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Characteristics of patients with acute peripheral arterial ischaemia — a single centre retrospective study

Charakterystyka pacjentów z ostrym niedokrwieniem tętniczym — badanie retrospektywne, jednoośrodkowe

Mariusz Kozak[1], Piotr Myrcha[2], Dawid Siemieniuk[1], Sonia Kardzis[1], Piotr Ciostek[2]

[1]Department of General, Vascular and Oncological Surgery, Mazovian Brodnowski Hospital, Masovian Voivodeship, Warsaw, Poland
[2]1st Chair and Department of General and Vascular Surgery, The Second Faculty of Medicine, Medical University of Warsaw, Poland

Abstract

Introduction. Acute peripheral arterial occlusion is a serious medical condition that requires an immediate action. Delays in diagnosis or treatment could lead to death or serious disability. The appropriate and early clinical evaluation of acute ischaemia is crucial. The goal of therapy for both acute embolic and thrombotic occlusion is reperfusion of the ischaemic organ.

Materials and methods. The aim of this study was a retrospective analysis of the demographic and epidemiological data of patients admitted to Surgical Department of Mazovian Brodnowski Hospital in Warsaw from 2014 to 2018 due to displaying symptoms of acute peripheral arterial ischaemia. 208 patients were evaluated. Our analysis included anthropometric parameters, history of cardiovascular and other important chronic diseases, and addictions. The aetiology, localisation, and type of primary surgery were also assessed.

Results. The analysed group contained 112 men (53.8%, average age: 67.9 years) and 96 women (46.2%, average age: 76.4). We find a statistically significant correlation was found between epidemiological factors [*i.e.* age, hypertension, atrial fibrillation (AF), peripheral artery disease, myocardial infarction, and smoking] and gender. Embolic ischaemia occurred in 50.5% of cases. Thrombosis was diagnosed in the remaining 49.5%. Lower extremity ischaemia occurred most frequently (81.3%). Open embolectomy/thrombectomy was the primary surgery in 155 cases. We find significance of the aetiology in relation to the type of intervention and to the ischaemia localisation, but there was no significance in terms of mortality. The presence of ischaemic heart disease, atherosclerosis and tobacco smoking were relevant factors affecting the aetiology of acute ischaemia.

Conclusion. Acute arterial ischaemia can occur regardless of gender. Embolic and thrombotic aetiologies occur with a very similar frequencies. Upper extremity arterial thrombosis occurs very rarely. An embolism is more often responsible for acute intestinal ischaemia. In patients with atherosclerosis and a history of previous vascular surgery, the presence of a vascular graft/stent graft is associated with a higher risk of arterial thrombosis. Among patients with AF and who were receiving vitamin K antagonists, the average level of international normalized ratio was non-therapeutic.

Key words: atherosclerosis, acute ischaemia, embolus, thrombosis, peripheral artery disease, atrial fibrillation

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Address for correspondence: lek. Mariusz Kozak, Oddział Chirurgii Ogólnej, Naczyniowej i Onkologicznej, Mazowiecki Szpital Bródnowski, ul. Kondratowicza 8, 03–242 Warszawa, Poland, e-mail: kozakmariusz88@gmail.com

Introduction

Acute peripheral arterial occlusion is a serious medical condition that requires an immediate reaction. A delay in diagnosis or treatment can lead to death or serious disability. The appropriate and early clinical evaluation of acute ischaemia is crucial to identify the aetiology of the ischaemic organ. Acute arterial ischaemia can be caused by various factors (Table 1) [1]. The clinical manifestation of acute arterial occlusion depends on the affected organ. A painless acute onset of a neurologic deficit suggests brain ischaemia. Pain, loss of sensation, and later loss of motor function with coexisting low body temperature, pale extremities and pulselessness may be symptoms of upper/lower limb acute ischaemia. Bowel ischaemia manifests as abdominal pain, nausea, vomiting, intestinal paralysis and sometimes diarrhoea [2].

Despite having the same effect as that of acute ischaemia, the clinical presentation of acute embolism versus thrombosis may be different (Table 2) [3]. Most arterial emboli originate from the heart. Atrial fibrillation (AF) is the most common cause of embolism. The most frequent manifestations of cardiac embolic events are strokes and peripheral ischaemic events. Clots formed in the left side of the heart are responsible for 55–87% of peripheral arteries emboli including visceral vessels [4].

The goal of therapy for both acute embolic and thrombotic occlusion is reperfusion of the ischaemic organ. Intravenous heparin administration is the first step in treatment. This prevents propagation of the thrombus both proximally and distally, while maintaining the patency of collateral vessels. Therefore, it will help to reduce the extent of the ischaemic injury. The restoration of arterial blood flow requires open surgery or endovascular intervention (thrombolysis or thrombectomy). The type of treatment depends on the degree of limb ischaemia, the occlusion localisation, the cause of the occlusion (embolic vs. thrombotic), and the general condition of the patient [5].

The aim of this study was a retrospective analysis of the demographic and epidemiological data of patients admitted to the Department of General and Vascular Surgery from January 2014 to November 2018 due to symptoms of acute peripheral arterial ischaemia.

Table 1. Acute arterial ischaemia

Embolic	Thrombotic
Atherosclerotic heart disease (CAD, MI, arrhythmia)	Atherosclerosis
Valvular heart disease (rheumatic, degenerative, congenital, bacterial, prosthetic)	Low flow states (CHF, hypovolemia, hypotension)
Artery-to-artery (aneurysm, atherosclerotic disease)	Genetic states of hypercoagulation
Idiopathic	Vascular grafts (progression of disease, intimal hyperplasia)
Paradoxical embolus	Arterial plaque rupture
Trauma	Aortic/arterial dissection
Iatrogenic	External compression
Other (air, amniotic fluid, fat, tumour, drugs, chemicals)	Trauma
	Iatrogenic

CAD — coronary artery disease; MI —myocardial infarction; CHF — congestive heart failure

Table 2. Differences in clinical presentation of acute arterial ischaemia (embolism vs. thrombosis)

Clinical presentation	Embolism	Thrombosis
Cardiac dysrhythmia	Yes	No
Onset	Sudden	Sudden or slower
Severity of signs and symptoms	Severe	Less severe
History of claudication or rest pain	No	Yes
Risk factors for peripheral vascular disease*	No	Yes
Contralateral pulse exam (limb ischaemia)	Normal	Abnormal
Exam findings of chronic limb ischaemia**	No	Yes

*Risk factors include cardiac disease, prior myocardial infarction, hyperlipidaemia, stroke, family history of peripheral vascular disease, smoking, and diabetes mellitus; **diminished hair growth, thin skin, thick nails, and arterial ulcerations

Materials and methods

Between January 2014 and November 2018, 212 patients were admitted to our Department with a diagnosis of acute arterial ischaemia. An eventual total of 208 patients were evaluated. Four patients were excluded due to the lack of full data. Analysis included basic anthropometrical parameters, a history of cardiovascular and other important chronic diseases, and addictions. The aetiology (embolic or thrombotic), the localisation (lower limb, upper limb, viscera), and the type of primary surgery was also assessed. Laboratory tests at admission were included. Mortality during hospitalisation and within three to 12 months after discharge was also considered. Patients with acute myocardial infarction, arterial injury or ischaemic stroke were excluded from evaluation. Basic statistical analysis regarding variables was made (*t*-Student, χ^2, p value)

Results

The analysed group contained 112 men (53.8%) aged from 31 to 101 years (average 67.9) and 96 women (46.2%) aged from 41 to 95 (average 76.4). The incidence of ischaemic heart disease was similar in the male and female groups, but its complications were significantly more common in men. Myocardial infarction (MI) occurred in 8.3% of the women, but in 25% of the men, despite the fact that males are more often treated invasively [percutaneous coronary intervention (PCI), coronary artery bypass grafting (CABG)]. The appearance of peripheral artery disease (PAD) was more frequently observed in the group of men. Atrial fibrillation was diagnosed twice as often as in women. In the female group stroke, hypothyroidism, peptic ulceration and arthritis were more frequently reported (Table 3). A statistically significant correlation between epidemiological factors (age, hypertension, AF, PAD, MI, PCI, smoking) and gender was found.

Embolic ischaemia occurred in 105 (50.5%) patients. Thrombosis was diagnosed in 103 (49.5%) cases. Lower extremity ischaemia occurred most frequently (81.3%). There were 30 cases of upper extremity ischaemia (14.4%), nearly all as a result of emboli (29 patients). Acute mesenteric ischaemia (AMI) was observed in nine patients (4.3%); in six of these cases superior mesenteric artery/celiac trunk embolism and in the remaining three cases thrombosis due to visceral vessel atherosclerosis.

Open embolectomy/thrombectomy was the primary surgery in 155 cases (74.5%). 54 such procedures (25.7%) were performed due to thrombosis. Endovascular mechanical thrombectomy was performed in 25 cases (12.0%) on 22 patients. Direct catheter thrombolysis (DCT) was the first choice for 26 patients (12.5%). Primary amputation was performed in two patients with thrombosis (1.0%) (Figure 1). Among patients with PAD and a history of previous vascular surgeries, occlusion caused by graft thrombosis occurred in 26 cases (12.5%). Of these, 16 concerned previous femoro-popliteal, one case ilio-femoral, one case femoro-femoral, and eight cases aorto-bifemoral bypass. Only one (0.5%) patient with a history of PAD (ilio-femoral bypass) and atrial fibrillation was admitted with acute limb ischaemia caused by graft embolic occlusion. Thrombosis after previous endovascular treatment occurred in five patients (2.4%) — in three after peripheral stent grafts — one after aortic stent graft — and one after bare stent graft. Popliteal artery aneurysm was the cause of acute limb ischaemia in three cases (1.4%); of these, one case was a primary aneurysm thrombosis, and two cases were of secondary stent graft thrombosis. There was statistical significance of the aetiology in correlation with the type of primary intervention and the ischaemia localisation.

There was no significance in the in-hospital and post-hospitalisation mortality. Overall in-hospital mortality was 13% (27 patients) — 15 deaths in consequence of embolism, and 12 deaths in the course of thrombosis. Post hospitalisation mortality, within three to 12 months of follow up, was 39 (18.8%). Seven patients died due to a stroke, and seven due to myocardial infarction. Peripheral arterial disease and its complications were responsible for seven deaths (3.4%). Cancer was the cause of death of four patients (1.9%). In the other 14 cases (6.7%) of post-hospitalisation death, the cause was different or unknown. Overall mortality in the study group was 66 (31.7%). Table 4 shows the detailed characteristics concerning the aetiology and localisation of ischaemia.

The comparative cardiovascular factors regarding thrombotic or embolic cause of ischaemia are summarised in Table 5. The presence of ischaemic heart disease (IHD), PAD and tobacco smoking were relevant factors according the aetiology of acute ischaemia.

Thrombotic peripheral arterial ischaemia occurred in 100 of 123 patients with a history of PAD (81.3%). Among 85 patients without a history of PAD, arterial thrombosis was observed in three cases (3.5%; one case PAA thrombosis, two cases of idiopathic thrombosis).

Laboratory tests analysis was divided into groups of either thrombotic (T) or embolic (E) aetiology. Mean haemoglobin level was similar in both groups (12.6 g/dL vs. 12.3 g/dL). Mean platelet level in the thrombotic group was 271.8 × 10^3/mL vs. 236.4 × 10^3/mL in the embolic group. Average serum creatinine level was 2.3 mg/dL (T) vs. 1.2 mg/dL (E). International normalized ratio (INR) vas similar in both groups: 1.26 (T) vs. 1.31 (B).

15 patients with a history of AF were treated by vitamin K antagonists (VKA). In this group, INR was below the therapeutic level (mean 1.7). Anticoagulants taken before hospitalisation were divided into two groups in relation to the

Table 3. Comorbidities in correlation with gender

Parameter	Female	Male		p value
Number of pts. (years)	96 (46.2%)	112 (53.8%)	–	–
Age (average)	41–95 (76.4, SD: 10.9)	31–101 (67.9, SD: 11.1)	t(206) = 5.57	**p < 0.005**
BMI (average)	27.1 (SD: 5.37)	25.7 (SD: 4.05)	t(89) = 1.28	p > 0.05
Coronary disease:	41 (42.7%)	44 (39.3%)	$\chi^2(1) = 0.3$	p > 0.05
• myocardial infarction	8 (8.3%)	28 (25.0%)	$\chi^2(1) = 10.2$	**p < 0.01**
• percutaneous coronary intervention	5 (5.2%)	15 (13.4%)	$\chi^2(1) = 4.0$	**p < 0.05**
• coronary artery bypass grafting	1 (1.04%)	6 (5.36%)	$\chi^2(1) = 2.9$	p > 0.05
Chronic obstructive pulmonary disease	3 (3.1%)	7 (6.3%)	$\chi^2(1) = 1.1$	p > 0.05
Peripheral artery disease (PAD)	40 (41.7%)	83 (74.1%)	$\chi^2(1) = 22.5$	**p < 0.0005**
Carotid stenosis	2 (2.1%)	5 (4.5%)	$\chi^2(1) = 0.9$	p > 0.05
Hyperlipidaemia	19 (19.8%)	23 (20.5%)	$\chi^2(1) = 0.1$	p > 0.05
Hypertension	70 (72.9%)	78 (69.6%)	$\chi^2(1) = 4.2$	**p < 0.05**
Diabetes	30 (31.3%)	22 (19.6%)	$\chi^2(1) = 3.7$	p > 0.05
Atrial fibrillation (AF):	43 (44.8%)	25 (22.3%)	$\chi^2(1) = 11.9$	**p < 0.001**
• paroxysmal AF	11 (25.6%)	5 (20.0%)	$\chi^2(1) = 2.6$	p > 0.05
Ventricular arrhythmia	1 (1.0%)	3 (2.7%)	–	–
Neurological symptoms:				
• transient ischaemic attack (TIA)	0 (0.0%)	3 (2.7 %)	–	–
• stroke:				
– ischaemic	19 (19.8%)	13 (11.6%)	$\chi^2(1) = 2.7$	p > 0.05
– haemorrhagic	5 (5.2%)	3 (2.7%)	$\chi^2(1) = 0.9$	p > 0.05
Chronic kidney disease	8 (8.3%)	9 (8.0%)	$\chi^2(1) = 0.0$	p > 0.05
Deep vein thrombosis (DVT)	0 (0.0%)	2 (1.8%)	–	–
Pulmonary embolism (PE)	2 (2.1%)	0 (0.0%)		–
Active cancer	5 (5.2%)	4 (3.6%)	–	–
Hypothyroidism	1 (1.0%)	1 (0.9%)	–	–
Hyperthyroidism	4 (4.2%)	2 (1.8%)	$\chi^2(1) = 1.1$	p > 0.05
Peptic ulcer	8 (8.33%)	2 (1.8%)	$\chi^2(1) = 2.9$	p > 0.05
GI tract bleeding	1 (1.0%)	2 (1.8%)	–	–
Arthritis	6 (6.1%)	3 (2.7%)	$\chi^2(1) = 0.1$	p > 0.05
Alcohol abuse	2 (2.1%)	11 (9.8%)	–	–
Smoking:	25 (26.0%)	45 (40.2%)	$\chi^2(1) = 11.2$	**p < 0.001**
• pack-years (average)	29.7	38.1	–	–

presence of AF or PAD (Table 6, Figure 2A, B). Coexistence of both diseases was found in 34 patients (16.4%). Statistical analysis showed a significant correlation between the occurrence of AF/PAD and anticoagulants/antiplatelet drugs administration before hospitalisation.

Discussion

Acute arterial ischaemia caused by an embolism secondary to valvular heart disease was the most common cause. Thrombosis occurred on the base of severe, vulnerable

Table 4. Aetiology, localisation and detailed characteristics of ischaemia

Parameter	Embolism		Thrombosis
Total	105 (50.5%)		103 (49.5%)
Lower extremity		169 (81.3%)	
	70 (33.7%)		99 (47.6%)
Upper extremity		30 (14.4%)	
	29 (13.9%)		1 (0.5%)
Acute mesenteric ischaemia		9 (4.3%)	
	6 (2.9%)		3 (1.4%)
Type of primary intervention			
Open surgery		155 (74.5%)	
	101 (48.6%)		54 (26.0%)
Endovascular thrombectomy		25 (12.0%)	
	3 (1.4%)		22 (10.6%)
Direct catheter thrombolysis (DCT)		26 (12.5%)	
	1 (0.5%)		25 (12.0%)
Primary amputation	0 (0.00%)		2 (1.0%)
Vascular graft occlusion	1 (0.5%)		26 (12.5%)
Stent occlusion	0 (0.00%)		5 (2.4%)
Popliteal artery aneurysm (PAA)	–		3 (1.4%)
In-hospital mortality		Overall: 27 (13.0%)	
	15 (7.2%)		12 (5.8%)
Post-hospitalisation mortality		Overall: 39 (18.8%)	
	25 (12.0%)		14 (6.7%)
	χ^2		p value
Type of primary intervention	**54.031**		**0.000**
Previous vascular surgeries	–		–
Location	**32.820**		**0.000**
In-hospital mortality	0.383		0.536
Post-hospitalisation mortality	3.819		0.051

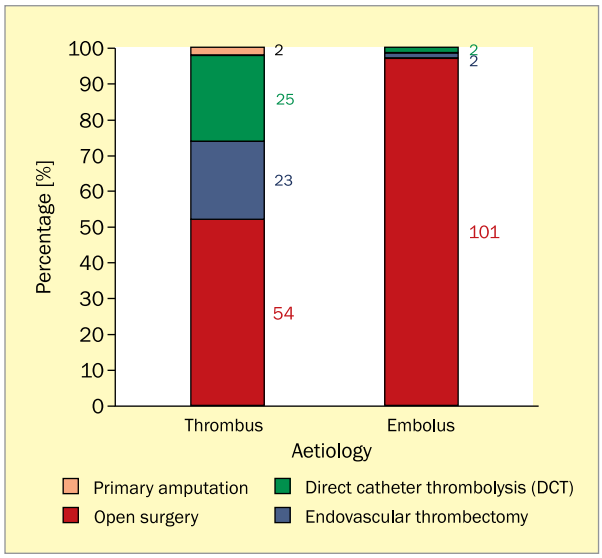

Figure 1. Type of primary intervention depending on the aetiology

atherosclerotic lesions [6]. Theories concerning the aetiology of acute ischaemia have changed over recent years. More recent studies have confirmed the increasing rate of a thrombotic cause of acute ischaemia [7].

In our presented study, the number of patients was comparable in both groups. In the material presented by Hemingway et al., acute limb ischaemia caused by arterial thrombosis was observed four times more often compared to an embolism [8], and a similar result was demonstrated by Genovese et al. [9]. After excluding thrombosis related to previous surgery, the primary cause of ALI was similar to our material. Serum creatinine level was higher in the thrombotic group and it has been proved that impaired renal function is a risk factor for PAD and thrombotic complications [10]. Some studies have shown that patients with acute limb ischaemia have a slightly higher rate of cerebrovascular disease (CVD) [11]. Our study showed no difference between the thrombotic and embolic groups in terms of CVD rate. The thrombosis group represents an

Table 5. Comparison of cardiovascular factors regarding the aetiology of acute ischaemia

Parameter	Total	Embolism	Thrombosis		p value
Average BMI	26.3	26.6	26.1	t(89) = 0.71	p > 0.05
PAD	123 (59.1%)	23 (21.9%)	100 (97.1%)	**$\chi^2(1) = 124.2$**	**p < 0.0005**
Diabetes	52 (25.0%)	30 (28.6%)	22 (21.4%)	$\chi^2(1) = 1.6$	p > 0.05
Smoking	63 (30.3%)	23 (21.9%)	40 (38.8%)	**$\chi^2(1) = 10.0$**	**p < 0.01**
IHD	85 (40.9%)	51 (48.6%)	34 (33.0%)	**$\chi^2(1) = 5.5$**	**p < 0.05**
MI	36 (17.2%)	15 (14.3%)	21 (20.4%)	$\chi^2(1) = 2.2$	p > 0.05
CVD	43 (20.7%)	20 (19.1%)	23 (22.3%)	$\chi^2(1) = 0.8$	p > 0.05
Carotid stenosis	7 (3.4%)	4 (3.8%)	3 (2.9%)	$\chi^2(1) = 0.2$	p > 0.05

BMI — body mass index; PAD — peripheral artery disease; IHD — ischaemic heart disease; MI — myocardial infarction; CVD — cerebrovascular disease (transient ischaemic attack/stroke)

Table 6. Anticoagulants and antiplatelet drugs administration before hospitalisation

	Disease (no. of patients)	AF (68)	PAD (123)
Antithrombotic drug	VKA	16 (23.5%)	8 (6.5%)
	Anti-IIa	4 (5.9%)	3 (2.4%))
	Anti-Xa	6 (8.8%)	6 (4.9%)
	LMWH	3 (4.4%)	2 (1.6%)
	ASA	6 (8.8%)	23 (18.7%)
	SAPT	2 (2.9%)	13 (10.6%)
	DAPT	1 (1.5%)	15 (12.2%)
	None	37 (54.4%)	53 (43.1%)
	χ^2	p value	
AF	50.342	0.000	
PAD	19.275	0.004	

AF — atrial fibrillation; PAD — peripheral artery disease; VKA — vitamin K antagonists; Anti-IIa — direct thrombin inhibitor; Anti-Xa — factor Xa inhibitor; LMWH — low molecular weight heparin; ASA — acetylsalicylic acid only; SAPT — single antiplatelet therapy (clopidogrel or cilostazol); DAPT — dual antiplatelet therapy

extremely high percentage of PAD (97.1%). Active smoking was observed more often (38.8%) in the thrombotic group. Smoking is also an obvious risk factor for atherosclerosis and renal failure [12].

In the analysed group of patients treated due to arterial embolism while receiving VKA, the INR level was non-therapeutic (mean 1.7) [13]. In the groups of patients with AF and PAD history, there was a very high rate of patients without any antithrombotic treatment before hospitalisation (AF 54.4%. PAD 43.1%).

Acute upper limb ischaemia occurs less frequently than the lower limb variation. The most common cause of arm ischaemia is a cardiac embolism. Atherosclerosis, except of the subclavian arteries, is rare in upper limb arteries. Thoracic outlet syndrome and proximal subclavian artery aneurysm are other rare causes of embolisation. Arm ischaemia threatens the limb to a lesser extent, and the treatment decision is thus less urgent. The main reason

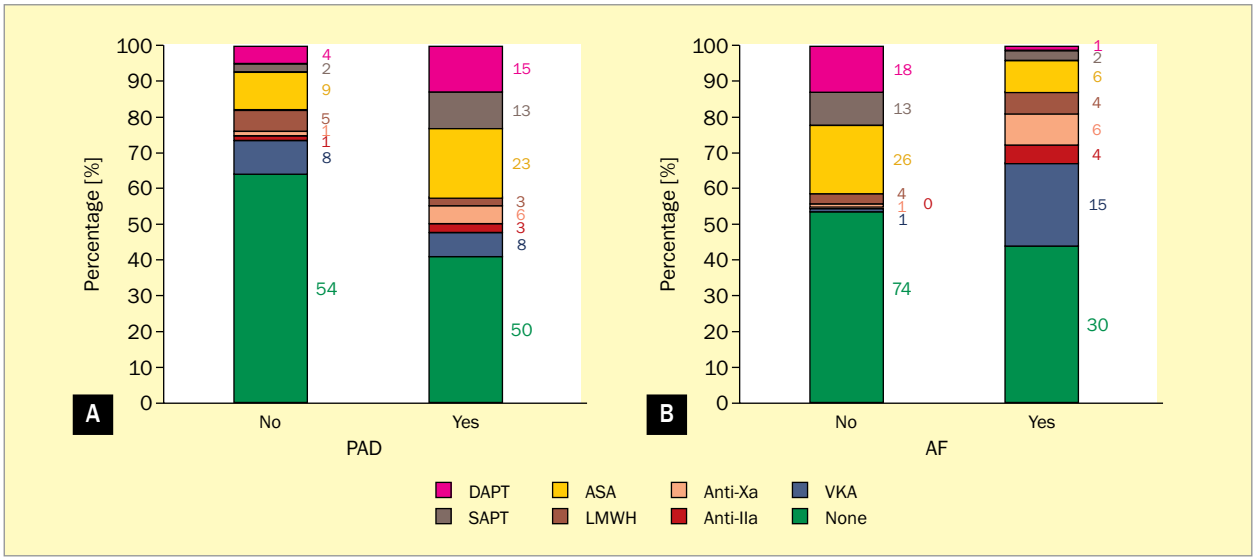

Figure 2A, B. Anticoagulants and antiplatelet drugs administration in correlation to presence of peripheral artery disease (PAD)/atrial fibrillation (AF); DAPT — dual antiplatelet therapy; SAPT — single antiplatelet therapy; ASA — acetylsalicylic acid; LMWH — low molecular weight heparin; Anti-Xa — factor Xa inhibitor; — direct thrombin inhibitor; VKA — vitamin K antagonists;

is to prevent late complications such as arm fatigue and chronic pain [14–16].

Acute mesenteric ischaemia (AMI) is uncommon. Women are affected three times more often than men [17]. Arterial embolism is the most common pathophysiology of AMI [18]. In contrast, data from our study shows that AMI occurred 3.5 times more often in the male group (seven males vs. two females) despite a significantly lower AF rate.

Popliteal artery aneurysm is relatively uncommon, with an estimated incidence rate of 0.1–2.8% and has been shown to be a rare cause of thromboembolism [19].

Our study presents the comprehensive characteristics of patients with acute arterial ischaemia. However, in order to draw clinical conclusions, a multi-centre analysis and a larger group of patients would be required.

Conclusions

Acute arterial ischaemia occurs regardless of gender. In our material, ischaemia caused by embolus and thrombus occurred with similar frequencies. Upper extremity arterial thrombosis occurs very rarely. An embolism is more often responsible for acute intestinal ischaemia. In patients with a history of PAD and a history of previous vascular interventions, the presence of a vascular graft/stent graft is associated with a higher risk of arterial thrombosis. Among patients with AF and receiving VKA, the average of level of INR is non-therapeutic.

Conflict(s) of interest

The authors report no conflict of interest.

Streszczenie

Wstęp. Ostra niedrożność tętnicy obwodowej może prowadzić do niedokrwienia zaopatrywanego przez nią narządu wymagającego pilnej reakcji. Opóźnienie w rozpoznaniu i leczeniu może doprowadzić do śmierci lub inwalidztwa.

Materiał i metody. Celem pracy była retrospektywna analiza danych demograficznych i epidemiologicznych pacjentów z objawami ostrego niedokrwienia przyjętych do kliniki autorów w latach 2014–2018. Badana grupa obejmowała 112 mężczyzn (53,8%; średni wiek 67,9 roku) i 96 kobiet (46,2%; średni wiek 76,4 roku). Ocena uwzględniała dane antropometryczne, wywiad chorób układu sercowo-naczyniowego, innych chorób przewlekłych i uzależnień. Analizowano przyczynę i lokalizację niedokrwienia oraz rodzaj interwencji chirurgicznej.

Wyniki. Zauważono istotny związek między płcią a wiekiem, nadciśnieniem tętniczym, migotaniem przedsionków, miażdżycą obwodową, zawałem serca, paleniem tytoniu. Niedokrwienie na podłożu zatorowym wystąpiło w 50,5% przypadków, a zakrzepica tętnicza — w 49,5%. Niedokrwienie kończyny dolnej występowało najczęściej (81,3%). Otwarta embolektomia/trombektomia była pierwotną operacją w 155 przypadkach. Stwierdzono istotny związek między etiologią niedokrwienia a chorobą niedokrwienną serca, niedokrwieniem kończyn dolnych, paleniem tytoniu, rodzajem interwencji i lokalizacją zmian. Nie stwierdzono istotnej różnicy w śmiertelności.

Wnioski. Ostre niedokrwienie tętnicze może wystąpić niezależnie od płci. Ostre niedokrwienie kończyny górnej w następstwie zakrzepu tętniczego występuje bardzo rzadko. Zator jest częściej odpowiedzialny za ostre niedokrwienie jelit. Pacjentów z miażdżycą tętnic obwodowych i po przebytych operacjach naczyniowych cechuje zwiększone ryzyko zakrzepicy tętniczej. Wśród pacjentów z wywiadem migotania przedsionków przyjmujących antagonistów witaminy K wartość międzynarodowego współczynnika znormalizowanego jest często nieterapeutyczna.

Słowa kluczowe: miażdżyca, ostre niedokrwienie, zator, zakrzep, choroba tętnic obwodowych, migotanie przedsionków

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