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ORIGINAL ARTICLE

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Application of Laserobaria 2.0_S device in the treatment of hard-to-heal wounds of mixed etiology — own experience

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Abstract

Introduction: *The formation of hard-to-heal wounds can have many causes and is most often the result of the influence of several patient health factors. Some of the most difficult to treat effectively are wounds resulting from complications of diabetes, known as diabetic foot syndrome.*

Material and methods: *Fifty-two patients (mean age 67 years ± 11.5) were eligible. All patients had chronic wounds of varied etiology in the lower limb, the previous treatment of which had not been satisfactory. Therapy parameters were selected individually; in addition to standard therapy, topical physical agents such as light therapy, pulsed electromagnetic field (PEMF), ozone therapy, and oxygen therapy were included in the treatment. Each therapeutic cycle lasted 10 consecutive days (excluding Saturdays and Sundays), and each treatment lasted approximately 1 hour.*

Results: *The analgesic effect of PEMF therapy was reported at 60% according to the VAS scale assessment. Pain was reduced from the third day of treatments, including for patients in whom pharmacological pain relief did not produce a clear improvement. Wound improvement, through granulation, after the first 10-day treatment cycle was observed in 40.5% of patients (14 k, 7 m). Four patients dropped the continuation of treatment because they did not see healing progress. Six patients dropped out of the next treatment cycle for other reasons (high cost of therapy, long distance of the clinic from home, and other socio-economic reasons).*

Conclusions: *The high efficiency of combining standard treatment with innovative physical treatments allows for better patient care, which accelerates the necessary therapeutic steps toward holistic patient treatment. The authors recommend further multicenter, randomized, blinded trials to develop the optimal dosage to maximize the therapeutic effect and shorten the time to complete wound closure.*

Keywords: diabetic foot syndrome; chronic wounds; topical physical agents; light therapy; pulsed electromagnetic field (PEMF) therapy; ozone therapy; oxygen therapy

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Introduction

The formation of hard-to-heal wounds can have many causes and is most often the result of the influence of several patient health factors. Some of the most difficult to treat effectively are wounds resulting from complications of diabetes, known as diabetic foot syndrome.

The main determinants of the development of diabetic foot ulcers are neuropathy and lower limb ischemia. As the disease progresses, there is a severe degeneration of the tissues of the lower limb, which manifests itself in swelling, severe pain, and the development of serious infections within even minor cuts and skin injuries. Tissues within the wound, as a result of impaired functioning of the blood system, are unable to effectively fight off foci of infection or conduct a proper and effective regeneration process. Such a situation promotes increased infectious colonization of the wound and further degeneration of adjacent tissues, which can eventually even lead to osteitis.

The treatment of patients with hard-to-heal extremity wounds requires a multidisciplinary team that, in inpatient, outpatient, and at home, will be able to effectively provide assistance to the patient by performing the necessary procedures, properly dressing the wound, and educating the patient and his family.

Often application of all good practices and conventional methods of treating hard-to-heal wounds is insufficient and additional measures must be taken, using the latest available methods.

The article describes the clinical experience of the wound healing process using the innovative Laserobaria 2.0_S device. The device allows for local oxygen therapy, ozone therapy, magnetotherapy, red light therapy, and UV light therapy.

In the period from July 2021 to May 2022, the Alfamedica Silesia North Medical Center provided therapy for hard-to-heal wounds of mixed etiology using a combined physical therapy method with the Laserobaria 2.0_S device manufactured by INVENTMED Sp. z o.o. for 52 patients.

The following paper presents the detailed therapeutic effects and methodology of using the Laserobaria 2.0_S device.

Material and methods

Description of the population

Fifty-two patients (mean age 67 ± 11.5 years), 23 women (mean age 68 ± 9.8), and 29 men (mean age 66 ± 12.6) in the present group were qualified for treatment with combined physical therapies. All of the patients had chronic wounds in the lower extremity, the previous treatment of which had not been satisfactory, and the persistent state of wound infection posed, in many cases, a real risk of having partial limb amputation. The etiology of the wounds varied, and a detailed breakdown by the condition is in preparation (Table 1, 2).

Table 1. Demographic description of patients

Total				
M	SD	Min	Max	N
66.8	11.5	38	91	52
Women				
M	SD	Min	Max	N
67.6	9.8	38	78	23
Men				
M	SD	Min	Max	N
66.2	12.6	45	91	29

Table 2. Distribution of patients by age groups

Age range	Women	Men
> 70	12	12
60–70	7	7
50–60	2	7
40–50	1	3
30–40	1	0

Each patient was treated with drug therapy. If necessary, the wound was treated surgically before treatment with Laserobaria 2.0_S. On each treatment day, the dressing was changed and the wound was cleaned in an outpatient setting (Fig. 1).

Description of therapeutic measures

Phototherapy — during the treatment, light is emitted with wavelengths in the red light range. This wavelength of light, according to the laws of photobiology, allows penetration through cells in highly absorbent bands. For most tissues in the body, the main chromophores are hemoglobin and melanin, which have high-absorption bands in the mentioned range [1]. Light radiation is absorbed by the skin, stimulating the skin's natural healing processes and reducing pain. Red light increases blood flow and oxygen and causes the production of oxygen free radicals acting destructively against bacteria [2]. Light therapy is very effective in treating skin ulcers caused by diabetes. Wound decontamination and the device itself are achieved by light-emitting diodes, which emit ultraviolet light. It can also be used to treat psoriatic lesions or atopic dermatitis [3].

Magnetotherapy — Magnetic fields have a beneficial effect on tissue respiration and regeneration processes. Magnetic influence at the cellular level primarily

Figure 1. An overview photo of the Laserobaria 2.0_S therapy kit

stimulates the production of calcium-dependent compounds, Calmodulin (CAM+) [4]. This is an essential cellular process for tissue growth and regeneration. Also through its anti-inflammatory and anti-oedematous effects, combined with the enhancement of beta-endorphin secretion processes, it has a strong analgesic effect, which is of great importance in pain patients. In the case of therapeutic medicine, thanks to the proper selection of the field frequency to the transmembrane impedance of the cells, effective therapeutic values oscillate around a few militesla. This feature makes it possible to construct devices that are small, safe, and convenient to use. It has also been shown that a PEMF (Pulsed Electromagnetic Field) acts on the structures of cell membranes by changing their properties, induces an immune enzymatic response, and has an effect on collagen and creatine formation [5]. The above features also translate into the high effectiveness of magnetic field therapy for osteoarticular diseases and injuries. Bones subjected to PEMF treatment knit together faster and their density increases significantly [6].

Oxygen therapy — is one of the most effective methods of delivering oxygen to all cells of the body. The use of pressure higher than atmospheric pressure deprives oxygen of its physiological barriers to penetration through tissues, allowing oxygen to penetrate poorly circulated areas, such as wounds. TOT (Topical Hyperbaric Oxygen Therapy) which is categorized as low-pressure oxygen therapy is effective for treating necrotic and gangrenous wounds. Topical oxygen therapy has several advantages over classical hyperbaric therapy in that it is safer and less expensive; due to the reduced pressure (0.5–1.3 ATA), the risk of oxygen poisoning is reduced, it facilitates the application of spot treatment, etc. Providing more oxygen to the tissue during recovery is a key element of successful therapy. In chronic wounds, a high oxygenation gradient is observed in the tissues, especially between the center of the wound and its periphery. The partial pressure of oxygen (po2) varies from 0–10 mm Hg in the center of the wound to 60 mm Hg at the wound periphery, while the po2 concentration in arterial blood averages 100 mm Hg. Providing supplemental oxygen to the treated tissue, as well as other methods to promote tissue oxygenation, accelerates the healing process. Oxygen penetrates not only red blood cells — but its concentration also increases in plasma, the lymphatic system, and cerebrospinal fluid. Oxygen therapy promotes physiological processes in the body, improving tissue regeneration and wound healing in conditions such as diabetic foot, and complications after radiation therapy of soft tissues and bone. It also promotes neovascularization or the formation of new vessels in the event of injury or disease. It reduces inflammation and has proven efficacy in a number of disease entities [7].

Ozone therapy — is among one of the most effective antiseptic methods. Ozone is the most potent bactericidal, fungicidal, and virucidal agent. It oxygenates cells, has a detoxifying effect, improves cell metabolism, improves blood circulation, reduces clumping of red blood cells, improves oxygen transport and blood flow, increases oxygen absorption by tissues, destroys fungi, bacteria, and viruses, and prevents their re-emergence [8].

Dosage and selection of therapeutic agents

Therapy parameters were selected for each patient individually, but general principles of wound management according to TIME recommendations were applied [9] and thus respectively:

— for patients who had severe pain and/or severe swelling of the limb, magnetotherapy was included;
— intensive biocidal therapy with ozone was used for patients whose wounds were at risk of infection or had a local infection-threatening systemic infection (W.A.R. Wounds at Risk score ≥ 3);
— for patients with a wound at low risk of infection (W.A.R. < 3), the limb was subjected to red light stimulation;
— oxygen therapy was used in every case.

UV light

UV light therapy is characterized by the wide variation in dosage and wavelength ranges used observed in the literature. Due to the undefined consensus on dosage and the least favourable benefit-risk ratio of other methods, UV light therapy was abandoned in the cases described. Recent meta-analyses, however, indicate that UV dosing in the low-energy range can provide therapeutic benefits with very short exposure times (< 5min) without serious side effects [10]. It is likely to be harmless for the patient to use UV light therapy (used in the UV-A device — low harm to the body), but the therapeutic value remains to be verified. The proposed dosage is 0.1 J/cm^2 with an exposure time of no more than 2 minutes at the beginning of therapy.

Ozone therapy

Ozone is administered at the beginning of treatment to clear the limb of biofilm and, in particular, inactivate viruses within the wound. Sealing the treatment chamber at the beginning of the treatment also allows ozone to remain inside the chamber after ozone therapy until the chamber is unsealed or ozone is displaced by oxygen. This approach makes it possible to extend the effective duration of ozone exposure for another several minutes (the half-life of ozone is 20 minutes) [11] (Table 3).

Flow rate: 3.5 l/min, capacity: 400 mg/h

Table 3. Duration of ozone therapy, number of treatments

Number of treatments	57
Average time	15
Median	15
Min	5
Max	30

Pulsed electromagnetic field

Based on previous experience using magnetic fields and taking advantage of the possibility of almost free shaping of magnetotherapy parameters, the following device setting parameters were used (Table 4, 5).

Table 4. Dosage of slow-variable magnetic field

	Bipolar	Unipolar
Triangle 4 mT, 5 Hz	12	13
Triangle 4 mT, 10 Hz	3	2
Triangle 4 mT, 15 Hz	0	2
Triangle 4 mT, 20 Hz	1	0
Triangle 4 mT, 40 Hz	4	3
Triangle 2 mT, 60 Hz	0	1
Sinus, 4.3 mT, 5 Hz	1	0
Sinus, 4.3 mT, 10 Hz	1	0
Sinus, 4.3 mT, 40 Hz	2	0

Table 5. Magnetic field trapping time

Treatment time with PEMF	[min]
Medium	14
Median	12
Maximum	20
Minimum	10

A total of 45 sessions (450 treatments) were performed using magnetic fields. Settings that showed wide therapeutic efficacy were: 4 mT, 5 Hz, triangular waveform, and bipolar.

Oxygen therapy

Oxygen with a concentration above 90% and a maximum pressure of 500 Pa or 1000 Pa above atmospheric pressure was supplied to the therapy chamber. During oxygen therapy, an atmosphere of increased pressure and increased oxygen concentration was maintained in the chamber. After the end of oxygen therapy, pressure equalization occurred, but it can be assumed with a high degree of probability that an elevated oxygen concentration was maintained in the chamber (Table 6, 7).

Concentration > 98%

Table 6. Oxygen dosage by time

	Pressure [Pa]	Time [min]
Average	570	34
Median	500	30
Min	500	10
Max	1000	60

Table 7. Distribution of maximum pressure dosage

	Number of treatments
500 Pa	61
1000 Pa	10

Red light

The Laserobaria 2.0_S device allows omnidirectional irradiation of the limb being treated inside the therapy chamber. The unique arrangement of the irradiation panels inside the chamber, along with its finish in a way that maximizes light reflection, makes it one of the few devices available on the market that effectively delivers light radiation evenly over the entire surface of the limb being treated (Table 8).

Radiation area: 1435 cm^2

Radiation power: 2000 mW

Table 8. Red light dosage

	Dose [J/cm^2]	Time [min]
Average	0.85	10
Median	0.84	10
Min	0.42	5
Max	1.67	20

Number of red light treatments performed: 35

Combination of physical therapeutic agents

In addition to medical contraindications to the use of selected therapeutic agents, the duration of the procedure is also an important limitation. For financial reasons, standardization of the medical service, and patient convenience, the duration of a single treatment should not exceed one hour. Therefore, in some cases, choices had to be made between therapies, to maximize the duration of the most appropriate form in a given case.

The general rule of thumb for combining therapeutic agents is similar effects of agents. So, for example, ozone can combine with UV light therapy, for maximum biocidal effect. Magnet therapy and red light therapy accelerate the process of angiogenesis and increase blood flow, so both therapies will act complementarily and work well in combination with oxygen therapy.

For reasons of time constraints, therapy should be planned in such a way as to maximize the duration of effect of the therapeutic agents prescribed to the patient, by appropriately arranging the sequence of successive therapies.

In all the cases described above, regardless of the choice of individual therapies, they were performed in the following order: ozone therapy, magnetotherapy, oxygen therapy, and red light therapy (Table 9, Fig. 2).

Table 9. Occurring combinations of treatments

	Ozone + PEMF + Oxygen	Ozone + Oxygen + Red Light	PEMF + Oxygen + Red Light	Ozone + Oxygen	PEMF + Oxygen	Ozone + PEMF + Oxygen + Red Light
W	9	7	4	3	2	3
M	12	12	4	4	5	4
Total	21	19	8	7	7	7

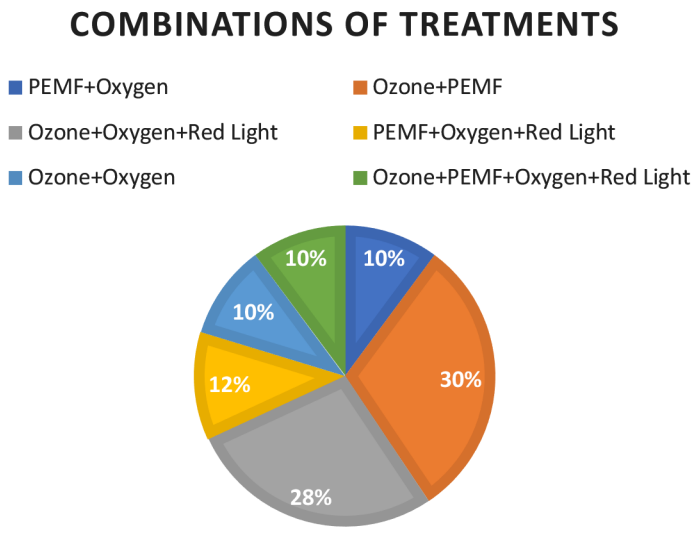

Figure 2. Graph showing the incidence of combined treatments

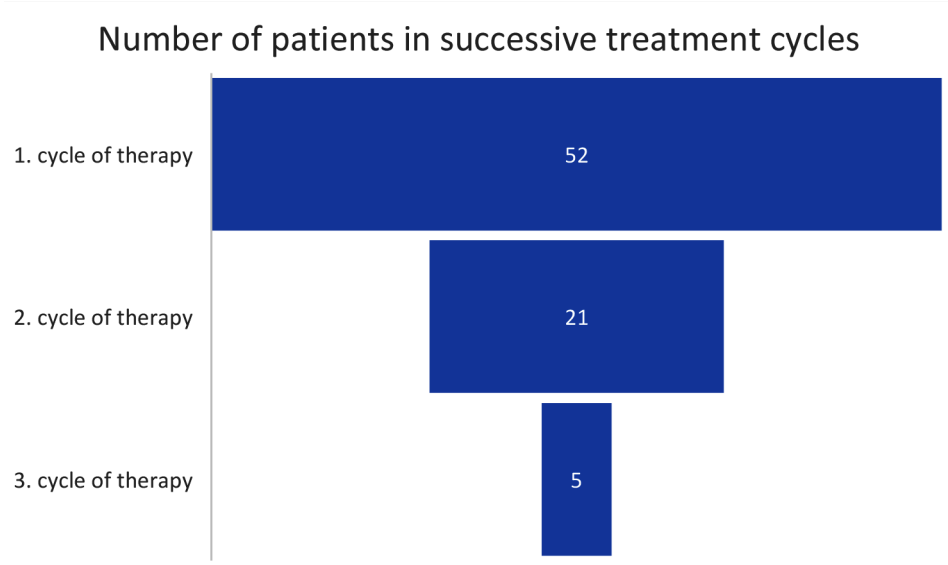

Figure 3. Graph of the number of patients in successive treatment cycles

Results

Each treatment cycle lasted 10 consecutive days (excluding Saturdays and Sundays), and each treatment lasted about 1 hour (including time for patient preparation and device disinfection).

Analgesic effect

The pain-relieving effect for the 43 PEMF therapies performed was recorded at 60% according to the VAS scale assessment. Pain was reduced from the third day of the treatments, including for patients in whom pharmacological pain relief did not produce a marked improvement.

Wound healing

Wound improvement, through granulation, after the first 10-day treatment cycle was observed in 40.5% of patients (14 k, 7 m). Of the initial group of 52 patients, 31 patients were qualified for repeat therapy. 4 people dropped out of continuing treatment because they saw no therapeutic progress. 6 people dropped out of the next treatment cycle for other reasons (high cost of therapy, long distance of the clinic from their homes, and other socio-economic reasons). The third treatment series was performed on 5 patients (Fig. 3).

Conclusions

The inclusion of the Laserobaria 2.0_S therapeutic chamber, which allows the wound to be affected by several physical therapy agents during treatment, in combination with intensified nursing care, which is meant daily cleaning and dressing of wounds, creates favorable conditions for tissue regeneration.

A dramatic and rapid improvement in the patient's well-being is noticeable, and hard-to-heal wounds often persisted for many months until therapy began to begin to heal.

The high effectiveness of the therapeutic method of combining standard treatment with innovative physical methods allows for better patient care, by relieving pain it allows for stronger compression therapy, effective infection control reduces risk factors for revascularization procedures, which accelerates the necessary therapeutic steps towards holistic patient treatment.

The authors recommend further multicenter, randomized, blinded trials to develop the optimal dosage to maximize the therapeutic effect and reduce the time to complete wound closure.

Conflict of interest

None.

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Effect of diosmin and diosmetin on the level of pro-inflammatory factors in the endothelium artificially induced with inflammatory stimuli

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Abstract

Introduction: *Diosmin and its aglycone diosmetin are phlebotropic drugs used in the treatment of chronic venous insufficiency (CVI). Diosmin increases the elasticity and tension of blood vessel walls, exhibits an antiedematous effect, and acts as an anti-inflammatory agent. As it is commonly known that the endothelium layer plays a significant role in the physiology and pathophysiology of the cardiovascular system, this paper investigates the effect of diosmin and diosmetin on modulating the levels of pro-inflammatory factors in an endothelial cell culture (HUVEC) stimulated by lipopolysaccharide (LPS) or phorbol (PMA).*

Material and methods: *A normal human umbilical vein/vascular endothelium cell line HUV-EC-C (HUVEC) was stimulated with lipopolysaccharide (LPS) or phorbol 12-myristate-13-acetate (PMA). Cell viability was assessed using NR and MTT assays. The levels of human IL-1β, IL-6, IL-10, COX-2, and PGE2 were measured using ELISA kits.*

Results: *Depending on the agent used to initiate inflammation, different levels of factors associated with this state were obtained. Diosmetin significantly decreased the levels of pro-inflammatory IL-1β and IL-6 as well as COX-2 in PMA-treated cells. Meanwhile, diosmin did not affect the interleukins but it lowered COX-2 and increased PGE-2. Upon the LPS stimulation of HUVEC cells, diosmetin increased the levels of PGE2, IL-1β, COX-2, and nitric oxide (NO), while diosmin increased NO and IL-6.*

Conclusions: *Diosmin and diosmetin have different impacts on the levels of pro-inflammatory factors depending on the inflammation inducer. Diosmetin more effectively modulated inflammation than diosmin, suggesting that the attachment of the sugar moiety to the aglycone attenuates its activity.*

Keywords: diosmin; diosmetin; lipopolysaccharide; phorbol 12-myristate 13-acetate; endothelial cells

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Introduction

Diosmin (5,7,3-trihydroxy-4'-methoxyflavone 7-rutinoside) and its aglycone — diosmetin belong to polyphenols with a confirmed wide range of biological activities [1–3]; however the impact of these flavonoids, especially diosmin, on the cardiovascular system has the greatest significance in medicine. In vivo studies evidenced that diosmin shows a strong protective effect on blood vessels via an increase in the elasticity and tension of blood vessel walls and a reduction of venous pressure and venous stasis in the lower limb. It is also shown to be active in facilitating lymph flow in the lymphatic system and reduces the permeability of capillary walls and thus has an anti-edematous effect [4, 5]. Moreover, it alleviates oxidative stress linked with the inflammation process [6, 7]. For these reasons, diosmin is widely used to support the treatment of Chronic Venous Disease (CVD). CVD is a functional and morphological abnormality of the venous system and it is manifested by skin lesions, swollen legs, and structural changes in the vein wall, such as varicose veins and venous leg ulcers which considerably decrease the quality of life [5, 8].

The role of the endothelium layer in the physiology and pathophysiology of the cardiovascular system is still a subject of interest [9, 10]. It is known that a properly functioning endothelium layer in normal conditions not only constitutes an anticoagulant layer, but also maintains the local balance between pro- and anti-inflammatory factors. Dysfunctions of this layer, e.g. inappropriate activation or over-activation, can lead to local changes in the stability and functionality of this barrier and, consequently, not only to disturbances in homeostasis in the vessels themselves but also to multiple organ failure. Initiation of endothelial inflammation is a known factor contributing to the development of e.g. atherosclerosis [11] since endothelial cells function both as target and effector cells during inflammation [12]. Besides significant pathological changes in the expression of adhesive molecules such as VCAM-1 or ICAM-1, subendothelial retention of lipoproteins also changes the recruitment of specific blood cells and adhesion to endothelial cell membranes. Moreover, microenvironmetal changes in the production of specific pro-inflammatory cytokines like IL-10 or IL-1β as well as compounds or intermediary factors of the arachidonic pathway (COX-2, PGE2, or NO) are also observed [13]. These all factors released by endothelial cells after induction with various stimuli can both be a process of defense of the blood vessel epithelium or lead to its clinically manifested dysfunction [12]. The regulating and balance-keeping factors released by endothelial cells have been quite well studied; however, factors directly controlling systemic endothelial inflammation are still in the discovery phase [14]. Analysis of the level of inflammatory factors released by endothelial cells in the presence of diosmin or diosmetin may therefore help to indicate a target for potential control or modulation of inflammation and the unfavorable phenomena occurring in blood vessels. Therefore, the aim of the present paper was to investigate the influence of popular phlebotonics diosmin and diosmetin on the modulation/regulation of artificially induced inflammation in a human endothelial cell culture model. Bacterial lipopolysaccharide (LPS) or phorbol ester (PMA) were used as a stimuli to induce inflammation.

Material and methods

Cell line

A normal human umbilical vein/vascular endothelium cell line HUV-EC-C (HUVEC) (ATCC® CRL-1730™) was used in this study. The cells were cultured as monolayers in 25 cm^2 culture flasks (NuncTM, Roskilde, Denmark) coated with PureColTM ultrapure collagen type I (INAMED Biomaterials, Fremont, CA, USA) at a 3.1 mg/ml concentration (about 12 $\mu g/cm^2$). The cell line was maintained in CS-C medium (Sigma) supplemented with 75 μg/ml of endothelial cell growth factor (ECGF) (Sigma, St Louis, MO, USA) and antibiotics (100 U/ml penicillin, 100 μg/ml streptomycin (Sigma) at 37°C in a humidified atmosphere with 5% CO_2.

Experimental design

The cells were cultured in 24-well (for ELISA, nitric oxide level, and staining) or 96-well (viability) plates (NuncTM). The cells were seeded on the well bottom at a density of 1×10^5 cells/ml. After 24 h of inoculation, the medium was renewed, and the cells were stimulated with lipopolysaccharide (LPS) from Escherichia coli serotype 0111:B4 (Sigma) (10 μg/ml for 2 h) or phorbol 12-myristate-13-acetate (PMA) (Sigma) (1 μg/ml for 30 min). The concentrations were selected based on literature data and our previous experiments. After cell stimulation, the medium was renewed, and diosmin (5 μM) or diosmetin (5 μM) (for ELISA, staining, and NO analysis) or the compounds in the range of 0–100 μM (for toxicity tests) were added. Then, the culture was conducted for a further 24h. After that time, culture supernatants were collected and analyzed for the levels of cytokines (IL-1β, IL-6), serine protease (uPA), and its receptor (uPAR). In turn, MMP activity was determined in the supernatants from the well bottom and inserts for comparison.

Both diosmin and diosmetin stock solutions were prepared by solubilization in a mixture of DMSO/culture medium (1:1). The stock solution concentration was

10 mM. At the highest working concentration of both compounds used in the research (100 μM), the DMSO concentration did not exceed 0.5%. In our previous papers, we showed no toxicity and no interference of this DMSO amount with the results.

Neutral Red (NR) uptake assay

The cells were grown in 96-well multiplates for 24 h in 100 μl of CS-C culture medium with the supplements and diosmin (5 μM) or diosmetin (5 μM). Subsequently, the medium was discarded and 0.4% NR (Sigma) solution medium was added to each well. The plate was incubated for 3 h at 37°C in a humidified 5% CO_2/95% air incubator. After incubation, the dye-containing medium was removed, the cells fixed with 1% $CaCl_2$ in 4% paraformaldehyde, and the incorporated dye was solubilized using 1% acetic acetate in a 50% ethanol solution (100 μl). The plates were gently shaken for 20 min at room temperature, and the extracted dye absorbance was measured spectrophotometrically at 540 nm using an E-max Microplate Reader (Molecular Devices Corporation, Menlo Park, CA, USA).

MTT assay

Cell viability after incubation with diosmin or diosmetin was determined in a standard spectrophotometric 3-(4,5-dimethylthiazole-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay. The cells grown in the 96-well multiplates in 100 μl of culture medium were incubated for 24h with the flavonoids. After that time, an MTT solution (5 mg/ml, 25 μl/well) (Sigma) was added, and further incubation was conducted for the next 3 h. The yellow tetrazolium salt was metabolized by viable cells to purple formazan crystals. The reaction was catalyzed by mitochondrial succinyl dehydrogenase. The crystals were solubilized overnight in a 10% sodium dodecyl sulfate (SDS) in a 0.01M HCl mixture. The product was quantified spectrophotometrically by absorbance measurement at 570 nm wavelength using an E-max Microplate Reader (Molecular Devices Corporation, Menlo Park, CA, USA).

Nitric oxide (NO) measurement

Nitrate, i.e., a stable end product of NO, was determined in the culture supernatants with a spectrophotometric method based on the Griess reaction. Briefly, the cells were induced with LPS or PMA and incubated for 24 h with diosmin or diosmetin. Thereafter, 100 μl of the supernatant was plated in 96-well flat-bottomed plates in triplicate and incubated with 100 μl of Griess reagent (1% sulphanilamide/0.1% N-(1-naphthyl)ethylenediamine dihydrochloride) (Sigma) in 3% H_3PO_4 (POCH Gliwice, Poland) at room temperature for 10 min. The optical density was measured at 550 nm using a microplate reader (Molecular Devices Corp., Emax, Menlo Park, CA, USA). A standard curve was achieved using 0.5–25 μM sodium nitrite ($NaNO_2$) for calibration.

May-Grünwald-Giemsa (MGG) staining

The MGG staining performed in this study facilitates only visualization of morphological changes in cells induced by the culture conditions. The cells at a density of 1×10^5 cells/ml were cultured in Petri dishes (35 mm). After treatment with LPS or PMA, the medium was changed, and the cells were incubated with diosmin or diosmetin for 24 h. After incubation, the cells were fixed with methanol for 5 min and stained with the May-Grünwald dye diluted in an equal volume of water for 2 minutes. Thereafter, the dye was removed and the Giemsa stain, previously diluted (1 vol. Giemsa: 19 vol. water), was added for 20 min. The dishes were rinsed three times with distilled water and dried. The observation was performed under a light microscope (Olympus BX51, Tokyo, Japan).

ELISA assay

The levels of human IL-1β, IL-6, IL-10, COX-2, and PGE2 (Elabscience, Houston, TX, USA) were measured immunoenzymatically (ELISA) using commercially available kits according to the manufacturer's instructions. Briefly, 100 μl of samples were added to appropriate plate wells. After incubation (2 h) and a series of washing, enzyme-conjugated secondary antibodies (100 μl) were added to the wells and incubated for 1 h. After washing, detection was performed by adding 100 μl of the enzyme-substrate to the wells. After 30 min of incubation, the color reaction was stopped by adding 2M H_2SO_4 to each well. The optical density of the end product was determined using a microplate reader (Molecular Devices Corp., Emax) at 450 nm. The concentrations of the cytokines in the analyzed samples of supernatant were calculated on the basis of a standard curve. The detection limit was 4.69 pg/ml (IL-1β, IL-6 and IL-10), 0.19 ng/ml (COX-2), and 18.75 pg/ml (PGE2).

Statistical analysis

The results are presented as means ± SD of three independent experiments ($n = 3$). The data were analyzed using a one-way analysis of variance ANOVA followed by Dunnett's multiple comparison post-hoc test. Differences were considered significant at $p \leq 0.05$.

Results and Discussion

Diosmin has long been widely used for the treatment of CVD because it relieves the symptoms, improves the

quality of patient's life, and is well tolerated [15]. It has already been shown that this polyphenol may exhibit anti-inflammatory properties by modulation of the local level of soluble factors (cytokines, chemokines), thus inducing the development of e.g. inflammation in tissue [16–18]. In our research, we artificially induced inflammation in umbilical vein endothelial cells (HUVEC) to estimate changes in the level of basic inflammatory factors after diosmin/diosmetin treatment.

The initial investigation involving the determination of the direct biological activity of diosmin and diosmetin on human umbilical vein cells (HUVEC) was based on toxicological analyses. The effect of these factors on cellular metabolism was checked with the MTT method (Fig. 1) and the stability of cell membranes was checked using the Neutral Red (NR) uptake assay (Fig. 2).

It was shown that diosmin at a concentration above 10 μM reduced the metabolic activity of the cells by 9% in comparison to the untreated control, while diosmetin had an opposite effect and, from the concentration of 10 μM, stimulated the metabolic activity in the cells by 8.5%, compared to the untreated control. In turn, both substances at a concentration exceeding 10 μM disturbed the stability of cell membranes and reduced the viability of the cells in the culture by more than 15% at the concentration of 100 μM, compared to the untreated control.

The detailed microscopic observation of the morphology of epithelial cells after MGG staining (Fig. 3) showed that diosmetin at 5 μM induced no significant morphological changes relative to the untreated cells in the control conditions; however, treatment of the control cells with diosmin caused slight cytoplasm contraction and separation of the cells from each other.

Although some adverse effects of diosmin at 5 μM were observed on cell morphology, we decided to continue the investigation with this concentration. Preliminary experiments showed the lower concentration was not effective and the differences between control and cells treated with diosmin/diosmetin were hard to estimate.

To assess the anti-inflammatory activity of investigated compounds, inflammation in endothelial cells was induced using LPS and PMA LPS is known to initiate the inflammatory signaling pathway by activation of the NF-κB factor. This takes place through phosphorylation and subsequent degradation of IκB-α. Consequently, the active form of NF-κB is released from this complex. The active form of NF-κB regulates gene transcription of nitric oxide synthase (NOS), COX-2, or selected pro-inflammatory cytokines [19]. In turn, PMA is an important factor activating protein kinase C (PKC). PKC controls the function of other proteins by phosphorylation of the serine and threonine hydroxyl groups

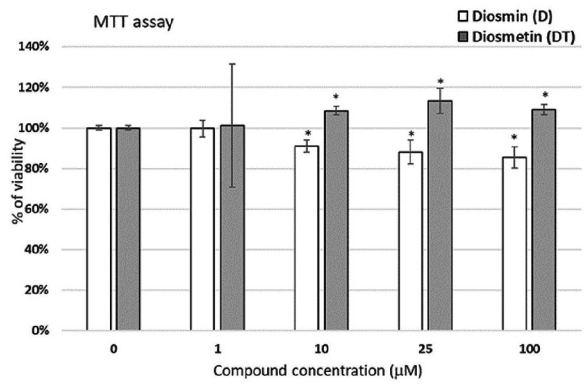

Figure 1. Cell metabolic activity determined by means of the MTT assay. The analysis was performed after 24h culture of human umbilical vein endothelial cells (HUVEC) with diosmin or diosmetin (0–100 μM)

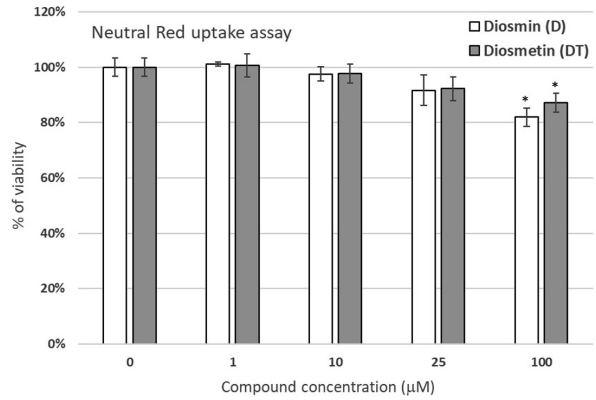

Figure 2. Neutral Red (NR) uptake assay performed after 24h culture of human umbilical vein endothelial cells (HUVEC) with diosmin or diosmetin (0–100 μM)

found in these proteins. Their role is to modulate events within the cell membrane, regulate transcription, or mediate immune response processes. Their impact on the induction of inflammation is therefore different.

The concentration of LPS and PMA, which demonstrated no toxicity in the assumed experimental time interval, was based on our previous studies. As can be seen (Fig. 3) treatment of the cells with LPS did not cause any morphological changes; however, for PMA-treated cells adverse effects including cytoplasm contraction, separation of the cells from each other and vacuolization appeared in single cells were observed.

In the LPS or PMA pre-incubated cells treated with diosmin, further contraction of the cytoplasm and cell separation were visible. Moreover, in the case of the pre-incubation with PMA, vacuolization was pronounced in individual cells. In turn, in the LPS or PMA pre-incubated cells treated with diosmetin sharpening of cell shapes and the appearance of vacuoles in the cells treated with PMA was found.

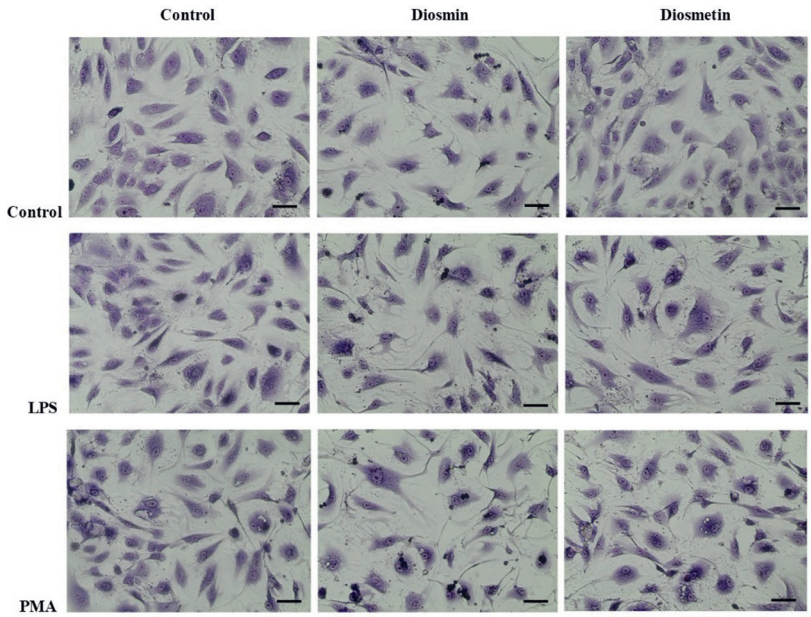

Figure 3. May-Grünwald-Giemsa (MGG) staining of human umbilical vein endothelial cells (HUVEC) incubated with diosmin or diosmetin (5 μM) for 24 h, prior to 2-h pre-treatment with *E. coli* LPS (10 μg/ml) or 30-min treatment with PMA (1 μg/ml). Magnification 200×. Bar = 20 μm

To assess the anti-inflammatory effect of diosmin or diosmetin, the level of IL-1β, IL-6, and IL-10 was monitored in endothelial cell culture pre-treated with LPS or with PMA (Fig. 4).

As can be observed, diosmin/diosmetin induced the production of cytokines but this was not surprising because all exogenous factors disturb cell homeostasis. Moreover, it should be also noted that the up-regulation of IL-1β and IL-6 was accompanied by an increase of IL-10; therefore, the balance between pro-inflammatory and anti-inflammatory cytokines has been almost maintained. Such an increased level of cytokines does not need to be considered as an adverse effect. Inflammation is necessary to initiate local adaptive immunity in endothelial cells which may lead to the induction of an epithelial-derived defense reaction that would bring our experimental conditions closer to in vivo reality. It also means that the epithelium was reactive and sensitive to experimental conditions.

The stimulation of inflammation with LPS or PMA resulted in a significant increase in the level of IL-6 (approx. 10-fold and 12-fold, respectively) in comparison to the untreated control and simultaneously, the level of IL-10 was only 3–3.5 — fold higher. No positive effect of diosmin on the level of cytokines in LPS/PMA-induced cells was found and even it slightly increased the production of IL-6. In turn, diosmetin lowered the level of IL-6 (approx. 2-fold) and slightly lowered IL-10 in PMA-induced cells and therefore, the balance between these factors was improved. Diosmetin did not affect the level of these interleukins in the cells pre-incubated with LPS; however, it significantly induced IL-1β.

The influence of diosmin on interleukins was also reported by Ali et al., who showed that diosmin treatment significantly reduced plasma concentrations of IL-1β and IL-6 in diabetic rats [17]. A similar effect was described by Carballo-Villalobos et al. [18].

In the further part of our study, the influence of diosmin/diosmetin on cyclooxygenase 2 (COX-2) and the other markers of inflammation including prostaglandin E2 (PGE2) and NO in cells with induced inflammation were investigated. Cyclooxygenases (COXs) are intracellular enzymes that catalyze the conversion of arachidonic acid to various forms of prostaglandins (PGs), thromboxanes, and hydroxyeicosatetraenoic acids. Various mitogens may induce inflammation mediated by COX-2 and then changes in COX-2 activity are closely related to PGE2 and NO levels. COX-2 is considered to be linked with a lot of symptoms in CVD including inflammation, pain, increased angiogenesis, and vascular permeability [9, 10].

As can be seen in Figure 5, in the control conditions, diosmin and diosmetin did not significantly change the level of COX-2 produced by the HUVEC cells. On the other hand, both compounds lowered the level of COX-2 in PMA pre-treated cells in a significant manner. In these conditions, diosmetin showed higher inhibitory activity than diosmin. In LPS-stimulated cells, no effect for diosmin was noted, meanwhile diosme-

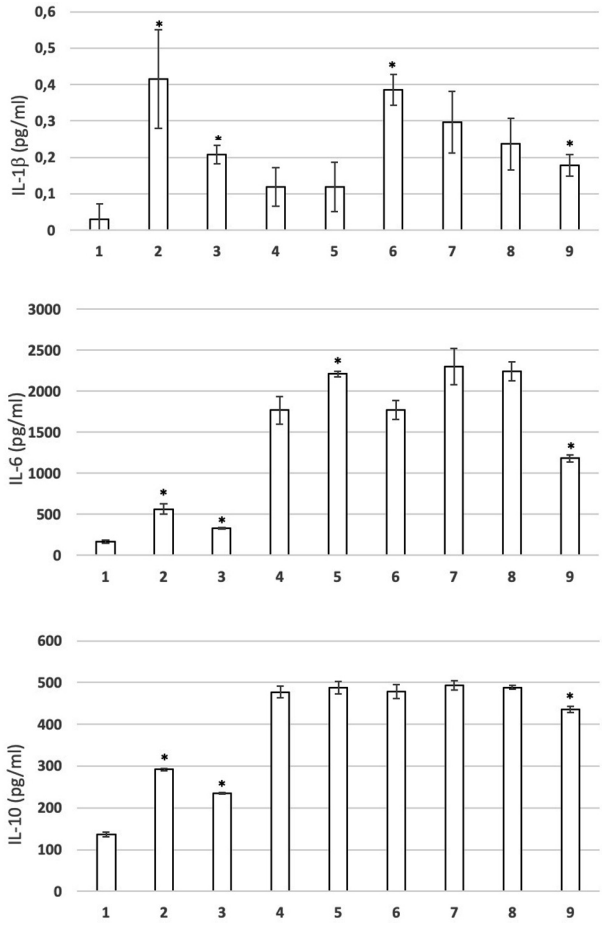

Figure 4. Effect of diosmin or diosmetin (5 μM) on interleukin level (A- IL-1β, B- IL-6, C-IL-10) in endothelial cells (HUVEC) pre-incubated with lipopolysaccharide (LPS) or phorbol 12-myristate-13-acetate (PMA). 1–3: Control, Value after cell treatment with diosmin, Value after cell treatment with diosmetin; 4–6: similarly to 1–3 but the cells were pre-incubated with LPS; 7–9: similar to 1–3 but the cells were pre-incubated with PMA. The data are mean ± SD (n = 3). One-way analysis of variance ANOVA followed by Dunnett's multiple comparison post-hoc tests.; *p-value of ≤ 0.05 vs. the respective control was considered significant

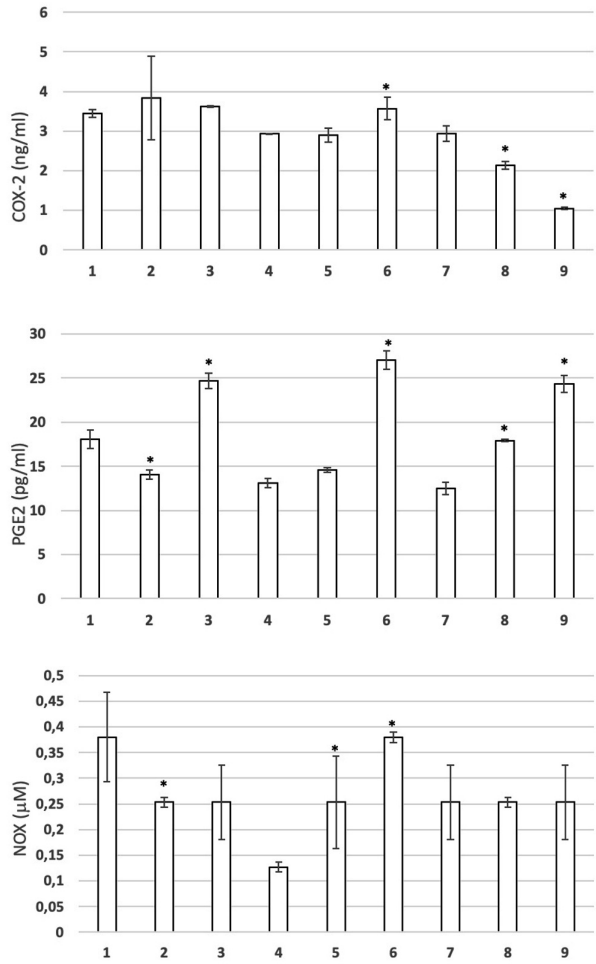

Figure 5. Effect of diosmin or diosmetin (5 μM) on COX-2, PGE2, and NO release by endothelial cells (HUVEC) pre-incubated with lipopolysaccharide (LPS) (10 μg/ml for 2 h) or phorbol 12-myristate-13-acetate (PMA) (1 μg/ml for 30 min). 1–3: Control, Value after cell treatment with diosmin (5 μM), Value after cell treatment with diosmetin (5 μM); 4–6: similarly, to 1–3 but the cells were pre-incubated with LPS; 7–9: similar to 1–3 but the cells were pre-incubated with PMA. The data are mean ± SD (n = 3). One-way analysis of variance ANOVA followed by Dunnett's multiple comparison post-hoc test.; *p-value of ≤ 0.05 vs. the respective control was considered significant

tin stimulated slightly the release of this enzyme. It should be observed that the PMA, LPS, and diosmin reduced the level of PGE2 in relation to control. In contrast, diosmetin turned out to be a potent inducer of PGE2, both in cells with as well as without induced inflammation. A moderate increase of PGE2 was also observed in PMA-induced cells after diosmin treatment. The decrease of NO was observed for all investigated conditions compared to the control, with the exception of LPS cells treated with diosmetin, where NO was on the same level as in HUVEC cells. LPS lowered NO the most effectively and surprisingly diosmin and diosmetin increased NO levels in LPS-induced cells.

Our study confirmed the results reported by Berkoz et al., who found that diosmin decreased NO and PGE2 production through inhibition of the expression of phosphorylated-ERK, p38, and p-IκB-α [19].

To sum up, the influence of diosmin/diosmetin on changes of investigated factors in cells with induced inflammation varied depending on the inducer; however, it seems that aglycone form more effectively modulates the inflammation. It significantly decreased the level of pro-inflammatory IL-1β and IL-6 as well as COX-2 in PMA-treated cells. Meanwhile, diosmin did not affect the interleukins but it lowered COX-2.

Interestingly, we found that decreases in COX-2 were accompanied by increases in PGE2 and it suggested the production of PEG2 in such conditions maybe connected with COX-1 activity. It is in line with the literature data. In vitro studies proved that diosmetin stimulated PGE2 via COX-1 more effectively than via COX-2 [20].

Our investigation showed the activity of both tested flavonoids varies depending on the presence or absence of inflammation as well as the inflammatory stimuli and it may depend not only on typical already known pathways but also on other factors of signal transducers differently expressed in different experimental conditions. The study confirmed the conclusions formulated by Lopez-Posadas et al., who stated, that the activity of flavonoids strongly depends on experimental conditions. Depending on the agent used to initiate inflammation, different levels of factors associated with this state were obtained [21].

Conflict of interest

None.

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Serum level of αII-spectrin breakdown products (SBDPs) as a potential marker of brain ischemia--reperfusion injury after carotid endarterectomy

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Abstract

Introduction: *Stroke remains one of the main causes of morbidity and mortality worldwide. Carotid endarterectomy (CEA) reduces the incidence of ischemic stroke or death in patients with symptomatic carotid artery stenosis more effectively than pharmacological therapy alone. SBDPs (spectrin breakdown products): SBDP120, SBDP145, and SBDP150 are the product of proteolysis of αII-spectrin (280 kDa) — an important structural component of the neuronal cytoskeleton, particularly present in axons. Increased serum level of SBDPs was previously observed in traumatic brain injury, subarachnoid hemorrhage (SAH), or brain ischemia.*

Material and methods: *The aim of our study was to investigate changes in serum levels of SBDP120 and SBDP145 in patients undergoing uncomplicated CEA. The study included 22 patients with severe carotid artery stenosis, qualified for CEA. Blood samples were taken from the antecubital vein at three different intervals (24 h before CEA, 12 and 48 h after surgery). SBDP's serum levels were measured by a commercially available enzyme-linked immunosorbent assay (ELISA).*

Results: *The study showed that serum SBDP120 levels were significantly decreased 48 h after CEA when compared to the level before the surgery. SBDP145 levels were significantly decreased 12 h after the procedure and then remained at a similar level 48 h after CEA.*

Conclusions: *In patients with high-grade carotid artery stenosis SBDP120 and SBDP145 serum level decreases after an uncomplicated CEA, therefore alterations from this curve may be a marker of neurological complications after the procedure. Higher SBDP levels before the procedure may represent brain damage caused by chronic ischemia.*

Keywords: carotid endarterectomy; carotid artery stenosis; stroke; αII-spectrin breakdown products

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Introduction

Stroke remains one of the main causes of morbidity and mortality worldwide, being an important concern of global public health [1]. The definition of a stroke, developed by the World Health Organization (WHO) is a, rapidly developing clinical signs of focal disturbance of cerebral function lasting more than 24 hours with no apparent cause other than of vascular origin" [2]. Ischemic stroke is a more common type than hemorrhagic stroke, and accounts for over 85% of all strokes [3]. The etiology of ischemic stroke (IS) includes atherothrombotic stroke, embolic stroke, cerebral hypoperfusion, and venous thrombosis, with atherothrombotic occlusion of the carotid artery being a major contributor to IS or transient ischemic attack (TIA) [4].

Carotid endarterectomy (CEA) is a surgical procedure, that reduces the incidence of IS or death in patients with severe (≥ 70 to 99% of stenosis), symptomatic (IS, TIA, or retinal TIA) carotid artery stenosis more effective than the pharmacological therapy alone [5–8]. However, this method is not completely free of complications in the perioperative period, and this may include: micro and macro embolism resulting in brain ischemia or ischemia-reperfusion injury and brain edema, caused by clamping and declamping of the internal carotid artery (ICA) during the CEA [9–12].

αII-spectrin (280 kDa) is an important structural component of the neuronal cytoskeleton, particularly present in axons. It plays a crucial role in neuronal integrity. Calpain and caspase-3 are proteolytic enzymes (proteases), which are involved in oncotic necrosis and apoptotic cell death. After injury, αII-spectrin can become a substrate for both enzymes, producing different SBDPs (spectrin breakdown products): SBDP 120, SBDP145, and SBDP150, that have been studied as biomarkers of axonal damage [13–15]. According to previous experimental studies, SBDP 145 and SBDP150 are mainly produced by calpain proteases, and SBDP120 is the product of caspase-3 [14]. SBDPs have been previously found to correlate with the severity of the brain damage after traumatic brain injury (TBI) determined by the GCS score, computed tomography (CT) infarct volume, and 6-month outcome, therefore it may be a potential marker of the severity of brain injury after TBI [16–20].

Spectrin breakdown products were also investigated in patients with aneurysmal subarachnoid hemorrhage (aSAH), relative to development of vasospasm. Serum concentrations of SBDPs were increased before the clinical detection of vasospasm and decreased to baseline after successful treatment [21–24].

In rats, an experimental ischemia, caused by the occlusion of the middle cerebral artery, lead to a strong increase in a level of SBDP120 and SBDP145 six hours after the occlusion in brain tissue and in cerebrospinal fluid (SBDP145), but not in the serum [25].

The advantage of SBDPs as brain damage monitoring biomarkers is the potential to investigate both calpain and caspase-3 activity; SBDP120 is a sensitive marker of caspase-3 activation connected to apoptotic cell death, while SBDP145 and SBDP150 measure a calpain activation associated with oncotic cell death and less with the apoptotic cell death [13, 18].

Material and methods

The patients were admitted to the Department of Vascular Surgery and Angiology of Medical University in Lublin, Poland, and were scheduled to undergo CEA due to internal carotid artery stenosis. The inclusion criteria were: carotid artery stenosis > 50% in symptomatic patients (symptoms of stroke/TIA < 6 months before), or > 60% in asymptomatic patients with at least 1 feature suggesting higher stroke risk on best medical therapy (BMT). The exclusion criteria were: inability to give informed consent, complete occlusion of the internal carotid artery, intracranial artery lesion more significant than the proximal carotid lesion, brain damage in the course of other nervous system diseases, prior ipsilateral CEA, history of disabling stroke (modified Rankin score ≥ 3), active inflammation and expected survival time < 5 years. The study involved 22 patients aged from 57 to 82 with a mean age of 71.36 (standard deviation = 6.51) years. The degree of internal carotid artery stenosis ranged from 70 to 90%. A Neurological examination was performed by a neurologist prior to and after CEA. In this neurological examination, there were no deviations from the normal state in all patients included in the study. Conventional CEA was performed under local anesthesia without the use of a shunt. CEA was performed through a longitudinal arteriotomy, running from the carotid bifurcation to the anterolateral surface of the internal carotid artery (ICA). The carotid artery was clamped, and the arteriotomy was closed with primary sutures. No postsurgical complications were observed. Demographic information and pertinent medical history of the patients are summarized in Table 1.

The degree of internal carotid artery stenosis was determined based on a high-resolution USG Doppler examination, performed with a Toshiba Aplio 500 device with a high-frequency (11 MHz) linear probe. The sonographer was a vascular medicine specialist who was unaware of the subject's clinical state.

Table 1. Characteristics of patients

Patient ID	Sex	Age	Location	%	Stroke/TIA	Symptoms	Other diseases
1	M	74	R	90	No	Tinnitus, hypoacusis	None
2	F	68	L	90	No	Tinnitus, dizziness	Diabetes, arterial hypertension, ischemic heart disease
3	M	57	R	70	No	None	Ischemic heart disease
4	M	78	R	80	No	Visual disturbances	Diabetes, arterial hypertension
5	M	74	L	90	No	Tinnitus, dizziness	Diabetes, arterial hypertension, ischemic heart disease
6	F	67	R	90	Stroke	Dizziness	Diabetes, arterial hypertension
7	M	67	L	90	Stroke	Hemiparesis	Diabetes, arterial hypertension
8	F	79	L	80	No	None	Arterial hypertension
9	M	78	R	90	Stroke	Hemiparesis	Arterial hypertension
10	F	63	L	90	No	Tremor	Diabetes, arterial hypertension
11	M	63	L	80	No	None	Arterial hypertension, ischemic heart disease
12	M	74	R	90	Stroke	None	Arterial hypertension
13	M	63	L	90	Stroke	Hemiparesis	Arterial hypertension
14	F	82	L	80	No	Dizziness	Arterial hypertension
15	M	74	L	90	No	None	Diabetes, arterial hypertension, ischemic heart disease
16	M	76	L	80	Stroke	None	Arterial hypertension
17	M	76	L	85	TIA	None	Diabetes, arterial hypertension, ischemic heart disease
18	F	64	L	90	TIA	None	Diabetes, arterial hypertension
19	F	72	L	70	No	None	Arterial hypertension
20	M	77	L	90	Stroke	Hemiparesis	Arterial hypertension
21	M	67	R	90	Stroke	Hemiparesis	Diabetes, arterial hypertension
22	M	77	L	80	No	Dizziness, visual disturbances	Arterial hypertension

ID — identification, M — male, F — female, TIA — transient ischemic attack, L — left, R — right

Based on Doppler studies, patients were qualified for the CEA procedure as determined by the guidelines set forth by the European Society of Vascular Surgery. Patients with severe carotid artery stenosis were identified using criteria established by NASCET (North American Symptomatic Carotid Endarterectomy Trial) according to the following formula: % ICA stenosis = (1-[narrowest ICA diameter/diameter normal distal cervical ICA]) × 100 [8].

Serum samples were taken from the antecubital vein of patients at three different times: within 24 hours preoperatively to CEA, 12 h postoperatively, and 48 hours postoperatively.

Serum for specific protein analysis was obtained by centrifugation of whole blood at 3000 rpm (603 × g) for 15 min in a laboratory centrifuge (MPW-350R; MPW Medical Instruments, Warsaw, Poland) at a temperature of 4°C and stored in –80°C prior analyses. Plasma without signs of hemolysis was analyzed using a quantitative sandwich enzyme-linked immunosorbent assay (ELISA) technique. The protocols were adapted from a commercially developed assay manufactured by Bioassay Technology Laboratory (BT Lab, Zhejiang, China). The concentrations of human alpha II-spectrin breakdown products: SBDP 120 (Cat. No: E3791Hu) and SBDP145 (Cat. No: E4005Hu) were quantified based on the optical density (OD) at 450 nm using the BioTek ELx808™ Absorbance Microplate Reader (BioTek, Winooski, VT, USA). Samples for each participant were diluted to fit the range of the standard curve and run in duplicate on the same plate. Briefly, the plates have been pre-coated with a human antibody, specific for each analyzed protein. A specific biotinylated antibody was added to sample each well. Then, streptavidin-HRP was added to the sample and standard wells. After incubation, the plates were washed with washing buffer

Table 2. Serum levels of SBDP120 and a comparative analysis

	N	SBDP 120 level [ng/ml]				p
		Mean	Median	SD	SE	
Before	20	122.138	125.696	53.402	11.941	p = 0.0267
12 h after	22	114.720	116.150	51.367	10.951	
48 h after	22	91.812	85.156	39.980	8.523	
Difference				Significance		
Before — 12h after				p = 0.3212		
Before — 48h after				p = 0.0146*		
12h after — 48h after				p = 0.0546		

SE — standard error; SD — standard deviation, N — number of patients; *statistically significant

5× with an automatic plate washer. Substrate solutions were added and once again the plates were incubated. The reaction was terminated by the addition of a stop solution. The concentration of protein levels in samples was calculated based on the standard curves using the average of the duplicate values.

The distribution of the collected data was evaluated using the Shapiro-Wilk's test, showing normal distribution for SBDP120, and not normal for SBDP145. Furthermore, data on the SBDP120 levels were analyzed using one-way repeated measures ANOVA test with post hoc t-test using Bonferroni correction. For the SBDP145 non-parametric methods: one-way repeated measures ANOVA Friedman, and Wilcoxon tests were used to determine differences between the variables.

Correlation analysis was performed using the Spearman rank correlation.

The SBDP120 and SBDP145 values were expressed in ng/ml, and. The values of $p < 0.05$ were considered significant.

The study was approved by the Ethics Committee of the Lublin Medical University (KE-0254/82/2021) (29.04.2021).

Results

The repeated measures ANOVA test showed that a sampling time significantly ($p < 0.05$) affected serum SBDP120 levels; $F(2, 38) = 3.99$, $p = 0.027$. Serum SBDP120 concentrations in patients and a comparative analysis are presented in Table 2.

The post-hoc paired t-test using a Bonferroni corrected $\alpha = 0.0166$ (0.05/3) indicated that the SBDP120 level was statistically significantly decreased 48 h after CEA as compared with the levels measured prior to surgery ($p < 0.0166$, Fig. 1). However, the difference in serum SBDP120 levels prior to surgery 12 h after CEA, and 12 h after CEA compared to 48 h after the procedure was not statistically significant ($p > 0.0166$).

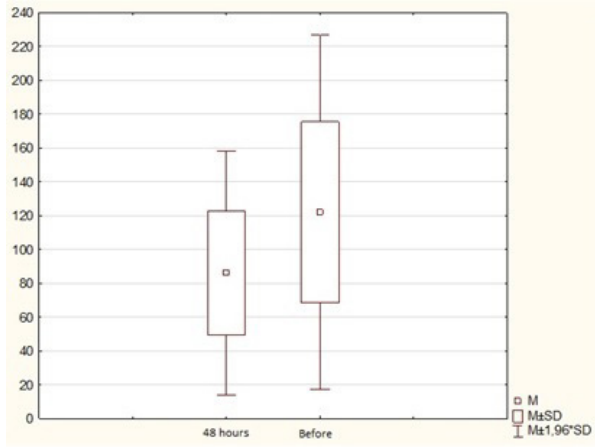

Figure 1. SBDP120 levels in patients before and 48 h after the procedure, Bonferroni $p = 0.0146$* (M — mean; SD — standard deviation); *statistically significant

There was no difference in serum SBDP-120 concentrations in three measurements between males and females ($p > 0.05$). The difference in serum SBDP-120 concentrations between younger (<69 years) and older (> 69 years) patients in the three measurements was not significant ($p > 0.05$).

SBDP145 serum concentration also decreased 12 h after the CEA surgery compared to the preoperative period, and then after 48 h did not significantly change compared to the level 12 h after the procedure. Serum SBDP145 concentrations in patients and a comparative analysis are presented in Table 3.

The repeated measures ANOVA test showed that a sampling time significantly ($p < 0.05$) affected serum SBDP145 levels; $p = 0.00783$.

The post-hoc paired Wilcoxon test indicated that the SBDP145 level was statistically significantly decreased 12 h after CEA as compared with the levels measured prior to surgery ($p < 0.0072$, Fig. 2). However,

Table 3. Serum levels of SBDP145 and a comparative analysis.

	N	SBDP 145 level [ng/ml]				p
		Mean	Median	SD	SE	
Before	21	9.110	7.370	4.009	0.875	p = 0.0078
12 h after	21	8.451	6.770	4.673	1.019	
48 h after	22	8.444	7.665	3.882	0.828	
Difference				Significance		
Before — 12h after				p = 0.00719*		
Before — 48h after				p = 0.130546		
12h after — 48h after				p = 0.614272		

SE — standard error; SD — standard deviation, N — number of patients; *statistically significant

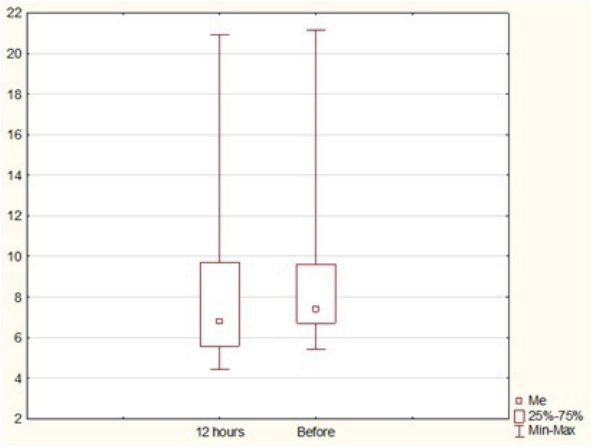

Figure 2. SBDP145 levels in patients before and 12 h after the procedure, p = 0.0146* (Me — median); *statistically significant

the difference in serum SBDP145 levels prior to surgery 48 h after CEA (p = 0.130546), and 48 h after CEA compared to 12 h after the procedure (p = 0.614272) was not statistically significant.

Moreover, there was no difference in serum SBDP-145 concentrations in three measurements between males and females (p > 0.05). The difference in serum SBDP-145 concentrations between younger (< 69 years) and older (> 69 years) patients in three measurements was not significant (p > 0.05).

Discussion

αII-spectrin breakdown products are the molecules, that were previously investigated as potential biomarkers of brain damage in numerous neurological pathologies such as traumatic brain injury (TBI), subarachnoid hemorrhage and ischemic stroke (in rats), or in Alzheimer's disease. However, up to now, it has not been studied in a perioperative period of carotid endarterectomy. Therefore, our study is the first to reveal, that SBDP120 and SBDP145 serum levels decrease after an uncomplicated CEA.

Preclinical studies, on the animal rat model, conducted by Pike et al. (2004), and Ringger et al. (2002) provided the first evidence, that SBDPs can be detected in CSF after ischemic-reperfusion brain injury and traumatic brain injury, and therefore can be used as biochemical markers in a rodent model of transient focal stroke in rats [26, 27].

Farkas et al. (2005), investigated a group of 12 TBI patients with raised intercranial pressure and found that SBDP levels were elevated, compared to the controls, concluding they can be useful in the clinical monitoring of patients with TBI [28].

Early in 2006, Cardali et al. held a prospective, case-controlled study, including 8 patients with severe TBI in which SBDP levels were measured in a CSF at 6, 12, 24, 48, 72, and 96 h following the injury. Authors found, that in TBI patients SBDP levels were significantly increased compared to control patients at all time points examined and that in patients with worse outcomes SBDP's levels remained elevated or failed to decline. The study provided the first evidence, that SBDPs could be a reliable marker of severe TBI in humans [29].

Later, Pineda et al. (2007), examined levels of SBDPs in cerebrospinal fluid (CSF) from adults with severe TBI and the relationship between these levels, severity of injury, and clinical outcome in a group of 41 patients with severe TBI, defined by a Glasgow Coma Scale (GCS) score of < or = 8. SBDP level was measured at 6, 12, 24, 48, 72, 96, and 120 h following TBI and analyzed for SBDPs. The authors concluded, that SBDP levels in CSF were significantly increased in TBI patients at several time points after injury, compared to control subjects. The time course of calpain-mediated SBDP150 and SBDP145 differed from that of caspase-3-mediated SBDP120 during the post-injury period examined. Mean SBDP values measured early after injury correlated with the severity of injury, computed tomography (CT) scan findings, and outcome at 6 months post-injury [30].

Brophy et al (2009), investigated a group of 38 patients with severe TBI, finding a positive correlation between patients with longer elevations in intercranial pressure, and the level of SBDP120, SBDP 145, and SBDP150, and was the first attempt to describe CSF exposure and kinetic characteristics of SBDPs after severe TBI. Authors observed evidence of a greater production of calpain-mediated biomarkers (SBDP145, SBDP150), than caspase–3–mediated biomarkers (SBDP120) in the acute phase following severe TBI [18].

Mondello et al (2010) found that levels of SBDP120 were significantly higher in older patients than in younger patients, suggesting increased apoptotic processes in elderly people. Moreover, the study showed that CSF SBDP levels can predict injury severity and mortality after severe TBI, and can be useful complements to clinical assessment [31].

After that, a couple of other studies confirmed the diagnostic and prognostic utility of SBDPs in TBI [20, 32–34].

In 2023 a meta-analysis held by Liu et al, including 10 studies and 417 participants, confirmed, that SBDPs can be useful biomarkers for the diagnosis and prognosis of TBI [35].

SBDPs were also investigated, as a potential marker of aneurysmal subarachnoid hemorrhage (aSAH), in a group of 40 patients (20 with aSAH, and 20 controls), by Papa et al. (2018). The study revealed that SBDPs could serve as an indicator of aSAH, and are associated with the severity of hemorrhage and early mortality [24].

Similar results were obtained by Lewis et al (2007), who concluded that SBDP levels were significantly increased in patients with aSAH, and increased significantly over baseline level up to 12 hours before the onset of cerebral arterial vasospasm. Moreover, differential expression of SBDPs suggests oncotic necrotic proteolysis may be predominant in acute brain injury after aSAH and cerebral arterial vasospasm [36].

SBDPs have also been investigated as potential indicators of brain damage caused by ischemia in the rat model in some preclinical studies. Zhang et al. [2002], found that the activity of calpains and caspases in the adult rat brain following 10 min of transient forebrain ischemia is increased. Western blots of cortical, striatal, and hippocampal homogenates demonstrated an alpha-spectrin cleavage pattern indicative of predominant calpain activity, with a peak between 24 and 48 h after reperfusion [37]. Pike et al (2004), examined the accumulation of SBDPs in CSF of rodents subjected to 2 hours of transient focal cerebral ischemia produced by occlusion of the middle cerebral artery followed by reperfusion. The study showed that levels of SBDPs (especially SBDP120) were increased in CSF after injury, while were undetectable in the control group [26]. Ren et al (2013), investigated SBDP level in rats with ischemic and hemorrhagic strokes. αII-spectrin breakdown products (SBDP150, SBDP145) were strongly increased after 6h after induced ischemia while remaining on the normal level in hemorrhagic stroke [25].

Spectrin breakdown products were not previously investigated in the perioperative period of carotid endarterectomy. However, there were some other molecules, considered as the brain damage markers, that were previously studied before and after this procedure.

The molecules that have been best recognized under these circumstances are neuron-specific enolase (NSE) and S-100B protein.

Connolly ES Jr et al. (2001) investigated a group of 25 patients who underwent CEA, divided into: injured (those who exhibited significant declines in neuropsychometric test performance), and uninjured patients, finding that injured patients presented significantly higher S100B levels, compared with uninjured patients, at 24, 48, and 72 hours after surgery. There were no significant differences in neuron-specific enolase levels for injured and uninjured patients at any time point [38].

Brightwell et al. investigated NSE and S100B levels in a group of 52 patients with carotid artery stenosis, of whom 28 underwent CEA and 24 carotid artery stenting (CAS). Baseline levels of NSE and S100B were significantly higher compared to the normal population. S-100β increased significantly at 24 hours in patients with a post-operative neurological deficit ($p = 0.015$) and in those with emboli detected by the perioperative trans-cranial Doppler examination. Also, a non-significant trend of transient rise of S-100β levels in the CAS group was observed, while levels in the CEA group appear unchanged. NSE appeared to rise at 48 hours post-operatively in the CEA group and decline in the CAS group, but these differences were also not statistically significant [39].

Rasmussen et al. (2006) measured serum levels of neuron-specific enolase (NSE) and S100B in a group of 22 patients undergoing carotid endarterectomy, pre- and postoperatively (12, 24, 36 and 48 h. after the CEA). In the study group, NSE level was significantly higher before carotid artery surgery and decreased postoperatively, while S100B level did not significantly change. No correlation between the change in cognitive function and the changes in blood levels of either NSE or S-100β protein was found [40]. These results were similar to those obtained in our study, where serum levels of SBDP120 and SBDP145 decreased after the CEA.

The other study, held by Mussack et al on a group of 46 patients with carotid artery stenosis, treated with CEA or CAS, investigated serum levels of S-100B pro-

tein in the perioperative period of CEA and CAS. The authors found that CEA but not CAS caused a transient increase in the S-100B serum levels, which later returned to baseline levels. In addition, prolonged elevation of S-100B serum levels was associated with the development of postoperative neurological deficits [41].

NSE and S100-B were not the only markers, that were studied in the perioperative period of CEA.

Terlecki et al. (2014) held a study on a group of 40 patients undergoing CEA or CAS, investigating perioperative plasma levels of kynurenic acid (KYNA). Baseline plasma KYNA concentrations before the surgery were higher in patients with unstable carotid plaque undergoing CEA than in patients with stable carotid plaque undergoing CEA and patients undergoing CAS. Moreover, KYNA concentration increased during the postoperative period in all studied groups. Higher plasma KYNA concentrations were observed in patients with postoperative neurological disorders [42].

Later, Ilzecki et al. investigated a group of molecules — potential biomarkers of brain damage — in the perioperative period of uncomplicated CEA, in the group of 25 patients. Serum Carnosine Dipeptidase 1 (CNDP1), Ubiquitin C — Terminal Hydrolase L1 (UCHL1), Microtubule-associated protein tau (MAPt) and myelin basic protein (MBP) levels were significantly decreased 12 h after CEA when compared to the level before the surgery, and then normalized 48 h after CEA [43, 44]. Three other molecules: glial fibrillary acidic protein (GFAP), neurofilament light polypeptide (NEFL), and brain lipid-binding protein (FABP7) levels did not statistically significantly change in the perioperative period of CEA [45, 46]. In contrast, the serum level of NSE was statistically significantly increased 48 h after CEA as compared with the levels measured 12 h after surgery and before surgery ($p < 0.05$) [47].

In our study, the level of SBDP120 and SBDP145 statistically significantly decreased after uncomplicated CEA, but the molecules showed different time curves, with SBDP 120 level decreasing gradually with the lowest level 48 hours after CEA, while SBDP145 decreased after 12 hours, and then stayed at the same level 48 hours after CEA. This difference may be explained by the different pathophysiological pathways for both of the molecules, where SBDP 145 is mainly produced by calpain proteases, and SBDP120 is the product of caspase-3.

The results obtained in our study are similar to some of the previous research, in which the serum level of brain damage markers (CNDP1, UCHL1, MAPt, MBP) significantly decreased in uninjured patients, after the uncomplicated CEA. The reason for that may be a normalization of perfusion after an uncomplicated CEA. Higher baseline levels of brain damage markers such as SBDP120 and SBDP145 could be a result of chronic brain ischemia caused by a high-grade internal carotid artery stenosis which could be responsible for the chronic damage of the brain. Therefore, it is reasonable, that when the perfusion normalizes, SBDP's levels fall with time. Similar results obtained by Rasmussem and Brightwell who investigated NSE levels before and after uncomplicated CEA, and Ilzecki, who investigated levels of CNDP1, UCHL1, MAPt, and MBP seem to support this hypothesis. On the other hand, some other brain damage markers levels, like S100B and KYNA appeared to rise after CEA, which may be a result of their higher sensitivity in detecting silent brain ischemia after the CEA, caused by clamping and declamping of the artery, microemboli, ischemia-reperfusion, etc.

The study was conducted on a group of 22 patients, which can be considered as one of the limitations of this research. The other could be a lack of a control group of healthy subjects, or a group of patients with neurological complications after the CEA, however, the aim of the study was to show how SBDPs react in patients undergoing uncomplicated CEA. The studies including patients with neurological complications could be a matter of study in the future.

Conclusions

Higher levels of SBDP and SBDP145 before the CEA may represent brain damage caused by chronic ischemia, which is reduced by successful, uncomplicated CEA.

SBDP 120 and SBDP145 serum levels decrease after an uncomplicated CEA in patients with high-grade carotid artery stenosis therefore alterations from this curve may be a marker of neurological complications after the procedure.

SBDPs may not be enough sensitive markers to detect silent ischemia, caused by CEA (clamping and declamping of the artery, microemboli, ischemia--reperfusion injury).

Up to now, our study is the first to investigate the influence of the uncomplicated CEA on the level of SBDPs, and it presents the data on a characteristic time curve of this molecule in the perioperative period of CEA.

Due to the limitations of our study, there is a need for further investigations on a bigger group of patients, including patients with neurological complications after the CEA, and a control group of healthy subjects.

The knowledge of how different brain damage marker levels are affected by CEA, may in the future lead to the development of a diagnostic panel, useful in detecting neurological complications after the procedure.

Conflict of interest

None.

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Visinin-like protein (VLP-1) as a potential marker of brain damage after carotid endarterectomy — preliminary study

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Abstract

Introduction: *Stroke is the second leading cause of disability and death worldwide. Carotid endarterectomy (CEA) reduces the incidence of ischemic stroke or death in patients with sympatomatic carotid artery stenosis more effectively than pharmacological therapy alone. Visinin-like protein 1 (VLP-1) is a potential marker of brain injury. An increased serum level of VLP-1 was observed in neurodegenerative diseases, ischemic stroke, and traumatic brain injury.*

Material and methods: *The objective of the study was to report the changes in serum level concentrations of VLP-1 in patients undergoing CEA. The study group consisted of 22 patients with severe carotid artery stenosis, qualified to CEA. Serum levels of VLP-1 were measured by an enzyme-linked immunosorbent assay (ELISA) test at 24 h before CEA, 12 and 48 h after the surgery.*

Results: *Serum VLP-1 levels were significantly reduced 48 h after CEA compared to the levels before and 12 h after surgery.*

Conclusions: *VLP-1 serum level decreases after an uncomplicated CEA in patients with high-grade carotid artery stenosis. Alterations in this curve may be a marker of neurological events after the procedure. Higher VLP-1 baseline levels before CEA may reflect brain damage caused by chronic ischemia.*

Key words: carotid endarterectomy; carotid artery stenosis; stroke; visinin-like protein

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Introduction

Stroke is the second leading cause of disability and death worldwide, especially in low-and middle-income countries [1]. The most common etiology of ischemic stroke (IS) is atherothrombotic occlusion of the carotid artery, and the others include embolic stroke, cerebral hypoperfusion, and venous thrombosis [2].

Carotid endarterectomy (CEA) is a surgical procedure that reduces the incidence of IS or death in patients

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with severe (≥ 70 to 99% of stenosis), symptomatic (IS, TIA, or retinal TIA) carotid artery stenosis more effective than pharmacological therapy alone [3–6]. However, this method is not completely free of complications in the perioperative period, and this may include micro and macro embolism resulting in brain ischemia or ischemia-reperfusion injury and brain edema, caused by clamping and declamping of the internal carotid artery (ICA) during the CEA [7–10].

Visinin-like protein 1 (VLP-1) is a neuron-specific molecule from the highly homologous family of neuronal calcium sensor (NCS) proteins [11], which are involved in several calcium-dependent signal transduction processes in neurons [12]. VLP-1 is responsible for multiple roles in normal neuron function, such as regulation of neuronal ion channels, membrane traffic, learning, neuronal growth, and survival, however, it is also a neurotoxic factor under the condition of the disruption of calcium homeostasis caused by stroke [13, 14]. In this case, calcium overload, an increased level of cytosolic Ca2+ concentration in neurons may lead to the involvement of NCS proteins in numerous necrotic and apoptotic pathways in the central nervous system (CNS) [15].

In 2006, Laterza et al. found VLP-1 in the cerebrospinal fluid (CSF) of a rat model of stroke and in the plasma from patients after stroke, suggesting it to be a potential marker of brain injury [16]. Subsequently, the potential to diagnose ischemic stroke using VLP-1 was confirmed in a pilot study conducted by Stejskal et al. [17]. Recently, Li et al. found that an increase in the level of VLP-1 in patients after stroke can serve as an independent predictor of cognitive dysfunction [18]. In 2020 Liu et al. concluded that serum levels of VLP-1 were associated with poor clinical outcomes in stroke patients [14].

Changes in the VLP-1 level can also be observed in neurodegenerative diseases such as Alzheimer's disease (AD) [19]. A recent meta-analysis conducted by Hao in 2021, which contained 51 studies, confirmed that the level of VLP-1 increased in AD, compared to healthy controls, which confirmed that it could be a valuable marker for the diagnosis of AD [20]. The serum level of VLP-1 also increased after an epileptic seizure, suggesting that it may be a useful biomarker for seizure-induced neuronal injury [21]. Down-regulation of VLP-1 has been reported in amyotrophic lateral sclerosis [ALS] [22]. Later, Liebl et al. suggested, that VLP-1 is a redox sensor that integrates Ca2+ homeostasis and the level of oxidative stress within a cell, and that the presence of VLP-1 dimers and aggregates correlates with the progression of motor neuron disease [23].

VLP-1 was also investigated as a possible biomarker of traumatic brain injury. Wu et al. found that VLP-1 may be a suitable biomarker for the identification of sports-related concussion (SRC) [24]. Similar results were obtained by Bradley-Whitman et al. [25], who found that the serum level of ubiquitinated-VLP-1 was significantly elevated after the brain injury in a well-characterized rat unilateral cortical contusion model. In contrast, Shahim et al. did not observe a significant difference in the plasma level of VLP-1 at 1 h after the concussion compared to the pooled baseline preseason levels, in a group of 288 professional ice hockey players [26].

In the light of the above findings, the aim of our study was to investigate changes in serum level of VLP-1 in patients undergoing CEA.

Material and methods

Patients

The study group consisted of patients with internal carotid artery stenosis, scheduled to undergo CEA in the Department of Vascular Surgery and Angiology of Medical University in Lublin, Poland. The study involved 22 patients aged from 57 to 82 with a mean age of 71.36 (standard deviation = 6.51) years. The degree of internal carotid artery stenosis ranged from 70 to 90%. The inclusion criteria were carotid artery stenosis > 50% in symptomatic patients (symptoms of stroke/TIA < 6 months before), or > 60% in asymptomatic patients with at least 1 feature suggesting higher stroke risk on BMT. The exclusion criteria were: inability to give informed consent, complete occlusion of the internal carotid artery, intracranial artery lesion more significant than the proximal carotid lesion, brain damage in the course of other nervous system diseases, prior ipsilateral CEA, history of disabling stroke (modified Rankin score ≥ 3), active inflammation and expected survival time < 5 years. A Neurological examination was performed by a neurologist prior to and after CEA. In this neurological examination, there were no deviations from normal state in all patients included in the study. Conventional CEA was performed under local anesthesia without the use of a shunt. CEA was performed through a longitudinal arteriotomy, running from the carotid bifurcation to the anterolateral surface of the internal carotid artery ICA. The carotid artery was clamped, and the arteriotomy was closed with primary sutures. No postsurgical complications were observed. Demographic information and pertinent medical history of the patients are summarized in Table 1.

The estimation of internal carotid artery stenosis degree

The degree of internal carotid artery stenosis was determined based on a high-resolution USG Doppler examination, performed with a Toshiba Aplio 500 de-

Table 1. Characteristics of patients

Patient ID	Sex	Age	Location	%	Stroke/TIA	Symptoms	Other diseases
1	M	74	R	90	No	Tinnitus, hypoacusis	None
2	F	68	L	90	No	Tinnitus, dizziness	Diabetes, arterial hypertension, ischemic heart disease
3	M	57	R	70	No	None	Ischemic heart disease
4	M	78	R	80	No	Visual disturbances	Diabetes, arterial hypertension
5	M	74	L	90	No	Tinnitus, dizziness	Diabetes, arterial hypertension, ischemic heart disease
6	F	67	R	90	Stroke	Dizziness	Diabetes, arterial hypertension
7	M	67	L	90	Stroke	Hemiparesis	Diabetes, arterial hypertension
8	F	79	L	80	No	None	Arterial hypertension
9	M	78	R	90	Stroke	Hemiparesis	Arterial hypertension
10	F	63	L	90	No	Tremor	Diabetes, arterial hypertension
11	M	63	L	80	No	None	Arterial hypertension, ischemic heart disease
12	M	74	R	90	Stroke	None	Arterial hypertension
13	M	63	L	90	Stroke	Hemiparesis	Arterial hypertension
14	F	82	L	80	No	Dizziness	Arterial hypertension
15	M	74	L	90	No	None	Diabetes, arterial hypertension, ischemic heart disease
16	M	76	L	80	Stroke	None	Arterial hypertension
17	M	76	L	85	TIA	None	Diabetes, arterial hypertension, ischemic heart disease
18	F	64	L	90	TIA	None	Diabetes, arterial hypertension
19	F	72	L	70	No	None	Arterial hypertension
20	M	77	L	90	Stroke	Hemiparesis	Arterial hypertension
21	M	67	R	90	Stroke	Hemiparesis	Diabetes, arterial hypertension
22	M	77	L	80	No	Dizziness, visual disturbances	Arterial hypertension

ID — identification; M — male; F — female; TIA — transient ischemic attack; L — left; R — right

vice with a high-frequency (11 MHz) linear probe. The sonographer was a vascular medicine specialist who was unaware of the subject's clinical state.

Based on Doppler studies, patients were qualified for the CEA procedure as determined by the guidelines established by the European Society of Vascular Surgery [27]. Patients with severe carotid artery stenosis were identified using criteria established by NASCET (North American Symptomatic Carotid Endarterectomy Trial) according to the following formula: % ICA stenosis = (1-[narrowest ICA diameter/diameter normal distal cervical ICA]) × 100 [6].

Biochemical analysis of visinin-like protein 1

Serum samples were taken from the antecubital vein of the patients at three different times: within 24 hours preoperatively to CEA, 12 hours postoperatively, and 48 hours postoperatively.

Serum for the analysis of specific proteins was obtained by centrifugation of whole blood at 3000 rpm (603 × g) for 15 min in a laboratory centrifuge at a temperature of 4°C and stored at –80°C prior to analyses. Plasma without signs of hemolysis was analyzed using a quantitative sandwich enzyme-linked immunosorbent assay (ELISA) technique. The protocols were adapted from a commercially developed assay manufactured by Bioassay Technology Laboratory (BT Lab, Zhejiang, China). The concentrations of visinin-like protein 1 (VLP-1); Cat. No: E4118Hu were quantified based on the optical density (OD) at 450 nm using the BioTek ELx808™ Absorbance Microplate Reader (BioTek, Winooski, VT, USA). The samples for each participant were diluted to fit the range of the standard curve and

Table 2. Serum levels of visinin-like protein 1 (VLP-1) and a comparative analysis

VLP-1 level (μg/l)						
	N	Mean	Median	SD	SE	p
Before	22	0.065	0.060	0.022	0.00477	p = 0.00041*
12 h after	22	0.054	0.053		0.024	0.00514
48 h after	22	0.0417	0.042		0.018	0.00392
Difference					**Significance**	
Before — 12h after					p = 0.03251	
Before — 48h after					p = 0.00009*	
12h after — 48h after					p = 0.00639*	

*statistically significant; SE — standard error; SD — standard deviation; N — number of patients

run in duplicate on the same plate. Briefly, the plates were precoated with a human antibody, specific for each analyzed protein. A specific biotinylated antibody was also added to each sample. Then, streptavidin-HRP was added to the sample and standard wells. After incubation, plates were washed with 5× washing buffer with an automatic plate washer. Substrate solutions were added and once again the plates were incubated. The reaction was terminated by the addition of a stop solution. The concentration of protein levels in samples was calculated based on the standard curves using the average of the duplicate values.

Statistical analysis

The distribution of the collected data was evaluated using the Shapiro-Wilk test showing normal distribution for VLP-1. Furthermore, the data on the VLP-1 levels were analyzed using the one-way repeated measures ANOVA test with post hoc student's t-test using Bonferroni correction. Correlation analysis was performed using the Spearman rank correlation. The VLP-1 values were expressed in μg/l. The values of $p < 0.05$ were considered significant.

Results

The repeated measures ANOVA test showed that a sampling time significantly affected ($p < 0.05$) serum VLP-1 levels; $F(2, 42) = 12.96$, $p = 0.00041$. Serum VLP-1 concentrations in patients and a comparative analysis are presented in Table 2.

The post-hoc paired student's t-test using a Bonferroni corrected $\alpha = 0.0166$ (0.05/3) indicated that the VLP-1 level was statistically significantly decreased 48 h after CEA as compared to the levels measured prior to surgery (Fig. 1), and 12 h after the surgery (Fig. 2) ($p < 0.0166$). However, the difference in serum

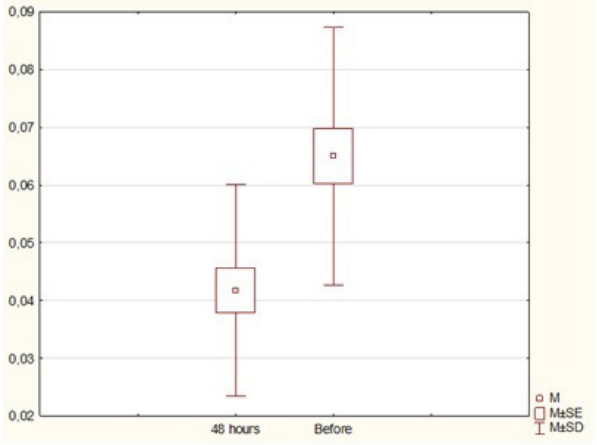

Figure 1. Serum visinin-like protein 1 (VLP-1) levels in patients before and 48 hours after the procedure, Bonferroni p = 0.00009** (M — mean; SE — standard error; SD — standard deviation); *statistically significant

VLP-1 levels prior to surgery and 12 h after CEA (Fig. 3) was not statistically significant ($p > 0.0166$).

There were no differences in serum VLP-1 concentrations in three measurements between males and females ($p > 0.05$). The difference in serum VLP-1 concentrations between younger (< 69 years) and older (> 69 years) patients in the three measurements was also not significant ($p > 0.05$). There was no correlation between serum creatinine level and the level of VLP-1 in all three measurements ($p > 0.05$).

Discussion

Our study revealed that the serum VLP-1 level decreased statistically significantly 48h after CEA compared to the levels measured before surgery and 12h after surgery.

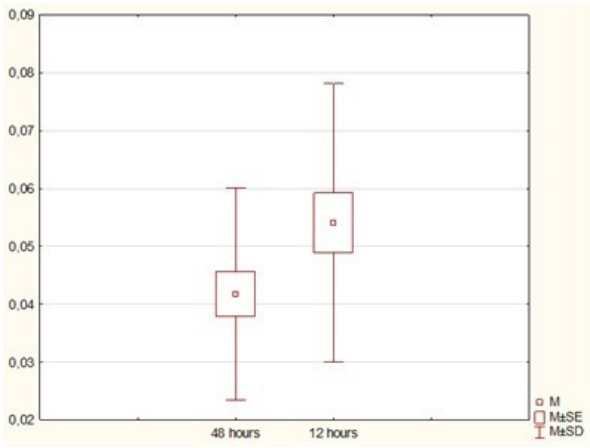

Figure 2. Serum visinin-like protein 1 (VLP-1) levels in patients 48 and 12 hours after the procedure, Bonferroni p = 0.00639** (M — mean; SE — standard error; SD — standard deviation); *statistically significant

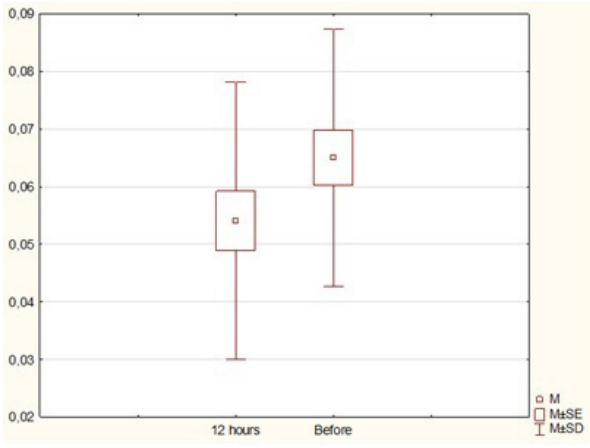

Figure 3. Serum visinin-like protein 1 (VLP-1) levels in patients before and 12 hours after the procedure, Bonferroni p = 0.03251. (M — mean; SE — standard error; SD — standard deviation)

To the best of our knowledge, this study is the first to evaluate the influence of the uncomplicated CEA on the level of VLP-1, and it presents data on a characteristic time curve of this molecule in the perioperative period of CEA.

At the beginning of 2006, Laterza et al. identified VLP-1 in cerebrospinal fluid from a rat model of a retrospectively collected stroke, and in plasma from 18 patients after stroke [16].

In 2011 Stejskal et al. developed the ELISA sandwich method for the determination of VLP-1. The study was held on a group of 33 patients: 17 healthy subjects and 16 suffering from ischemic stroke. The authors presented a statistically significant ($p < 0.01$) difference in the level of VLP-1 in both serum and cerebrospinal fluid (CSF), between these two groups, assuming that VLP-1 may be an independent marker of brain injury. The authors did not find significant differences in VLP-1 concentration between men and women in either serum or CSF in the group of healthy subjects, nor in the group of patients with ischemic stroke. The limitations of the study included a small number of patients and the selection of the control group, which did not allow one to estimate the precision for differentiating stroke from other neurological diseases [17].

A larger group of 110 patients with a stroke, was investigated by Li et al. in 2018. The authors found that in the stroke group, the level of VLP-1 was significantly ($p < 0.001$) higher than that in the control group, and in the patients with cognitive dysfunction, the level of VILIP-1 was higher than that in the normal cognition group. Authors therefore concluded that this molecule can serve as a predictor for cognitive dysfunction after stroke [18].

In 2020 Liu et al. investigated a group of 80 stroke patients and found that infarct volume and serum VLP-1 concentrations were highly and significantly correlated, and VLP-1 levels showed a strong association with poor stroke outcome [14].

In contrast, the study conducted by Park et al. in 2013 in a group of 175 patients found that the peripheral blood level of VLP-1 did not increase after stroke and was therefore not associated with stroke outcome, probably due to sampling of blood markers within 24 hours after stroke onset, when the release of proteins from the damaged brain to peripheral blood has not reached the peak yet [28].

Up to now, VLP-1 has not been investigated in the perioperative period of carotid endarterectomy; however, some other molecules, considered markers of brain damage, were previously studied before and after this procedure.

In 2001 Connolly ES Jr et al. conducted a study on a group of 25 patients who underwent CEA, measuring serum levels of S100B protein and neuron-specific enolase before (24h and pre-clamping), and after (24, 48, and 72 hours) the procedure. The study group was divided to: injured (those who exhibited significant declines in neuropsychometric test performance), and uninjured patients. As a result, injured patients presented significantly higher S100B levels, compared with uninjured patients, at 24, 48, and 72 hours after surgery ($P < 0.05$). However, S100B levels were elevated not only during the postoperative period but also during the preclamp period. Although the mechanism of cerebral injury among CEA patients demonstrating a decrease in neuropsychometric test performance is unknown, hypoperfusion or microemboli could be responsible. There were no significant differences in neuron-specific

enolase levels for injured and uninjured patients at any time point [29].

Our study showed that VLP-1 levels decreased after CEA. Rasmussen et al. presented similar results. The authors measured serum levels of neuron -specific enolase (NSE) and S100B, a different marker of brain damage, in a group of 22 patients undergoing carotid endarterectomy, preoperatively and postoperatively (12, 24, 36 and 48 h after CEA). The results showed that NSE level was significantly higher before carotid artery surgery and decreased postoperatively, while S100B level did not significantly change. The authors found no correlation between the change in cognitive function and the changes in blood levels of NSE or S100B protein [30].

The same molecules were investigated by Brightwell et al. [31], on a group of. 52 patients with carotid artery stenosis, of whom 28 underwent CEA and 24 carotid artery stenting (CAS). Both NSE and S100B were significantly higher at the baseline compared to the normal population. After the intervention, there was a non--significant trend of a transient rise of S100B levels in the CAS group, while the levels in the CEA group appeared unchanged. NSE appeared to increase at 48 hours postoperatively in the CEA group and decline in the CAS group, however, differences were not statistically significant. S100B alone increased significantly at 24 hours in those patients with postoperative neurological deficit ($p = 0.015$), and in those with emboli detected by the perioperative transcranial Doppler examination.

Mussack et al. conducted a study on a group of 46 patients with carotid artery stenosis, treated with CEA or CAS, and found that CEA but not CAS was associated with a transient increase in serum levels of S-100B, which later returned to baseline levels. The prolonged elevation of serum S-100B levels corresponded to the development of postoperative neurological deficits [32].

Earlier, a study group from our Department investigated a number of different molecules, that were potential brain damage markers, in the perioperative period of CEA.

In 2014 Terlecki et al. investigated the plasma level of kynurenic acid (KYNA) in a group of 40 patients, who underwent CEA or carotid artery stenting (CAS). Patients who underwent CEA were divided into groups with stable and unstable carotid artery plaque. KYNA level was measured before surgery and 1, 6, 24, and 48 hours after surgery. The authors found that the baseline value of plasma KYNA concentrations determined before surgery were higher in patients with unstable carotid plaque undergoing CEA than in patients with stable carotid plaque undergoing CEA and patients undergoing CAS. Independent of the baseline KYNA level, its concentration increased during the postoperative period in all studied groups. Higher plasma KYNA concentrations were noted in patients with postoperative neurological disorders. KYNA value was associated with the degree of inflammation measured by NLR (neutrophil-lymphocyte ratio) [33].

Later, in 2016 Ilzecki et al. investigated serum levels of several molecules in the perioperative period of patients undergoing uncomplicated CEA. Serum levels of carnosine dipeptidase 1 (CNDP1) and terminal hydrolase L1 (UCHL1) Ubiquitin C decreased significantly 12 h after CEA compared to the level before surgery and then normalized 48 h after CEA [34]. Microtubule--associated protein tau (MAPt) and myelin basic protein (MBP) presented a similar time curve, and significantly decreased 12 hours after CEA compared to the level before the surgery ($p < 0.05$), but then normalized 48 hours after CEA [35]. Three other molecules: glial fibrillary acidic protein (GFAP), neurofilament light polypeptide (NEFL), and brain lipid-binding protein (FABP7) levels were not statistically different between all the three measurements ($p > 0.05$) [36, 37].

In the other study, published by Ilzecki et al. in 2016, authors showed in the group of 25 patients undergoing uncomplicated CEA, that the serum level of NSE was statistically significantly increased 48 h after CEA as compared with the levels measured 12 h after surgery and prior to surgery ($p < 0.05$) [38].

Therefore, the results obtained in our study appear to be similar to some of the previous research, in which the serum level of brain damage markers (CNDP1, UCHL1, MAPt, MBP) significantly decreased in uninjured patients, after the uncomplicated CEA. The reason for that could be chronic brain ischemia caused by a high-grade internal carotid artery stenosis which could be responsible for the chronic damage of the brain, and therefore higher baseline level of brain damage markers such as VLP-1. Then, after the CEA, when the perfusion normalizes, the VLP-1 level drops with time. Similar results obtained by Rasmussem and Brightwell, who investigated NSE levels before and after uncomplicated CEA, and Ilzecki, who investigated levels of CNDP1, UCHL1, MAPt, and MBP seem to support this hypothesis. However, other levels of some other brain damage markers, such as S100B and KYNA appeared to increase after CEA.

The reason why different molecules established as brain damage markers act differently after CEA surgery remains unknown. It is possible, that some of them show higher sensitivity in detecting damage to the brain, and only these could detect small injuries of the brain such as silent ischemia after the CEA, caused by clamping and declamping the artery, microemboli, ischemia-reperfusion etc.

Higher VLP-1 levels before the procedure may represent brain damage caused by chronic ischemia, which is reduced by successful, uncomplicated CEA. Chronic cerebral hypoperfusion (CCH) has previously been investigated to activate a molecular and cellular injury cascade that leads to the breakdown of the blood-brain barrier (BBB) and neurodegeneration [39]. Therefore, brain damage markers, such as VLP 1, may be elevated, and found in the peripheral blood, due to a BBB impairment.

Up to now, there is no data on the possibility of release of the VLP-1, e.g. directly from the atherosclerotic plaque. However, there is some evidence of the presence of VLP-1 in extra-neuronal tissues. Buttgereit et al. [40] described VLP-1 expression in the human heart, rat cardiomyocytes, and H9c2 cells, and demonstrated that VLP-1 regulates the cell surface localization of natriuretic peptide receptor B. Dai et al. have shown that VLP-1 is expressed in pancreatic beta-cells and modulates insulin secretion [41]. Guerrico et al. showed that VLP-1 decreased cell adhesion and invasiveness of highly invasive squamous carcinoma cells in mice [42]. In addition, Akagi et al. demonstrated a prognostic role for VLP-1 at the mRNA level, suggesting its possible usefulness as a predictor of lymph node metastasis and a poor prognosis in colorectal cancer [43].

The authors are aware that one of the limitations of our study is the small study group (22 patients), without a control group of healthy subjects or patients with neurological complications after the CEA. However, the aim of the study was to investigate how the VLP-1 level acts in patients who underwent successful, uncomplicated CEA, and therefore it can be treated as a pilot study, while there is still a need for the next, more complex research taking into account these issues in the future.

The other limitation is only one surgical technique of CEA (primary suture), without the use of a shunt in all of the patients. However, in a group of 22 patients differentiating the surgical technique and dividing the study group into smaller subgroups could make the statistical analysis unreliable.

Conclusions

On the basis of the obtained results, it may be concluded that alternations in the curve of the serum level of VLP-1 may be a marker of neurological complications after the CEA procedures, however, further investigations are needed. Additionally, higher VLP-1 baseline levels before CEA may reflect brain damage caused by chronic ischemia.

Conflict of interest

None.

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VIA MEDICA

CASE REPORT

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An unusual case of a true aneurysm of the dorsalis pedis artery in a young man — an eight years observation

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Abstract

We present a case of a 21-year-old man, physically active, a few months after a torsion injury of the left ankle periodically began to have persistent problems similar in nature to Raynaud's phenomenon in the left foot, especially after exposure to cold and prolonged immobilization of the ankle, in ski shoes, for example. Initial Duplex Doppler ultrasonography revealed an abnormal lateral course of the distal segment of the left anterior tibial artery and the initial section of the dorsalis pedis artery and a small true aneurysm of the dorsalis pedis artery in the talus area. The changes were confirmed by a Computed Tomography Angiography test. At the same time, the immune and inflammatory origin of reported symptoms was excluded. After conservative treatment (rest, avoidance of cold temperatures, aspirin at a dose of 75 mg/day), relief of the symptoms was achieved during six-month medical supervision. During further observation, patient started again his physical activity (soccer, skiing). After 8 years of onset, he remains asymptomatic. He is observed as an out-patient.

Key words: true aneurysm; dorsalis pedis artery

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Introduction

Aneurysms below the popliteal artery is a very rare phenomenon, especially in the dorsalis pedis artery. The majority of aneurysms are of known origin, mainly traumatic or iatrogenic. However, true aneurysms of the dorsalis pedis artery occur very rarely. According to the review of the literature, only 20 cases of varied and often unclear etiology have been identified so far [1], two of them are related to bilateral synchronous changes [1, 2]. Due to limited occurrences of these anomalies, there is little clinical data on the natural history and symptomatology. Consequently, precise therapeutic procedures have not been established clearly and must be considered individually, depending on the case.

Case report

A 21-year-old man, actively involved in sport (soccer, skiing), was sent to our hospital due to the occurrence of troublesome symptoms for several months similar in nature to the symptoms of Raynaud's phenomenon: sudden tingling, numbness, pain and blanching of the great toe and pain on the plantar side of the left foot (Fig. 1). The symptoms appeared for the first time while skiing in minus temperatures and have reappeared periodically since, especially after prolonged immobilization of the foot or exposure to cold, and the

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Figure 1. Paleness of the third and fourth toes of the right foot

symptom suppression period varied and sometimes even lasted a few days.

In an interview, the patient reported that a torsion injury of the left ankle occurred about one year before — treated conservatively. Moreover, medical history revealed removal of the left palatine tonsil, hypo-sensitization therapy for grass pollen allergy and Gilbert's syndrome detected five years before. There was no data on the anamnesis leading to other potential vascular pathologies in this patient or in his family members. The patient did not report any complaints from other areas of the body, including the other limbs.

Physical examination of the left foot revealed unchanged skin with proper warmth comparable with that of the opposite side and full mobility of the ankle joint. The pulse was present in all the places on the lower extremities where it is typically found, including dorsal arteries of the foot, which was confirmed by ABI measurement at rest using the blind Doppler method. Inconclusive results were obtained in a nail fold capillaroscopy test of the big toes, but the morphology of capillaries pointed more to the secondary nature of Raynaud's symptoms. The basic laboratory tests showed no significant deviations, except for a slightly elevated level of bilirubin with a predominance of the intermediate fraction, observed in Gilbert's syndrome. Proper marking of inflammation indicators and tests for the presence of various common autoantibodies, including crioglobulin, excluded the inflammatory and immune background of reported disorders.

The Duplex Doppler ultrasonography revealed a correct picture of the aorta, iliac arteries, femoral and lower leg arteries, and those of the right foot. On the left leg, however, attention was drawn to the distal segment to an unusual course of the anterior tibial artery and the initial section of the dorsalis pedis artery; this course was more lateral and twisting around the lateral malleolus, and the dorsalis pedis artery had

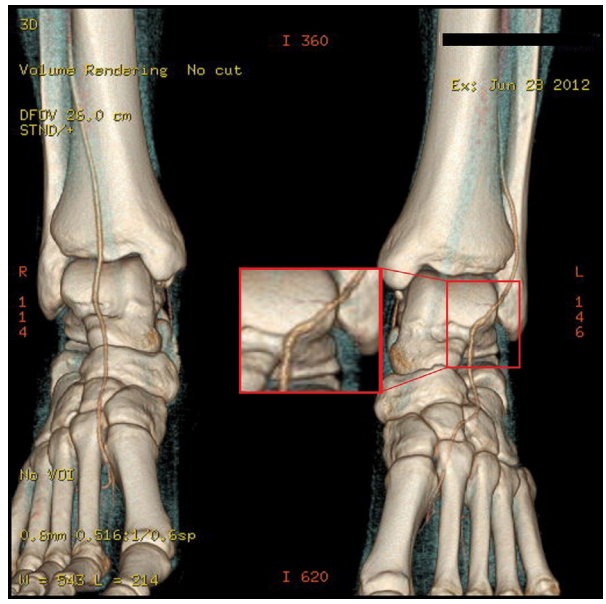

Figure 2. Angio CT — atypical localization of tibial anterior artery and dorsalis pedis artery aneurysm

a short, aneurysm extension in the talus area. In order to further refine the assessment, a contrast Computed Tomography Angiography test was done, which confirmed the atypical course of the above-mentioned arteries and allowed for a better view of a small (20 mm long × 6 mm wide) fusiform aneurysm of the left dorsalis pedis artery with an associated thrombus, slightly narrowing the lumen (Fig. 2).

On the basis of test results and the whole clinical picture, it was decided to continue conservative treatment and behavioral observation. As part of the treatment, Aspirin at a dose of 75 mg/day as well as avoiding injuries, low temperatures, and any overloading of the left lower limb was recommended. The patient reported for a check-up after about six months, reporting improvements in the form of only occasional occurrence of symptoms of very low intensity and rapid recovery from them. The dimensions of the aneurysm did not increase, based on the ultrasonography control test. After 8 years of onset, he remains asymptomatic. The patient started again his physical activity as before. He is further monitored as an out-patient. Periodical duplex doppler ultrasound assessment revealed patency of the vessel with stabile aneurysm diameter (Fig. 3).

Discussion

The dorsal artery of the foot is a very rare location for the occurrence of aneurysms. The most common of these are false aneurysms, arising mainly as a result of a non-penetrative blunt trauma, such as twisting the ankle or bruising the area, but also as a result of a penetrating trauma caused by a sharp object or fractures [3].

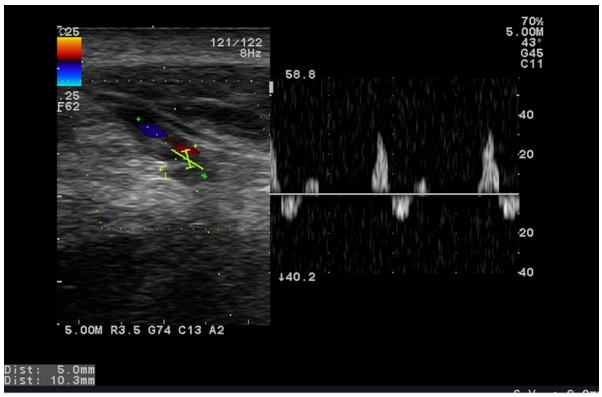

Figure 3. USG doppler as a control examination after 8 years

latrogenic causes should also be mentioned, such as cannulation of the dorsal digital veins of the foot [4], surgical removal of a gelatinous cyst on the tendon [5], or other orthopedic procedures, especially in the field of ankle arthroscopy[6–8]. All of these situations may result in breaking the continuity of the vessel wall, the escape of blood into the surrounding tissues around the fibrous capsule, and the formation of a false aneurysm.

True aneurysms of the dorsalis pedis artery are even less common. In some reported cases, particularly in patients with such risk factors as diabetes [5, 9–11] and hypertension [3, 5, 9, 12–14], the possible cause of the aneurysm can be seen in the underlying degeneration of the wall caused by atherosclerosis, which has been repeatedly confirmed by histopathology [1, 9, 13]. Another possible etiology is an inflammatory (*mycotic*) aneurysm, which could arise as a result of several situations, 55 such as bacterial embolism with coexisting bacterial endocarditis, generalized sepsis, use of infected intravascular catheters or stents, intravenous drug use and, less often, by the spread of infection to the wall of the artery by continuity from the surrounding tissues [3]. Other possible reasons include cellular degeneration of the tunica media, Ehlers-Danlos syndrome, or other collagenopathies [13]. Among potential factors that predispose to the formation of a true aneurysm, the role of injuries is brought to attention, especially repetitive microtraumas conducive to the formation of thin artery walls and thereby accelerating the formation of an aneurysm [1, 3, 9].

Symptoms of an aneurysm of the dorsalis pedis artery primarily include a pulsating tumor, pain, tenderness and sometimes itching [9, 15]. Additional symptoms such as compression of adjacent structures (e.g., a vein or a nerve) or foot pain when taking a certain position of the body (e.g., vajrasana sitting position), may depend on the location and size of the aneurysm [13]. It is also worth mentioning that the discomfort associated with wearing shoes, which in addition causes pain by chronic irritation, may even increase the risk of acute ischemia, contributing to the formation of *in situ* thrombosis or embolism [3].

Because there are slight chances of aneurysms occurring below the level of the popliteal artery, including the dorsalis pedis artery, their natural history is little known compared to aortic and popliteal artery aneurysms. Such complications as spontaneous rupture of an aneurysm of the dorsalis pedis artery [12] or acute ischemia of the forefoot due to thrombosis of an aneurysm and systemic embolism, have been reported in literature [16]. It is partly because there is a possibility of such complications occurring that most authors believe that any changes in this area should be operated. On the basis of several reported cases, it is believed that small and so-called "asymptomatic" aneurysms can be successfully monitored even over several years [13]. Possibilities of surgery include ligation of changes and cutting out or leaving, and in some cases, implementing reconstruction of the vessel, particularly in patients with underlying plantar arch artery insufficiency or failure or occlusion of the posterior tibial artery [5, 9, 13].

This report, against the background of many previous works [3, 5, 9], confirms that the Duplex Doppler ultrasonography is sufficient for the diagnosis and initial evaluation of a small aneurysm of the dorsalis pedis artery. Thanks to its non-invasiveness, availability, and low cost, it is also a very useful test to continue monitoring the changes. Other methods, such as Computed Tomography Angiography or Magnetic Resonance Imaging, are extremely useful particularly in the more accurate assessment of vascular anomalies; however, they are characterized by difficult accessibility, a higher cost, and require a contrast agent. Contrast angiography and digital subtraction angiography are considered to be more sensitive tests, but also more invasive, therefore they are reserved for the assessment of diagnostically difficult changes or applied for planning simultaneous therapeutic intervention.

Conclusions

Due to the small size of the aneurysm defined in the present patient, uncharacteristic symptoms appearing periodically, and subjective improvement after conservative treatment, it was decided to leave the patient for further ambulatory observation. We considered surgical treatment if the symptoms worsen or the size of the aneurysm increases, but after eight years of observation, the patient is still asymptomatic.

Conflict of interest

None.

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CASE REPORT

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Internal carotid artery dissection due to direct mechanical damage caused by the ipsilateral elongated styloid process. A 4-year follow-up

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Abstract

Internal carotid artery dissection (ICAD) is a complex clinical problem with a multi-causal etiology, in which the intima of the artery ruptures and is detached by the inflowing blood. Causes include trauma, intense exercise, vomiting, prolonged retroflexion of the neck, and spontaneous dissection. The therapy for this condition consists of treatment with anticoagulants or through endovascular intervention in recurrent cases. The aim of this paper is to present a case of ICAD in a young woman complicated by an ischemic stroke caused by an elongated styloid process. This abnormality was found in 3D computed tomography. In the described case, it was decided to start pharmacotherapy and withdraw from the endovascular treatment due to the technical difficulties of the procedure. The patient had been followed up regularly up to 4 years after the incident.

An elongated styloid process may be the cause of Eagle's syndrome classified into two types: classical type, and the rare carotid artery type, a component of which is ICAD. It is estimated that the styloid process in this form occurs in 4% of the population, which may indicate that the amount of ICAD caused by this variant of the styloid process is underestimated and should be included in the differential diagnosis of ischemic stroke in young people.

Key words: carotid artery dissection (CAD); elongated styloid process (ESP); transient ischemic attack (TIA); Eagle's syndrome

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Introduction

Carotid artery dissection (CAD) is a multicausal condition where the layers of the carotid artery are spontaneously separated [1]. It is often caused by neck injuries, especially extreme neck rotations or extensions [2]. This can lead to recurrent ischemic events such as transient ischemic attack (TIA) [3]. CAD is a major cause of stroke in young (< 50 years old) patients [4]. Therapy of carotid artery dissection is based on anticoagulants which protect patients from peripheral embolism and following cerebral ischemia [2]. This procedure is often sufficient and pathological lesions heal up spontaneously in a six-month time [2].

Case report

A 36-year-old woman, with a history of 3 miscarriages, polycystic ovaries syndrome, and MTHFR gene mutation (heterozygous) diagnosed 3 years earlier

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was admitted to the Department of Neurology due to symptoms of a TIA and severe headache. 3 days prior to admission the patient had suffered a right-sided jolt of the body caused by a German Shepherd.

Neurological examination revealed weakness and stiffness of the left side of the body, central facial palsy, and dysarthria. Computed Tomography (CT) imaging showed a hyperdense middle cerebral artery (MCA) in the M1 segment. Ischemic lesions in basal ganglia on the right side were depicted in the MR scan. 2 hours after the onset of symptoms recombinant tissue plasminogen activator thrombolytic therapy was administered. The total dose was calculated at 59 mg (6 mg with an intravenous bolus and 53 mg by intravenous infusion over 1 hour). At the same time, Angio-CT was performed, which showed occlusion and features of right internal carotid artery (RICA) dissection. Subsequently, the patient underwent the mechanical thrombectomy procedure. In the control CT examination performed after 24 hours, a small hemorrhagic area in the posterior part of the basal ganglia on the right side was seen. After the mechanical thrombectomy, the patient was treated with 5000 IU (International Units) low molecular weight heparin and two antiplatelet drugs — 150 mg acetylsalicylic acid (ASA), 75 mg clopidogrel and 20 mg atorvastatin.

After two weeks of hospitalization, the patient was discharged from the Neurology Department in good general condition and was referred to the Department of Angiology. Duplex Doppler ultrasonography examination of carotid arteries done at an Angiology clinic revealed a turbulent flow with a peak systolic velocity (PSV) over 3 m/s and two lumens with the reversed flow in a false lumen in the RICA. No abnormalities were found in the carotid arteries on the left side as well as in external and common carotid arteries on the right side. A follow-up Angio-CT scan done at that time revealed the cause of the patient's carotid artery dissection. The 3-dimensional reconstruction showed an elongated right styloid process (SP), which abutted with its end to the arterial wall of ICA (Fig. 1, 2). Its length, measured from the temporal bone junction to the tip of the process, was 31 mm (Fig. 3). It was decided to consult the patient with vascular surgeons, who chose not to apply a carotid stent because of the high risk of intraprocedural stroke and the need to use a long stent given that dissection involved extra- and intracranial segments of ICA. Instead, the patient remains on drug treatment consisting of 75 mg ASA and 20 mg atorvastatin. LMWH and clopidogrel were discontinued 6 months after the incident. In addition, she is under constant supervision at follow-up visits held every 3–6 months in the Department of Angiology where the carotid flow in doppler ultrasound is measured.

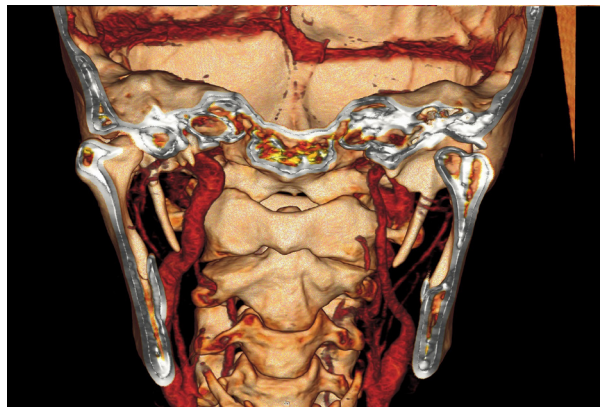

Figure 1. 3D reconstruction of angiography CT scan showing the site of right internal carotid artery damage caused by the ipsilateral styloid process

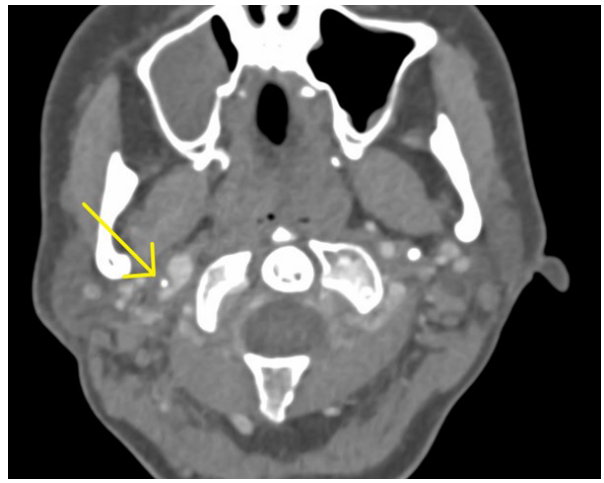

Figure 2. Axial reconstruction of angiography CT scan showing the tip of the styloid process compressing the right internal carotid artery

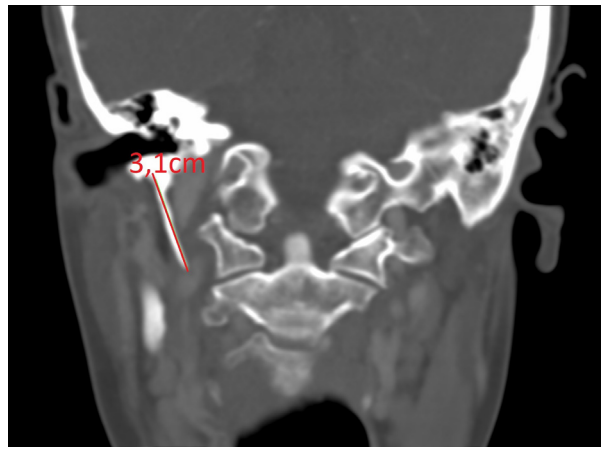

Figure 3. Coronal reconstruction of angiography CT scan showing the length of the right styloid process

Currently, the dissection is stabilized, the carotid flow gradually decreases and totals 2 m/s. Figure 4 presents the most recent USG (January 2023) duplex-doppler examination of RICA in our patient.

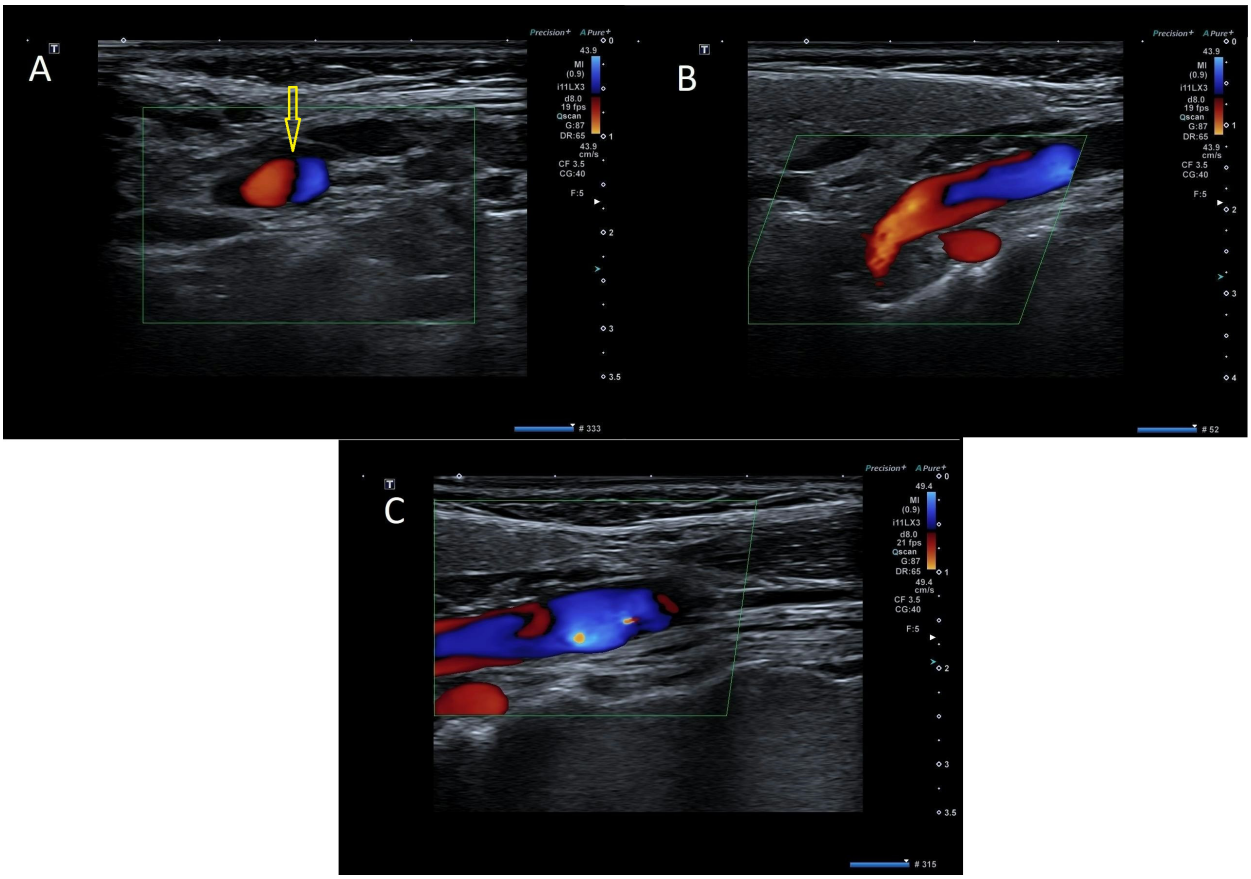

Figure 4. Duplex-doppler ultrasonography examination of RICA shows a dissection flap (yellow arrow [**A**]) separating the true and the false lumen. Retrograde flow is visible in the latter (**B**, **C**). The measured PSV value was 173 cm/s

The neurological condition of the patient was reassessed during the follow-up visit in February 2023 — the patient presented a mild weakness in the left limbs.

Discussion

The annual prevalence of internal carotid artery dissection is 2.5–3 cases per 100,000 [5, 6]. CAD is responsible for almost 20% of strokes in young adults and for about 2,5% among older patients [5, 7]. However, this incidence could be undiagnosed due to slight clinical symptoms [8]. Moreover, according to Paciaroni et al. CAD is more likely to occur during winter than in summer [9].

CAD can be divided based on the segment of the artery which was involved. It can be classified as the dissection of the vertebral or carotid segment and as the dissection of the intracranial or extracranial segment [8]. The most common, with 75% prevalence, are dissections of extracranial segments [10].

CAD mostly occurs spontaneously or after neck or head trauma which leads to a tear in the intimal layer of the carotid artery which creates an intramural hematoma [11]. The hematoma can result in stenosis and thrombus formation which results in cerebral ischemia. The risk factors of CAD are excessive physical exercise, emesis, long-lasting retroflection, or bronchoscopy [2]. The genetic factors are Ehlers-Danlos syndrome, Marfan's syndrome, Osteogenesis Imperfecta, or Behcet's disease [2].

The course of carotid artery dissection can be asymptomatic and that is why this condition is often undiagnosed [8]. Headache occurs among 2/3 patients and is often described as severe, acute, stabbing, or pounding and is localized on the side of the dissection [2, 6]. Other clinical manifestations of CAD are cranial nerve palsies, ipsilateral Horner's syndrome, and retinal or cerebral ischemia [8]. The symptoms of cerebral ischemia are episodes of *amaurosis fugax*, TIA, and brain stroke [2].

The most common, easily accessible, and noninvasive examination to diagnose carotid artery dissection is doppler ultrasound [2]. This procedure also allows monitoring of the course of CAD in later periods [2]. Doppler ultrasound should be always verified by neuroimaging techniques including magnetic resonance imaging (MRI), computerized tomographic angiography (CT), and conventional angiography [2, 8]. Angiography

is an invasive examination, which is associated with some mild complications, but allows one to implement endovascular treatment or to plan surgical procedures [2].

In the case described here, a three-dimensional Angio-CT scan revealed the cause of the ICAD. According to the literature, the styloid process is classified as elongated when it exceeds 30 mm in length [12]. About 4% of styloid processes are found to be elongated, but of these, only about 4% present with symptoms [13, 14]. Eagle syndrome is a rare condition caused by an ESP which interferes with the neighboring structures leading to various symptoms [13]. The typical Eagle syndrome is associated with sore throat, otalgia, and foreign body sensation in the throat due to compression of the ESP on the glossopharyngeal nerve, while the rare carotid type is caused by compression of the carotid artery in its extracranial segment, causing cerebrovascular symptoms such as syncope, dizziness, or transient ischemic attacks. There are a handful of reports on mechanical injury to the internal carotid artery caused directly by the styloid process [15–17]. Nevertheless, an ESP is considered a risk factor for CAD that can lead to ischemic stroke. Given the prevalence of ESP, the differential diagnosis of ischemic stroke in young individuals should include this abnormality of the styloid process once other causes have been ruled out.

Drug treatment of carotid artery dissection primarily consists of antithrombotic therapy: anticoagulant and antiplatelet therapies [18]. According to Misztal et al. who reviewed the literature of the treatment of CAD, there is no significant difference in the survival rate of patients who used anticoagulants or antiplatelet drugs, which means that both of them can be successfully used [2, 19]. However, for patients with recurrent ischemic incidents, an endovascular intervention should be considered [2]. Surgical procedures are indicated only in special cases such as enlarging of dissection range, presence of critical hemodynamically arterial stenosis, and presence of aneurysm which is bigger than the twofold dimension of the normal internal carotid artery, but for the majority of patients, endovascular therapy is preferred [2].

The prognosis of carotid artery dissection is good if no ischemic stroke or irreversible eye lesions occurred [2]. Most cases of carotid artery dissection can be conservatively treated with anticoagulation or antiplatelet drugs and have good clinical outcomes, with anatomic resolutions and low rates of recurrence [20].

Conflict of interest

None.

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16–17 kwietnia 2021 r., Wrocław

SESJA PLAKATOWA/POSTER SESSION

Przestrzeganie zasad profilaktyki przeciwobrzękowej u kobiet leczonych z powodu raka piersi a występowanie obrzęku limfatycznego

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Wstęp: Obrzęk chłonny jako powikłanie pooperacyjne raka piersi jest kliniczną manifestacją mechanicznej niewydolności układu limfatycznego. Dostępne metody i systemy rehabilitacji skupiają się w pierwszych etapach na profilaktyce przeciwobrzękowej.

Cel: Celem pracy było sprawdzenie poziomu zastosowania się pacjentek leczonych z powodu raka piersi do zasad profilaktyki przeciwobrzękowej oraz skali problemu występowania obrzęku limfatycznego.

Materiał i metody: Materiał badawczy stanowiło 60 kobiet (średnia wieku 61,2 roku) po przebytej radykalnej mastektomii, usprawnianych w Świętokrzyskim Centrum Onkologii w Kielcach. Kwestionariusz ankiety obejmował pytania dotyczące przestrzegania zasad profilaktyki przeciwobrzękowej. Analizę statystyczną przeprowadzono za pomocą oprogramowania statystycznego PQ-Statver.1.4.8.322.

Wyniki: Prawostronną mastektomię zastosowano u 40% badanych, lewostronną u 53,33%, a obustronna operacja dotyczyła 6,67% kobiet. Wszystkie badane (100%) deklarowały znajomość zasad profilaktyki przeciwobrzękowej, a 78,33% ankietowanych potwierdzało stosowanie się do nich. Samodzielne wykonywanie autodrenażu wskazywało 81,67% ankietowanych. Korzystanie z wyrobów uciskowych deklarowało 20% kobiet. Problem występowania obrzęku limfatycznego kończyny górnej stwierdzono u 55% badanych, a 23,33% doświadczyło także stanów zapalnych — infekcji „róży" nasilające objawy choroby.

Wnioski:

1. Kobiety leczone z powodu raka piersi Świętokrzyskim Centrum Onkologii w Kielcach przestrzegają niektórych zasad profilaktyki przeciwobrzękowej.
2. Spośród wszystkich zasad profilaktyki przeciwobrzękowej najliczniejsza grupa badanych stosuje się do zaleceń wykonywania autodrenażu.
3. Nieliczna grupa kobiet leczonych z powodu raka piersi korzysta z rękawa uciskowego okrągłodzianego.
4. Pomimo przestrzegania niektórych zasad profilaktyki przeciwobrzękowej występowanie obrzęku limfatycznego odnotowano u ponad połowy badanych.
5. Istnieje wskazanie do wprowadzenia szerszego nadzoru nad działaniami edukacyjnymi wobec powyższej grupy chorych, dla monitorowania ryzyka wystąpienia obrzęku limfatycznego.

Compliance with the principles of anti-edema prophylaxis among women treated for breast cancer and the occurrence of lymphedema

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Introduction: Lymphoedema as a post operation complication of breast cancer is a clinical manifestation of the mechanical failure of the lymphatic system. The available methods and systems of rehabilitation focus in the first stages on anti-edema prevention.

Aim: The aim of the study was to check the level of compliance of patients treated for breast cancer with the principles of anti-edema prophylaxis and the scale of the problem of lymphoedema.

Material and methods: The research material concerned 60 women (average age 61.2 years) after radical mastectomy, who underwent rehabilitation at the Holycross Cancer Centre in Kielce. The survey questionnaire included questions about compliance with the principles of anti-edema prophylaxis. Statistical analysis was performed using the PQ-Statver statistical software. 1.4.8.322.

Results: Right-sided mastectomy was performed in 40% of patients, left-sided in 53.33%, and bilateral surgery was performed in 6.67% of women. All respondents (100%) declared that they knew the rules of anti-edema prophylaxis, and 78.33% of the respondents confirmed that they followed them. Self-draining was indicated by 81.67% of the respondents. The use of compression products was declared by 20% of women. The problem of upper limb lymphoedema was found in 55% of respondents, and 23.33% also experienced inflammation — an infection of "rose" intensifying the symptoms of the disease.

Conclusions:

1. Women treated for breast cancer at the Holycross Cancer Centre in Kielce adhere to some principles of anti-swelling prophylaxis.
2. Among all the principles of anti-oedematous prophylaxis, the largest group of respondents follows the recommendations of self-draining.
3. A small group of women treated for breast cancer use a round-shaped compression sleeve.
4. Despite the observance of some principles of anti-edema prophylaxis, the occurrence of lymphedema was reported in over half of the respondents.
5. There is an indication to introduce wider supervision over educational activities in the above group of patients in order to monitor the risk of lymphedema.

Key words: breast cancer; lymphedema; anti-edema prophylaxis

Ocena skuteczności kompleksowej terapii przeciwobrzękowej wśród kobiet leczonych z powodu raka piersi

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Wstęp: Kompleksowa terapia przeciwobrzękowa (KTP) jest powszechnie stosowaną metodą w walce z obrzękiem limfatycznym u kobiet po radykalnym leczeniu raka piersi. W jej skład wchodzą łącznie stosowane: manualny drenaż limfatyczny, kompresjoterapia, ćwiczenia ruchowe oraz pielęgnacja skóry.

Cel: Celem pracy była ocena skuteczności kompleksowej terapii przeciwobrzękowej u kobiet po mastektomii jednostronnej.

Materiał i metody: Grupę badaną stanowiło 70 kobiet (średnia wieku 62 lata) będących po zabiegu mastektomii jednostronnej usprawniane w Świętokrzyskim Centrum Onkologii w Kielcach z powodu obrzęku limfatycznego kończyny górnej po stronie operowanej piersi.

Najliczniejszą część grupy (61%) stanowiły kobiety po przebytej mastektomii lewostronnej. Połowę badanych (50%) stanowiły kobiety będące więcej niż 5 lat po zabiegu operacyjnym.

Leczenie uzupełniające radioterapią zastosowano u 76% kobiet, a leczenie w postaci chemioterapii przebyło 89% badanych.

Kwestionariusz ankiety obejmował pytania dotyczące występowania obrzęku limfatycznego oraz pomiary obwodów kończyn górnych na niżej wymienionych poziomach: 10 cm poniżej stawu barkowego, 10 cm powyżej stawu łokciowego, staw łokciowy, 10 cm poniżej stawu łokciowego, 3 cm przed stawem promieniowo-nadgarstkowym, staw promieniowo-nadgarstkowy, śródręcze.

Analizy wyników przeprowadzono za pomocą pakietu statystycznego PQStat ver. 1.6. Wyniki analizowanych skal w zależności od kończyny przeprowadzono analizą wariancji dla powtarzanych pomiarów.

Wyniki: Obrzęk limfatyczny po zabiegu mastektomii jednostronnej najczęściej występował w części proksymalnej (46%), kolejno w części proksymalnej i dystalnej (30%), a najrzadziej w części dystalnej (24%). Umiejscawiał się najczęściej na ramieniu (39%), następnie na przedramieniu (27%), kolejno w okolicach łokcia (16%), w dłoni (10%) oraz w okolicach pachy (7%). Większość badanych kobiet (56%) zgłosiło problem występowania bólów w okolicy kończyny górnej po stronie operowanej piersi. Najliczniejsza grupa badanych (21%), u których występował ból określiła go jako rozpierający. Większość, czyli 67% ankietowanych wskazuje na obecność chorób współtowarzyszących. Problem występowania infekcji róży zgłosiło 16% ankietowanych. Uszkodzenia po radioterapii (zwłóknienia) zgłosiło 68% ankietowanych. U większości (79%) badanych kobiet kolor skóry kończyny górnej był w normie. U najliczniejszej (68%) grupy badanych stwierdzono osłabione napięcie mięśni kończyny górnej. Dodatni wynik testu Stemmera dotyczył 20% ankietowanych, podobnie dodatni wynik testu „dołka” dotyczył 20% ankietowanych. Upośledzenie funkcji chwytnej ręki zgłosiło 19% badanych. Problem związany z zaburzeniami czucia okolicy operowanej zgłosiło 34% ankietowanych.

Wyniki pomiarów obwodów kończyn górnych na różnych poziomach wykazują tę samą tendencję. Różnice między tymi wynikami są wysoce istotne ($p < 0,0001$) i różnice te dotyczą zarówno porównania kończyny zdrowej do chorej jak i porównania wyników przed i po terapii. Oznacza to, że w wyniku leczenia obserwuje się wysoce istotny ($p < 0,01$) spadek obwodów tego pomiaru, co pozytywnie świadczy o terapii. Porównanie kończyny zdrowej do chorej po leczeniu metodą KTP wskazuje, że obrzęk jest istotnie wyższy ($p < 0,01$)

w kończynie chorej. Natomiast wyniki pomiarów po terapii nadal różnią się wysoce istotnie ($p < 0,01$) od kończyny zdrowej. Oznacza to, iż choć istnieje pozytywny wpływ terapii to nie skutkuje ona taką poprawą by uzyskać efekt typowy dla kończyny zdrowej.

Wnioski:

1. Obrzęk limfatyczny po mastektomii jednostronnej najczęściej umiejscowiony jest w części proksymalnej kończyny górnej strony operowanej.
2. Zastosowanie kompleksowej terapii przeciwobrzękowej istotne zmniejszenia obrzęk limfatyczny kończyny strony operowanej piersi.
3. Choć istnieje pozytywny wpływ kompleksowej fizykalnej terapii udrażniającej, to nie skutkuje ona taką poprawą by uzyskać efekt typowy dla kończyny zdrowej.
4. Kompleksowa fizykalna terapia udrażniająca jest skuteczną metodą zwalczania obrzęku limfatycznego u kobiet po mastektomii.

Assessment of the effectiveness of comprehensive anti-edema therapy in women treated for breast cancer

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Introduction: Comprehensive Anti-Edema Therapy is a commonly used method in the fight against lymphedema among women after radical treatment of breast cancer. It includes: manual lymphatic drainage, compression therapy, physical exercises and skin care.

Aim: The aim of the study was to evaluate the effectiveness of the Comprehensive Anti-Edema Therapy in women after unilateral mastectomy.

Material and methods: The study group consisted of 70 women (average age 62) who underwent unilateral mastectomy and were rehabilitated at the Holycross Cancer Centre in Kielce due to lymphoedema of the upper limb on the side of the operated breast. Half of the respondents (50%) were women who were more than 5 years after surgery. Adjuvant radiotherapy was used in 76% of women, and chemotherapy was used in 89% of respondents. The questionnaire included questions about the presence of lymphedema and measurements of the circumference of the upper limbs. The analyzes of the results were performed using the statistical package PQStat ver. 1.6. The results of the analyzed scales depending on the limb were performed using the variance analysis for repeated measurements.

Results: Lymphoedema following unilateral mastectomy was most common (46%) in the proximal part. Most of the surveyed women (56%) reported the problem of pain in the upper limb area on the side of the operated breast. 67% of respondents indicate the presence of comorbidities. The problem of rose infection was reported by 16% of respondents. Damage after radiotherapy (fibrosis) was reported by 68% of respondents. A positive result of the Stemmer test concerned 20% of the respondents, a similar positive result of the "hole" test concerned 20% of the respondents. Impaired grasp function was reported by 19% of respondents. The problem related to sensory disorders in the operated area was reported by 34% of respondents. The results of measurements of upper limb circumferences at different levels show the same trend. The differences between these results are highly significant ($p < 0.0001$) and these differences concern both the comparison of the healthy limb to the diseased limb and the comparison of the results before and after treatment. This means that as a result of treatment, a highly significant ($p < 0.01$) decrease in the circuits of this measurement is observed, which positively proves the therapy. The comparison of the healthy limb to the diseased limb after treatment with the comprehensive anti-edema therapy method shows that the edema is significantly higher ($p < 0.01$) in the diseased limb. On the other hand, the results of the measurements after the therapy still differ significantly ($p < 0.01$) from the healthy limb. This means that although there is a positive effect of the therapy, it does not result in such an improvement as to obtain the effect typical for a healthy limb.

Conclusions:

1. Lymphoedema after unilateral mastectomy is most often located in the proximal part of the upper limb of the operated side.
2. The use of Comprehensive Anti-Edema Therapy significantly reduces lymphatic edema on the extremity of the operated breast.
3. Although there is a positive effect of Comprehensive Anti-Edema Therapy, it does not result in such an improvement as to obtain the effect typical of a healthy limb.

4. Comprehensive Anti-Edema Therapy is an effective method of combating lymphoedema in women after mastectomy.

Key words: breast cancer; lymphoedema; comprehensive anti-edema therapy

Dietary intervention assessment in cases of patients suffering from lymphedema and lipedema — case study

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Introduction: In cases of lymphedema and lipedema, the use of caloric restrictions and introducing physical activity do not cause the expected results — there is no edema reduction. Patients' nutritional status assessment is used to determine the level of obesity and fat distribution in the body. The goal of treating patients is achieving healthy body weight, because overweight and obesity can contribute to further obesity increase. Measuring resting metabolism by indirect calorimetry allows us to calculate the actual energy demand and determine the energy value of a diet. The use of a balanced diet with proper calories and low content of refined carbohydrates which is rich in anti-inflammatory ingredients is intended for the reduction of edema these patients suffer from.

Aim: Assessing the effectiveness of dietary intervention in reducing lymphedema and lipedema.

Case description: We describe a case of a 26-year-old patient with lymphedema and a 44-year-old patient with lipedema. Both women came to a dietician to verify their diets, define nutritional mistakes as well as to gather information and suggestions on how to act in order to decrease body fat in their limbs. In the first case (lymphedema) an excess of visceral fat was found in the lower limbs. The resting metabolism measured by indirect calorimetry was 1421 kcal. The patient received diet equal to 1700 kcal. After 3 months her body weight dropped by 2.8 kg, total body fat went down by 2.1% — left leg 0.38 kg, right leg 0.42 kg and visceral fat by 1. In the second case (lipedema) we saw obesity including excess of visceral fat and extra body fat in lower limbs. The resting metabolism measured by indirect calorimetry was 1578 kcal. This patient received a diet equal to 2000 kcal, and after 4 months it was decreased to 1700 kcal. Results were measured every 1.5 months. After 8 months the patient lost 6.6 kg, body fat dropped by 3.3% - left leg 0.84 kg, right leg 0.86 kg and visceral fat by 2.

Results: The prescribed dietary intervention turned out effective with lymphedema and lipedema patients. The effect was decreased body weight, lower body fat in affected body limbs and diminished visceral fat.

Conclusions: Authors of countless research papers point to nutritional recommendations as ways to treat lymphedema and lipedema patients. Edema makes it difficult to define the real energy demand, thus hindering applying a diet that would help to reduce body weight. Suggested body weight control should be based on a properly balanced nutritional plan designed for a particular patient. Additionally it is necessary to define which elements of the diet have influence on edema, due to the fact there are no reports on the effectiveness that diet can have on lymhedema and lipedema reduction. It is advisable to continue research and observations that would consider the relations between diet applied and the size of lymphedema and lipedema.

Key words: body fat percentage, obesity, nutritional mistakes, diet

Ocena zastosowania kompresji w profilaktyce obrzęku kończyn dolnych u kobiet aktywnych fizycznie w czasie ciąży i połogu — doniesienia wstępne

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Wstęp: Obrzęki kończyn dolnych wraz z dolegliwościami dotyczą nawet około 80% kobiet w III trymestrze ciąży. W oparciu o rekomendacje wydaje się, że zastosowanie profilaktycznej kompresji w postaci podkolanówek w połączeniu z aktywnością fizyczną w ciąży i połogu jest skutecznym rozwiązaniem, ale wymaga potwierdzenia badaniem zgodnie z *evidence-based medicine*.

Cel: Ocena zastosowania kompresji w profilaktyce obrzęku kończyn dolnych u kobiet aktywnych fizycznie w okresie ciąży i połogu.

Materiał i metody: 51 kobiet w ciąży, które spełniały kryteria (m.in. brak przeciwwskazań do aktywności fizycznej) zostało losowo przydzielonych do grupy CG (z kompresją podkolanówki uciskowe okrągłodziane

w ccl1 18–21 mm) lub do grupy NCG (bez kompresji). Projekt ukończyło 38 pacjentek. W przypadku wystąpienia obrzęku (przyrost objętości o ≥ 10%) w grupie NCG również włączono kompresję (NCG + C). W obu grupach wykonano badanie Dopplerem naczyń kończyn dolnych w II trymestrze ciąży i po połogu, pomiary obwodów i objętości podudzi (II, III trymestr i połóg) oceniono stan układu żylnego w skali CEAP oraz poziom aktywności fizycznej (kwestionariusz IPAQ w wersji długiej).

Wyniki: Obrzęk kończyn dolnych w rejonie stóp i podudzi stwierdzono u 5 pacjentek z grupy NCG w III trymestrze ciąży, dobrano kompresję i zakwalifikowano do grupy NCG + C. U jednej pacjentki wcześniej stwierdzono refluks, u pozostałych 4 obrzęk wystąpił mimo braku istotnych odchyleń w pierwszym badaniu Dopplerem. Pacjentki z grupy NCG + C w I i II trym. ciąży były najbardziej aktywne fizycznie.

Stwierdzono istotne obniżenie poziomu aktywności fizycznej u wszystkich kobiet w III trymestrze ciąży. Zaobserwowano istotną zależność pomiędzy intensywnym wysiłkiem fizycznym a wzrostem objętości kończyn, a także wzrostem objętości kończyn a brakiem wysiłku fizycznego. Zaobserwowano także subiektywnie odczuwane zmniejszenie dolegliwości w grupach z kompresją.

Wnioski: Kompresja z niskim ciśnieniem wpływa na zmniejszenie obrzęków u kobiet w okresie ciąży i połogu. Stosowanie ucisku i aktywności fizycznej w profilaktyce obrzęków kończyn dolnych u kobiet w ciąży wymaga dalszych badań.

Physiotherapy after liposuction with skin excision (mLIPO) — case report

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Introduction: The upper limb lymphedema occurs in 20–30% of patients with breast cancer after the surgical treatment. Physiotherapy, including the complex decongestive therapy (CDT), is the main conservative treatment of lymphedema. Liposuction with skin excision (mLIPO) is one of the surgical treatments of lymphedema, which is used more often than others because of the lack of effectiveness of the conservative treatment. The addition of the adequate physiotherapy to the surgical treatment may be crucial for achieving long-term effects.

Material and methods: A 51-year-old female with breast cancer underwent a mastectomy with ALND, chemotherapy and radiotherapy (RT). The patient developed secondary lymphedema on the right upper limb (stage III) and was admitted for the modified liposuction with skin excision (mLIPO). The compression therapy (CT) with compression in the range of 23–40 mm Hg (class 2) was started following the surgery and continued during the hospitalization and convalescence period (4 weeks). Then the patient was admitted for a 3-week rehabilitation in the Rehabilitation Unit of the Maria Sklodowska-Curie National Research Institute of Oncology Branch in Gliwice. We administered a physiotherapy program with the aim to improve the functionality of the upper limb and optimize the lymphedema. It included manual lymphatic drainage (SLD), compression therapy (CT), exercises improving muscle pomp of the upper limb, myofascial release (MFR) (used to manage scar tissues on chest and upper limb), sensorimotor exercises (used to teach patient the correct position of the scapula).

Results: As a result of PT the range of movement (ROM) of the right shoulder joint improved (most noticeable in flexion: from 138° to 152° and abduction: from 139° to 165°). Significant pain reduction was reported (from 10 to 1 in VAS scale). We observed an increase in the muscle strength (improvement in the grip force was recorded using dynamometer). We managed to achieve the optimization of lymphedema (reduction in the arm and forearm circumferences > 2 cm and better gliding of the fascia).

Conclusions: The physiotherapy after the surgical treatment of lymphedema using liposuction with skin excision increases the long-term effectiveness of this treatment and improves functionality of the upper limb.

Key words: lymphedema; liposuction; physiotherapy

The assessment of the influence of manual lymphatic drainage on biochemical parameters in people with improper weight. The description of chosen cases

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Introduction: Lymphatic drainage is usually used as a manual therapy in people after oncological surgeries,

chemotherapy, radiotherapy and as well as in overweight individuals. Lymphatic drainage contributes to the increase of lymph circulation. It can partly cause accelerated removal of damaged metabolites, increased dynamic of body fluids and decreased activity of sympathetic nervous system. It is particularly used in the treatment of lymphedema and lipedema which can be a result of genetic defects, venostasis, excessive physical effort, injuries or oncological diseases. The literature also reports about rare cases which suggests that not only the lymphatic system disorder can cause lymphedema, but may also lead to the increased risk of hypertension, atherosclerosis or insulin resistance.

Aim: Evaluation of the impact of manual lymphatic drainage on carbohydrate and lipid metabolism in the group of three chosen women.

Material and methods: The research realization was approved by Independent Bioethics Committee for Scientific Research at Medical University of Gdańsk (approval number: Uchwała nr NKBBN/692/2019-2020). The patients were recruited from Poradnia Kardiologii i Chorób Wewnętrznych in Gdynia. The therapy of three women, in the age ranging from 30 to 59 years old, was presented. The patients were subjected to the therapy of lymphatic drainage of abdomen ten times (30 minutes, 2–3 times per week).

There was also a blood test conducted-before and after the therapy. The test included: glycated haemoglobin HbA1c, C-peptide, C reactive protein, lipid panel and blood glucose (point 0 and 120). The patients were given a health questionnaire. The obesity level was defined by the BMI (Body Mass Index) and WHR indicator (weight to hip ratio).

Results: Patient nr 1 (CT): 59 years old, 27,5 kg/m^2; average pressure — 122/85 mm Hg; before/after respectively — HbA1c 5,5%/5,6%; glucose0' — 91/95 mm/dl; glucose120' — 103 mm/dl; total cholesterol — 253/239 mg/dl; HDL — 51/47 mg/dl; LDL — 177/169 mg/dl; triglycerides — 125/109 mg/dl; CRP — 3,6/3 mg/l; C-peptide — 2.95/2.23 ng/ml.

Patient nr 2 (NH): 30 years old, BMI — 35.42 kg/m^2; average pressure — 120/77 mm Hg; before/after respectively HBA1C — 5,6%/5,6%; glucose0' — 105/b.z. mg/dl; glucose120' — 69 mg/dl; total cholesterol — 194/211 mg/dl; HDL — 57/55 mg/dl, LDL — 111/144 mg/dl, triglycerides — 131/61 mg/dl; CRP — 1.3/1.9 mg/l; C-peptide — 2.4/1.9 ng/ml.

Patient nr 3 (CA): 49 years old, BMI — 21,67 kg/m^2; average pressure — 121/74 mm Hg; before/after respectively HBA1C — 5,6%/5,6%; glucose0' — 97/94 mg/dl; glucose120'' — 81 mg/dl; total cholesterol — 213/214 mg/dl, HDL — 67/66 mg/dl; LDL — 135/134 mg/dl; triglycerides — 51/67 mg/dl, CRP < 1/2 mg/l, C-peptide — 1,16/1.21 ng/ml.

Conclusions: The therapy in overweight patient resulted in a decrease of: CRP, few elements of lipid panel, triglycerides, C-peptide. In the case of obese patient, there was an increase of: lipid panel and CRP. However, there was also a decrease in C-peptide and triglycerides. In the case of the patient with proper BMI, the results were the most stable. The continuation of research is necessary to establish if manual lymphatic drainage may be helpful in the treatment of early phases of insulin resistance in obese people.

Key words: manual lymphatic drainage; obesity; overweight; metabolic syndrome; carbohydrate metabolism; lipid metabolism

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SESJA PLAKATOWA/POSTER SESSION

Porównanie skuteczności diety niskowęglowodanowej i wysokotłuszczowej oraz diety z umiarkowaną zawartością węglowodanów i tłuszczu w zmniejszaniu masy ciała oraz parametrów składu ciała u pacjentek z obrzękiem tłuszczowym

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Wstęp: Obrzęk tłuszczowy to zaburzenie charakteryzujące się nadmiernym gromadzeniem podskórnej tkanki tłuszczowej, szczególnie w kończynach dolnych, z wyłączeniem stóp. Leczenie otyłości u tych pacjentów jest kluczowym elementem terapii. Celem pracy było porównanie skuteczności dwóch diet: niskowęglowodanowej i wysokotłuszczowej (LCHF, *low carbohydrate high fat diet*) oraz z umiarkowaną zawartością tłuszczu i węglowodanów (MCMF, *medium carbohydrate medium fat diet*) w zmniejszaniu masy ciała oraz parametrów składy ciała u pacjentek z obrzękiem tłuszczowym.
Materiał i metody: Grupa składała się z 91 kobiet (średni wiek: 44,0 ± 13,5 roku) ze zdiagnozowanym obrzękiem tłuszczowym. Badane kobiety zostały podzielone na 2 grupy. W jednej grupie zastosowano dietę z niską zawartością węglowodanów (6% energii) i wysoką zawartością tłuszczu (> 70% energii) (LCHF; n = 45), a w drugiej grupie dietę o średniej zawartości tłuszczu (39% energii) i węglowodanów (39% energii) (MCMF; n = 46). Obie diety zastosowano przez okres 16 tygodni. Pomiary antropometryczne zostały zebrane na początku i na końcu badania.
Wyniki: Obie diety przyczyniły się do istotnego obniżenia parametrów składu ciała i obwodów wśród badanych pacjentek. Różnice w masie ciała wynosiły –8.2 ± 4.1 kg (w diecie LCHF) *vs.* –2,1 ± 1,0 kg (w diecie MCMF); p < 0,0001. Zawartość tkanki tłuszczowej zmniejszyła się o –4,2 ± 2,1% w grupie LCHF i o –0,9 ± 0,5% w diecie MFMC; p < 0,0001. Dieta LCHF przyczyniła się do zmniejszenia obwodów pasa i bioder w większym stopniu niż dieta MCMF. Obwody ud i łydek uległy znacznemu zmniejszeniu w obu grupach, ale bardziej efektywne w grupie LCHF.
Wnioski: Skuteczniejsza w obniżaniu masy ciała, zawartości tkanki tłuszczowej oraz obwodów kończyn dolnych okazała się dieta LCHF niż MCMF.

Comparison of the effectiveness of low-carbohydrate, high-fat diet with moderate-carbohydrate and fat diet in reducing body weight and body composition parameters in patients with lipedema

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Introduction: Lipedema is a disorder characterized by an excessive accumulation of subcutaneous body fat, particularly in the lower extremities excluding feet. Management of obesity among patients with lipedema is a key component in its treatment. The aim of this study was to compare the effectiveness of two diets: low carbohydrate high fat (LCHF) and medium carbohydrate medium fat (MCMF) in reducing body weight, body fat and lower limb circumference in patients with lipedema.
Material and methods: The study group consisted of 91 women (mean age: 44.0 ± 13.5 years) with lipedema. The participants were divided into two groups following two interventional diets for 16 weeks: low-carb high fat diet (LCHF, n = 45) (6% energy from carbohydrates; > 70% energy from fat) and medium-carb and fat diet (MCMF, n = 46) (39% energy from fat and carbohydrates, equally), which were applied to indicated caloric restrictions. Anthropometric measurements were made at the baseline and after 16 weeks.
Results: Both LCHF and MCMF diets contributed to significant reductions in body composition parameters and body circumferences in patients with lipedema. The difference of body weight after dietary intervention was: –8.2 ± 4.1 kg *vs.* –2.1 ± 1.0 kg for LCHF and MCMF diet, respectively ($p < 0.0001$). The percentage body fat decreased by –4.2 ± 2.1% in LCHF group, and by –0.9 ± 0.5% in MCMF diet ($p < 0.0001$). LCHF diet contributed to greater reduction of waist and hips circumferences than MCMF diet. The circumferences of thighs and calves decreased significantly in both groups, but more effective in LCHF group.

Glycocalyx — clinical aspects

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Properties and clinical role of the glycocalyx (GCX). The barrier of the inner vessel wall is not only formed by the vascular endothelium. The barrier consists of a functionally little-known structure — GCX (1–2 nm on the surface of the Era, 0.1 μm on the endothelium). Let's compare with the size of the erythrocyte! The permeability and thus the sequestration of fluid from the IVP to the IST varies significantly according to the quality and immediate functional state of GCX. GCX is affected by the charge of the ions of the infused solution repulsive force of zeta-potential (see also stability of fat emulsion). A small change in the variable and regulated permeability across GCX barrier leads to significant changes in fluid sequestration from the IVP to the IST (biological amplification). The escape or retention of crystalloids in the systemic circulation is largely determined by GCX.
Conclusion and implications for the design of new ionic formulations of infusion solutions. The negative charge of erythrocytes reflects the properties of endothelial GCX. The GCX hub informs about its quality. The GCX repulsive forces of the erythrocyte surface and the surface of the endothelium are influenced by the „ionic cocktail" of the infusion solution with which it comes into contact. The GCX quality of the capillary wall determines the rate of crystalloid transfer from the IVP to the ISP and thus the length of time the crystalloid remains in the circulation. Theoretically, this opens the way to the development of infusion solutions developed on new principles that are based on the function of GCX.

Zwężenie w początkowym odcinku żyły szyjnej wewnętrznej zaburza odpływ przez tę żyłę i może zmieniać geometrię zastawki zlokalizowanej w dolnym odcinku żyły: wyniki cyfrowego modelowania przepływu

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Wstęp: Obecnie uważa się, że zastawki żyły szyjnej wewnętrznej są podstawową przyczyną zaburzonego przepływu przez te żyły. Innym potencjalnym źródłem zaburzeń są zwężenia tworzące rodzaj dławika w jej górnym odcinku, na przykład spowodowane przez wydłużony wyrostek rylcowaty kości skroniowej.

Materiał i metody: W pracy użyto oprogramowania do cyfrowego modelowania przepływu COMSOL Multiphysics. Modele żył posiadały sztywne zwężenie w początkowym i elastyczną zastawkę w dolnym odcinku. Przepływ modelowano w warunkach przepływu laminarnego, połączonego z mechaniką strukturalną, stosując podejście badające interakcję między płynem i strukturą, gdzie zależność naprężenia ścinającego do odkształcenia ścinającego była Newtonowska. Materiał budujący zastawkę był izotropowo linearnie elastyczny.

Wyniki: W modelach żył z symetryczną dwupłatkową zastawką i bez zwężenia w górnym odcinku lub z niewielkim zwężeniem, przepływ był niezaburzony i laminarny. Płatki zastawki symetrycznie otwierały się i zamykały na skutek wirów powstających za zastawką. W przypadku większego stopnia zwężenia centralny strumień przepływu odchylał się od osi naczynia i powstawały obszary z odwróconym kierunkiem i separacją przepływu. W przypadku zastawki dwupłatkowej wiry powodujące asymetrię przepływu były obecne na całym przebiegu modelowanego naczynia, zaś płatki zastawki były zniekształcane przez asymetryczny przepływ.

Wnioski: Wyniki naszego badania sugerują, że utrudniony odpływ krwi przez żyły szyjne wewnętrzne jest prawdopodobnie głównie wywołany przez patologiczne struktury położone w ich górnych odcinkach, a nie przez patologiczne zastawki szyjne, które do tej pory były głównym obiektem badań. Dodatkowo, nieprawidłowości zastawki mogą być pogłębione przez zwężenie zlokalizowane w górnym segmencie żyły.

Stenosis at the beginning of the internal jugular vein compromises outflow through this blood vessel and can alter the geometry of the jugular valve located downstream: results of numerical modeling of blood flow

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Introduction: Currently, pathological jugular valves are thought to be the main cause of altered hemodynamics in the internal jugular veins. The alternative cause of disturbances are the nozzle-like strictures in their upper parts, for example enlarged styloid processes.

Material and methods: Computational fluid mechanics software, COMSOL Multiphysics, was used for the numerical simulation of the real-time blood flow. The 2-dimensional computational domain involved stenosis at the beginning of the modeled vein and a flexible valve downstream. The laminar flow modeling was coupled with structural mechanics, using the fluid-structure interaction approach, where the constitutive relation for shear stress to shear strain was considered Newtonian. The material of the venous valve was considered isotropic linear elastic.

Results: In the vein models with symmetric 2-leaflet valve and without upstream stenosis, or with minor stenosis, the flow was undisturbed and laminar. Valve leaflets opened and closed symmetrically, due to the vortices developing downstream of the valve. In the case of major stenosis, the centerline velocity was positioned asymmetrically and areas of reverse flow and flow separation developed. In the 2-leaflet model with major stenosis, vortices evoking flow asymmetry were present for the entire course of the model, while the valve leaflets were distorted by asymmetric flow.

Conclusions: Our modeling suggests that an impaired outflow through the internal jugular veins is likely to be caused by pathological strictures in their upper parts, instead of pathological jugular valves that of as yet were the main target of clinical research. In addition, the jugular valve pathology can be exacerbated by strictures located in the upper segments of these veins.

Symulacje odpływu krwi żylnej z mózgu w modelach złożonych z żyły szyjnej wewnętrznej i żylnego splotu kręgowego

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Wstęp: Krew odpływa z mózgu przez dwie alternatywne drogi: żyły szyjne wewnętrzne lub żylny splot kręgowy. Ta pierwsza dotyczy głównie pozycji leżącej, zaś przez drugą krew odpływa w pozycji pionowej. Niewiele wiadomo, jak zmiany patologiczne żyły szyjnej wewnętrznej wpływają na ten wzorzec odpływu.
Materiał i metody: Symulacje przepływu w modelach zapewniających alternatywny przepływ przez żyłę szyjną wewnętrzną lub żylny splot kręgowy wykonano przy użyciu oprogramowania do obliczeniowej mechaniki płynu: Flowsquare+. Mierzono objętości przepływające przez każdą z tych dróg: w modelach odpowiadających geometrii żyły szyjnej wewnętrznej w pozycji leżącej oraz pionowej, jak i w przypadku patologicznych zwężeń tej żyły.
Wyniki: W modelu odpowiadającym pozycji leżącej większość krwi odpływała przez żyłę szyjną, zaś w modelu odpowiadającym pozycji pionowej znaczna część krwi kierowała się do kręgowej drogi odpływu. W ten sposób wykazaliśmy, że nasze modelowanie przepływu było poprawne. Przesunięcie odpływu do kręgowej drogi odpływu było jeszcze większe w modelach ze zwężeniem żyły szyjnej wewnętrznej w jej górnym odcinku, szczególnie współwystępujących ze stenostyczną zastawką tej żyły.
Wnioski: Nasze cyfrowe modelowanie przepływu wnosi nowe spojrzenie na anatomiczne podstawy zaburzonego odpływu żylnego z mózgu spowodowanego przez nieprawidłowości położone poza jamą czaszki.

Simulations of the venous outflow from the brain in models comprising the internal jugular vein and the vertebral venous plexus

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Introduction: Blood flow out of the brain through two alternative pathways: internal jugular veins and vertebral venous plexus. The former route is mainly utilized in the supine body position, the latter in the upright one. Little is known how a pathology of the internal jugular vein affects this pattern.
Material and methods: With the use of computational fluid mechanics software the Flowsquare+ we simulated blood flow the models that enabled alternative outflow through the internal jugular vein or vertebral venous plexus. We measured the volumes flowing through each of these pathways, in the models resembling geometry of the internal jugular vein in the supine and standing body positions, as well as in the settings of pathological strictures of the internal jugular vein.
Results: In the model resembling the supine body position a majority of blood flew out through the jugular pathway. In the model resembling upright body position there was a shift of flow towards the vertebral pathway. This demonstrated that our modeling was correct. This shift of outflow was even higher in the models with strictures in the upper part of the internal jugular vein, especially those coexisting with stenotic jugular valve.
Conclusions: Our in silico studies provide new insight into anatomical background of impaired cerebral venous outflow caused by extracranial abnormalities.

Tętniak tętnicy skroniowej powierzchownej — opis przypadku

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Wstęp: Pierwszy przypadek tętniaka tętnicy skroniowej powierzchownej (TTSP) został opisany w 1742 roku. Od tego czasu zgłoszono niecałe 400 przypadków. Klasyfikacja obejmuje tętniaki rzekome oraz tętniaki prawdziwe stanowiące 5–8% opisanych przypadków.
Opis przypadku: 37-letnia chora została przyjęta do Kliniki celem pogłębienia diagnostyki z powodu powiększającego się od trzech miesięcy guza lewej okolicy skroniowej. W wywiadzie podawała tępy uraz

okolicy skroniowej lewej przed kilkoma laty. Po urazie narastające, pulsujące bóle głowy, początkowo bez wyczuwalnego guza. TTSP lewej uwidoczniono za pomocą ultrasonografii dopplerowskiej, a następnie potwierdzono w obrazie TK. W badaniach laboratoryjnych nie stwierdzono istotnych nieprawidłowości, w tym wartości parametrów zapalnych były prawidłowe. Pacjentkę przedstawiono do klasycznej operacji chirurgicznej resekcji tętniaka.
Dyskusja: W diagnostyce różnicowej guza w okolicy skroniowej należy uwzględnić zmiany skórne, stany zapalne naczyń, głównie olbrzymiokomórkowe zapalenie tętnic oraz zmiany nowotworowe takie jak nerwiak nerwu twarzowego, guz ślinianki przyusznej. TTSP najczęściej są wynikiem tępego urazu okolicy skroniowej. Podstawą leczenia pozostaje otwarta resekcja chirurgiczna. W przypadku umiejscowienia tętniaka w początkowym odcinku tętnicy skroniowej powierzchownej, z uwagi na bliskość nerwu twarzowego warto rozważyć interwencję endowaskularną.

Superficial temporal artery aneurysm — a case report

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Introduction: The first case of superficial temporal artery aneurysm (STAA) was reported in 1742. It is a rare pathology, approximately 400 cases have been reported since then. It can be classified into pseudoaneurysm or spontaneous true aneurysm, 5–8% of all analysed cases.
Case report: A 37-year-old female with a 3-month history of progressively enlarging left temporal mass. The patient reported a history of blunt head trauma over the previous few years. After the incident, she observed an increasing left area headache and no mass associated with the injury at the beginning. The left STAA was first diagnosed with a doppler ultrasound. The diagnosis was confirmed with a CT angiogram. Laboratory tests showed no significant abnormalities, including the values of inflammatory parameters were normal. She was presented for surgical resection of the aneurysm.
Discussion: In the differential diagnosis of left temporal area mass subcutaneous hematoma, inflammatory diseases such as giant cell arteritis, neoplastic disease such as facial nerve schwannoma, and parotid gland tumour should be taken into consideration. STAA in most of the reported cases was associated with blunt head trauma and was diagnosed after 2–6 weeks after the injury incident. Surgical resection of the aneurysm is the most common treatment modality. However endovascular treatment might be considered in a selected group of patients.

Czynniki pro- i anty-angiogenne w zespole stopy cukrzycowej po rewaskularyzacji wewnątrznaczyniowej tętnic kończyn dolnych

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Wstęp: Jedną z metod terapii zespołu stopy cukrzycowej (ZSC) jest przezskórna angioplastyka (PTA) tętnic kończyn dolnych. Niemniej jednak, PTA nie zawsze skutkuje pełnym wygojeniem owrzodzenia. Zaburzenia angiogenezy u pacjentów z ZSC nie są oczywiste i jednoznaczne. Ponadto, zmiany w stężeniach czynników pro- i anty-angiogennych po PTA nie były do tej pory analizowane na szerszą skalę.
Materiał i metody: Do badania włączono 21 pacjentów (71,4% mężczyzn, wiek 64,6 ± 1,7 roku) z ZSC, zakwalifikowanych do PTA. Procesy angiogenne były oceniane przed zabiegiem oraz w trakcie późniejszej obserwacji poprzez pomiar w surowicy krwi stężeń 5 pro- oraz 2 anty-angiogennych czynników. Ocena kliniczna i pomiary hemodynamiczne przeprowadzano 1 dzień przed oraz 1 dzień po zabiegu, jak również 1 i 3 miesiące po PTA.
Wyniki: Podczas 3-miesięcznej obserwacji, 7 pacjentów uzyskało całkowite wygojenie owrzodzeń. Wśród analizowanych czynników, poziom anty-angiogennej angiopoetyny 1 był znamiennie obniżony po PTA w porównaniu ze stężeniem przed zabiegiem (1636,9 *vs.* 3440,5 pg/ml, p = 0,37). Wśród czynników pro-angiogennych, stężenie naczyniowo-śródbłonkowego czynnika wzrostu A (VEGF-A) istotnie spadło po zabiegu (16,23 *vs.* 26,32 pg/ml, p = 0,19). Poziom czynnika wzrostu fibroblastów (FGF) również uległ obniżeniu po 1 miesiącu w porównaniu do stężenia przed PTA (3,5 *vs.* 5,9 pg/ml, p = 0,02).
Wnioski: Skuteczny technicznie zabieg wewnątrznaczyniowy nie zawsze jest równoznaczny z całkowitym wygojeniem owrzodzenia. Patomechanizm tego zjawiska nie jest wciąż w pełni wyjaśniony, jednak zaburzenia w neoangiogenezie podczas procesu gojenia tkanek może pełnić kluczową rolę. Konieczne wydaje się przeprowadzenie analizy w subgrupach celem określenia przyczyn powyższych obserwacji.

Pro- and anti-angiogenic factors in diabetic foot syndrome after endovascular revascularization of lower limb arteries

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Introduction: Percutaneous transluminal angioplasty (PTA) is one of the treatment forms for diabetic foot syndrome (DFS). However, PTA does not always result in complete ulcer healing. Angiogenesis impairments among patients with DFS are not always clear and conclusive. Moreover, changes in pro- and anti-angiogenic factors after PTA have not been analyzed on a wider scale.

Material and methods: The study included 21 patients (age 64.6 ± 1.7 lat, 71.4% male) with diabetic foot syndrome, qualified for PTA. Angiogenic processes were assessed by 5 pro- and 2 anti-angiogenic factors levels measured in the serum before PTA and during follow-up period. Clinical condition and hemodynamical parameters were assessed before PTA, 1 day, 30 days, and 3 months after the procedure.

Results: During 3-month observation, 7 patients achieved complete ulcer healing. Among all analyzed factors, the level of anti-angiogenic angiopoietin 1 was significantly lowered after PTA compared to the level before the intervention (1636.9 *vs.* 3440.5 pg/ml, p = 0,37). However, among pro-angiogenic factors, the concentration of vascular endothelial growth factor A (VEGF-A) significantly decreased after PTA (16.23 *vs.* 26,32 pg/ml, p = 0.19). The level of fibroblast growth factor (FGF) also significantly lowered after 1 month compared to the level before PTA (3.5 *vs.* 5.9 pg/ml, p = 0.02).

Conclusions: Technically successful angioplasty does not always result in ulcer healing. The pathomechanism of this phenomenon is still not fully understood, but neo-angiogenesis disturbations in tissue repair may play an essential role. However, analysis between subgroups seems to be necessary to identify the causes of obtained results.

Mnogie tętniaki rzekome tętnicy udowej powierzchownej i podkolanowej u pacjenta z posocznicą gronkowcową leczonego wcześniej za pomocą angioplastyki balonem uwalniającym paclitaxel z powodu restenozy w stencie

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Wstęp: Brakuje doniesień na temat ryzyka powstawania tętniaków rzekomych u pacjentów leczonych DEB, szczególnie mnogich.

Wyniki: 75-letni pacjent został przyjęty (12.07.2022 r.) z powodu nagłego bólu prawego uda w miejscu tętniącego guza. W dniu 01.07.2022 r. pacjent był wypisany z innego oddziału tutejszego szpitala; zalecono przyjmowanie między innymi 40 mg prednizonu. W badaniu USG przy przyjęciu stwierdzono liczne tętniaki rzekome okalające drożne stenty w prawej tętnicy udowej powierzchownej i podkolanowej (implantowane 2017 r., DEB — 22.12.2020 r.). W badaniu angio-TK kończyny dolnej prawej potwierdzono obecność drożnych stentów w tętnicy udowej powierzchownej i podkolanowej oraz licznych tętniaków rzekomych, z których największy lokalizował się w 1/3 górnej uda; prezentował cechy aktywnego krwawienia, miał wymiary 32 × 18 mm na długości 30 mm (wielkość zacieku 10 × 18 × 24 mm) i był otoczony skrzepliną 43 × 54 × 63 mm. Wymiary pozostałych tętniaków rzekomych w przekrojach poprzecznych od góry w kierunku dystalnym wynosiły: 14 × 17; 5 × 2; 6 × 3; 12 × 10; 10 × 13 mm. Obserwowano wysokie wartości CRP (292 mg/dl), a z krwi wyhodowano *Staphylococcus aureus* przy braku gorączki. Włączono leczenie celowane kloksacyliną *iv.* 4 × 2 g, odroczono zabieg wewnątrznaczyniowy. Tętniaki rzekome na udzie powiększały się jednak, pacjent się anemizował, wymagał przetoczeń 4j koncentratu krwinek czerwonych. W dniu 27.07.2022 roku przeprowadzono amputację prawej kończyny dolnej na poziomie uda z powodu pogarszania się stanu miejscowego i ogólnego oraz utrzymującej się bakteriemii.

Dyskusja: U prezentowanego pacjenta, jako przyczynę powstania mnogich tętniaków rzekomych tętnicy udowej powierzchownej i podkolanowej po prawie 2 latach

od zastosowania DEB, rozważamy nałożenie zakażenie gronkowcowego stentu na toksyczny efekt paclitaxelu.

Numerous pseudoaneurysms of right superficial femoral and popliteal arteries in patient with Staphylococcus aureus bloodstream infection who two years before was treated endovascularly with paclitaxel eluting balloon due to in-stent restenosis

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Introduction: Data concerning occurrence of pseudoaneurysm, especially numerous, in patients treated with DEB and DES are lacking.
Results: Male patient, 75 y. old was admitted on 12th of July 2022 due to sudden thigh pain and presence of pulsatile tumor. On first of July 2022 patient was discharged from another hospital ward. Among other things, the use of 40 mg prednisone was recommended. At admission numerous pseudoaneurysms circumflexing stents implanted into superficial femoral and popliteal arteries were found in USG examination (stenting — 2017, DEB — 12.2020). The computed tomography angiography (CTA) of legs confirmed presence of numerous pseudoaneurysms along superficial femoral artery. The largest was located in 1/3 upper part of thigh and had signs of active hemorrhage (blood flow dimensions: 32 × 18 × 30 mm; blood patch dimensions: 10 × 18 × 24 mm; and cloth: 43 × 54 × 63 mm). The transversal dimensions of remain pseudoaneurysms amounted to (from top to bottom): 14 × 17; 5 × 2; 6 × 3; 12 × 10; and 10 × 13 mm. Moreover, among other things, we observed: elevated C-reactive protein blood concentration (292 mg/dl) and positive blood bacterial cultures (*Staphylococcus aureus*) without fever. Culture guided antibiotic therapy with cloxaciline 4 × 2 g i.v. was applied, endovascular therapy was postponed, external compression was not tolerated. Pseudoaneurysms in thigh enlarged in size, patient required blood transfusions. On July 27, 2022, the right lower limb was amputated at the level of the thigh due to local and general deterioration and persistent bacteremia.
Discussion: In presented case, as the cause of numerous pseudoaneurysms developed in superficial femoral and popliteal arteries after two years after DEB use, we consider overlapping of stent infection with toxic effect of paclitaxel.

Litotrypsja wewnątrznaczyniowa (SHOCKWAVE) tętnicy udowej powierzchownej i podkolanowej w leczeniu niedokrwienia zagrażającego utratą kończyny pacjenta z IV stopniem kalcyfikacji naczyń

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Wstęp: Zwapnienie tętnic może dotyczyć błony środkowej i/lub wewnętrznej naczynia i mieć charakter ekscentryczny, koncentryczny lub ogniskowy. Jego nasilenie może decydować o skuteczności zabiegu rewaskularyzacyjnego, jego wynikach wczesnych oraz odległych. W leczeniu wewnątrznaczyniowym takich pacjentów zaleca się: stosowanie balonów tnących, wysokociśnieniowych, stentów o dużej sile radialnej, stentgraftów, aterektomów rotacyjnych i kierunkowych, a ostatnio także litotrypsję wewnątrznaczyniową (IVL). W Polsce dostępne są tylko zestawy SKOCKWAVE dedykowane tętnicom segmentu udowo- podkolanowego (M5), ale wprowadzane są systemy do tętnic biodrowych i tętnic goleni (M5+, S4).
Opis przypadku: Mężczyzna 72-letni został przyjęty z powodu niedokrwienia zagrażającego utratą lewej (3.12.2021, Rutherford 6) oraz prawej (31.01.2022, Rutherford 4) kończyny dolnej. Wykonano wewnątrznaczyniowe zabiegi udrożnienia tętnic udowych powierzchownych w świetle naczynia, a następnie litotrypsję wewnątrznaczyniową tętnicy udowej powierzchownej i podkolanowej balonem 60 × 5,5 mm z dobrym efektem angiograficznym, bez powikłań zatorowych, bez stosowania DEB i implantacji stentów. W obserwacji ambulatoryjnej, po 6 miesiącach od interwencji, potwierdzono utrzymywanie się poprawy klinicznej, a ultrasonograficznie — pierwotną drożność naczyń obu ud.
Dyskusja: Do dnia dzisiejszego w Klinice Angiologii SU nr 2 wykonano 40 zabiegów litotrypsji wewnątrznaczyniowej, przeważnie u pacjentów z niedokrwieniem zagrażającym utratą kończyny, z dobrym efektem klinicznym: mediana czasu drożności pierwotnej 272

± 42 dni, jedna amputacja po 37 dniach od zabiegu z powodu zmian w tętnicach goleni oraz jeden zgon tego pacjenta (82 lata) po 35 dniach od amputacji. Nie obserwowano innych powikłań.

Endovascular lithotripsy (SHOCKWAVE) of superficial femoral and popliteal arteries in therapy of chronic limb threatening ischemia in patient with IV grade vessel calcification

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Introduction: Arterial calcification may concern both intimal and medial vessel layer, and have form concentric, eccentric and focal. Severity of arterial calcification may affect technical success of procedure, as well as its early and long-term outcomes. In therapy of patients with severe arterial calcification are recommended: cutting balloons, high pressure balloons, stents with high radial force, stengrafts, rotational and directional atherectomy, and recently, also endovascular lithotripsy (IVL). The systems dedicated for femoro-popliteal vascular segment (M5) are available currently in Poland, however, it is planned to provide systems for aorto-iliac and popliteal segments (SHOCKWAVE M5+, S4).
Case report: Seventy-two years old male patient was admitted due to chronic limb threatening ischemia of left (Rutherford 6, 12/3/2021) and right (Rutherford 4, 01/31/2022) legs. During both procedures patency was restored intra-luminary in superficial femoral and popliteal arteries, and next, endovascular lithotripsy using 60 × 5.5 mm balloons was performed, with good direct, angiographic effect, without distal embolization, dissection and perforation. DEB's and stents were not used. During 6-month ambulatory follow-up clinical improvement maintained, and primary vessel patency was confirmed in ultrasonography.
Discussion: Until now we performed 40 procedures of endovascular lithotripsy, mainly in patients with chronic limb threatening ischemia, with good clinical outcome. Median of primary patency is 272 ± 42 days, with one amputation after 37 days after intervention due to lack of run-off, and one death (in the same patient, 82 y, old) on 35 day after leg amputation. The other complications were not observed.

Z deszczu pod rynnę — przypadek 72-letniej pacjentki z przewlekłym niedokrwieniem grożącym utratą kończyny

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Wstęp: Przewlekłe niedokrwienie grożące utratą kończyny (CLTI) jest stanem klinicznym, w którym w przebiegu choroby tętnic obwodowych (PAD) występuje ból spoczynkowy, martwica lub owrzodzenie przez > 2 tygodni. PAD występuje u ponad 200 mln osób, z czego 10% to CLTI, istotnie zwiększające ryzyko zgonu sercowo-naczyniowego.
Opis przypadku: 72-letnia pacjentka obciążona internistycznie, z obustronnym CLTI została przyjęta do rewaskularyzacji prawej kończyny dolnej. Cztery miesiące wcześniej, po nieudanej próbie udrożnienia SFA, wszczepiono żylny pomost udowo-podkolanowy, wykonano endarterektomię CFA i DFA oraz udrożnienie i PTA POP i BTK. Klinicznie występowała niegojąca się rana prawego przodostopia po amputacji 7 miesięcy wcześniej (WIfI 6) oraz obustronny ból spoczynkowy. Udrożniono pomost udowo-podkolanowy, co skutkowało przeciekiem w odcinku środkowym, w miejscu tym wszczepiono stent kryty. Kontrolna angiografia wykazała wielopoziomowe naruszenie ciągłości pomostu i zakontrastowanie tkanek go otaczających, w związku z tym do jego światła podano trombinę zatrzymując krwawienie. U chorej w ciągu godziny po zabiegu wystąpiły objawy ogniskowe, które wraz z wynikiem obrazowania naczyń mózgowia i perfuzji, pozwoliły na rozpoznanie udaru niedokrwiennego. Powtórna analiza obrazów angiograficznych nie wykazała obecności przetok łączących pomost z układem żylnym, a USG tętnic dogłowowych i obrazowanie serca nie uwidoczniły zmian wskazujących na źródło udaru. W ciągu tygodnia od zabiegu objawy ogniskowe stopniowo ustąpiły, a ukrwienie kończyny dolnej prawej było porównywalne do stanu wyjściowego.
Wnioski: Rewaskularyzacja, będąca jedyną szansą na zachowanie kończyny, u pacjentów z CLTI jest obarczona bardzo dużym ryzykiem wystąpienia incydentów sercowo-naczyniowych w okresie okołozabiegowym.

When bad goes worse — a 72-year-old patient with chronic limb-threatening ischemia case report

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Introduction: Chronic limb-threatening ischemia (CLTI) is a clinical state when PAD coexists with rest pain, gangrene or an ulceration > 2 weeks. There are > 200 million of PAD patients worldwide and about 10% of them have CLTI, which significantly increases cardiovascular risk of death.
Case report: A 72-year-old female with multiple internal diseases and bilateral CLTI was admitted to revascularize right lower limb arteries. 4 months prior to admission, the patient has undergone a right side hybrid revascularization with a creation of femoro-popliteal bypass using venous graft after an ineffective attempt to recanalize SFA, CFA&DFA endarterectomy and recanalization and PTA of popliteal and BTK arteries. Clinically there was a non-healing wound of right forefoot after amputation 7 months earlier (WIfI 6) and resting pain of both extremities. A recanalization of the venous bypass caused a leakage in its medial part, so a covered stent was implanted. A control angiography revealed a multilevel destruction of the bypass with contrasting of the surrounding tissues and because of that bovine thrombin was injected to the lumen of the vessel. Within an hour after procedure the patient has developed focal signs and after brain imaging gave a diagnosis of ischemic stroke. Re-analysis of angiographic images did not reveal presence of fistulas between bypass and venous system, carotid ultrasound and cardiac imaging did not reveal any changes indicating the source of stroke. Within one week after the surgery, the focal signs gradually subsided and the blood supply to the right lower limb was comparable to the baseline condition.
Conclusions: Revasularization, which is the only chance for limb preservation, is associated with very high periprocedural risk of cardiovascular events.

Angioplastyka ujścia prawej żyły jajnikowej jako metoda redukcji nadciśnienia wrotnego u pacjentki z nieskutecznym endoskopowym tamowaniem krwawienia żylakowego do przewodu pokarmowego

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Wstęp: Wewnątrznaczyniowe leczenie nadciśnienia wrotnego polega albo na embolizacji splotów okołoprzełykowych (np. BRTO, *balloon-occluded retrograde transvenous obliteration*) albo na przezskórnym wykonaniu przetoki wrotno-systemowej (np. TIPS, *transjugular intrahepatic porto-systemic shunt*).
Opis przypadku: 77-letnia pacjentka została przyjęta do Kliniki Gastroenterologii w dniu 16.11.2021 roku z powodu krwistych wymiotów. Mimo codziennych endoskopowych zabiegów opaskowania żylaków przełyku i żołądka, nie udało się powstrzymać krwawienia do przewodu pokarmowego wymagającego przetaczania 2–4 j. koncentratu krwinek czerwonych na dobę. W badaniu angio-TK nie uwidoczniono miejsca krwawienia, stwierdzono jednak krążenie oboczne ze znacznie poszerzoną żyłą jajnikową prawą (ŻJP). Upatrując poszerzenie ujścia ŻJP do żyły głównej dolnej, jako szansę poprawy odpływu krwi z krążenia trzewnego i redukcji nadciśnienia wrotnego, w dniu 25.11.2021 roku chorą zakwalifikowano do zabiegu angioplastyki ujścia ŻJP balonem 14 mm, uzyskując szybki odpływ, wcześniej zalegającego kontrastu w ŻJP. Krwawienie ustąpiło i chora nie wymagała przetoczeń. Pacjentka zmarła jednak w przebiegu „śpiączki wątrobowej" w dniu 03.12.2021 roku.
Dyskusja: W omawianym przypadku analiza fazy żylnej angio-TK pozwoliła na uwidocznienie względnego zwężenia żyły jajnikowej, która została uznana za miejsce naturalnego, ale niewydolnego shuntu wrotno- systemowego. Angioplastyka ujścia prawej żyły jajnikowej spowodowała zatrzymanie utrzymującego się krwawienia, najwyraźniej jednak nasiliła „przeciek" neurotoksyn do krążenia systemowego, stając się, obok krwi zalegającej w przewodzie pokarmowym, jednym z czynników zaostrzających encefalopatię wątrobową; ta, z kolei, doprowadziła do zgonu chorej.

Right ovarian vein angioplasty as a method of reduction in portal hypertension in female patient with variceal bleeding into digestive tract and inefficient endoscopic treatment

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Introduction: Endovascular treatment of portal hypertension rely on either sclerotherapy/coiling of periesophageal varices (e.g. balloon-occluded retrograde transvenous obliteration, BRTO) or percutaneously making portosystemic shunt (e.g. transjugular intrahepatic porto-systemic shunt, TIPS).
Case report: Female patient, 77 years old was admitted to Clinic of Gastroenterology on November 16, 2021, due to bloody vomiting. Numerous procedures of variceal banding failed and maintained variceal bleeding required everyday blood transfusions due to anemia. Computed tomography visceral angiography (CTVA) showed in venous phase collaterals of visceral veins anastomosed with significantly dilated right ovarian vein (ROV). We assumed that angioplasty of ROV ostium to vena cava inferior, which was too narrow in relation to blood excess in visceral circulation, might be the way for improvement in visceral blood outflow and reduction in portal hypertension. Such procedure was performed on November 25, 2022 from jugular access with balloon 14mm, achieving fast outflow of contrast from ROV to vena cava. During clinical observation the hemorrhage to digestive tract stopped, patients did not require blood transfusion. However, patient died on December 03, 2021, due to exacerbated liver encephalopathy.
Discussion: In presented case, the venous phase of CTVA made possible to image relative narrow ROV ostium, which was assumed as natural but insufficient portosystemic shunt. ROV ostium angioplasty leaded to stopping of variceal bleeding, however we cannot exclude, that, at the same time, it increased the leak of endotoxins, escalating liver encephalopathy, which, in turn, caused patient's death.

Udrożnienie żyły podobojczykowej za pomocą teleskopowego systemu Navicross

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Wstęp: Powikłaniem założenia cewnika dializacyjnego do żyły centralnej może być jej zwężenie lub niedrożność.
Opis przypadku: Pacjentka lat 45, dializowana na cewniku permanentnym w prawej żyle szyjnej wewnętrznej od stycznia 2021 roku, po wytworzeniu przetoki tętniczo-żylnej na prawym ramieniu (05.02.2021 r.), została przyjęta do Kliniki w dniu 22.02.2022 roku z powodu nagłego obrzęku kończyny górnej prawej, żylnego krążenia obocznego na ścianie klatki piersiowej oraz tętniaków ramienia żylnego przetoki. Zabieg wewnątrznaczyniowy wykonano z dostępu przez ramię żylne przetoki. Udało się pokonać niedrożność żyły podobojczykowej i ramienno-głowowej lewej prowadnikiem 0,014'', ale nie można było przeprowadzić cewnika. W celu zwiększenia „siły podparcia", na cewnik Naviscross 0,018'' nałożono „teleskopowo" drugi cewnik do udrożnień Navicross 0,035''. Dzięki temu połączeniu udało się wprowadzić cewniki do żyły głównej górnej, a w jego świetle przeprowadzić sztywny prowadnik 0,035'', co umożliwiło wykonanie angioplastyki żylnej balonem 4, 10 i 14 mm z dobrym efektem angiograficznym, IVUS i klinicznym. Po 3 miesiącach doszło do nawrotu niedrożności żyły i tym razem nie udało się udrożnić naczynia. Chora poprosiła o podwiązanie przetoki z powodu utraty funkcjonalności dłoni prawej.
Dyskusja: Nie można wykluczyć, że całkowitemu zamknięciu żyły ramienno-głowowej prawej i utracie dostępu do dializ zapobiegłaby kolejna, ale wcześniejsza angiografia z implantacją krótkiego stentu lub angioplastyka balonem uwalniającym paclitaxel, ale odpowiedniego stentu nie posiadano, a balony lekowe dedykowane do żył centralnych nie są dostępne w Polsce. W większości przypadków standardowa angioplastyka ramienia żylnego przetoki dializacyjnej zapewnia jej drożność na 3–6 miesięcy.

Subclavian vein patency restoration using telescoping Navicross system

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Introduction: A complication of a dialysis catheter insertion may be narrowing or occlusion of central veins.
Case report: Forty-five years old female patient, who was dialyzed using dialysis catheter inserted to right jugular vein since January 2021, after creation of arterio-venous fistula, brachial-cephalic (02/05/2021 r.), was admitted on February 22, 2022, due to sudden oedema of upper limb, collaterals on chest wall, and aneurysms of venous branch of fistula. Endovascular procedure was performed through 6F access via right cephalic vein. Subclavian and brachiocephalic vein occlusion was crossed using guidewire 0,014'', however it was impossible to put catheter through. To increase support power the catheter Navicross 0.035'' was put telescoping on catheter 0.018''. Vena cava superior was reached and guidewire 0.035'' can be carried through. Venous angioplasty was performed using 4, 10 and 14 mm balloon catheter with good angiographic and IVUS result. Clinically disappearance of right arm swelling and improvement in dialysis quality indices was achieved. After 3 months symptoms recurred, and rescue procedure failed. Patient asked for fistula ligation due to loss of right-hand functionality.
Discussion: We cannot exclude that occlusion of right subclavian vein and loss of vascular access for dialysis could be prevented thorough earlier elective venous angioplasty with drug eluting balloon (DEB), and/or use of dedicated short stent. However, such accessories were no available in Poland. In majority cases, venous branch angioplasty of arterio-venous fistulas for dialysis help to maintain its patency and functionality for 3–6 months.

Przetoka tętniczo-żylna w nerce prawej jako przyczyna niewydolności prawej komory serca

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Wstęp: Przetoka tętniczo-żylna w krążeniu dużym jest wymieniana jako przyczyna przewlekłej niewydolności serca (CHF) ze zwiększoną pojemnością minutową serca.
Opis przypadku: 45-letnia kobieta została przyjęta do Kliniki Ginekologii 27.03.2022 roku z powodu podejrzenia nowotworu jajnika prawego. Pacjentka była konsultowana przez angiologa z powodu szmeru skurczowego w jamie brzusznej stwierdzonego przez kardiologa podczas kwalifikacji do zabiegu. W 01.2022 roku rozpoznano u niej prawokomorową CHF. W badaniu echokardiograficznym stwierdzono między innymi poszerzenie prawej komory serca, ciężką niedomykalność zastawki trójdzielnej (SPS 55 mm Hg). W angiologicznym badaniu USG jamy brzusznej przy przyjęciu stwierdzono wodobrzusze, poszerzenie żyły nerkowej prawej i żyły głównej dolnej od poziomu jej odejścia oraz poszerzenie UKM nerki prawej, w którym stwierdzono niskooporowy przepływ. Wysunięto podejrzenie przetoki tętniczo-żylnej nerki prawej, co potwierdziła ponowna analiza angio-TK ze stycznia 2022 roku. Chorą zakwalifikowano do implantacji stentgraftu (BeGraft Peripheral, Bentley, 6,0) do tętnicy nerkowej prawej. W trakcie zabiegu doszło jednak do perforacji naczynia i konieczna była embolizacja tętnicy nerkowej. Podczas wizyty kontrolnej w dniu 15.07.2022 roku chora nie prezentowała objawów CHF, nerka prawa o długości 65mm miała prawidłową echostrukturę. Stężenie kreatyniny i markerów nowotworowych Ca125, HE4 było w normie. Badanie echokardiograficzne było prawidłowe.
Dyskusja: Badanie fizykalne jamy brzusznej było kluczowe dla rozpoznania przetoki tętniczo-żylnej w nerce prawej, gdyż zmiany USG w nerce można było traktować jak poszerzenie UKM, łatwe do wytłumaczenia obecnością guza jajnika. Wewnątrznaczyniowe

zamknięcie przetoki tętniczo-żylne wyleczyło chorą z CHF.

Arterio-venous fistula in right kidney as a cause of right heart failure

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Introduction: Arteriovenous fistula in a systemic circulation is listed as a cause of chronic heart failure (CHF) with increased ejection fraction and cardiac output.
Case report: Female, 45-years old patient was admitted on March 27, 2022 to Clinic of Gynecology due to suspicion of right ovarian cancer. Patient was consulted by angiologist because of abdominal murmur. In 01/2022 she was hospitalized in another voivodship and was diagnosed as having exacerbated CHF of right ventricle. In echocardiography were found, e.g.: significant right ventricle dilatation, severe tricuspid insufficiency (SPS 55 mm Hg). In abdominal ultrasonography performed by angiologist at admission were found, e.g.: ascites, extension of right renal vein and cava vein, dilated pelvicalyceal system of right kidney with low-resistant blood flow in Doppler imaging. Presence of renal arteriovenous fistula was suspected. It was confirmed in renal hilus in reanalysis of CTA imaging made in 01/2022. Patient was qualified for stent graft implantation (BeGraft Peripheral, Bentley, 6.0). The endovascular procedure was complicated by rupture of renal artery, therefore distal part of renal artery embolization was necessary. During control visit on July 15, 2022, patient was asymptomatic. In USG, right kidney was diminished (65 mm, corex-12 mm). Blood creatinine and cancer biomarkers (Ca125, HE4) concentrations normalized; echocardiography was normal.
Discussion: In this case physical examination (abdominal murmur) was a key point in diagnosis of arteriovenous fistula, because without it, the ultrasound findings of right kidney might be recognized only as dilated pelvicalyceal system secondary to right ovarian tumor. Endovascular closure of arteriovenous fistula healed cardiac failure in this patient.

Zespół antyfosfolipidowy nałożony na trzewną postać choroby Takayasu

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Wstęp: Choroba Takayasu, jako schorzenie autoimmunologiczne, może ona przebiegać w postaci zespołów nakładania.
Opis przypadku: Mężczyzna 40-letni został przyjęty 14.09.2010 roku z powodu martwicy palców stopy prawej. W angio-TK rozpoznano owrzodzenie aorty, niedrożność pnia trzewnego i tętnicy krezkowej górnej. Wykonano badania w kierunku trombofilii, zapaleń naczyń i chorób tkanki łącznej, które wypadły negatywnie. Zalecono leczenie przeciwmiażdżycowe, hipotensyjne oraz warfarynę. W obserwacji ambulatoryjnej owrzodzenia palców wygoiły się, a obraz kliniczny zdominowało oporne nadciśnienie tętnicze na podłożu zwężenia prawej tętnicy nerkowej, którą stentowano w dniu 02.10.2015 roku. W dniu 08.12.2016 roku pacjenta hospitalizowano z powodu marskości nerki prawej (niedrożność stentu), progresji zwężenia aorty. W dniu 15.02.2017 roku pacjenta hospitalizowano z powodu powierzchownych owrzodzeń kończyn dolnych (stopy, golenie, uda). W badaniach laboratoryjnych stwierdzono wzrost miana 3 biomarkerów zespołu antyfosfolipidowego (APS). W kwietniu 2017 roku pacjent został ponownie przyjęty z powodu zespołu nerczycowego (białkomocz 7,5 g/dl, kreatynina 4,2 mg/dl). Po włączeniu steroidoterapii w ciągu tygodnia uzyskano redukcję białkomoczu. Po 3 miesiącach, rozpoznano APS, włączono ASA z warfaryną Owrzodzenia kończyn dolnych wygoiły się po 3–4 miesiącach. Do czerwca 2022 roku pacjent pozostawał w stanie stabilnym, leczony między innymi azatiopryną 1 x 50 mg, aspiryną, warfaryną.
Dyskusja: Trzewna postać choroby Takayasu może objawiać się zatorowością obwodową, nadciśnieniem tętniczym, a zespół antyfosfolipidowy- owrzodzeniami skórnymi i martwicą o lokalizacji nietypowej dla niedokrwienia, które zagojono leczeniem immunosupresyjnym i przeciwzakrzepowym.

Antiphospholipid syndrome overlapping visceral form of Takayasu disease

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Introduction: Takayasu disease, as autoimmunological disease it can course with overlapping syndromes.
Case report: Forty years old male patient was admitted on 09/14/2010, due to toes necrosis of right foot. In computed tomography angiography (CTA) imaging were found: aorta ulcer, occlusion of visceral trunk and superior mesenteric artery. Thrombophilia, vasculitis, and connective tissue diseases were not confirmed. Antiatherogenic, hypotensive therapy and warfarin were recommended. Toys ulcers healed, but the main clinical problem was resistant hypertension cause by right renal artery stenosis, which was stented on 10/2/2015. On 12/8/2016, patient was hospitalized due to right kidney cirrhosis (stent occlusion). On 02/15/2017, patient was admitted due to fast progressing leg skin ulcers. In laboratory examinations elevated titre of 3 biomarkers of antiphospholipid syndrome (APS). In April of 2017 patient was readmitted due to signs of nephrotic syndrome (daily proteinuria 7.5 g/day, creatine — 4.2 mg/dl). After steroidotherapy proteinuria was reduced; APS was diagnosed after obtaining repeated positive blood biomarkers after 3 months; aspirin and warfarin were recommended again. Leg skin ulcers healed after 3–4 months. Until June 2022 patient remain in good state. Patient is treated, i.a. with azathioprine 1 x 50 mg, aspirin, and warfarin.
Discussion: Visceral form of Takayasu disease may manifest as blue toe syndrome, and arterial hypertension. Antiphospholipid syndrome may lead to occurrence of leg skin superficial ulcers with localization not typical for leg ischemia, which can be managed with immunosuppressive therapy and anticoagulants.

Tętnica promieniowa jako alternatywny dostęp do zabiegu angioplastyki i stentowania tętnic obwodowych

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Wstęp: Zabiegi obwodowe najczęściej przeprowadza się z dostępu pachwinowego, systemem 6F. Celem zmniejszenia liczby powikłań miejscowych wprowadza się systemy nisko-profilowe (4F) z dostępu promieniowego.
Opis przypadku: 59-letni pacjent został przyjęty z powodu chromania prawej kończyny dolnej. W USG oraz angio-TK uwidoczniono niedrożność prawej tętnicy biodrowej wspólnej. W dniu 23.02.2022 roku nakłuto lewą tętnicę promieniową i wprowadzono introduktor 4F, 90 cm do dystalnego odcinka aorty brzusznej. Za pomocą prowadnika Glidewire Advantage™ oraz cewnika Rubicon™ (0,014") pokonano niedrożność prawej tętnicy biodrowej. Po predylatacji balonem 3 mm implantowano stent Astron-Pulsar™ 7 x 60 mm. W angiografii kontrolnej uwidoczniono prawidłowo posadowiony stent i brak zwężenia rezydualnego. W miejscu wkłucia nie obserwowano krwiaka ani cech tętniaka rzekomego. W kontroli po 3 miesiącach od zabiegu pacjent nie zgłaszał chromania, potwierdzono w USG drożność stentu.
Dyskusja: Zmiana standardowego dostępu naczyniowego na promieniowy umożliwiła osiągnięcie sukcesu technicznego przy użyciu niskoprofilowego systemu oraz przyspieszyła uruchomienie chorego i jego powrót do sprawności. Wykorzystanie takiego dostępu poprawia bezpieczeństwa zabiegu, skraca czas hospitalizacji, unieruchomienia i utrzymywania opatrunku uciskowego.

Radial artery as an alternative access to angioplasty and arterial stenting

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Introduction: The most frequently used vascular access for angioplasty procedures is the ipsi- or contralateral femoral artery with the use of 6F introducers. Low-profile systems are increasingly used to reduce the number of local complications. Changing access point to the radial artery, as in coronarogrphy, can also reduce complications and improve comfort. The described case shows a patient undergoing successful angioplasty and stenting of the common iliac artery using radial artery access.

Case report: A 59-year-old patient was admitted due to claudication of the right leg. The USG-Doppler and computed tomography angiography examinations showed an occlusion of the right common iliac artery. On February 23, 2022, the left radial artery was punctured and the 4F, 90 cm introducer was introduced into the distal segment of the abdominal aorta. The occlusion was crossed with the Glidewire Advantage TM and the Rubicon TM catheter (0.014"), then after predilatation with a 3mm balloon catheter, the Astron-Pulsar TM 7 x 60 mm stent was implanted. Final angiography showed a correctly positioned stent with no residual stenosis. There was no hematoma or pseudoaneurysm at the injection site. During the standard follow-up, 3 months after the procedure, the patency of the stent was confirmed by USG and clinically resolved from intermittent claudication.

Discussion: The change of the vascular access to the radial artery made it possible to achieve technical success with the use of a low-profile system and accelerated the patient's mobilization and recovery. The use of such access contributes to the improvement of procedure safety, shortening the length of hospitalization, immobilization and compression.

Angioplastyka balonowa tętnicy udowej powierzchownej z wykorzystaniem dostępu poprzez kolaterale

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Wstęp: Osiągnięcie sukcesu technicznego zabiegu wewnątrznaczyniowego w 20% wymaga nakłucia obwodowego. Wiąże się ono z wydłużeniem procedury, wzrostem ryzyka powikłań. W opisywanym przypadku udrożnienie retrograde przeprowadzono, wykorzystując kolateralę łączącą tętnicę głęboką uda (PFA) z tętnicą udową powierzchowną (SFA).

Opis przypadku: W dniu 02.02.22 roku u 67-letniego mężczyzny wykonano zabieg endowaskularny z powodu niegojącej się martwicy palców lewej kończyny dolnej. W angiografii uwidoczniono niedrożność od odejścia lewej SFA, a przepływ odtwarzał się w dystalnym odcinku tętnicy. Podjęto próbę standardowego udrożnienia, jednak nie udało się wprowadzić prowadnika do kikuta proksymalnego SFA. Wobec uwidocznienia szerokiej kolaterali PFA, łączącego się z drożnym odcinkiem SFA zadecydowano o próbie udrożnienia wstecznego tą drogą. Z wykorzystaniem cewników Vert oraz Rubicon™ przeprowadzono prowadnik Asahi Gladius™ 0,014" do SFA i wykonano wsteczne udrożnienie, następnie przeprowadzono balon Sapphire Pro™ 1,5 mm i wykonano predylatację. Następnie z prądem krwi, przeprowadzono kolejny prowadnik i wykonano angioplastykę balonową cewnikami balonowymi 3 mm i 6 mm z dobrym efektem. W angiografii kontrolnej SFA była drożna, niezwężona, nie obserwowano powikłań. W standardowej kontroli po 3 miesiącach uwidoczniono prawidłową drożność SFA, bez cech restenozy a klinicznie uzyskano wygojenie ognisk martwicy.

Dyskusja: W omawianym przypadku wykorzystanie kolaterali do udrożnienia wstecznego ograniczyło konieczność nakłuwania innych tętnic i związanego z tym ryzyka ich uszkodzenia, co jest szczególnie niepożądane u pacjentów z zespołem stopy cukrzycowej.

Balloon angioplasty of the superficial femoral artery using collateral access

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Introduction: Technical success of endovascular procedure due to chronic total obstruction requires a peripheral access in 20%. However, puncture of an peripheral vessel is associated with the prolongation of procedure, and increased risk of complications. In the described case, retrograde revascularization was performed using collaterals connecting the branch of the profunda femoris artery (PFA) with the superficial femoral artery (SFA).

Case report: On 02/02/2022 in 67-year-old patient endovascular revascularization of left lower limb due to non-healing finger necrosis. Angiography revealed an occlusion of the left SFA with no visible stump and the flow was reconstructed in the distal segment of the SFA. An insertion of guidewire into the proximal stump of the SFA failed. Due to the visualization of the wide collateral vessel of the PFA, connecting with the patent segment of the SFA, it was decided to attempt to retrograde restoration using this route. With the use of Vert and RubiconTM catheters, the Asahi GladiusTM 0.014" wire was carried out into the SFA and retrograde revascularization was performed. Then the Sapphire ProTM 1.5mm balloon catheter was delivered and predillation was performed. Then, thorough the bloodstream way, another guidewire was delivered and balloon angioplasty was performed with 3 and 6 mm balloon catheters gathering good angiographic results. On control angiography, the SFA was patent, and no complications were observed. Standard control after 3 months showed patency of the SFA, without restenosis, and clinically healing the necrosis foci and prolonged claudication distance.

Discussion: In the discussed case, the use of collaterals for retrograde revascularization reduced the need to puncture other arteries and the risk of their damage.

Ocena jakości życia pacjentek z zespołem biernego przekrwienia miednicy mniejszej

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Wstęp. Przewlekły ból miednicy dotyka około 25% kobiet, jedną z przyczyn jest zespół przekrwienia biernego miednicy (PCS) w następstwie niewydolności żył i splotów żylnych miednicy mniejszej. Rozpoznanie opiera się na podstawie objawów oraz badań obrazowych USG + doppler, CT, NMR żył miednicy. Epidemiologia oraz wpływ na jakość życia kobiet jest w dalszym ciągu niewystarczająco zbadana. Celem badania była ocena jakości życia pacjentek z PCS.

Materiały i metody: W badaniu wzięły udział pacjentki przyjmowane na Oddział Angiologii celem leczenia wewnątrznaczyniowego metodą embolizacji żył miednicy. Zostały poproszone o wypełnienie kwestionariusza opracowanego przez Uniwersytet w Manchesterze odpowiednio przetłumaczony przez nasz zespół oraz dostosowany do językowo do grupy odbiorców.

Wyniki: 81% pacjentek zgłaszało dolegliwości jak ból i dyskomfort, a 63% doświadczało przewlekłego bólu miednicy przez ponad 3 miesiące. Ból występował podczas menstruacji (57,6%), a także przez resztę miesiąca u ponad połowy badanych (50,8%), przy defekacji (30,5%) i podczas stosunku seksualnego (46%). Negatywne konsekwencje bólu miednicy obejmowały utratę apetytu (50,8%) oraz zaburzenia snu (73%). Prawie 2/3 pacjentek twierdziło, że nie jest w stanie przezwyciężyć bólu — 40% kobiet próbowało złagodzić objawy poprzez przewlekłe stosowanie niesteroidowych leków przeciwzapalnych lub opioidów. Średnia samoocena jakości życia w skali VAS (1-100) wyniosła 70 i była znacząco niższa niż w populacji polskiej (81,4).

Wnioski: Badanie wykazało, że przewlekły ból miednicy ma negatywny wpływ na jakość życia kobiet. Odpowiednia diagnostyka i rozpoznawanie schorzenia oraz leczenie objawów, a także przyczyn leżących u ich podłoża powinny być dostępne i powszechnie stosowane przez lekarzy praktyków.

The impact of pelvic venous disorders on quality of life of female patients

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Introduction: Chronic pelvic pain affects almost 25% women worldwide. One of its causes is pelvic vein incompetence (PVI) which impacts about 15–20% of women's lives, yet its epidemiology and quality of life (QoL) in these patients is very poorly studied. The aim of our study was to assess the quality of life in the patients suffering from pelvic venous disorders.
Materials and methods: In study we enrolled women admitted to Department of Angiology for endovascular treatment. All women were requested to fill special questionnaire based on disease-specific symptoms form designed by University of Manchester.
Results: As many as 81% of the respondents reported ailments such as pain and discomfort on the day of answering the questionnaire. Furthermore, 63% of the questioned women experienced chronic pelvic pain for over 3 months. The reported pain occurs not only during menstruation (57.6%) but throughout the rest of the month as well in over half of the responders (50.8%). It is often immersed with defecation (30.5%) and sexual intercourse (46%). The negative consequences of the pelvic pain included loss of appetite (50.8%) and sleep disturbances (73%). Almost two-thirds of the patients claimed not to be able to overcome the pain. As a consequence 40% of women attempted to alleviate the symptoms by taking the medication. Mean self-assessed quality of life on VAS scale (1-100) equaled 70 lower than Polish general population (81.4).
Conclusions: The study revealed that chronic pelvic pain caused by PeVD often compels women to submit their everyday lives to it. Therefore, prompt diagnosis and efficient treatment of not only symptoms, but also the underlying causes should be readily available as it could directly contribute to increasing the QoL of the patients with PeVD.

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