Abdominal aortic aneurysms: insights into mechanical and extracellular matrix effects from mouse models

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Abdominal aortic aneurysms (AAAs) manifest with progressive luminal dilatation and a high risk of aortic rupture. In the past two decades, the mechanisms of this devastating disease have been explored using multiple mouse models. Since early 2000, three AAA mouse models have often been used, including angiotensin II infusion,[1] periaortic application of calcium chloride,[2] and intraluminal perfusion of elastase.[3] In 2012, Bhamidipati et al[4] modified the intraluminal perfusion of the elastase model with an easier surgical procedure involving periadventitial application. However, just as with the intraluminal elastase perfusion model, the luminal dilatation was modest, with no aortic rupture. Recently, Lu et al[5] modified this mouse model to provoke more severe pathologic manifestations. In addition to the periadventitial application of elastase, the mice are administered β-aminopropionitrile (BAPN) in their drinking water. Prolonged administration of BAPN leads to progressive luminal dilatation of the infrarenal aorta, thrombosis, and spontaneous infrarenal aortic rupture, mimicking several aspects of human AAAs.[5] This model has become popular for studying the pathogenesis and mechanisms of AAAs.[6-8]

In this issue, Gueldner et al[9] reported on the mechanical and matrix effects using the periadventitial elastase mouse model with different durations of BAPN administration. They performed mechanical testing of fresh aortic sections to determine the tangent modulus (representing the aortic stiffness) and ultimate tensile strength (UTS; representing the maximal elasticity). Compared to the sham group, the mice administered elastase alone had an increased tangent modulus but no change in the UTS. These data support the notion that the infrarenal aortic damage by elastase application resulted in increased wall stiffness but no change in wall strength at 2 weeks after elastase application. The administration of BAPN for 4 or 14 days after elastase application did not change either the tangent modulus or UTS. In contrast, administration of BAPN for 8 weeks reduced both the tangent modulus and the UTS. These data support that prolonged administration of BAPN leads to progressive structural and functional impairment of the already damaged aortic wall by periaortic elastase application.

Subsequently, the authors performed quantitative structural matrix protein analysis. Considering the complex pathology and intraluminal thrombus in mice administered BAPN for 8 weeks, that group was excluded from the comparisons. The mice administered elastase alone had less insoluble elastin and a low content of collagen. Administration of BAPN for either 4 or 14 days did not change the elastin level. Collagen was modestly higher in the mice administered BAPN for 4 days but not for 14 days. To understand why aortic aneurysms are more frequent in the infrarenal region, the authors compared the descending thoracic aorta and infrarenal aorta in the sham group. The infrarenal aorta had a lower tangent modulus and higher collagen content but no difference in the UTS or elastin compared with the descending thoracic aorta.

In conclusion, the study by Gueldner et al[9] determined temporal alterations of biomechanical properties and matrix profiles during AAA formation using periadventitial elastase application with the BAPN administration mouse model, providing important insights into the pathologic and mechanistic complexity of human AAAs.

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