УДК 617-089 DOI: https://doi.org/10.17816/mechnikov97149



Гендерные особенности критической ишемии нижних конечностей

Н.И. Глушков, П.Д. Пуздряк, А.Н. Агурбаш, А.В. Разепин, М.А. Иванов

Северо-западный государственный медицинский университет им. И.И. Мечникова, Санкт-Петербург, Россия

Обоснование. Критическая ишемия нижних конечностей у больных атеросклерозом ведет к негативным последствиям из-за высокой вероятности появления многоуровневых изменений, а также поражения коронарного и каротидного бассейнов.

Цель исследования — изучить гендерные особенности критической ишемии нижних конечностей атеросклеротического генеза по итогам реконструктивных вмешательств.

Материалы и методы. Выполнены артериальные реконструкции у 261 пациента с периферическим атеросклерозом (95 женщин и 166 мужчин) с учетом особенностей оперативных вмешательств и анализом осложнений и количества ампутаций в ранние сроки.

Результаты. В группе женщин отмечено более высокое пульсовое давление и достоверно более частое поражение тибиальных артерий (p < 0.05). Тромбоз оперированного сегмента чаще наблюдали у мужчин на стадии критической ишемии. При операции на стадии клаудикации осложнения носили единичный характер.

Выводы. Эффективность реконструктивной помощи для мужчин и женщин с периферическим атеросклерозом на стадии клаудикации определяет необходимость оперативного вмешательства при отсутствии результатов консервативного лечения.

Ключевые слова: периферический атеросклероз; критическая ишемия; гендерные различия.

Как цитировать:

Глушков Н.И., Пуздряк П.Д., Агурбаш А.Н., Разепин А.В., Иванов М.А. Гендерные особенности критической ишемии нижних конечностей // Вестник Северо-Западного государственного медицинского университета им. И.И. Мечникова. 2021. Т. 13. № 4. С. 47—52. DOI: https://doi.org/10.17816/mechnikov97149

Рукопись получена: 29.11.2021 Рукопись одобрена: 13.12.2021 Опубликована: 29.12.2021



DOI: https://doi.org/10.17816/mechnikov97149

Gender peculiarities of critical lower limb ischemia

Nikolay I. Glushkov, Petr D. Puzdryak, Anastasia N. Agurbash, Anatoly V. Razepin, Mikhail A. Ivanov

North-Western State Medical University named after I.I. Mechnikov, Saint Petersburg, Russia

BACKGROUND: Development of critical ischemia of lower limbs in patients with atherosclerosis causes negative consequences due to the high probability of detecting multilevel changes, as well as identifying coronary and carotid pools.

AIM: The aim of the study was to investigate gender differences in critical lower limb ischemia of atherosclerotic genesis following reconstructive interventions.

MATERIALS AND METHODS: Arterial reconstructions have been performed in 261 patients with peripheral atherosclerosis (95 women and 166 men). The specific features of reconstructive interventions have been taken into account; complications and the number of amputations have been analyzed in the early period.

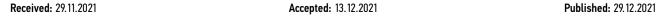
RESULTS: Higher pulse pressure has been registered in the female group; tibial arteries have been affected significantly more frequently (p < 0.05). Thrombosis of the operated segment has been observed more frequently in the male patients at the stage of critical ischemia; in the case of claudication the complications were sporadic.

CONCLUSIONS: The best results of reconstructive care in men and women with peripheral atherosclerosis at the claudication stage determine the vector of active tactics in the absence of conservative treatment results.

Keywords: peripheral atherosclerosis; critical ischemia; gender differences.

To cite this article:

Glushkov NI, Puzdryak PD, Agurbash AN, Razepin AV, Ivanov MA. Gender peculiarities of critical lower limb ischemia. *Herald of North-Western State Medical University named after I.I. Mechnikov.* 2021;13(4):47–52. DOI: https://doi.org/10.17816/mechnikov97149





BACKGROUND

The incidence of peripheral arterial disease of atherosclerotic origin is comparable to the incidence of malignant neoplasms [1]. Critical limb ischemia (CLI) in patients with atherosclerosis results in negative consequences due to the high probability of multilevel changes and damage to the coronary and carotid systems [2].

The need for reconstructive intervention on several segments does not coincide with the concept of minimally invasive interventions performed on patients with critical ischemia [3]. Patients with claudication are afraid of angiosurgery, even if conservative therapy is ineffective [4]. In women, CLI often occurs without traditional intermittent claudication, reducing the time for medical decisions [5]. Thus far, no risk factors for the complicated course of multilevel peripheral arterial disease with the development of CLI in patients of different genders have been identified.

The study aimed to analyze the gender characteristics of CLI of atherosclerotic genesis based on reconstructive intervention results.

MATERIALS AND METHODS

The work was based on the follow-up of 261 patients with multilevel atherosclerotic lesions of the vessels of the lower extremities. Ninety-five female patients comprised the main group (81 with CLI and 14 with claudication). The control group included 166 men (123 with CLI and 43 with Fontaine—Pokrovsky grade IIb ischemia). All patients

underwent reconstructive interventions, the results of which were analyzed in the early stages. During the first 30 days after surgery, the incidence of thrombosis of the operated segment, postoperative bleeding, the number of infectious complications and amputations, and the incidence of cerebrovascular accidents were recorded. The aspects of comorbid conditions in men and women, variants of atherosclerotic lesions according to TASC-II, and types of interventions were studied.

Diabetes mellitus was diagnosed when the glycated hemoglobin level was >6.5% or when the patient received appropriate treatment. Arterial hypertension was analyzed according to the recommendations of the international classification (American College of Cardiology/American Heart Association Hypertension Guidelines, 2017). Chronic kidney disease was diagnosed based on the Kidney Disease: Improving Global Outcomes (2013) guidelines. Chronic heart failure was analyzed according to the New York Heart Association classification (1964). The diagnosis of postinfarction cardiosclerosis was established in the presence of a history of myocardial infarction and cicatricial changes on the electrocardiogram.

The characteristics of the operated patients are presented in Table 1.

The characteristics of vascular bed lesions according to TASC-II and options for interventions are presented in Table 2.

The statistical processing of the results was performed using the Statistica 10 data analysis package. The quantitative characteristics are presented as the mean \pm standard deviation. The qualitative characteristics were presented

Table 1. Characteristics of the operated patients

Таблица 1. Характеристика оперированных больных

Indicators	Women	Men	p
Age, years	71.1 ± 9.5	63.2 ± 8.9	p < 0.05
Mean systolic pressure, mmHg	140 (130; 160)	140 (130; 150)	<i>p</i> < 0.05
Pulse pressure, mmHg	62.4 ± 16.6	55.6 ± 11.7	<i>p</i> < 0.05
Smoking, n (%)	18 (22.2)	57 (46.3)	<i>p</i> < 0.05
Grade II/III arterial hypertension, n (%)	88 (93.0)	152 (92.0)	No significant differences
Grade II/III chronic heart failure, n (%)	27 (28.4)	25 (15.0)	<i>p</i> < 0.05
Grade II/III angina, n (%)	35 (37.0)	55 (33.0)	No significant differences
Postinfarction cardiosclerosis, n (%)	20 (21.0)	21 (12.6)	<i>p</i> < 0.05

Table 2. Characteristics of the variants of atherosclerotic lesions and types of surgical interventions

Таблица 2. Характеристика вариантов атеросклеротического поражения и разновидностей оперативных воздействий

Indicators	Women	Men	р
Damage to the femoropopliteal segment type C/D according to TASC-II, $n\ (\%)$	57 (60)	104 (63)	No significant differences
Damage to the tibial segment, n (%)	14 (15)	10 (6)	p < 0.05
Type of intervention			
Bypass, n (%)	19 (20)	47 (21)	No significant differences
Endarterectomy, n (%)	45 (47)	82 (49)	No significant differences
Endovascular, n (%)	32 (33.7)	33 (19.9)	<i>p</i> < 0.05

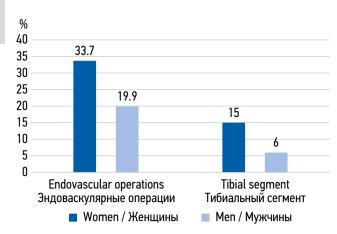


Fig. 1. Differences in the incidence of tibial segment involvement and needs for endovascular care in the study groups

Рис. 1. Различия в частоте поражения тибиального сегмента и потребности в эндоваскулярной помощи в исследуемых группах

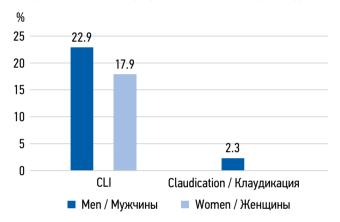
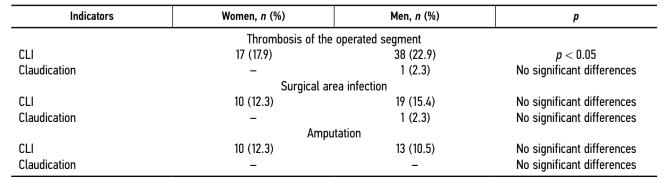


Fig. 3. The frequency of thrombosis of the operated segment in the analyzed groups against the background of critical ischemia of the lower extremities and claudication. CLI — critical lower limb ischemia Рис. 3. Частота тромбоза оперированного сегмента в анализируемых группах на фоне критической ишемии нижних конечностей и клаудикации. CLI — критическая ишемия нижних конечностей

as the relative frequencies and expressed as percentages. The significance of the distribution of qualitative characteristics was determined using the χ^2 test. Differences between the groups were considered significant at p < 0.05.

Table 3. Early postoperative complications and amputations **Таблица 3.** Ранние послеоперационные осложнения и ампутации



Note, CLI — critical limb ischemia.



Fig. 2. The value of perioperative blood loss in the analysis groups **Puc. 2.** Величина периоперационной кровопотери в анализируемых группах

RESULTS

The expected differences in the age of the operated patients were revealed as well as the later development of ischemia in female patients. The duration of critical ischemia before surgical treatment was longer in female patients (77.7% of the patients operated on 1 month after the onset of CLI symptoms versus 48% in male patients). In CLI development in men and women, an unequal role was played by increased pulse pressure. Significantly higher pulse pressure was noted in female patients (p < 0.05). In CLI patients, chronic heart failure, postinfarction cardiosclerosis, and abdominal obesity were more often recorded than in the control group (p < 0.05). Female atherosclerosis was characterized by lesions of the tibial segment, which affected the frequency of endovascular revascularization (Fig. 1).

The amount of surgical blood loss was greater in the control group, which was associated with the predominance of conventional suprainguinal reconstructions in men (Fig. 2).

A comparative analysis of early postoperative complications showed different results in patients with critical ischemia and claudication (Table 3). Thrombosis of the operated segment was most often registered in men at the CLI stage. The minimum number of complications was recorded in patients with claudication (Fig. 3).

There were no significant gender differences in the analyzed groups in terms of the incidence of cerebrovascular accidents in the early stages.

A beneficial clinical outcome (elimination of CLI and increase in walking distance) was registered in 141 (84.9%) men and 78 (82.1%) women with CLI. At the claudication stage, a positive clinical result was achieved in all operated patients.

DISCUSSION

Hormonal gender characteristics affect the timing of the manifestation of peripheral atherosclerosis and CLI; in most cases, clinical manifestations occur much earlier in men [6], as confirmed in this study.

The clinical signs of peripheral arterial disease in female patients differ from the traditional symptoms of claudication, making it difficult to diagnose even in CLI [7]. Three-quarters of the patients analyzed were operated on within >1 month from the onset of CLI manifestations, which could cause infectious complications and amputations in this group (12.3%).

Another characteristic of female atherosclerosis that affected the incidence of complications was a deviation in pulse pressure [8]. In this study, female patients showed significantly higher pulse pressure values, associated with a high incidence of chronic heart failure, postinfarction cardiosclerosis, and abdominal obesity in the main group.

In the presence of a multilevel peripheral arterial disease, the predominant lesion of certain segments in men and women was not the same [9]. Changes in the tibial segment were more common in the main group, leaving the possibility for endovascular revascularization.

REFERENCES

- 1. Krishna SM, Moxon JV, Golledge J. A Review of the pathophysiology and potential biomarkers for peripheral artery disease. *Int J Mol Sci.* 2015;16(5):11294–11322. DOI: 10.3390/ijms160511294
- 2. Matsushita K, Kwak L, Yang C, et al. High-sensitivity cardiac troponin and natriuretic peptide with risk of lower-extremity peripheral artery disease: the Atherosclerosis Risk in Communities (ARIC) Study. *Eur Heart J.* 2018;39(25):2412–2419. DOI: 10.1093/eurheartj/ehy106
- **3.** Puzdriak PD, Shlomin VV, Bondarenko PB, et al. Comparison of the results of hybrid and open surgical treatment of multilevel arterial disease of lower extremities (in Russian only). *Russian Journal of Cardiology and Cardiovascular Surgery.* 2019;12(3):227–234. (In Russ.). DOI: 10.17116/kardio201912031227
- **4.** Glushkov NI, Potashov TA, Ivanov MA, et al. Optimal terms of revascularization in patients with peripheral atherosclerosis *Preventive and Clinical Medicine*. 2020;3(76):70–76. (In Russ.)

The optimal timing of reconstruction in patients with a multilevel peripheral arterial disease before or after the development of CLI is subject to discussion. In the presence of claudication, the number of complications is usually less, which should be considered when determining the approach to treatment of a particular patient [10]. More hazardous complications were registered in CLI patients, implying the need to reduce the time between establishing a diagnosis and surgery.

Thrombosis of the operated segment, among complications after a reconstructive intervention, is most often registered in men with CLI. Repeated reconstructions achieved an acceptable clinical result in several patients; however, such postoperative consequences prove the benefit of revascularization in men with no effect from the conservative treatment of claudication [11].

CONCLUSIONS

Metabolic disorders in female patients with a multilevel peripheral arterial disease often lead to the development of CLI and complications after revascularization. The efficiency of reconstructive care in men and women with peripheral atherosclerosis at the stage of claudication determines the need for surgical intervention in the absence of conservative treatment results.

ADDITIONAL INFORMATION

Funding. The study had no external funding.

Conflict of interest. The authors declare no conflict of interest. The limitation of this study is the lack of results in the treatment of critical ischemia in the long term.

All authors made a significant contribution to the study and preparation of the article and read and approved the final version before its publication.

- **5.** Man JJ, Beckman JA, Jaffe IZ. Sex as a biological variable in atherosclerosis. *Circ Res.* 2020;126(9):1297–1319. DOI: 10.1161/CIRCRESAHA.120.315930
- **6.** Jelani Q, Mena-Hurtado C, Burg M, et al. Relationship between depressive symptoms and health status in peripheral artery disease: role of sex differences. *J Am Heart Assoc.* 2020;9(16):e014583. DOI: 10.1161/JAHA.119.014583
- 7. Pérez-López FR, Larrad-Mur L, Kallen A, et al. Differences in cardiovascular disease: hormonal and biochemical influences. *Reprod Sci.* 2010;17(6):511–531. DOI: 10.1177/1933719110367829
- **8.** Fanlo-Maresma M, Candás-Estébanez B, Esteve-Luque V, et al. Asymptomatic carotid atherosclerosis cardiovascular risk factors and common hypertriglyceridemia genetic variants in patients with systemic erythematosus lupus. *J Clin Med.* 2021;10(10):2218. DOI: 10.3390/jcm10102218

9. Giannopoulos S, Shammas NW, Cawich I, et al. Sex-Related Differences in the Outcomes of endovascular interventions for chronic limb-threatening ischemia: results from the liberty 360 study. *Vasc Health Risk Manag.* 2020;16:271–284. DOI: 10.2147/VHRM.S246528 **10.** Altreuther M, Mattsson E. Long-term results after femoral thrombendarterectomy combined with simultaneous endovascular

intervention in intermittent claudication and critical ischemia. *SAGE Open Med.* 2020;8:2050312119900860. DOI: 10.1177/2050312119900860 **11.** Muluk SC, Muluk VS, Kelley ME, et al. Outcome events in patients with claudication: a 15-year study in 2777 patients. *J Vasc Surg.* 2001;33(2):251–257. DOI: 10.1067/mva.2001.112210

СПИСОК ЛИТЕРАТУРЫ

- 1. Krishna S.M., Moxon J.V., Golledge J. A Review of the pathophysiology and potential biomarkers for peripheral artery disease // Int. J. Mol. Sci. 2015. Vol.16, No. 5. P. 11294—11322. DOI: 10.3390/ijms160511294
- 2. Matsushita K., Kwak L.,Yang C. et al. High-sensitivity cardiac troponin and natriuretic peptide with risk of lower-extremity peripheral artery disease: the Atherosclerosis Risk in Communities (ARIC) Study // Eur. Heart J. 2018. Vol. 39, No. 25. P. 2412–2419. DOI: 10.1093/eurheartj/ehy106
- 3. Пуздряк П.Д., Шломин В.В., Бондаренко П.С. и др. Сравнение результатов гибридного и открытого хирургического лечения многоуровневого поражения артерий нижних конечностей // Кардиология и сердечно-сосудистая хирургия. 2019. Т. 12, № 3. С. 227—234. DOI: 10.17116/kardio201912031227
- **4.** Глушков Н.И., Поташов Т.А., Иванов М.А. и др. К вопросу об оптимальных сроках реваскуляризации у лиц с периферическим атеросклерозом // Профилактическая и клиническая медицина. 2020. Т. 3, № 76. С. 70–76.
- **5.** Man J.J., Beckman J.A., Jaffe I.Z. Sex as a biological variable in atherosclerosis // Circ. Res. 2020. Vol. 126, No. 9. P. 1297–1319. DOI: 10.1161/CIRCRESAHA.120.315930
- **6.** Jelani Q., Mena-Hurtado C., Burg M. et al. Relationship between depressive symptoms and health status in peripheral artery disease:

role of sex differences // J. Am. Heart Assoc. 2020. Vol. 9, No. 16. P. e014583. DOI: 10.1161/JAHA.119.014583

- 7. Pérez-López F.R., Larrad-Mur L., Kallen A. et al. Differences in cardiovascular disease: hormonal and biochemical influences // Reprod. Sci. 2010. Vol. 17, No. 6. P. 511–531. DOI: 10.1177/1933719110367829
- **8.** Fanlo-Maresma M., Candás-Estébanez B., Esteve-Luque V. et al. Asymptomatic carotid atherosclerosis cardiovascular risk factors and common hypertriglyceridemia genetic variants in patients with systemic erythematosus lupus // J. Clin. Med. 2021. Vol. 10, No. 10. P. 2218. DOI: 10.3390/jcm10102218
- **9.** Giannopoulos S., Shammas N.W., Cawich I. et al. Sex-Related Differences in the Outcomes of endovascular interventions for chronic limb-threatening ischemia: results from the liberty 360 study // Vasc. Health Risk Manag. 2020. Vol. 16. P. 271–284. DOI: 10.2147/VHRM.S246528
- **10.** Altreuther M., Mattsson E. Long-term results after femoral thrombendarterectomy combined with simultaneous endovascular intervention in intermittent claudication and critical ischemia // SAGE Open Med. 2020. Vol. 8. P. 2050312119900860. DOI: 10.1177/2050312119900860 **11.** Muluk S.C., Muluk V.S., Kelley M.E. et al. Outcome events in patients with claudication: a 15-year study in 2777 patients // J. Vasc. Surg. 2001. Vol. 33, No. 2. P. 251–257. DOI: 10.1067/mva.2001.112210

AUTHORS INFO

Nikolay I. Glushkov, MD, Dr. Sci. (Med.), Professor; ORCID: https://orcid.org/0000-0001-8146-4728; e-mail: nikolay.qlushkov@szgmu.ru

Petr D. Puzdriak, MD;

ORCID: https://orcid.org/0000-0003-2631-3622; Scopus Author ID: 57194489779; ResearcherID: K-9787-2016; e-mail: hirurg495@yandex.ru

Anastasiya N. Agurbash;

ORCID: https://orcid.org/0000-0003-1247-3481; e-mail: nastaagurbash@mail.ru

Anatoly V. Razepin;

ORCID: https://orcid.org/0000-0003-0470-4681; e-mail: razepint@rambler.ru

* Mikhail A. Ivanov, MD, Dr. Sci. (Med.), Professor; address: 47 Piskarevsky Ave., Saint Petersburg, 195067, Russia; ORCID: https://orcid.org/0000-0002-4756-6488; e-mail: iv30407302007@yandex.ru

* Corresponding author / Автор, ответственный за переписку

ОБ АВТОРАХ

Николай Иванович Глушков, д-р мед. наук, профессор;

ORCID: https://orcid.org/0000-0001-8146-4728;

e-mail: nikolay.qlushkov@szgmu.ru

Петр Дмитриевич Пуздряк;

ORCID: https://orcid.org/0000-0003-2631-3622; Scopus Author ID: 57194489779; ResearcherID: K-9787-2016; e-mail: hirurg495@yandex.ru

Анастасия Николаевна Агурбаш;

ORCID: https://orcid.org/0000-0003-1247-3481; e-mail: nastaagurbash@mail.ru

Анатолий Васильевич Разепин;

ORCID: https://orcid.org/0000-0003-0470-4681; e-mail: razepint@rambler.ru

* Михаил Анатольевич Иванов, д-р мед. наук, профессор; адрес: Россия, 195076, Санкт-Петербург, Пискаревский пр., д. 47; ORCID: https://orcid.org/0000-0002-4756-6488; e-mail: iv30407302007@yandex.ru