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Reply

We appreciate the insights that Dr. Merryman offers regarding degenerative aortic valve disease (DAVD) and our recent article (1). He emphasizes the point that the aortic valve interstitium plays a paramount role in the process of valve degeneration. The authors agree that the interstitium, along with the endothelium, generates an inflammatory milieu that promotes DAVD, and that structural changes in the interstitium and endothelium are inherent to the disease process. We attempted to discuss this in our review but perhaps should have further emphasized the importance of the interstitium to this process.

We agree with Dr. Merryman that matrix remodeling and degradation may result from direct effects on the interstitium (2,3). The effects of cytokines within the interstitium include the upregulation of matrix metalloproteinase (MMP), which causes valvular remodeling by degrading the extracellular matrix (4). As we state in our article, MMP seems to regulate valve plasticity, but its overexpression in DAVD leads to elastin degradation in the interstitium, which may contribute to adverse remodeling (5,6). We highlight the transformation of myofibroblasts into an osteogenic phenotype under the influence of cytokines, which alter expression of MMP and bone morphogenic protein (BMP) (7,8). Aortic valve remodeling is strongly linked to altered expression and cytokine production in the myofibroblasts of the interstitium.

In our review we discuss the hemodynamic and mechanical forces that affect the aortic side of the valve and the structural remodeling of the endothelium on that surface. The cascade of downstream effects initiated by endothelial disruption leads to the changes described above. As Dr. Merryman postulates, there may be further effects caused by altered stress transfer from variably oriented collagen fibers in the interstitium of aging valves. We agree that this process may contribute to the pathological changes described in DAVD. However, Dr. Merryman's statement that nearly all DAVD pathology originates in the fibrosa may exclude other important processes contributing to this pathology. In addition, although Dr. Merryman has shown that transforming growth factor β1 alters smooth muscle alpha-actin and type I collagen C-terminal propeptide in an in vitro model, the notion that DAVD in vivo is largely predicated on transforming growth factor β1 activation may be a generalization (9).

In conclusion, we agree that the interstitium and the myofibroblasts therein play a critical role in the pathogenesis of DAVD. Stress transfer within the interstitium likely contributes to matrix remodeling and cytokine activation, but further studies are needed to confirm current studies and determine the relative importance of this pathway.

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Vascular Closure Devices: Begin With the End in Mind

In their review of the history and future of vascular closure devices, Dauerman et al. (1) discuss a variety of factors that affect vascular complication rates. They note that there are cautions and contraindications regarding the use of vascular closure devices and indicate that post-procedure femoral angiography is a "significant advance" in reducing complications, because it identifies the 13% of patients with nonfemoral sheath insertion and also those with insertion above the inferior epigastric artery.

We would liken this practice to secondary prevention. As important as that is, most of us would like to achieve primary prevention and prevent incorrect sheath location. To achieve that, it has been widely recommended that pre-procedure fluoroscopy of the femoral head would help to reduce inaccurate sheath insertion and lower complication rates.

Unfortunately, the authors do not even mention the most accurate method of sheath insertion: the use of needle-guided vascular ultrasound imaging. Invasive and interventional cardiologists relying on surface or fluoroscopic landmarks depend upon normal anatomy and palpation to guide their punctures. In percutaneous coronary intervention procedures this is uncomplicated about 98% of the time, as noted in the article and by the NNECVDG (Northern New England Cardiovascular Disease Study Group) Registry.

In our experience, routine ultrasound use can substantially lower this small but costly complication rate. It has long been advocated in the anesthesia community for safe and successful central venous access. Prospective data to prove this claim are, unfortunately, not yet available for femoral access.

In the cardiac catheterization laboratory, ultrasound is sometimes used for the "difficult patient," relegating it to a situation that disrupts the flow of the procedure and may be frustrating, since rare use on the most difficult patients makes for a long learning curve. Routine ultrasound use, however, can be done very quickly