

Dependency of Nuclear Deformation of Smooth Muscle Cells on Tissue Stretch Direction May Explain Anisotropic Response of Aortic Wall to Hypertension

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Abstract: Aortic wall thickens in response to hypertension. Many studies reported that the wall thickening occurs to maintain the wall stress in the circumferential direction at a constant level. In case of the longitudinal direction, however, there are few studies suggesting the constancy of the stress. Such anisotropic response may be attributable to the circumferential alignment of the smooth muscle cells (SMCs) in the wall [1]. However, to the authors' knowledge, there are no study discussing the underlying mechanism of the anisotropic response. It has been reported that mechanical deformation of the nuclei causes transcription upregulation [2]. This might suggest that the deformation of the nuclei may stimulate protein syntheses by upregulating transcriptions and thus causes wall thickening. If this is the case, SMC nuclei in the aortic walls may deform larger in response to circumferential stretch than in the longitudinal stretch. To check this hypothesis, we have observed the deformation of the SMC nuclei in the aortic wall of mice during the circumferential and longitudinal stretches. Thoracic aortas harvested from adult male mice were cut open longitudinally. Rectangular specimens of 1 mm x 3 mm, whose major axis coincided with the circumferential or longitudinal direction, were excised from the cut-open segments, stained with Hoechst 33342 (Molecular Probes) for nuclei, and attached to a laboratory-made tensile tester [3] to stretch them in their major axis direction in normal saline at room temperature. Deformation of the nuclei was observed from the intimal side with a confocal laser scanning microscope. It was significantly smaller than that of the macroscopic deformation of the specimen. Nuclear deformation was ~25% of the macroscopic deformation in the longitudinal stretch, and was significantly smaller than that in the circumferential stretch (~50% of the macroscopic deformation). These results suggest that the relative insensitivity of the aortic tissues to stress change in the longitudinal direction may partly be caused by the smaller deformation of the nuclei in this direction.

Keywords: Mechanical adaptation; mechanotransduction; wall thickening

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