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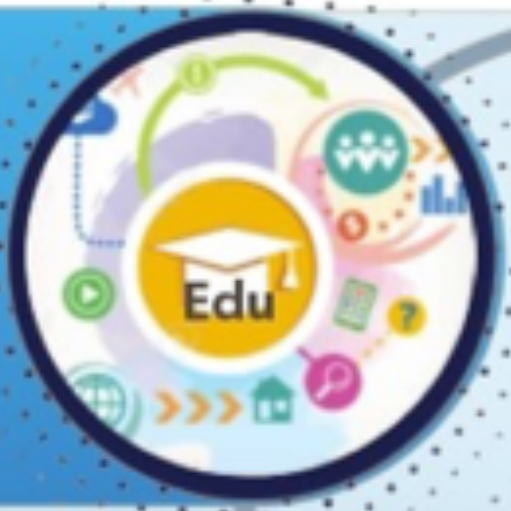

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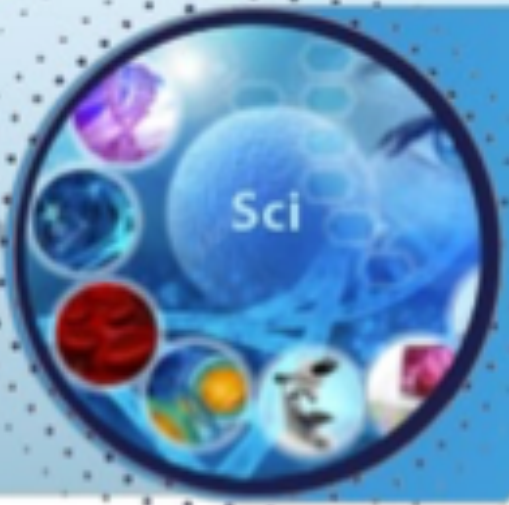

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Interrelationship Between Diabetic Foot Syndrome and Coronary Artery Disease

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ABSTRACT

Background: *Diabetic foot syndrome (DFS) and coronary artery disease (CAD) are two of the most devastating complications of type 2 diabetes mellitus (T2DM), frequently coexisting and interacting through overlapping vascular, metabolic, and inflammatory pathways. Understanding their pathophysiological interdependence is essential for effective management of high-risk diabetic populations.*

Methods: *This narrative review synthesizes current literature on shared mechanisms linking DFS and CAD, including endothelial dysfunction, atherogenesis, systemic inflammation, and impaired microcirculation. Emphasis is placed on epidemiological data, cardiovascular risk stratification, and clinical outcomes in patients with combined DFS and CAD.*

Results: *T2DM accelerates atherosclerosis and promotes multivessel coronary involvement, while also contributing to peripheral ischemia and neuropathy characteristic of DFS. Chronic hyperglycemia, oxidative stress, dyslipidemia, and platelet hyperreactivity play central roles in both coronary and peripheral artery disease. Patients with both conditions exhibit significantly higher rates of amputation, cardiac events, and mortality, underscoring the need for integrative management approaches.*

Conclusion: *DFS and CAD share a common pathophysiological foundation and should be regarded as manifestations of systemic diabetic angiopathy. Risk prediction and treatment strategies must account for the bidirectional impact of these conditions. Early cardiovascular screening in DFS patients and individualized vascular intervention planning are essential to improve limb and life prognosis.*

Keywords: *Diabetic foot, coronary artery disease, type 2 diabetes mellitus, endothelial dysfunction, atherosclerosis, systemic inflammation, ischemia.*

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INTRODUCTION

The global burden of type 2 diabetes mellitus (T2DM) continues to rise, accompanied by a surge in vascular complications that significantly reduce both quality and length of life. Among the most critical are coronary artery disease (CAD) and diabetic foot syndrome (DFS), which frequently coexist and reflect systemic macroangiopathic progression [1,2]. While CAD has long been recognized as the leading cause of death in diabetic patients, DFS remains a major cause of non-traumatic lower-limb amputation and long-term disability. The concurrence of these two complications is not accidental but arises from shared pathophysiological mechanisms rooted in chronic hyperglycemia, oxidative stress, and inflammation [3,4].

Patients with DFS often harbor unrecognized or underdiagnosed myocardial ischemia. Silent ischemia is particularly prevalent in this cohort due to concurrent peripheral neuropathy, which blunts anginal symptoms [5]. Conversely, individuals with established CAD and T2DM are more likely to develop lower-extremity arterial disease and microcirculatory insufficiency that precipitate ulceration and gangrene [6].

Endothelial dysfunction serves as a unifying pathological substrate. Chronic hyperglycemia disrupts nitric oxide signaling, promotes non-enzymatic glycation of vascular proteins, and accelerates lipid oxidation—all of which compromise vascular integrity and repair [7]. The result is widespread atherosclerotic disease, with multivessel involvement observed both in the coronary circulation and the peripheral arteries of the lower limbs [8]. Moreover, T2DM patients frequently exhibit a distinct pattern of diffuse, subcritical coronary lesions, which are prone to plaque rupture despite appearing non-significant angiographically [9].

From a clinical standpoint, the presence of DFS is now recognized as a powerful independent predictor of adverse cardiovascular events. Studies indicate that the five-year mortality after major limb amputation in diabetic patients can exceed 50%, rivaling that of several malignancies [10]. Likewise, patients with DFS and concurrent CAD face increased risk of perioperative complications, prolonged hospitalization, and poor limb salvage outcomes, particularly when their cardiac function is compromised [11].

Despite this well-established bidirectional risk, management approaches often remain siloed. DFS is typically addressed by vascular or diabetic foot care teams, while CAD is managed within cardiology departments. This separation may delay risk recognition and reduce opportunities for coordinated care. In addition, most current revascularization algorithms for DFS do not incorporate myocardial functional reserve as a determinant of procedural sequence, even though cardiac output directly affects distal limb perfusion [12].

Integrating cardiovascular and peripheral vascular assessments into a single clinical framework is therefore essential. Recent guidelines advocate for comprehensive risk stratification using clinical, hemodynamic, and anatomical parameters to inform individualized treatment planning in high-risk patients with combined DFS and CAD [13]. However, practical implementation of such integrative strategies remains inconsistent, particularly in resource-limited settings.

This review aims to consolidate the current understanding of the pathophysiological interplay between DFS and CAD in patients with T2DM, highlighting epidemiological associations, shared mechanisms of vascular injury, and the clinical consequences of dual pathology. Recognizing DFS as a surrogate marker of systemic vascular disease and integrating cardiometabolic considerations into diabetic foot management may improve both limb preservation and cardiovascular survival outcomes [14,15].

MAIN PART

Pathophysiological Convergence of DFS and CAD in T2DM)

The pathophysiological convergence of diabetic foot syndrome (DFS) and coronary artery disease (CAD) in the context of type 2 diabetes mellitus (T2DM) is now understood to reflect not merely the coexistence of complications but a common systemic vascular pathology. Central to this interplay is chronic hyperglycemia, which initiates a cascade of cellular and molecular events that compromise vascular structure and function across both macro- and microvascular domains [1].

Endothelial dysfunction represents a pivotal early manifestation of diabetic angiopathy. Prolonged exposure to elevated glucose levels leads to increased production of reactive oxygen species (ROS), impaired nitric oxide (NO) bioavailability, and the formation of advanced glycation end-products (AGEs), all of which disrupt endothelial homeostasis. These abnormalities reduce vasodilatory capacity, enhance vascular permeability, and stimulate expression of adhesion molecules, thus facilitating leukocyte infiltration and vascular inflammation [2]. In coronary vessels, these mechanisms accelerate the development of atheromatous plaques, while in

peripheral arteries they lead to progressive occlusion and ischemia of the lower limbs [3].

Moreover, the atherosclerotic burden in T2DM is characteristically diffuse, affecting multiple arterial territories simultaneously. Coronary angiographic studies have demonstrated that diabetic patients frequently present with multivessel disease and a higher incidence of complex lesions, including long-segment stenoses and distal occlusions [4]. In the peripheral vasculature, these same individuals often exhibit critical limb ischemia and distal vessel calcification, both of which complicate revascularization efforts and contribute to the progression of DFS [5].

Another common feature is the impaired capacity for neovascularization and collateral vessel formation. This is particularly significant in the diabetic foot, where tissue hypoxia is compounded by neuropathy and impaired angiogenic signaling. Similar defects in angiogenesis have been observed in the myocardium of diabetic patients with ischemic cardiomyopathy, suggesting a global impairment in vascular adaptation [6].

In addition to structural alterations, diabetic vascular pathology is marked by chronic low-grade inflammation. Elevated serum levels of interleukin-6, tumor necrosis factor-alpha, and high-sensitivity C-reactive protein have been documented in both DFS and CAD populations, correlating with disease severity and progression [7]. This inflammatory state not only contributes to endothelial injury but also promotes thrombogenicity through increased platelet aggregation and procoagulant activity [8]. Consequently, patients with T2DM and combined DFS-CAD often exhibit heightened susceptibility to both arterial occlusion and stent thrombosis, presenting a challenge for both medical and interventional management.

The clinical implications of this shared pathogenesis are substantial. DFS serves as a clinical marker of advanced systemic atherosclerosis and should prompt active cardiovascular screening. Conversely, the presence of CAD in a diabetic patient should raise concerns about unrecognized peripheral ischemia, especially in the presence of neuropathy that may mask classic symptoms such as intermittent claudication [9].

Taken together, the coexistence of DFS and CAD reflects a syndrome of global diabetic vasculopathy, where cardiac and limb perfusion are mutually dependent and pathophysiologically inseparable. Effective management therefore requires an integrated approach that simultaneously addresses coronary perfusion, limb salvage, and glycemic control, guided by accurate cardiovascular and angiographic risk stratification [10–12].

Epidemiological Associations and Clinical Coordination Challenges

Epidemiological data have consistently demonstrated a high degree of overlap between diabetic foot syndrome (DFS) and coronary artery disease (CAD) in individuals with type 2 diabetes mellitus (T2DM). Studies indicate that more than 70% of patients presenting with DFS have either previously diagnosed or subclinical CAD, a proportion that increases with age, disease duration, and poor glycemic control [1]. Moreover, nearly one-third of patients undergoing major lower-extremity amputation due to DFS die within the first year postoperatively, with cardiovascular events representing the leading cause of mortality [2].

DFS is now widely recognized as an independent predictor of major adverse cardiovascular events (MACE), including myocardial infarction, stroke, and cardiovascular death. The five-year mortality rate following high-level amputation in diabetic patients can exceed 50%, underscoring the profound systemic burden carried by individuals with advanced peripheral disease [3]. Conversely, diabetic patients with CAD are more likely to exhibit occult lower-extremity arterial disease and tissue hypoxia, which may remain undetected until the development of ulceration or infection. Peripheral neuropathy, a hallmark of DFS, further obscures symptom recognition and delays timely diagnosis [4].

Despite this robust epidemiological connection, clinical coordination between specialties remains suboptimal. In many healthcare systems, DFS and CAD are managed in separate institutional silos—vascular surgery and diabetology on one side, cardiology and internal medicine on the other. This organizational separation hinders the timely identification of high-risk patients and precludes the implementation of shared therapeutic pathways. It also limits the integration of cardiovascular risk assessment into the decision-making process for lower-limb revascularization [5].

Guideline-based management algorithms frequently overlook the bidirectional impact of cardiac and limb ischemia. For instance, standard protocols for diabetic foot revascularization focus primarily on angiographic feasibility and limb viability, without systematically accounting for myocardial perfusion or left ventricular function. However, impaired cardiac output can directly influence the success of distal tissue perfusion, particu-

larly in the setting of borderline vascular anatomy or microcirculatory compromise [6].

Moreover, recent studies suggest that cardiac dysfunction may not only reduce limb salvage potential but also increase the risk of perioperative complications. Diabetic patients with reduced left ventricular ejection fraction undergoing lower-extremity interventions exhibit higher rates of hemodynamic instability, arrhythmia, and postoperative deterioration [7]. In this context, stratifying patients according to both cardiac and peripheral vascular profiles become critical for optimizing treatment sequencing and resource allocation.

Some authors have proposed integrated scoring systems that include cardiac status, glycemic control, wound depth, and anatomical vascular parameters to predict outcomes in patients with combined DFS and CAD. While these models have shown promise in retrospective analyses, they remain underutilized in routine practice due to limited validation and lack of consensus regarding their clinical application [8]. Additionally, in regions with constrained access to advanced imaging modalities, risk assessment often relies on subjective clinical judgment, which may introduce variability in care.

Consequently, there is a pressing need for the development and dissemination of standardized algorithms that incorporate cardiovascular risk stratification into the therapeutic planning for DFS. Such frameworks should enable clinicians to determine not only the technical feasibility but also the physiological appropriateness of limb revascularization, especially in patients with compromised myocardial reserve [9,10].

Ultimately, viewing DFS and CAD as mutually reinforcing manifestations of systemic diabetic macroangiopathy demands a shift in both mindset and organizational structure. By promoting interdisciplinary collaboration and shared clinical decision-making, healthcare providers can better address the complex interplay of cardiac and peripheral vascular disease, improving long-term outcomes in this vulnerable population.

Therapeutic Perspectives and Future Directions

The recognition of diabetic foot syndrome (DFS) as a systemic vascular disease with prognostic implications extending beyond limb preservation has significant therapeutic consequences. Recent international guidelines emphasize the importance of multidisciplinary care models for patients with DFS and coexisting coronary artery disease (CAD), recommending close collaboration between diabetologists, vascular surgeons, cardiologists, and rehabilitation specialists [1]. These integrative strategies are particularly crucial for high-risk individuals with reduced left ventricular function, multilevel arterial disease, or recurrent ulceration.

One of the key principles emerging from recent literature is the necessity of tailoring revascularization strategies to the individual patient's cardiovascular profile. In those with well-compensated cardiac function, primary endovascular intervention targeting the lower extremity may be performed safely with high success rates. However, in patients with advanced CAD, especially with reduced ejection fraction or unstable angina, preliminary coronary assessment and revascularization should be considered prior to peripheral procedures to mitigate intraoperative risk and improve perfusion adequacy [2].

The timing and sequencing of interventions remain areas of ongoing debate. While "limb-first" approaches may be favored in the setting of limb-threatening ischemia, the "heart-first" strategy may be more appropriate for patients with severe myocardial dysfunction or recent cardiac events [3]. Hybrid pathways involving simultaneous or staged revascularization have also shown promise, but require logistical coordination and careful risk stratification. Prospective studies comparing these models remain limited, and further randomized trials are needed to establish evidence-based algorithms [4].

Beyond procedural considerations, systemic optimization is paramount. Intensive glycemic control, lipid-lowering therapy, and antiplatelet regimens form the cornerstone of macrovascular protection in diabetic patients, yet are often underprescribed in those with foot complications due to perceived frailty or focus on local treatment. Integration of secondary cardiovascular prevention into diabetic foot care pathways has been shown to reduce mortality and improve healing rates [5].

Emerging technologies may further enhance risk prediction and guide therapy. Non-invasive vascular imaging, tissue oxygenation metrics, and machine learning algorithms capable of integrating metabolic, anatomical, and hemodynamic variables hold promise for refining prognostic models in patients with combined DFS and CAD [6,7]. However, these tools require rigorous validation and equitable access to ensure their utility across diverse healthcare settings.

Ultimately, DFS and CAD must be conceptualized not as isolated complications of diabetes, but as interconnected expressions of advanced systemic vascular disease. Their joint presence demands a unified clinical response that transcends disciplinary boundaries. Personalized therapeutic strategies, grounded in accurate risk stratification and multidisciplinary coordination, of-

fer the best opportunity to improve survival, preserve limb function, and reduce the global burden of diabetic macroangiopathy [8–10].

CONCLUSION

The convergence of diabetic foot syndrome (DFS) and coronary artery disease (CAD) in patients with type 2 diabetes mellitus (T2DM) is emblematic of systemic vascular pathology that transcends localized complications. Rather than distinct entities, these conditions represent interconnected manifestations of chronic endothelial dysfunction, accelerated atherogenesis, and impaired tissue perfusion. Their coexistence is associated with markedly elevated risks of limb loss, cardiovascular events, and mortality.

Despite robust evidence linking DFS and CAD through shared pathophysiological and epidemiological pathways, clinical management remains fragmented. The absence of integrated diagnostic frameworks and unified therapeutic strategies undermines timely risk stratification and coordinated care. To improve outcomes, clinicians must adopt a systems-level perspective—one that simultaneously evaluates coronary and peripheral arterial disease, optimizes metabolic control, and coordinates revascularization efforts in a personalized, risk-oriented manner.

Future research must focus on validating predictive models that incorporate cardiac function, vascular anatomy, metabolic status, and inflammatory markers to guide treatment sequencing. Multidisciplinary teams and standardized care algorithms will be critical in translating scientific insights into clinical benefit. As the prevalence of T2DM continues to rise, integrating cardiac and limb-focused strategies will be essential to mitigate the global burden of diabetic macroangiopathy.

Ethical Approval:

This article is a narrative literature review and does not involve original research with human or animal subjects. Therefore, ethical approval was not required.

Conflict of Interest:

The author declares no conflicts of interest.

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Author Contributions:

Kamalov S.T.: Conceptualization, literature analysis, writing, and final revision of the manuscript.

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DIABETIK OYOQ SINDROMI VA YURAK ISHEMIK KASALLIGINING O‘ZARO BOG‘LIQLIGI

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ANNOTATSIYA

2-tip qandli diabet bilan og‘rigan bemorlarda diabetik oyoq sindromi (DOS) va yurak ishemik kasalligi (YIK) ko‘pincha birga uchraydi va bu holatlar tomirlar, metabolizm va yallig‘lanish mexanizmlari bilan chambarchas bog‘langan. Ushbu adabiy tahlil DOS va YIK o‘rtasidagi umumiy patofiziologik mexanizmlarni o‘rganadi, jumladan endotelial disfunktsiya, ateroskleroz, periferik ishemiya va tizimli yallig‘lanishni. Tadqiqot natijalari shuni ko‘rsatadiki, bu ikki asoratning birgalikda mavjud bo‘lishi bemorlarning amputatsiya, yurak-qon tomir asoratlari va o‘lim xavfini keskin oshiradi. DOS holatida YIK uchun faol skrining, shuningdek, miokard zahirasini hisobga olgan holda individual davolash strategiyalarini ishlab chiqish zarur. Vaskulyar kasalliklarning umumiy modeli sifatida DOS va YIK ni yagona, tizimli yondashuvda baholash bemorlarning hayot va oyoqni saqlab qolish prognozini yaxshilashga yordam beradi.

Kalit so‘zlar: Diabetik oyoq, yurak ishemik kasalligi, qandli diabet, endotelial disfunktsiya, ateroskleroz, ishemiya.

ВЗАИМОСВЯЗЬ СИНДРОМА ДИАБЕТИЧЕСКОЙ СТОПЫ И ИШЕМИЧЕСКОЙ БОЛЕЗНИ СЕРДЦА

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АННОТАЦИЯ

Синдром диабетической стопы (СДС) и ишемическая болезнь сердца (ИБС) являются двумя наиболее тяжёлыми осложнениями сахарного диабета 2 типа, которые часто сосуществуют и развиваются на фоне общих сосудистых, воспалительных и метаболических нарушений. Настоящий обзор посвящён анализу патогенетических механизмов, объединяющих СДС и ИБС, включая эндотелиальную дисфункцию, атерогенез, хроническую ишемию и системное воспаление. Отмечается, что пациенты с СДС имеют высокую частоту скрытой или недиагностированной ИБС, а одновременное наличие обеих патологий значительно увеличивает риск ампутаций, сердечно-сосудистых событий и летальности. Подчёркивается необходимость кардиологического скрининга при СДС, интеграции миокардиального статуса в планирование сосудистых вмешательств и реализации персонализированной стратегии лечения. Рассмотрение СДС и ИБС как двух аспектов системной диабетической ангиопатии позволяет обосновать необходимость междисциплинарного подхода к ведению пациентов с высокой сосудистой коморбидностью.

Ключевые слова: Синдром диабетической стопы, ишемическая болезнь сердца, сахарный диабет 2 типа, эндотелиальная дисфункция, атеросклероз, ишемия.