Editorial Comment

The Role of Adventitial Vasculature In Restenosis: A New View of an Old Problem*

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There has recently been a reawakening in the appreciation of the importance of the adventitia in the response to vascular injury. As early as 1915, a role of the adventitia had been postulated in the arterial response to, (and possibly the progression of), atherosclerosis when Allbutt described inflammatory cells in atherosclerotic arteries (1). Schwartz and Mitchell later noted a correlation between the degree of adventitial inflammation and the severity of atherosclerotic disease in the overlying arterial wall (2). Adventitial inflammation has also been described in studies of experimental hypercholesterolemia in nonhuman primates (3).

Although initial experiments into the mechanism of restenosis focused on deendothelialization as the primary injury (4), pathologic studies in humans have documented that the mechanism of angioplasty was due to tearing of the media with exposure of deep media and adventitia (5). Pigs have been used as models for postangioplasty restenosis with some success mainly because of the similarity in size to humans and the use of catheters and devices identical to those used clinically. After coronary overstretch injury, there is an intense amount of adventitial proliferation two to three days after injury. By seven days after injury this adventitial proliferation abates, and there is a relatively small amount of proliferation at and near the torn medial end. By two weeks after injury the proliferative response is nearly complete. Pulse-label studies have suggested that the proliferating cells in the adventitia migrate from the adventitia to form the neointima (6). In addition, the chronic remodeling seen after vascular injury seems to be related to a phenotypic change in the adventitia because it acquires markers for actin. Thus, it seems that the adventitia plays a critical role in the response to angioplasty-like injuries. Therefore, the characterization of the blood supply to this important area and the changes that occur after injury is crucial to developing an understanding of the mechanism of restenosis.

The article written by Kwon and colleagues (7) will be of significant importance in the elucidation of the mechanism of the vascular response to injury. The authors used microscopic computed tomography techniques to construct a three-dimensional pattern of the vasa vasorum. They found that in normal coronary arteries there were two types of vasa. First-order vasa arose primarily from branch points and ran longitudinally along the vessel wall. Second-order vasa arose from the first-order vasa and ran circumferentially in a plexus around the vessel wall. After balloon injury, the authors found that the density of the vasa vasorum increased, and it seemed that the newly formed vasa were mainly second order vasa. In addition, these investigators found a correlation between the number of vasa vasorum and the percent luminal stenosis.

The findings in this article constitute a major step forward in the understanding of the mechanism of the arterial response to vascular injury, and particularly, to restenosis. A key question will be whether the proliferation of the vasa vasorum is necessary for the cellular proliferation and remodeling. With the advent of drugs that inhibit neovascularization and the ability to deliver drugs locally, the findings of Kwon et al. may have a major role in the development of a successful pharmacologic treatment for the prevention of restenosis.

References