
EXPERIMENTAL AND NUMERICAL STUDY OF AORTIC GROWTH AND REMODELING UNDER GESTATIONAL HYPOBARIC HYPOXIA

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Abstract

Cardiovascular diseases are one of the main causes of death and morbidity worldwide (1). However, their pathogenesis and consequences are not fully understood, particularly regarding potential changes in structural and functional properties of the arterial wall (2). It is known that the arterial wall can modify its shape, structure, and properties in the face of external perturbations such as aging, vascular diseases, and surgical interventions. These changes are triggered with the goal of maintaining a state of mechanical homeostasis. This kind of alteration is commonly studied within the context of growth and remodeling (G&R) phenomena, which is closely related to the production, removal or degradation of microconstituents of the arterial wall. Such alterations may be reflected in variation in mass and alteration of the mechanical properties of the vascular tissue.

One notable condition associated with alterations in the external environment that may have implications at the physiological level is high-altitude hypobaric hypoxia (HH). This phenomenon is defined by a reduction in oxygen partial pressure in comparison to normal conditions (normoxia). Its clinical significance is evident in organisms inhabiting highlands at an altitude of 2500 meters above sea level (3).

To investigate these effects, a coupled experimental-numerical study was conducted with the objective of determining the long-term impact of gestational exposure to hypobaric hypoxia on the thoracic aorta. To this end, the experimental groups utilize one-year-old guinea pigs as animal model. One group of animals was subjected to hypoxic hypobaric conditions during gestation, corresponding to a partial pressure of oxygen equivalent to 4600 meters above sea level. A second (control) group of animals was subjected to normoxic normobaric conditions.

Several ex-vivo biomechanical tests, including planar biaxial tensile, axial stretch and ring opening, were conducted on the thoracic aortas of animals studied. Concurrently, histological measurements were performed to determine the composition of the main load-bearing

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components of the artery wall. The data obtained from these experiments was used to calibrate a mechanobiological G&R model formulated by Latorre et al. (2020) (4).

The G&R model adopted considers a constrained mixture model approach (G&R-CMM) (5) to take into account the distinctive properties of each constituent and assumes mechanobiological equilibrium to describe the long-term, stationary state of the grown tissue. This condition is precisely suited to the experimental data available, as one year of age corresponds to a stage of adulthood in the cardiovascular development of guinea pigs.

The main findings illustrate the long-term impact of HH exposure during gestation, as evidenced by biomechanical parameters, residual deformation, and microstructural composition. The G&R-CMM model characterization provides insight into the mechanobiological phenomena and mechanisms governing G&R on aortic tissue under gestational hypoxic hypobaric conditions.

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