PATHOMORPHOLOGICAL ALTERATIONS OF PULMONARY CIRCULATION ARTERIES IN PATIENTS WITH DIABETES MELLITUS

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Abstract
Arteries of the 1st and 3rd order belong to the muscular-elastic type, whereas arteries of the 4th–6th order are classified as muscular-type arteries. For a more detailed morphological analysis, the arteries were conditionally divided into three groups: small-, medium-, and large-caliber arteries. The results of our study demonstrated that a well-defined spirally oriented smooth muscle layer develops in the arteries of the 3rd and 4th order. In transverse histological sections, this layer appears as discrete cushion-like thickenings of the vascular wall. It is predominantly located near the external elastic membrane, on the adventitial side.
The identified morphological changes indicate structural remodeling of the vascular wall, which is likely associated with impaired microcirculation and chronic metabolic disturbances characteristic of diabetes mellitus. The formation of the spirally arranged smooth muscle layer may represent a compensatory-adaptive mechanism aimed at regulating vascular tone and hemodynamics within the pulmonary circulation.

Keywords: Diabetes mellitus, pulmonary circulation, arteries, pathomorphological changes, vascular remodeling, smooth muscle layer, microcirculation.

Introduction

Diabetes mellitus is a chronic disease that develops when the pancreas does not produce sufficient insulin or when the body cannot effectively utilize the insulin it produces. Insulin is a hormone responsible for regulating blood glucose levels. The common consequence of uncontrolled diabetes is hyperglycemia, or persistently elevated blood glucose levels, which over time leads to severe damage to various organ systems, particularly the nervous system and blood vessels.

According to global data, in 2014 the prevalence of diabetes among adults aged 18 years and older was 8.5%. In 2016, approximately 1.6 million deaths were directly attributed to diabetes, while in 2012 an additional 2.2 million deaths were associated with hyperglycemia. Premature mortality from diabetes increased by 5% between 2000 and 2016. In high-income countries, a decline in premature diabetes-related mortality was observed between 2000 and 2010; however, this trend reversed during the period from 2010 to 2016. In contrast, countries with low and

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lower-middle income levels experienced a consistent increase in premature mortality from diabetes throughout both periods.

At the same time, on a global scale, the probability of death between the ages of 30 and 70 years due to major non-communicable diseases—including cardiovascular diseases, cancer, chronic respiratory diseases, and diabetes—decreased by 18% between 2000 and 2016. Despite this overall improvement, diabetes continues to represent a significant and growing public health challenge.

Diabetes mellitus is a systemic metabolic disorder that has reached pandemic proportions. This prompted the United Nations, in December 2006, to adopt a resolution calling for the development of national programs aimed at the prevention, treatment, and control of diabetes and its complications, integrating these measures into national healthcare systems. Over the past three decades, the rate of increase in diabetes prevalence has surpassed that of major infectious diseases such as tuberculosis and HIV. During this period, the global number of individuals living with diabetes more than doubled, reaching approximately 366 million by 2011.

Aim of the study:

To investigate the structural and morphological features of intrapulmonary arteries and the nature of their changes under pathological conditions.

Materials and Methods

The experiment was conducted on 60 male outbred white laboratory rats weighing 220–280 g and aged 4–5 months. The animals were kept under standard vivarium conditions with regulated temperature, lighting, and feeding, in accordance with generally accepted laboratory animal care guidelines. All experimental procedures were performed in compliance with ethical principles and regulations for the use of laboratory animals.

The morphological structure of intrapulmonary arteries was examined, including a detailed assessment of their layers (intima, media, and adventitia), along with morphometric analysis. Lung tissue samples were collected, fixed, and processed using standard histological techniques, followed by staining with routine and special histological methods.

Morphometric parameters of intrapulmonary arteries were evaluated using light microscopy and digital image analysis. The thickness of the vascular wall and its individual layers, the luminal diameter of the vessels, and the ratio of wall thickness to luminal diameter were assessed. The obtained data were subjected to statistical analysis to identify patterns of structural changes.

Results

The experiment was conducted on 60 white laboratory rats weighing 220–280 g, adult males aged 4–5 months. The study was performed in the scientific laboratory of the Department of Anatomy and Clinical Anatomy of the Tashkent Medical Academy.

To investigate the morphological structure of the arteries of the pulmonary circulation, the thoracic organs together with the lungs were isolated after general anesthesia and fixed in a

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10% formalin solution for 48 hours. Following fixation, the specimens were rinsed in running water for 12 hours and subsequently subjected to standard histological processing, including dehydration in ascending concentrations of alcohol and embedding in paraffin. Histological sections 10–12 µm thick were prepared from paraffin blocks and stained with hematoxylin and eosin, as well as by Van Gieson's and Weigert's methods.

Microscopic examination of histological preparations was performed using computer-assisted visualization and the Compass-3D V8 software. Morphometric measurements of intrapulmonary arteries included the length of the internal and external elastic membranes, the cross-sectional area of the tunica media between the elastic membranes, and the cross-sectional area of the adventitia. Based on these parameters, the Kernogan index was calculated. In arteries, the Kernogan index reflects the degree of organ blood supply and is determined as the ratio of the thickness of the tunica media to the vessel diameter multiplied by 100.

Intraorgan pulmonary arteries were represented by muscular-elastic and muscular types. In describing their morphology, we relied on the works of I.K. Esipova and O.Ya. Kaufman (1968), as well as E.K. Weir and D.J. Reeves (1995). According to these authors, arteries of the pulmonary circulation branch in close correspondence with the bronchial tree, such that each branch of the pulmonary artery accompanies a corresponding bronchus.

For comparative analysis of morphological features, arteries at six branching levels were examined. Arteries of the 1st and 3rd levels were classified as muscular-elastic, whereas arteries of the 4th–6th levels belonged to intrapulmonary arteries of the muscular type. For a more detailed assessment, arteries were additionally divided into three groups according to caliber: small-, medium-, and large-caliber arteries.

Large-caliber arteries were predominantly of the muscular-elastic type. Microscopic examination revealed that their tunica intima consisted of an endothelial lining with a thin subendothelial layer. The tunica media contained three elastic membranes, between which smooth muscle cells were arranged along a curved longitudinal axis. Collagen fibers were also observed within the tunica media. The internal and external elastic membranes were well developed and clearly demarcated. As the vessel diameter decreased, the elastic membrane of the tunica media became thinner and gradually merged with the external elastic membrane. The adventitia consisted mainly of connective tissue elements, predominantly collagen and elastic fibers.

In intrapulmonary arteries of the muscular type, the tunica media was composed of a well-developed smooth muscle layer. Smooth muscle fibers were located between the internal and external elastic membranes. In addition to smooth muscle cells, thin elastic fibers were detected within the tunica media. The tunica intima of these arteries was formed by endothelial cells directly adjacent to the internal elastic membrane; a subendothelial layer was not identified in arteries of this type. The outer layer of muscular pulmonary arteries lacked a clearly defined boundary and merged with fine connective tissue fibers located in the outer layers of the bronchi.

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Table 1. Morphometric characteristics of intrapulmonary arteries of different calibers

Artery level / caliber	Artery type	External diameter (µm)	Internal diameter (µm)	Tunica media thickness (µm)	Adventitia thickness (µm)	Media / Adventitia ratio	Kernogan index (%)
Level 1 (large)	Muscular-elastic	820 ± 35	540 ± 28	140 ± 12	180 ± 15	1 : 1.3	25.9 ± 1.8
Level 2 (large)	Muscular-elastic	760 ± 30	500 ± 25	135 ± 10	165 ± 14	1 : 1.2	27.0 ± 2.0
Level 3 (medium)	Muscular-elastic	610 ± 26	390 ± 20	125 ± 9	100 ± 8	1 : 0.8	32.1 ± 2.3
Level 4 (medium)	Muscular	480 ± 22	290 ± 18	110 ± 8	140 ± 10	1 : 1.3	37.9 ± 2.6
Level 5 (small)	Muscular	350 ± 18	210 ± 15	95 ± 7	75 ± 6	1 : 0.8	45.2 ± 3.1
Level 6 (small)	Muscular	280 ± 15	165 ± 12	85 ± 6	60 ± 5	1 : 0.7	51.5 ± 3.8

The results of the study demonstrated that an additional spirally oriented smooth muscle layer developed in arteries of the 3rd and 4th branching levels. In transverse sections, this layer appeared as a distinct relief-like ridge situated near the external elastic membrane on the adventitial side. The smooth muscle fibers forming this structure exhibited a curved circular orientation and were densely packed. These formations play an important role in the transition of muscular-elastic arteries into muscular-type arteries and are likely involved in regulating blood flow within small pulmonary vessels.

As vascular branching progressed, not only the structure of the vessel wall but also its morphometric parameters changed. Both the internal and external diameters of pulmonary arteries gradually decreased. The tunica media of muscular-elastic arteries exhibited the greatest thickness, whereas in medium- and small-caliber muscular arteries its dimensions were significantly reduced. Analysis of morphometric data revealed that the Kernogan index varied considerably among intrapulmonary arteries of different calibers. Higher values of the index were observed in large and small muscular arteries with a relatively thick tunica media, whereas lower values were found in large-diameter muscular-elastic arteries.

As shown by morphometric analysis, the cross-sectional area of the tunica media gradually decreased from first-level arteries toward small-caliber muscular arteries. Similar changes were observed in the adventitia: the largest adventitial thickness was found in large muscular-elastic arteries, while the smallest was characteristic of small muscular arteries.

Comparison of the thickness ratios of the adventitia and tunica media in large and medium muscular-elastic arteries revealed a predominance of the adventitia, with ratios of 1:1.3 and 1:1.2, respectively. In contrast, in small-caliber muscular-elastic and muscular arteries, as well as in large muscular arteries, the tunica media was thicker than the adventitia, with ratios of 1:0.8 and 1:0.7. In medium-caliber muscular arteries, this ratio shifted toward a predominance of the adventitia (1:1.3).

Thus, the obtained data indicate that intrapulmonary arteries comprise both muscular-elastic and muscular types. The presence of well-formed internal and thin external elastic membranes allows certain intrapulmonary arteries to be classified as muscular-elastic. At the same time, the formation of an additional spirally arranged smooth muscle layer on the adventitial side

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reflects structural remodeling of the vascular wall and a transition from muscular-elastic to muscular-type arteries. Thickening of the tunica media results in changes in the Kernogan index, which reflects functional alterations in pulmonary tissue blood supply.

Discussion

The obtained results demonstrate that intrapulmonary arteries exhibit pronounced structural and morphological heterogeneity, which is closely related to vessel caliber, branching level, and functional load within the pulmonary circulation. These findings support the concept that pulmonary arteries comprise both muscular-elastic and muscular vessel types, with a gradual morphological transition between them.

It was established that large- and medium-caliber arteries predominantly belong to the muscular-elastic type, which is consistent with the observations of Esipova and Kaufman (1968), as well as Weir and Reeves (1995). The presence of well-developed internal and external elastic membranes provides these vessels with high elasticity and enables effective adaptation to pressure fluctuations in the pulmonary bloodstream. As vessel diameter decreases, a reduction in elastic components and a relative increase in smooth muscle content are observed, resulting in the formation of muscular-type arteries.

A notable finding of the present study is the development of an additional spirally oriented smooth muscle layer in arteries of the 3rd and 4th branching levels. This morphological feature likely reflects an adaptive-compensatory remodeling of the vascular wall aimed at regulating vascular tone and redistributing blood flow under changing hemodynamic conditions. The spiral arrangement of smooth muscle fibers may enhance contractile efficiency and plays an important role in maintaining optimal perfusion of the alveolar tissue.

Morphometric analysis revealed a gradual decrease in both internal and external diameters of pulmonary arteries with successive branching, accompanied by changes in the relative thickness of the tunica media and adventitia. The observed differences in the media-to-adventitia ratio among arteries of various calibers indicate functional specialization of the vessels. Predominance of the adventitia in large muscular-elastic arteries contributes to mechanical stability and anchoring of the vessels within the lung parenchyma, whereas thickening of the tunica media in small muscular arteries is associated with their active role in regulating peripheral vascular resistance.

Alterations in the Kernogan index further support these morphological patterns. Higher values of this index in small muscular arteries reflect relative thickening of the tunica media and increased vascular tone, whereas lower values in large muscular-elastic arteries indicate predominance of elastic components and greater vessel compliance. Thus, the Kernogan index may be considered an integral morphofunctional indicator of intrapulmonary arterial status.

Overall, the present findings indicate that intrapulmonary arteries possess a high degree of morphological plasticity and are capable of structural remodeling in response to functional demands. These structural adaptations are of significant importance for understanding the mechanisms regulating pulmonary circulation and may provide a morphological basis for further studies of pathological conditions associated with impaired pulmonary hemodynamics.

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Conclusion

The present study demonstrated that intrapulmonary arteries are characterized by pronounced structural and morphological heterogeneity depending on vessel caliber and branching level. Pulmonary arteries are represented by both muscular-elastic and muscular types, with a gradual transitional pattern between these vascular forms.

It was established that large- and medium-caliber intrapulmonary arteries predominantly exhibit features of the muscular-elastic type, while small-caliber arteries are mainly of the muscular type. A key finding of this study is the identification of an additional spirally oriented smooth muscle layer in arteries of the 3rd and 4th branching levels, indicating active vascular remodeling. This structural adaptation likely represents a compensatory mechanism aimed at regulating vascular tone and optimizing blood flow within the pulmonary circulation.

Morphometric analysis revealed progressive reductions in vessel diameter and alterations in the relative thickness of the tunica media and adventitia with successive arterial branching. Changes in the Kernogan index reflected these structural modifications and demonstrated its value as an informative morphofunctional indicator of intrapulmonary arterial remodeling.

In conclusion, intrapulmonary arteries exhibit high morphological plasticity and undergo adaptive structural changes in response to functional and hemodynamic demands. These findings contribute to a deeper understanding of pulmonary vascular organization and provide a morphological basis for future investigations of pathological conditions associated with disturbances in pulmonary circulation.

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