo odstawiono klopidogrel, utrzymano deksametazon dożylnie 2 × dziennie, kolejno 8 i 4 mg oraz przetaczano dziennie 1 opakowanie koncentratu krwinek płytkowych w kolejnych dobach.

W 15. dobie u pacjentki zaobserwowano niewielką ilość wybroczyn krwotocznych pod obiema piersiami (ryc. 3). W kolejnych dobach obserwowano stopniowy wzrost stężenia PLT (tab. 1). Łącznie pacjentce przetoczono 4 opakowania koncentratu krwinek płytkowych. Stopniowo redukowano dawki podawanych glikokortykosteroidów. Po wzroście stężenia PLT powyżej 30 tys./µl do terapii włączono klopidogrel, a następnie ponownie dołączono kwas acetylosalicylowy. U chorej w okresie hospitalizacji nie zaobserwowano dodatkowych epizodów o charakterze zakrzepowym i krwotocznym. W 22. dobie hospitalizacji, w stanie stabilnym pacjentkę wypisano z kliniki z wynikiem stężenia PLT:

177 tys./µl. W miesięcznej obserwacji chorej nie stwierdzono niepokojących sygnałów.

Dyskusja

Małopłytkowość indukowana heparyną występuje u 0,1–5% pacjentów leczonych heparynami [3]. Wyróżnia się dwa typy tej jednostki chorobowej. Typ 1 nie ma tła immunologicznego, zmniejszenie stężenia PLT jest łagodne, występuje zwykle w ciągu pierwszych 2–4 dni terapii, zwykle brak jest klinicznych następstw. Typ 2 charakteryzuje się tłem immunologicznym, spadek stężenia PLT jest większy (> 50%) [4]. Powyższe rozpoznanie należy rozważyć, gdy liczba płytek spada poniżej 100 tys./ml, zwykle 5–10 dni od włączenia heparyn w leczeniu [5]. Podczas diagnostyki HIT zaleca się oznaczenie przeciwciał przeciwheparynowych, jednak ze względu na małą dostępność badanie to jest rzadko wykorzystywane. Postępowanie w HIT obejmuje odstawienie heparyn oraz wdrożenie alternatywnej terapii przeciwzakrzepowej. Zaleca się stosowanie argatrobanu, lepirudyny, fondaparynuksu lub doustnego antykoagulantu niebędących antagonistami witaminy K — najlepiej rywaroksaban [4]. W opisanym przypadku spadek stężenia PLT rozpoczął się w 13. dobie hospitalizacji, był gwałtowny oraz nasilał się pomimo odstawienia heparyn, co wskazuje na prawdopodobny mechanizm immunologiczny. Ze względu na bardzo niski poziom PLT oraz pojawienie się wybroczyn krwotocznych, zdecydowano o przetoczeniu koncentratu krwinek płytkowych oraz wdrożeniu steroidoterapii. Dodatkowym wyzwaniem terapeutycznym u opisywanej chorej była konieczność leczenia przeciwpłytkowego związana z implantacją stentu. Według zaleceń pacjenci z implantowanym stentem w przebiegu NSTEMI powinni otrzymywać podwójną terapię przeciwpłytkową obejmującą kwas acetylosalicylowy oraz inhibitor P2Y12 do 12 miesięcy [6]. Autorzy, uwzględniając zalecenia konsultującego hematologa, zdecydowali się na krótkotrwałe odstawienie leków przeciwpłytkowych.

W opisywanym przypadku, ze względu na pojawienie się objawów skazy krwotocznej, pod postacią wybroczyn, odstąpiono od wdrożenia alternatywnego leczenia przeciwzakrzepowego. Obecnie brakuje szczegółowych i jednoznacznych zasad postępowania w przypadku współwystępowania ostrego zespołu wieńcowego i HIT, w związku z czym poszczególne decyzje muszą być podejmowane indywidualnie w zależności od oceny sytuacji klinicznej.

Konflikt interesów

Nie zgłoszono.

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81-year-old patient with tachycardia–bradycardia syndrome after bilateral mastectomy with pacemaker pocket infection

Przypadek 81-letniej pacjentki z zespołem tachykardia–bradykardia po obustronnej mastektomii z infekcją loży stymulatora w wywiadzie

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Abstract

The case report presents a history of an 81-year-old woman with paroxysmal atrial fibrillation, treated with apixaban at a reduced dose, who has a DDD pacemaker implanted in March 2018 due to tachycardia-bradycardia syndrome. In the interview were left-hand mastectomy in 2012 and right-hand mastectomy in October 2022 caused by breast cancer. In November 2022 the patient was admitted to the Department of Cardiology to stimulate system removal because of a pacemaker pocket infection. Then, according to the interview of sick sinus syndrome, the electrocardiogram Holter monitoring was made and due to its results the patient was qualified for repeated electrotherapy. Considering the general clinical view it was decided to implant the leadless MICRA pacemaker.

Key words: tachycardia-bradycardia, sick sinus syndrome, pacepocket infection, MICRA

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Introduction

Tachycardia–bradycardia syndrome is a manifestation of sick sinus syndrome. It is a disorder of the sinoatrial node. The condition is caused by a not fully functional pacemaker and damaged impulse transmission. The implication of this is bradycardia after fast supraventricular rhythm episodes [1]. The dysfunction occurs mostly in older but can appear at any age. One in 600 cardiac patients of 65 years of age or older develops sinus node dysfunction [2]. The treatment of the disease includes pacemaker implantation, which may cause complications. Most studies show complication rates after dual-chamber pacemaker implantation — 4.8% at 30 days, 5.5% at 90 days and 7.5% at 3 years [3]. Infections after 12 months after the procedure account for approximately 1.3% of complications [4].

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Case report

81-year-old woman with paroxysmal atrial fibrillation, treated with apixaban in reduced dose, after DDD pacemaker implantation in march 2018 due to tachycardia-bradycardia syndrome was admitted to the Department of Cardiology of the University Clinical Hospital in Bialystok on 5.11.2022 to stimulate system removal because of pacemaker pocket infection. The patient complained about fatigue and weight loss. In the interview were also: left-hand mastectomy in 2012 and right-hand mastectomy with lower axillar lymph nodes removal in 13.10.2022 caused by breast cancer, left upper limb lymphatic oedema, arterial hypertension, hypothyroidism, organic mood disorders.

At admission, the patient was cachectic, conscious in logical contact and slightly demented. In physical examination: blood pressure 137/57 mm Hg, heart rate 58/min., SpO_2 98%, without fever, lymphatic oedema of the left upper limb, in the left subclavian area - large wound with big skin loss and purulent content leakage moreover severe redness and swelling with the partially emerged stimulating system. Furthermore, in the right axillary fossa a tuberous, palpatory immobile and hard change, size of approximately 5 × 5 cm was observed. The abdomen was soft and indolent with negative peritoneal symptoms. In electrocardiogram (ECG) — effective atrial and chamber stimulation with a chamber rhythm of 58/min. In laboratory tests, the patient showed mild anaemia (haemoglobin 9.4 g/dL), slight hyperpotassaemia (K+ 5.4 mmol/dL), mixed hyperlipidaemia and low inflammatory parameters. Blood cultures were negative. In transthoracic echocardiography left ventricle with preserved global systolic function (ejection fraction 52%) and second-degree diastolic dysfunction was shown, moderate regurgitation of the mitral and tricuspid valves, and leads of pacemakers in the right cavities of the heart. In treatment applied: vancomycin (empirically) 3 × 500 mg *i.v.*, Clexane 2 × 40 mg *s.c.* (apixaban was cancelled), perindopril 1 × 1.25 mg *p.o.*, levothyroxine 112 mcg 1 × 1 *p.o.*, sertraline 50 mg *p.o.* On 7.11.2022 patient underwent a procedure of pacing system removal without complications.

Simultaneously parts of leads were taken due to microbiological examination. After pacemaker removal in ECG, a first-degree atrioventricular block was observed. During a couple of next days after the procedure there was slight bleeding between the wound edges and seeping the dressing with blood. According to that, the decision to readminister anticoagulant therapy was held. Apixaban was introduced again on the fourth day after the procedure. The state of the patient remained stable. The next days showed progressive renal function impairment — glomerular filtration rate dropped to 34 mL/min from 45 mL/min originally. Vancomycin concentration in serum was above the therapeutic range. After consultation with the hospital microbiologist, the dose was reduced to 2 × 500 mg until the result of the pacemaker leads culture. It turned that from wound swab and leads there was a growth of resistance to vancomycin *Staphylococcus lugdunensis*. It was necessary to change the therapy — aimed antibiotic therapy with cloxacillin 2 g every 6 hours *i.v.* was started, it needed to remain for 14 days. Blood screening showed severe anaemia (haemoglobin 8 g/dL) — taking into account recent neoplasm history and general clinical condition 1 unit of blood was transfused. According to the interview of sick sinus syndrome, the ECG Holter monitor was made. It showed sinus rhythm 40–82/min., average 62/min., 24 pauses lasting > 2 seconds in sinus pause mechanism, moreover 3 episodes of bradycardia < 40/min. (minimum 30/min.). A decision to qualify the patient for pacemaker implantation was made. It was decided to implant the leadless MICRA pacemaker after ending the antibiotic therapy. In 8.12.2022 patient was readmitted to the Department of Cardiology of University Clinical Hospital. From the previous hospitalisation, the patient did not report any symptoms. On 10.12.2022 in general anaesthesia IPG Micra RV was implanted without complications.

Conclusions

The new generation leadless pacemakers are the optimal solution of electrotherapy for patients in elderly age with a difficult visceral approach or in states that do not allow for implantation of a traditional pacemaker. In this case, the patient had a mastectomy in the area where the new pacemaker was about to be implanted. That is why the patient needed over-standard treatment. The last mastectomy operation happened nearly a month before, it was too soon to implant a new pacemaker safely — it would have to be located in the right subclavian area.

According to all above, the most optimal and beneficial solution was to implant IPG Micra.

Discussion

The most common reason for pacemaker implantation is sick sinus syndrome (SSS). Interestingly, the risk of sudden cardiac death and more over the entire time of living in this group of patients is similar to the general population. Although, apart from this SSS may lead to transient bradycardia, which may appear as dizziness, collapse, decreased effort tolerance or increased exhaustion. The published data expressly say that patients with asymptomatic SSS do not earn any profit from pacemaker implantation. According to that, only electrocardiographically proven symptomatic SSS is an indication for the procedure [1] which causes significant improvement in life quality [4]. Unfortunately, even in the presence of full indications for pacemaker implantation, the possibility of complications must be

considered in such therapy. Most of the complications resulting from cardiac pacing and cardiac resynchronization therapy occur in the postoperative period [5]. In this case, the pacemaker box infection is a late complication [3]. According to data, such an infection after 12 months after the procedure accounts for approximately 1.3% of complications [4]. In the present case the infection developed after over 4 years. The patient had undergone serious surgery about a month before — right-hand mastectomy — which was a counter-indication to another traditional pacemaker placement. The IPG Micra was considered the most optimal treatment. A leadless pacemaker is a new type of device, which is especially beneficial in young patients with long-life perspectives when there is a need for a lead exchange or reimplantation but also in old who have limited vascular approach. Such pacemakers do not need a battery that is located under the skin in a subclavian area which had a critical meaning in this case. Moreover, there is no risk of lead fracture or dislocation which is a common reason for pacemaker dysfunction [1].

Conflict of interest

None declared.

Streszczenie

W niniejszej pracy przedstawiono przypadek 81-letniej pacjentki z wywiadem napadowego migotania przedsionków, leczonej przeciwkrzepliwie apiksabanem w dawce zredukowanej, po implantacji stymulatora typu DDD w marcu 2018 roku z powodu zespołu tachykardia–bradykardia. W wywiadzie stan po zabiegu mastektomii lewostronnej w 2012 roku, a w październiku 2022 roku — mastektomii prawostronnej z powodu raka piersi. W listopadzie 2022 roku chora została przyjęta do Kliniki Kardiologii Uniwersyteckiego Szpitala Klinicznego w Białymstoku w celu usunięcia układu stymulującego ze względu na zakażenie loży stymulatora. Ze względu na wcześniejszy wywiad zespołu chorego węzła po usunięciu układu wykonano badanie elektrokardiograficzne metodą Holtera i ponownie zakwalifikowano pacjentkę do elektroterapii. Z uwagi na całokształt obrazu klinicznego zdecydowano o implantacji stymulatora bezelektrodowego typu Micra.

Słowa kluczowe: tachykardia–bradykardia, zespół chorego węzła, infekcja loży stymulatora, MICRA

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Newly diagnosed congenitally corrected transposition of the great arteries in physically active 73-year-old men

Nowo rozpoznane skorygowane przełożenie wielkich pni tętniczych u aktywnego fizycznie siedemdziesięciolatka

Amelia Joanna Mądrecka[1], Marcin Antoni Konopka[1], Edyta Kostarska-Srokosz[2], Wojciech Król[1], Marek Kuch[2], Wojciech Braksator[1]

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Abstract

A 73-year-old Caucasian male, so far engaged in regular, recreational physical activity, was admitted to the hospital due to a progressive decline in efficiency. As a result of the performed diagnostics, a congenitally corrected transposition of the great arteries with failure of the systemic ventricle was diagnosed. Despite the coexisting congenital heart defect, the patient remained physically active for several dozen years and performed high-intensity exertions.

Key words: CCTGA, congenitally corrected transposition of the great arteries, echocardiography, heart failure

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Case report

Seventy-three-year-old Caucasian man with decades of regular physical activity was admitted to the hospital due to severe dyspnea. Since a year before hospitalization, a subjective reduction in exercise tolerance. Since 2–3 months, non-specific chest pains and a tendency to edema in legs. Several days before hospitalization, intensified exertional dyspnea followed by orthopnea. Coexisting medical conditions — several years of history of hypertension and type 2 diabetes treated with oral medications. In youth, spontaneous pneumothorax occurred during an alpine expedition, with subsequent empyema treated with drainage. The patient underwent echocardiographic examinations several times — enlargement of the heart cavities with mildly reduced or normal contractility has been reported; the difficult imaging conditions were emphasized each time.

On admission to the hospital, the patient presented fair general condition, with orthopnea and dyspnea at rest, elevated blood pressure, signs of pulmonary congestion, and pitting edema in both legs. A chest radiograph shows right-side pleural effusion, a significantly enlarged outline of the heart, mesocardia (Figure 1).

In laboratory tests, elevated values of cardiac troponin I (hsCTn I: 1321 to > 1046 ng/L; n = 34 ng/L), increased values of B-type natriuretic peptide (BNP: 10512 pg/mL; n = = 125 pg/mL), and D-dimer (DD: 1852 ng/mL; n = 730 ng/mL).

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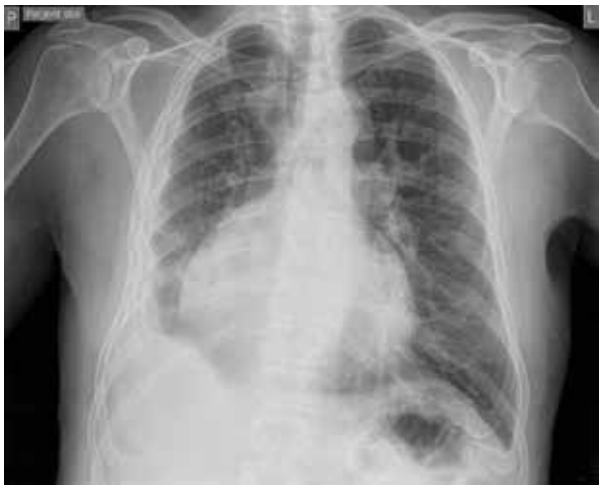

Figure 1. Chest radiography. Enlarged heart silhouette, shading in the area of the right diaphragmatic-costal sinus and along the side of the chest. Discrete parenchymal densities in the lower field of the right lung; mesocardia

Congenitally corrected transposition of the great arteries (CCTGA) was diagnosed on the basis of echocardiography. It was the first diagnosis of congenital heart disease in this patient. The heart was visualized from the sub-sternal projection (Figure 2). Examination showed an enlarged, spherical right ventricle (which is a systemic ventricle) with features of myocardial hypertrophy and significant impairment of systolic function (ejection fraction of 30%). The tricuspid valve was connected with the systemic ventricle, and mild regurgitation was present. Great arteries were extending from the heart with a parallel course characteristic of CCTGA. The pulmonary valve was with a mild regurgitation. The atria remained in a typical location. The ventricular septal defect and other coexisting heart defects were not visualized.

Coronary angiography was performed — the right coronary artery arising in a place typical for the left, left coronary artery arising in a place typical for the right; coronary arteries without atherosclerotic changes.

The Holter electrocardiogram device recorded numerous additional ventricular beats, including pairs and episodes of non-sustained ventricular tachycardia (Figure 3).

After the treatment, typical for congestive heart failure (diuretics, beta-blockers, angiotensin-converting enzyme inhibitors), a quick improvement of the general condition, reduction of BNP, and reduction of cardiac arrhythmias was achieved. In a follow-up, Holter electrocardiogram device recorded no complex forms of ventricular arrhythmia.

It should also be emphasized that the described patient remained physically active for most of his life (over 50 years), undertaking efforts of moderate and high intensity. In the last years, played squash regularly (3–4 trainings/week for 90 min) and participated in sports competitions. Additionally, about 30 minutes of brisk (5 km/h) walking a day. For about a year, resistance exercises 2–3 times a week for 60 minutes, swimming or aerobics. In his youth, the patient is actively hiking in the mountains. At 24 years of age climbed Kilimanjaro. Despite the congenital heart defect, the patient undertook intense physical activity for several dozen years and remained asymptomatic until old age.

Discussion

Congenitally corrected transposition of the great arteries is a rare cardiac malformation characterized by discordant atrioventricular (right atrium connected to the left ventricle, left atrium to the right ventricle) and ventricular-arterial

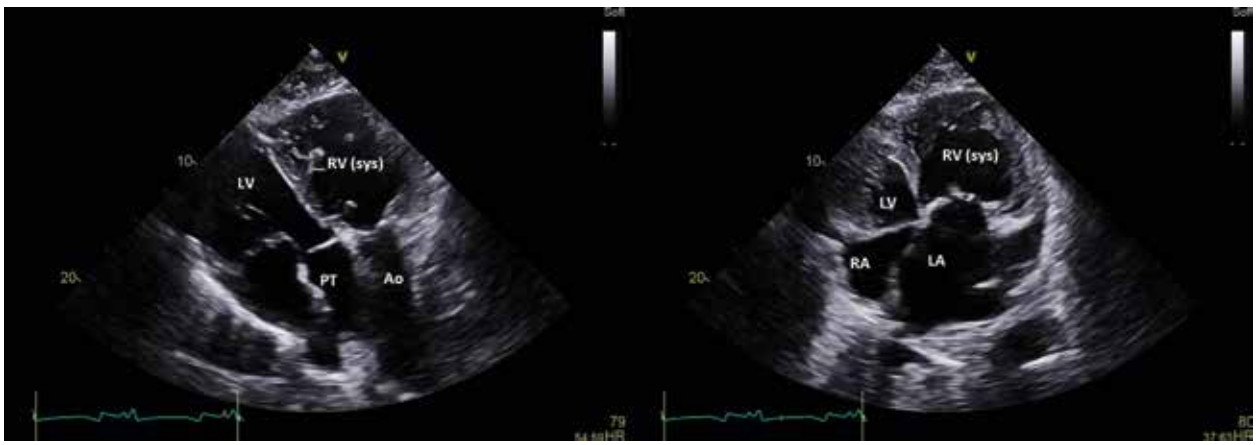

Figure 2. Echocardiographic examination, substernal projections. Enlarged, spherical right ventricle with myocardial hypertrophy, with significant impairment of contractility (ejection fraction 30%). Great arteries arising from the heart with a parallel course characteristic of congenitally corrected transposition of the great arteries; Ao — aorta; LA — left atrium; LV — left ventricle; PT — pulmonary trunk; RA — right atrium; RV (sys.) — right ventricle (systemic)

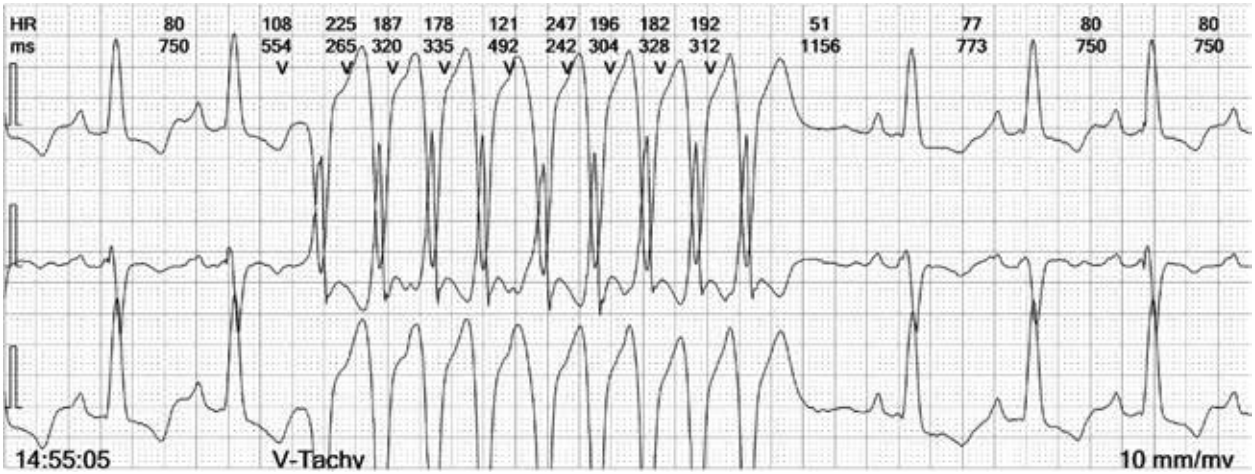

Figure 3. Holter electrocardiogram device. Non-sustained ventricular tachycardia

connection (aorta connected to the right ventricle, pulmonary trunk connected to the left ventricle). It accounts for 1% of congenital heart defects [1] and occurs in 1 in 33 thousand live births [2]. We distinguish a complex form in which the above-mentioned changes are accompanied by other anomalies, most often ventricular septal defect (70%) or valvular pulmonary stenosis (40%), and an isolated form, which may remain undiagnosed for a long time. The first symptoms appear most often in the fourth decade of life, when systemic ventricular dysfunction, tricuspid regurgitation, or complete atrioventricular block develop [3]. The average life expectancy of patients with CCTGA without associated defects is approximately 60 years, with accompanying defects — 40 years. Patients most often die of heart failure or ventricular arrhythmia [4].

One of the factors leading to progressive heart failure is the fact that the systemic ventricle is vascularized by the right coronary artery, which may lead to insufficient perfusion of the hypertrophied myocardium, and consequently to its progressive dysfunction, as muscle hypertrophy is not accompanied by an adequate proliferation of capillary vascularization. [2]

Another hypothesis is that the unfavorable shape of the systemic chamber results from remodeling aimed at maintaining adequate arterial pressure [5]. The presented patient belongs to a small group described in the literature who remained asymptomatic up to the age of 70. The oldest patient with newly diagnosed CCTGA described so far was 88 years old [6], and the oldest surviving patient was 92 years old [7].

Physical activity undertaken by people with congenital heart disease requires a systematic medical assessment: subjective and physical examination, additional tests, assessment of training intensity, and further medical supervision. Parameters of prognostic importance include ventricular function with the assessment of the ejection fraction, pulmonary artery pressure, presence of cardiac arrhythmias, the value of resting/exercise saturation, and width of the aorta [3].

Conflict of interest

None declared.

Streszczenie

Siedemdziesięciotrzyletni mężczyzna rasy kaukaskiej, dotychczas podejmujący regularną, rekreacyjną aktywność fizyczną został przyjęty do szpitala z powodu postępującego spadku wydolności. W wyniku przeprowadzonej diagnostyki rozpoznano skorygowane przełożenie wielkich pni tętniczych z niewydolnością komory systemowej. Pomimo współistniejącej wrodzonej wady serca pacjent przez kilkadziesiąt lat pozostawał aktywny fizycznie i wykonywał wysiłki o dużej intensywności.

Słowa kluczowe: ccTGA, skorygowane przełożenie wielkich tętnic, echokardiografia, wysiłek fizyczny, niewydolność serca

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CASE REPORT

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Spongy cardiomyopathy with the first clinical manifestation at the age of 90 years

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Abstract

The present paper reports a case of a 90-year-old woman, admitted to the hospital because of decompensated heart failure *de novo*. Echocardiography examination revealed characteristic spongy cardiomyopathy: excessive trabeculation and occurrence of deep intertrabecular recesses. Standard treatment for heart failure was initiated, achieving clinical improvement. The case indicates, that spongy cardiomiopathy diagnosis can be made at a very advanced age and does not always mean a bad prognosis.

Key words: spongy cardiomyopathy, heart failure, echocardiography

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Introduction

Spongiform cardiomyopathy also known as left ventricular noncompaction (LVNC) is considered a rare form of cardiomyopathy with a genetic basis [1]. The hallmark is abnormal left ventricular (LV) trabeculation with deep intertrabecular recesses communicating with the LV cavity. The lesions are mainly located in the LV apex, LV inferior and lateral wall, below the papillary muscles, less commonly affecting the interventricular septum, and may also involve the right ventricular (RV) muscle [2–4]. The clinical manifestation can range from completely asymptomatic cases diagnosed incidentally on echocardiography to severe heart failure (HF). The following triad of symptoms is typical of spongiform cardiomyopathy: HF, supraventricular and ventricular arrhythmias, including sudden cardiac death and thromboembolic events [4].

The diagnosis can be made based on transthoracic echocardiography. The most commonly used criteria are those of Jenni et al. [3]. These include the finding of two layers of myocardium: a thin epicardial compacted (C) layer and a much thicker endocardial noncompacted (NC) layer; NC to C ratio should be above 2:1 in the end-systolic phase.

Until recently, this form of cardiomyopathy was mainly diagnosed in children. It is estimated to represent 9% of all cardiomyopathies in young patients [4]. In contrast, over the past decade or so, there has been an increasing number of cases reported in adults, including elderly patients [5–7].

The prognosis of patients with this form of cardiomyopathy is poor, with a risk of sudden death exceeding 50% in a symptomatic patient population [8].

Case report

A 90-year-old female patient, treated psychiatrically for many years for personality disorders with signs of dementia and for hypertension, taking the following medications permanently: doxepin 3 × 25 mg, promethazine 2 × 25 mg, quetiapine 3 × 25 mg , perindopril 1 × 5 mg, amlodipine 1 × 5 mg, was admitted for the first time in her life to the

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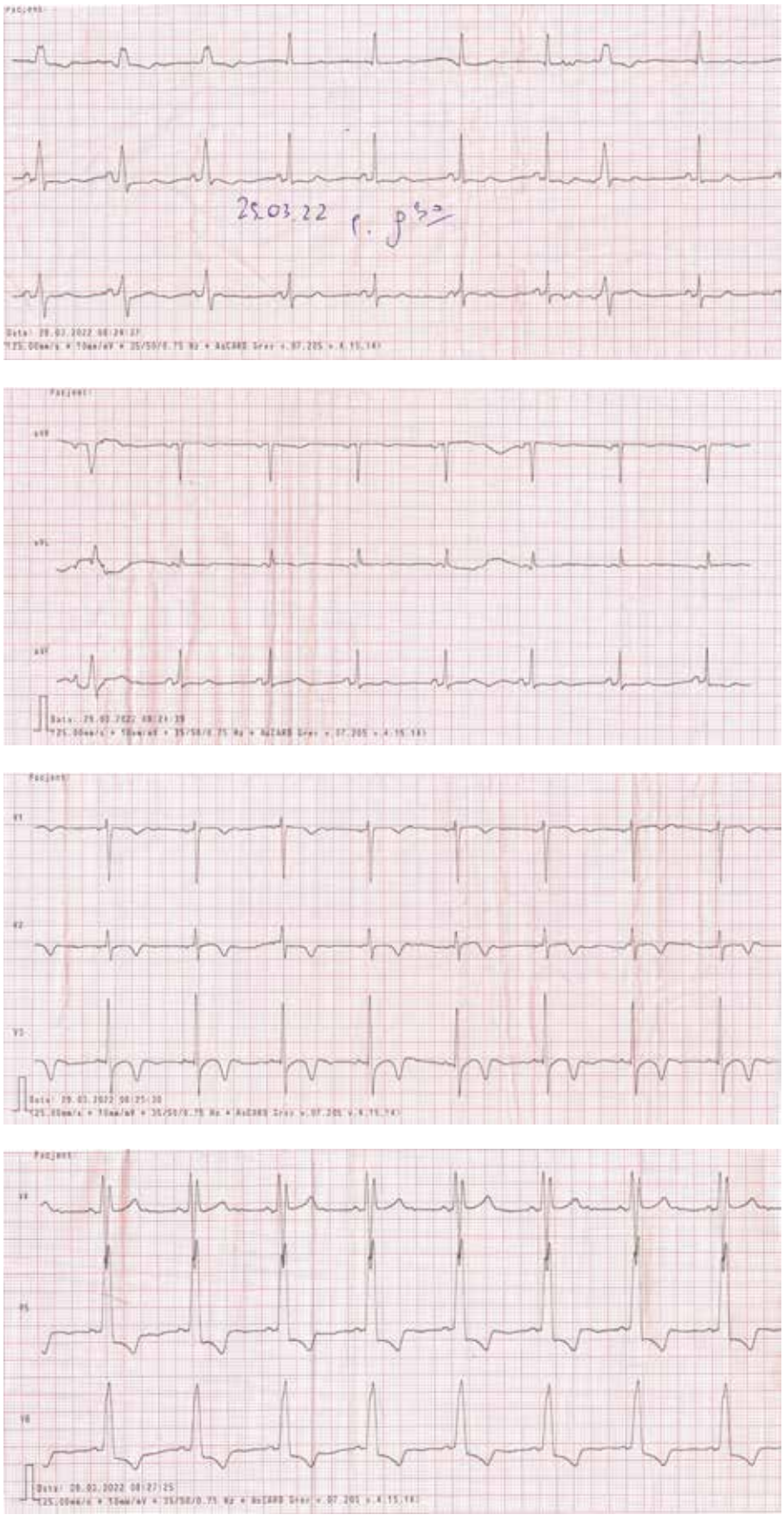

Figure 1. Electrocardiography recording during hospital admission. Intermittent left bundle branch block

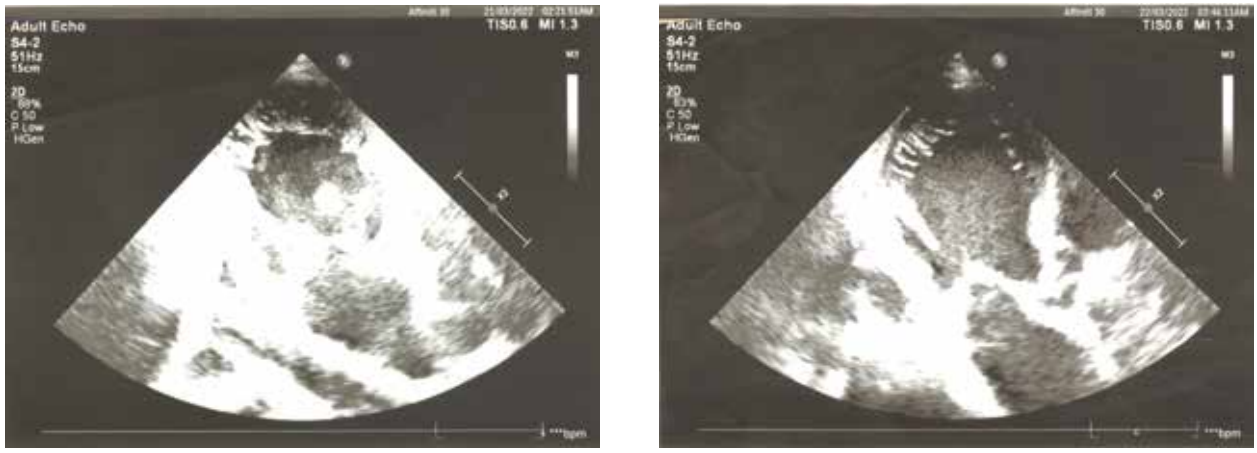

Figure 2. Transthoracic echocardiography. The presence of increased left ventricle trabeculation with deep recesses; noncompacted to compacted ratio greater than 2:1

Internal Medicine Ward in February 2022 due to dyspnoea at rest. Physical examination revealed BP 120/70 mm Hg, regular heart function, muffled heart sounds, muted vesicular breath sounds at the base of the lungs, slight periosteal oedema.

Laboratory tests showed the following abnormalities: moderate anaemia (Hb 10.6 g/dL), reduced creatinine clearance (Cockcroft-Gault GFR: 30 ml/min) and moderate hyponatraemia (Na 133 mmol/l).

The electrocardiography (ECG) recording (Figure 1) revealed intermediate heart axis, sinus rhythm 60/min, disturbed by single atrial premature beats with aberration, intermittent left bundle branch block (LBBB), signs of left atrial hypertrophy/enlargement, possible LV hypertrophy. Chest X-ray revealed the following abnormalities: opacity at the base of both lungs, possibly representing pleural fluid, with a greater amount on the right side, and fibrostreaky opacities in the lower fields of both lungs. Echocardiography was performed, which showed moderate enlargement of the left heart cavities and RV cavities, generalized LV hypokinesia with severely reduced ejection fraction (approximately 20–22%), high-grade LV diastolic dysfunction (restrictive mitral inflow pattern, E/E'sept = 22.5), impaired RV longitudinal systolic function (TAPSE 15 mm), low mitral, aortic and tricuspid regurgitation, high probability of pulmonary hypertension (RVSP: 51 mm Hg), low amount of pericardial fluid (up to 8 mm near the right atrium). In the region of the LV apex there was evidence of excessive trabeculation with deep recesses communicating with the LV cavity, passing into the middle segments of the lateral, anterior, and former posterior wall (Figure 2).

The psychiatric treatment, as recommended by the specialist, was modified: doxepin, which can promote the occurrence of hyponatraemia, was discontinued and the dose of quetiapine was increased. The following medications were added to the therapy: torasemide 1 × 10 mg, eplerenone 1 × 25 mg, bisoprolol 1 × 1.25 mg and a non-vitamin-K antagonist oral anticoagulant (eliquis 2 × 2.5 mg).

The treatment resulted in a significant clinical improvement — resolution of dyspnoea at rest, resolution of periosteal oedema. A follow-up ultrasound examination revealed regression of the amount of pericardial fluid and a reduction in the amount of pleural fluid. The patient refused to have a Holter monitor fitted but intermittent LBBB and single premature supraventricular beats were observed in the 12-lead ECG recordings performed and repeated several times during her stay on the ward.

The patient was discharged home with a recommendation for follow-up visits in the Cardiology Outpatient Clinic. The patient's family was informed of the genetic basis of the disease and immediate family members were advised to report to the Cardiology Outpatient Clinic.

Conclusions

The case presented in this paper, in which LVNC was detected at a very advanced age, proves that the disease does not always have to mean a poor prognosis. In the patient, the first clinical manifestation was the appearance of signs of HF. There was no history of embolic complications or loss of consciousness. The literature reports cases of LVNC patients in whom life-threatening arrhythmias or HF already appeared in childhood [4, 8]. There are also reports of good long-term prognosis in patients with this form of cardiomyopathy [9], which can be confirmed by the case presented in this paper. One year and 7 days have passed since the patient was discharged from hospital and we know that she is alive.

Conflict of interest

None declared.

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Kardiomiopatia gąbczasta z pierwszą manifestacją kliniczną w wieku 90 lat

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Streszczenie

W niniejszym tekście przedstawiono przypadek 90-letniej pacjentki, leczonej z powodu zaburzeń depresyjnych i nadciśnienia tętniczego, przyjętej na oddział wewnętrzny z powodu zdekompensowanej niewydolności serca *de novo*. W wykonanym badaniu echokardiograficznym stwierdzono cechy kardiomiopatii gąbczastej: wzmożone beleczkowanie i głębokie zachyłki między beleczkami. Włączono leczenie typowe dla niewydolności serca, uzyskując istotną poprawę kliniczną. Przypadek ilustruje, że rozpoznanie tej postaci kardiomiopatii może zostać postawione w bardzo zaawansowanym wieku, a tym samym nie zawsze oznacza złe rokowanie.

Słowa kluczowe: kardiomiopatia gąbczasta, niewydolność serca, echokardiografia

Folia Cardiologica 2023; 18, 3: 145–148

Wstęp

Kardiomiopatia gąbczasta, zwana także kardiomiopatią z niescalenia mięśnia lewej komory (LVNC, *left ventricular noncompaction*), jest uważana za rzadką postać kardiomiopatii o podłożu genetycznym [1]. Cechą charakterystyczną jest nieprawidłowe beleczkowanie mięśnia lewej komory (LV, *left ventricular*) z głębokimi zachyłkami między beleczkami, komunikującymi się z jamą LV. Zmiany lokalizują się głównie w koniuszku LV, na jej ścianie dolnej i bocznej, poniżej mięśni brodawkowatych, rzadziej dotyczą przegrody międzykomorowej, mogą też obejmować mięsień prawej komory [2–4]. Manifestacja kliniczna może być różna: od przypadków całkowicie bezobjawowych, rozpoznanych przypadkowo w trakcie badania echokardiograficznego aż po ciężką niewydolność serca (HF, *heart failure*). Typowa dla kardiomiopatii gąbczastej jest triada objawów: HF, nadkomorowe i komorowe zaburzenia rytmu, w tym nagłe zgony sercowe oraz epizody zakrzepowo-zatorowe [4].

Rozpoznanie można postawić na podstawie badania echokardiograficznego przezklatkowego. Najczęściej stosowane są kryteria Jenni i wsp. [3]. Obejmują one stwierdzenie obecności dwóch warstw mięśnia sercowego: cienkiej nasierdziowej warstwy scalonej oraz znacznie grubszej wsierdziowej warstwy niescalonej, stosunek warstwy niescalonej do scalonej powinien wynosić powyżej 2:1 w fazie późnoskurczowej.

Do niedawna ta postać kardiomiopatii była rozpoznawana głównie u dzieci. Szacuje się, że stanowi ona 9% wszystkich kardiomiopatii u młodych pacjentów [4]. Natomiast w ciągu ostatnich kilkunastu lat coraz więcej przypadków opisywanych jest u dorosłych, w tym u pacjentów w podeszłym wieku [5–7].

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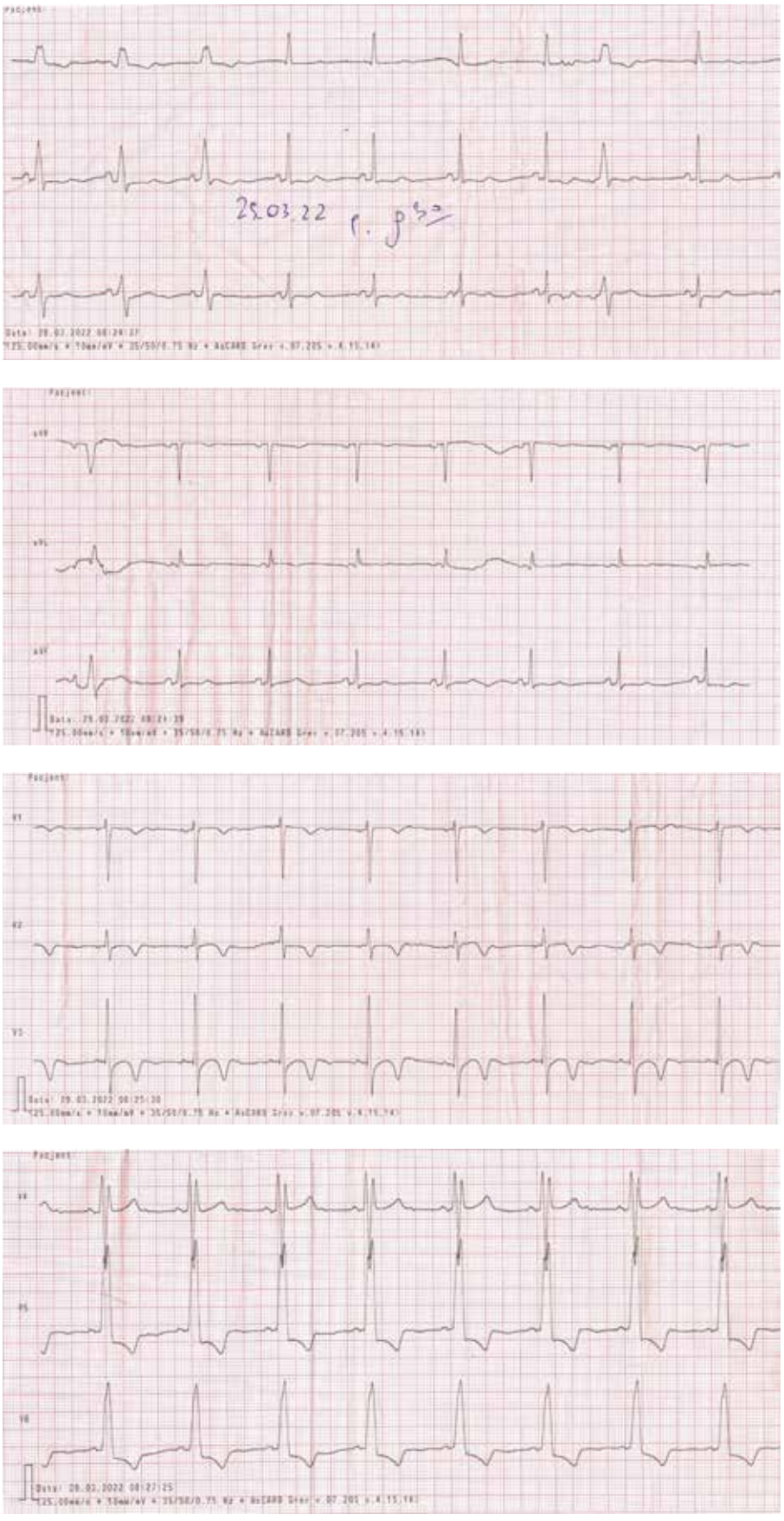
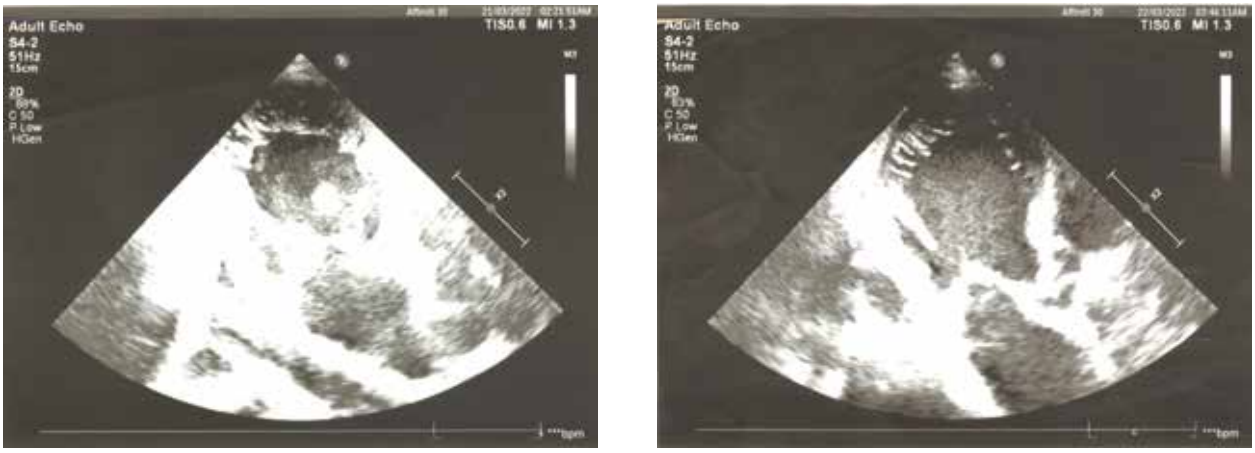


Rycina 1. Zapis elektrokardiograficzny podczas przyjęcia do szpitala. Intermitujący blok lewej odnogi pęczka Hisa



Rycina 2. Badanie echokardiograficzne przezklatkowe. Widoczne wzmożone beleczkowanie mięśnia lewej komory z głębokimi zachyłkami; stosunek warstwy niescalonej do scalonej powyżej 2:1

Rokowanie u chorych z tą postacią kardiomiopatii jest poważne, ryzyko nagłego zgonu w populacji chorych objawowych przekracza 50% [8].

Opis przypadku

Dziewięćdziesięcioletnia pacjentka, leczona od wielu lat psychiatrycznie z powodu zaburzeń osobowości z cechami otępienia oraz z powodu nadciśnienia tętniczego, przyjmująca na stałe następujące leki: doksepina 3 × 25 mg, prometazyna 2 × 25 mg, kwetiapina 3 × 25 mg, peryndopryl 1 × 5 mg, amlodypina 1 × 5 mg, została przyjęta po raz pierwszy w życiu na oddział wewnętrzny w lutym 2022 roku z powodu duszności spoczynkowej. W badaniu fizykalnym: ciśnienie tętnicze 120/70 mm Hg, czynność serca miarowa, tony serca głuche, ściszenie szmeru pęcherzykowego u podstawy płuc, niewielkie obrzęki okołokostkowe.

W badaniach laboratoryjnych z odchyleń od normy stwierdzono następujące nieprawidłowości: miernego stopnia niedokrwistość (Hb 10,6 g/dl), obniżony klirens kreatyniny (GFR wg Cockrofta i Gaulta: 30 ml/min) oraz miernego stopnia hyponatremię (Na 133 mmol/l).

W zapisie EKG (ryc. 1) wykazano: oś serca pośrednia, rytm zatokowy 60/min, zaburzony pojedynczymi przedwczesnymi pobudzeniami przedsionkowymi z aberracją, intermitujący blok lewej odnogi pęczka Hisa (LBBB, *left bundle branch block*), cechy przerostu/powiększenia lewego przedsionka, możliwość przerostu LV. W badaniu radiologicznym klatki piersiowej nieprawidłowości to: zacienienie u podstawy obu płuc mogące odpowiadać płynowi w jamach opłucnych, większa ilość po stronie prawej, zacienienia pasmowato-włókniste w dolnych polach obu płuc. Wykonano badanie echokardiograficzne, w którym stwierdzono mierne powiększenie jam lewego serca i prawej komory, uogólnioną hypokinezę lewej komory z ciężko obniżoną frakcją wyrzutową (ok. 20–22%), dysfunkcję rozkurczową LV dużego stopnia (restrykcyjny typ napływu mitralnego; E/E'sept = 22,5), upośledzoną funkcję skurczową włókien podłużnych prawej komory (TAPSE 15 mm), małą niedomykalność mitralną, aortalną i trójdzielną, duże prawdopodobieństwo nadciśnienia płucnego (ciśnienie skurczowe w prawej komorze: 51 mm Hg), małą ilość płynu w worku osierdziowym (do 8 mm koło prawego przedsionka). W rejonie koniuszka LV stwierdzono obecność nadmiernego beleczkowania z obecnością głębokich zachyłków komunikujących się z jamą LV, przechodzących na segmenty środkowe ściany bocznej, przedniej i dawnej tylnej (ryc. 2).

Zmodyfikowano leczenie psychiatryczne, zgodnie z zaleceniami specjalisty: odstawiono doksepinę, mogącą sprzyjać występowaniu hyponatremii i zwiększono dawkę kwetiapiny. Dołączono do leczenia następujące leki: torasemid 1 × 10 mg, eplerenon 1 × 25mg, bisoprolol 1 × 1,25 mg oraz doustny antykoagulant niebędący antagonistą witaminy K (eliquis 2 × 2,5 mg).

W wyniku zastosowanego leczenia uzyskano istotną poprawę kliniczną — ustąpienie duszności spoczynkowej oraz obrzęków okołokostkowych. W kontrolnym badaniu ultrasonograficznym stwierdzono regresję ilości płynu w worku osierdziowym i zmniejszenie ilości płynu w jamach opłucnych. Pacjentka nie wyraziła zgody na założenie rejestratora Holter EKG, natomiast w wykonanych zapisach 12-odprowadzeniowego EKG, powtarzanych kilkakrotnie w czasie pobytu na oddziale obserwowano intermitujący LBBB i pojedyncze przedwczesne pobudzenia nadkomorowe.

Wypisano pacjentkę do domu z zaleceniem kontroli w poradni kardiologicznej. Rodzinę chorej poinformowano o genetycznym uwarunkowaniu choroby i zalecono zgłoszenie się do poradni kardiologicznej najbliższych członków rodziny.

Podsumowanie

Przedstawiony przypadek wykrycia niescalenia mięśnia LV w bardzo zaawansowanym wieku dowodzi, iż choroba nie zawsze musi oznaczać złe rokowanie. U pacjentki pierwszą manifestacją kliniczną było pojawienie się cech HF. W wywiadzie nie było powikłań zatorowych ani utrat przytomności. W piśmiennictwie opisywane są przypadki pacjentów z LVNC, u których groźne dla życia zaburzenia rytmu lub HF pojawiały się już w dzieciństwie [4, 8]. Istnieją także doniesienia o dobrym długofalowym rokowaniu u pacjentów z ta postacią kardiomiopatii [9], czego potwierdzeniem może być zaprezentowany przypadek. Minął rok i 7 dni od wypisania pacjentki ze szpitala i wiemy, że żyje...

Konflikt interesów

Nie zgłoszono.

Piśmiennictwo

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Foreign body ingestion by a paediatric patient: case analysis and legal issues

Połknięcie ciała obcego przez pacjenta pediatrycznego — analiza przypadków oraz wątki prawne

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Abstract

Foreign body ingestion by paediatric patients is a common problem in medical practice. This article aims to analyse the clinical picture, the aetiology and to comment on the legal liability that the caregiver or the manufacturer may incur in such cases. The presented data come from a 3-year period from a medical centre in Kielce and were analysed retrospectively. The study involved 75 children. Educating caregivers to pay more attention to where they place dangerous objects or to buying toys consisting of small parts may contribute to the reduction of the percentage of patients with the described issues.

Key words: paediatric patient, respiratory foreign body, gastrointestinal foreign body, responsibility for supervision of a minor, manufacturer's liability

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Introduction

Children as the individuals most vulnerable to danger are subject to special legal protection. This protection stems from the basic legal institution in family law, which is parental authority. Parental authority is granted to parents on the birth of a child and continues until the child reaches the age of majority. Parental authority implies the legal responsibility of parents towards their children. Ensuring that the child is adequately protected in terms of his or her health, which, apart from his or her well-being, is the most important aspect of his or her existence, is an important task of the parents in the process of child-rearing. The exercise of parental authority can be reviewed by the guardianship court at any time. If a child is neglected, the family court can restrict parental authority and even, in extreme circumstances, order the termination of parental authority. The ingestion of foreign bodies by paediatric patients may be a consequence of inadequate care of the child. Inadequate care may, in turn, result from the improper exercise of parental authority by the child's parents or their negligence in taking care of the minor.

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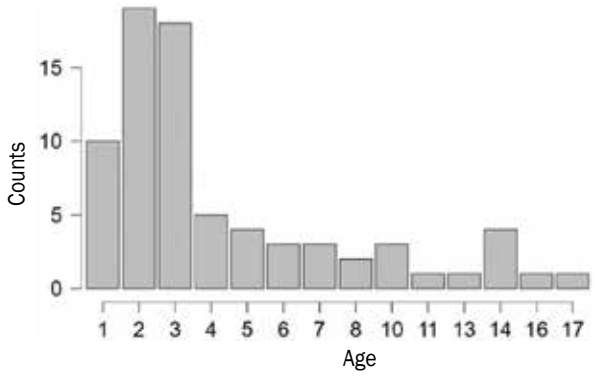

Figure 1. Age distribution of respondents

Table 1. Type of object ingested and mean age of the patient

Object swallowed	Mean	Number of patients	Standard deviation
1.00 chemicals	2.778	18	2.1298
2.00 batteries	3.706	17	3.3868
3.00 coins	4.231	13	2.2787
4.00 other	6.370	27	5.2120
Total	4.533	75	4.0079

Methodology and discussion of study results

The data came from a 3-year period (April 2017–June 2020) from a medical centre in Kielce and were analysed retrospectively. Patients up to 18 years of age were selected from all cases. Of the 75 children, 47 were male. The mean age of the patients was 4 years 6 months, and most patients were under 5 years of age (Figure 1, Table 1). There were 47 patients residing in an urban area and 28 coming from a rural area. The patients ingested or aspirated: 18 chemical products, 17 batteries, 13 coins and 27 items from the category "other". The category "other" includes, among others, glass, drawing pins, office staples, buttons, razor blades, *etc*. Of the cases analysed, 73 consisted of foreign bodies in the digestive tract, of which 19 were poisonings. Foreign bodies in the respiratory system accounted for 2 cases only. The study shows a significant relationship with respect to the type of foreign body swallowed and age (Table 2). Young children were more likely to swallow chemical items, while older children were more likely to swallow objects belonging to the category of "other". The analysis of cases has been performed based on the criterion of consequences of obstruction of the respiratory tract, gastrointestinal tract and poisoning.

Table 2. Type of object swallowed by gender of the patient

Type of object swallowed	Coin	Detergent	Batteries	Other
Girls	2	8	7	11
Boys	9	10	10	16

The table excludes the 2 cases where the objects were aspirated

The mean age of the patients was 5 years old. The histogram shows a higher number of swallowed objects in younger children compared to older ones. Due to the high skewness and kurtosis of the age distribution (values of both parameters exceed twice their standard deviations), the relationship between age and specificity of swallowed objects was tested using a non-parametric test. The Kruskal–Wallis test allowed us to reject the null hypothesis of no relationship between the variables. The character of this relationship is shown in Table 1, which illustrates the variation in mean age values of the children in groups defined by types of objects.

The data collected shows that younger children are more likely to consume chemicals, while older children are more likely to consume items in the "other" category.

Airway obstruction

A foreign body aspiration is a common event among paediatric patients. Children under 3 years of age are at the most risk due to their narrow airways and immature protective neuromuscular mechanisms [1]. Usually, the event is discovered by caregivers immediately due to a sudden attack of coughing, dyspnoea and wheezing in the child. Complete airway obstruction may also occur, resulting in rapid respiratory failure, cyanosis and unconsciousness. In both cases, the foreign body must be removed from the airway as soon as possible to regain function. Occasionally, however, situations also occur in which foreign body aspiration is not immediately discovered and the symptoms are mild. The object remains in the airway for a long time — months or even years, giving symptoms of chronic respiratory disease such as asthma [2], emphysema, atelectasis, or pneumonia, which may lead to misdiagnosis. Therefore, all cases of patients in whom conservative treatment has failed to bring improvement should be reviewed.

Foreign body in the gastrointestinal tract

Foreign body ingestion is a common problem among paediatric patients. The cases collected were grouped into 4 categories based on the type of object ingested: coins (11 cases), batteries (17 cases), detergent (18 cases) and others (27 cases). The "other" category included pieces of

glass, plastic parts, buttons, blocks, *etc*. The swallowed foreign body may be located in any part of the gastrointestinal tract — proximal or distal part of the oesophagus and stomach. Due to the variety of foreign bodies, including size, shape, length, number and location, they may give different clinical presentations. Symptoms that a patient may experience after swallowing a foreign body include coughing, vomiting, salivation, dysphagia, a feeling of having something stuck in the throat, and abdominal pain [3]. In some cases, the caregivers may be unaware of the foreign body swallowed by children due to their asymptomatic or non-specific symptoms. They discover that the child has ingested the object for the first time after finding the foreign body in the stool. Rarely, cases of foreign body ingestion require endoscopic or surgical removal, and the objects cause obstruction or mucosal damage in the oesophagus or stomach, or even perforation and necrosis of the intestinal wall. It is necessary to consider the type of foreign body ingested in relation to age and possible complications.

Poisoning

The household substances most commonly ingested by children are non-pharmaceutical products [4]. Pharmaceuticals, due to caregivers' awareness of their effects and the fact that they are meant to be ingested, are better stored than cleaning products. Caregivers do not consider the possibility of ingestion of detergents, believing it to be preposterous; however, children may find the colourful appearance of, for example, candy-like laundry capsules, attractive. Poisoning can be divided into three categories, based on the object of ingestion: cosmetics, detergents, and a category including swallowing items coated with a poisonous agent (e.g., old toys covered in lead paint) and direct ingestion of a toxic substance (e.g., mercury from a broken thermometer). Fortunately, most products in the above categories are not toxic in small quantities. Only a few household products, such as caustic cleaners, due to their content of strong acids or bases, may cause toxicity and sometimes even death in young children [4]. Parents should be educated about the assistance they can provide, as any attempt to neutralise the ingested substance may provoke an exothermic reaction or cause it to pass back through the oesophagus, causing additional injury.

Neglect and parental authority

Neglect is a form of child abuse and can include both physical and psychological abuse. Throughout history, many attempts have been made to define this phenomenon. Today, neglect is defined as a failure to meet a child's needs necessary for his or her proper development — the needs related to nutrition, clothing, shelter, hygiene or medical care [5]. Neglect, according to the Polish language dictionary, is a lack of care for something, or a bad condition of someone or something resulting from a lack of care [6]. Neglect is a consequence of intentional or unintentional actions, most often by adults, towards a child with different levels of satisfaction and regulation of their vital needs. It should be emphasized that neglect is connected with a potential or actual threat to the conditions of a child's proper psychological and physical development, and its essence consists of a failure to provide the child with appropriate conditions for development in the sphere of health, education, emotion, or adequate nutrition. Neglect is passive in its nature. It can consist of a permanent attitude, persistent behaviours or an isolated incident with significant consequences that causes harm to the child [7]. Parents do not always fulfil their responsibilities of care and upbringing properly, with examples such as resulting in neglect or leaving a child without proper care [8].

Parental neglect of a child is a consequence of the parents' improper exercise of parental authority over the minor. The child, as the weakest individual in the family group, has always been subject to parental authority [9]. The use of the term "parental authority" in Polish law until 2008 was not questioned. The discussion started with the amendment of the Family and Guardianship Code of 6 November 2008. However, it resulted in a decision not to change the term "parental authority" [10]. Parental authority is a legal relationship linking directly the parents with their minor child, by granting to the parents a conglomerate of rights and duties in relation to the child in the area of custody, representation and management of the child's property, functionally linked to the process of the child's upbringing [11]. Parental authority encompasses all the duties and rights of the parents towards the child, aimed at ensuring proper custody and guarding of the child's interests. This category also includes the parents' competencies with regard to both the person of the child and its property [12]. Parental authority is a fundamental institution of family law which ensures the proper functioning of the child in society. The exercise of parental authority depends exclusively on the parents who exercise it. If parental authority is vested in both parents, each of them is obliged and entitled to exercise it, but the essential matters concerning the child are decided jointly by the parents, and in the absence of an agreement between them, the guardianship court decides [13]. Parental authority is inextricably linked with parental supervision over the child. This supervision is not limited to the day-to-day care of the child but includes methods of indirect influence such as upbringing [14]. Linking supervision with the concept of parental authority seems natural and has been confirmed in the literature [15]. It is noted that the most important

feature of parental authority is the protective function [16]. Czerederecka [17] points out that "The most important feature of parental authority is considered to be the protective function, and the child's best interest as the overriding goal".

International legal regulations also refer to parental responsibility. It is worth mentioning the Convention of 20 November 1989 on the Rights of the Child [18] as an example. Article 18(1) of this Convention states that both parents share responsibility for the upbringing and development of the child. Parents, or in certain cases legal guardians, have the primary responsibility for the upbringing and development of the child. The best interests of the child are to be their primary concern. Parental responsibility is also referred to in Council Regulation 2201/2003/EC of 27 November 2003 on jurisdiction and the recognition and enforcement of judgments in matrimonial matters and matters of parental responsibility [19].

Parents' responsibilities towards the child

As a part of the physical development of the child, the parents are obliged to take care of the child's health and life, of his/her full physical fitness [20]. The situation threatening the child's best interest, and not only this interest's violation, is a premise for the guardianship court to issue appropriate orders to immediately prevent the violation of the child's best interest, regardless of whose side the reasons resulting in such a state of affairs were [21]. Whoever, having the duty of care or supervision over a minor under 7 years of age or over another person incapable of recognizing or defending himself or herself against danger, allows such person to remain in circumstances dangerous to human health, shall be subject to the penalty of a fine or the penalty of a reprimand [22]. The subject of an offence under Art. 106 of the Misdemeanours Code is always a minor under the age of 7, as well as another person incapable of recognizing or defending him or herself against danger. Thus, the legislature recognizes a minor under the age of 7 as a person incapable of recognizing or defending himself or herself against danger, while above this age — only depending on the individual characteristics of the person [23]. Compliance with the duty of care, care and supervision consisting in ensuring the personal safety of the ward, and protecting him/her from physical and mental consequences of dangerous situations is the object of protection in this case [24]. Special protection concerns the health and development of minors under 7 years of age and helpless persons, which may be damaged as a result of allowing these persons to stay in dangerous places [25]. It must be emphasized that a minor under 7 years of age is not, on the grounds of Article 106 of the Misdemeanours Code, a separate subject from persons incapable of recognizing or defending themselves against danger. This is evidenced by the wording of this provision, which provides for a minor under 7 years of age and a person other than such a minor, who is incapable of recognizing or defending him or herself against danger [26].

A child, being in the custody of the parents, is subject to special care. The parents, but also the guardians who currently supervise the minor, are obliged to guard the safety of the child's health and life. The cases of ingestion of foreign bodies by paediatric patients presented in this article occurred in the situations of improper care of a minor, which constitutes negligence in the proper exercise of care and supervision over the child. If the doctor has a justified suspicion that the ingestion of the foreign body occurred due to improper care, he or she should inform the competent authorities, i.e., the police, the prosecutor's office or the family court. In such a case, the doctor is exempt from the obligation of medical confidentiality.

Responsibility of the manufacturer

In order to assess the prerequisites for the legal responsibility of parents for improper care of the minor, it is important to establish whether parents exercise due diligence in terms of supervision. Such supervision includes exercising care, especially in situations or places where the minor may experience harm, such as a public road or a large-format shop, but also in the home environment, through the appropriate selection of toys [27]. Under current law, all toys should bear appropriate markings, including the most important ones concerning age restrictions and whether the child can play with the object alone or under adult supervision. Toys and their parts and, in the case of fixed toys, their fastenings, must have the requisite mechanical strength and, where appropriate, stability so that the loads to which they are subjected during use do not cause them to break or become detached in such a way as to present a risk of physical injury or harm to the user. Accessible edges, protrusions, cords, cables and fastenings on toys must be designed and manufactured in such a way as to minimise the risk of injury from contact with them. Toys must be designed and manufactured in such a way that they do not present a hazard or that hazards caused by the movement of their parts are minimised [28].

In jurisprudence, there are cases of holding the manufacturer of preparation, as a result of which a minor suffered health impairment, jointly responsible. In one of the cases, the court examined whether the product ingested by a minor had appropriate protection against opening and whether its label was correct. A manufacturer of a highly corrosive product admitted to general circulation and available in most shops on the lower shelves should eliminate the danger of easy opening and consumption of this product, which is in accordance with the principles

of social co-existence, especially the principle of health protection, protection of young children and not exposing them to avoidable danger. Having analysed the facts of the case, the Court of Appeal concluded that the defendant's conduct and the momentary inattention of the parents were co-factors in the tragic event. It was not possible to consider them as exclusive (and thus to assume, as the plaintiff would have had it, that the sole cause of the event was the defendant's defective conduct or — as the defendant requested — that the parents should bear sole responsibility for it). Undoubtedly, a proper reaction by the parents could have prevented the tragedy. Had the unsecured product not been in the shop, it would not have happened either [29].

A product is considered to be movable even if incorporated into another movable or immovable, as well as animals and electricity [30]. A product is (considered) unsafe if it does not ensure the safety that can be expected, taking into account the normal use of the product. Whether a product is safe or not is determined by the circumstances at the time it was placed on the market, in particular how it was presented on the market and what information was given to the consumer about the product's characteristics. A product may not be deemed unsafe simply because a similar improved product was later placed on the market. Before giving a toy to a child, parents should check whether it has small hidden parts that the child can swallow. It is the duty of the parents in the first instance to prevent a minor from swallowing a foreign body. As pointed out by the Court of Appeal in Łódź in one of its judgments, it is not unlawful to manufacture an unsafe product and place it on the market if the potential buyer, based on the available information, can learn about the properties of the unsafe item that the buyer intends to purchase and use for its intended purpose. On the other hand, it is unlawful, since it is contrary to the principle of fairness to the buyer and fairness in commercial relations to market products with unsafe characteristics, even though available commercial information indicates otherwise [31]. Therefore, it should be concluded that the manufacturer, when placing a product on the market, is not responsible for its manufacturing and marketing, because it is the purchaser (parents) who have the obligation to find out, based on available information, that the product (toy) is unsafe.

Summary

As long as children continue to put objects in their mouths, foreign body ingestion will be a problem that paediatricians will have to deal with. As technology develops faster and faster, new toys are being developed that have in their structure many small parts that children like to put in their mouths. Their size can cause swallowing that goes unnoticed by the parent. While the ingested object can be pointed out by the parent, the chemical is often found outside the original packaging, so the guardian may not be able to precisely identify the type of substance ingested, making it difficult to provide prompt and accurate treatment. Parental authority is a fundamental institution of family law and is inextricably linked to the protection of the child's best interest. Neglect in exercising supervision and care over a child, defined as failure to meet the child's needs necessary for his or her proper development, may lead to an offence under Article 106 of the Misdemeanours Code, according to which anyone who, having the duty of care or supervision over a minor under 7 years of age or over another person incapable of recognizing or defending himself/herself against danger, allows that person to remain in circumstances dangerous to human health, is subject to a fine or reprimand. Parents should exercise due diligence in their care and supervision of a minor. To determine the responsibility of the parents for the damage, it is necessary to analyse all the circumstances, including whether due diligence was exercised on their part. Where parents fail to exercise their rights and duties under parental authority, the guardianship court may issue an order restricting or, in extreme cases, withdrawing their parental authority. Responsibility for the ingestion of foreign objects by a child will lie primarily with the parent, but also with the guardian who supervised the child. It is therefore important to educate parents and carers to pay more attention to where dangerous objects are placed. This will reduce the proportion of patients with the aforementioned conditions. The responsibility of the toy manufacturer is equally important as that of parents and carers. The manufacturer, in fact, before placing a product on the market, should ensure that the toy is appropriately labelled, so that parents can verify that the toy is suitable for children to play with.

Conflict of interest

None declared.

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Streszczenie

Połknięcie ciała obcego przez pacjentów pediatrycznych stanowi częsty problem w praktyce medycznej. Celem artykułu jest analiza obrazu klinicznego, etiologii i przedstawienie uwag dotyczących odpowiedzialności prawnej, jaką może ponieść w takim przypadku opiekun lub producent. Prezentowane dane pochodzą z placówki medycznej w Kielcach, zbierane w ciągu trzech lat i zostały przeanalizowane w sposób retrospektywny. W badaniu udział wzięło 75 dzieci. Edukacja opiekunów, by większą uwagę przykładali do miejsc odkładania przedmiotów niebezpiecznych czy kupowania zabawek składających się z drobnych części, może się przyczynić do zmniejszenia odsetka pacjentów z opisanymi przypadłościami.

Słowa kluczowe: pacjent pediatryczny, ciało obce w układzie oddechowym, ciało obce w układzie pokarmowym, odpowiedzialność za nadzór nad małoletnim, odpowiedzialność producenta

Folia Cardiologica 2023; 18, 3: 149–154

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