Toward a targeted approach to diabetes-related peripheral arterial occlusive disease

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Data on the histologic and molecular patterns of vascular remodeling in diabetes are still lacking. In their study, Narayanan et al[1] elegantly compare the arterial response to balloon-mediated carotid injury in diabetic rats with nondiabetic rats and provide a pathophysiologic and transcriptomic database for differences in vascular response without and with insulin resistance. They successfully apply novel bioinformatics tools in this established model of arterial injury to analyze gene expression and regulation associated with balloon injury. The authors' work is relevant, impactful, and timely. Diabetes mellitus constitutes a global health burden. The results of the National Health and Nutrition Examination Survey show that the prevalence of diabetes has nearly doubled over the last three decades.[2] This pervasive disease often presents with unique patterns of peripheral atherosclerosis.[3] The outcomes of percutaneous intervention in this group have heretofore seemed worse than in nondiabetic patients.[4] In an era where the number of endovascular interventions performed has increased continually, understanding the arterial response to treatment delivery and minimizing negative vascular remodeling are of the utmost importance to guide future therapeutic advances.[5]

This article shows the mechanisms underlying the distinct and inferior outcomes of endovascular revascularization in this high-risk population. In a simulated percutaneous transluminal angioplasty model consisting of Fogarty balloon arterial stretch, insulin-resistant type 2 diabetic rats showed significantly greater neointimal thickness driven by increased numbers of contractile smooth muscle cells and an aberrant inflammatory response. Goto-Kakizaki rats exhibited sustained upregulation of smooth muscle cell proliferation genes for ≤6 weeks after injury.

To date, treatment algorithms are rarely based on phenotypes of vascular response, limiting the application of personalized medicine. Strides in endoluminal device development have been made in parallel with but not in conjunction with the steadfast discovery of molecular markers of intimal response.[6] Therapeutic targeting of vascular growth and remodeling modifiers is long awaited. This work establishes a rich database of gene expression associated with arterial healing and has the potential to serve as the cornerstone for personalized vascular medicine. The optimal endovascular treatment for symptomatic peripheral arterial occlusive disease could combine not only a mechanical solution for a sustained hemodynamic treatment, but also a biologic therapy targeting patient-specific vascular healing pathways.

To decrease postintervention neointimal hyperplasia and its sequela restenosis, drug-coated balloons and drug-coated and -eluting stents are commonly used in contemporary practice. In this study, the authors used a conventional balloon-mediated injury that is a closer model for plain old balloon angioplasty. Future studies may, thus, include this important variable.

In summary, this study provides granular animal data on the delayed vascular healing associated with diabetes after endovascular intervention. Additional translational science is needed to further understand the diabetic arterial response to the vast array of available endovascular therapies and help to guide treatment selection as well as potentially target vascular remodeling on a molecular level. Clinicians know that a one-size-fits-all endovascular treatment protocol is insufficient; the long-term durability of peripheral endovascular intervention may require the application of transcriptomics to target patient-specific mechanisms of vascular response after revascularization.

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