

лихоманки, головного болю (86.2%), блювоти (69.9%), судом (1.6%), порушення свідомості (17.8%) і менингеального синдрому (80.2%). Етіологічний чинник був встановлений у 20.3% пацієнтів. У 41.4% пацієнтів спостерігались неврологічні ускладнення. Летальний наслідок спостерігався у 7.3% пацієнтів. Головним збудником гострих бактеріальних менингітів виявився *S. pneumoniae* – 56.0%, друге місце посіла *N. meningitidis* – 36.0%, третє поділили між собою *S. aureus* і *L. monocytogenes* (по 4.0% випадків). Частими ускладненнями виявлялися набряк мозку (90.2%), парези кінцівок (11.7%) і епілептичні припадки (7.8%). Розповсюдженість гострих бактеріальних менингітів склала 0.86 на 100 тис населення в рік в співвідношенні між чоловіками і жінками 1.5:1 та загальною річною смертністю 0.06 на 100 тис населення.

Ключові слова: бактеріальний менингіт, епідеміологія, етіологія, дорослі.

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лихорадки, головної болю (86.2%), рвоти (69.9%), судорог (1.6%), порушення свідомості (17.8%) і менингеального синдрому (80.2%). Етіологічний фактор був встановлений у 20.3% пацієнтів. У 41.4% пацієнтів спостерігались неврологічні ускладнення. Летальний наслідок спостерігався у 7.3% пацієнтів. Головним збудником гострого бактеріального менингіта виявився *S. pneumoniae* – 56.0%, друге місце посіла *N. meningitidis* – 36.0%, третє поділили між собою *S. aureus* і *L. monocytogenes* (по 4.0% випадків). Частими ускладненнями були отек мозку (90.2%), парези кінцівок (11.7%) і епілептичні припадки (7.8%). Розповсюдженість гострого бактеріального менингіта склала 0.86 на 100 тис населення в рік в співвідношенні між чоловіками і жінками 1,5:1 та загальною річною смертністю 0.06 на 100 тис населення.

Ключевые слова: бактериальный менингит, эпидемиология, этиология, взрослые.

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MORPHOLOGICAL JUSTIFICATION OF THE STEPWISE DOSED BALLOON ANGIOPLASTY APPLICATION COMPARED TO STANDARD METHODS IN PATIENTS WITH DIABETIC FOOT

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The main reason for the development of lower extremities gangrene in diabetes mellitus is impairment of their blood supply. In recent decades, endovascular surgical treatment has played a significant role in restoring blood supply. However, the issues of complications that arise after such interventions, the reasons for their occurrence, what morphological changes occur in the atherosclerotic artery wall during their implementation remain understudied. Therefore, experimental research to study the local changes that occur in the arteries of the lower extremities during balloon angioplasty, especially in patients with ischemic diabetic foot, is an urgent problem of modern interventional surgery. The purpose of the study was to provide a morphological justification for the use of stepwise dosed balloon angioplasty using balloons of different diameters and lengths compared to standard methods in patients with ischemic form of diabetic foot syndrome. An experimental study was performed on 20 lower limbs that were amputated at the hip level for foot gangrene in patients with ischemic form of diabetic foot syndrome. The first group included 5 (25.0%) lower extremities, in which immediately after the surgery, sections of the tibial arteries with stenosis of more than 75% were sampled. Group II included 5 (25.0%) amputated lower extremities, which immediately after the surgery were performed a typical balloon angioplasty. Group III included 10 (50%) amputated lower extremities, in which the method of stepwise dosed balloon angioplasty was tested. According to the results of experimental studies, it was found that mainly when performing staged dosed angioplasty according to the proposed method, the inner elastic membrane of the artery was clearly pronounced, had insignificant areas of fragmentation. At the same time, the outer elastic membrane was quite well pronounced throughout the whole length, had insignificant areas of fragmentation and they were much less in number than in those cases when angioplasty was performed according to standard methods. Moreover, in the outer membrane, where vasa vasorum and vascular nerves were located, they remained almost unchanged. Reducing the number and sizes of arterial membranes' dissection, their fragmentation when performing staged dosed balloon angioplasty by the proposed method using balloons of different diameters and lengths permits to recommend it in practice to reduce the incidence of thrombotic complications in the early postoperative period.

Key words: arteries, atherosclerosis, arterial occlusion, diabetes mellitus, diabetic foot, balloon angioplasty.

The work is a fragment of the research project "Development of modern scientifically based principles of stratification, monitoring and prognostication of surgical diseases and injuries course", state registration No.0120U101176.

Over the past 10-15 years, the incidence of diabetes mellitus (DM) in Ukraine has almost doubled to more than 1.5 million people. The syndrome of diabetic foot (DFS) occurs in every fourth patient and ends in almost half with high amputation of one or both lower extremities [3]. Two thirds of patients die from gangrene of the lower extremities, and its development in patients with diabetes is observed many-fold more frequently than in the general population. [6, 7].

The main reason for the development of the lower extremities gangrene in diabetes mellitus is an impairment of their blood supply [11, 12]. The main method of restoring blood flow in this disease is surgical revascularization, but this method can be used to a limited extent in patients with virtually no distal blood flow and with the presence of severe comorbidities. In addition, there is currently no reliable

assessment criterion that permits to select patients for surgical revascularization [1]. The situation is further complicated by the fact that against the background of diabetes mellitus, the infragenicular arteries are most often affected [3, 7, 12].

At the same time, the problems of complications after endovascular intervention for chronic ischemia of the lower extremities and technical difficulties during their implementation are insufficiently studied and clarified in the domestic and world literature [5]. There is almost no literature on morphological changes that occur in atherosclerotic artery wall during balloon angioplasty in patients with diabetes mellitus. Depending on these data, it is possible to predict the development of some complications that occur in the early postoperative period after endovascular interventions [10]. Therefore, experimental study of local changes that occur in peripheral arteries during balloon angioplasty, particularly in patients with ischemic form of DFS, is an urgent problem of modern interventional surgery, [9].

The purpose of the study was to provide a morphological justification for the use of stepwise dosed balloon angioplasty using balloons of different diameters and lengths compared to the standard method in patients with ischemic form of diabetic foot syndrome.

Materials and methods. The study was performed on 20 lower limbs that were amputated at the level of the thigh for foot gangrene in patients with ischemic DFS. This experimental study was approved by the Commission on Ethics and Bioethics of the Ukrainian Medical Stomatological Academy at the Ministry of Health of Ukraine.

Amputated limbs for the experiment were divided into 3 groups. Group 1 consisted of 5 lower extremities, in which immediately after the operation, sections of the infragenicular arteries were taken at the site of stenosis (75% or more). Group 2 also included 5 lower extremities, on which immediately after the operation an experimental typical one-stage conventional angioplasty under pressure from 8 to 22 atm was performed with antegrade (through the femoral artery) insertion of a Pacific Plus OTW balloon into the posterior or anterior infragenicular arteries. Group 3 included 10 (50%) amputated lower extremities, on which we tested our proposed method of stepwise dosed balloon angioplasty.

The method of stepwise dosed balloon angioplasty lied in the fact that in the lumen of one of the infragenicular arteries a conductor was inserted behind the affected area, through which a balloon catheter for angioplasty was inserted and there was a gradual increase in pressure with exposure for 5 minutes at 3/4 of the nominal pressure with gradual pressure increase by 1 atm for 1 minute, and exposure for 5 minutes when reaching the required diameter of the balloon catheter. This study was performed on areas of the posterior or anterior great infragenicular arteries up to 10 cm long, with balloons corresponding to the diameter of the selected vessel and ranging from 2 to 3.5 mm and the length of 2 to 4 cm. Raising the pressure in the balloon causes the gradual influence on the arterial wall, reduces its trauma and helps to preserve the integrity of the arterial intima (performed under the control of arteriography).

General histological study methods were applied.

Results of the study and their discussion. Morphological changes in the walls of the infragenicular arteries of group 1 in atherosclerosis were evidence of its initial stages. In the cross sections of the vessels, the intima at the site of atherosclerotic plaque had the form of an intermittent lining, due to the partial destruction of endothelial cells. Undamaged endothelial cells had unevenly spaced hyperchromic nuclei that protrude into the vascular lumen. The walls were segmentally thickened with the formation of plaques, which were based on actively proliferating fibroblasts and cells of smooth myocytes of the subendothelial layer. The nuclei of the latter in these places were arranged in several layers, perpendicular to the inner surface of the vessel. The fibrous structures of the plaque in places had a loose appearance, which was an evidence of mucoid edema. The middle membrane of the arteries under the plaque was thin. The outer elastic membrane was without visible changes. The loose fibrous connective tissue of the adventitia contained unevenly full-blooded blood vessels located in small groups.

Assessing the results of histological examination of the infragenicular arteries of group 2 (after angioplasty according to the standard method, in which the selected diameter cylinders were installed in the site of atherosclerotic lesions of the vessel with the simultaneous achievement of the required balloon diameter) showed that the inner elastic membrane was loosened and exfoliated. In some areas, exfoliation of the intima and inner elastic membrane with a layer of smooth myocytes of the middle membrane was observed in the places of ballooning (fig. 1A).

In the media membrane, on the border with adventitia, small hemorrhages were detected in the intercellular space. The outer elastic membrane was not clearly visualized, but areas of collagen and elastic fibers fragmentation were also observed in it (fig. 1B).

The outer membrane of the artery was represented by loose fibrous connective tissue, in which perivascular cell infiltration was determined.

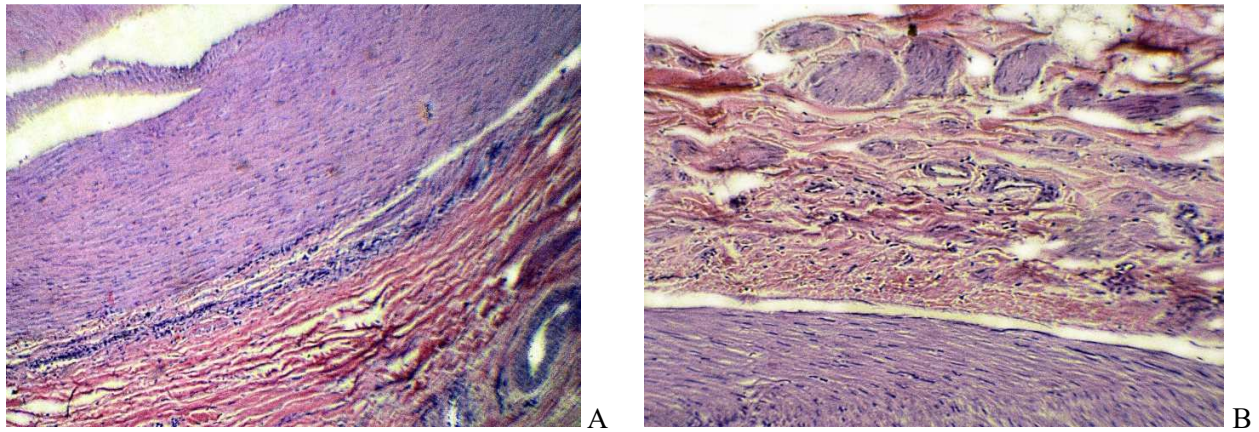


Fig. 1. The wall of the anterior great infragenicular artery after balloon angioplasty by standard methods: A - exfoliation of the intima with a layer of smooth myocytes of the media; B - adventitial exfoliation with hemorrhage. Hematoxylin and eosin staining. Magnification: Oc: 10; Ob: 10

In group 3, histological examination of the anterior infragenicular artery wall, when performing balloon angioplasty by our proposed stepwise, dosing method, showed that the inner membrane consisted of endothelial cells, which had a polygonal shape and were located on the inner elastic membrane (fig. 2A).

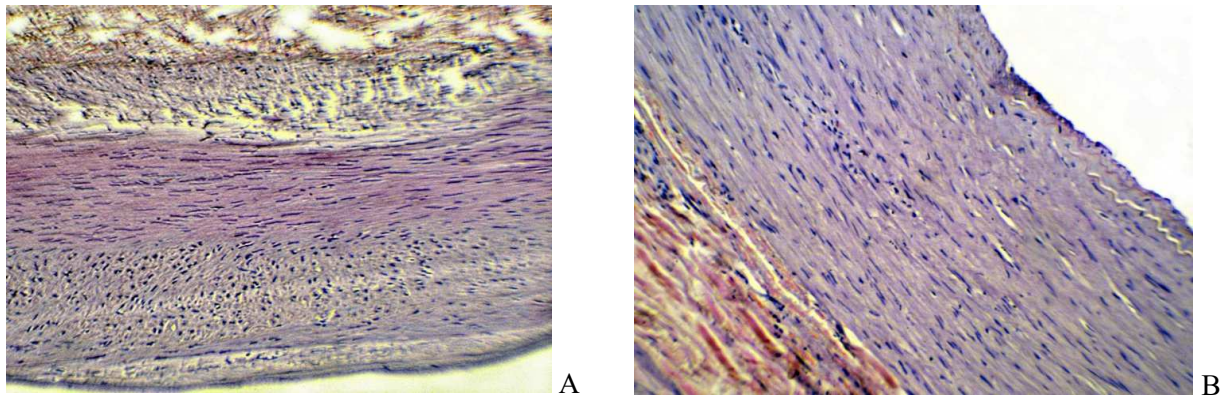


Fig. 2. The wall of the anterior infragenicular artery during balloon angioplasty by stepwise, dosed achievement of nominal pressure in the balloon: A - preservation of intima, media and adventitia; B - slight stratification in the media and outer membranes. Hematoxylin and eosin staining. Magnification: Oc: 10; Ob: 10.

Endothelial cells were stretched along the vessel, the subendothelial layer consisted of thin elastic and collagen fibers, which were also located along the vessel. Single smooth myocytes and low specialized connective tissue cells were located between the fibers. The inner elastic membrane was clearly defined, had insignificant areas of fragmentation, almost a continuous contour. In the specimens there were single areas of intima and internal elastic membrane exfoliation (fig. 2B).

The media membrane consisted of smooth myocytes, between which there were single collagen and elastic fibers, making a framework for them (fig. 2A, B).

Comparing the architectonics of the media membrane to group 2 (balloon angioplasty, which was performed according to the standard method), it was found that the stepwise, dosed method of balloon angioplasty showed a lower frequency of these stratifications and their insignificant size.

The outer elastic membrane was quite well pronounced throughout, but had insignificant areas of fragmentation and at the same time, they were less numerous than in cases where angioplasty was performed according to standard methods.

The outer membrane was represented by loose fibrous connective tissue in which the vasa vasorum and the nerves of the vessels were localized, which remained almost unchanged in the analysis of histological specimens.

Due to the rapid development of endovascular surgery, it has become possible to use endovascular revascularization methods for distal lesions. This largely applies to balloon angioplasty and stenting of the infragenicular arteries. Recently, the use of balloon angioplasty is proposed to be considered in patients with critical lower extremity ischemia as a first-line intervention [12].

Prospects for the use of balloon angioplasty were determined by the following factors: achieving adequate results, reducing the number of complications, the possibility of repeated interventions, low mortality. All this opened up great opportunities in the application of this method in the treatment of critical ischemia of the lower extremities. Endovascular treatment methods had a relatively low risk of

complications with a high level of success [12], therefore some researchers predict the technical success of endovascular treatment in impaired patency of the lower extremities arteries at 91% [4].

Therefore, according to experimental research on histological study of changes that occurred in the atherosclerotic wall of the infragenicular arteries and during balloon dilatation in various ways, it was established that mainly when performing stepwise dosed angioplasty according to the proposed method, the internal elastic artery membrane was sufficiently pronounced, had insignificant fragmentations with an almost continuous contour. At the same time, the outer elastic membrane was quite well pronounced throughout, had insignificant areas of fragmentation and they were much smaller than in those cases when angioplasty was performed according to standard methods. Moreover, the outer membrane was represented by loose fibrous connective tissue, where there were vasa vasorum and vascular nerves, which remained almost unchanged. The obtained data do not contradict those previously published [2].

Conclusion

Reducing the number and size of arterial membranes exfoliations, their fragmentation when performing stepwise dosed balloon angioplasty according to the proposed method using balloons of different diameters and lengths, permits to recommend its use in practice to reduce the incidence of thrombotic complications in the early postoperative period.

References

1. Asamov RE, Khamidov BP, Abdulayev BP. Endovaskulyarnoye lecheniye kriticheskoy ishemii nizhnikh konechnostey u bolnykh sakharnym diabetom. Vestnik ekstrennoy meditsiny. 2012; 3: 90-93. [in Russian]
2. Bolshakov IN, Shestakova LA, Kotikov AR, Kaptyuk GI. Eksperimentalnyy aterogenez u krysa. Morfologicheskaya rekonstruktsiya stenki magistralnoy arterii polisakharidnymi biopolimerami. Fundamentalnyye issledovaniya. 2013; 10-3: 557-563. [in Russian]
3. Zaporozhchenko BS; Shishlov VI; Khaylov MP; Gorbunov AA; Shishlova LA; Shevchenko VG; Muravyev PT. Kompleksnoye lecheniye bolnykh s sindromom «diabeticheskoy stopy» i obliteriruyushchimi zabolevaniyami arteriy nizhnikh konechnostey v stadii kriticheskoy ishemii. Suchasni medychni tekhnolohiyi. 2011; 3-4: 121-124. [in Russian]
4. Pityk AI. Oslozhneniya endovaskulyarnykh vmeshatelstv u bolnykh pri kriticheskoy ishemii tkaney nizhnikh konechnostey. Klinichna khirurgiya. 2014; 12: 39-42. [in Russian]
5. Rusyn VI, Korsak VV, Popovych YAM, Rusyn VV. Bezposeredni uskladnennya endovenoznykh vtruchan pry khronichniy ishemiyi tkanyn nyzhnikh kintsivok. Klinichna khirurgiya. 2014; 9: 41-43. [in Ukrainian]
6. Margolis DJ, Malay DS, Hoffstad OJ. Prevalence of Diabetes, Diabetic Foot Ulcer, and Lower Extremity Amputation Among Medicare Beneficiaries, 2006 to 2008: Data Points No. 1. Feb. 17 2011; Available at: <http://www.ncbi.nlm.nih.gov/books/NBK63602/>
7. Peregrin JH, Kožnar B, Kováč J, Laštovičková J, Novotný J, Vedlich D, et al. PTA of Infrapopliteal Arteries: Long-term Clinical Follow-up and Analysis of Factors Influencing Clinical Outcome. Cardiovasc Intervent Radiol. 2010; 33:720-5. Available at: <https://doi.org/10.1007/s00270-010-9881-3>
8. Liu M, Tang Zh, Li G, Qu Sh, Zhang Yu, Ren Zh, et al. Janus-like role of fibroblast growth factor 2 in arteriosclerotic coronary artery disease: Atherogenesis and angiogenesis. Atherosclerosis. 2013; 229(1):10-7. Available at: <https://doi.org/10.1016/j.atherosclerosis.2013.03.013>.
9. Bakker K, Apelqvist J, Lipsky BA, Van Netten JJ; International Working Group on the Diabetic Foot. The 2015 IWGDF guidance documents on prevention and management of foot problems in diabetes: development of an evidence-based global consensus. Diabetes Metab Res Rev. 2016; 32(1):2-6. Available at: <https://doi.org/10.1002/dmrr.2694>
10. Byrne RM, Taha AG, Avgerinos E, Marone LK, Makaroun MS, Chaer RA. Contemporary outcomes of endovascular interventions for acute limb ischemia, Journal of Vascular Surger. 2014; 59(4):988-95. Available at: <https://doi.org/10.1016/j.jvs.2013.10.054>
11. Baril DT, Chaer RA, Rhee RY, Makaroun MS, Marone LK, Endovascular interventions for TASC II D femoropopliteal lesions, Journal of Vascular Surgery. 2010; 51(6):1406-12. Available at: <https://doi.org/10.1016/j.jvs.2010.01.062>
12. Stoner MC, Calligaro KD, Chaer RA, Dietzek AM, Farber A, Guzman RJ, et al. Reporting standards of the Society for Vascular Surgery for endovascular treatment of chronic lower extremity peripheral artery disease. Journal of Vascular Surgery. 2016; 64(1):1-21. Available at: <https://doi.org/10.1016/j.jvs.2016.03.420>
13. Zeller T, Baumgartner I, Scheinert D, Brodmann M, Bosiers M, Micari A, et al. Drug-Eluting Balloon Versus Standard Balloon Angioplasty for Infrapopliteal Arterial Revascularization in Critical Limb Ischemia. J Am Coll Cardiol. Oct 2014; 64(15):1568-76. Available at: <https://doi.org/10.1016/j.jacc.2014.06.1198>

Реферати

**МОРФОЛОГІЧНЕ ОБҐРУНТУВАННЯ
ЗАСТОСУВАННЯ ПОЕТАПНОЇ ДОЗОВАНОЇ
БАЛОННОЇ АНГІОПЛАСТИКИ У ПОРІВНЯННІ
З СТАНДАРТНОЮ МЕТОДИКОЮ У ХВОРИХ
З ШЕМИЧЕСЬКОЮ ФОРМОЮ СИНДРОМУ
ДІАБЕТИЧНОЇ СТОПИ**

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Сидоренко А.В.**

В останні десятиліття значне місце у відновленні кровообігу відіграють ендovasкулярні методи хірургічного лікування. Однак, залишаються недостатньо вивченими питання ускладнень, які виникають після

**МОРФОЛОГИЧЕСКОЕ ОБОСНОВАНИЕ
ПРИМЕНЕНИЯ ПОЭТАПНОЙ ДОЗИРОВАННОЙ
БАЛОННОЙ АНГИОПЛАСТИКИ В СРАВНЕНИИ
СО СТАНДАРТНОЙ МЕТОДИКОЙ У БОЛЬНЫХ
С ИШЕМИЧЕСКОЙ ФОРМОЙ СИНДРОМА
ДИАБЕТИЧЕСКОЙ СТОПЫ**

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В последние десятилетия значительное место в восстановлении кровоснабжения играют эндоваскулярные методы хирургического лечения. Однако, остаются недостаточно изученными вопросы осложнений, которые

проведення таких втручань, причини їх виникнення, які морфологічні зміни відбуваються у атеросклеротично змінених стінці артерії при їх проведенні. Метою дослідження було дати морфологічне обґрунтування застосування поетапної дозованої балонної ангиопластики з використанням балонів різного діаметру і довжини у порівнянні з стандартною методикою у хворих з ішемічною формою синдрому діабетичної стопи. Згідно отриманих результатів експериментальних досліджень встановлено, що в основному при виконанні поетапної дозованої ангиопластики за запропонованим способом внутрішня еластична перетинка артерії чітко виражена, має не значні ділянки фрагментації. При цьому, зовнішня еластична перетинка виражена достатньо добре на всьому протязі, має не значні ділянки фрагментації і їх було значно менше чим у тих випадках коли виконувалась ангиопластика за стандартною методикою. Причому, у зовнішній оболонці, де знаходилися судини судин та нерви судин, вони збереглися майже без змін. Зменшення кількості і величини розшарувань оболонок артерії, їх фрагментації при виконанні поетапної дозованої балонної ангиопластики за запропонованим способом з використанням балонів різного діаметру і довжини дозволяє рекомендувати її використання у практичній діяльності для зменшення частоти виникнення тромботичних ускладнень у ранньому післяопераційному періоді.

Ключові слова: діабетична стопа, балонна ангиопластика

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возникают после проведения таких вмешательств, причины их возникновения, какие морфологические изменения происходят в атеросклеротически измененной стенке артерии при их проведении. Целью исследования было изучить в эксперименте морфологические изменения, которые происходят в стенке берцовых артерий при проведении баллонной ангиопластики у больных с ишемической формой синдрома диабетической стопы. Согласно полученным результатам экспериментальных исследований установлено, что в основном при выполнении поэтапной дозированной ангиопластики по предложенному способу внутренняя эластичная перепонка артерии четко выражена, имеет не значительные участки фрагментации. При этом, внешняя эластичная перепонка выражена достаточно хорошо на всем протяжении, имеет не значительные участки фрагментации и их количество было значительно меньше чем в тех случаях, когда выполнялась ангиопластика по стандартной методике. Причем, во внешней оболочке, где находились сосуды сосудов и нервы сосудов, они сохранились почти без изменений. Уменьшение количества и величины расслоений оболочек артерии, их фрагментации при выполнении поэтапной дозированной баллонной ангиопластики по предложенному способу с использованием баллонов различного диаметра и длины позволяет рекомендовать ее применять в практической деятельности для уменьшения частоты тромботических осложнений в раннем послеоперационном периоде.

Ключевые слова: диабетическая стопа, балонная ангиопластика

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NOVEL NON-INVASIVE SEVERITY MARKERS IN IDIOPATHIC PULMONARY FIBROSIS

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Idiopathic pulmonary fibrosis is a severe, steadily progressive disease. Lack of specific signs and presence of individual variations in the course of the disease indicate the need to find additional non-invasive markers for diagnosis, estimation of the disease severity and monitoring of treatment effectiveness. Therefore, this study aimed to determine activities of gelatinase A and gelatinase B activities, as well as progelatinase B/lipocalin complex in patients with moderate and severe IPF. It was found that increased gelatinase A and gelatinase B activities correlated with the disease progression. Increased activities of progelatinase B and its active form at different stages of the disease can be used as markers of the severity of the fibrotic process, while gelatinase A activity can indicate its stage. Changes in the progelatinase B/lipocalin complex activity reflect clinical signs and symptoms during the idiopathic pulmonary fibrosis course and are associated with the severity of the disease.

Keywords: idiopathic pulmonary fibrosis, gelatinases A and B, progelatinase B/lipocalin complex.

The work is a fragment of the research projects "Improving of diagnosis, comprehensive prevention and treatment of respiratory and comorbid diseases in industrial workers and residents of the industrial area", state registration No. 0117U004787 and "Pharmacological approaches on prevention of respiratory failure development in patients with a chronic obstructive pulmonary disease (COPD) in combination with cardiovascular diseases", state registration No. 0115U002017.

Idiopathic pulmonary fibrosis (IPF) is a severe and potentially fatal disease, which is defined by a radiological and histopathological pattern of interstitial pneumonia. The triggering mechanisms of this disease remain unclear [12]. The diagnosis of IPF is based on a set of clinical signs, lung biopsy data, and a typical high-resolution computed tomography pattern [11], provided that other diseases that cause pulmonary fibrosis are excluded [13]. IPF predominantly affects elderly patients. Among the adult population, IPF is usually diagnosed in patients older than 55 years. The average survival rate is 3-5 years and it directly depends on the patient's age at the time of diagnosis: in patients diagnosed between 66 and 69 years of age the survival was almost 8 years compared with 4.5 years in patients diagnosed at the age of 75-79 years and only 2.5 years in patients over 80 years of age [10].

Clinical signs of IPF are not sufficiently specific and coincide with those of other diseases of the interstitial lung disease group [1]. Currently, the high-resolution computed tomography has been