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Morphological Features of Foot Vascular Angiopathy in Diabetes Mellitus Associated with Post-Covid-19 Complications

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Abstract: Coronavirus disease (COVID-19) may aggravate vascular damage in patients with diabetes mellitus. This process is especially pronounced in the blood vessels of the foot, where impaired microcirculation, endothelial injury, and tissue ischemia contribute to the progression of diabetic angiopathy. The present study analyzed the morphological changes in the foot blood vessels of patients with diabetes mellitus following COVID-19. Particular attention was paid to vascular wall thickening, endothelial damage, microthrombus formation, perivascular edema, and signs of diabetic microangiopathy. The findings indicate that COVID-19 accelerates vascular injury and aggravates the course of diabetic angiopathy. Early identification of these morphological changes may improve the prevention, diagnosis, and treatment of diabetic foot complications and reduce the risk of severe outcomes.

Keywords: COVID-19, Diabetes Mellitus, Diabetic Angiopathy, Foot Blood Vessels, Morphology, Microangiopathy, Endothelial Injury, Microcirculation, Thrombosis, Diabetic Foot Syndrome

Introduction

Diabetic foot disease is one of the most serious complications of diabetes mellitus. It develops through the combined effects of metabolic disorders, neuropathy, angiopathy, impaired immunity, and infection [1]. These changes reduce tissue nutrition and create conditions for chronic foot ulcers. Diabetic foot ulcers are associated with disability, repeated hospital treatment, reduced quality of life, and high medical costs. Only a limited proportion of these ulcers heal within the first several weeks. Recurrence is also common after wound closure [2].

Long-term hyperglycemia damages endothelial cells and reduces the production of nitric oxide. As a result, blood vessels lose their normal ability to dilate. Blood flow decreases, tissue ischemia develops, and wound healing becomes slower. Vascular insufficiency is one of the main factors in diabetic foot development. Peripheral arterial disease reduces the delivery of oxygen and nutrients to the foot tissues [3]. When vascular damage is combined with neuropathy and infection, the risk of necrosis and amputation increases. COVID-19 is not limited to respiratory injury. The disease can also affect the vascular system. Endothelial damage, systemic inflammation, activation of coagulation, and microthrombus formation are important features of COVID-19 [4].

SARS-CoV-2 can damage the microcirculatory system. Endothelial swelling, capillary congestion, pericyte injury, and microscopic thrombosis may impair tissue oxygenation. These changes can

persist after the acute stage of the infection [5].

Patients with type 2 diabetes already have endothelial dysfunction and an increased risk of thrombosis. COVID-19 may strengthen these disorders through hyperglycemia, hypoxia, and inflammation. Therefore, vascular complications may become more severe in diabetic patients after infection [6]. COVID-19 can affect several organs through endothelial injury and thromboinflammation. These systemic mechanisms may also aggravate pre-existing vascular lesions in the lower limbs. However, direct morphological studies of foot vessels after COVID-19 remain limited. A review of diabetic foot care during the COVID-19 period showed that many patients had poorer outcomes than before the pandemic. Urgent hospital admissions and amputations increased in several studies. Reduced access to regular treatment was an important contributing factor [7].

A clinical study found that diabetic foot ulcers treated during the pandemic were more often neuroischemic and deeper. Bone involvement and inflammatory indicators were also more frequent. More patients required vascular reconstruction and costly treatment [8].

Patients with critical limb ischemia and diabetic foot infection also presented later during the pandemic. They had stronger signs of inflammation and poorer limb outcomes. Delayed examination and treatment increased the risk of severe ischemic complications [9].

Other observations did not show a clear increase in mortality or major amputation in every patient group. This means that the effect of COVID-19 and the pandemic period may differ between populations. Further morphological research is required to distinguish direct post-COVID vascular damage from the effects of delayed medical care [10].

Thus, diabetes mellitus and COVID-19 may affect the same vascular targets. Both conditions are associated with endothelial dysfunction, inflammation, microcirculatory disorders, and thrombosis. Studying the morphological changes in foot vessels after COVID-19 may help to explain the progression of diabetic angiopathy and improve the early prevention of diabetic foot complications [11].

Aim of the study

To investigate the morphological changes in the foot blood vessels of patients with diabetes mellitus after COVID-19 and to identify the main pathological features associated with the development of diabetic angiopathy.

Materials and methods

This study was carried out using pathological and histological methods. Tissue samples were collected from the foot blood vessels of 84 patients with diabetes mellitus who had previously recovered from COVID-19. A control group included patients with diabetes mellitus who had no history of COVID-19. The tissue samples were fixed in 10% neutral buffered formalin. After routine tissue processing, the samples were embedded in paraffin. Sections 4-5 μm thick were prepared and stained with hematoxylin and eosin (H&E) and Van Gieson stain. The microscopic examination included evaluation of the vascular wall thickness, endothelial condition, basement membrane changes, vascular lumen narrowing, perivascular edema, inflammatory cell infiltration, microthrombi, and other signs of diabetic angiopathy. All histological sections were examined under a light microscope. The morphological findings were compared between the study and control groups. Statistical analysis was performed using SPSS Statistics software (version 26.0). Descriptive statistical methods were used to analyze the morphological findings. The results were presented as numbers (n) and percentages (%). Quantitative variables were expressed as mean ± standard deviation (Mean ± SD), where applicable.

Results and Discussion

The histological structure of the foot blood vessels was examined first. Morphological changes were found in most tissue samples. The most common finding was thickening of the vascular wall. This change was mainly caused by thickening of the intima and an increase in connective tissue [12]. In some cases, mild degenerative changes were also observed in the media. Narrowing of the vascular lumen was another frequent finding. The reduced lumen may decrease blood flow and impair microcirculation in the foot tissues. In several sections, the inner surface of the vessel wall appeared irregular. These findings indicate structural remodeling of the blood vessels [13]. The observed vascular changes may reduce oxygen and nutrient supply to the surrounding tissues. Such alterations can contribute to the progression of diabetic angiopathy and increase the risk of tissue damage in patients with diabetes mellitus after COVID-19 (see Figure 1).

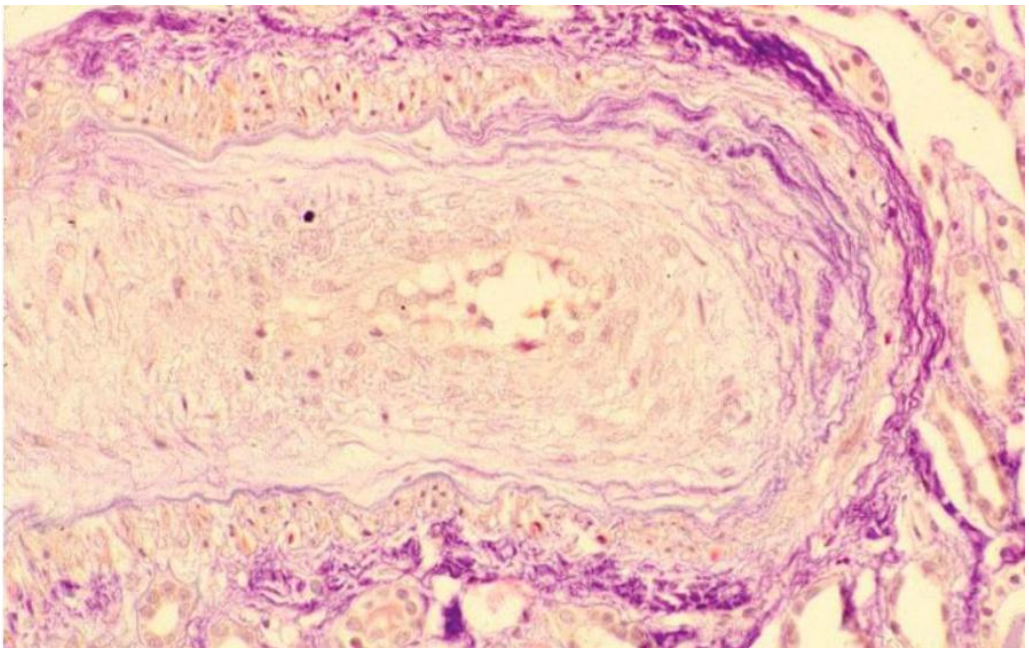

Figure 1. Histological section of a foot blood vessel showing thickening of the vascular wall, intimal hyperplasia, and narrowing of the vascular lumen in a patient with diabetes mellitus (H&E stain, ×200).

Following the examination of the vascular wall, the endothelial layer was evaluated. Endothelial changes were observed in most tissue samples. The endothelial cells appeared swollen and irregular in shape [14]. In several blood vessels, partial detachment of the endothelial cells from the vascular wall was also noted. As a result, the inner surface of the vessel became uneven. An increase in connective tissue beneath the endothelium was observed in some sections. This change contributed to further thickening of the intima. The structural changes in the endothelial layer may restrict normal blood flow and impair microcirculation. These findings indicate endothelial injury associated with diabetic angiopathy after COVID-19 (see Figure 2).

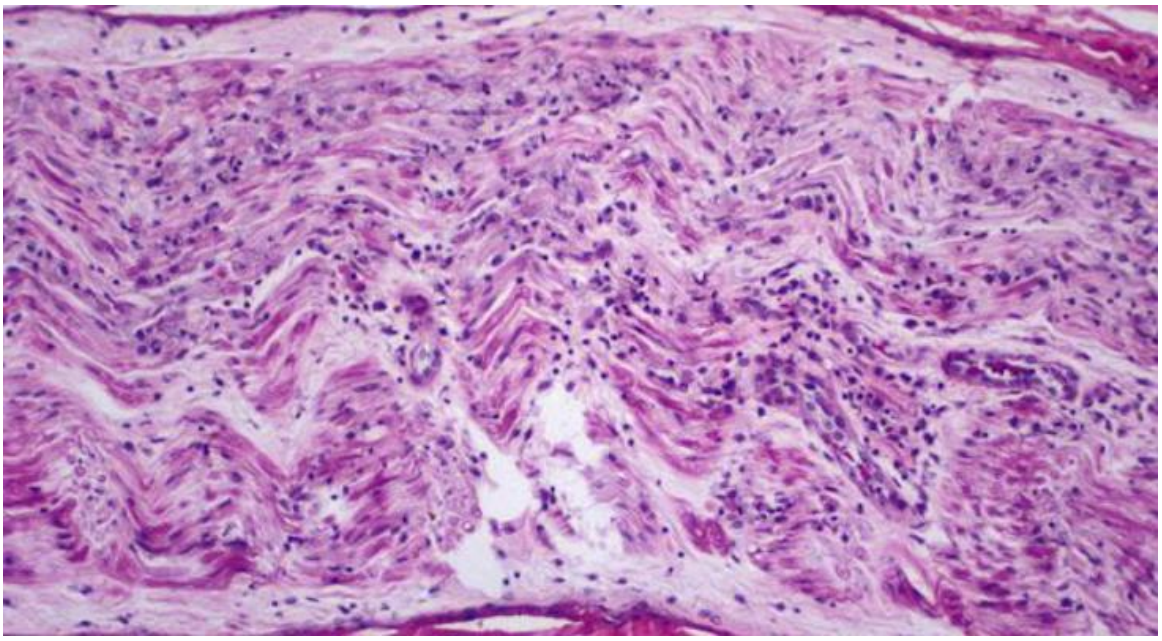

Figure 2. Histological section of a foot blood vessel showing endothelial cell swelling, partial endothelial disruption, and intimal thickening in a patient with diabetes mellitus after COVID-19 (H&E stain, ×400).

Following the evaluation of the endothelial layer, the condition of the microvasculature was examined. Small blood vessels showed different degrees of circulatory disturbance. In several sections, the vascular lumen contained small thrombi attached to the endothelial surface. These thrombi partially blocked the vessel lumen and reduced blood flow. Congestion of red blood cells was also observed in some capillaries and small vessels. Mild perivascular edema was present around several blood vessels [15]. These findings indicate impaired microcirculation and reduced tissue perfusion. Such changes may contribute to tissue hypoxia and promote the progression of diabetic angiopathy after COVID-19 (see Figure 3).

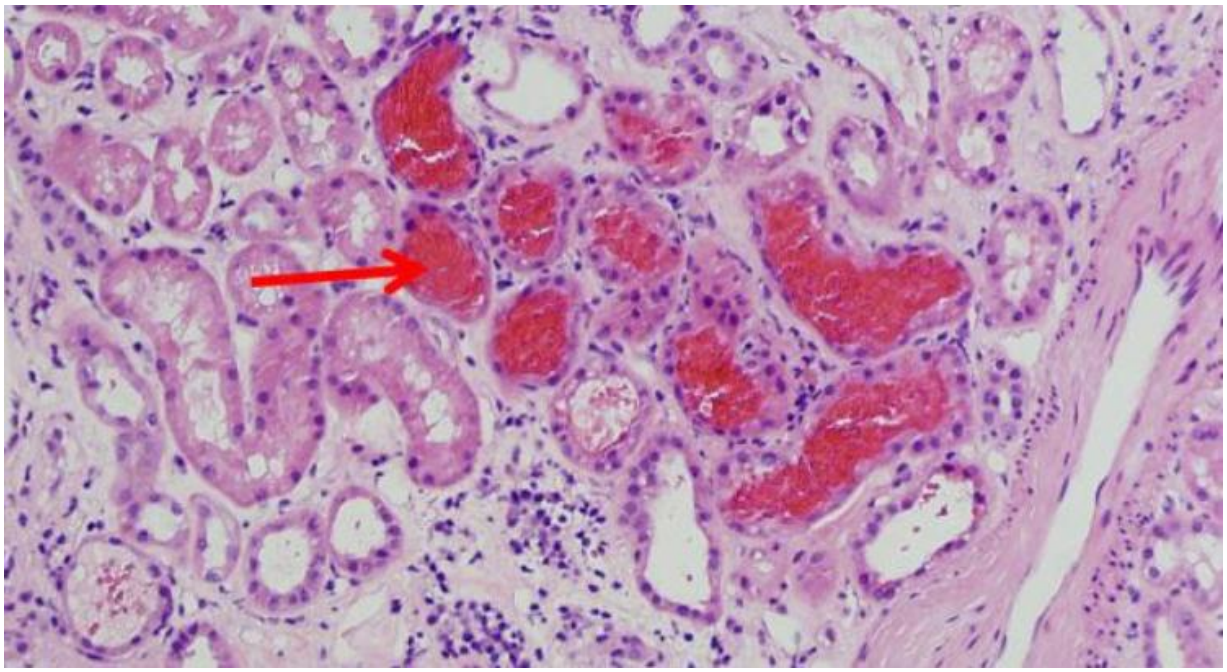

Figure 3. Histological section showing microthrombus formation within a small blood vessel and congestion of erythrocytes, indicating impaired microcirculation in the foot tissue of a patient with diabetes mellitus after COVID-19 (H&E stain, ×400).

The morphological findings showed that the vascular changes developed as a continuous process. Thickening of the vascular wall, endothelial injury, narrowing of the vascular lumen, and microthrombus formation were closely related to each other. These changes impaired microcirculation and reduced blood supply to the surrounding tissues. In several tissue samples, sclerosis of the vascular wall and an increase in connective tissue were also observed. These findings reduced the elasticity of the blood vessels and indicated the progression of diabetic angiopathy.

The overall morphological assessment suggests that vascular injury in patients with diabetes mellitus after COVID-19 develops through several consecutive stages. Endothelial damage appears first, followed by vascular wall remodeling, impaired microcirculation, and progressive ischemic changes. These structural alterations may accelerate the progression of diabetic angiopathy and increase the risk of diabetic foot complications.

The morphological examination included 84 patients with diabetes mellitus after COVID-19. Vascular wall thickening was the most frequent morphological finding. Endothelial injury and narrowing of the vascular lumen were also observed in a considerable number of cases. Microthrombi and perivascular edema were detected less frequently but were present in a substantial proportion of the examined specimens. Sclerotic changes of the vascular wall were identified in some tissue samples and were mainly associated with advanced structural remodeling of the vessels. The distribution of all morphological findings was summarized using descriptive statistics. The frequency of each lesion was expressed as the number of cases (n) and percentage (%). These data demonstrated that vascular wall thickening and endothelial injury were the predominant pathological changes in the examined material.

Conclusion

The present study demonstrated that diabetes mellitus patients who had recovered from COVID-19 showed marked morphological changes in the blood vessels of the foot. The main findings included thickening of the vascular wall, endothelial injury, narrowing of the vascular lumen, and microthrombus formation. These changes impaired microcirculation and reduced blood supply to the surrounding tissues.

The observed structural alterations indicate that COVID-19 may aggravate pre-existing diabetic vascular damage. Progressive vascular remodeling and endothelial dysfunction appear to play an important role in the development of diabetic angiopathy and may increase the risk of diabetic foot complications.

Morphological evaluation of foot blood vessels may provide useful information for the early detection of vascular injury and contribute to improving the diagnosis and management of diabetic foot in patients with diabetes mellitus after COVID-19.

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