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## Leriche syndrome – the analysis of 502 cases. Novel or already known issues?

### Zespół Leriche'a – analiza 502 przypadków. Nowe czy znane aspekty?

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Leriche syndrome, atherosclerosis of the aorta, carotid arteries and other peripheral arteries, screening, Doppler ultrasound

#### Słowa kluczowe

zespół Leriche'a, miażdżycy aorty, tętnic szyjnych i obwodowych, screening, USG-Doppler

#### Conflict of interest

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None  
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#### Summary

**Introduction.** Leriche described a specific constellation of symptoms in 1923. Current techniques enable physicians to quickly diagnose patients with this syndrome, while surgical and endovascular techniques. Only few authors noticed that there are some clinical and epidemiological differences in the population of patients with Leriche syndrome (LS).

**Aim.** The primary aim of this study was to evaluate the incidence and severity of atherosclerotic lesions in extracranial segments of carotid arteries in patients with atherosclerosis of abdominal aorta and arteries of the lower extremities suffering from Leriche syndrome. The additional aim was to analyse a population of patients with Leriche syndrome in terms of epidemiological and risk factors for atherosclerosis and its clinical manifestation.

**Material and methods.** Study group consisted of 1000 patients treated for chronic diseases of aorta and lower limb arteries and LS was diagnosed in 502 of them. Each patient had an duplex ultrasound of extracranial segments of carotid arteries performed. Statistical analysis of the obtained results was performed with regard to age, sex, atherosclerosis risk factors, cardiovascular diseases and previous vascular surgeries.

**Results.** Atherosclerotic lesions in carotid arteries were found in 72.7% of LS patients. Stenoses of over 50%, 70% and occlusions were found in 9.1 and 17.3%, 4.3 and 8.1%, 2.9 and 10.5% of patients with isolated form of LS and LS with concomitant arterial lesions, respectively. These differences were statistically significant.

**Conclusions.** A strong positive correlation between the severity and multi-level localisation of atherosclerotic lesions, and incidence and severity of carotid lesions was observed. Statistically significant differences concerning age, sex, carotid lesion distribution and the presence of > 50%, > 70% stenoses and occlusion was observed between patients with isolated Leriche syndrome and patients with multi-level atherosclerotic lesions in the arteries. The results of the study suggest that there are two different populations of patients with LS. The clinical differences between these two patient populations are probably caused by various arterial pathomorphology.

#### Streszczenie

**Wstęp.** Zespół Leriche'a został opisany w 1923 roku. Dzięki metodom diagnostycznym możliwe jest jego rozpoznanie, a operacje chirurgiczne i wewnątrznaczyniowe pozwalają skutecznie go leczyć. Zaledwie kilku autorów zwróciło uwagę na pewne odmienności kliniczne i epidemiologiczne dotyczące patologii tętnic u pacjentów z zespołem Leriche'a.

**Cel pracy.** Pierwszorzędowym celem tego badania była ocena częstości występowania i rozległości zmian miażdżycowych w pozaczaskowych odcinkach tętnic szyjnych u pacjentów z miażdżycą aorty brzusznej i tętnic kończyn dolnych, u których rozpoznano zespół Leriche'a. Dodatkowym celem badania była analiza populacji pacjentów z zespołem Leriche'a pod kątem epidemiologii i czynników ryzyka miażdżycy oraz jej manifestacji klinicznej.

**Materiał i metody.** Badanie przeprowadzono na grupie 1000 osób leczonych z powodu przewlekłych chorób aorty brzusznej i tętnic kończyn dolnych, wśród których było 502 chorych z zespołem Leriche'a (ZL). U wszystkich pacjentów zbadano pozaczaskowe odcinki tętnic szyjnych metodą kolorowego Dopplera. Dokonano analizy statystycznej wyników oraz wieku badanych, płci, czynników ryzyka miażdżycy, chorób układu krążenia i przebytych operacji naczyniowych.

**Wyniki.** Zmiany miażdżycowe w TSZ stwierdzono łącznie u 72,7% pacjentów z ZL. Zwężenia > 50%, > 70% i niedrożności naczyń szyjnych obserwowano w grupie IZL z częstością wynoszącą odpowiednio 9,1; 4,3 i 2,9%, natomiast w grupie WZL: 17,3; 8,1 i 10,5%. Różnice pomiędzy grupami osiągnęły istotność statystyczną.

**Wnioski.** Wśród pacjentów z zespołem Leriche'a stwierdzono silną dodatnią zależność pomiędzy stopniem zaawansowania oraz wielopoziomą lokalizacją zmian w tętnicach kończyn dolnych a częstością występowania i stopniem zaawansowania zmian w tętnicach szyjnych. Stwierdzono istotną statystycznie różnicę pod względem wieku, płci, obecności i rozkładu zmian w tętnicach szyjnych oraz zwężeń > 50%, 70% i niedrożności, pomiędzy pacjentami z IZL a pacjentami z WZL. Na podstawie wyników przeprowadzonego badania można przypuszczać, że mamy do czynienia z dwiema populacjami pacjentów z zespołem Leriche'a, a różnice kliniczne pomiędzy nimi są prawdopodobnie spowodowane odmienną patomorfologią tętnic.

## INTRODUCTION

Clinical manifestation of occlusion of aortic bifurcation and/or iliac arteries includes a group of symptoms indication chronic limb ischemia. It was first described by French surgeon Rene Leriche (1-4). Predisposing factors include male sex and other risk factors for atherosclerosis (5, 6). Modern imaging modalities facilitate the diagnosis of Leriche syndrome, and surgical reconstruction methods and endovascular procedures provide effective therapy for such patients (7-10). Many articles concerning Leriche syndrome have been published, yet only few authors observed some discrepancies in the arterial pathology and heterogeneity of patient population, both in terms of clinical and epidemiological factors (4, 11).

## AIM

The primary aim of this study was to evaluate the incidence and severity of atherosclerotic lesions in extracranial segments of carotid arteries in patients with atherosclerosis of abdominal aorta and arteries of the lower extremities suffering from Leriche syndrome.

The additional aim was to analyse a population of patients with Leriche syndrome in terms of epidemiological and risk factors for atherosclerosis and its clinical manifestation.

## MATERIAL AND METHODS

The study was performed in a group of 1000 patients reporting to the Copernicus Memorial Voivodeship Comprehensive Centre for Oncology and Traumatology, Lodz, Poland (Wojewódzkie Wielospecjalistyczne Centrum Onkologii i Traumatologii im. M. Kopernika w Łodzi), who had been treated there due to chronic disease of aorta and lower limb arteries. A total of 502 patients with Leriche syndrome have been identified in this population, 94 of which were women (18.7%) and 408 were men (81.3%) aged 39 to 86 years old (mean age  $58.69 \pm 9.95$ ). Ultrasound examination of abdominal aorta, arteries of lower limbs and extracranial segments of carotid arteries were performed in Imaging Diagnostic Laboratory by the same, experienced physician (PK) using a PowerVision 6000 SSA-370A device (TOSHIBA) equipped with convex (3-6 MHz) and linear (8-12) transducers.

Each patient had a duplex Doppler ultrasound of abdominal aorta and arteries of lower limbs performed (colour coded ultrasound – CCU) to determine the type, localisation and severity of atherosclerotic lesions and to evaluate the disturbances in arterial blood flow. It was assumed for the analysis, that stenoses of 50% or greater, including vessel occlusion, are hemodynamically significant. The patients with Leriche syndrome were divided into two groups depending on the localisation of the lesions:

Group A – isolated atherosclerotic lesions in aorto-iliac segment: 207 subjects (41.2%), 53 of which were women (25.6%) and 154 were men (74.4%) aged 39 to 78 years (mean age  $56.24 \pm 8,81$  years).

Group B – atherosclerotic lesions in femoro-popliteal segment, concomitant to atherosclerotic lesions in aorto-iliac segment: 295 subjects (58.8%), 41 women (13.9%) and 254 men (86.1%), aged 40 to 86 years (mean age  $61.15 \pm 9.05$  years).

The ultrasound evaluation of atherosclerotic lesions in extracranial segments of carotid arteries was performed based on analysis of flow velocities and its spectrum. The degree of arterial stenosis was based on calculation of percent diameter stenosis, which compared the diameter of the greatest stenosis with the diameter of intact internal carotid artery over the stenosis using NASCET method. The percent diameter stenosis of the carotid arteries calculated by the computer was used to qualify the patients into one of the following six subgroups:

- a – no atherosclerotic lesions (0%),
- b – low grade stenosis (1-29%),
- c – medium-grade stenosis, hemodynamically insignificant (30-49%),
- d – medium-grade stenosis, hemodynamically significant (50-69%),
- e – high-grade stenosis (70-99%),
- f – arterial occlusion (100%).

The analysis of obtained data was based on the data provided by the patient during anamnesis, including their age, sex, atherosclerosis risk factors (smoking – S, diabetes – DM, arterial hypertension – HA, hypercholesterolemia – Chol), atherosclerosis-related

diseases (ischemic heart disease – IHD, myocardial infarct), as well as cardiac and vascular surgeries performed due to atherosclerosis.

**Statistical analysis**

Obtained results were subjected to statistical analysis using both Excel and Statgraphics Plus v. 5.0 software. The structure of patients estimated according to the observed features was described using fractions. Structure indices were used to describe the qualitative features (non-measurable) in the studied group of patients. If the group was small the indices were presented as fractions, not percentages. For measurable (quantitative) features an arithmetic mean was calculated, as an average value, and standard deviation, as the dispersion of the values. Maximal and minimal values were presented as well. To compare the calculated arithmetical means a test for two means was used: a) for large samples (for  $n_1, n_2 > 30$ ), b) for small samples (for  $n_1, n_2 < 30$ ). The differences between studied parameters (incidences, arithmetical means) were considered statistically significant when the calculated test value was equal or larger from the critical value read from the table of  $\chi^2$  distribution (normal, Student's t) for appropriate number of degrees of freedom and probability of bias  $p < 0.05$ . Correlation analysis was performed to determine the relationship between the values of the studied features. Regression equations were computed for significant correlations, linear correlation coefficients (Pearson's r) and regression equations  $y = ax + b$  were calculated. Student's t distribution with N-2 degrees of freedom was used to estimate the correlation significance.

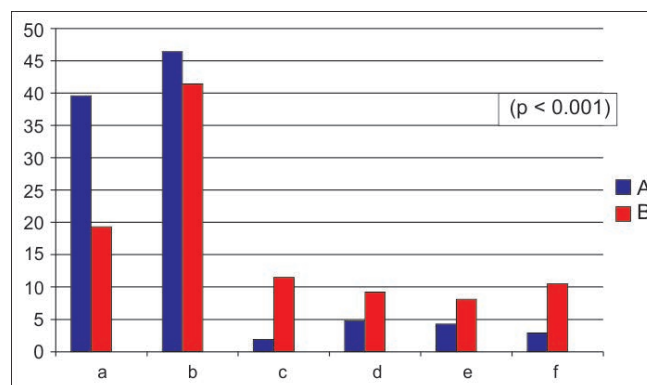
**RESULTS**

In a population of 1000 patients, atherosclerotic lesions in aorto-iliac segment (Leriche syndrome) were detected in 502 subjects (50.2%). They were isolated in 207 patients (42.2%), while concomitant femoropopliteal lesions were found in 295 subjects (58.8%). Atherosclerotic lesions in extracranial segments of carotid arteries were detected in 363 patients (72.3%) diagnosed with Leriche syndrome. Medium- (> 50%) and high-grade (> 70%) carotid artery stenoses were found in 70 (14%) and 33 (6.6%) of patients, respectively. Carotid artery occlusion was observed in 37 subjects (7.4%). The incidence of atherosclerotic lesions in carotid arteries was higher in group B and was twice as high for  $\geq 50\%$  and  $\geq 70\%$  stenoses than in group A. The carotid artery occlusion was detected thrice as often in group B, than in group A. The presence of atherosclerotic lesions in carotid arteries in the entire population and particular groups of patients is presented in table 1. The distribution of atherosclerotic lesions in carotid arteries in the studied population of patients with Leriche syndrome is presented in figure 1. The analysis of risk factors and other anamnesis-relevant data for the entire studied population and groups A and B are as follows (tab. 2).

**Tab. 1.** Characteristic of carotid lesions in patients with Leriche syndrome

Carotid arteries	Total	%	A	%	B	%
No stenosis	139	27.7	82	39.6	57	19.3
Any stenosis	363	72.3	125	60.4	238	80.7
$\geq 50\%$	70	14.0	19	9.1	51	17.3
$\geq 70\%$	33	6.6	9	4.3	24	8.1
Occlusion	37	7.4	6	2.9	31	10.5

A – patients with isolated atherosclerotic lesions in aorto-iliac segment; B – patients with multi-level atherosclerotic lesions in aorta and arteries of the lower extremities



**Fig. 1.** Distribution of carotid arteries lesions in particular groups of patients with Leriche syndrome

A – patients with isolated atherosclerotic lesions in aorto-iliac segment; B – patients with multi level atherosclerotic lesions in aorta and arteries of the lower extremities; a – no atherosclerotic lesions (0%); b – low grade stenosis (1-29%); c – medium-grade stenosis, hemodynamically insignificant (30-49%); d – medium-grade stenosis, hemodynamically significant (50-69%); e – high-grade stenosis (70-99%); f – arterial occlusion (100%)

**Tab. 2.** Incidence of atherosclerosis risk factors and cardiovascular data in patients with Leriche syndrome

Group	n	S	DM	Chol	HA	Heart	CNS	Surgery
A	207	162	12	12	51	35	15	16
%	41.2	78.3	5.8	5.8	24.6	17.0	7.25	7.7
B	295	221	17	11	67	44	19	29
%	58.8	74.9	5.8	3.7	22.7	15.0	6.4	9.8

A – patients with isolated atherosclerotic lesions in aorto-iliac segment; B – patients with multi level atherosclerotic lesions in aorta and arteries of the lower extremities; S – smoking; DM – diabetes mellitus; Chol – hypercholesterolemia; HA – arterial hypertension; Heart – atherosclerotic complications concerning coronary arteries (ischemic heart disease, myocardial infarct); CNS – atherosclerotic complications concerning cerebral arteries (TIA, stroke); surgery – surgical repair of atherosclerotic lesions in aorta and arteries of lower extremities (bypass grafting, PTA/stenting, limb amputation, other procedures)

A difference between both groups was observed for mean age:  $56.24 \pm 8.81$  years in group A and  $61.15 \pm 9.05$  in group B, and it was statistically significant ( $p < 0.05$ ). Statistically significant differences were observed for sex distribution in both groups ( $p < 0.001$ ). Both the presence and distribution of atherosclerotic lesions in carotid arteries were statistically significantly different in both groups ( $p < 0.001$ ). The incidence of lesions observed in carotid arteries, including medium- ( $\geq 50\%$ ), high-grade ( $\geq 70\%$ ) stenoses and occlusions was statistically significantly different in the stud-

ied groups. The analysis of atherosclerosis risk factors considered individually and together did not reveal and statistically significant difference between the groups. The distribution of incidence of carotid artery lesions in studied groups was similar in terms of the number of risk factors.

## DISCUSSION

The occlusion of distal aorta and/or iliac arteries, referred to as Leriche syndrome affects 30-40% of patients with chronic limb ischemia (CLI) (1-4). It is more common among men than women in their third-sixth decade of life and is associated with the following risk factors: arterial hypertension, diabetes, hyperlipidaemia and smoking (5, 6, 10).

The age of our patients ranged from 39 to 86 years, while mean age was  $58.69 \pm 9.95$  years. Patients with isolated aorto-iliac lesions were statistically significantly younger than those with concomitant femoro-popliteal changes ( $56.24 \pm 8.81$  vs.  $61.15 \pm 9.05$ ). There were 94 women (18.7%) and 408 men (81.3%) in the group of 502 patients with Leriche syndrome. A greater percentage of women was observed in the group of patients with isolated aorto-iliac lesions than in group with concomitant femoro-popliteal changes (1:3 vs. 1:5). The analysis of risk factors in the studied population revealed that there were insignificantly higher rate of smokers and subjects with hypercholesterolemia and arterial hypertension in ISL group. The incidence of diabetes mellitus was the same in both groups.

Typical clinical manifestation of Leriche syndrome include: erectile dysfunction in the form of difficulty in maintaining erection and male impotence, lower limb fatigue and more common buttock claudication, skin paleness and no palpable pulse over femoral artery/arteries (4). Advanced form of the disease is characterised by total impotence, cyanosis and progressive limb necrosis (4). The severity of clinical symptoms and the speed at which it progresses depends on, but not limited to, the nature of the pathology, its severity and localisation, the duration in which the disease develops and the presence and efficacy of collaterals (4, 5, 9-14). The involvement of arteries below the inguinal ligament is usually associated with more pronounced clinical manifestation (11).

In our group more severe symptoms of chronic limb ischemia were observed patients with multi-level lesions when compared to patients with isolated form of Leriche syndrome. Grades IIB, III and IV according to Fontaine's classification of clinical severity were observed two, three and four times more often in the group of patients with concomitant femoro-popliteal lesions than in ISL group.

The physical examination supplemented by non-invasive screening tests (such as ankle-brachial index and oscillometry) allow to detect and classify clinical severity of CLI (4, 12, 13). Modern imaging modalities such as ultrasound, computed tomography angiography and magnetic resonance angiography and digital

subtraction angiography allow to diagnose patients with early stages of Leriche syndrome (7-10). Due to widespread availability they make it possible to detect and evaluate the nature and severity of pathologic lesions within aorta and arteries of the lower extremities (14). Their specificity and sensitivity in detecting particular vascular pathologies in patients with Leriche syndrome, such as arterial thrombosis or atherosclerosis, varies however between modalities (6, 15). The results of research indicate, that CTA and MRA are more sensitive than ultrasound in detecting thrombotic changes (7).

A differentiated ultrasound image of observed lesions, both in the aortic wall and stenosed or occluded arterial segments, was found in the studied group of 502 patients with Leriche syndrome. Hypo- and isoechoic changes, typical for thrombosis were observed more common in aorta and iliac arteries of patients with isolated Leriche syndrome, while calcifications are atherosclerotic plaques were found less frequently. On the other hand, hyperechoic lesions, typical for atherosclerosis and calcifications leading to their stenoses or occlusion were observed more frequently in patients with multi-level lesions, localised below inguinal ligament as well.

Aortic occlusion was first described by Robert Graham in 1814 (1). Till 1899 Welch described a total of 14 cases of thrombotic occlusion of aortic bifurcation (16). In 1940, French surgeon, Rene Leriche, presented a surgical technique for patients with aortic bifurcation occlusion, which included a resection of pathologically changed vessels and bilateral lumbar sympathectomy (3). In 1948, in collaboration with Morel, they presented not only a complete description of clinical manifestation of the syndrome, characterised the underlying aortic and arterial pathology, but also presented surgeries, which they performed (4). The previously proposed surgical technique for aorto-iliac occlusion was supplemented by the surgical thrombectomy, which was first performed by Dos Santos one year earlier (4, 17). In modern vascular surgery, thrombendarterectomy (TEA) is used as an independent intervention or as addition to reconstructive procedures, such as aortobiliac (AIB) or aortobifemoral bypass grafting (AFB). In high-risk patients extra-anatomical procedures are performed, i.e. axillary-bifemoral bypass or femoro-femoral bypasses in patient with unilateral iliac occlusions. Minimally invasive endovascular techniques are an alternative for the above-mentioned surgical techniques, as they are associated with less complications. These techniques include percutaneous transluminal angioplasty (PTA) and stenting of stenosed or occluded arterial segments (10, 18).

Both Leriche and Morel, as well as other researchers, pointed out the chronic nature of the disease and its relatively slow, but unceasingly progressive course, leading in most patient who were treated conservatively to complete impotence and limb necrosis (4, 19, 20). They described pathological lesions in

aorto-iliac segment characteristic for this entity based on post-mortem examinations and intraoperative findings (4). They found that the main cause for occlusion was progressive thrombosis of distal abdominal aorta, which they clearly distinguished from well-known and described in the literature "aortic saddle embolus" of cardiac origin. The latter was associated with rapidly developing syndromes of bilateral acute limb ischemia (21-26). According to their description the thrombosis, which in most patients started in common iliac arteries, gradually affected more proximal aortic bifurcation. It was less common for the thrombosis to begin in aorta and then progress in distal direction towards iliac arteries. In some cases thrombosis affected only one iliac artery, but over time they caused also the occlusion of the contralateral side. The progressive process lead eventually to a total aorto-iliac occlusion affecting long segment of the vessels up to the level of renal arteries (4, 8, 19). Moreover, the authors emphasised the various nature of pathological lesions. In some cases the common iliac arteries were hard looking like „string-like sticks" with no visible lumen. In other cases the outer arterial wall was smooth and even, but its lumen thrombosed, which was associated with intensive periarterial inflammation which involved adjacent structures of retroperitoneal space. In some patients there were atherosclerotic lesions in aorta, which hampered surgery, while in others there was an organised thrombus within the aortic lumen, which did not adhere to the endothelium (4).

It was confirmed in our material during intraoperative evaluation of aorta and arteries in 123 patients with Leriche syndrome undergoing open surgery. In patients with isolated aorto-iliac occlusion the vessel wall was frequently intact and elastic, while the thrombus was removed from the vessel lumen. In patients with multi-level lesions the arteries were atherosclerotically changes, hard on palpation. Atherosclerotic plaques were frequently observed in their occluded lumen.

When compared with patients with multi-level lesions (group B), patients with isolated aorto-iliac changes (group A) showed:

- lower mean age (A –  $56.24 \pm 8.81$  years vs. B –  $61.15 \pm 9.05$ ),
- higher percentage of women (A – 1:3, B – 1:5),

- lower incidence of lesions within carotid arteries (6:8), including medium- and high-grade (1:2, 1:2) as well as occlusions (1:3),
- lower intensity of clinical symptoms of chronic limb ischemia.

The ultrasound and intraoperative findings in patients with isolated lesions were more characteristic for thrombosis, while in patients with concomitant femoro-popliteal lesions the lesions typical for arterial atherosclerosis and calcifications were observed.

It therefore may be concluded that the incidence of carotid artery lesions in patients with Leriche syndrome is dependent on the severity and localisation of lower limb lesions and are more common in subjects with multi-level lesions. Statistically significant differences between both groups were found for age, sex and the distribution of incidence of carotid artery lesions. The ultrasound and intraoperative evaluation demonstrated that there were two types of pathological arterial changes. Thrombotic lesions were more common in isolated aorto-iliac lesions, while atherosclerotic changes were more frequent in patients with multi-level disease. These observations lead to hypothesis that patients with Leriche syndrome form a inhomogeneous group in terms of underlying pathology and epidemiological and clinical factors.

## CONCLUSIONS

1. A strong positive correlation was observed in patients with Leriche syndrome between the severity and multi-level localisation of atherosclerotic lesions, and incidence and severity of carotid lesions.
2. Statistically significant differences concerning age, sex, carotid lesion distribution, as well as the presence of > 50%, > 70% stenoses and occlusion was observed between patients with isolated Leriche syndrome and patients with multi-level atherosclerotic lesions in the arteries of lower extremities.
3. The results of the study suggest that there one can distinguish two different populations of patients with Leriche syndrome.
4. The clinical differences between these two patient populations are probably caused by various arterial pathomorphology.

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