

Inelastic properties of the thoracic and abdominal aorta in response to elevated homocysteine and cholesterol in a rabbit model of atherosclerosis

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Abstract

The mechanical behavior of vascular tissue is characterized by various inelastic effects. From a theoretical perspective, it is therefore advantageous to develop experimental protocols that allow for the separation of equilibrium and rate-dependent phenomena. A recent study on the porcine thoracic aorta showed that the equilibrium response cannot be reliably captured with continuous loading protocols, as rate-dependent effects occur even at low deformation rates [1]. The assumption of quasi-stationarity thus proved insufficient for isolating the equilibrium relation, making the interpretation of such tests ambiguous. Alternatively, the equilibrium response can be assessed using step-wise relaxation protocols, which enable the separation of dissipative properties in a single test. In the present study, the aforementioned methodology was applied to investigate the mechanical changes of the thoracic and abdominal aorta in a rabbit model of atherosclerosis. In this regard, high homocysteine, elevated cholesterol conditions, and their combination were induced in rabbits by specific diets and intravenous

homocysteine injections. Additionally, balloon injury to the intima of the abdominal aorta was used to accelerate atherosclerosis progression [2]. Hyperhomocysteinemia, defined as an elevated level of homocysteine in the blood, is considered an independent risk factor for atherosclerosis and, more generally, cardiovascular disease. Its relationship to aortic biomechanics and its influence on the macromolecular constituents of the aorta have been little explored to date. For this reason, we performed an extensive mechanical characterization using equibiaxial extension tests, including (i) continuous cyclic tests and (ii) cyclic stepwise relaxation tests to characterize the inelastic behavior of both aortic segments. The mechanical investigations were complemented by microstructural analyses to assess changes in the structural constituents, i.e., collagen, elastin, and smooth muscle cells, using multi-photon microscopy and histology. Our study reveals significant remodeling of the media and changes in mechanical properties in response to the treatments. More specifically, a cholesterol-rich diet leads to softening of both the thoracic and abdominal aorta. In contrast, high homocysteine conditions, obtained by a combination of a B vitamins and choline-deficient diet and homocysteine injections, caused collagen deposition in the intima and stiffening of the abdominal aorta, even without hypercholesterolemia. This suggests an independent role of homocysteine in the progression of atherosclerosis. Finally, when comparing the aortic regions, more pronounced inelastic phenomena were always measured in the abdominal aorta, where atherosclerosis has progressed the most due to balloon injury, thus suggesting changes in tissue viscoelasticity as an indicator of wall integrity [3].

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