You can never step twice in the same river

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“You can never step twice in the same river,” so Heraclitus of Ephesus (535-475 BCE) explained the concept of the *panta rhei* (everything flows), which beautifully represents the first clear definition of space-time relativity. It took the genius of Albert Einstein to integrate this concept fully into the restricted relativity theory paradigm, finally making easy to understand for everyone that although we live in a 3-dimensional world, we live in it 4-dimensionally.

Although for most diseases the dimension of time is irrelevant, cardiovascular medicine has some peculiarities that make space-time thinking relevant. The average heartbeat accomplishes a full cycle in less than a second, moving all structures by a few centimeters and in the process displacing a significant volume of blood from the heart chambers to the great vessels. The novel technique of 4-dimensional magnetic resonance imaging represents in fact the possibility of coupling spatial acquisition with time resolution. It encodes the velocity of flowing blood at each voxel in the volume, enabling fluid dynamics to be visualized by means of dedicated software. Because of the complexity of postprocessing and relatively long acquisition times, this technique is not yet routine in clinical use, but it holds potential as a groundbreaking technique to understand further the consequences of reconstructive or replacement heart valve and aortic surgical therapies. We have also recently used this fascinating technology to visualize optimal flow inside the sinuses of Valsalva,¹ something Leonardo da Vinci magically and beautifully sketched in his *Corpus of Anatomical Studies* in the Windsor collection of Queen Elizabeth II.

The article by Bollache and colleagues² in this issue of the *Journal* interestingly confirms the power of 4-dimensional magnetic resonance imaging to evaluate regional structural characteristics. This elegant study shows that for patients with bicuspid aortic valves, increased aortic valve-mediated wall shear stress is significantly associated with elastic fiber thinning, particularly with aortic valve stenosis and in the earlier stages of aortopathy. In turn, elastic fiber thinning correlates with impaired tissue biomechanics.

Luca P. Weltert, MD (left), and Ruggero De Paulis, MD (right)

Central Message

The recent use of 4-dimensional magnetic resonance imaging, with its potential for measuring wall shear stress, is contributing greatly to shedding light on this controversial issue.

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These findings, clearly confirmed by histopathologic study of aortic tissue samples resected at surgery, further implicate valve-mediated hemodynamics in the progression of bicuspid aortic valve aortopathy. The information provided by this study starts to unravel the controversies and discussions about the origin of aortopathy in the context of a bicuspid valve or in relation to various morphologic types of bicuspid valve. The long-standing argument as to whether the aortopathy is genetically predetermined or rather depends on the eccentric flow hammering the aortic wall and initiating a degenerative process is beginning to be clarified. On the basis of the current data of Bollache and colleagues,² we have finally arguments to assert that a bicuspid stenotic valve with time might induce progressive wall degeneration at the site where the jet impacts the aortic wall. The first direct consequence of this notion is the possibility that earlier aortic valve replacement might stop the process and, to some extent, prevent aortic dilatation. At the moment, other forms of aortopathy, such as the “root phenotype,” similar to patients with Marfan syndrome and often associated with bicuspid valve insufficiency, appear to be genetically mediated, but the scientific evidence is still lacking, and a similar epigenetic mechanism may well be involved. For the time being, however, in both cases, waiting too long before surgery seems to increase the chance of aortic dilatation and its related consequences.

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