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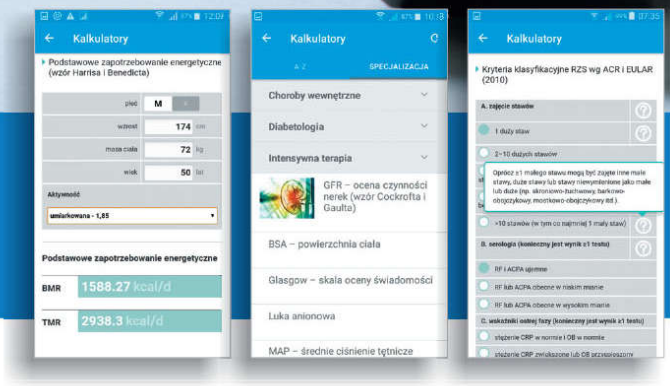

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Teamwork in trauma resuscitation

Zespołowy model resuscytacji okołourazowej

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Abstract. The purpose of the paper is to evaluate the duration of trauma resuscitation within the Trauma Resuscitation Area in patients with multiple injuries, and the possible time-savings related to introducing a teamwork model. The retrospective evaluation includes the medical documentation of patients treated in the Emergency Department of the Warsaw Military Institute of Medicine in 2015. The calculation covers the median value, and the first and third quartile of the total activity time of the trauma team in the resuscitation area. The second stage includes repeated simulation of resuscitation in a trauma room setting, using a CPR manikin. The resuscitation times were measured for trauma teams of two or three members. The results are presented in tabular and descriptive forms. The introduction of a trauma teamwork model in trauma patient care may shorten resuscitation time and increase its effectiveness. Regular team training and improvements in communication within the trauma team are key factors that improve the quality of the treatment process.
Key words: Trauma Team, multiple injuries treatment, medical simulation

Streszczenie. Celem pracy była ocena czasu trwania resuscytacji okołourazowej prowadzonej w obrębie obszaru resuscytacyjno-zabiegowego SOR wobec chorych z wielonarządowymi obrażeniami ciała oraz ocena możliwości skrócenia jej trwania poprzez wdrożenie zespołowego modelu postępowania. Przeprowadzono retrospektywną ocenę dokumentacji medycznej chorych leczonych w 2015 roku w SOR CSK MON WIM w Warszawie (SOR WIM). Obliczono medianę oraz pierwszy i trzeci kwartyl całkowitego czasu działania zespołu urazowego w obszarze resuscytacyjno-zabiegowym SOR. W dalszej kolejności przeprowadzono powtarzalne symulacje działań resuscytacyjnych w warunkach sali zabiegowej, wykorzystując fantom ćwiczebny. Zmierzono czas trwania czynności resuscytacyjnych wykonywanych przez zespoły dwu- i trzyosobowe. Wyniki przedstawiono w formie tablarycznej i opisowej. Wdrożenie zespołowego modelu postępowania z pacjentami urazowymi może skrócić czas trwania resuscytacji okołourazowej i zwiększyć jej efektywność. Regularne treningi zespołów udzielających pomocy poszkodowanym oraz poprawa komunikacji pomiędzy osobami podejmującymi czynności ratunkowe mają kluczowe znaczenie dla poprawy jakości udzielanej pomocy.
Słowa kluczowe: zespół urazowy, leczenie wielonarządowych obrażeń ciała, symulacja medyczna

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Introduction

Treating a patient with multi-organ injuries is a continuous process. It starts at the site of the event, continues during transportation, at the hospital emergency department (HED), and is completed at a specialist department. The time from the injury to definitive treatment, often provided in the operating room, is a crucial element of this process. Due to its importance, this time is referred to as the "golden hour" [1-4]. The speed and effectiveness of the actions undertaken are of great importance to the survival, degree of disability or future quality of life for the patient.

According to an Institute of Rescue Medicine Report from 2002, 20% of casualties admitted to hospitals died within 6 hours of hospital treatment. In the view of this document, 13.3% of deaths could have been avoided with better workflow, a wider range of diagnostic tests, proper anti-shock management or a faster decision regarding surgical intervention [5].

In order to improve survival rates following the most severe trauma, in 2010 a network of trauma centres was created in Poland, based on 14 specialist hospitals. They were established to provide comprehensive and multispecialty healthcare for patients suffering from severe injuries. Presently, the centres are functionally separated parts of hospitals, allowing for fast diagnosis and treatment of trauma patients, according to the current science in this area [6, 7].

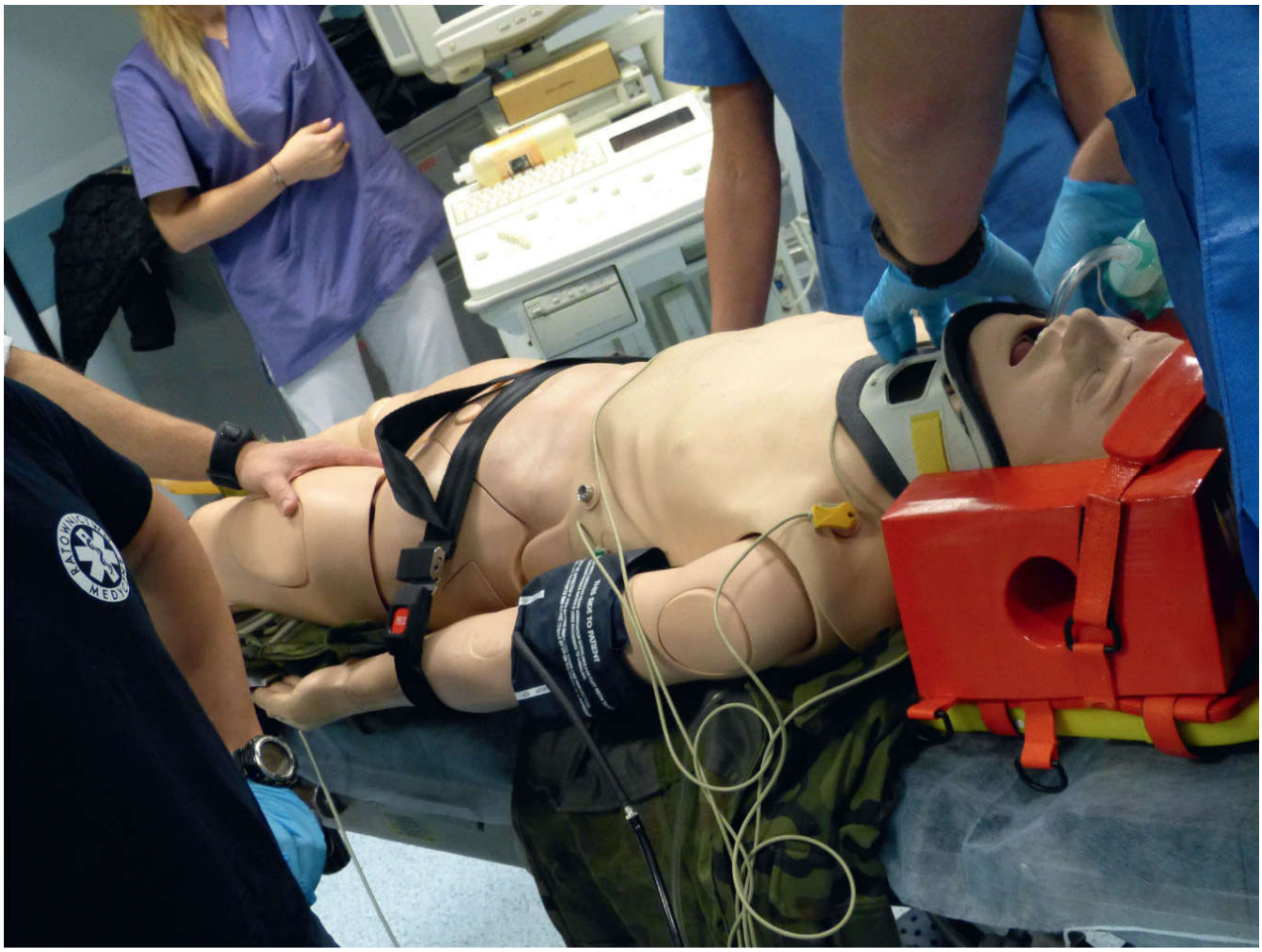

Figure 1. CPR manikin used in simulated trauma resuscitation. Operating Room of ED.
Rycina 1. Fantom wykorzystywany w symulowanej resuscytacji okołourazowej. Sala zabiegowa SOR.

The principles of resuscitation of trauma patients are included in management standards, based on the guidelines developed by scientific associations. Advanced Trauma Life Support (ATLS), a set of recommendations prepared by the American College of Surgeons, has played a major role in that respect for years [8-10]. The problem of management of patients with multiple and multi-organ injuries is also explored in numerous publications and scientific studies. Nevertheless, no significant progress is observed in the current medical knowledge in this field or in the diagnostic and therapeutic options offered by treatment facilities. This is mostly due to the financial limitations of the centres treating multi-organ trauma. Therefore, the only option to improve the outcomes for trauma patients is to improve the organisation of the work of trauma teams, in order to reduce the time of resuscitation and preliminary diagnostics in the HED, and to introduce the definitive treatment in the operating room sooner. Our own experience, as well as literature data, suggest that this is possible if a teamwork model for the management of trauma patients treated in the HED is introduced.

Aim of the study

The aim of this study is to assess the duration of trauma resuscitation performed on patients with multi-organ injuries in the Trauma Resuscitation Area of the HED, as well as to evaluate the possibility of reducing this time by implementing a teamwork management model.

Methods

In order to assess the duration of trauma resuscitation, defined as the full scope of preliminary diagnostics and early treatment of injuries, a retrospective assessment of the medical record of patients treated in 2015 at the HED of the Central Clinical Hospital of the Ministry of National Defence, Military Institute of Medicine in Warsaw (MIM HED) was performed. The analysis covered the time between the transfer of the trauma patient by the Medical Rescue Team (MRT) to the HED trauma team and the imaging diagnostic tests in the CT laboratory in the case of stable patients, or urgent surgical treatment in the case of critical patients. The median and the first and third quartiles of the total time of work of the trauma team in the Trauma Resuscitation Area were calculated. In every case the protocol of trauma resuscitation followed the ATLS guidelines, and covered the initial assessment (ABCDE – airway patency and C-spine stabilisation, respiratory assessment, circulation assessment and neurological exam, followed by undressing the patient), monitoring of the vital functions (SBP, HR, RR, SaO_2), collection of blood samples for laboratory tests, and second assessment (trauma examination according to ITLS and FAST), with concurrent performance of rescue procedures, following the medical indications. The results are presented in tables and described.

To assess the possible reduction of the duration of trauma resuscitation, repeated simulations of resuscitation procedures were carried out in the operating room, following the above protocol, with the use of a manikin and medical equipment used in the HED (Fig. 1). The duration of resuscitation activities performed by two- and three-person teams was measured. The results were analysed statistically, and presented in tables.

Results

The adopted methods indicate that the MIM HED treated 321 patients with multiple and multi-organ trauma in 2015.

Table 1. Duration of trauma team action in resuscitation area (hh:mm:ss)
Tabela 1. Czas działania zespołu urazowego w obszarze resuscytacyjno-zabiegowym SOR (gg:mm:ss)

	1st quartile	median	3rd quartile
Time	00:29:00	00:38:00	00:48:00

Table 2. Duration of trauma patient simulated resuscitation
Tabela 2. Czas trwania symulowanej resuscytacji pacjenta urazowego

	2-person team	3-person team	difference
1st test	00:03:35	00:02:44	**20%**
2nd test	00:03:06	00:02:27	**21%**
3rd test	00:03:02	00:02:15	**25%**
	11%	18%	

Table 1 presents the mean times of the trauma team acting in the resuscitation area, which were calculated according to the adopted methods. Table 2 presents the measured times of the simulated resuscitation of a trauma patient, performed in the operating room, using a manikin, in two- and three-person teams.

In both groups, the duration of resuscitation in each subsequent test was shorter. In the third test, the resuscitation was shorter by 11% and 18%, respectively. The duration of trauma resuscitation performed by 3-person teams was significantly shorter compared to the same activities conducted by 2-person teams. The analysis of the results demonstrated an improvement in subsequent tests by 20%, 21% and 25%, respectively. The best result of a three-person team was 38% better than the worst result achieved by a two-person team.

Discussion

Since medical personnel need to provide patients suffering from the most severe trauma with specialist treatment, they have to be highly competent and familiar with the medical science related to emergency cases and the care of patients with multi-organ trauma. The rules for the resuscitation and initial treatment of trauma patients indicate that the personnel are obliged to perform intense rescue activities from the moment the patient enters the HED. These activities should be consistent with prehospital management, and they should result in the diagnosis and treatment of life-threatening injuries, determination of the nature and scope of other pathologies, as well as establishing diagnostic and therapeutic priorities [11-13].

Western trauma centres operate according to procedures specifying the criteria for activating a trauma team, its members, the location of the members by the patient's bed and their tasks [12-14]. Trauma teams are activated when a trauma patient needs to be resuscitated. Every member of a trauma team has different tasks and the members carry out rescue procedures almost simultaneously, which reduces the duration of resuscitation activities. The tasks of a trauma team include determining the character and scope of injuries sustained, resuscitation and stabilisation of vital functions, setting priorities and the order of treatment, as well as preparing and transporting the patient to the place of definitive treatment [13].

Considering the literature data, the optimal results for the treatment of patients with multi-organ trauma require teamwork-based treatment and pre-planning of the activities of team members during the trauma-related resuscitation phase [14-16]. This principle allows the team members to perform their assigned tasks simultaneously, which reduces the duration of preliminary treatment and thus increases the likelihood of survival of the trauma patient.

The study of the data regarding the HED at the Military Institute of Medicine reveals that the median time of trauma resuscitation performed in the resuscitation area was 38 minutes and the first and the third quartiles were 29 and 48 minutes, respectively. The subsequent medical simulation demonstrated that it is possible to reduce the duration of resuscitation activities by 20-25%, if a trauma centre implements a teamwork-based action model, and assigns particular tasks to individual team members. The collaboration of the trauma team was further improved by proper information flow between the personnel members performing the rescue activities. Clear, concise messages and, importantly, acknowledgement of their reception, followed by proper feedback, significantly improved the team's effectiveness and helped to eliminate potential errors. According to the literature data, changing the work organisation of trauma teams reduces the time to commencement of life-saving procedures, thereby reducing both early and late trauma fatality [14-16]. An optimal level of collaboration between the team members is an important factor affecting efficient rescue action. It is possible to achieve with frequent and intensive training, which results in an improved and sustained ability to provide help by all the team members. The effectiveness of the trauma team depends on numerous factors, such as knowledge and skills, the work environment and the ability to deal with the emotional burden induced by the tasks performed [16]. Frequent trainings using various scenarios, and working in mixed teams (physician, nurse, paramedic) significantly improve the efficiency, and reduce the time of rescue action. They also limit the stress that adversely affects the decision-making process and situational awareness in individual team members, including mutual monitoring and ongoing control of the quality of the procedures. Practising simulated rescue procedures allows every healthcare professional to learn the weak and strong points of other team members, to predict their needs, and to constantly improve the quality and effectiveness of individual activities.

Debriefing [16] is an indispensable element. It consists of analysing the patient management, discussing the actions performed, detecting weak points and deviations from the management guidelines, and drawing conclusions in the "lesson learned" pattern, which enables each person undertaking rescue activities to assess their level of knowledge and skills. Debriefing should be based on comments and observations from each person engaged in the rescue action, and it should result in concrete conclusions, leading to improved teamwork quality. The implementation of a "more we, less me" approach, through an emphasis on the work of the team perceived as a group of equal partners, sharing the responsibility for the final outcome of the decisions taken, significantly affects the long-term improvement of the collaboration.

The Polish system for the treatment of trauma patients needs improvement in a number of aspects. Patients with multiple and multi-organ injuries who are admitted to an emergency room should be provided with medical care by a highly-qualified team capable of immediately starting effective and well-organised resuscitation activities, which result in stabilisation of the patient's condition, as well as identifying and definitively treating the trauma sustained. In order for rescue activities to be optimal, trauma team members should perform their clearly pre-defined tasks concurrently [13, 16]. Without prior planning of the rescue action, the initial treatment of the trauma patient may cause chaos, decreasing the effectiveness of patient care and increasing the risk of diagnostic errors. In view of the above, it is crucial that the teamwork model of management of trauma patients is implemented in HED and trauma centres.

Conclusions

- Implementation of the teamwork model of management of trauma patients may reduce resuscitation times.
- Regular training based on medical simulations can significantly improve the effectiveness of the work of trauma teams.

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Effect of Simvastatin therapy on the serum concentration of matrix metalloproteinases

Wpływ leczenia simwastatyną na stężenie surowiczych metaloproteinaz

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Abstract. Statins exert a protective effect on the lungs, inhibiting the pro-inflammatory MMP induction which is crucial in COPD pathogenesis. The aim of this study was to assess the effect of a three-month simvastatin treatment of selected MMP concentrations in blood serum on lung function and clinical parameters in patients with stable COPD. A prospective single-center study was conducted in 39 males and 11 females (aged from 47 to 80 years) randomly allocated to two groups: the study group - receiving simvastatin (Zocor 40 mg) and the control group - not receiving the drug. A total of 26 patients in the statin group and 24 in the control group completed the study. No significant differences were found between the study group and control group in respect of mMRC results (p=0.6458), spirometry parameters measured with FEV_1%N, FVC% N and FEV%FVC and in concentration changes of MMP-1 (p=0.6468), MMP-9 (p=0.0651) and MMP-12 (p=0.3309). The treatment had a positive effect (p=0.0053) on the CAT results of the COPD clinical course. A significant decrease in MMP-1 concentration (p=0.0454) in the statin group in comparison with the control group was shown only in the subgroup of patients with FEV_1 <50%N. In stable COPD, Simvastatin treatment has no significant effect on the decrease in serum concentration of specific MMP-1, MMP-9 and MMP-12, crucial in disease pathogenesis.
Keywords: chronic obstructive pulmonary disease, metalloproteinases, statins

Streszczenie. Statyny wywierają ochronny wpływ na płuca, co może wynikać z hamowania indukcji prozapalnych metaloproteinaz *[matrix metalloproteinase* - MMP), istotnych w patogenezie przewlekłej obturacyjnej choroby płuc (POChP). Cel. Ocena wpływu trzymiesięcznego leczenia simwastatyną na stężenia wybranych surowiczych MMPs, funkcję płuc oraz parametry kliniczne u chorych na stabilną POChP. Materiał i metoda. Badanie prospektywne jednoośrodkowe u 39 mężczyzn i 11 kobiet (47-80 lat) przydzielonych losowo do grupy badanej - leczonej simwastatyną (Zocor 40 mg) i kontrolnej - nieotrzymującej leku. Wyniki. Badanie ukończyło 26 chorych w grupie statyny i 24 z grupy kontrolnej. Nie stwierdzono istotnych różnic w zakresie wyników mMRC (p = 0,6458), parametrów spirometrycznych mierzonych FEV_1%N, FVC% N, FEV%FVC oraz zmian stężeń MMP-1 (p=0,6468), MMP-9 (p=0,0651) i MMP-12 (p=0,3309) pomiędzy grupami. Zastosowane leczenie wpłynęło korzystnie (p=0,0053) na przebieg kliniczny POChP mierzony testem CAT. Istotne zmniejszenie stężenia MMP-1 w grupie statyny w porównaniu z grupą nieleczonych chorych wykazano tylko w podgrupie pacjentów z FEV_1 <50%N (p=0,0454). Wnioski. Leczenie simwastatyną u chorych ze stabilną POChP nie wpływa znamiennie na surowicze stężenia swoistych MMP-1, MMP-9 i MMP-12 istotnych w patogenezie choroby.
Słowa kluczowe: przewlekła obturacyjna choroba płuc, metaloproteinazy, statyny

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Introduction

Chronic obstructive pulmonary disease (COPD) is a complex, progressive disease posing a significant health-related, social and economic problem. The underlying chronic inflammation causes not only local lesions in the respiratory system, but also affects the entire body, and the course of coexisting conditions.

For years, spirometry has been the basic and most commonly used test of the severity and progression of the disease, despite the fact that it is not closely correlated with the clinical symptoms and other quality of life indicators [1]. New, well-defined biomarkers for the disease are being sought to enable its classification, the monitoring of its course and therapeutic effectiveness. Recently, the role of metalloproteinases in the pathogenesis of COPD has been emphasised. Their excessive local effect contributes to the promotion of destructive processes, which triggers compensation mechanisms, resulting in emphysema lesions. Their

significantly elevated concentrations are correlated with deteriorated pulmonary function, whereas in the lungs of healthy individuals they are practically absent [2].

In COPD patients, compared to symptomatic and "healthy" smokers, the highest level of elastin degradation was demonstrated, correlated with excessive MMP-9 secretion by macrophages [3], and with the degree of pulmonary functional impairment [4, 5] increasing further in the exacerbation phase [6].

MMP-12 is not only a direct cause of the degradation of pulmonary parenchyma, but also demonstrates pro-inflammatory properties, as it affects the release of TNF-alpha from macrophages [7], and the synthesis and release of IL-8 from the bronchial epithelial cells. The fragments of extracellular matrix (ECM) produced in the process of proteolysis demonstrate a chemotactic response to inflammatory cells [8]. In transgenic mice with a deactivated MMP-12-coding gene, no emphysema lesions were found, despite exposure to tobacco smoke [9], which inspired the studies on the possibility of using MMP inhibition in therapy and the prevention of COPD.

Increased expression of the human MMP-1 gene in the lungs of transgenic mice was associated with the development of emphysema shortly after birth [10]. Its over-expression in the human bronchial epithelial cells was found in smokers and COPD patients [11].

The results of experimental and clinical studies reveal evidence for the relation between MMP-1, MMP-9 and MMP-12 and the presence of emphysema and COPD pathogenesis.

Statins demonstrate a protective effect on the lungs, inhibiting the development of experimentally induced emphysema, which may result from blocking the induction of pro-inflammatory MMPs [12], or from the direct effect on fibroblasts [13]. Statins limit neutrophil inflammation by inhibiting the secretion of IL-8 and granulocyte-macrophage colony-stimulating factor (GM-CSF) from the bronchial epithelial cells [14], which demonstrates a protective effect on the development of emphysematous lesions due to the activity of elastase and other proteases [12].

The aim of the study

The principal aim of the study was to assess the effect of a three-month long simvastatin therapy on the blood serum concentrations of selected MMPs. Moreover, their usefulness in the assessment of disease severity and of the effectiveness of the applied treatment was evaluated.

Material and method

The study was conducted between June 2010 and April 2014 in patients diagnosed with COPD, treated at the Clinical Department of Pulmonology and Allergology of the Military Research Hospital and Polyclinic no. 10, and the Pulmonology Clinic, in the stable phase of the disease. The study protocol was approved by the Bioethical Committee of the Military Institute of Medicine in Warsaw. All patients received detailed information about the purpose and scope of the study, and signed an informed consent form prior to the start of study procedures. Sixty-eight COPD patients were included in the study; active or former smokers with a history of at least 10 pack-years of tobacco smoking, without a history of exacerbation within 6 week before signing the consent. Finally, 50 patients were qualified, and randomised into two groups. The study group (n = 26) received simvastatin (Zocor, MSD) at a dose of 40 mg/d for 3 months, and the control group (n = 24) did not receive the medicine. The analysed group comprised 11 (22.0%) females and 39 (78.0%) males aged 47-80 years old. The mean age of the females was 61.9 ± 4.9 years, which did not differ significantly from the age of the males, 62.0 ± 8.8 years (p = 0.9814).

COPD was diagnosed based on spirometric test results, GOLD criteria and medical history. Due to the small number of patients with a mild (FEV_1 ≥80%) or very severe obstruction (FEV_1 <30%), further analysis involved the two groups of patients being subdivided according to disease severity, with an FEV_1 percentage value of 50% as the criterion. The first subgroup comprised patients with a severe or very severe obstruction (FEV_1 <50%), and the second subgroup included those with a mild or moderate obstruction (FEV_1 ≥50%).

The exclusion criteria were as follows:

- presence of large emphysematous bullae or bronchiectasis in radiological examinations,
- significant abnormalities in the thoracic anatomy,
- chronic circulatory insufficiency, NYHA III or higher, or signs of its exacerbation,
- acute coronary syndromes,
- myocardial infarction or unstable coronary disease within 6 months prior to signing the consent.
- history of percutaneous coronary intervention or aortocoronary bypass within a year prior to the study,
- insufficiency of other organs,
- neoplastic disease,
- coagulation disorders,
- early post-operative period or recent (within 3 months) serious trauma,
- BMI <20.

Table 1. Baseline characteristics of patients
Tabela 1. Wstępna charakterystyka chorych

	Study group N = 26	Control group N = 24	P
	Mean ±SD *Median (Q1-Q3)	Mean ±SD *Median (Q1-Q3)	
Age (years)	61.3 ± 8.3	61.3 ± 8.3	0.5584
Males (%)	69.2	87.5	0.1110
Present smokers (%)	26.9	29.2	0.8756
mMRC points	1.62 ± 0.70	1.83 ± 0.76	0.2519
CAT points	16.35 ± 6.18	16.50 ± 6.23	0.9306
FEV_1 (%)	58.9 ± 18.8	57.0 ± 18.7	0.7233
FVC (%)	95.3 ± 16.5	96.2 ± 17.1	0.8594
FEV1/FVC	50.0 ± 13.6	47.0 ± 14.4	0.4585
CHL (mmol/l)	5.56 ± 1.36	5.68 ± 1.20	0.7518
LDL (mmol/l)	3.75 ± 1.22	3.80 ± 1.08	0.8894
HDL (mmol/l)	1.32 ± 0.35	1.51 ± 0.46	0.1058
TG (mmol/l)	1.89 ± 0.88	1.52 ± 0.46	0.0762

CAT – COPD Assessment Test, FEV_1 – forced expiratory volume in one second, FVC – forced vital capacity, HDL – high-density lipoprotein, LDL – low-density lipoprotein, mMRC – modified questionnaire of the Medical Research Council, SD – standard deviation, TG – triglycerides

Table 2. Concentrations of matrix metalloproteinases in each group
Tabela 2. Stężenia metaloproteinaz w analizowanych grupach

Metalloproteinases (pg/ml)	Study group		Control group		P
	Median	Q1-Q3	Median	Q1-Q3	
MMP-1	98.1	29.8 - 228.3	69.9	27.8 - 133.8	0.4736
MMP-9	637.5	289.1 - 1495.0	453.2	98.8 - 913.7	0.2262
MMP-12	3.76	1.80 - 8.26	2.00	1.20 - 9.11	0.5258

All patients were assessed in a medical interview, including a survey questionnaire: a modified Medical Research Council questionnaire (mMRC) [15], a COPD Assessment Test (CAT), and in a physical examination. Then, each patient received a spirometric examination, an ECG and an echocardiographic test, and venous blood samples were collected for laboratory tests. The blood was collected in the morning, before a meal, using Greiner Bio-one vacuum tubes. Serum assays included a lipid profile and basic laboratory tests. The remaining blood serum was frozen at -80°C and stored for MMP determination. Procarta Immunoassays kits by Affymetrix and a Luminex 100 device were used to determine MMP-1, MMP-9 and MMP-12 concentrations. The assays are based on the xMAP technology, using microspheres stained with fluorescent dyes.

The spirometric examinations were performed using a MasterScope device (JLAB version 5.21) by Jaeger, before and 20 minutes after the inhalation of 40 µg of salbutamol. After three months, all patients were re-subjected to the same study procedures.

Table 3. Changing mMRC, CAT and spirometry components in each group
Tabela 3. Zmiana mMRC i CAT składowych badania spirometrycznego w analizowanych grupach

Change in the parameter	Study group N = 26	Control group N = 24	P
	Mean ±SD	Mean ±SD	
Δ mMRC (points)	-0.08 ± 0.39	0.13 ± 0.34	0.6458
Δ CAT (points)	-1.80 ± 2.29	0.25 ± 2.61	0.0053
Δ FEV_1 (l)	0.05 ± 0.18	0.06 ± 0.16	0.8631
Δ FEV_1 (%)	1.9 ± 5.7	1.8 ± 5.1	0.9557
Δ FVC(MAX) (l)	0.11 ± 0.40	0.08 ± 0.33	0.7611
Δ FVC (%)	-2.5 ± 9.1	2.9 ± 8.0	0.8792
Δ FEV/FVC (%)	2.5 ± 14.6	0.2 ± 5.5	0.3930

CAT – COPD Assessment Test, FEV_1 – forced expiratory volume in one second, FVC – forced vital capacity, mMRC – modified questionnaire of the Medical Research Council, SD – standard deviation

Statistical analysis

The study results obtained were analysed statistically. The Lilliefors test was used to verify the normality of the distribution of the variables. For the tests with a distribution similar to normal, the arithmetic mean and standard deviation (SD) were derived, a t-Student's test for independent and dependent variables was used to compare the means. Levene's test was used to assess

the equality of variances. If the distribution varied considerably from the normal range, the median, and the first and third quartiles were calculated, and the significance of the differences between the groups was verified using the non-parametric Mann-Whitney U test and the Wilcoxon test. The Chi-square test (c^2) was used to assess the proportions in the groups. The correlations between the variables were evaluated with Spearman's r correlation coefficient. The statistical significance was established at p = 0.05. The calculations were performed using the Statistica 7.1 software.

Results

The initial patient characteristics are presented in Table 1.

The study group comprised 18 (69.2%) males and 8 (30.8%) females, and the control group comprised 21 (87.5%) males and 3 (12.5%) females. the mean number of pack-years was 39.3 ± 15.9 in the study group and 41.8 ± 16.4 in the control group.

The groups did not differ considerably in demographic characteristics, tobacco use, therapy of COPD or comorbidities, initial spirometic parameters or lipidogram components. The results are presented in Table 2.

Results after the treatment period

Clinical course

The applied treatment significantly (p = 0.0053) affected the clinical course of COPD measured with CAT. In the study group, a significant (p = 0.0006) reduction by 1.80 ± 2.29 points was observed, whereas in the control group, an insignificant (p = 0.6431) increase by 0.25 ± 2.61 points was found. No significant effect of the treatment with the statin on the mMRC score was observed. The results are presented in Table 3.

After 3 months of treatment, in the study group, a significant reduction in total cholesterol concentration (p < 0.0001), LDL concentration (p < 0.0001) and triglyceride levels (p = 0.0030) was found.

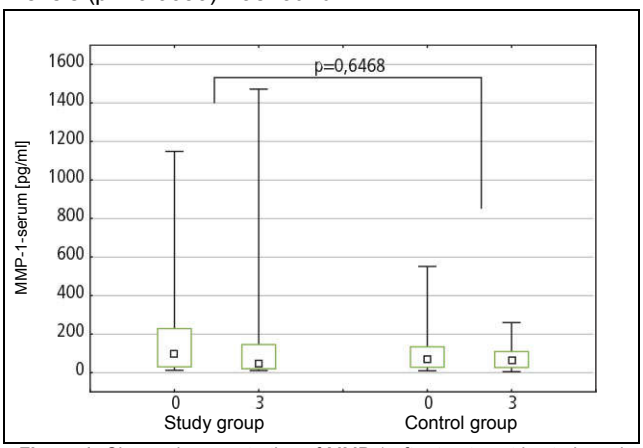

Figure 1. Changed concentration of MMP-1 after treatment in study and control subgroups

Rycina 1. Zmiana stężenia MMP-1 po leczeniu w grupie badanej i kontrolnej

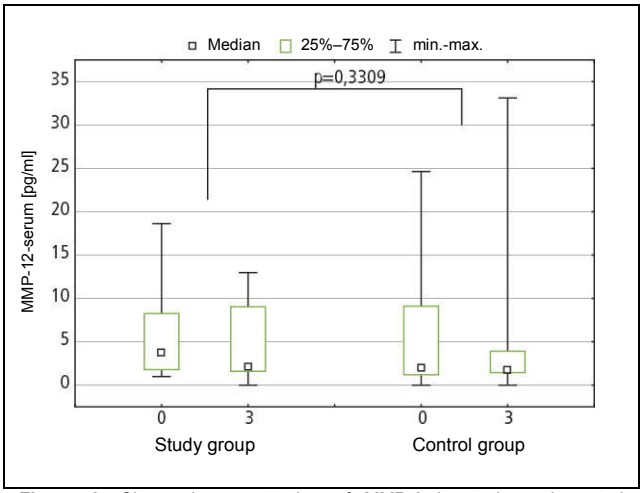

Figure 2. Changed concentration of MMP-9 in study and control subgroups after treatment

Rycina 2. Zmiana stężenia MMP-9 po leczeniu w grupie badanej i kontrolnej

Table 4. Concentration of matrix metalloproteinases in each group
Tabela 4. Stężenie metaloproteinaz w analizowanych grupach

Metalloproteinases (pg/ml)	Study group			Control group		
	At the beginning of the study	After 3 months of treatment	P	At the beginning of the study	After 3 months of treatment	P
	Median Q1-Q3	Median Q1-Q3		Median Q1-Q3	Median Q1-Q3	
MMP-1	98.1 29.8 - 228.3	46.5 19.7 - 145.6	0.1618	69.9 27.8 - 133.8	64.1 26.7 - 109.1	0.0291
MMP-9	637.5 289.1 - 1495	480.9 198.0 - 987.7	0.0163	453.2 98.8 - 913.7	458.2 99.0 - 897.2	0.4140
MMP-1/2	3.76 1.80 - 8.26	2.17 1.60-9.04	0.1060	2.00 1.20 - 9.11	1.80 1.45-3.91	0.8137

Metalloproteinases

The treatment had different effects on the concentrations of the analysed metalloproteinases. The results are presented in Table 4 and in Figures 1-3.

An insignificant (p = 0.6468) decrease of serum MMP-1 concentration by 19.15 pg/ml was observed in the study group, and by 10.89 p/ml in the control group.

After three months of therapy, a significant (p = 0.0163) reduction of MMP-9 by 175.6 pg/ml was found in the study group. No significant difference (p = 0.0651) in the changes was observed between the analysed groups.

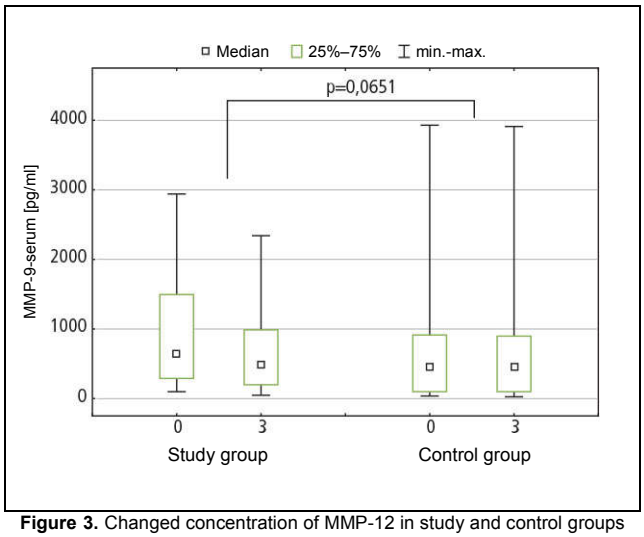

Figure 3. Changed concentration of MMP-12 in study and control groups after treatment

Rycina 3. Zmiana stężenia MMP-12 po leczeniu w grupie badanej i kontrolnej

An insignificant reduction of MMP-12 concentration by 0.620 pg/ml was observed in the study group, and no change was found in the control group. No differences in SIA were observed between the groups (p = 0.3309).

Treatment outcomes according to the severity of obstruction

Clinical course measured with mMRC and CAT

The three-month treatment period resulted in a significant improvement in the CAT point scores in the second subgroup, and an insignificant improvement in the first subgroup.

The degree of perceived dyspnoea measured according to the mMRC was insignificantly reduced in both subgroups. The results are presented in Table 5.

Lipid profile

In both subgroups, significant reductions in total cholesterol and LDL concentrations were observed, without a statistically significant difference between the subgroups. The results are presented in Table 6.

Metalloproteinases

A significant difference (p = 0.0454) in changes of MMP-1 concentrations between the subgroups was observed: MMP-1 concentration was significantly reduced by 20.8 pg/ ml in patients from the second subgroup, and insignificantly increased by 5.3 pg/ml in the first subgroup. No significant changes were found in the concentrations of the remaining MMPs. The results are presented in Table 7.

Table 5. Changed mMRC and CAT after treatment in each subgroup
Tabela 5. Zmiana mMRC i CAT po okresie leczenia w podgrupach chorych

Tests (point)	First subgroup (FEV <50%)			Second subgroup (FEV ≥50%)		
	Study group N = 9	Control group N = 10	P	Study group N = 17	Control group N = 14	P
	Mean ±SD	Mean ±SD		Mean ±SD	Mean ±SD	
Δ MRC	0.00 ± 0.50	-0.30 ± 0.48	0.2012	-0.12 ± 0.33	0.00 ± 0.00	0.1967
Δ CAT	-0.89 ± 2.47	0.50 ± 2.42	0.2326	-2.31 ± 2.09	0.07 ± 2.81	0.0129

CAT – COPD Assessment Test, mMRC – modified questionnaire of the Medical Research Council, SD – standard deviation

Table 6. Changed concentration of lipid profile components in each subgroup
Tabela 6. Zmiana stężenia składowych profilu lipidowego w analizowanych podgrupach chorych

Lipid profile components (mmol/l)	First subgroup (FEV <50%)			Second subgroup (FEV ≥50%)		
	Study group N = 9	Control group N = 10	p	Study group N = 17	Control group N = 14	p
	Mean ±SD	Mean ±SD		Mean ±SD	Mean ±SD	
Δ CHL	-1.32 ± 0.79	0.01 ± 0.25	0.0001	-1.51 ± 0.81	-0.12 ± 0.26	<0.0001
Δ LDL	-1.34 ± 0.67	0.07 ± 0.34	<0.0001	-1.48 ± 0.69	0.01 ± 0.24	<0.0001
Δ HDL	-0.01 ± 0.22	-0.02 ± 0.12	0.9077	0.10 ± 0.34	-0.19 ± 0.18	0.0072
Δ TG	-0.14 ± 0.33	0.07 ± 0.63	0.3860	-0.44 ± 0.58	0.24 ± 0.62	0.0039

Table 7. Changes in concentration of inflammatory biomarkers in study and control subgroups
Tabela 7. Zmiany stężeń biomarkerów zapalnych w podgrupie badanej i kontrolnej

Metalloproteinases (concentration)	First subgroup (FEV <50%)			Second subgroup (FEV ≥50%)		
	Study group N = 9	Control group N = 10	P	Study group N = 17	Control group N = 14	P
	Median 0.1 ± 0.3	Median Q1-Q3		Median Q1-Q3	Median Q1-Q3	
Δ MMP-1 (pg/m)l	5.3 -27.5 ± 131.6	-5.4 -26.6 ± 2.5	0.3284	-20.8 -181.9 ± -7.6	-15.1 -33.8 ± -6.2	0.04835
Δ MMP-9 (pg/ml)	-131.7 -733.9 ± 478.3	-8.4 -421.9 ± 34.6	0.7898	-175.6 477.4 ± -20.4	-18.0 135.5 ± 35.1	0.0516
Δ MMP-12 (pg/ml)	-1.28 -3.25 ± 0.21	0.00 -2.50 ± 0.20	0.8590	-0.62 -2.74 ± 0.56	0.10 -0.15 ± 1.11	0.1798

Discussion

Recently, the importance of chronic systemic inflammation in COPD has been emphasised, which is reflected in the new definition of the disease [16]. Persistent inflammation of the respiratory tract and a protease-antiprotease imbalance lead to an increased concentration of circulating inflammatory markers and cytokins, such as IL-6, CRP, fibrinogen and TNF-alpha [17], which play an important role in the development of extrapulmonary symptoms and comorbidities, e.g. cardiovascular diseases, metabolic syndrome, osteoporosis or exhaustion [18]. It is also associated with an increased risk of death due to cardiovascular incidents and lung cancer [19]. In this study, we determined concentrations of selected metalloproteinases: MMP-1, MMP-9 and MMP-12, which could be potential new markers specific for the disease's pathogenesis. After 3 months of treatment with simvastatin, no statistically significant changes in MMP-1 and MMP-12 serum concentrations were observed, compared to the control group. In the study group, the level of MMP-9 was statistically significantly elevated (0.0163), and the difference in the change between the study and control groups was at the statistical trend level (p = 0.0772).

The majority of previous studies on the effect of statins on the activity of individual MMPs assessed the material collected at the site of the ongoing pathological process: macrophages [20], vascular epithelial cells [21] or vascular smooth muscles [22], indicating a positive effect, measured by the reduction of their local expression. Relatively few of these studies focus on the effect of 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors (HMG-CoA) on the activity of metalloproteinases in COPD.

Lee et al. demonstrated that simvastatin used systemically alleviates the functional and structural damage to the pulmonary tissue induced by a 16-week exposure to tobacco smoke in rats. Korean scientists were the first to suggest that the important protective effect of simvastatin in emphysema may result from the inhibition of pro-inflammatory MMP-9 induction in the lungs [12]. This hypothesis was confirmed in further studies on isolated rat macrophages, in which MMP-9 induction with cigarette smoke extract (CSE) was inhibited. Kamio et al. demonstrated that statins could inhibit the secretion of MMPs from human foetal lung fibroblast strain (HFL-1). The authors suggest that, via this mechanism, the medicines directly improve the remodelling and reduce emphysema [13]. In a study using a murine model, Takahashi et al. demonstrated that simvastatin reverses the elatsase-induced emphysematous lesions by the inhibition of m-RNA expression of interferon, TNF-alpha and MMP-12 [23].

An analysis of the relationships between MMPs and the spirometric parameters describing the severity of the disease revealed a surprisingly significant reduction of MMP-1 concentration in the statin group, but only in the subgroup of patients with mild and moderate COPD. There are no publications assessing the relationship between MMP-1 concentration and lung function, so it is difficult to compare the results of our study with others. Only in genetic studies, Joos et al. demonstrated that the expression of the MMP-1 specific allele was associated with a rapid deterioration of pulmonary function in smokers, and with the development of emphysema [24]. Therefore, it may be assumed that the relation between MMP-1 concentration and the degree of obstruction is observed only in the COPD phenotypes involving MMP-1 polymorphisms that were not assessed in this study.

According to the available literature, the study presented is one of few evaluating the usefulness of the major groups of metalloproteinases as biomarkers of systemic inflammation in COPD patients. Clinical studies demonstrated that high serum concentrations of MMPs, especially MMP-9, may reflect an increased remodelling process. Brajer and Batura [25], who analysed MMP-9 concentrations in patients with moderate and severe COPD, compared with healthy smokers, revealed that in COPD patients, MMP-9 concentration was significantly higher than in the control group, and its values varied according to the severity of obstruction, and were negatively correlated with FEV_1 and FEV_1/FVC% values. Similarly, the study by Omachi et al., who observed patients with a relatively homogeneous COPD phenotype involving $alpha_1$-antitrypsin deficiency for a year, revealed a significant, positive correlation between plasma MMP-9 concentration, more frequent COPD exacerbations, accelerated reduction of TLCO (transfer factor for carbon monoxide), and decreased density of pulmonary parenchyma, assessed in thoracic CT [26]. Therefore, based on the premises from the above studies, a reduction in plasma elastolytic activity, measured by MMP-9 concentration, was expected, especially in the group of patients with severe COPD, which could support the beneficial therapeutic effect of statins in the inhibition of remodelling.

In the present study, a statistically significant reduction of MMP-9 concentration was observed as a result of statin therapy; however, compared to the control group, the change was not significant. Also in a study by Kaczmarek and Sładek [27] the authors did not observe a statistically significant difference in MMP-9 concentrations in the entire group of treated patients, or any correlation between MMP-9 and the severity of the disease in analogical subgroups of COPD severity. Similarly, John and Crockcroft [27] did not find any changes in serum MMP-9 concentration after 6 weeks of treatment of patients with stable COPD. However, the dosage used by the researchers was lower, and the duration of intervention was shorter than in our study.

Due to the discrepancy between the results of individual reports, further studies are required, involving extensive clinical material, and considering the material representative for the local environment (a study is in preparation).

Study limitations

The study had a few limitations, the most significant being the relatively small size of the population studied. However, the sample was sufficient to find the baseline lack of statistically significant differences between the control group and the study group in demographic parameters, the disease advancement and the studied indicators of inflammation. Another important limitation was the determination of COPD severity based only on the spirometric parameters according to the GOLD 2009 guidelines, valid at the time of study planning. Further modifications from 2011, also taking into consideration clinical symptoms, particularly the history of exacerbations, would probably contribute to important outcomes. It was an open-label study, without placebo

control; however, the analysis focused primarily on the assessment of biochemical and spirometric parameters, independent of the placebo effect. Therefore, the demonstrated changes in these parameters should be assumed to depend on the medicine used. The patients were observed for 3 months, and the studied parameters were determined only at the beginning and at the end of the study. An extended observation period and assessment at other points in time would allow for a better evaluation of the effect of simvastatin treatment on the serum biomarkers, and the demonstration of potential correlations with clinical parameters and pulmonary function.

Conclusions

A three-month therapy with simvastatin in patients with stable COPD does not significantly reduce serum concentrations of specific MMPs relevant for the pathogenesis of the disease. Only a trend ($p = 0.0651$) of MMP-9 reduction as a result of the treatment was observed. A significant decrease of MMP-1 concentration in the group of patients receiving the statin, compared to the untreated group, was demonstrated only in the subgroup of patients with mild and moderate COPD. Therefore, a careful conclusion could be drawn that a simvastatin presents a better therapeutic effect, measured as a reduction in MMP-1 secretion, in patients with a less advanced disease, and with a lower degree of pulmonary damage. Formulating a final conclusion is difficult due to a small size of the studied groups, and the relatively short time of observation.

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Assessment of the fear of neurosurgery under general anesthesia

Ocena poziomu lęku przed zabiegami neurochirurgicznymi w znieczuleniu ogólnym

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Abstract. Patients awaiting surgery experience different levels of anxiety before general anaesthesia. The goal of this research was to assess the main source of anxiety caused by anaesthesia, and study its relationship with, among other things, gender, age and education. A questionnaire consisting of 21 questions was presented to patients a day before undergoing surgery during a pre-anaesthetic visit. The questions were related to the demographics of the patients and to their fear of anaesthesia. 100 questionnaires have been analysed. 89% of patients reported a fear of general anaesthesia (96% of females and 84% of males). Concern about the surgery was expressed by 96% of females and 78% of males. The level of anxiety increased with the patients' age (<45 y/o - 80%, >45 y/o - 95%). Prior experience with anaesthesia and neurosurgery lowered the level of fear (first anaesthetic - 94%, subsequent anaesthesia - 87%; first neurosurgery - 93%, subsequent neurosurgery - 81%). Patients with chronic diseases reported a higher level of fear than patients without (91% *vs* 86%). Level of anxiety was greater in patients having a family history of chronic disease, before brain surgeries, and in patients with higher BMI. The anxiety was lower in patients with neurological symptoms. There was no correlation between the level of anxiety and education, residence or surgery lead time. Fear of general anaesthesia is a common phenomenon in surgical patients. The anxiety is greater in females, patients over 45 and people with concurrent diseases.
Keywords: fear of anaesthesia, preoperative anxiety, questionnaires

Streszczenie. Cel. Pacjenci oczekujący na zabieg operacyjny odczuwają różnego stopnia strach przed znieczuleniem ogólnym. Celem badania było określenie głównej przyczyny lęku spowodowanego anestezją oraz opracowanie zależności stopnia nasilenia strachu w odniesieniu między innymi do płci, wieku i poziomu edukacji. Metody. Ankiety zawierające 21 pytań przekazywane były pacjentom w przededniu zabiegu podczas konsultacji anestezjologicznej. Pytania dotyczyły danych demograficznych pacjenta oraz odnosiły się do lęku przed anestezją. Wyniki. Analizie poddano 100 kwestionariuszy. 89% pacjentów zgłaszało występowanie lęku przed znieczuleniem ogólnym, w tym 96% kobiet i 84% mężczyzn. Strach przed zabiegiem operacyjnym odczuwało 96% kobiet i 78% mężczyzn. Poziom odczuwanego lęku zwiększał się z wiekiem (<45. rż. - 80%, >45. rż. - 95%). Wcześniejsze doświadczenia w dziedzinie anestezji i neurochirurgii zmniejszały poziom odczuwanego lęku (pierwsze znieczulenie ogólne - 94%, kolejne - 87%; pierwsza operacja neurochirurgiczna - 93%, kolejna - 81%). Obecność chorób przewlekłych powodowała występowanie lęku u 91%, ich brak u 86% pacjentów. Poziom lęku zwiększał się w przypadku występowania choroby przewlekłej w rodzinie, operacji w obrębie mózgowia czy dużej masy ciała pacjenta, a zmniejszał się w przypadku występowania objawów neurologicznych. Nie zaobserwowano znamiennej zależności pomiędzy odczuwaniem lęku a stopniem wykształcenia, miejscem zamieszkania czy czasem oczekiwania na zabieg. Wnioski. Niepokój związany ze znieczuleniem ogólnym jest zjawiskiem powszechnym u pacjentów chirurgicznych. Poziom lęku jest szczególnie nasilony u kobiet, u osób po 45. roku życia oraz u osób z chorobami towarzyszącymi.
Słowa kluczowe: lęk przed znieczuleniem ogólnym, niepokój przedoperacyjny, kwestionariusze

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Introduction

Fear of general anaesthesia is common among patients awaiting a surgical procedure. In the case of a planned procedure, the anxiety is associated more with the anaesthesia itself and its potential complications, than with the surgery [9]. The fear may adversely affect the initiation of anaesthesia, and disturb the patient's convalescence period [15]. A high level of anxiety results in an increased incidence of tachycardia, arrhythmia and arterial hypertension [17], as well as increasing the need for propofol and sevoflurane during the introduction of anaesthesia [6, 8]. It also increases the risk of postoperative nausea, vomiting and pain, and prolongs convalescence. Anxiolytics appear to be helpful, but their use requires special monitoring until the patient is transferred to the operating room, increasing the need for additional medical personnel [4, 16]. During the consultation with the anaesthesiologist, most of the time is dedicated to determining the patient's general condition and comorbidities. Sometimes the quality of the details about the anaesthesia delivered to the patient becomes a secondary concern. They tend to be incomplete and imprecise, which results in doubts and anxiety. Both the quantity and quality of information should be adjusted to the individual expectations of the patient [10]. The anaesthesiological consultation can calm the patient, and its significance should not be underestimated, regardless of time constraints [2].

Aim of the study

The aim of the study was to determine the principal source of fear of general anaesthesia, and to explore the correlation between the degree of anxiety and factors such as sex, age and education.

The analysis of the results will help to offer special care to the patients most predisposed to fear. A stronger feeling of safety and greater patient satisfaction will result in improved doctor-patient co-operation.

Material and methods

The study was approved by the Bioethical Committee in Łódź. Patients provided written consents to participate in the medical experiment. The study involved 100 patients awaiting surgery in the Department of Neurosurgery and Peripheral Nerve Surgery, Military Medical University Teaching Hospital in Łódź – Central Veterans' Hospital. To determine the level of anxiety, survey questionnaires comprising 21 questions were used – attachment no. 1 (sample questionnaire [Fig. 1]).

Patients received the questionnaires on the day preceding their surgery, during the anaesthesiological consultation. The exclusion criteria were as follows:

- lack of patient co-operation,
- urgent procedures,
- block anaesthesia,
- age under 18 years old,
- history of mental illness,
- patients unable to respond to questions on their own (patients in poor general condition, blind etc.).

Patients completed questionnaires independently, without the assistance of the anaesthesiologist or any accompanying people.

The results were analysed to determine the correlation between the level of fear of general anaesthesia and sex, age, education, place of residence, presence of comorbidities, neurological symptoms, type of procedure (affecting the brain / spine), time of waiting for the procedure or experience associated with possible previous general anaesthesia or neurological surgery.

Results

The study involved 100 subjects, aged 19-87 years old. Forty-five per cent of the subjects were women, 76% were from urban areas, 10% had primary education, 23% had basic vocational education, 39% had secondary education and 28% had higher education. A total of 69% of the subjects had been under general anaesthesia before. Fifty-seven percent of the subjects declared that they completely understood the information about the procedure, and 70% declared a complete understanding of the information about the anaesthesia. Eighty-nine percent of the patients reported fear of general anaesthesia, 92%- fear of pain, and 58% were afraid of nausea and vomiting. The principal cause of the fear of general anaesthesia was associated with an inability to wake up after the procedure (44%), 13% of subjects were afraid of regaining consciousness during the surgery, and 16% were anxious about the pain during the procedure. 79% of the subjects declared that the medical personnel provided them with the sense of safety: for 63% it was the anaesthesiologist, and for 53% it was the nurses.

Significant differences were found between the experience of fear by male and female patients – attachment no. 2 (Fig. 2-3): different levels of fear of general anaesthesia were reported by 96% of women and 84% of men. The degree of fear of the surgical procedure was similar: 96% in women and 78% in men.

The level of anxiety increased with age, from 80% in subjects <45 years old to 95% in those >45 years old.

Questionnaire regarding the fear of neurosurgical procedures under general anaesthesia

Complete the questionnaire by underlining the most suitable answer or crossing the right box

SEX: ☐ F ☐ M WEIGHT: ..... kg

AGE: ..... years old HEIGHT: ..... cm

EDUCATION: ☐ Primary ☐ Vocational ☐ Secondary ☐ Higher

PLACE OF RESIDENCE: ☐ city ☐ country

CHRONIC DISEASES

CARDIAC DISORDERS (ischaemic heart disease, heart attack, circulatory insufficiency)	☐ yes	☐ no	☐ I don't know
ARTERIAL HYPERTENSION	☐ yes	☐ no	☐ I don't know
RESPIRATORY DISORDERS (pneumonia, asthma, COPD)	☐ yes	☐ no	☐ I don't know
DIABETES	☐ yes	☐ no	☐ I don't know
GASTROINTESTINAL DISORDERS (gastric and duodenal ulcers, liver disorders, pancreatic disorders)	☐ yes	☐ no	☐ I don't know
NEUROLOGICAL DISORDERS (stroke, epilepsy, aneurysms, CNS tumours, degenerative disc diseases)	☐ yes	☐ no	☐ I don't know
KIDNEY DISORDERS (kidney stones, kidney failure)	☐ yes	☐ no	☐ I don't know
	☐ yes	☐ no	
NEUROLOGICAL SYMPTOMS	☐ yes	☐ no	

WHAT SYMPTOMS (provide a list): .....

.....

IS THERE A FAMILY HISTORY OF NEUROLOGICAL DISEASES ☐ yes ☐ no

WHAT DISEASES (provide a list): .....

.....

NEUROSURGICAL PROCEDURE ☐ yes ☐ no
FIRST / NOT FIRST
(underline the applicable)

Type of procedure: .....

.....

How long did you wait for the procedure: .....

.....

Understanding of the information about the surgical procedure

☐ Definitely yes ☐ Rather yes ☐ Rather no ☐ No

Understanding of the information about the anaesthesia

☐ Definitely yes ☐ Rather yes ☐ Rather no ☐ No

HAVE YOU EVER BEEN UNDER GENERAL ANAESTHESIA?

☐ yes ☐ no ☐ I don't know

ARE YOU AFRAID OF GENERAL ANAESTHESIA?

☐ Definitely yes ☐ Rather yes ☐ Rather no ☐ No

WHAT IS THE MAIN CAUSE OF YOUR FEAR OF GENERAL ANAESTHESIA? (mark one answer)

☐ Inability to wake up after the procedure ☐ Regaining consciousness during the procedure ☐ Experiencing pain during the procedure ☐ Other: .....

FEAR OF THE SURGERY

☐ Definitely yes ☐ Rather yes ☐ Rather no ☐ No

FEAR OF PAIN

☐ Definitely yes ☐ Rather yes ☐ Rather no ☐ No

FEAR OF OTHER SYMPTOMS

☐ Nausea ☐ Vomiting ☐ OTHER (WHAT SYMPTOMS? provide a list).....

THE SENSE OF SAFETY ENSURED BY:

☐ Doctors ☐ Nurses ☐ Anaesthesiologist ☐ Leaflets

Figure 1. Questionnaire about anxiety before neurosurgeries under general anaesthesia
Rycina 1. Ankieta dotycząca poziomu lęku przed zabiegami neurochirurgicznymi w znieczuleniu ogólnym

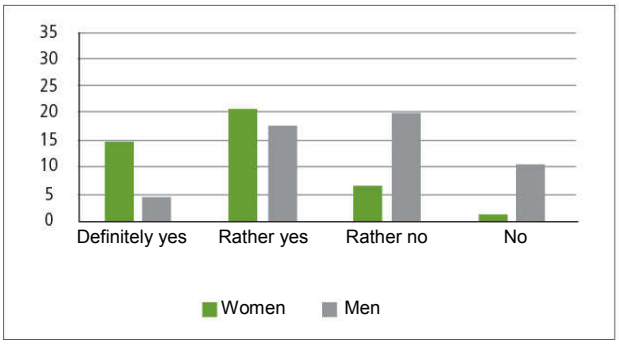

Figure 2. Level of anxiety before general anaesthesia
Rycina 2. Poziom lęku przed znieczuleniem ogólnym

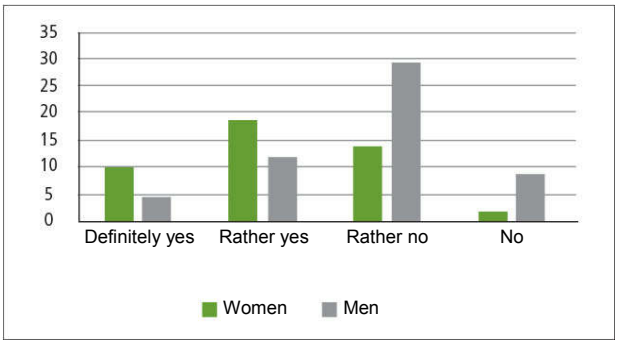

Figure 3. Level of anxiety before surgery
Rycina 3. Poziom lęku przed operacją

This correlation was probably due to a higher incidence of comorbidities, and a higher awareness of the risks associated with medical procedures at older ages (the presence of chronic diseases was the source of fear in 91% of patients, the absence of chronic diseases was associated with fear in 86% of patients). The presence of neurological symptoms, paradoxically, contributed to a reduction of the fear of anaesthesia (86% vs 90% in the absence of neurological symptoms), whereas the occurrence of a neurological disorder in the family increased the fear (100% vs 88.5% in the absence of such a disorder). The level of fear correlated with the area being operated on: it was higher in the case of brain procedures than in surgeries involving the spinal area (100% vs 88%). Previous experience with anaesthesia and/or neurosurgery contributed to a reduced level of fear (the first general anaesthesia – 94%, a subsequent one – 87%; the first neurosurgery – 93%, a subsequent one – 81%). The fear of anaesthesia increased with body weight (BMI <30 kg/m^2 – 87%, BMI >30 kg/m^2 – 100%).

No significant relationship was observed between anxiety and education level (primary – 90%, vocational – 83%, secondary – 92%, higher – 89%) or place of residence (city – 88%, country – 92%). The time of waiting for the surgery had only a slight effect on the level of fear; however, it was slightly higher in the case of a short waiting period (up to a month – 91%, over a month – 88%).

Discussion

The results presented clearly indicate that the majority of patients (89%) experienced various degrees of fear of general anaesthesia. The results of our own study are slightly higher than in the studies by Mavridou et al. (81%) and Mitchell (82.4%) [9, 11]. Both our study and numerous other studies confirm that the principal differences in experiencing fear were associated with sex, and the anxiety in women was considerably higher [14]. It is probably due to social conditioning, as demonstrating weakness and fear by men is considered undesirable. Moreover, women spend the time before surgery in a different way: they prefer the company of close friends or relatives, or talking to other patients, whereas men choose reading books and leaflets about the surgery, or listening to music [9].

Both the study by Nagramp et al. and our observations confirm that patients with chronic diseases experience higher levels of fear. The awareness of an increased risk of complications during anaesthesia is associated with higher anxiety [12]. Theories regarding the relationship between age and fear vary. Our results clearly demonstrate that patients over 45 years old report a higher degree of fear, whereas Shevde K. et al. and Clifton proposed a contrary hypothesis [1, 14]. It is surprising that previous experience with anaesthesia only reduced the anxiety to a limited degree. Possibly this is due to a lack of exhaustive information offered before the previous anaesthesia and surgery [3, 9, 14]. As the principal causes of fear of general anaesthesia, patients indicate an inability to wake up after the procedure and regaining consciousness during the surgery. The education level and place of residence do not affect the degree of anxiety [9, 14].

Patients waiting for procedures under general anaesthesia demonstrate a higher level of fear than those operated on under local anaesthesia, and the anxiety occurs earlier. They also expect more information, provided earlier [11].

A significant number of patients believe that they have not received sufficient information about general anaesthesia; according to Mavridou et al. 78%, and according to Kain et al. as many as 85% [5, 10].

The details about anaesthesia have different effects on a patient's behaviour: both excessive and insufficient information may cause anxiety. According to a study by Mitchell, 46% of patients expect detailed information, and 14% would like to receive moderately specific information. This means that 60% of patients need detailed information [11].

Conclusions

- Fear of general anaesthesia is common in patients undergoing procedures in anaesthesia.
- The anxiety is particularly strong in women patients over 45 years of age and patients experiencing comorbidities.

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Platelet parameters and metabolic disorders in patients with arterial hypertension

Parametry płytkowe a zaburzenia metaboliczne u chorych z nadciśnieniem tętniczym

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Abstract. Arterial hypertension (AH) frequently coexists with metabolic disorders, an activated inflammatory and thrombogenic state, as well as increased secretion of adipokines. Mean platelet volume (MPV) and its ratio to platelet count (MPV/PLT) was shown to relate to cardiovascular risk. The evaluation was to show any correlation between platelet parameters and the laboratory indices of cardiometabolic disorders in hypertensives. In 137 subjects (94 males, mean age 44.9 years) with untreated AH, the correlations of platelet parameters (MPV, PLT, MPV/PLT) with a concentration of, among other things, the following analytes were assessed: fasting glucose, LDL cholesterol, HDL cholesterol, triglycerides, creatinine and resistin, with special regard to gender. There were no significant differences in the mean values of platelet parameters between males and females. In females, MPV and MPV/PLT correlated significantly with the concentration of resistin (R=0.43; p=0.005; R=0.39; p=0.011, respectively), creatinine (R=0.40; p=0.007; R=0.48. p=0.001) and HDL-C (only for MPV/PLT: R=-0.32; p=0.039). No such significant relations were observed in males. In hypertensive females the platelet parameters are associated with some cardiometabolic disorder indicators, which may be pathophysiologically relevant and should be further investigated.
Keywords: resistin, arterial hypertension, platelets, cardiovascular risk

Streszczenie. Wstęp. Nadciśnienie tętnicze (NT) często współistnieje z zaburzeniami metabolicznymi, wzmożoną aktywnością zapalną i prozakrzepową, a także zwiększonym wytwarzaniem adipocytokin. Średnia objętość płytek krwi (MPV) oraz stosunek średniej objętości płytek do ich liczby (MPV/PLT) wykazują związek z ryzykiem sercowo-naczyniowym. Cel. Ocena związku między parametrami płytkowymi a wykładnikami zaburzeń kardiometabolicznych u chorych z NT. Metody. U 137 pacjentów (94 mężczyzn; średni wiek 44,9 lat) z nieleczonym NT uwzględniając płeć, oceniono związek morfologicznych parametrów płytkowych (MPV, PLT, MPV/PLT) między innymi ze stężeniem glukozy na czczo, cholesterolu frakcji HDL, LDL, triglicerydów (TG), kreatyniny i rezystyny. Wyniki. Nie zaobserwowano istotnych różnic między płciami w zakresie wartości średnich parametrów płytkowych. Jedynie u kobiet MPV i MPV/PLT korelowały istotnie ze stężeniem rezystyny (odpowiednio: R=0,43; p=0,005; R=0,39; p=0,011), kreatyniny (R=0,40; p=0,007; R=0,48; p=0,001) oraz HDL (tylko MPV/PLT: R=-0,32; p=0,039). U mężczyzn nie stwierdzono istotnych powiązań analizowanych parametrów. Wnioski. U kobiet z NT parametry płytkowe wykazują związek z wybranymi wskaźnikami zaburzeń kardiometabolicznych, co może mieć znaczenie patofizjologiczne. Wartość kliniczna tych obserwacji wymaga dalszych badań.
Słowa kluczowe: rezystyna, nadciśnienie tętnicze, płytki krwi, ryzyko sercowo-naczyniowe

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Introduction

Arterial hypertension (AH) is a disease associated with a number of metabolic disorders, chronic activation of the inflammatory process, and an increased risk of thrombosis. These may contribute to AH-related complications in various organs, and accelerated progression of comorbidities [1, 2]; therefore, researchers are looking for the markers for unfavourable pathophysiological phenomena associated with AH.

Recently, the role of platelet count (PLT) in the general systemic processes related to disturbed cardiovascular function has been emphasised. Endothelial dysfunction and chronic inflammation of the vascular wall lead to secretion of thrombocyte-stimulating cytokines. The mean platelet volume (MPV) and the ratio between MPV and the number of thrombocytes in a blood volume unit (MPV/PLT) are indicative of an inflammatory activation, e.g. with IL-3 and IL-6. It may suggest their relation to the macrophage function, as macrophages play an important role in the production of metabolically active compounds, including resistin, an adipocytokine involved in a number of cardiovascular processes [3-6].

Previously, platelet parameters as the markers of inflammation were tested primarily in gastroenterological diseases [7], laryngological disorders [8] and dermatological conditions [9]. There are also reports indicating the prognostic value of these parameters in certain groups of cardiac patients [6].

Therefore, it seems reasonable to study the relationships between platelet parameters and the recognised cardiovascular risk factors, as well as with new biochemical indicators of cardiometabolic disorders.

Aim of the study

The aim of the study was to assess the correlation between platelet parameters and selected indicators of cardiometabolic disorders in hypertensive patients.

Material and methods

The analysis was conducted in a group of 137 patients (mean age: 44.9 ±10.4 years) with arterial hypertension defined as increased blood pressure (BP) for at least 3 months. Their clinical details are presented in Table 1. The exclusion criteria were the following:

- confirmed secondary AH,
- confirmed chronic renal failure (GFR <60 ml/min/1.73 m^2 acc. to MDRD formula),
- other serious comorbidities: systolic heart failure, cardiomyopathy, significant arrhythmias, significant valvular disease, chronic obstructive pulmonary disease, previously diagnosed diabetes, polyneuropathy, peripheral vascular disease,
- aged < 18 years and > 75 years,
- body mass index (BMI) > 40 kg/m^2,
- mental diseases that prevent full cooperation with the patient,
- cardiac rhythm other than sinus rhythm (including permanent cardiac pacing).

Table 1. Basic characteristics of the study group
Tabela 1. Ogólna charakterystyka badanej grupy

	n (137)
Age (years), mean ± SD	44.9 ± 10.4
Males, n (%)	94 (68.6%)
SBP (mmHg), mean ± SD	141 ± 13
DBP (mmHg), mean ± SD	90 ± 9
HR (bpm), mean ± SD	73.5 ± 10.7
BMI (kg/m^2), mean ± SD	29 ± 4.27
Creatinine (mg/dl), mean ± SD	0.84 ± 0.16
eGFR (ml/min/1.73 m^2), mean ± SD	100 ± 18.9
MPV (fl), mean ± SD	9.29 ± 1.00
PLT (10^3/mm^3), mean ± SD	229.5 ± 53.4
MPV/PLT (-), mean ± SD	0.044 ± 0.001
Resistin (ng/ml), mean ± SD	9.42 ± 3.69
TC (mg/dl), mean ± SD	223.9 ± 39.6
HDL (mg/dl), mean ± SD	57.7 ± 18.6
LDL (mg/dl), mean ± SD	145.1 ± 34.1
TG (mg/dl), mean ± SD	158.2 ± 78.4
FG (mg/dl), mean ± SD	98.6 ± 11.3

BMI – body mass index, DBP – diastolic blood pressure, eGFR – MDRD-derived estimated glomerular filtration rate, FG – fasting glucose, HDL – high-density lipoproteins, HR – heart rate, LDL – low-density lipoproteins, MPV – mean platelet volume, PLT – platelet count, SBP systolic blood pressure, TC – total cholesterol, TG – triglycerides

Patients using hypotensives were asked to discontinue the therapy for at least 7 days prior to hospitalisation. The study protocol was approved by the Bioethics Committee at the Military Institute of Medicine (Agreement No. 21/WIM/2011), and all participants gave their written informed consent to participate in the study. The project was registered in the ClinicalTrials.gov database (NCT01996085).

In the clinical study, special consideration was given to the history of cardiovascular risk factors, such as age, sex, tobacco smoking, family history of cardiovascular diseases, systolic blood pressure (SBP) and diastolic blood pressure (DBP), and the constitutive factors (height, body weight, BMI and waist circumference).

Laboratory tests were performed using fasting peripheral venous blood, collected in the morning (7:30 – 8:30). The analysis included concentrations of: creatinine, fasting glucose (FG), total cholesterol (TC), low-density

lipoproteins (LDL) and high-density lipoproteins (HDL), triglycerides (TG) and resistin (assays performed using Human Resistin Immunoassay Quantikine® ELISA, R&D Systems). The value of the estimated glomerular filtration rate (eGFR) was calculated using the MDRD formula. The blood count analysis covered the following platelet parameters: PLT, MPV and MPV/PLT ratio.

The statistical analysis was performed using Microsoft Office Excel 2010 and Statistica 7.0 (StatSoft Inc.). Visual inspection and Kolmogorov-Smirnov test were used to assess the distribution of variables. Linear correlations were determined based on the Pearson's correlation coefficient and Spearman's rank correlation coefficient. Student's t-test and Mann-Whitney U-test were used for comparisons in subgroups (separately for men and women). Statistical significance was set at $p < 0.05$.

Results

Basic characteristics of the study group

Male subjects, with a significant rate of overweight and obese patients, dominated in the study group (Table 1). Increased TC and TG concentrations are noteworthy, as they indicate a considerable incidence of metabolic disorders. The metabolic characteristics of the study group are discussed in detail in the previous study prepared by our team [2].

Correlations in the group

In the analysis of the relationship between the platelet parameters and selected indicators of metabolic disorders for the entire group, no statistically significant correlations were found.

Correlations in the subgroups of men and women

No significant differences between men and women were found regarding absolute values of the platelet parameters. Men and Women demonstrated a similar platelet count (PLT: 225.0 ± 52.6 vs 240.1 ±54.5 $10^3/mm^3$; p = 0.067), platelet volume (MPV: 9.26 ± 1.02 vs 9.36 ± 0.99 fl; p = 0.659), and MPV/PLT value (0.044 ± 0.013 vs 0.042 ± 0.222; p = 0.223).

Table 2. Correlations between platelet parameters and several indicators of metabolic disorders in the whole group
Tabela 2. Korelacje między parametrami płytkowymi a wybranymi wykładnikami zaburzeń metabolicznych w całej grupie

MPV correlations vs	R	P
Age	0.08	0.328
SBP	0.05	0.505
DBP	0.07	0.403
BMI	0.06	0.535
Creatinine	0.07	0.448
eGFR	0.11	0.194
TC	0.12	0.164
HDL	0.11	0.207
LDL	0.06	0.498
TG	0.04	0.661
Glucose	0.07	0.452
Resistin	0.11	0.213
MPV/PLT correlations vs	R	P
Age	0.02	0.801
SBP	0.01	0.985
DBP	0.07	0.403
BMI	0.06	0.461
Creatinine	0.14	0.100
eGFR	0.14	0.100
TC	0.08	0.383
HDL	0.02	0.812
LDL	0.01	0.896
TG	0.01	0.947
FG	0.10	0.243
Resistin	0.07	0.447

BMI – body mass index, DBP – diastolic blood pressure, eGFR – MDRD-derived estimated glomerular filtration rate, FG – fasting glucose, HDL – high-density lipoproteins, HR – heart rate, LDL – low-density lipoproteins, MPV – mean platelet volume, p – statistical significance, PLT – platelet count, R – correlation coefficient, SBP systolic blood pressure, TC – total cholesterol, TG – triglycerides

A separate analysis of the relationships between the platelet parameters and selected indicators of metabolic disorders in the subgroups of men and women revealed significant differences between the subgroups. The correlations in the female subgroup were statistically significant for MPV and resistin (R = 0.43; p = 0.005), creatinine (R = 0.40; p = 0.007) and eGFR (R = -0.33; p = 0.034), as well as for MPV/PLT (R = 0.39; p = 0.011) and resistin (R = 0.39; p = 0.011), creatinine (R = 0.48; p = 0.001), GFR (R = -0.39; p = 0.009) and HDL-C (R = -0.32; p = 0.039). No significant correlations were found for other variables, or in the male subgroup (Table 3).

Table 3. Correlations between platelet parameters and several indicators of metabolic disorders in the subgroups of males and females

Tabela 3. Korelacje między parametrami płytkowymi a wybranymi wykładnikami zaburzeń metabolicznych w podgrupach kobiet i mężczyzn

MPV correlations *vs*	**Women**		**Men**	
	R	**P**	**R**	**P**
Age	0.18	0.237	0.06	0.581
SBP	0.08	0.620	0.06	0.551
DBP	0.11	0.476	0.11	0.269
BMI	0.14	0.383	0.05	0.635
Creatinine	0.40	0.007	0.05	0.618
eGFR	0.33	0.034	0.02	0.828
TC	0.2	0.192	0.10	0.323
HDL	0.27	0.077	0.06	0.557
LDL	0.02	0.881	0.09	0.403
TG	0.23	0.135	0.00	0.999
FG	0.03	0.872	0.10	0.340
Resistin	0.43	0.005	0.02	0.857
MPV/PLT correlations vs	**Women**		**Men**	
	R	**P**	**R**	**P**
Age	0.10	0.506	0.04	0.703
SBP	0.14	0.373	0.08	0.432
DBP	0.19	0.227	0.02	0.830
BMI	0.04	0.813	0.04	0.704
Creatinine	0.48	0.001	0.03	0.787
eGFR	0.39	0.009	0.03	0.781
TC	0.17	0.280	0.09	0.393
HDL	0.32	0.039	0.17	0.116
LDL	0.03	0.827	0.1	0.358
TG	0.27	0.084	0.17	0.104
FG	0.16	0.309	0.01	0.905
Resistin	0.39	0.011	0.05	0.645

BMI – body mass index, DBP – diastolic blood pressure, eGFR – estimated glomerular filtration rate according to MDRD formula, FG – fasting glucose, HDL – high-density lipoproteins, HR – heart rhythm,
LDL-C – low-density lipoproteins, MPV – mean platelet volume, p – statistical significance, PLT – platelet count, R – correlation coefficient, SBP – systolic blood pressure, TC – total cholesterol, TG – triglycerides

Discussion

The results presented reveal previously unknown pathophysiological relations in AH patients. They indicate a relationship between the platelet parameters and certain metabolic disorders, as well as renal function, although only in female patients. The correlations were not found in the male subgroup. A strong relationship between the platelet parameters and resistin observed in women may suggest that the adipokine is involved in connecting metabolic disorders with the platelet function.

Previous scientific reports demonstrate that in the general population, elevated MPV values are a significant prognostic factor for both stable coronary disease and acute coronary syndrome. The relationship we demonstrated in the female subgroup between MPV and resistin concentration, HDL-C levels and glomerular filtration suggests that platelets may be involved in a number of complex pathomechanisms associated with AH and an increased cardiovascular risk [3-6, 11]. The relation between the platelet parameters and resistin may be explained by their dependence on the macrophage function. Platelets produce factors that increase MPV (IL-6), as well as resistin concentration [4, 12]. Elevated MPV in renal dysfunction may be associated with activation of prothrombotic processes and with oxidative stress [13].

The results obtained demonstrate differences between the analysed interactions in male and in female patients: in the subgroup of men, the correlations observed in women are not found. It may be due to general differences between sexes, as well as to differences in the pathomechanisms associated with AH. For instance, relationships have been observed between the platelet volume and menstruation or the use of contraceptives [10]. This phenomenon requires further studies involving larger groups of patients.

The results presented reveal that in women, the platelet parameters as associated with metabolic disorders, including the concentration of resistin, a diabetogenic adipocytokine. Therefore, continuation of the studies on their prognostic value regarding the development of AH complications (coronary disease, cerebral stroke, renal disease) and metabolic disorders (e.g. diabetes) seems justified.

Limitations

The study presented is limited by the small size of the study group, and an imbalance between the number of male and female subjects. Hormonal evaluation and consideration of the menstrual cycle phase would be a great benefit; however, the data were not available. It should also be noted that the results presented apply to patients with AH and without other comorbidities, so they

cannot be extrapolated to the entire population of AH patients.

Conclusions

In women with uncomplicated AH, the platelet parameters are related to various indicators of metabolic and functional disorders. The clinical significance of these correlations requires further studies involving larger groups of patients.

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Refractive change following combined glaucoma and cataract surgery. Comparison of penetrating and nonpenetrating procedures

Zmiany refrakcji oka w następstwie łączonych zabiegów przeciwjaskrowych. Porównanie zabiegów penetrujących i niepenetrujących

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Abstract. An analysis of refractive changes with an assessment of astigmatism following penetrating (trabeculectomy, iridencleisis) and non-penetrating (nonpenetrating deep sclerectomy) glaucoma surgery. The prospective study involved 37 patients (37 eyes), of whom 21 underwent a penetrating glaucoma procedure and 16 a nonpenetrating procedure. Before the surgery and 6 months post-operatively, autorefractometry data was collected and analysed. The arithmetical mean of astigmatism, spheroequivalent, centroid, mean astigmatism (with the rule - WTR, against the rule - ATR, oblique), and surgically induced astigmatism (SIA) were calculated. The arithmetic mean of astigmatism before surgery for penetrating procedures was 0.84 ±0.51 D and 0.98 ±0.73D for nonpenetrating ones. Six months post-op, it was 0.98 ±0.73D and 1.07 ±0.72D, respectively. The centroid for penetrating surgery at day 0 was 0.13 D ax 150.8° and after 6 months 0.32 D ax 3°. Preoperatively, it was oblique and postoperatively it shifted into the ATR direction. In nonpenetrating procedures, the centroid was 0.21D ax 56.6° and 0.4D ax 64.8° after surgery. It was directed ATR pre- and post-op. SIA at 6 months was 1.24 ±0.74D for penetrating and 1.22 ±0.95D for nonpenetrating. No differences between the groups was shown for SIA (p=0.641). No differences were reported in SIA and refrective changes (in the form of the arithmetic mean of cylinder and spheroequivalent) in individual groups, and between them, pre- and post-op. Both procedures shift astigmatism in the ATR direction.

Key words: astigmatism, surgically induced astigmatism, centroid, astigmatism vector analysis, cataract and glaucoma surgery, trabeculectomy, deep sclerectomy

Streszczenie. Cel. Analiza zmian refrakcji oka z oceną astygmatyzmu po zabiegach penetrujących (fako-trabekulektomia i fako-wkleszczenie) oraz niepenetrujących (fako-sklerektomia głęboka niepenetrująca). Materiał i metody. Do badania prospektywnego włączono 37 pacjentów (37 oczu) - 21 po zabiegach penetrujących i 16 po niepenetrujących. Analiza na podstawie autorefraktometrii przed zabiegiem i 6 miesięcy po zabiegu. Wyliczono średnią wartość astygmatyzmu, sferoekwiwalent, centroid, trend astygmatyzmu (zgodny z regułą, przeciwny regule i skośny), a także astygmatyzm indukowany chirurgicznie (SIA). Wyniki. Średnia arytmetyczna astygmatyzmu przed operacją dla zabiegów penetrujących wyniosła 0,84 ±0,51D, a dla zabiegów niepenetrujących 0,98 ±0,73D. Po zabiegu odpowiednio 0,98 ±0,73D i 1,07 ±0,72D. Centroid w zabiegach penetrujących przed zabiegiem wynosił 0,13 D ax 150,8°, po zabiegu 0,32 D a x 3°. Centroid uległ zmianie ze skośnego na przeciwny regule. W procedurach niepenetrujących centroid przed zabiegiem wynosił 0,21 D ax 56,6°, a po zabiegu 0,4D ax 64,8°. Przed operacją i po niej był przeciwny regule. SIA 6 miesięcy po zabiegu wynosił 1,24 ±0,74D w zabiegach penetrujących i 1,22 ±0,95D w niepenetrujących. Nie wykazano różnic dla SIA między grupami (p=0,641). Wnioski. Nie wykazano różnic w SIA i zmianach refrakcji (sferoekwiwalent, cylinder) w poszczególnych grupach, a także między nimi przed zabiegiem i po nim. Oba typy generują astygmatyzm przeciwny regule.

Słowa kluczowe: astygmatyzm, astygmatyzm indukowany chirurgicznie, centroid, analiza wektorowa astygmatyzmu, chirurgia jaskry i zaćmy, trabekulektomia, sklerektomia

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Introduction

Penetrating procedures are the most frequently performed glaucoma procedures in the world. However, they are associated with complications due to hypotony caused by increased aqueous humour outflow, particularly in the first days following surgery. Hypotony is associated with flattening of the anterior chamber, maculopathy and choroidal detachment. Presently, non-penetrating procedures are more frequently conducted, as their safety profile is considerably better, with a relatively minor difference in terms of effectiveness [1]. In the facility where the material was obtained, non-penetrating procedures are routinely used in primary open angle glaucoma, and in the case of lens opacity, a combined surgery with simultaneous removal of the cataract is performed. Glaucoma and cataracts are very often coexistent, which is mostly due to patients' age. An important indicator of safety of the procedure is visual acuity, directly affected by refractive changes. The aim of the study is to assess the refractive changes in the eye, and to provide a detailed evaluation of astigmatism following glaucoma surgery. The stabilisation period for post-operative astigmatism is still being studied. Cunliffe et al. [2] demonstrated stabilisation only 2 months following penetrating procedures, Dietze et al. [3] and Willekens et al. [4] observed stabilisation after 3 months, Claridge at al. [5] and Hong et al. [6] reported changes until the 12th month. In our study, we assessed stabilisation after 6 months.

Material and methods

The analysis involved data obtained from 37 patients (37 eyes) diagnosed with glaucomas and cataracts, qualified for surgical treatment. The patients were operated on in the years 2006-2007 in the Department of Ophthalmology of the Military Institute of Medicine. The study was prospective. It involved patients qualified for penetrating procedures (iridencleisis, trabeculectomy) and non-penetrating procedures (non-penetrating deep sclerectomy) (Table 1). The indications for surgery included progression of glaucomatous lesions due to unregulated intraocular pressure, intolerance to local glaucoma therapy, or problems with patient compliance. Patients with a history of ophthalmological surgery were excluded from the study, as it could affect refraction, and patients with other eye diseases which could potentially reduce visual acuity (e.g. advanced macular or retinal lesions, unregulated diabetes with retinopathy, a history of uveitis, or corneal pathologies). Patient under 18 years of age were not qualified for the surgery.

Table 1. Summary of demographic data
Tabela 1. Podstawowe dane demograficzne

Type of procedure	Penetrating	Non-penetrating
Procedures	16 phacotrabeculectomies, 5 phacoiridencleisis	16 non-penetrating deep phacosclerectomies
Number of patients	21	16
Age (years)	74.09 ± 9.01	72.75 ± 6.97
Right/left eye	13/8	8/8
Sex female/male	14/7	8/8

The study followed the guidelines of the Declaration of Helsinki, and it was approved by the Bioethical Committee of the Military Institute of Medicine.

Pre-operative examination

General medical histories and detailed ophthalmological histories were collected. The anterior and posterior eye sections were examined in detail with the use of a slit lamp. For the purpose of this study, before the procedure and 6 months after the procedure, a keratometric examination of the cornea was performed using an automatic autorefractometer (Tomey, RC-800, US). All of the surgeries were performed by the same experienced surgeon (M.R.).

Surgical technique

Phacotrabeculectomy

Sedation. Local anaesthesia. Retrobulbar 2% Xylocaini. Bridle suture on the superior rectus muscle. Retractor. Dissection of the ocular conjunctiva from the top, excision of the Tenon's capsule, scraping off the vascular episcleral lamina. Incision into the sclera and preparation of an episcleral flap. Puncturing of the opening of the anterior chamber in the limbus and 2.8 mm from the temple. Viscoelastic agent into the anterior chamber. Anterior circular capsulotomy. Hydrodissection and hydrodelineation. Phacoemulsification of the lens nucleus. Irrigation and aspiration of cortical masses. Viscoelastic agent into the anterior chamber. Implantation of a foldable lens from an injector into the capsule. Puncturing of the opening of the anterior chamber under the flap. Viscoelastic agent into the anterior chamber. Excision of the trabecular flap with a punch. Basal iridectomy. Endodiathermy. Two single nylon sutures on the scleral flap. Single vicryl sutures on the ocular conjunctiva. Addition of a viscoelastic agent into the anterior chamber. Dressing.

Phacoiridencleisis

Sedation. Local anaesthesia. Retrobulbar 2% Xylocaini. Bridle suture on the superior rectus muscle. Retractor. Dissection of the ocular conjunctiva from the top and from the temple, scraping off of the vascular episcleral lamina, incision into the sclera and preparation of a semi-elliptical superficial episcleral flap. Puncturing of the opening of the anterior chamber in the limbus from the temple. Opening of 2.2 mm in the clear cornea from the temple. Viscoelastic agent into the anterior chamber. Continuous circular capsulorhexis, moderate. Hydrodissection and hydrodelineation. Phacoemulsification of the nucleus. Irrigation and aspiration of cortical masses. Viscoelastic agent into the anterior chamber. Implantation of a posterior chamber intraocular lens from an injector into the lens capsule. Centring. Incision of the sclera and provoked, spontaneous positioning of the peripheral iris, without outflow of the aqueous humour. Longitudinal incision of the incarcerated iris, and positioning it with the pigmented epithelium facing upwards. Viscoelastic agent into the anterior chamber. Two single nylon sutures on the superficial scleral flap. Single sutures on the ocular conjunctiva. Rinsing of the anterior chamber. Sealing the wounds. Dressing.

Phacosclerotomy

Sedation. Local anaesthesia. Retrobulbar 2% Xylocaini. Bridle suture on the superior rectus muscle. Retractor. Dissection of the ocular conjunctiva from the top, scraping off of the vascular episcleral lamina, diathermocoagulation of bleeding vessels, incision of the sclera and preparation of a superficial flap and a deep (smaller) episcleral flap. Puncturing of the opening of the anterior chamber in the limbus, 2.2 mm from the temple. Viscoelastic agent into the anterior chamber. Anterior circular capsulotomy. Hydrodissection and hydrodelineation. Phacoemulsification of the lens nucleus. Irrigation and aspiration of cortical masses. Viscoelastic agent into the anterior chamber. Implantation of a foldable lens from an injector into the capsule. Dissection of the deep scleral flap to the scleral spur and Descemet's membrane. Removal of the roof of the Schlemm's canal. Confirmation of filtration. Two single nylon sutures on the superficial scleral flap. Single vicryl sutures on the ocular conjunctiva. Rinsing of the anterior chamber. Sealing the wounds in the limbus. Dressing.

Post-operative protocol

The fixed appointment schedule involved control visits on days 1 and 7 following the surgery, then in the first, third and sixth months after the surgery. The analysis of refractive changes included the data from the visit before the surgery, and the appointment 6 months after the procedure. After the surgery, all patients received antibiotic drops, steroid drops and non-steroid anti–inflammatory drops for 4 weeks.

Analysis of astigmatism

The mean astigmatism for individual patient cohorts was calculated using two methods [7, 8]. The first involved the arithmetic mean of the cylindrical dioptres, without the axial values. The spheroequivalent was also calculated. It is a sum of the sphere and half of the cylinder. The arithmetic mean (of the cylinder or equivalent) is used to compare absolute values. The difference in the cylinder value calculated by simple subtraction may illustrate the mean change in the cylinder value in a given group. All calculations were made using positive cylindrical dioptres.

The other method consisted of calculating the centroid, i.e. mean astigmatism including the axis. The centroid enables a summary vector analysis, as well as an assessment of the astigmatism trend directed with the rule (WTR), against the rule (ATR) or oblique. It is the only method of calculating the mean astigmatism for the entire group of data, including its direction (axis). Without the centroid, the astigmatism trend for a group of data cannot be calculated.

Vector method – detailed description

The data regarding astigmatism, routinely presented as polar values (cylinder, axis), were transformed to points that can be placed on the Cartesian system (axes x, y). To do this, the following formulas were used:

$x = cyl*\cos(2*axis)$

$y = cyl*\sin(2axis)$

Then, the change of the astigmatism vector was calculated:

$cyl = \sqrt{(x^2+y^2)}$

$angle = 1/2 *(\tan^{-1}(y/x))$

if x >0 and y>0	angle = axis
if x <0	angle = axis +90°
if x >0 and y<0	angle = axis + 180°
if x = 0, and y <0	angle = 135°
if x = 0, and y >0	angle = 45°
if x = 0 and y = 0	angle = 0°
if y = 0, and x <0	angle = 90°
if y = 0, and x >0	angle = 0°

The calculations were made for each pair of data separately, so that the vector change could be determined for individual patients. In order to estimate the vector change for the entire study group, the centroid was calculated based on the mean of all x values, and the mean of all y values obtained in the analysed group.

The centroid results were presented graphically on a double-angle graph. The range of axis on the graph is 0° to 180°. It is the most appropriate method of presenting astigmatism, as the vector returns to the same value

when it reaches 180°. The centroid is found within an ellipsis, whose arms are determined by the standard deviation of the x and y values.

The surgically induced astigmatism (SIA) was calculated with the method proposed by Jaffe and Clayman [9] (Figure 1), where the SIA is the result of the vectors before and after surgery. It is used to assess the effect of the procedure on refraction of the eye.

Statistical analysis

The calculations were made using Statistica 10.0 PL software. The analysis included standard descriptive statistics, the normality of distribution was assessed using the Shapiro-Wilk test, the Mann-Whitney U-test was used to compare the groups, the chi-squared test was used for nominal data, and the Wilcoxon pair test for analyses in groups.

Results

The study involved 37 patients (37 eyes). Glaucoma surgery and phacoemulsification to remove a cataract were performed simultaneously. Penetrating surgeries were performed in 21 eyes, phacotrabeculectomy in 16 eyes, and phacoiridencleisis in six eyes. Non-penetrating deep phacosclerectomy was conducted in 16 patients. The mean age of the patients was 73.38 ± 8.14 years, and did not differ between the groups. In the analysed material, 60% of the subjects were women, and 56% of eyes were right (Table 1).

The arithmetic mean of astigmatism before the surgery was 0.84 ± 0.51D for penetrating procedures, and 0.98 ± 0.73D for non-penetrating ones; 180 days after the surgery, the values were 0.98 ± 0.73D and 1.07 ± 0.72D, respectively. Surgically induced refractive changes based on the cylinder from an autorefractometer at 180 days following the procedure were 0.02 ± 0.73 and -0.47 ± 0.81, respectively. No statistical differences were found regarding cylinder values before the surgery and 6 months after the procedure in individual groups, i.e. penetrating procedures (p = 0.959) and non-penetrating procedures (p = 0.076). The data are presented in Table 2.

The distribution of astigmatism in both studied periods is presented in a cumulative percentage plot. It is noteworthy that in most patients in both groups the astigmatism values were low at 1.5-2.0D. Only in a small group of patients, the astigmatism was > 2.0D (Fig. 2-3).

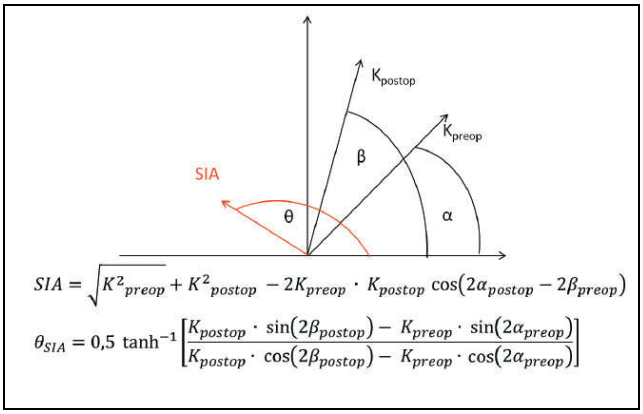

Figure 1. Formula for calculating surgically induced astigmatism (SIA). K $_{preop}$ is the vector of astigmatism before surgery, K $_{postop}$ is the vector of astigmatism after surgery

Rycina 1. Wzór na obliczenie astygmatyzmu indukowanego chirurgicznie (SIA). K $_{preop}$ - wektor astygmatyzmu przed operacją, K $_{postop}$ - wektor astygmatyzmu po operacji.

The mean astigmatism with the axis for the group undergoing penetrating procedures was 0.13 D ax 150.8° before surgery, and 0.32 D ax 3° after surgery. The centroid changed from oblique to against the rule (Fig. 4). In non-penetrating procedures, the centroid was 0.21 D ax 56.6° before surgery, and 0.4D ax 64.8° after surgery. Both before and after surgery, it was against the rule (Fig. 5).

The surgically induced astigmatism, calculated using the vector method presented by Jaffe and Clayman [9] six months after the procedure was 1.24 ± 0.74D in the case of penetrating procedures, and 1.22 ± 0.95D in non-penetrating surgeries. No differences in SIA between the groups were demonstrated (p = 0.641). (Table 3).

Discussion

Based on the data (Table 2) the mean astigmatism before and after surgery oscillated around one, and did not increase after the procedure. Moreover, in both groups, over 80% of patients had astigmatism of <1.5D prior to the procedure, and the same level was maintained six months following the surgery in the sclerectomy group. After a penetrating operation, approximately 60% of patients were within this range. Similar data were reported by Egrilmez et al. [8] and Claridge et al. [5].

Table 2. Data presenting values of cylinder and spheroequivalent. Arithmetic mean of cylinder with standard deviation, median, range before and 180 days after surgery. Statistical comparison within groups and between them.
Tabela 2. Dane dotyczą wartości cylindra i sferoekwiwalentu. Średnia arytmetyczna z odchyleniem standardowym, mediana, zakres wartości w okresie przez zabiegiem i 180 dni po zabiegu. Porównanie statystyczne w grupach i między grupami.

		Cylinder (cylindrical dioptres)			Spheroequivalent (SE) (spherical dioptres)		
Period	**Data**	**Penetrating**	**Non-penetrating**	**P***	**Penetrating**	**Non-penetrating**	P*
Day 0	Mean ±SD	0.84 ± 0.51	0.98 ± 0.73	0.561	0.30 ± 2.20	0.89 ± 3.51	0.747
	Median	0.83	0.77		0.50	0.37	
	Range	0.06; 1.93	0.16; 3.20		4.87; 2.62	8.25; 5.25	
Day 180	Mean ±SD	1.08 ± 0.67	1.07 ± 0.72	0.449	0.25 ± 1.12	0.00 ± 1.83	0.837
	Median	0.83	0.95		0.00	0.00	
	range	0.31; 2.39			3.25; 1.00	3.75; 2.87	
Day 180 - Day 0	Mean difference	0.02 ± 0.73	0.47 ± 0.81		0.35 ± 1.92	0.21 ± 2.78	
P^1		0.959	0.07		0.721	0.959	

*SD – standard deviation
P* – based on Mann-Whitney U-test, comparison between the groups
P^1 – based on the Wilcoxon's pair test, analysis in a given group
Significance at $p < 0.05$

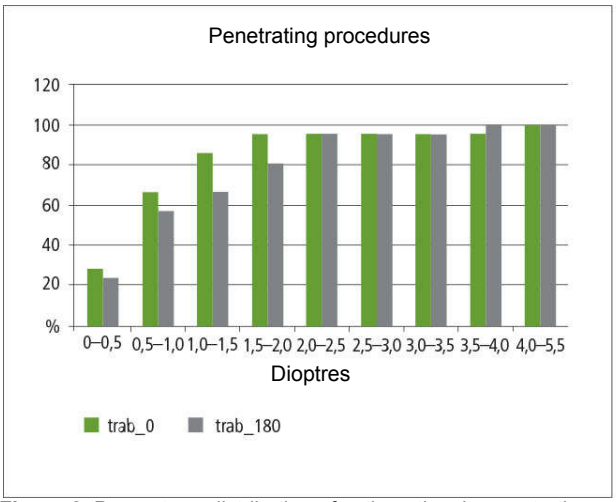

Figure 2. Percentage distribution of astigmatism in penetrating surgeries
Rycina 2. Wykres skumulowanego odsetka astygmatyzmu w grupie penetrującej

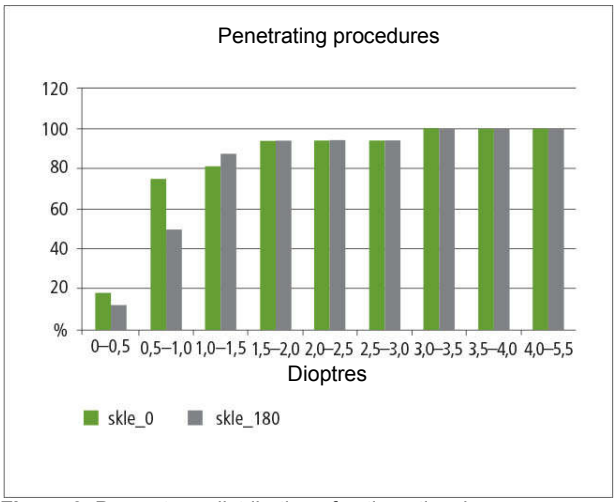

Figure 3. Percentage distribution of astigmatism in nonpenetrating surgeries
Rycina 3. Wykres skumulowanego odsetka astygmatyzmu w grupie niepenetrującej

Astigmatism based on the arithmetic mean of the cylinder and refraction based on the spheroequivalent did not differ between the study groups. In addition, no differences were observed within the groups before and after surgery. El-Saied et al. [10], similarly, did not find a difference using the vector method. Moreover, as in the presented study, their analysis did not reveal any differences in the groups before and after surgery. Similar observations, i.e. no change in mean astigmatism, were made by Willekens et al. for trabeculectomy [4]. Egrilmez et al. [8] noticed statistically significant differences in mean astigmatism between penetrating and non-penetrating procedures in the third and sixth months following surgery, in the favour of non-penetrating surgeries.

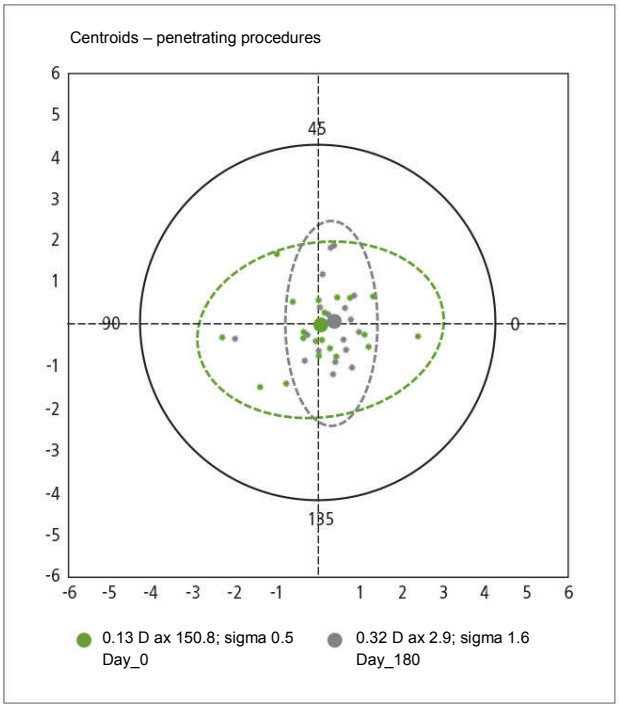

Figure 4. Mean astigmatism (centroid) for penetrating procedures on double angle plot. Red represents preoperative data. Blue represents postoperative data at 180 days. Single points represent the data of particular patients.

Rycina 4. Średni astygmatyzm (centroid) dla operacji penetrujących na wykresie zdwojonego kąta. Kolor czerwony przed zabiegiem. Kolor niebieski 180 dni po zabiegu. Pojedyncze punkty symbolizują dane dla poszczególnych pacjentów.

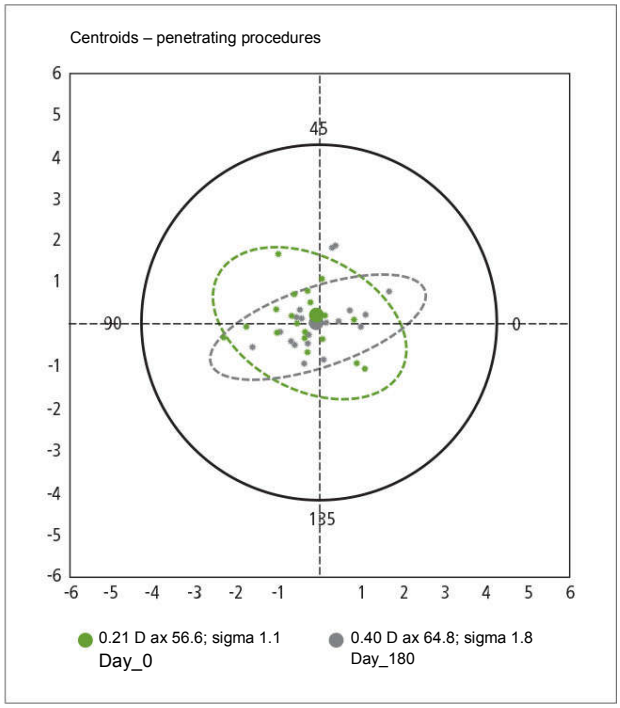

Figure 5. Mean astigmatism (centroid) for nonpenetrating procedures on double angle plot. Red represents preoperative data. Blue represents postoperative data at 180. Single points represent the data of particular patients.

Rycina 5. Średni astygmatyzm (centroid) dla operacji niepenetrujących na wykresie zdwojonego kąta. Kolor czerwony przed zabiegiem. Kolor niebieski 180 dni po zabiegu. Pojedyncze punkty symbolizują dane dla poszczególnych pacjentów.

Table 3. Surgically induced astigmatism (SIA) calculated with Jaffe and Clayman's methods [9]
Tabela 3. Astygmatyzm indukowany chirurgicznie (SIA), obliczony na podstawie metod zaproponowanych przez Jaffe i Clayman [9]

SIA (dioptres)				
Procedure	**Mean ±SD**	**Median**	**Range**	**P**
Penetrating	1.24 ± 0.74	1.05	0.44-3.05	0.641
Non-penetrating	1.22 ± 0.95	0.96	0.16-3.56	

P based on Mann-Whitney U-test, significance p <0.05
*SD – standard deviation

The mean astigmatism for the axis for the groups undergoing penetrating surgeries was 0.13 D ax 150.8° before the procedure, and 0.32 D ax 3° after the operation. The centroid changed from oblique to against the rule (Fig. 4). Egrilmez et al. [8] reported astigmatism against the rule after six months following the procedure. Kook et al. [11] noticed astigmatism with the rule until the third month following the procedure, whereas after 12 months there was a shift against the rule. Similar results were reported by Hong et al. [6], although their follow-up was continued until the 12th month. Delbeke et al. [12] described astigmatism with the rule six months following the surgery. Willekens et al. [4] also presented the tendency for astigmatism with the rule, most pronounced in the first month following the procedure, but persisting until the end of the 18-month long follow up period.

In non-penetrating procedures the centroid was 0.21 D ax 56.6° before the procedure, and 0.4D ax 64.8° after the surgery. Both before and after the surgery it was against the rule (Fig. 5). Egrilmez et al. [8] observed in the group of non-penetrating procedures, astigmatism with the rule, from the first day until the end of six months following the procedure.

The differences in the direction of post-operative astigmatism may have various causes. The surgical technique [13], using cauterisation, the size of the filtering bleb, the upper lid dropping after the procedure [5], the flap suturing technique [4], the time of removing the anchor sutures in the cornea or sclera [14], or the sutures in the conjunctiva [15].

Surgically induced astigmatism is a result of the vector before and after surgery (Fig. 1), and is generated by the

surgical procedure. SIA in the study groups was limited, and comparable with the results reported in the literature. Six months after surgery it was 1.24 ± 0.74D in the group of penetrating procedures, and 1.22 ± 0.95D in the non-penetrating surgery group. Żarnowski et al. [16] reported values of 0.4-1.1D after three months, depending on the technique of trabeculectomy. Kumari et al. [17] presented the values of 1.08 - 1.4D, and Pfeiffer et al. [14] reported approximately 1.2D. Egrilmez et al. [8] reported 0.62D for sclerotomy, and 1.24D for trabeculectomy. The difference was considered statistically significant from the third month.

From a clinical point of view, shifts in the vector of astigmatism are transient, as confirmed by many authors cited in this study.

To conclude, based on the data obtained in our study, non-penetrating and penetrating procedures with simultaneous cataract removal are equivalent regarding the induction of post-operative astigmatism and surgically induced astigmatism. No differences in SIA and refractive changes were demonstrated in individual groups before and after the surgery.

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Concomitance of immediate-type allergies in a patient with Crohn's disease and celiac disease – a case report

Współistnienie alergii typu natychmiastowego u pacjentki z chorobą Leśniowskiego-Crohna oraz celiakią – opis przypadku

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Abstract. The paper presents the case of a 42-year-old female suffering from Lesniewski-Crohn's and celiac disease with parenteral complications: aphthous ulcers, recurrent aphthous stomatitis, cholelithiasis, autoimmune hepatitis and an immediate-type allergy to household dust mites with symptoms of asthma, rhinitis, conjunctivitis and allergic chronic, and angioneurotic oedema of the upper lip. The patient was also diagnosed with Hashimoto's thyroiditis and had a complication after immunosuppression therapy in the form of pulmonary fibrosis.
Key words: immediate-type allergy to household dust mites, Lesniowski-Crohn's disease, Crohn's disease, celiac disease, local and parenteral complications

Streszczenie. Przedstawiono przypadek 42-letniej pacjentki chorującej na chorobę Leśniowskiego-Crohna oraz celiakię, u której wystąpiły liczne powikłania pozajelitowe: owrzodzenia błony śluzowej jamy ustnej, aftowe zapalenie jamy ustnej, kamica żółciowa, autoimmunologiczne zapalenie wątroby oraz współistnienie alergii typu natychmiastowego na roztocza kurzu domowego pod postacią astmy oskrzelowej, alergicznego nieżytu nosa i zapalenia spojówek, a także nawracające obrzęki naczynioruchowe wargi górnej. U pacjentki stwierdzono również chorobę Hashimoto oraz powikłanie po leczeniu immunosupresyjnym - włóknienie płuc.
Słowa kluczowe: alergia typu natychmiastowego na roztocza kurzu domowego, choroba Leśniowskiego-Crohna, celiakia, powikłania miejscowe i pozajelitowe

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Introduction

Crohn's disease is an inflammatory condition of the intestines, classified as a non-specific intestinal inflammation, whose aetiology is unknown. It is commonly considered an autoimmune disease associated with the Th1 and Th17 lymphocytes [1, 2]. Susceptibility to the disease is conditioned by a mutation of the NOD2 (nucleotide oligomerisation domain) protein, also referred to as CARD 15 (caspase recruitment domain family), localised on chromosome 16 regulating macrophage activation in response to bacterial lipopolysaccharides. The presence of two alleles of the mutated gene increases the risk of Crohn's disease

incidence 20-40 times [2, 3]. Pro-inflammatory cytokines play an important role in the development of the inflammatory process. A gene polymorphism for IL23R is found, similarly to psoriasis [3, 4], and the presence of a *NOD2/CARD 15* gene mutation conditions early onset of the disease [3, 4]. Crohn's disease is a full-thickness, granulomatous inflammation that can affect any part of the gastrointestinal tract, from the oral cavity to the rectum [3, 4]. Characteristic of the condition is the presence of segmental lesions in the small and large intestine, separated by healthy segments. They may take the form of small mucosal ulcerations. Intestinal complication can occur in the course of the disease: interloop abscesses, intestinal strictures, perirectal lesions, intestinal perforation, haemorrhages, colorectal cancer, and extraintestinal complications. Extraintestinal complications include: uveitis, conjunctivitis, optic neuritis, ulceration in the oral cavity, aphthous stomatosis, specific granulomatous lesions of the oral cavity and lips, pericarditis, myocarditis, acute pancreatitis (the presence of antibodies against the cells of the exocrine part of the pancreas), autoimmune hepatitis, cholelithiasis, urolithiasis, amyloidosis, thromboembolic complications, autoimmune haemolytic thrombocytopenic purpura, anaemia due to an iron deficiency, anaemia due to a vitamin B_{12} and folic acid deficiency [3-5].

The study presents the case of a patient with Crohn's disease, who experienced multiple extraintestinal complications, and immediate hypersensitivity to dust mites in the form of bronchial asthma, allergic rhinitis, conjunctivitis, Quincke's angioedema, coeliac disease, Hashimoto's disease, and pulmonary fibrosis due to an adverse effect of the applied immunosuppressive treatment (mesalazine, sulfalazine, azathioprine, 6-mercaptopurine).

Case report

Patient aged 37 years old, unemployed, presently receiving a disability benefit, came to the allergology clinic in August 2012 due to wheezing, dry cough, rhinitis, ocular pruritus and transient urticaria. The patient has a history of Crohn's disease, coeliac disease, right ventricular hypertrophy, polycycstic ovary syndrome, laparoscopic ovarian cyst removal, and salicylate intolerance. Family and individual history: maternal grandmother– bronchial asthma, father – diabetes, son – hypersensitivity to milk protein, daughter – urticaria and hypersensitivity to pollen and to hymenoptera venom (wasp).

Physical exam

In the physical examination, mucosal abnormalities in the form of oral aphthas and ulceration were found, as well as a pulmonary oedema, individual wheezing and fibrillation with hyperventilation, limited obesity.

Additional tests

- Complete blood count with differential: slight anaemia (Hb 11.9 g/dl, HCT 37%, erythrocytes 4.64 x 10^3 µl, PLT 311, leukocytes 9.1 x 10^6/µl), creatinine 0.88 mg/dl
- ASO 93 IU/ml (<200), d-dimer concentration 460 µg FEU/l (<500 µg/FEU/l), urinalysis – without change, 3 faecal tests for parasites and lamblia cysts – not found
- Specific IgE panel in the serum (Phadia AB, Sweden) – serum concentrations of specific IgE confirmed hypersensitivity to house dust mites (specific IgE antibody; Phadia AB, Sweden): SD1 (dust mites) in class 3 and for SD2 (dust mites) in class 3, specific IgE in the serum for other allergens; the combinations of grass, trees, weeds, latex and gluten were negative (class 0)
- Total IgE of 37.5 IU/ml (<100)
- Lung X-ray: pulmonary parenchyma without thickening, normal heart silhouette
- Spirometry: normal lung ventilation

The rhinitis, conjunctivitis, dyspnoea and cough were attributed to IgE-dependent hypersensitivity to household dust mites. Anti-dust mite prophylaxis and symptomatic treatment when the symptoms occur were advised.

A gluten-free diet was also recommended, due to the diagnosis of coeliac disease. Due to painful oral ulceration, the patient had a laryngological and stomatological consultation with a doctor specialising in mucosal disorders. A biopsy of the lower lip was performed, and two salivary glands were collected for histopathological examination. Sjogren's syndrome was excluded (the histopathological picture did not meet the diagnostic criteria for the disease). In December 2012, due to increased pain symptoms in both wrist joints, the patient was referred for diagnostics and treatment of the lumbosacral and cervical spine, and the knee joints, to the department of rheumatology (Public Healthcare Institution in Starachowice), where she was diagnosed with degenerative joint and spine disease, and further observation due to a suspected systemic connective tissue disease was recommended. During hospitalisation, antinuclear antibodies (ANA) with a speckled pattern at 1:320 were found. At the end of May and beginning of June 2013, the patient was hospitalised at the internal diseases department (Starachowice) due to very strong pain symptoms in the middle abdomen, and stools with mucus. Liver damage was confirmed, probably following

the treatment of Crohn's disease with azathioprine (ALT 118 U/i, AST 28 U/l). Moreover, cholecystolithiasis was observed. The patient also reported to the hospital gastrology clinic in Warsaw (where she had follow-up visits once a month or once every two months), and her treatment was adjusted: azathioprine was substituted for mercaptopurine. In the following months (July/August 2013), the dyspnoea and fatigue increased. The patient was referred to the Clinic of Lung Diseases (Starachowice) for a pulmonological consultation and exclusion of drug-induced interstitial pneumonia and pulmonary fibrosis. A thoracic HRCT was performed, revealing: focal densities in the apex of the oblique fissure of the left lung, approximately 6 mm in diameter, suggestive of focal fibrosis, and a single small nodule of approx. 3 mm in diameter in the upper dorsal part of the left lung, which could also correspond to a focal fibrosis – for verification in 3 to 6 months. At the same time (August 2013) the patient experienced oedema and redness in the left submandibular area, causing strong local pain. The GP prescribed an antibiotic, and referred the patient to the otolaryngological department (in Skarżysko-Kamienna), where she was diagnosed with sialolithiasis of the left submadibular salivary gland. After clinical improvement – alleviation of pain and reduction of the lesion in the salivary gland area – the patient was qualified for a planned surgical procedure to remove the left submandibular salivary gland. Due to further progression of the disease (symptoms of general weakness, transient dyspnoea, pain in the pharynx and oesophagus when swallowing, and oedema of the upper lip) the patient was hospitalised in November 2013 in the Department of Infectious Diseases and Allergology of the Military Institute of Medicine in Warsaw. A thoracic HRCT was performed at the hospital and revealed discrete striated densities in the 7th segment of the left lung. Apart from that, the lungs were free from focal lesions. No fluid was found in the pleural cavities. The heart and large vessels did not demonstrate signs of pathology. Material for histopathological examination was collected during the gastroscopy (*oesophagitis refluxiva and mucosa duodeni normalis*). The patient consulted with a maxillofacial dentist. Samples from the mucosa of the upper lip were collected (a tangentially cut segment of epithelium with a superficial ulceration, under the epithelium profuse infiltrations of small lymphocytes B [CD20+] and T [CD3+] and plasma cells [CD138], an image of a non-specific inflammatory process), C_3 – 156 mg/dl (90-180); inhibitor C_1 >88.0% (normal range >68%). During the entire course of the disease, the patient experienced oral ulceration, difficulty with swallowing, abdominal pains, pruritus and pain in the eyes, transient oedema of the upper lip and dyspnoea.

In June 2014, in the Department of Otolaryngology in Warsaw, the patient had the left submandibular salivary gland removed surgically, without complications.

During the next hospitalisation in the Department of Internal Diseases and Gastroenterology in Warsaw, at the end of August and the beginning of September 2014, an abdominal MR examination was performed, revealing a focal lesion of 23 x 17 mm in the L3 cord, with angioma morphology. Between 11 and 16 September 2014, the patient was hospitalised at the Department of Internal Diseases and Rheumatology in Warsaw, 137 Wołoska St., due to a suspected connective tissue disease. The patient was diagnosed with musculoarticular pain syndrome, of fibromyalgia type. In November 2014, she attended the Daily Rehabilitation Centre, Public Healthcare Institution in Starachowice due to strong spinal pain, for rehabilitation treatment. Another sudden hospitalisation (January/February 2015) at the General Surgery Department in Starachowice due to strong abdominal pain (symptoms of exacerbated cholelithiasis and gall bladder abscess) involved laparoscopic cholecystectomy. The postoperative period was complicated by an episode of dyspnoea on the 2nd day after the procedure, which subsided after intervention (Ventolin). Due to choking, problems with swallowing, dyspnoea and an enlarged thyroid, the patient was referred to an endocrinologist (March 2015), who diagnosed her with nodular thyroid disease – Hashimoto's disease in the phase of euthyreosis. The patient was qualified for observation and periodic controls of the thyroid. For the entire follow-up period, due to bronchial asthma in the allergology clinic, the patient was also treated by a gastrologist and internist. She used second generation antihistamines (cetirizine dihydrochloride, loratadine), inhaled steroids, and long- and short-acting β_2-mimetics. Due to her general condition, including liver damage and multiple complications, the patient was disqualified by gastroenterologists, and did not receive biological treatment (with monoclonal antibodies).

Discussion

In the international literature, there is a publication from Taiwan, describing a retrospective study involving 5260 patients (the study period covered the years 2000-2005), confirming that in the group of patients with non-specific intestinal inflammation, the risk of bronchial asthma is four times higher than in the general population [6]. Asthma and non-pulmonary allergic diseases in the course of non-specific intestinal inflammation were also described [7].

Some researchers point to the coexistence of atopic dermatitis and Crohn's disease, and to an increased risk of Crohn's disease in the patients with atopic dermatitis

[8-10]. A cohort study conducted in Germany in the years 2005-2011 confirmed that atopic dermatitis is associated with a considerably elevated risk of rheumatoid arthritis, non-specific intestinal inflammation (including Crohn's disease), and a reduced incidence of type 1 diabetes [11].

An immediate allergy to foods, including cow's milk (28.6%), beef, sea food, wheat, walnuts (10.7% each), peanuts, chestnuts (7.1% each), strawberries, tomatoes, sesame seeds, bananas, barley, apples, olives, soy, potatoes, kiwi fruit, cocoa and oranges (3.6% each) was observed in Iranian children suffering from non-specific intestinal inflammation. The study was conducted in the years 2013-2015 in Teheran (skin prick tests, skin specific IgE antibodies). In this group of patients, an increased incidence of food allergies was observed, compared to the general population, e.g. a cow milk's allergy was found more often in ulcerative colitis than in Crohn's disease. Often it was a multiple allergy.

The occurrence of coeliac disease in patients with non-specific intestinal inflammation is unclear. Several cases of the coexistence of the diseases in one family, or in one patient, are presented in the literature [13-16]. After the diagnosis of coeliac disease, the presented patient was recommended to follow a gluten-free diet. This condition is not present in the patient's family. Her father has diabetes.

This case illustrates how in Crohn's disease over a short observation period (3 years), multiple complications, as presented above, may occur (local, extraintestinal). Also, concurrent immediate allergies may be found in the form of bronchial asthma, allergic conjunctivitis or Quincke's angioedema, which may be caused by a number of autoimmune diseases (Crohn's disease, Hashimoto's disease). Due to hypersensitivity to household dust mites, anti-dust mite prophylaxis and symptomatic treatment are recommended (antihistamines, β2-mimetics as required and inhaled steroids). A patient with such problems requires the comprehensive care of many specialists, including a gastroenterologist/internist, an allergologist, a neurologist and a dentist, as well as life-long medical supervision.

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Drug-induced interstitial lung disease in a patient with bronchial asthma – a case report

Lekopochodne śródmiąższowe zapalenie płuc u pacjenta z astmą oskrzelową – opis przypadku

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Abstract. Acute interstitial pneumonia (AIP) is a sudden onset disease. Respiratory failure develops rapidly in the majority of cases and frequently requires mechanical ventilation. The characteristic radiographic findings in computed tomography resemble diffuse ground-glass opacity. The article presents the case of a clinically difficult 41-year old patient with a several year history of bronchial asthma and rapidly progressing respiratory failure. Laboratory tests were dominated by leukocytosis, a high CRP level; the levels of antibodies ANA, cANCA, pANCA were within the reference range. Initial empirical antibiotic therapy was not successful. The addition of immunosuppressive drugs led to an improvement. The clinical data from a physical examination and a differential diagnosis indicate a possible hypersensitivity reaction to acetylsalicylic acid.
Key words: acetylsalicylic acid, acute interstitial pneumonia, asthma, DILD, drug-induced interstitial lung disease

Streszczenie. Ostre śródmiąższowe zapalenie płuc (AIP) to choroba o dynamicznym przebiegu. W większości przypadków niewydolność oddechowa narasta szybko i często wymaga mechanicznego wspomagania wentylacji. Charakterystyczne są rozległe zmiany o typie mlecznej szyby w badaniach obrazowych (tomografia klatki piersiowej). W niniejszej publikacji prezentujemy przypadek 41-letniego pacjenta z wieloletnim wywiadem astmy oskrzelowej oraz gwałtownie narastającą niewydolnością oddechową. W badaniach dodatkowych leukocytoza, zwiększone stężenie CRP, przeciwciała ANA, cANCA i pANCA w wartościach nieprzekraczających norm laboratoryjnych. Początkowa antybiotykoterapia empiryczna była nieskuteczna. Dołączenie leków immunosupresyjnych spowodowało poprawę. Dane kliniczne z badania podmiotowego oraz diagnostyka różnicowa wskazują na możliwość reakcji nadwrażliwości na kwas acetylosalicylowy.
Słowa kluczowe: lekopochodne śródmiąższowe zapalenie płuc, DILD, ostre śródmiąższowe zapalenie płuc, astma, kwas acetylosalicylowy

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Background

Acute interstitial pneumonia (AIP), also known as Hamman-Rich syndrome, is a rapidly progressing interstitial lung disease. It mostly affects middle-aged patients. The course of the disease is dynamic, and its beginning is non-specific, including muscular pain, headache, general weakness, cough and dyspnoea. Dominating signs in the physical examination include tachycardia, tachypnea, cyanosis and crackles over the entire lung field. The risk of rapidly increasing respiratory failure is high: it develops in the majority of cases, and requires mechanical ventilation. AIP needs to be differentiated from IPF (idiopathic pulmonary fibrosis),

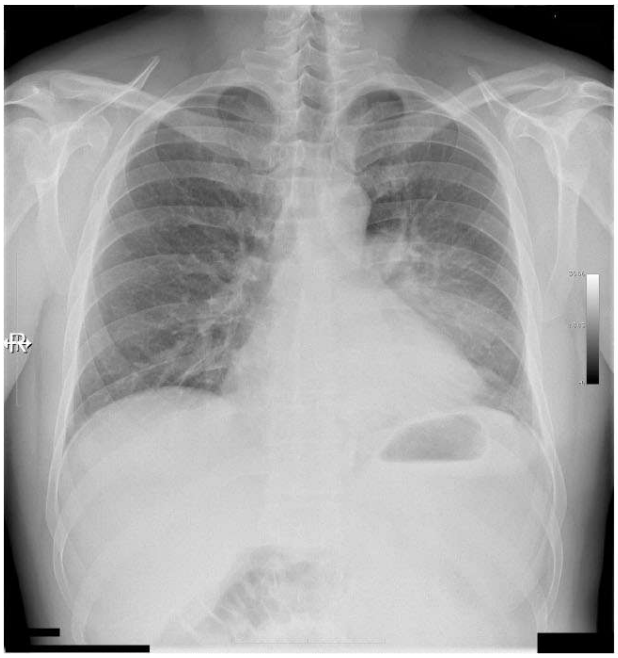

Figure 1. X-ray - on admission
Rycina 1. Badanie RTG w dniu przyjęcia

Figure 2. CT scan of the chest without contrast
Rycina 2. Obraz TK klatki piersiowej bez kontrastu

exacerbations of connective tissue diseases and severe respiratory infections.

In the initial stages of the disease, the radiological changes are limited; with the development of the pathological process, vesicular densities and ground-glass opacities occur. Treatment involves immunosuppressive medicines, e.g. glucocorticosteroids, cyclophosphamide, azathioprine and vincristine. Prognosis is unfavourable, as approximately 60% of patients die in the acute phase of the disease, mostly within six months from the onset. In patients who survive an acute episode, remission involving reduced lung volume may occur.

In the literature, there are reports of drug-induced interstitial lung disease (DILD), whose symptoms are identical to those of AIP. However, in this case there is a strict correlation with the body's reaction to medicines (e.g. amiodarone, statins, geftinib, nitrofurantoin, amphotericin B, bleomycin, methotrexate, bromocriptine and others). Often the disease is caused by nonsteroidal anti-inflammatory drugs (NSAIDs) [1-5]. The most prominent one is acetylsalicylic acid (ASA). Another risk for the presented patient is an increased incidence of hypersensitivity to acetylsalicylic acid in the population of patients with asthma. In Poland, it is observed in 4.3% of individuals suffering from asthma [6, 7]. This may exacerbate this chronic disease after exposure to ASA. Moreover, acetylsalicylic acid is responsible for disturbed cytokine balance, which may result in disturbed immunological function and a pathological response of the immune system [6, 7].

A diagnosis is established based on differential diagnostics, by the process of elimination, and a positive history of medication [1-5]. Management is similar to AIP treatment [1, 2, 4].

Case report

A 41-year-old patient was admitted to the department of rheumatology due to pyrexia of up to 40°C, and dyspnoea persisting for 2 weeks. Before hospitalisation, the patient was treated at home with a NSAID, due to the diagnosis of a viral infection of the upper respiratory tract. A history of bronchial asthma, treated for several years, was revealed.

The physical examination at admission showed a severe general condition with resting dyspnoea, dull percussion sound over the lower left lung field, and massive, resonant crackles, merging over the entire lungs.

Additional tests revealed leukocytosis (WBC 16.80 x 10^9/l). A radiological thoracic examination demonstrated inflammatory densities in the left lung (Fig. 1). An empirical antibiotic therapy was introduced with amoxicillin, clavulanic acid and clarithromycin. The patient's condition deteriorated. Thoracic tomography revealed areas of ground-glass opacities in the upper lobe of the right lung, an area of high density in the middle

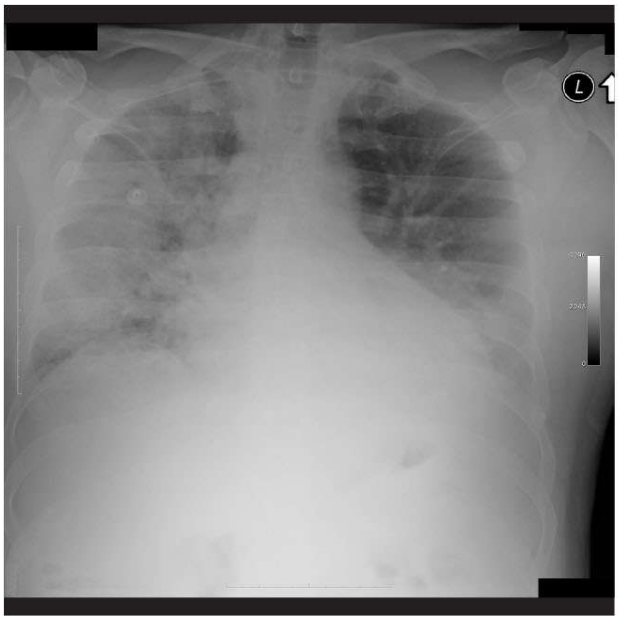

Figure 3. X-ray - progression of infiltration changes
Rycina 3. RTG kontrolne - progresja zmian naciekowych

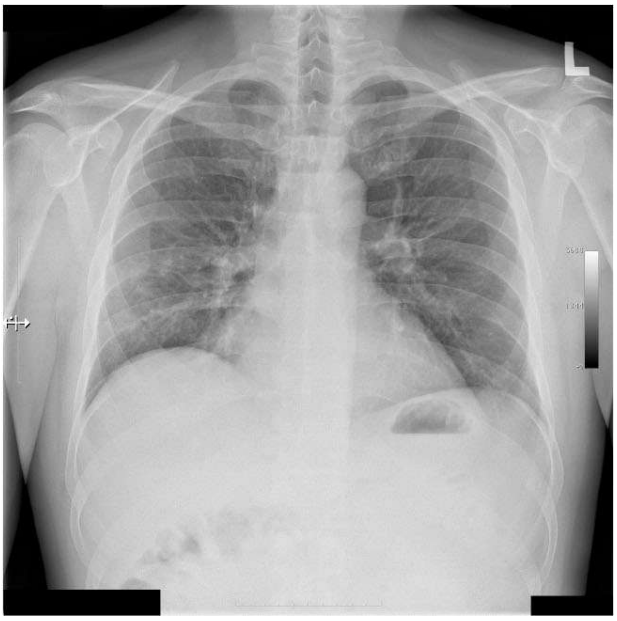

Figure 4. X-ray- regression of parenchymal density
Rycina 4. RTG przy wypisie - regresja zagęszczeń miąższowych

lobe, and massive parenchymal densities in the lower lobe of the right lung (Fig. 2). High fever and dyspnoea persisted. Due to a deteriorated general condition, and the progression of a lesion in the imaging test, the patient was transferred to the Department of Pulmonology.

In further diagnostics, additional tests revealed pH 7.46, pCO2 33.9 mm Hg, pO2 61.1 mm Hg, leukocytosis - WBC 21.50 x 109/l, RBC 4.41 x 1012/l, PLT 185 x 109/l, CRP 39.2 mg/dl, OB 73/h, procalcitonin 7.94 ng/ml, anti-HBc antibodies - non-reactive, HCV - non-reactive, HIV - non-reactive. An abdominal ultrasound showed a normal image of the organs.

Blood samples for cultures were collected, and antibiotic therapy was empirically corrected (piperacillin with amikacine, itraconazole, sulfomethoxazole + trimethoprim). A bronchofiberoscopy was performed, and the aspirate was submitted for a microbiological culture. The patient complained about strong pain in the left chest, alleviated only with narcotic medicines. Further imaging tests of the lungs revealed progression of the inflammatory lesions (Fig. 3). Due to signs of increasing respiratory insufficiency, non-invasive ventilation support was administered, with good results, as the blood oxygenation parameters improved: pH 7.44, pCO2 37.0 mm Hg, pO2 97.7 mm Hg. Further diagnostics to determine the infectious cause of the pneumonia were conducted. Test for A and B flu were performed (both results were negative), as well as two tests of infection with Legionella pneumophila (antigen in the urine was negative). Biochemical tests of viral infection (HCV, HIV, CMV) did not confirm a recent infection. The ANA and pANCA antibody titres were determined with negative results.

As the infectious nature of the disease had not been confirmed (negative blood cultures) and the clinical condition did not improve, glucocorticosteroide therapy was introduced: 1.0 g/d of methylprednisolone was administered, and for the following three days the dose was reduced. Antibiotic therapy was withdrawn, but the glucocorticosteroid doses were maintained. In subsequent imaging tests of the lungs, diffuse inflammatory lesions were still present. After the patient's condition was stabilised, a bronchofiberoscopic examination of the right middle lobe with a bronchoalveolar lavage (BAL) was conducted. Cytological assessment of the aspirate revealed numerous cells of respiratory epithelium, but reduced cellularity disqualified the material for objective assessment [8]. No eosinophils were found in it. Immunosuppresive treatment was continued, and azathioprine was introduced. In the subsequent days of hospitalisation, the signs of respiratory insufficiency subsided, the biochemical blood parameters and inflammatory parameters reached a normal laboratory range. A follow-up X-ray examination demonstrated regression of the lesions (Fig. 4). High doses of systemic steroids resulted in the disturbed metabolism of carbohydrates. The patient was diagnosed with type 3 diabetes. Short-acting insulin was introduced.

Discussion

AIP is a disease characterised by a dynamic course, a non-specific clinical picture, the severe condition of the patient, and an uncertain prognosis, with over a 60% mortality rate in the acute phase of the disease. Therefore, it is often difficult to recognise, and the diagnosis is established during therapy, based on the patient's response to treatment (as in the presented case).

Epidemiological data indicate that the disease most frequently affects middle-aged patients. The symptoms are suggestive of an infectious etiology. Tachypnea, tachycardia, crackles over the entire lung fields and cyanosis are found in the physical examinations. The dynamic course of the disease and pulmonary involvement lead to respiratory insufficiency, which requires mechanical ventilation [4, 5]. Changes in the radiological imagery in the early stages of the disease may be impossible to discern, then they progress rapidly and are visible in the form of vesicular densities and opacities, referred to as ground-glass opacification [1, 4, 5].

Differential diagnosis includes IPF, rapidly deteriorating systemic connective tissue diseases, infective respiratory diseases and drug-induced reactions.

Due to a lack of response to the administered anti-infective therapy and negative results of microbiological tests, infection was excluded. The cytological test results and the absence of antinuclear antibodies eliminated Churg-Strauss syndrome, Goodpasture syndrome or eosinophilic pneumonia.

Finally, having considered the clinical picture and the patient's history, and after exclusion of the above disease units, the diagnosis of DILD was established, with acetylsalicylic acid as the trigger for AIP symptoms.

The mechanism of the pathological process is not fully understood, although it is suspected that it is mediated by lymphocytes T [1, 4, 5]. According to the literature data, the incidence of DILD in men and women is similar, and independent of age [1]. It has been suggested that the development of symptoms depends on the dose of the medicine [1, 2, 4, 5]. In the discussed patient, despite numerous previous exposures to ASA, the symptoms occurred after ingestion of a high dose of the substance in an OTC preparation. Possible interactions between medicines are also considered, as in the presented case [1-4]. It should be noted that among NSAIDs, acetylsalicylic acid is mentioned as the most common trigger of DILD [1, 3, 5]. It is also in the group of substances which most often cause pulmonary injury due to hypersensitivity [1, 3, 5]. There are premises indicating an increased incidence of DILD in patients with chronic lung diseases – the presented patient had a diagnosis of bronchial asthma for several years [1, 5-7].

No universal management protocol has been established so far for AIP or DILD. Symptomatic treatment involves oxygen therapy and mechanical ventilation [1, 4, 5]. In pharmacotherapy glucocorticosteroids, cyclophosphamide, azathioprine or vincristine are used [1, 5]. In the case of DILD, it is clearly necessary to discontinue the agent triggering the symptoms [1-5].

The prognosis is unfavourable. Most patients who survive the acute phase of the disease (40%) die within the next six months. There is a risk of permanent reduction of the lung function, and of progressive pulmonary fibrosis. In some patients complete recovery is obtained [1, 5].

Conclusions

Acute interstitial pneumonia is a direct threat to a patient's life due to rapidly progressing respiratory insufficiency. Usually it is idiopathic, and in certain cases it is caused by the medicines used by the patient. Diagnosis of DILD consists of differential diagnostics and the elimination of other options, primarily infection. Patients, apart from ventilatory support, require therapy with high doses of immunosuppressives (glucocorticosteroids, cyclophosphamide, azathioprine and vincristine). Aggressive treatment, despite the risk of adverse effects and an unfavourable prognosis, may result in complete recovery, as in the presented case.

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High mortality risk pulmonary embolism in a patient with colitis ulcerosa

Zatorowość płucna dużego ryzyka zgonu u chorego z wrzodziejącym zapaleniem jelita grubego

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Abstract. The case report involves a 44-year old patient admitted to the hospital with symptoms of cardiogenic shock. The patient was suffering from colitis ulcerosa and had an episode of low mortality risk pulmonary embolism in the course of deep vein thrombosis and innate thrombophilia. As a result of anticoagulation treatment, the patient developed heparin-induced thrombocytopenia. Considering the patient's comorbid diseases, this article presents the connections between them as well as the possibility of their overlapping and mutual intensification, and related therapeutic decisions.
Key words: cardiogenic shock, colitis ulcerosa, pulmonary embolism, factor V Leiden mutation, heparin-induced thrombocytopenia

Streszczenie. Opisano przypadek 44-letniego pacjenta przyjętego do szpitala z objawami wstrząsu kardiogennego. Chory leczony przewlekle z powodu wrzodziejącego zapalenia jelita grubego. W wywiadzie przebyta zatorowość płucna małego ryzyka zgonu w przebiegu zakrzepicy żył podudzia oraz trombofili wrodzonej. Przebieg leczenia przeciwkrzepliwego powikłany małopłytkowością indukowaną heparyną. Przedstawiono implikacje kliniczne współistniejących chorób i decyzje terapeutyczne z nich wynikające.
Słowa kluczowe: wstrząs kardiogenny, wrzodziejące zapalenie jelita grubego, zatorowość płucna, mutacja czynnika V Leiden, małopłytkowość indukowana heparyną

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Introduction

Venous thromboembolism is a common disease, coexisting with other disorders, especially with a pulmonary embolism, which can result in a life-threatening, acute right ventricular heart failure.

Case report

A 44-year-old patient was admitted to the hospital in a critical condition, with symptoms of cardiogenic shock. A physical examination revealed pale skin, with significant signs of perspiration, a weak vesicular murmur over the lung fields, RR 70/50 mm Hg, HR 45/min, sO_2 92%. The patient also reported increased frequency of loose, bloody stools.

He was treated long-term due to ulcerative colitis. Moreover, the patient had a history of pulmonary embolism following lower limb deep vein thrombosis, and heterozygous V Leiden factor mutation. Based on the physical examination and medical history, a pulmonary embolism was suspected. As part of preliminary diagnostics at the HED, a thoracic angio-CT test was performed. A bilateral pulmonary embolism was demonstrated: a riding embolus in the pulmonary trunk bifurcation and in the bifurcation of both pulmonary arteries, embolic material in all the lobar arteries, and in most segmental arteries bilaterally.

Echocardiographic examination demonstrated signs of overload and impaired contractility of the right cardiac ventricle. No thrombi were found in the right heart cavities.

An ultrasound examination of lower limb veins did not reveal deep vein thrombosis.

Due to an increased risk of gastrointestinal haemorrhage, fibrinolytic therapy was not introduced. The patient received a continuous infusion of unfractionated heparin (UFH). Due to persistent hypotension, pressor amines had to be administered (noradrenaline). Over the following days, the patient's condition stabilised.

Instead of UFH, low molecular weight heparin (LMWH) was administered. The patient's general condition deteriorated. The blood pressure decreased, tachycardia occurred, and saturation was reduced to 86%. In addition, the patient complained about chest pain.

Another angio-CT examination was performed; no thrombi in the left pulmonary artery were demonstrated. In the proximal lobar segments of the right pulmonary artery, there was an excessive amount of embolic material, and the peripheral flow was impaired in the middle and lower lobar arteries. The patient was qualified for catheterisation of the pulmonary artery. A local procedure to restore the patency was performed (pig tail and MP catheter rotation, and aspiration thrombectomy), resulting in a limited angiographic improvement, especially in the upper lobar artery. The clinical condition improved. As a result of the procedure, and an increased risk of haemorrhagic complications, local thrombolytics were not administered. The antithrombotic therapy was adjusted (UFH instead of LMWH), pressor amines and oxygen were administered, and fluid therapy was continued. Due to a significant (>50%) reduction of the platelet count in the following days of hospitalisation, on the 15th day, the patient was diagnosed with heparin-induced thrombocytopenia. The antithrombotic treatment was corrected. UFH was discontinued, and fondaparinux was administered. Anti-platelet factor 4 (PF4) antibody titre was determined. On the 18th day of hospitalisation, in the morning, the patient suddenly lost consciousness. Bilateral pupil dilation was observed, as well as a lack of pupil response to light, flaccid right-sided hemiparesis and bilateral Babinski response. The symptoms subsided within an hour.

A CT examination of the central nervous system was performed, and it did not demonstrate signs of haemorrhage. The angio-CT of the cerebral vessels revealed a thrombus in the distal section of the basilar artery, closing the lumen of the left posterior cerebral artery, and the left superior cerebellar artery. After a consultation with an interventional radiologist and with a neurologist, surgery was dismissed, due to the high risk of cerebral stroke associated with the procedure. The conservative treatment was continued.

On the next day, in the evening, the patient experienced a reduction of the field of vision on the right side. A brain tomography was performed, demonstrating a fresh stroke focus in the left occipital lobe. After a consultation with a neurologist, the conservative treatment was continued.

A transoesophageal ECHO examination was performed. It revealed a thrombus wedged in the foramen ovale, and a leak through the interatrial septum at the level of the foramen ovale. The patient was initially qualified for a cardiosurgical procedure. The surgery was postponed due to a fresh stroke focus in the brain. The conservative treatment continued, and oral coagulants were introduced. The next ECHO examination did not demonstrate a thrombus in the atriums. The patient started rehabilitation.

After 37 days, the patient was discharged in a good general condition. Three months after the described thromboembolic incident, he had an endovascular procedure: closure of the opening in the interatrial septum.

Discussion

The presented juxtaposition of disease processes, the unexpected course, and complications associated with the treatment provide interesting material for analysis.

The Factor V Leiden mutation found in almost 5% of the Caucasian population is a mutation of a single gene. Due to the mutation, both the active and inactive form of coagulation factor V are resistant to active C protein (aPC), known as a natural coagulant. In this case, the natural process of haemostasis is disturbed, and the coagulation pathway promotes coagulation. Therefore, individuals with the FVL mutation are at increased risk of venous thromboembolism. It is estimated that the mutation is detected in 20-60% of patients with deep vein thrombosis (DVT) [1]. However, it is worth emphasising that not all individuals with the FVL mutation will develop venous thromboembolism. Nevertheless, once the mutation is discovered, the risk of venous thromboembolism should be reduced with primary prophylaxis (but also by preventing recurrence of the disease, if it occurred before).

Type II heparin-induced thrombocytopenia (HIT), found in the presented patient, is an autoimmune disease. Normally, heparin binds with PF4 of thrombocytes, thus blocking the coagulation process. The autoantibodies produced are oriented against the complexes of PF4 and heparin [2-4]. This results in changes leading to thrombocytopenia through two mechanisms. Firstly, thrombocytes with the IgG autoantibody are destroyed by macrophages in the spleen, secondly – and most importantly – the platelets are activated earlier, in an uncontrolled manner, and they

coagulate. This condition may also contribute to an increased risk of venous thromboembolism [3].

Due to the varied etiology of both disease units (the gene mutation in FVL and the autoimmune nature of type II HIT) it may be assumed that the FVL mutation increases the thrombotic risk in HIT, and the rate at which thrombocytopenia and thrombosis developed. Data indicate that heterozygous FVL mutation is not an additional risk factor for thrombosis in patients with HIT. It means that in both cases the thrombosis develops in a different way, but no correlation or mutual intensification of these processes have been demonstrated [5].

Pulmonary embolism (PE) is the most dangerous form of venous thromboembolism. In patients diagnosed with HIT, the risk of DVT increases. Therefore, PE is assumed to be a complication of HIT, and it may occur in up to 40% of cases [6, 7].

Diseases of the colon predispose to DVT as a post-operative complication. Venous thromboembolism is a frequent complication in these patients, and it is associated with increased mortality [8].

The risk of thrombosis is elevated in patients with inflammatory colon diseases, because they predispose to an increased risk of neoplasms. Iversen et al. studied patients operated on due to colorectal cancer, and observed DVT in 20% of the subjects [9].

Pre-operative screening in the form of ultrasonographic pressure test in patients with a newly diagnosed tumour revealed thrombosis in 7.5% of them [10].

Summing up, it is believed that inflammatory intestinal diseases are associated with up to a four times higher risk of venous thrombosis [11], which may also correlate with the scope of the inflammatory process [12].

Therapy of thromboembolic disease in patients with inflammatory colorectal diseases is difficult. On the one hand, there is the increased risk of haemorrhage from the damaged intestine; and on the other hand, the medicines used to treat both diseases may interact. The interaction of azathioprine and warfarin reduces the effect of the latter. It forces increasing the dose of warfarin by a factor of 3-4 times [13], which could make effective control of INR difficult.

This leads to a more frequent use of low molecular weight heparin instead of oral coagulants in patients with inflammatory intestinal diseases. However, using heparin is associated with a risk of HIT. In this group of patients, unfractionated heparin is more often used, as its $T_{1/2}$ is shorter. It helps to control the doses, and in patients with a risk of haemorrhage, this is very important. HIT develops more often following the use of unfractionated heparin than low molecular weight heparin [14].

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Alveolar hydatid disease – problems with diagnosis

Bąblowica wielojamowa wątroby – trudności diagnostyczne

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Abstract: Alveolar echinococcosis (alveolar hydatid disease) is caused by the larval form *of Echinococcus multilocularis.* The invasive nature of the parasite's growth and ability to spread to distant organs and the creation of secondary lesions makes alveolar hydatid disease similar to cancer. Alveolar hydatid disease does not have any specific symptoms so the diagnosis is based on imaging studies and serology. The case report presents a 75-year-old patient with weakness, weight loss and recurrent fever, who had been diagnosed with a tumor in the liver and adrenal gland and recurrent pleural effusion. In the past, the patient was treated for colorectal cancer. In order to determine the etiology of focal lesions, the patient underwent a series of examinations, including positron emission computed tomography (PET-CT) and magnetic resonance imaging (MRI) of the abdomen, as well as a surgical biopsy of the lesion. Histopathological examination of the sample demonstrated abnormalities that may be the result of parasitic infestation. The diagnosis of alveolar echinococcosis was based on clinical picture and positive serological results.
Keywords: *Echinococcus,* alveolar hydatid disease, alveolar echinococcosis, liver tumor

Streszczenie. Bąblowica wielojamowa (alweokokoza) wywoływana jest przez larwy bąblowca wielojamowego *Echinococcus multilocularis*. Naciekowy charakter wzrostu oraz zdolność do rozprzestrzeniania się larw do narządów odległych i tworzenia ognisk wtórnych upodabnia bąblowicę do choroby nowotworowej. Brak patognomonicznych objawów sprawia, że w rozpoznaniu alweokokozy podstawowe znaczenie mają badania radiologiczne i serologiczne. W artykule przedstawiono przypadek 75-letniego pacjenta zgłaszającego osłabienie, postępującą utratę masy ciała i nawracające stany podgorączkowe, u którego stwierdzono guza wątroby i nadnercza prawego oraz nawracający płyn w prawej jamie opłucnowej. W przeszłości pacjent był leczony z powodu raka jelita grubego. W celu ustalenia charakteru zmian ogniskowych u chorego wykonano szereg badań, w tym pozytonową tomografię komputerową (PET-CT) i rezonans magnetyczny (MRI) jamy brzusznej oraz biopsję chirurgiczną. W badaniu histopatologicznym pobranego wycinka stwierdzono nieprawidłowości wskazujące na inwazję pasożytniczą. Na podstawie obrazu klinicznego i dodatnich wyników testów serologicznych u pacjenta rozpoznano bąblowicę wielojamową.
Słowa kluczowe: *Echinococcus,* bąblowica wielojamowa, alweokokoza, guz wątroby

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Background

Alveolar hydatid disease (alveolar echinococcosis) is a zoonotic disease caused by the larval form of *Echinococcus multilocularis*, considered one of the most dangerous parasites for humans. The definitive hosts of *E. multilocularis* are foxes, wolves, raccoon dogs and dogs, which excrete the parasites' eggs in their faeces. Intermediate hosts include forest and field mammals, such as shrews and voles [1, 2]. Humans do not participate in the parasite's development cycle, but they can be infected by accidental ingestion of the eggs, which can be found on the hands after contact with infected animals (mainly foxes) carrying eggs on their fur [2, 3]. The risk factors for alveolar hydatid disease include drinking contaminated water or eating contaminated vegetables, forest fruit and mushroom, or working in agriculture in an area where foxes are often found.

According to the WHO, alveolar hydatid disease is endemic to South America, East Europe, Russia, East Asia and China [4]. Studies by Nahorski et al. demonstrate that in the years 1990-2011, 121 cases of alveolar echinococcosis were observed in Poland, primarily in the northeastern regions [5].

In the majority of patients, the primary lesion is found in the liver, where it forms a conglomerate of numerous, small cysts. The most frequent extrahepatic locations include the lungs, brain and peritoneum [5]. A characteristic feature of the primary lesion is the absence of a connective tissue sac, which facilitates penetration of the organ by a growing parasite and metastases to distant organs, which renders the process similar to neoplatic proliferation [6].

In most patients the infection is asymptomatic. Symptoms often occur years after the infection, and are associated mostly with the growth of the cysts, resulting in pressure on the adjacent tissue and organs, and depends on their location. The spontaneous or injury-induced breakage of a cyst may lead to anaphylactic shock.

Due to its limited incidence, alveolar hydatid disease is rarely considered in the differential diagnostics of a focal lesion, which may result in delayed diagnosis and improper treatment. Untreated alveolar echinococcosis leads to death in a few years [3, 7, 8]. This study presents the case of a patient with a history of colorectal cancer, examined due to focal lesions of an unknown nature in the liver and the right adrenal gland.

Case report

A 75-year-old patient, a forester, with coronary disease, a paroxysmal atrial flutter, hyperthyroidism and osteoarthritis, was admitted in May 2015 to the Department of Internal Diseases, Nephrology and Dialysis of the Central Clinical Hospital of the Ministry of National Defence, Military Institute of Medicine, due to body weight loss (8 kg within a month), weakness, a recurring subfebrile state and recurring fluid in the right pleural cavity.

Previously, in September 2014, the patient had a right hemicolectomy due to a non-pedunculated colon polyp, found in a preventative colonoscopy. The histopathological examination of the tissue removed during the surgery revealed *adenocarcinoma intramucosum*, infiltrating focally the lamina propria of the colonic mucosa. In order to assess the advancement of the neoplastic disease, an abdominal ultrasound examination was performed, which demonstrated a hypoechogenic area of 44 x 36 x 44 mm near the hepatic hilum. Due to the unknown nature of the lesion, a positron emission computed tomography examination (PET-CT) was conducted, and revealed a focus of 42 x 57 x 46 mm, with peripherally increased metabolic activity, in the 7th segment of the liver, and in the nodule of the right adrenal gland. The abdominal magnetic resonance imaging (MRI) demonstrated an infiltrative lesion with a minor and partial enhancement in segments 7/8 of the liver, infiltrating through the organ capsule, and covering the right adrenal gland. Both in the adrenal gland and in the liver, the described lesions were heterogeneous and composed of multiple individual cysts (Fig. 1). The abdominal and pelvic computed tomography (CT) test conducted in February 2015 revealed an infiltrative lesion in segment 7, of approximately 57 x 56 mm, encircling the inferior vena cava and the right hepatic vein, and infiltrating the right adrenal gland (29 x 20 mm), dilation of the biliary ducts, peripheral to the infiltration, in segment 7 of the liver, and a moderate stricture of the lumen of vena cava inferior, caused by the tumour (Fig. 2), which indicated progression of the disease, and suggested the hyperplastic nature of the lesion.

In order to verify the type of the lesion, in March 2015 a laparotomy was performed, samples for histopathological examination were collected from the hepatic tumour, and thermoablation of its remaining part was carried out. The procedure consisted of focal warming up of the tissue up to 45-50° C with an electric current, using leads introduced directly into the lesion, which caused protein denaturation. The histopathological examination of the biopsy material demonstrated fragments of the liver with necrotic foci, containing the remains of eosinophilic, twisted structures, corresponding to fragments of parasites surrounded by fibroblasts, histiocytes and eosinophils. No neoplastic cells were observed. The patient was referred to a local health centre.

In March 2015, the patient was hospitalised in the local hospital, where, based on a physical examination and medical interview, he was diagnosed with right-sided pneumonia. He received empirical antibiotic therapy with gentamycin, amoxicillin with clavulanic acid, and ciprofloxacin. Due to a large volume of fluid in the right pleural cavity, multiple thoracentesis procedures were performed during a 2-week long hospitalisation. As a result, approximately 400 ml of effusion fluid was collected in total. The results of cultures from the collected fluid were negative. The treatment lead to a clinical improvement. Despite the effective antibiotic therapy, the recurrent effusion in the right pleural cavity required pleural drainage, which resulted in rehospitalisation of the patient in April 2015.

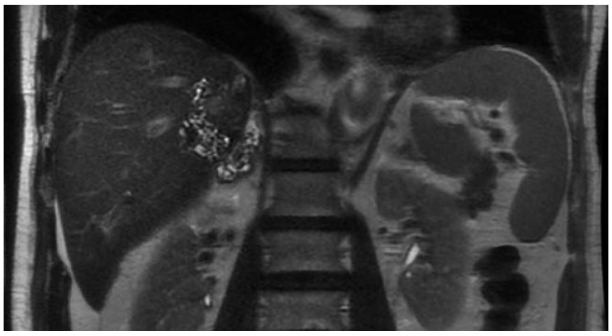

Figure 1. Magnetic resonance image (MRI) of abdomen - tumor in the liver. Photograph from patient medical records (Military Institute of Medicine).

Rycina 1. Zmiana ogniskowa w wątrobie w badaniu MRI jamy brzusznej. Zdjęcie z dokumentacji pacjenta (WIM CSK MON).

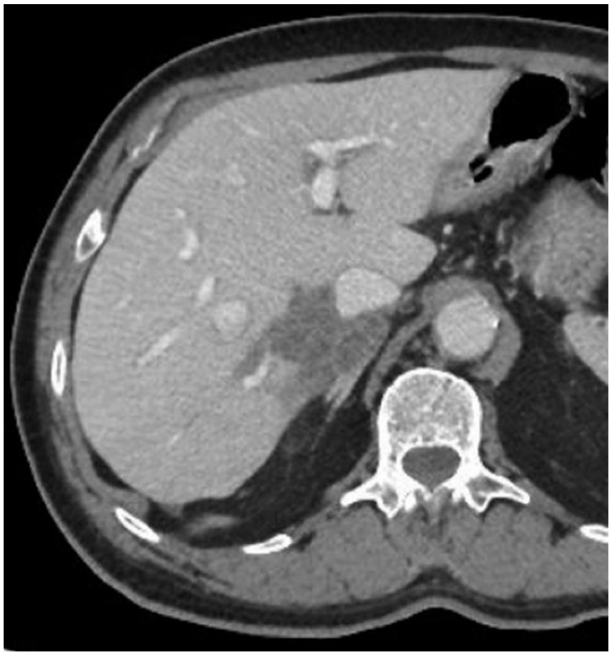

Figure 2. Computed tomography scan (CT) of abdomen - tumor in the liver. Photograph from patient medical records (Military Institute of Medicine).

Rycina 2. Zmiana ogniskowa w wątrobie w badaniu TK jamy brzusznej. Zdjęcie z dokumentacji pacjenta (WIM CSK MON).

Due to his deteriorating general condition, in May 2015 the patient was admitted to the Department of Internal Diseases, Nephrology and Dialysis of the Military Institute of Medicine. Additional tests revealed anaemia, eosinophilia, elevated inflammatory parameters, elevated hepatic parameters, and a reduced TSH concentration. The results of stool tests for parasites and virological tests for type B and C hepatitis were negative (Tab. 1).

Table 1. Results of laboratory tests (May 2015)
Tabela 1. Wyniki badań laboratoryjnych (maj 2015 r.)

Parameter	Value	Normal range
Haemoglobin	11.2 g/dl	11.0-18.0 g/dl
Haematocrit	33%	35-55%
Eosinophils	9.00%	0.5-6.0%
ESR	105 mm	0-20 mm
CRP	4.5 mg/dl	0-0.8 mg/dl
ALT	186 U/l	0-50 U/l
AST	114 U/l	0-50 U/l
ALP	269 U/l	40-129 U/l
GGTP	165 U/l	8-61 U/l
TSH	0.034 µIU/ml	0.27-4.2 µIU/ml
fT3	3.79 pmol/l	3.2-6.9 pmol/l
fT4	16.33 pmol/l	12-22 pmol/l

The tests revealed the presence of effusive fluid in the right pleural cavity, with signs of minor pneumothorax, and an area of atelectatic densities over the fluid. Bacterioscopic examination and cultures of the fluid obtained by thoracentesis gave negative results. Despite the thermoablation performed previously, the abdominal ultrasound demonstrated an irregular, hyperechogenic focal lesion of 33 x 44 x 58 mm, and a volume of 45 ml in hepatic segment 7, of unknown nature (suggestions included angioma, haematoma following resection of the lesion in the organisation phase, or a hyperplastic lesion), slightly dilated intrahepatic biliary ducts in both lobes, and a hyperechogenic lesion of 16 x 38 mm in the area of the right adrenal gland, adjacent to the lesion in the liver. An abdominal CT scan revealed a hypodense focal lesion of 51 x 60 x 64 mm, with central amorphous hyperdense foci, covering segment 7 of the liver, and transgressing its outline up to the adrenal field. Based on the clinical course of the disease and the imaging studies suggestive of a hyperplastic process, considering the histopathological examination results excluding the neoplastic nature of the lesion, and indicating a parasitic infection, together with the patient's line of work, alveolar hydatid disease was suspected. With the use of an ELISA test, specific IgG antibodies against the *Echinococcus* antigens were found. The diagnosis was confirmed with a Western-blot test, which presented the electrophoretic band pattern characteristic of an *E. multilocularis* infection. To determine the advancement of the disease, and to exclude CNS involvement, a head CT and ophthalmological examination were performed, although they did not reveal any significant abnormalities. Considering the reported general symptoms (e.g. body weight loss and weakness) and abnormal laboratory test results regarding thyroid function, modification of the

Table 2. TNM Classification of alveolar hydatid disease [9]
Tabela 2. Klasyfikacja PNM bąblowicy wielojamowej [9]

P - parasite present in the liver	Px - the primary tumour has not been assessed P0 - no detectable hepatic tumour P1 - peripheral lesion without biliary or proximal vascular involvement P2 - central lesion with biliary or proximal vascular involvement of one lobe P3 - central lesion with biliary and/or proximal vascular involvement of both lobes, or two hepatic veins, or both P4 - extension of each hepatic lesion along the portal vein, inferior vena cava or hepatic arteries and the biliary tree
N - involvement of neighbouring organs	Nx - not assessed N0 - no regional involvement of neighbouring organs N1 - regional involvement of neighbouring organs
M - presence or absence of distant metastatic lesions	Mx - not assessed M0 - no metastases detected (thoracic X-ray and head CT - no metastases) M1 - metastases present

Table 3. Stages of alveolar hydatid disease [9]
Tabela 3. Stopnie zaawansowania alweokokozy [9]

Stage I	P1 N0 M0
Stage II	P2 N0 M0
Stage IIIa	P3 N0 M0
Stage IIIb	P1-3 N1 MO P4 N0 M0
Stage IV	P4 N1 M0 any P any N M1

treatment with metizol (thiamazole) was introduced. After the diagnosis, the patient, in a stable condition, was referred to the Clinic of Infectious Diseases, where albendazole therapy was implemented, based on the received test results. Presently, the patient is in good general condition, and is under observation on an outpatient basis.

Discussion

Alveolar echinococcosis is asymptomatic until the cysts start exerting pressure. Due to the absence of pathognomonic symptoms, diagnosis is based on radiological imaging tests and serological examinations [4]. Abdominal ultrasonographic examination shows an irregular, poorly vascularised focal lesion of heterogeneous echogenicity, with areas of necrosis, calcifications and infiltration of the adjacent structures [9, 10]. The presence of multiple hyperechogenic foci may indicate an early stage of the alveolar hydatid disease. If a computed tomography scan reveals cysts with small, peripheral calcifications, and a lack of contrast enhancement of the septa in the cysts, it indicates alveolar echinococcosis. A multivesicular structure, visible in the magnetic resonance imaging test, and found in the presented case, is characteristic of alveolar hydatid disease (Fig. 1) [6, 7, 10]. According to WHO recommendations, the basic imaging test used in the diagnostics of alveolar hydatid disease is an ultrasonographic examination. Computed tomography and magnetic resonance imaging are performed in the case of atypical lesions, and in patients qualified for surgical treatment [3]. In the presented case, the initial ultrasound test did not allow an unambiguous diagnosis, so using more advanced diagnostic tools was necessary.

For the assessment of disease advancement, PNM classification based on the imaging test results has been developed. Category P refers to the hepatic location of the primary lesion, N describes infiltration of the adjacent organs, and M determines the presence of distant metastases of the disease (Tab. 2-3). The presented patient should be diagnosed with stage IIIb alveolar hydatid disease, due to adrenal involvement.

Laboratory tests are also used in the diagnostics of alveolar hydatid disease. They usually demonstrated increased activity of aminotransferases and cholestatic enzymes, as observed in the presented case. Determination of specific antibodies against antigens Em-2 plus and Em-18 using the ELISA method (sensitivity >90%, specificity of 95%), confirmed in a Western-blot test, is also useful in the diagnostic process. To verify the diagnosis of alveolar hydatid disease, histopathological and molecular tests of a tumour sample are used (detection of the parasite's molecular material with the PCR method). In the described case, the diagnosis was based on the results of serological tests.

Despite recent progress, treatment of alveolar hydatid disease is difficult. In the case of resectable lesions, the treatment of choice involves removal of the focal lesion with a healthy tissue margin. Patients with very advanced lesions infiltrating the hepatic hilum or the inferior vena cava, but without foci in other organs, may be qualified for liver transplantation. In the case of non-surgical or diffuse lesions, pharmacological treatment with albendazole is used [1, 11].

This study presents diagnostic problems in the patient with a hepatic focal lesion. The general symptoms reported by the patient indicated an advanced, generalised neoplastic disease, but distant metastases in a patient with colorectal cancer that does not invade the

basement membrane *(carcinoma in situ)* are unlikely. The risk of a primary liver tumour in a patient without a chronic hepatic parenchymal damage is also very limited, although the imaging test results indicated a hyperplastic disease. Due to the location of the focal lesion and the high risk of complications associated with a large-core needle biopsy conducted to verify the nature of the tumour, a surgical biopsy was performed. The clinical course of the disease, as well as the long-term involvement of the patient with forestry, indicating possible ingestion of unwashed forest fruit and contact with wild animals, which are considered the principal risk factors for the disease, directed further diagnostic procedures. As a result, alveolar hydatid disease was recognised, and treatment was implemented. Gradual reduction of the fluid volume in the pleural cavities could confirm the effectiveness of the therapy. The general symptoms observed at admission to the hospital (e.g. body weight loss and weakness) could also result from hyperthyroidism, especially considering the fact that modification of the treatment regimen with thiamazole resulted in reduced severity of the symptoms, and in stabilisation of the patient's condition.

Conclusions

The infiltrative character of the alveolar echinococcosis lesion, as well as the migration of larvae to distant organs, where they create secondary foci, render the disease similar to a neoplastic process. In the diagnostics of a primary lesion of uncertain nature, a differential diagnosis should cover rare conditions, including a zoonotic disease. Exhaustive diagnostics, including a detailed patient interview, help to establish an accurate diagnosis, and implement the proper treatment.

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Dietetic approach to chronic renal failure in the predialysis period

Postępowanie dietetyczne u pacjentów z przewlekłą chorobą nerek w okresie leczenia zachowawczego

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Abstract. Chronic kidney disease (CKD) is a structural or functional kidney dysfunction lasting at least 3 months. It affects approximately 11.9% of adults in Poland, while diabetic kidney disease is the most frequent cause of CKD. A special diet and nutrition assessment should accompany pharmacological treatment in patients with this disease. Low protein diets (LPDs) or very low protein diets (vLPDs) with ketoanalogs supplementation are desirable. A significant component of the diet, apart from protein content, should be an adequate supply of energy, both quantity and quality of fats and the content of mineral components such as sodium, potassium, phosphates and water-soluble vitamins. In recent years, attention has been paid to fructose intake, which enhances insulin resistance. Implementation of dietary recommendations may delay disease progression and renal replacement therapy. A proper diet favourably influences the nutritional status, metabolic disorders and quality of life of the patient; thus, it may contribute to a reduction in the direct and indirect costs of CKD treatment.
Keywords: chronic kidney disease, low-protein diet (LPD)

Streszczenie. Przewlekła choroba nerek (PChN) to zespół chorobowy rozwijający się na podłożu strukturalnego lub czynnościowego uszkodzenia nerek trwającego przynajmniej 3 miesiące. W Polsce aktualnie choruje około 11,9% dorosłych, a najczęstszą przyczyną jest cukrzycowa choroba nerek. Leczenie zachowawcze PChN obejmuje oprócz leczenia choroby podstawowej również leczenie dietetyczne i ocenę stanu odżywienia. W PChN stosuje się dietę ubogobiałkową (LPD) oraz bardzo ubogobiałkową (vLPD) suplementowaną ketoanalogami aminokwasów egzogennych. Istotnymi elementami diety, oprócz zawartości białka, są: odpowiednia podaż energii, ilość i jakość tłuszczów, zawartość składników mineralnych, takich jak sód, potas, fosforany, czy witamin rozpuszczalnych w wodzie. W ostatnich latach zwraca się uwagę na spożycie fruktozy, która nasila insulinooporność. Przestrzeganie odpowiednich zaleceń dietetycznych pozwala spowolnić przebieg choroby, opóźniając konieczność wdrożenia leczenia nerkozastępczego, wpływa korzystnie na stan odżywienia, towarzyszące zaburzenia metaboliczne i jakość życia pacjentów. Tym samym przyczynić się może do zmniejszenia kosztów bezpośrednich i pośrednich leczenia PChN.
Słowa kluczowe: dieta ubogobiałkowa, przewlekła choroba/niewydolność nerek

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Introduction

Chronic renal failure (CRF) is a disease syndrome that develops as a result of progressive and irreversible kidney function impairment, manifested by a reduced glomerular filtration rate (GFR). According to the Kidney Diseases Outcome Quality Initiative (K/DOQI) guidelines, it is a condition characterised by renal damage persisting for over 3 months, and/or a GFR reduced to <60 ml/million/1.73 m^2 for over 3 months [1].

The annual incidence of CRF is approximately 150 people in Poland, approximately 11.9% of the adult population suffer from CRF, and the rate of patients with end-stage renal failure is increasing dramatically; this is primarily due to the epidemic of diabetes, excessive weight and obesity [2].

Chronic renal failure results from a reduced number of active nephrons, due to glomerulosclerosis, tubular atrophy, and fibrosis of the renal interstitial tissue. From an epidemiological point of view, the primary causes

include; diabetic nephropathy, hypertensive nephropathy, glomerulonephritis and other diseases [1].

Due to pathological processes developing in the kidneys, the number of nephrons is reduced. As a result, the excretion of nitric metabolites decreases, and they accumulate in the blood serum. The renal adaptive mechanism in reaction to that situation involves hyperfiltration in the undamaged nephrons. Therefore, CRF is balanced (compensated) for many months or years, and creatinine concentrations are within the normal range, or slightly elevated. To determine the CRF stage, GFR should be calculated, based on the formulas including creatinine concentration, as well as the patient's age, sex, and race (the Cockroft-Gault formula or short MDRD, i.e. a formula developed in the Modification of Diet in Renal Disease Study). Glomerular hyperfiltration, occurring as a reaction to renal damage, is harmful. From a long-term perspective, it leads to glomerulosclerosis, thus accelerating the progression of CRF, as demonstrated by Brenner [3]. The factors contributing to glomerular hyperfiltration include a high protein diet and hyperglycaemia. Therefore, restricting protein intake is the main dietary recommendation for CFR patients.

The principles of a low-protein diet in CRF patients

Following a low-protein diet (LPD) is associated with reduced accumulation of the catabolic end products of protein, such as phosphates, organic acids, sulphates and urea, i.e. toxins which cause the symptoms of uremia. To reduce these symptoms, a low-protein diet was introduced in the first half of the 20th century. At that time, a restrictive potato diet was recommended, containing only 20-25 g of protein/d [4, 5]. In the 1970s, researchers observed that the diet was associated with a risk of malnutrition. The low-protein diet regained interest in the 1980s. Then animal models provided evidence that the long-term reduction of protein intake limited renal damage in histological tests, and delayed CRF progression. A low-protein diet demonstrates nephroprotective effects, as it reduces glomerular hyperfiltration, thus decreasing the progression of CRF. Numerous studies presented the effect of a low-protein diet on a delay in CRF progression; however, in some studies this influence was not observed [6, 7]. The greatest difficulty in conducting reliable studies in this area is patient compliance. The population of CRF patients largely comprises elderly people, with various degrees of education, who require individualised methods of nutritional education [8, 9].

Diet in CRF supports pharmacological treatment. Properly implemented and supervised nutritional therapy helps to inhibit renal damage and delay the necessity of renal replacement therapy, as well as preventing malnutrition and reducing the metabolic disorders associated with kidney diseases. CRF patients are at an increased risk of protein and energy malnutrition, which is an independent risk factor for elevated mortality rates in this group of patients. A low-protein diet in CRF must be closely monitored by a nephrologist and a nutritionist.

Energy value of the diet

The energy value for patients with CRF is the same as for healthy individuals. Energy requirement depends on age, sex, body weight and physical activity. The usually recommended value is approximately 35 kcal/kg i.b.w./d. In elderly patients, i.e. over 60 years old, who do not lead an active lifestyle, the energy requirement is reduced to 30 kcal/kg i.b.w. [10-12].

With planned protein reduction, the energy value of the diet is very important for the prevention of protein energy wasting (PEW). It should be monitored with daily dietary intake records and recommended methods of nutritional status assessment. The awareness of appetite disorders secondary to increasing uremia (uremic anorexia), which often result in a significant reduction of the food consumed, is an important element of proper nutrition. This phenomenon may be prevented by patient education, monitoring of intake, and the proper choice of foods, considering patient's taste preferences (e.g. a clear preference for acidic foods with a strong flavour, frequently declared by CRF patients).

The most accurate method of estimating energy requirement is based on calculating the resting metabolic rate (RMR), and considering the physical activity index typical for the patient.

Protein

In nutritional therapy of patients with chronic renal failure, the quality and amount of protein intake are the most important aspects. The protein content in the diet is calculated based on ideal body weight. A normal protein diet contains 0.8-1.0 g of protein/kg i.b.w. According to ESPEN (The European Society for Clinical Nutrition and Metabolism), in CRF patients treated conservatively, whose GFR is <70 ml/min/1.73 m^2, the recommended protein intake is 0.55-0.60 g/kg i.b.w./d. This ensures proper nitrogen balance [10]. The recommendations of the Team of the National Medical Consultant in Nephrology from 2010 include a protein intake of 0.8-1.0 g/kg i.b.w. for patients with CRF during conservative treatment , and 0.6-0.8 g/kg i.b.w. in patients with GFR <25 ml/min. [11]. Nephrology societies also present recommendations regarding protein content in the diet: NKF (National Kidney Foundation) recommends a protein intake of 0.6-0.75 g/kg i.b.w. in patients with GFR <25

ml/min, whereas ADA (American Dietetics Association) recommends this amount in a wider range of patients, i.e. in those with GFR 15-90 ml/min [9, 12, 13].

Complete protein (i.e. animal protein) should account for 50% of the total protein intake. A reduced amount of protein in the diet is possible in stable patients, who are under the care of a nutritionist.

In patients with GFR >70 ml/min/1.73 m^2, the recommended protein intake is the same as for healthy individuals, i.e. up to 1.0 g/kg i.b.w. However, periodical monitoring is important, so that the protein content in the diet does not exceed 1.0 g/kg i.b.w.

The dietary recommendations should be based on the patient's current metabolic parameters, as metabolic acidosis, chronic inflammation, resistance to anabolic hormones, anaemia and loss of appetite contribute to chronic renal failure. All these metabolically adverse symptoms may result in lean body mass wasting, and the development of protein and energy malnutrition. For safety reasons, protein reduction to <0.8 g/kg i.b.w./d should not be recommended in patients with reduced blood carbohydrate concentrations (HCO_3), with inflammation, or if greater reduction is difficult to accept.

In patients with severe renal failure (GFR 20-25 ml/min/1.73 m^2) a very low-protein diet (vLPD) may be administered, i.e. a protein intake of 0.3-0.4 g of protein/kg i.b.w./d. Administration of such a diet is possible only if essential amino acids or amino acid analogues are supplemented. Since 2006, the supplementation should follow the guidelines of international experts (International Advisory Board Meeting 2006): in patients with GFR <60 ml/min 1 tablet of ketoanalogues per 5 kg b.w. is used with vLPD [9, 14, 15]. Close monitoring by a nutritionist and careful analysis of the energy value in diets administered to patients are very important elements of therapy.

Practical implementation of low-protein diets in CRF patients is possible thanks to special low-protein starch products available on the market, such as starch bread (low in proteins), low-protein flour and pasta. The protein content in 100 g of low-protein products is several times lower than in traditional products (e.g. 100 g of traditional bread contains 5.9 g of protein, whereas the same amount of starch bread provides only 1.6 g of protein). Another important aspect associated with the use of low-protein products is a reduction of incomplete protein (from plant foods) in the diet. The range of low-protein products is gradually increasing. Presently, several dozen foods are available on the Polish market, including semi-finished goods and ready-made meals.

In the literature, there are also numerous studies on the use of vegetarian and vegan diets in CRF. Some present satisfactory results, but not all of them do. A vegan diet appears to be associated with a higher risk of malnutrition. It seems that vegetarian diets in patients with chronic renal failure is a good alternative option, especially in those who used to follow such diet, provided a nutritionist supervises the therapy, and certain vitamins are supplemented, e.g. vitamin B_{12} [9].

Carbohydrates

The energy from carbohydrates should amount to 55-60% of the energy value of the diet. Carbohydrates complete the energy value of the diet in CRF patients [10-13]. Their rates must be increased with care in patients with diabetic nephropathy. It is important to limit the intake of simple carbohydrates, and introduce complex carbohydrates. Recently, special attention has been paid to the presence of fructose in the diet of CRF patients.

Fructose is a simple sugar, commonly found in natural products, such as honey, sugar, fruit and some root vegetables. High-fructose syrups added as sweeteners to various foodstuffs, primarily to highly-processed ones, are found in juice, sweet beverages, jelly, jam, preserves and alcohol. In recent years, a regular increase in high-fructose syrup consumption has been observed, mostly due to economic and technological reasons [16, 17].

Initially, fructose was considered a safe sugar, as it does not elevate the concentration of insulin stimulating lipogenesis, so it should not contribute to an accumulation of fat tissue, and to metabolic diseases. However, studies show that consumption of excessive amounts of fructose leads to hyperuricemia, resulting in metabolic disorders, which increase the risk of CRF [18-23]. Uric acid damages kidneys through oxidative stress, stenosis of the renal vessels, and the development of arterial hypertension [18, 20]. Insulin resistance, type 2 diabetes, metabolic syndrome and cardiovascular diseases also contribute to CRF. In addition, a high-fructose diet may result is excessive transport of fructose into the kidneys, leading to inflammation [23]. A study demonstrated that such diet increased proteinuria, deteriorated general renal function, increased glomerulosclerosis, as well as contributed to glomerular hypertension, reduced blood flow through the kidneys, and diseases of the renal vessels [23]. Excessive intake of added sugars increases glucose conversion to fructose (fructogenesis) in the proximal tubule by induction of oxidative stress, insulin resistance, hyperglycaemia and hyperuricemia. All these disorders activate the polyol pathway. In normoglycaemic patients only 3% of glucose is metabolised through the polyol pathway, whereas in hyperglycaemic patients it is 30%. This pathway contributes to the development and progression of real damage, which indicates that not only

fructose, but also glucose, through endogenous transformation to fructose, may be nephrotoxic [19].

To assess the metabolic risk due to excessive fructose intake, the fructose index (FI) was developed. It is defined as the fructose-derived percentage of energy in the food. However, it should be emphasised that eating fruit rich in fructose, contrary to high-fructose syrups, does not pose a health risk. This is due to the fact that fruit contains antioxidants, polyphenols, potassium and fibre, which demonstrate effects opposite to those of fructose, especially regarding arterial hypertension and metabolic disorders. Moreover, occasional consumption of products containing high-fructose syrup is safe, as adverse metabolic effects are observed when the fructose intake exceeds 35% of the energy value in the diet [17]. Therefore, limited consumption of fructose, especially from highly processed foods, may reduce the risk of metabolic diseases contributing to chronic renal failure.

Fats

The energy from fats should cover 30% of the daily energy requirements. In patients with concurrent lipid disorders, the quantity and quality of fats in the diet should be modified on an individual basis. In patients with hypercholesterolemia and increased LDL cholesterol concentration, recommendations include reduction of fats to 25-35% of energy requirement, reduction of saturated fatty acids to 7%, and mono- and polyunsaturated fatty acids to 20% and 10% of the energy value of the diet. Factors important in the treatment of hypercholesterolemia include a dietary fibre content of 20-30 g/d, a cholesterol content of <200 mg/dl, and the presence of plant stanols and sterols at approximately 2 g/d in the diet.

Hypertriglyceridemia often occurs in chronic renal failure, due to an increased concentration of VLDL cholesterol, and a reduced level of HDL cholesterol. Apart from the limited content of fats in the diet (with very high triglyceride concentrations, i.e. >1,000 mg/dl, the energy from fats should be reduced to <15%), body weight reduction should be recommended in the therapy of hypertriglyceridemia, as well as increased physical activity, stabilisation of carbohydrate imbalance, reduced alcohol consumption and supplementation of omega-3 acids.

Minerals

Progressive reduction of glomerular filtration leads to a hydroelectrolytic imbalance. With reduced diuresis, hyperkalaemia is observed. In patients with increased serum potassium concentrations, after modification of the pharmacotherapy of arterial hypertension (ACE inhibitors, glucocorticosteroids, potassium preparations, multivitamins), nutritional factors should be considered. The best sources of potassium in a diet are raw fruit and vegetables, as well as fruit and vegetable juices. Patients with hyperkalaemia should reduce the intake of these products in their raw form (potassium content in the diet of approximately 1,500-2,000 mg/d). Double cooking of vegetables with water exchange can be used to reduce the potassium content.

Disturbed calcium and phosphorus metabolism results in reduced calcium concentrations and increased levels of phosphates in the blood serum, as well as in the development of secondary hyperparathyroidism. Reduced phosphorus intake plays an important role in the prevention of these disorders. For patients with GFR <25 ml/min, the recommended intake is 600-1,000 mg of phosphorus/d. A limited amount of this mineral in the diet effectively reduces the blood parathormone concentration. Calcium intake with food should not be increased, as most food products will also contain phosphorus. Calcium should be supplemented in the form of calcium carbonate preparations (1.5-2.0 g/d). In patients with chronic renal failure, gastrointestinal absorption of calcium is often impaired, as a consequence of $1,25(OH)_2D_3$ deficiency.

In patients with CRF and concurrent arterial hypertension, a reduction of sodium intake to 1,800-2,500 mg/d is also recommended.

In addition, water-soluble vitamins should be supplemented (ascorbic acid, folates, riboflavin, thiamine, pyridoxine), as well as selenium, magnesium and zinc, as, in patients with CRF, a deficiency of these substances is observed. Patients using vLDL with supplementation of amino acid ketoanalogues, or a vegetarian diet, should also supplement iron, especially if anaemia occurs. The guidelines regarding vitamin supplementation recommend administration of >1 mg/d of vitamin B_1, 1-2 mg/d of vitamin B_2, and 1.5-2.0 mg/d of vitamin B_6. However, vitamins soluble in fats (carotenoids, vitamins E and K) should be used carefully, as many cases of dangerous accumulation of these elements were reported in patients with uremia. Vitamin D analogues are administered at a dose adjusted to the other components of calcium and phosphorus metabolism [10-13].

Conclusions

A proper diet in the course of chronic renal failure may significantly support pharmacological treatment, and prevent malnutrition. It also helps to treat the metabolic disorders frequently associated with the disease. Proper protein intake is of key importance, and it should be determined on an individual basis, according to the GFR value. A low-protein diet (LPD) and very low-protein diet (vLPD) are used, with supplementation of essential amino acid ketoanalogues. In patients with disturbed metabolism of lipids and carbohydrates, it is necessary to modify the quantity and composition of fatty acids, as well as to reduce the intake of simple carbohydrates, especially fructose. A hydroelectrolytic imbalance often requires a reduced potassium intake, and with a disturbed calcium and phosphorus metabolism the intake of phosphates should be reduced. In patients with CRF and concurrent arterial hypertension, sodium intake should be limited. Supplementation of water-soluble vitamins and selenium, magnesium and zinc is recommended. Vitamins soluble in fat should be used with care. Following nutritional recommendations helps to delay the disease progression and implementation of renal replacement therapy. It has beneficial effects on the nutritional status, concurrent metabolic disorders, and the quality of life of patients. Therefore, it may reduce the direct and indirect costs of CRF therapy.

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Role of a psychologist in the surgical treatment of morbid obesity

Rola psychologa w chirurgicznym leczeniu otyłości olbrzymiej

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Abstract. Morbid obesity is a condition involving the excessive accumulation of body fat, exceeding normal levels, which can be life-threatening. A patient is diagnosed as morbidly, or severely, obese when their BMI exceeds 40 kg/m^2. When this is long-lasting, not only does it impair the normal functioning of the body, but it can also influence the progression of multiple comorbidities. Severe obesity affects the quality of life of patients on the health, psychological, and social levels. Nowadays, the obesity treatment program considered to be the most effective is bariatric surgery. As the causes, as well as the effects, of morbid obesity concern numerous aspects of a patient's functioning, it is essential to include specialists of diverse fields in the patient's care, by creating multidisciplinary teams. Psychologists play an indispensable role in the treatment process: using tailored tools and techniques, they conduct psychophysical assessments, diagnose causes of the disorder, then motivate, and support the patient at each stage of treatment. Obesity treatment is not a terminable process; it is a continuum. The process is marked by a certain risk of weight gain recurrence. Only a holistic approach to obesity therapy is effective.
Keywords: bariatric surgery, morbid obesity, psychologist's role

Streszczenie. Otyłość olbrzymia to stan nagromadzenia tkanki tłuszczowej w organizmie w stopniu przekraczającym wartości prawidłowe, które mogą zagrażać życiu. Rozpoznaje się ją, gdy pacjent uzyskuje BMI >40 kg/m^2. Utrzymując się przez dłuższy czas, stan ten zaburza prawidłowe funkcjonowanie organizmu i może wpływać na rozwój wielu chorób współtowarzyszących. Otyłość olbrzymia pogarsza jakość życia pacjentów w sferze zdrowotnej, psychicznej i społecznej. Obecnie za najskuteczniejszą metodę walki z otyłością chorobliwą uznaje się chirurgię bariatryczną. Ponieważ zarówno przyczyny, jak i konsekwencje otyłości dotyczą wielu sfer funkcjonowania chorego, istotne jest zespołowe podejście do leczenia otyłości olbrzymiej, angażujące specjalistów z różnych dziedzin. Niezastąpioną rolę w procesie leczniczym odgrywa psycholog, który indywidualnie dopasowując odpowiednie narzędzia i techniki psychologiczne, określa stan psychofizyczny chorego, diagnozuje przyczyny rozwoju otyłości oraz motywuje i wspiera pacjenta na każdym etapie leczenia. Leczenie otyłości nie jest procesem zamkniętym -to proces, który charakteryzuje się pewnym ryzykiem nawrotów zwiększenia masy ciała. Tylko holistyczne podejście do leczenia otyłości przekłada się na jej efektywność.
Słowa kluczowe: chirurgia bariatryczną, otyłość olbrzymia, rola psychologa

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Introduction

The incidence of obesity is assuming epidemic proportions [1]. Obesity is the state when the fat tissue in the body exceeds its physiological needs. This disease affects people in all age groups. The World Health Organisation [2] considers obesity the most dangerous chronic disease, due to the high risk of comorbidities [2, 3]. It is estimated that 65% of the global population live in countries where excessive weight and obesity contribute to higher mortality rates than malnutrition [4]. According to recent data, Poles are in a leading position in Europe regarding excessive weight and obesity, as the problem

affects over a quarter of society [5]. Morbid obesity contributes to a deteriorated quality of life for patients [6-10], and reduces their lifespan by 20 years on average [11-14]. Therefore, it is very important to provide a patient receiving bariatric treatment with the comprehensive care offered by a team of specialists, including a psychologist.

Causes of excessive body weight

The etiopathogenesis of obesity is complex. There are three principal factors contributing to its development.

Genetic factors

Obesity may be inherited in one gene, in multiple genes, or as part of a genetic syndrome. Studies demonstrate that a predisposition to obesity is caused by mutations in multiple genes. They may be associated with the regulation of energy absorption from food, basal metabolic rate, maturation of fat cells, and activity of the enzymes responsible for the metabolism of lipids and carbohydrates. As a result, the processes of energy storage dominate over energy expenditure. Obesity may be a component of genetic syndromes such as Prader-Willi syndrome, Laurence-Moon-Biedl syndrome, Cohen syndrome, Carpenter syndrome and others [15].

Environmental factors (lifestyle)

The environment comprises another group of risk factors contributing to the etiopathogenesis of obesity. The disease develops rapidly, and affects people of all ages, from birth to death. Presently, environmental factors, poor nutritional habits and lack of exercise are considered the most common causes of obesity. As a result, the body receives highly processed food, rich in calories, which supplies more energy than required. The excess energy contained in the food is stored in the form of fat tissue.

Psychological factors

Eating habits have become a means of regulating emotions as well as reducing the stress and tension of everyday life (emotional eating). We are often unable to monitor the food consumed during the activities engaging our attention, e.g. watching TV, working at a computer, or reading a book (habitual eating). As a result, the body receives more calories than it needs to maintain vital physiological processes.

Increased amounts of fat tissue may also be a consequence of hormonal abnormalities, organic cause-related (disorders of the hypothalamus), developmental defects or use of pharmacotherapy that leads to gaining body weight [5].

How to diagnose morbid obesity?

Obesity is diagnosed with the use of anthropometric methods. The most popular is the determination of body mass index (BMI), i.e. the ratio of body weight expressed in kilograms to height expressed in square metres. Normal body weight corresponds to a BMI index of 18.5 – 24.9 kg/m^2. If the BMI value is between 25 - 29.9 kg/m^2, the patient is considered overweight. Obesity is diagnosed when BMI is > 30 kg/m^2, and morbid obesity when BMI is >40 kg/m^2. The latter condition is life-threatening [11-13].

Treatment of obesity

The aim of obesity treatment is to reduce excessive body weight, which directly improves the patient's health status and sense of well-being. In the process of obesity therapy, it is very important to maintain the effects of reduced body weight. Obesity is usually treated conservatively; however, according to scientific reports, patients who manage to reduce their body weight experience a yo-yo effect after 5 years on average, or often exceed their initial body weight [16, 17]. This is due to the fact that nutritional awareness itself does not suffice to provide long-term results. Bariatric surgery, considered the most effective method of reducing excessive body weight, is an opportunity for patients suffering from morbid obesity [6, 9, 10, 18]. The level of advancement of the procedures varies [19].

Indications and contraindications for surgical treatment of obesity

According to European guidelines, the primary indication for the surgical treatment of obesity is the body weight criterion: BMI >40 kg/m^2 or BMI >35 kg/m^2 with concurrent obesity-induced diseases, including diabetes, arterial hypertension, lipid disorders, cardiac diseases, sleep apnoea, osteoarticular disorders and other. A bariatric procedure is indicated in patients whose body weight cannot be reduced with conservative treatment. The above recommendations apply to patients aged 18-60 years old. Representatives of other age groups are evaluated individually by the qualifying physician, with consideration of the benefits and risks associated with the surgery. The principal contraindications for a bariatric procedure include: expected lack of patient compliance following the surgical treatment, psychoactive substance abuse, pregnancy, unstable mental disorders (each case is analysed individually), or directly life-threatening comorbidities [12].

The role of a psychologist in managing a bariatric patient

Obesity is a chronic disease adversely affecting the level of a patient's life satisfaction [3], which influences the person's functioning in different areas of life [7, 20]. Very often, obese patients withdraw from social roles or everyday activities, and avoid contact with other people, which is associated with physical and mental suffering [21]. It is important to remember that bariatric surgery helps to reduce excessive body weight through modification of the gastrointestinal anatomy, but it does not change the behaviour and eating habits. The following aspects are crucial in obesity treatment: diagnosing the causes and mechanisms that led to the development of the disease; taking actions in order to change those mechanisms; and maintaining the effects of the therapy, as well as reducing the risk of regaining weight. This is the area of working with the patient where a psychologist plays the key role. The tasks of the psychologist vary at different stages of the bariatric treatment. The type and scope of psychological intervention should provide safe and effective help for the patient, so that the treatment of morbid obesity brings optimal results. There are three stages of therapy.

Qualification of a patient for bariatric surgery

At this stage, the psychologist learns about the patient's history, diagnoses the psychological mechanisms of the person's functioning, and analyses the causes of their obesity. The task is to assess the patient's psychological and physical condition (detecting potential eating disorders, depression, anxiety disorders etc.), and to prepare the patient for the surgery (informed consent to the procedure and conscious acceptance of associated lifestyle modifications or the need for long-term co-operation in the post-operative period). The psychologist also defines potential risks that could impair the patient's collaboration with the therapeutic team in the future. The process involves various diagnostic tools: an interview, observation, questionnaires and tests [22]. The collected information will be used to determine the patient's problems, and to direct further therapy.

Preparation of the patient for the surgery

One of the main conditions for the effectiveness of the treatment is the proper engagement and motivation of the patient. An individualised approach helps to reach the patient's resources and strengths, increases motivation, helps to fight procrastination and stimulate persistence in following the treatment. At this stage, the psychologist needs to provide education and instruction. The work with the patient involves a change of mind-set and the destructive perception of oneself, the world and food. The aim of psychological assistance is to explain and demonstrate the mechanisms that led to morbid obesity, as well as their effect on the patient's everyday life. Depending on the needs and therapeutic goals, the psychologist uses different techniques: intention implementation, mental simulation, attention techniques, breathing exercises, emotion self-regulation training, constructive rewarding, relaxation techniques and others. In a safe environment, the patient gains and perfects new nutritional and corrective habits, as well as develops the skills necessary to deal with difficult situations, experiences benefits from introducing changes, and regains control over their actions.

Sometimes patients experience strong discomfort during therapy, which affects their functioning in society and the roles they play. In these cases, psychotherapy is indicated [23].

Post-operative care

The aim of post-operative care is to stimulate motivation and perseverance in following medical recommendations. This is the period when the patient generalises new skills in their everyday functioning, and together with the psychologist, predicts potential risks, learns how to deal with difficulties, and searches for constructive solutions to prevent relapse. The psychologist's role is to inspire and support the patient in further treatment and maintaining the results obtained.

Co-operation between the bariatric patient and the psychologist is based on a safe and ethical therapeutic relationship, perceived primarily as a "meeting of two people" [22], and their interaction.

Conclusions

As obesity treatment is a complex problem, and the consequences of the disease affect many areas of one's life, bariatric patients should be under the care of a team of qualified specialists. A psychologist, who from the beginning supports and motivates the patient in the process of change and recovery, is of key importance. It is also worth noting that therapy for obesity, as with any chronic disease, is a very long, sometimes life-long process. Therefore, it requires the long-term support of a specialist team, strong motivation of the patient, and persistence. Regular co-operation with a psychologist can help the patient with effective and permanent reduction of excessive body weight, which is the only outcome that may be perceived as fully successful.

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Epidemiological monitoring by the Military Institute of Medicine of the prevalence of intestinal parasitic infections brought to Poland by PMC soldiers

Nadzór epidemiologiczny Wojskowego Instytutu Medycznego nad występowaniem zarażeń pasożytami jelitowymi oraz ich zawlekaniem do kraju przez żołnierzy PKW

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Abstract. Contemporary military operations involving Polish Military Contingents (PMC) are usually carried out under difficult environmental conditions, which favour bringing home pathogens of infectious and parasitic diseases. This fact has been confirmed by a number of studies conducted by the Military Institute of Medicine (MIM) between 2010 and 2014 as part of the program for the prevention of intestinal parasitic infections among participants of military operations, local population studies in areas of the PMC deployment in Afghanistan, Central African Republic and Kosovo, carried out between 2011 and 2016, and parasitological tests performed on soldiers from PMCs deployed to Afghanistan, Kosovo, Bosnia and Kuwait in 2015 and 2017. Since 2010, the Military Institute of Medicine has been the only research centre continuously involved in the epidemiological monitoring and elimination of intestinal parasitic infections among military personnel serving overseas. Out of concern for the continuity of the above-mentioned monitoring, and for the ongoing efficient elimination of intestinal parasitic infections among Polish soldiers, the MIM prepared a draft program for the prevention of intestinal parasitic infections for the coming years, which was sent to the Department of the Military Health Service for consecutive agreements.
Key words: intestinal parasites, Polish Military Contingents, soldiers

Streszczenie. Operacje współczesnego teatru działań z udziałem żołnierzy Polskich Kontyngentów Wojskowych (PKW) prowadzone są w ciężkich warunkach środowiskowych, które sprzyjają zawlekaniu do kraju macierzystego patogenów chorób infekcyjnych i inwazyjnych. Potwierdzają to badania realizowane przez Wojskowy Instytut Medyczny w latach 2010-2014 w ramach programu profilaktyki chorób pasożytniczych przewodu pokarmowego wśród uczestników operacji wojskowych, badania ludności miejscowej w rejonach stacjonowania polskich żołnierzy w Afganistanie, Republice Środkowej Afryki i Kosowie w latach 2011-2016, a także diagnostyka parazytologiczna żołnierzy PKW pełniących służbę w Afganistanie, Kosowie, Bośni i Kuwejcie prowadzona w latach 2015-2017. Wojskowy Instytut Medyczny nieprzerwanie od 2010 roku jest jedynym ośrodkiem zajmującym się nadzorem epidemiologicznym i eliminacją zarażeń pasożytami jelitowymi w środowisku żołnierzy PKW poza granicami państwa. W trosce o ciągłość ww. nadzoru i kontynuowanie skutecznej eliminacji zarażeń pasożytniczych wśród polskich żołnierzy WIM przygotował projekt programu profilaktyki chorób pasożytniczych przewodu pokarmowego na kolejne lata, który został przesłany do Departamentu Wojskowej Służby Zdrowia w celu dalszych uzgodnień.
Słowa kluczowe: pasożyty jelitowe, Polskie Kontyngenty Wojskowe, żołnierze

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Introduction

Contemporary military operations involving Polish Military Contingents (PMC) are usually carried out in difficult environmental conditions, which favour the spread of pathogens of infectious and parasitic diseases. This fact has been confirmed by a number of studies conducted by the Military Institute of Medicine (MIM) between 2010 and 2014 as part of the programme for the prevention of intestinal parasitic infections among 24,638 participants of military operations in the Polish Armed Forces, among whom 1396 were diagnosed with ascariasis, strongyloidiasis, giardiasis, amebiasis, teniasis and other intestinal parasites requiring unconditional treatment before the return of those PMC soldiers to their home country [1].

Studies conducted by the Military Institute of Medicine (MIM) under research projects between 2011 and 2014 among 3146 Afghan people, demonstrated infections with similar species of intestinal parasites (to those diagnosed in Polish soldiers) in as many as 38.9% of Afghans, which clearly indicated the source of infections of Polish soldiers serving in Afghanistan [2,3]. Further studies conducted by the MIM in 2014-2015, which involved 3209 residents of the Republic of South Africa, revealed infections with intestinal parasites in 69.5% of participants, while studies conducted between 2015 and 2016, involving 632 residents of Kosovo, confirmed infections in 12.0% of Kosovars, justifying the need to screen members of the PMC for intestinal parasites and to administer treatment to those infected before they return home in order to prevent the transmission of such parasites to Poland [3].

With an eye to continuing epidemiological monitoring in the regions of deployment of Polish soldiers, the Military Institute of Medicine, after concluding the programme for the prevention of parasitic diseases of the gastrointestinal tract of 2010-2014, has run diagnostics of parasitic infections since 2015 in the regions of PMC deployment and treated the infected before their return to Poland (the studies are financed from the Institute's own funds). All soldiers in PMC Afghanistan, PMC Kosovo, PMC Bosnia and PMC Kuwait diagnosed with parasitic diseases received appropriate antiparasitic treatment in the area of operation, to prevent the transmission of parasites to Poland. Table 1 presents the results of parasitological examinations for intestinal parasites, conducted by the Military Institute of Medicine among Polish soldiers in PMCs between 2015 and 2017.

After their return to Poland, before they are examined by a Military Medical Board and receive the results of the tests for parasites, PMC soldiers can have private and professional contacts with other people for at least 10-14 days. The probability of spreading an infection faeco-orally to family and friends through direct contact (dirty hands), and to random people in public places (toilets), is high during this time.

The programme for parasitic disease prevention, implemented in 2010-2014, made it possible to eliminate parasitic infections in more than a thousand Polish soldiers returning from areas of military operations to Poland, and thus prevented the spread of intestinal parasites among thousands of residents in Poland. The continuation of the programme using the Military Institute of Medicine's own funds in 2015-2017 made it possible to prevent the transmission of Platyhelminthes and Nemathelminthes.

It is worth noting that Military Medical Boards in Poland, pursuant to the Resolution of the Minister of National Defence of 23 December 2010 on certain healthcare benefits for professional soldiers [4] and the Resolution of the Minister of the National Defence of 13 June 2016 on acclimation leave and treatment and prevention camps [5], and based on agreements concluded with diagnostic laboratories, are conducting examinations for parasites of the gastrointestinal tract using the basic method of direct smears, which can detect intestinal parasites in only 30% of cases (provided that the examination is performed by laboratory staff experienced in parasite diagnostics) [6]. For the sake of comparison, the Military Institute of Medicine runs parasite diagnostics using five microscopic methods and a molecular biology method in collaboration with the Department of Tropical Parasitology of the Institute of Maritime and Tropical Medicine. Due to the limited parasite diagnostics offered by Military Medical Boards, it is worth considering the amendment of legal regulations, extending the methodology of examinations for the presence of parasites of the gastrointestinal tract in soldiers delegated to foreign countries and returning to Poland after completing their tour of duty. This is even more important, as, pursuant to the Resolution of the Minister of Health of 30 January 2013 on the list of infections and infectious diseases among soldiers, officers and employees of units and other people falling within the scope of the State Sanitary Inspection, Military Sanitary Inspection, State Sanitary Inspection of the Ministry of the Interior, Veterinary Inspection and Inspection of Environmental Protection [7] only two parasitic diseases of the gastrointestinal tract (giardiasis and cryptosporidiosis) are covered under epidemiological monitoring in Poland, while ascariasis, strongyloidiasis, enterobiasis, teniasis, amebiasis and a number of other parasitic infections are not subject to such monitoring. This is why neither the Chief Sanitary Inspectorate of the state nor the Chief Sanitary Inspectorate of the Polish Army possess sufficient knowledge of the presence and spread of parasitic intestinal infections among civilians and military personnel in Poland. This state of affairs has

Table 1. Tests for intestinal parasitic infections among soldiers serving in Polish Military Contingents in 2015 and 2017
Tabela 1. Badania w kierunku występowania zarażeń pasożytami jelitowymi wśród żołnierzy Polskich Kontyngentów Wojskowych w latach 2015-2017

PMC tour	date	number of examined individuals	number of infected individuals	% of infected individuals
1st tour of PMC Afghanistan	04/2015	116	16	13.8
2nd tour of PMC Afghanistan	11/2015	147	16	10.9
33rd tour of PMC Kosovo	04/2016	175	20	11.4
3rd tour of PMC Afghanistan	05/2016	143	17	11.9
11th tour of PMC Bosnia	08/2016	39	3	7.7
SOAT-50 Afghanistan (special forces)	08/2016	47	11	23.4
34th tour of PMC Kosovo	10/2016	201	22	10.9
4th tour of PMC Afghanistan	11/2016	167	17	10.2
1st tour of PMC Kuwait	12/2016	88	9	10.2
12th tour of PMC Bosnia	01/2017	23	4	17.4
SOAT-50 Afghanistan (special forces)	02/2017	42	5	11.9
35th tour of PMC Kosovo	03/2017	178	8	4.5
2nd tour of PMC Kuwait	04/2017	111	5	4.5
5th tour of PMC Afghanistan	05/2017	162	11	6.8
total		**1639**	**164**	**10.0**

source: Korzeniewski K. Own work

continued since 5/12/2008, i.e. the entering into force of the Act on preventing and combating infections and infectious diseases in people [8], which repealed the obligation to monitor infections by most intestinal parasites in the Polish population.

The Military Institute of Medicine has been the only centre dealing with the epidemiological monitoring and elimination of intestinal parasitic infections among PMC soldiers serving abroad since 2010. With an eye to continuing the monitoring and effective elimination of parasitic infections among Polish soldiers, the Head of the Military Institute of Medicine sent to the Head of the Military Medical Service Inspectorate (IWSZ) a draft programme for the prevention of parasitic diseases of the gastrointestinal tract for the years to come, which was approved by the Agency for Health Technology Assessment (AOTMiT) on 17/03/2015, provided that the remarks of the AOTMiT Transparency Council are taken into account. The draft programme, analysed and amended by the MIM, as suggested by the Transparency Council, was sent to the Head of the Department of Polish Military Medical Service (DWSZdr) on 15/04/2015.

On 23/12/2015 a meeting took place at the Bureau for Anti-Corruption Procedures, Ministry of National Defence, which saw the participation of representatives of DWSZdr, during which Col. Korzeniewski from MIM, the coordinator of the prevention programme in 2010-2014, presented in detail the assumptions, objectives, schedule of action, costs of implementation, reporting and the expected results.

According to DWSZdr it would originally be implemented in the form of an outsourced task, and in subsequent years as a prevention programme. DWSZdr sent for inter-ministerial negotiations a draft Decision of the Minister of National Defence on appointing the research institute – Military Institute of Medicine – with the task for defence and public safety, concerning the conducting of parasite screening among the military.

Further examinations of Polish Military Contingent soldiers for infections with intestinal parasites, still financed by the Military Institute of Medicine from its own funds, as well as the treatment of infected individuals before their return to Poland, are planned for Q4 2017 and 2018 (PMC Kosovo, PMC Afghanistan, PMC Kuwait, and PMC Iraq).

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Biogenic amines intolerance syndromes. Part I. Histamine and histamine intolerance

Zespoły nietolerancji amin biogennych. Część I. Histamina i nietolerancja histaminy

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Abstract. Histamine intolerance (HIT), like all so-called biogenic amines intolerance syndromes, is still a mysterious problem of modern allergology. Its pathomechanism involves an imbalance between the amount of histamines consumed with food and the degradation ability of the intestinal enzymatic barrier.
The main reasons are congenital and acquired deficiencies in the activity of enteral diamino oxidase (DAO), which is one of the histamine degrading enzymes. This results in the appearance of symptoms after the intake of foods containing histamines at concentrations harmless to the general population. HIT should be distinguished from histamine intoxication, when people with a fully functional enzymatic barrier experience symptoms after the ingestion of food containing an extremely high level of the mediator. The complex symptomatology of HIT, which is a classic example of a pseudoallergy, consists of numerous, non-specific symptoms. It often creates a serious diagnostic challenge for allergists. It seems that this syndrome is underdiagnosed and underestimated amid allergic diseases. Moreover, treatment is not easy due to difficulties in assessing the content of histamine in individual products. The literature review is presented below to outline the problem, and analyse controversial issues, and to review the current state of knowledge on HIT and other posthistamine reactions.
Key words: biogenic amines, diamine oxidase, diet therapy, food poisoning, histamine intolerance

Streszczenie. Nietolerancja histaminy (HIT), podobnie jak wszystkie tzw. zespoły nietolerancji amin biogennych, nadal jest zagadkowym problemem współczesnej alergologii. Jej patomechanizm polega na zaburzeniu równowagi pomiędzy ilością histaminy przyjmowanej z pokarmem a zdolnością do jej degradacji przez jelitową barierę enzymatyczną. Najczęstszą przyczyną są wrodzone i nabyte niedobory aktywności jelitowej diaminooksydazy (DAO), jednego z enzymów rozkładających histaminę, co powoduje wystąpienie objawów chorobowych po spożyciu produktów o nieszkodliwym dla ogółu populacji stężeniu histaminy. HIT należy odróżniać od zatrucia histaminą, kiedy to osoby o w pełni sprawnej barierze enzymatycznej odczuwają objawy po przyjęciu pokarmu zawierającego skrajnie duże stężenia mediatora. Złożona symptomatologia HIT, będąca klasycznym przykładem pseudoalergii, na którą składają się liczne objawy nieswoiste, często stanowi dla alergologów poważne wyzwanie diagnostyczne. Wydaje się, że jest to zespół rozpoznawany zbyt rzadko i niedoceniany wśród chorób alergologicznych. Leczenie również nie należy do łatwych, ze względu na trudności w ocenie zawartości histaminy w poszczególnych produktach. Poniżej przedstawiono przegląd piśmiennictwa w celu przybliżenia problemu i analizy kontrowersyjnych zagadnień, a także uporządkowanie aktualnego stanu wiedzy na temat HIT oraz pozostałych reakcji pohistaminowych.
Słowa kluczowe: aminy biogenne, diaminooksydaza, nietolerancja histaminy, terapia dietetyczna, zatrucie pokarmowe

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Introduction

Biogenic amine syndromes (BAS) are one of the forms of adverse food reactions in the recommendations of the American National Institute of Allergy and Infectious Diseases (NIAID) of 2010 [1]. In its most recent position, the European Academy of Allergy and Clinical Immunology (EAACI) adopted a similar classification on this food allergy, including it in a wider group of food intolerances, more precisely referred to as non-immunological adverse food reactions [2]. The common property of BAS is the lack of participation of any immunological mechanisms – both IgE-dependent and IgE-independent humoral, as well as cellular. However,

other, very diverse mechanisms appear, often of a mixed nature.

From a chemical point of view, amines are organic compounds with an amine group (ammonia derivative) as a functional group. Biogenic amines (BA) are a particular group of amines, which are created in plant and animal cells as a result of the process of decarboxylation of amino acids, playing a significant role in their physiology and pathology. Examples of products of decarboxylation of individual amino acids are presented in Table 1. For the human body, a significant source of BA is food with a high protein content, in which, with the presence of bacterial strains with a high activity of proteolytic enzymes during fermentation, processing and storage, they are created in higher amounts [3]. BA can be further metabolised, as a result of which compounds with very diverse actions are created. It has been proven that many species of bacteria are capable of the decarboxylation of amino acids: *Bacillus, Citrobacter, Clostridium, Escherichia, Klebsiella, Listeria, Micrococcus, Proteus, Pseudomonas, Shigella, Staphylococcus* and lactic acid bacilli [4].

An excess of BA consumed with food (or in pure form, for example phenethylamine) can cause the symptoms of poisoning, and in people with impaired mechanisms of their degradation, the symptoms can manifest even after consumption of foods with a low concentration. In this case, it is called BA intolerance or BAS, and such patients visit allergologists suspecting they have a food allergy. A differential diagnosis in such cases is difficult due to extensive symptomatology and relatively limited options within the scope of additional tests. A suspicion of BAS becomes more grounded after the exclusion of a real food allergy as the cause of the ailment. In practice, we most often come across intolerance of histamine (HIT), tyramine (TIT) or serotonin (SIT).

Table 1. Products of decarboxylation of individual amino acids
Tabela 1. Produkty dekarboksylacji poszczególnych aminokwasów

amino acid	product of decarboxylation
arginine	agmatine
cysteine	cysteamina
serine	ethanolamine
histidine	histamine
lysine	cadaverine
tyrosine	tyramine
threonine	propanolamine
ornithine	putrescine
tryptophan	serotonin
tryptophan	tryptamine
tyrosine	tyramine

Histamine

Histamine, originally referred to as β-Imidazolethylamine, is a biogenic amine of multiple properties participating in important physiological mechanisms. Detected a little earlier, it was finally synthesised in 1907 by two German chemists – Windaus and Vogt [5]. Three years later, Dale and Laidlaw, after a series of animal experiments, described an entire palette of physiological effects for this neurotransmitter and mediator, attributing the leading role in the pathogenesis of anaphylaxis to it [6]. Shortly after this discovery, the name "histamine" was proposed (Ancient Greek *histos* – tissue), emphasising its common presence in animal tissues. In the following years, skin reactions to histamine administration were described and the role of this mediator was identified in greater detail, which finally led to the introduction of drugs modulating its influence. These include the first and second generation H1 receptor antagonists for histamine (rH1), H2 and H3 receptor antagonists (rH2 and rH3), as well as some of the trinuclear antidepressants and neuroleptics.

From a chemical point of view, the structure of histamine is relatively simple. In the body, its basic source, especially in pathological conditions, are mast cells, in which it is formed from an exogenous amino acid – histidine, and the enzyme catalysing the synthesis is L-histidine decarboxylase (HDC), and its cofactor – pyridoxal phosphate, the active form of vitamin B_6. There are currently four known receptors for histamine – from rH1 to rH4, through which it exerts its physiological and pathological effects (Tab. 2) [7].

Histamine degradation

There are two main paths of histamine degradation (Fig. 1). Approximately 80% of the systemic histamine pool is degraded in the process of methylation catalysed by histamine-N-methyltransferase (HNMT) with the generation of N-methylhistamine [8]. Determination of the concentration of the mentioned metabolite in urine is a clinically useful indicator of systemic mast cell activation, for example in the course of anaphylaxis. The other path, applying to approximately 20% of the histamine present in the body, is oxidation by means of DAO. The product of this reaction is imidazole-4-acetaldehyde, which then, with the participation of aldehyde dehydrogenase (ADH), is transformed into an appropriate acid, to finally undergo the process of ribolysation. Interestingly, N-methylhistamine can be oxidised both by DAO and by monoamine oxidase (MAO) to N-methylimidazole-4-acetaldehyde, and then by ADH to the appropriate acid. However, the latter cannot be

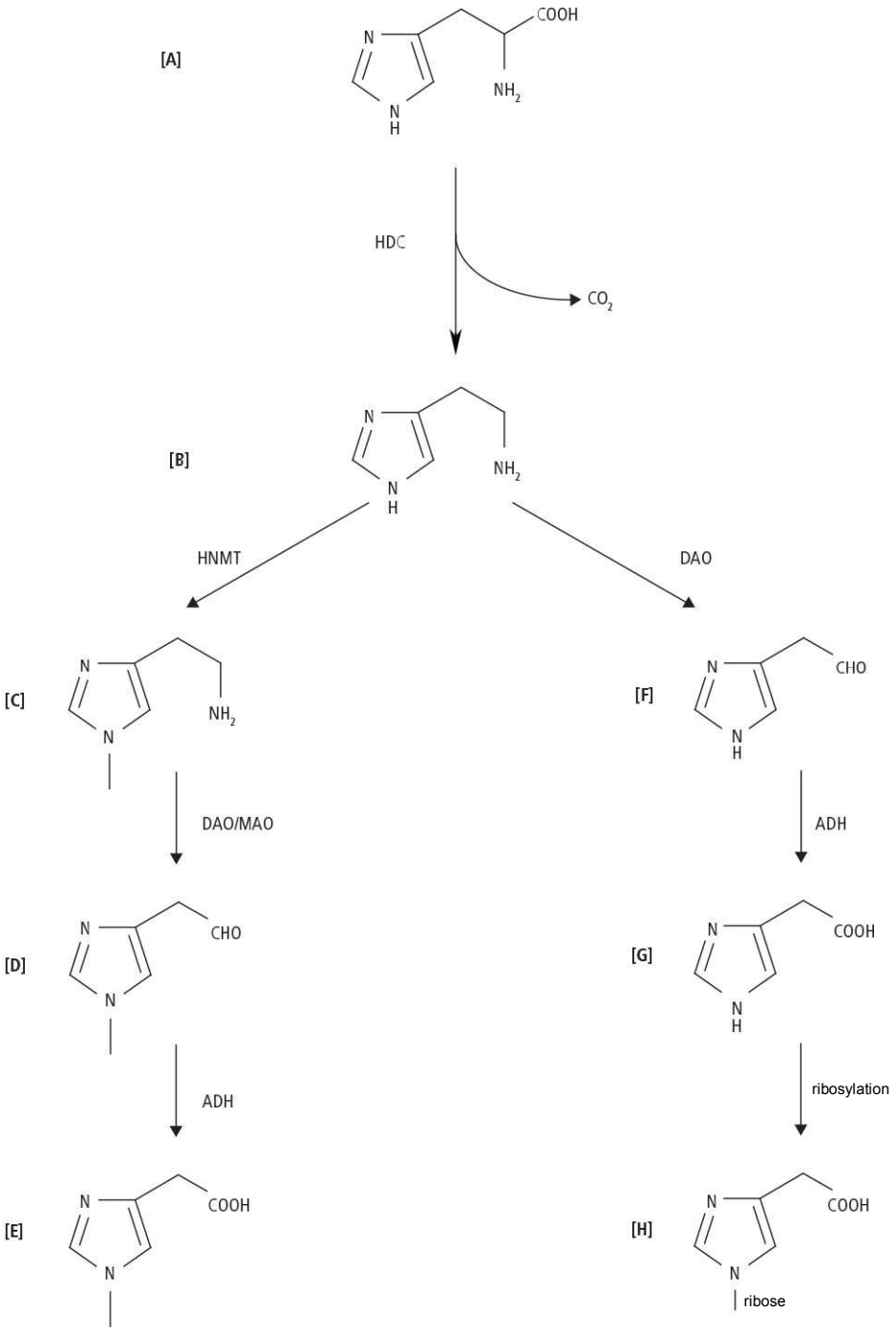
Table 2. Biological effects of histamine - receptor interactions [7]
Tabela 2. Biologiczne efekty oddziaływania histaminy na receptory [7]

type, G protein	cytoplasmic mediator	organ/tissue	effect	
H1	Gq	inositol triphosphate	vessels	increased permeability
				vasodilation
			smooth muscles	contraction
			cardiac muscle	positive chronotropic
			glands	mucus secretion
			eosinophils	stimulation of chemotaxis
				inhibition of apoptosis
			CNS	neurotransmission
H2	**Gs**	adenosine-3',5'-cyclic phosphate	vessels	vasodilation
			cardiac muscle	positive inotropic
				positive chronotropic
			stomach	stomach secretion
			bronchia	mucus secretion
				bronchospasm
			basophils	reciprocal inhibition
			granulocytes	inhibition of chemotaxis
			CNS	neurotransmission
H3	**Gi**	inositol triphosphate	mast cells	reciprocal inhibition
			CNS	neurotransmission
H4	**Gi**	phospholipase C	bone marrow	decrease in TNF secretion
			leukocytes	inhibition of IL-12 synthesis
			mast cells	inhibition of IL-16 synthesis
			intestine	stimulation of IL-10 synthesis

subjected to ribolysation due to the blocking of the imidazole group by the methyl residue.

It is important to keep in mind the different locations of these enzymes in the body. HNMT is responsible for histamine inactivation in nervous tissue, where it functions as a neurotransmitter. DAO, on the other hand, is necessary for the removal of the mediator once it is released into the extracellular space. Its presence is essential in the intestinal wall, where it allows the degradation of exogenous histamine ingested with food [9]. It is also abundantly present in the kidneys and placenta [10]. Significantly, there are numerous polymorphisms affecting the production and activity of proteins related to histamine metabolism. This also applies to HDC, rH1 and rH4, HNMT and DAO. It seems that some of these polymorphisms have pathophysiological significance. For example, some HNMT variants resulting in a reduced enzyme activity are related to the occurrence of atopic asthma and atopic dermatitis, whereas impaired DAO functioning leads to an increased risk of the appearance of hypersensitivity to nonsteroidal anti-inflammatory drugs [9, 11].

The activity of the latter mentioned enzyme is in any case subject to decrease by numerous agents, both endo- and exogenous. The former ones, apart from the already signalised genetically determined reduction of activity, also include acquired deficits, related to numerous enterocyte damage conditions. Here we can list infectious intestinal catarrh, parasitoses, non-specific inflammatory bowel diseases, absorption and intestinal flora disorders. DAO activity can also be reduced in the course of chronic renal failure, viral hepatitis, advanced cirrhosis and chronic urticaria. In order to function, the enzyme requires cofactors – vitamin B_6, vitamin C, and zinc and copper cations, which is why deficiencies of these microelements impair its activity. On the other hand, pregnancy can lead to a 500-times increase in DAO concentration due to its placental production [12].



[A] - histidine; [B] - histamine; [C] - N-methylhistamine; [D] - N-methylimidazole-4-acetaldehyde;
[E] - N-methylimidazole-4-acetic acid; [F] - imidazole-4-acetaldehyde; [G] - imidazole-4-acetic acid;
[H] - 1-ribosylimidazole-4-acetic acid.

Figure. Histamine metabolism (by the author)

Rycina. Metabolizm histaminy (rycina własna autora)

Table 3. Diamine oxidase inhibitors [12, 13]
Tabela 3. Inhibitory diaminooksydazy [12, 13]

control	medical substances
antiarrhythmic agents	quinidine, propafenone, verapamil
antibiotics	cefuroxime, isoniazid, doxycycline, clavulanic acid
bronchodilator agents	aminophylline, theophylline
mucolytic agents	acetylcysteine, ambroxol
antiemetic agents	metoclopramide, promethazine
psychiatric	amitryptyline, diazepam, MAO-A inhibitors, haloperidol
relaxants	alcuronium, pancuronium, D-tubocurarine
other	acriflavine, chloroquine, cimetidine, dihydralazine, estrogens, furosemide, metamizole

Exogenous agents also seem important, as some of the commonly used drugs are DAO inhibitors (Tab. 3) [13, 14]. The greatest clinical significance in this case is ascribed to isoniazid and other drugs inhibiting MAO activity. Similar activity is also exhibited by ethanol. Interestingly, the influence of histamine itself on the production of the enzyme is controversial. Introduction of a histamine-free diet in one study increased the DAO plasma activity to a statistically significant degree [15], whereas in another report, a low-histamine diet had no influence on it [16].

Pathomechanism and symptomatology of histamine intolerance

It seems that in the case of histamine, of greatest significance is the direct toxic activity of the mediator contained in the food on rH1 and rH3 – both in the intestinal wall and in other tissues. The term "post-histamine reactions" covers a wide spectrum of reactions of different intensities, which is partly determined by the dose of histamine in the consumed food, as well as the efficiency of the mechanism of its degradation in the body. Their final clinical effect also depends on many additional factors influencing histamine supply and degradation.

Dangerous post-histamine reactions include histamine intoxication. According to the American Food and Drug Administration (FDA) consumption of greater amounts of food containing histamine in a concentration of >500 mg/kg can cause the symptoms of histamine intoxication in healthy people. In such a situation, the consumed dose of histamine can exceed the quantitative capability of its decomposition by intestinal DAO. The excess of histamine is absorbed into blood circulation and the consequence is the appearance of the symptoms of histamine intoxication, dependent upon its content in the consumed food (nausea, emesis, itchiness, blisters, abdominal pain, diarrhoea).

Histamine intolerance (HIT) is identified if a posthistamine reaction occurs after consumption of food containing histamine in an amount that is harmless to healthy people. It is most often the result of the ineffective polymorphism of genes conditioning the intestinal DAO activity, as a result of which the activity of this enzyme is significantly decreased. It is estimated that this can apply to 1% of the population [14].

Clinic

Ailments caused by exogenous histamine are to a major extent identical to that of its endogenous release. The full scope of pseudoallergic symptoms is therefore observed, from local reactions to anaphylaxis. Reactions often appear 10-30 minutes after the consumption of histamine-rich food and they tend to self-limit and regress within 6-8 hours. The most frequent include facial flushing, headache, abdominal pain, diarrhoea and palpitations. The less frequent include: general flushing, nausea, emesis, urticaria, vasomotor oedema, xerostomia, wheezing breath, dyspnoea, cough, itchiness, hypotension and fainting. Some patients taste a pepper, metallic or bitter flavour. Case reports include cases of anaphylactic shock, heart failure, pulmonary oedema, supraventricular arrythmias, acute amblyopia and isolated hypotension. These symptoms can be life threatening, at least one fatality has been described [14, 17-20].

Most of the described pseudoallergic symptoms are the result of local or systemic rH1 activation. Nevertheless, in the case of central symptoms, such as headaches, nausea and emesis, the role of rH3 and the related neurotransmission disorders are emphasised [17].

These issue of the occurrence of chronic HIT is definitely more controversial. Some suspect such a situation in the case of deterioration of the course of allergic diseases, primarily spontaneous urticaria. Some authors also suggest the possibility of participation of

histamine in chronic fatigue syndrome, strong menstrual pains, insomnia, depression, anxiety and panic disorders [14].

Post-histamine reactions after the consumption of *Scombridae* fish

Reactions caused by the histamine contained in sea fish were first described in 1799 in Great Britain. However, further reports came as late as in the 1950s, when this matter was analysed due to an increase in the number of occurrences in Japanese literature. In the USA, the first cases were described in 1968 [17]. It has been noted that such reactions often occur after consumption of the flesh of *Scombridae* and *Scomberesocidae* fish, which is why the disorder caused by consumption of these fish is often referred to as scombroid food poisoning.

Credible epidemiological data concerning the appearance of such reactions come from the countries with high fish consumption rates, primarily the USA and Japan. According to reports submitted to the American Centers for Disease Control and Prevention (CDC), in the years 1998-2015 there were 389 recorded outbreaks and 1459 cases of scombroid food poisoning; 48 people were hospitalised (3.3%). The greatest number of outbreaks was identified in typically seaside states – in Hawaii, New York, Florida, and in California. Overall, the intoxication constituted approximately 0.39% of the cases of all the reported poisonings, but approximately 2% of the identified outbreaks. However, no fatality due to this cause has been recorded in the territory of the USA. There has been a clear decrease in incidences over the last twenty years – from 180 cases in 1998 to 23 in 2015. There is also a noticeable seasonal dynamic, with a peak in the spring-summer period and a decrease in the winter [21]. Japanese data also indicates a greater incidence than the American data – at the level of 150 cases per year. Japan is also where the largest outbreak was recorded, in 1973, with 2656 incidents [17].

Table 4. Bacterial species synthesizing histidine decarboxylase [18, 22]
Tabela 4. Rodzaje bakterii wytwarzające dekarboksylazę histydyny [18, 22]

Acinetobacter
Citrobacter
Clostridium
Enterobacter
Escherichia
Photobacterium
Proteus
Pseudomonas
Serratia
Vibrio

A disorder corresponding to both histamine intoxication and HIT can be observed after the consumption of *Scombridae* fish.

The toxic properties are primarily linked to the histamine-rich dark meat of the *Scombridae* fish. The commonly known species include tuna and mackerel, whereas the lesser known include oceanic bonito. The disease can also be caused by the meat of fish of other families, such as *Clupeidae, Engraulidae, Coriphaenidae* and *Pomatomidae* [22]. In this case the typically listed ones include sardines, mahi-mahi, bluefish and salmon. However, there is a noticeable distinctive toxic potential in some species. According to the American data 80% of the described cases are caused by the consumption of tuna and mahi-mahi, the latter being currently rarely consumed in Poland [17].

The meat of fish, even of the two species mentioned above, will not cause the symptoms in every case. Their occurrence is a resultant of the histamine content in the consumed food and individual sensitivity of the consumer to its activity. Histamine in the stored meat is created as a result of histidine decarboxylase activity produced by many bacteria (Tab. 4) [17, 23]. As in the case on any enzyme, the efficiency of its catalysis depends on environmental conditions – humidity, pH, electrolyte concentration, and especially temperature. Storage of fish in a cold store below 0°C prevents the production of histamine, but after even 2-3 hours at a temperature of 20°C it can accumulate in an amount sufficient to evoke the symptoms, even more so as the presence of live bacteria is not necessary for catalysis, just the enzyme they previously produced [24]. Moreover, after production, histamine is significantly resistant to physicochemical conditions, therefore thermal processing, freezing and conservation are often unable to lead to its removal from the food.

Histamine concentrations in fully fresh fish meat often amounts to <0.1 mg/kg. The concentration recognised as toxic is >500 mg/kg, whereas the maximum allowed concentration according to the European standards is

200 mg/kg for fresh fish and 400 mg/kg for fish preserved by immersion in brine [25]. According to the meta-analysis of Colombo et al. the average concentration of histamine in samples causing poisoning amounted to 1107 mg/kg with a 95% confidence interval of 423-2901 mg/kg [22]. There was no identified significant relation between the appearance of symptoms and gender, parallel consumption of alcohol, other specific foods or drugs in the report. However, the indicated risk factors include the intake of izoniazid, MAO inhibitors, congenital decreased DAO activity, as well as accompanying severe medical conditions, such as incorrectly controlled bronchial asthma or unstable heart disease.

It is known that sometimes the symptoms of scombroid food poisoning occur with relatively low concentrations of histamine in the suspect meat. Some authors suggest that even a concentration of 50-200 mg/kg can cause the symptoms in some cases. This can definitely be the result of low DAO activity, but attention is also focused on the possible participation in pathogenesis of compounds blocking degradation of the mediator, such as putrescine and cadaverine, or causing non-specific mast cell degranulation, such as urocanic acid [17, 22, 26, 27].

Poisoning with other foods

Data on histamine poisoning contained in foods other than fish are definitely more rarely. Harmful effects of histamine contained in certain types of cheese and red wine have been postulated for a long time (Tab. 5) [28]. This opinion is strongly based on experimental studies, both on people and animals. Pigs where the DAO activity was pharmacologically blocked after feeding with wine and cheese, manifested the symptoms of anaphylaxis with a mortality rate of more than 20%. Moreover, premedication with antihistamines (AH) prevented the occurrence of the disease in them [29, 30]. On the other hand, in a study with the participation of patients with chronic urticaria duodenal provocation, using as little as 120 mg histamine caused the appearance of diarrhoea, urticaria, headache, tachycardia and hypotension [31].

Regardless of these experimental premises, there is a surprisingly low number of well documented poisonings. In 103 analysed histamine poisoning outbreaks included in the last year's meta-analysis by Colombo et al. only two pertained to cheese, whereas all the others pertained to fish. The first of these reports, from 1967, pertained to a single male patient, a resident of Rotterdam, who was poisoned with old Gouda cheese. The histamine concentration in the sample was 850 mg/kg [32]. The second publication (from 1982) pertained to the collective poisoning of 6 people with Swiss cheese served in the canteen of an American navy aircraft carrier. In this case, the concentration was as high as 1870 mg/kg [22]. The included description convincingly indicates the possibility of poisoning with histamine contained in cheese. However, considering the fact that not a single poisoning of this type has been documented in the CDC database, this issue should be recognised as minor [21].

In the case of wine, there were suggestions of the histamine it contains in the pathogenesis of headaches and bronchospastic symptoms [33, 34]. However, in this case there is also a lack of credible proof confirming such a hypothesis, whereas experimental data is available indicating a lack of correlation between the content of histamine in wine and its intolerance. Moreover, it was actually low-histamine wine that caused a short-term significant increase of its concentration in the blood 10 minutes after consumption, which indicates a greater role played by the compounds contained in wine which non-specifically degranulate mast cells than that of histamine itself [35].

Table 5. Histamine concentration in different food products [27]
Tabela 5. Zawartość histaminy w wybranych pokarmach [27]

food product	histamine concentration	
cheeses	Harzer	390 mg/kg
	Gouda	29.5-180 mg/kg
	Roquefort	158 mg/kg
	Camembert	35-55 mg/kg
	Cheddar	34 mg/kg
	Tilsit	50-60 mg/kg
alcohols	red wine	0.6-3.8 mg/l
	white wine	0.003-0.120 mg/l
	sparkling wine	0.015-0.670 mg/l
	beer	0.021-0.305 mg/l
other	Westphalian ham	38-159 mg/kg
	spinach	38 mg/kg
	ketchup	22 mg/kg

Histamine intolerance in pathogenesis of other nosological units

There have been repeated suggestions of a relation between the histamine consumed in foods and the occurrence of aggravation of allergic diseases. Recent years have brought several new discoveries within his scope, critically verifying the widespread opinions.

The particularly interesting ones include last year's reports on chronic spontaneous urticaria (CSU), due to the as yet not fully explained etiopathogenesis of this nosological unit. Authors from a centre in Berlin conducted a study with the participation of 157 patients with a moderate or severe form of chronic spontaneous urticaria, that is, with an urticaria activity score (UAS7) at the level of at least 10 points. As many as 34% of them had a positive medical history of HIT, but this group was not significantly distinguished in terms of the severity of their symptoms. All the patients in the initial period were subjected to a diagnostic histamine-free diet, with low levels of other pseudoallergens, based on rice, potatoes, bread, butter, oil, salt, coffee, and tea. As a result, in 46% of participants, a good response to the diet was achieved, manifesting in the reduction of UAS7 by at least 7 points, and on average by 59% ($p < 0.0001$). Contrary to expectations, patients with HIT in their medical history did not react significantly better to the dietary treatment than the others. Next, a double-blind, placebo-controlled oral provocative challenge with 75 mg of histamine was conducted. It was generally positive in 38% of patients, as it caused an urticaria reaction in only 17% of them. Interestingly, no significant correlation between a positive medical history of HIT and a positive result of the provocative challenge with histamine was identified. Besides, only 2 out of 157 participants presented the full cause-and-effect course of events: symptoms of HIT in the past, a good response to the histamine-free diet and a positive result to the provocative challenge. Therefore, it seems that HIT can be a credible cause of only a few cases of chronic spontaneous urticaria, whereas a positive medical history of HIT is not a predictive factor of a good response to a histamine-free diet [36].

In other studies, the concentrations of histamine and N-tele-methylhistamine in urine were compared in patients with a documented food allergy and in healthy people. It was observed that in the course of a regular diet the concentrations are significantly higher in patients with an allergy, whereas after the implementation of a histamine-free diet they are reduced to the concentrations recorded in the healthy control group. This can be a result of the occurrence of enzymatic barrier disorders in the course of a food allergy. In the opinion of the authors, the concentrations of histamine and N-tele-methylhistamine in urine constitute a good marker differentiating an allergy from other gastroenterological diseases [37].

In the case of other allergic diseases the proof of the coexistence of HIT is primarily limited to descriptions of series of cases. For example, there were reports of the occurrence of recurrent idiopathic anaphylactic reactions in patients with an extremely reduced DAO activity. The inclusion of a histamine-free diet and second-generation antihistamines caused a regression of the fits, in some cases in their entirety [21]. Remission of the symptoms of atopic dermatitis after application of a histamine-free diet has also been reported [38].

Diagnosis and differentiation

Establishing a correct HIT diagnosis is not easy. As in the case of all the syndromes in allergology, a correct and scrupulous medical history is essential, as well as the skilful interpretation of different subjective, often not too characteristic symptoms. Attention should be paid to the clinical picture of the ailment, the time interval of 20-60 minutes typical of acute poisoning between the intake of food and the appearance of symptoms, the potential content of histamine in the consumed products, alcohols consumed in parallel, drugs used protractedly and temporarily that could have impaired DAO activity, the self-limiting nature of acute symptoms and their regression within 6-8 hours, as well as their improvement after taking AH. Due to the unclear relation often observed in HIT between the symptoms and the intake of food, it is recommended that the patient should keep a diet diary with regard to the products consumed and the symptoms appearing afterwards. In turn, in the case of histamine intoxication the allergological history of the patient is particularly significant, as well as an epidemiological inquiry. This may include a negative medical history of food allergies, while a once-off acute unwellness in the surrounding people allow the initial ruling out of an IgE-dependent allergy and direct the diagnostic course towards poisoning [12, 17].

A physical examination, unless conducted in the period of acute symptoms, identifies no significant irregularities. However, deviations typical of the conditions increasing the risk of histamine intoxication can potentially be identified, such as cirrhosis.

Additional tests are primarily meant to rule out the diseases which may manifest similar symptomatology. It would be optimal for cause-and-effect verification to determine the concentration of histamine in the food causing the symptoms, but this test is not easily accessible. To the extent possible, it is good to determine the concentration of N-methylhistamine and prostaglandin D_2 (PGD_2) in the urine and tryptase activity in the plasma in the case of a suspicion of acute

poisoning. In the case of HIT only the former of the listed parameters will be increased, as no systemic degranulation of mast cells has occurred. This allows differentiation with an anaphylactic reaction and mastocytosis. Other indicators, such as the concentration of chromogranin in the blood and 5-hydroxyindoleacetic acid and metanephrins in the urine allow the diagnosis of, respectively, carcinoid syndrome and *pheochromocytoma* [17].

Skin prick tests, including prick-to-prick, as well as measurement of the concentration of specific IgE-class antibodies are an important element of differentiation between histamine intoxication and food allergy. This results from the fact that even in the case of adults, a first-time occurrence of an allergy, for example to fish meat, though rare, is possible. In these cases the possibility of a prior inhaled allergy is suspected [39].

In the case of typical chronic symptoms of HIT, diagnostic procedures are recommended towards gastroenterological diseases, particularly coeliac disease and lactose intolerance [26]. A double-blind, oral provocative challenge with histamine and a following assessment of its concentration in the serum, as well as a determination of DAO activity in the intestinal mucosa would be desirable. Genetic tests can be considered regarding DAO gene polymorphisms. However, all these tests are mainly available within the framework of scientific studies [12].

Therefore, more easily available diagnostic tests are being sought. In this context, there were interesting studies of the kinetics of changes in the blister size in a skin prick test with 1% aqueous solution of histamine hydrochloride. Receiver operating characteristic (ROC) curves of 75 people were compared with the ones of 81 people with HIT. Although no significant difference in the diameter of maximum blister sizes were identified, it was proven that both groups differ significantly in terms of the blister size assessed 50 minutes after the test. At this time in 64 people in the HIT group, the blister found had a minimum diameter of 3 mm, whereas in the control group this was true for as few as 14 ($p < 0.0001$). Diagnostic parameters were calculated for this test, called by the authors the Histamine 50-Skin-Prick Test: sensitivity 79%, specificity 81.3%, positive predictive value 82.1%, negative predictive value 78.2% [10]. This test can become a valuable addition to the double-blind provocative challenge with histamine, which primarily assesses DAO activity, which is why it cannot be treated as the diagnostic gold standard and, according to some authors, in 50% of cases remains unreliable [8, 40]. Observation of a post-histamine blister for 50 minutes is, on the other hand, possible in any allergy clinic. In addition, another component of histamine degradation in the body, that is the HNMT enzyme, which is dominant in the skin, is analysed.

Pharmacological prevention and treatment

There is a lack of randomised, blinded trials concerning the procedure in the case of histamine intoxication. Therefore, it seems rational to extrapolate the experience from treatment of systemic conditions of histamine release, such as anaphylaxis, as well as to use the data from case reports and literature reviews.

In cases with a mild or moderate course, it is suggested that rH1 antagonists are administered, such as cetirizine, diphenhydramine and chlorpheniramine. An rH2 antagonist can also be added, and promethazine in the case of nausea. It is important to manage an appropriate fluid therapy. In a severe form of poisoning, adrenaline should be administered immediately intramuscularly, and fluids after that or – if there is no effect – dopamine. It is recommended to administer a glycocorticosteroid, such as methylprednisolone [17].

The data on the pharmacological prevention of histamine intoxication symptoms is poor. There are no studies with the preventive use of rH1 and rH2 antagonists before the consumption of histamine-rich meals. However, in some cases, consideration of such a procedure seems justified, for example in patients taking isoniazid or MAO inhibitors protractedly [17].

Implementation of rH1 and rH2 antagonists is also suggested for HIT. In the case of intensified symptoms, appearing on a daily basis, AH doses necessary to control the disease can be twice as large as the standard ones. Recommendations in older literature also included chromones and supplementation of vitamin C, vitamin B_6, zinc and copper, which does not seem that well-founded at the moment. In the case of patients with HIT, drugs known to have the potential to degranulate mast cells should be administered with caution. If their use is absolutely necessary, for example of muscle relaxant drugs and radiocontrast agents, premedication with AH and glycocorticosteroid should be considered.

DAO supplementation can be a very effective approach to long-term HIT treatment [12]. There is a promising report from last year by Italian researchers on the application of a Daosin preparation, containing an enzyme obtained from porcine kidneys. 14 patients with a previous positive reaction to the reduction of histamine in the diet were qualified for the study. Ten of them manifested plasma DAO activity deficiency, described as a level of <10 U/ml. Next, the participants were given Daosin orally – 1 capsule, 2 times a day, 15 minutes before a meal, for a minimum of 14 days. As a result, 13 patients felt an improvement within the scope of at least a single symptom associated with HIT [26].

Table 6. Products allowed in a low histamine diet [15]
Tabela 6. Produkty dozwolone w diecie ubogohistaminowej [15]

control	products	reservations
dairy products	milk, sour cream, butter, margarine, cheese, cottage cheese, eggs	
meat	cooked ham, beef, veal, pork, lamb, poultry	except for long-maturing products
fish	flounder, cod, trout, hake, perch	fresh, or frozen shortly after being caught
fruit	all, excluding strawberries, raspberries, citrus fruit, bananas, kiwi, plums, papaya	
vegetables	all, excluding tomatoes, spinach, avocado, eggplant	
cereal products	bread, cookies, noodles, cereal flakes, rice, corn, millet, buckwheat	
desserts	rice pudding, compote, sorbets, ice creams, yoghurts, curd cheeses, vanilla cream	only fruit versions permitted
sweets and other	honey, home-made fruit jams, hard fruit candy and fruit chewing gums, popcorn	
drinks	water, soda water, home-made fruit and vegetable juices	

Further studies are necessary, including blinded and randomised trials. The results presented are, however, important inasmuch as the mentioned preparation is relatively cheap. Furthermore, although it is not sold in Polish pharmacies, starting in April of this year an equivalent has been available; the dietary supplement HISTAsolv.

Non-pharmacological prevention and dietary procedures

Primary HIT prevention most of all concerns the maintenance of a highly efficient cold chain in food production and sanitary supervision. Although current EU regulations define the allowed level of histamine in fish meat, they are not possible to apply in the case of fish from amateur fishing.

There is definitely more data available on the issue of dietary procedures, although they often contradict each other. This even applies to the assessment of the histamine content in particular foods. In one of the systematic reviews, prepared by Spanish researchers, huge discrepancies were shown in classifications of products in different publications. For example, the following were at the same time assessed as high-, mid- and low-histamine: strawberries, cooked ham, blue cheese, yoghurts and green tea. Even the determinations by analytical laboratories were diametrically opposed to each other, such as in the case of spinach, ketchup, and Cheddar and Swiss cheeses. This indicates there are issues with the methodology, as well as variations in the histamine concentrations in different samples of the same food. This does not facilitate dietary consultancy, even more so as the labels of food products do not include their histamine content [41].

The mechanism of action of the diet itself also remains controversial. The studies mainly covered allergic diseases with a suspected HIT component. As indicated, in accordance with the study by Siebenhaar et al. a histamine-free and low-pseudoallergen diet leads to a significant decrease in the activity of chronic spontaneous urticaria. The authors suggest, however, that it is not the lack of histamine that is the decisive factor in this case. On the other hand, in another study from last year, the application of a less restrictive histamine-poor diet (Tab. 6) over a period of 3 weeks caused a decrease in the UAS4 score from an average of 9.05 to 4.23 ($p = 0.004$). The improvement concerned 42 out of 56 participants. Interestingly, there were also earlier observations of a decrease in plasma DAO activity in these patients, which is explained by the authors with the up-regulation phenomenon which appeared earlier. The study also recorded a significant improvement in quality of life after the introduction of the diet, which was a surprise to the authors due to its theoretically unfavourable impact within this scope. Therefore, it seems that a histamine-poor diet is an effective, simple and cheap therapeutic tool in the case of chronic spontaneous urticaria. Following the diet for 3-4 weeks can result in distinguishing of the disease process [14]. In the case of other allergic diseases, there is a lack of strong proof in reference to the favourable effects of a histamine-poor diet. Nevertheless, an analysis of previous reports indicates that it is justified to recommend limitation of histamine consumption in all cases of its intolerance, congenital DAO deficiencies and mast cell hyperplasia [41].

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Maj. Kazimierz Rudolf Fritz, PhD (1896-1979) – defender of Lviv, insurgent of Warsaw, a large-hearted and generous-spirited man

Mjr dr Kazimierz Rudolf Fritz (1896-1979) - obrońca Lwowa, powstaniec warszawski, człowiek wielkiego serca i ducha

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Abstract. The article presents the Polish military physician after whom the Doctors' Retirement House in Warsaw is named. Kazimierz Rudolf Fritz was born in Drohobych, on 11 March 1896. In 1916, he graduated from a renowned middle school (gymnasium) in his hometown. In November 1918, as a cadet, he participated in the defense of Lviv, the battle between the Polish inhabitants of the city (mostly middle school and university students) and the Ukrainian soldiers of Dmytro Vitovsky, who staged a coup d'état. In 1925, he graduated from the Faculty of Medicine at Jan Kazimierz University in Lviv. In the interwar period, he served in several military hospitals. From 1936 he was a head of the dermatological ward in the 7th Regional Hospital in Poznań. During the German occupation, he worked at the Ujazdowski Hospital and as a doctor of this institution he took part in the Warsaw Uprising in 1944. After the end of World War II, he headed the dermatological ward at the City Hospital in Chorzów. Doctor Fritz was the originator and one of the founders of the Doctors' Retirement House in Warsaw. He died on 9 November 1979, at the age of 83.
Key words: Fritz, defence of Lviv, Warsaw Uprising, Ujazdowski Hospital, Drohobych

Streszczenie. Artykuł przedstawia sylwetkę polskiego lekarza wojskowego, który jest patronem Domu Lekarza Seniora w Warszawie. Kazimierz Rudolf Fritz urodził się 11 marca 1896 roku w Drohobyczu. W 1916 roku ukończył renomowane gimnazjum w swym rodzinnym mieście. W listopadzie 1918 roku jako podchorąży wziął udział w Obronie Lwowa, czyli bitwie o miasto jego polskich mieszkańców (głównie studentów i gimnazjalistów) z ukraińskimi żołnierzami Dmytra Wytowskiego, który przeprowadził zamach stanu. W 1925 roku ukończył Wydział Lekarski Uniwersytetu Jana Kazimierza we Lwowie. W okresie międzywojennym służył w kilku szpitalach wojskowych. Od 1936 roku był szefem oddziału dermatologicznego w 7. Szpitalu Okręgowym w Poznaniu. Podczas okupacji niemieckiej pracował w Szpitalu Ujazdowskim, jako lekarz tej placówki wziął udział w Powstaniu Warszawskim. Po zakończeniu II wojny światowej prowadził oddział dermatologiczny w Szpitalu Miejskim w Chorzowie. Doktor Fritz był pomysłodawcą i jednym z fundatorów Domu Lekarza Seniora w Warszawie. Zmarł 9 listopada 1979 roku w wieku 83 lat.
Słowa kluczowe: Fritz, Obrona Lwowa, Powstanie Warszawskie, Szpital Ujazdowski, Drohobycz

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Early life, education and military service

The famous statement by Marshal Józef Piłsudski, comparing Poland to a bagel, which argues that the most valuable assets come from the borderlands, is frequently quoted when the most meritorious Poles from the eastern districts of the former Republic of Poland are presented. This elite company must certainly include Maj. Kazimierz Rudolf Fritz, PhD, a Polish military physician from the land of Lwów, and who deserves the highest recognition for his life's values and achievements. June 2017 marks the 15th anniversary of the naming of the K.Fritz Doctors' Retirement House in Warsaw, a perfect opportunity to remember and broadly present the profile of this extraordinary physician and remarkable man.

Kazimierz Rudolf Fritz was born on 11 March 1896 in Drohobych, in the land of Lwów (this part of the Republic of Poland was at the time under Austro-Hungarian rule), to Ludwik Fritz (1863-1945) and Antonina née Czemeres (1859-1931). The family was an affluent one and they were members of the local elite. The father was a horse-drawn vehicle manufacturer, which allowed them to accumulate significant wealth. All seven of the Fritz children (Kazimierz, Józef, Wiktoria, Jan, Maria, Zofia and Roman) received a thorough education, adhering to the family's values [1]. Young Kazimierz Fritz attended the renowned Gymnasium (middle school) in Drohobych, which provided excellent schooling. The quality of the school can be proven by the fact that it was attended by personalities who later distinguished themselves in various fields, for example Bruno Schulz (1892-1942, fine artist, writer, respected artist), Stanisław Maczek (1892-1994, Lt. Gen., 1st Armoured Division Commander), Michał Tokarzewski-Karaszewicz (1892-1964, Division Commander, the first commander of the Union of Armed Struggle (ZWZ)) and many others. The outbreak of World War I interrupted the process of education and resulted in the oldest students being drafted into the Austrian army. This included Kazimierz Fritz.

A special regulation of the k.k. Minister of Religion and Public Education from 17 September 1915 introduced accelerated matriculation examinations for students performing military service. Young Fritz seized this opportunity and passed his matriculation examination on 27 January 1916 in his school, before an examination board headed by Józef Staromiejski [2-4].

During his service, he obtained the rank of officer cadet and in 1917, he was seconded to medical studies at the Faculty of Medicine of the Jan Kazimierz University in Lwów. In November 1918 he actively participated in the defence of Lwów against a Ukrainian coup d'état staged by Dmytro Vitovsky, joining the staff of the "Technik" Hospital (in the building of the Technical University) and

Figure 1. Maj. Kazimierz Rudolf Fritz, PhD (1896-1979), 1940s (Central Medical Library: KOL L-2065)
Rycina 1. Mjr dr Kazimierz Rudolf Fritz (1896-1979), lata 40. XX wieku (Główna Biblioteka Lekarska: KOL L-2065)

the "Dwójka" Hospital (in the House for War Invalids at 35 Kleparowskiej St.), where he could observe the world-famous surgeon, Gen. Prof. Ludwik Rygier (1850-1920). His participation in the defence of Lwów was a source of great pride for Fritz up until his last days. From 10 July up until 1 October 1919 he served as sanitary liaison officer for sanitary matters with the Military Command of the Former Prussian Partition [5-8]. After the cessation of military actions and the following disarmament, in 1921 the Sanitary Department of the Ministry of Military Affairs issued a decision to second the medical students serving in the army to universities, with the view of obtaining full professional competence.

Kazimierz Fritz – a seasoned soldier, already promoted to lieutenant in April 1919, after 12 months promoted to captain, and awarded one of the highest military orders – the Cross of Valour (No 27716) – returned to Lwów, to the Faculty of Medicine of the Jan Kazimierz University. The system of schooling for military students was not that different from that for civilians, except that during summer holidays they usually received additional military training, were assigned to a military unit and temporarily performed additional functions. Capt. Medic Kazimierz Fritz was initially a member of the staff of the Local Hospital in Stryj, later transferred to the 9th

Figure 2. Former Military Hospital No. 2 “Dwójka", where Kazimierz Fritz served as a cadet during the defence of Lwów in 1918, presently the Lviv State University of Life Safety, Lviv, 2006 (by Z. Lviv, 2005)
Rycina 2. Dawny Szpital Wojskowy nr 2 „Dwójka", gdzie podchorąży K. Fritz służył podczas Obrony Lwowa w 1918 roku, obecnie Lwowski Państwowy Uniwersytet Bezpieczeństwa Życia, Lwów, 2006 (fot. Z. Kopociński)

Heavy Artillery Regiment, at the same time assigned permanently to study at the Jan Kazimierz University. During the holiday break in 1924 (12 July – 6 September) he attended a special sanitary course at the Military Sanitary School in Warsaw. Fritz obtained his medical diploma on 4 July 1925 at the Faculty of Medicine of the Jan Kazimierz University in Lwów, while the authorisation to practise the profession was issued in 1926 by the Voivodeship Office in Stanisławów [6, 7, 9].

The interwar period

Immediately after he graduated, Capt. K. Fritz, PhD was appointed a junior physician with the 48th Kresy Rifles Infantry Regiment in Stanisławów, and a year later transferred to the same post with the 19th Relief of Lwów Infantry Regiment in Lwów. At that time, his main field of professional interest was dermatology, a speciality of particular significance in the army, due to wide-spread skin (questionable conditions of hygiene in barracks) and venereal diseases. On 23 December 1927, he took the position of the head of the department of skin and venereal diseases in the 9th Regional Hospital in Brest-on-the-Bug. This helped him gain experience and vital skills regarding dermatological diseases, which resulted in him achieving the title of a specialist in this medical field. At that time, the facility located on the Hospital Island of the Brest Fortress was one of the most

important military medical centres in the country; it offered advanced specialised care in most medical fields. The department of skin and venereal diseases was administered by an experienced and recognised physician, Maj. Robert Funk, PhD, under whose watchful eye Fritz expanded his professional knowledge [6, 7, 9, 10]. The peak of Fritz's career in the military was his promotion to the rank of major with seniority on 1 January 1931. In October of the same year, he received the position of clerk in the District Sanitary Command of the 9th Corps in Brest-on-the-Bug. His direct supervisors, Col. Adolf Jacewski, PhD, and then Col. Tomasz Krzyski, PhD made it possible for him to continue his practice in the department of skin and venereal diseases in the 9th District Hospital. This proved especially beneficial for gaining both knowledge and experience in dermatology at a level allowing him to take over administration of such a department.

In January 1936 Maj. Fritz, PhD left the ever-so-hospitable Brest for good and set out for the capital of the Greater Poland, where he became the senior head of an 85-bed department of skin and venereal diseases at the 7th District Hospital. This was a dream come true for this medic from Drohobych, as he became the head of a significant department in his favourite field of medicine in one of the most prominent military hospitals of the interwar period. His success in his professional life also contributed to stability in his private life – in 1939 Fritz married a Polish woman born in St Petersburg – Antonina Purtal [7, 9, 11, 12].

World War II and German occupation

Unfortunately, the political situation in Europe at that time was becoming less beneficial for Poland and the violent attitude of the neighbouring countries gave no hope for further peaceful coexistence. As part of the preparation for a potential armed conflict, the military sanitary authorities organised various types of trainings. From 1 October 1938 up until 1 May 1939 Maj. Fritz, PhD participated in the Second Course for Large Formation Sanitary Chiefs whose primary purpose was to prepare the management personnel to command medical subdivisions on the future battlefield. The knowledge he gained there was soon to be used in practice. On 1 September 1939, after the Third Reich's attack on Poland, this dermatologist from Poznań became the commandant of the 701st Field Hospital (formed by the Reserve Personnel of the 7th District Hospital) with the 14th Infantry Division in Poznań. With his unit, he followed the whole heroic combat trail of the soldiers commanded by Maj. Gen. T Kutrzeba, and after the capitulation worked in a prison hospital in Łowicz [11, 13, 14]. A great number of physicians from the 7th District Hospital were sent to the Ujazdowski Hospital in Warsaw, headed by a former commandant of the Poznań facility, Col. prof. Teofil Kucharski (1889-1955). In December 1939 Maj. Fritz, PhD joined the staff of the famous *Rzeczpospolita Ujazdowska* (Ujazdów Republic).

It is worth mentioning that Poles inhabiting the capital of Greater Poland, including many families of Poznań military physicians, had no choice but to leave their city. Antonina Fritz was no exception, and she was forced to leave her home at 30 Słowackiego St. and set off for Warsaw where her husband had already been sent. Ujazdowski Hospital was at the time a genuine refuge for both military medical personnel as well as injured soldiers. The staff consisted mainly of professional officers, which was conductive to building mutual trust and the development of underground activity. Col. Leon Strehl, PhD (1891-1960) took command. Throughout the whole occupation, aside from providing regular medical services and taking extended care of war invalids, the facility hosted medical training of the medical personnel for the purposes of the Home Army (AK), secret schooling for medical students, and a medical committee deciding on disability enabling formal release from a prisoner-of-war camp. Taking into consideration its attitude in the defensive war of 1939, the occupation and the Warsaw uprising, Ujazdowski Hospital undeniably deserves the highest combat award, which was applied for in 1947 by its commandant, Col. prof. T Kucharski. For more than 10 years, the co-authors of this article have been making constant efforts to realise the request of the Ujazdów Republic's commandant and award the facility with the Virtuti Militari, without any success thus far [9, 15, 16].

In the fighting capital

At the outbreak of the Warsaw uprising on 1 August 1944 the command of the Ujazdowski Hospital was yet again handed over to Col. prof. T Kucharski, while Maj. Fritz stood guard along with other medics. It should be emphasised that since the very beginning of the fighting, the facility provided medical assistance to all injured, including Germans. On the 5 August 1944, the occupant's army reached the facility and ordered its evacuation. At 9 am of the following day, a unit was formed out of 1491 people selected from patients and personnel, and sent to the re-established Ujazdowski Hospital at 19 Chełmska St. The facility was the most important health care centre in Lower Mokotów at the time and its staff was comprised of devoted military physicians, including Col. prof. T. Kucharski, Col. Mieczysław Naramowski, PhD, Maj. Kazimierz Fritz, PhD and Maj. Witold Waligórski, PhD. In these extremely severe conditions, constantly under fire and accompanied by bombing raids, with no basic

medical supplies or food, the entire staff of the hospital provided medical assistance, often putting their own life and health at risk. On 30 August 1944 the Germans bombed the hospital, which was sheltering 800 injured (150 of them died). After this tragic event, the commandant of the facility ordered an evacuation to Upper Mokotów, where Col M. Naramowski, PhD had opened a facility at 91 Puławska St. while some of the personnel were sent to Sadyba. By the time the epic uprising came to an end, Ujazdowski Hospital was in Milanówek and then, in November 1944, it was transferred to Kraków, where it was disbanded in 1945 and the patients were admitted to local field hospitals. The dermatologist, Maj. Fritz, PhD, accompanied the Republic of Ujazdów on its entire incredibly heroic combat trail [7, 17, 18].

After the war

World War II and its consequences took a toll on Dr. Fritz's life. The new reality did not permit any public mention of Lwów or Drohobych, where his family was expatriated from, while according to his deceitful identity document, his place of birth was now in the USSR. Warsaw was completely destroyed and the former 7th Regional Hospital in Poznań no longer existed. Fritz moved to Upper Silesia, where he became active joined in reconstructing the Polish health care system. He worked in the Social Insurance Office in Chorzów, where he also established a dermal-venereological clinic. In 1955, he founded a Dermatology Department in the Municipal Hospital in Chorzów, which he governed until his retirement in 1966. Through his work, he earned enormous respect from the people of Upper Silesia. After he retired, he moved back to Warsaw and lived with his wife at 3/18 Śliska St. He was an active member of the Polish Medical Association (PTL). He was the founder and initiator of the Doctors' Retirement House. At a PTL meeting on 22 April 1978, he donated 1 million PLN for that cause, which was a huge amount of money at that time, and in his will bequeathed another 800 thousand PLN. Unfortunately, he did not witness the opening of his dream facility, as he died on 9 November 1979. He was buried in the family grave in Old Powązki Necropolis in Warsaw, section 84, row 5, space 19. The Retirement House was established only in 1992, and on 21 June 2002, by a decision of the Minister of Health, the facility was named after its most prominent donor and co-founder, Dr. Kazimierz Fritz. This year, we celebrate the 15th anniversary of this great event. It is undoubtedly a moving expression of tribute for the Drohobych-born medic of small size (1.67 m) but enormous spirit and heart [7, 9, 20].

For his loyal service, courage during the war and years of committed work in various health care units, Fritz received many awards, including two Crosses of Valour, the Order of the Cross of Independence, the Gold Cross of Merit, the Knight's Cross of Polonia Restituta (1972) and a badge “For Exemplary Work in Health Care” [7]. It is important to mention the fact that the Fritz family, being of Austrian origin (the mother of Fritz's father was Austrian) and having received an offer to sign the Reichslist, remained loyal to their country during the occupation, even though it had disastrous consequences. Józef Fritz, Kazimierz Fritz's brother, a Lvovian paediatrician, was murdered along with his wife, Elżbieta (they were compelled to go into hiding due to her Jewish origin) in the Gross-Rosen German concentration camp.

The tombstone of Maj. Kazimierz Fritz, PhD contains an incredibly meaningful engraving: “A defender of Lwów” (“Obrońca Lwowa”). He was always extremely proud of his participation in a battle of such importance and returning the most loyal city to the Republic. However, sadly, the colleagues of Fritz, PhD buried in the Defenders of Lwów Cemetery (for example, the world-famous surgeon, Gen. prof. Ludwik Rydygier), were deprived of such an engraving on their tombstones, following a decision by the Ukrainian authorities. Taking away a title of honour from Polish national heroes who died or were killed paying the price of blood and sacrifice, is difficult to understand in a civilised world. Maybe the most significant symbolic award for Maj. Kazimierz Fritz, PhD for all his achievements and sacrifices is the humble engraving on his tombstone which shall never be removed – “A defender of Lwów”.

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In memory of a Professor of Medicine, Bronisław Stawarz (1934-2017)

Wspomnienie o Profesorze Bronisławie Stawarzu (1934-2017)

On 11 May 2017, Col. prof. Bronisław Stawarz, MD, PhD, a wonderful husband, father, grandfather, educator of many generations of surgeons and urologists, passed away. A man of great sensitivity, always loving towards his family, and respectful towards friends, colleagues and students.

Professor Stawarz graduated from the Faculty of Medicine of the Medical University of Lublin in 1958. Initially, he worked at the Surgery Department of the Municipal Hospital in Przemyśl. In 1964, he was drafted into military service and served in the Military Hospital in Przemyśl as a surgery department assistant.

From 1967, he was permanently associated with the Szaserów Hospital, which formed part of JKP WAM, then CKP WAM, and most recently WIM. In the period 1967-1971, he was an assistant in the department of trauma surgery and orthopaedics and from 1971 in the 2nd Clinical Hospital headed by prof. Smolarek, and worked his way up the career ladder.

In 1982, he was made Head of the Urology Clinic at which post he stayed until 2002. From 2003 he was a consultant in the Urology Clinic of WIM.

Professor Stawarz was a widely educated surgeon and urologist. He obtained the second degree specialisation in general and paediatric surgery and in urology. He also completed many scientific internships, for example in Roland Klinik in Bremen, University Hospital in Munich, Copenhagen, Ulm, Stuttgart and Los Angeles.

Over time, he was awarded the following academic degrees and titles: MD, PhD in 1972, MD, Doctor Habilitatus in 1980, Associate Professor in 1988 and Full Professor in 1995. He was promoted to the rank of colonel of the Polish Army in 1981.

The professor's scientific output consists of 205 papers and conference communications.

He belonged to many associations and organisations, including the Association of Polish Surgeons (TChP), the Polish Urological Association (PTU), the Polish Society of Andrology, the European Association of Urology and the European Association for Endoscopic Surgery.

He was also an active member of the medical council, with an enormous contribution in increasing the prestige of military physicians. In 1989, he was elected the first president of the Military Medical Chamber, kept this role for two terms and later on was an active member of the Supreme Medical Court for several more terms.

He participated in the work of the Scientific Councils of CSK WAM and WIM and was a member of many Examination Boards regarding surgery and urology.

He was the supervisor of seven doctoral dissertations and the reviewer of many post-doctoral and doctoral dissertations. He was also the reviewer in many publishing committees, e.g. “Military Physician”, “Scalpel”, and “Polish Journal of Urology”.

His scientific, educational and research activities were distinguished with a 1st Degree Award of the Science and Technology Development Chairman, the Commission of National Education Medal, the PTU Certificate in recognition of merit in the field of urology and awards of the WAM Rector and CKP WAM Commandants.

He particularly valued the award for his social work. He was given the St. Brother Albert Adam Chmielowski Award for many years of selfless help that he offered to pensioners. A patient could always count on his support. He would provide medical consultation both on the phone and in person.

He was awarded many departmental decorations. In 1985, he was awarded the Knight's Cross of the Order of Polonia Restituta and in 2001, he received the Officer's Cross of the Order of Polonia Restituta.

He was a wonderful man, a great and unusually intelligent teacher and a keen observer of life, gifted with a remarkable memory. Thanks to these features, he was a fine clinician, a gifted surgeon and a skilful head of a medical team.

The broad knowledge, enormous experience and exceptional organisational skills that the professor had were always highly valued by his colleagues, including physicians and nurses.

He was very witty and his humour was contagious and could cheer up anyone in their hard work at the hospital.

Young physicians loved to hear his stories about medicine, difficult medical cases and his own experience – it was an important element in the education of young surgeons and urologists. For many years, even after he retired, he maintained contact with his students and always supported them in solving medical problems.

Despite the workload resulting from treating patients, being the head of a department and working in court, he never neglected his responsibilities towards his family. He brought up two daughters with his wife, Lilianna Stawarz (a specialist in paediatrics and allergology): Beata and Lilianna. He was an attentive, loving husband and father and after the birth of two grandchildren – a caring grandfather. Beside medicine, his family was the most important part of his life.

Professor Stawarz had many hobbies. Unfortunately, due to a constant lack of time, he rarely had the opportunity to enjoy them. He loved fishing, an activity which let him fully escape from his everyday responsibilities at least for a short while. He also spent his spare time on good books.

Professor Stawarz was liked in the medical community, mostly for his kindness, empathy, openness and good sense of humour.

We will miss all of that.

With huge regret, we said goodbye to our Bronisław, a true friend who always kept in touch with us, despite his retirement due to a long and serious illness.

He is gone forever but will remain in our hearts and memory as a role model of a physician and a man.

Professor Bronisław Stawarz was buried in the cemetery in Bródno, Warsaw.

Bronek, rest in peace
Honour his memory