Bridging the translational gap: immune-metabolic dysregulation in age-related metabolic and vascular diseases in real-world populations

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Age-related metabolic and vascular diseases—such as type 2 diabetes, obesity, hypertension, and atherosclerosis—are leading contributors to morbidity and mortality worldwide. While traditionally studied in isolation, these conditions share overlapping pathophysiological mechanisms, particularly at the intersection of immune and metabolic dysfunction. Increasing evidence supports the existence of common immune-metabolic disturbances, including chronic low-grade inflammation (inflammaging), immune cell dysregulation, mitochondrial dysfunction, and altered nutrient sensing[1]. These factors contribute to endothelial dysfunction, insulin resistance, oxidative stress, and tissue remodeling—the hallmarks of both metabolic and vascular decline in aging. Despite significant advances in immunometabolism and aging biology, our understanding of how these immune-metabolic alterations develop and interact during aging remains incomplete. Key shared pathways—such as activation of the NLRP3 inflammasome, impaired AMPK and mTOR signaling, macrophage polarization, and immune senescence—have been identified[2]. However, the causal relationships between these processes and their temporal dynamics across different tissues are still poorly defined. Moreover, heterogeneity in aging phenotypes, sex differences, and the influence of environmental and genetic factors further complicate the elucidation of unifying mechanisms. This lack of integrative understanding presents a major barrier to the development of effective, targeted interventions for age-related cardiometabolic diseases[3]. Current therapeutic strategies often address individual risk factors rather than the underlying systemic dysfunctions. There is an urgent need for interdisciplinary approaches that combine systems biology, longitudinal studies, and mechanistic research to map the complex crosstalk between the immune and metabolic systems during aging. In this review, we synthesize current knowledge on common immune-metabolic mechanisms driving age-related metabolic and vascular conditions, highlight key gaps in the field, and propose future research directions. A deeper understanding of these shared pathways could pave the way for innovative therapies aimed at delaying or preventing multiple age-associated diseases through immune-metabolic modulation.

LITERATURE

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