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Neovascularization and Intraplaque Hemorrhage in Atherosclerotic Plaque Destabilization-A Mathematical Model

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Abstract: Observational studies have identified angiogenesis from the adventitial vasa vasorum and intraplaque hemorrhage (IPH) as critical factors in atherosclerotic plaque progression and destabilization. Here we propose a mathematical model incorporating intraplaque neovascularization and hemodynamic calculation for the quantitative evaluation of atherosclerotic plaque hemorrhage. An angiogenic microvasculature based on histology of a patient's carotid plaque is generated by two-dimensional nine-point model of endothelial cell migration. Three key cells (endothelial cells, smooth muscle cells and macrophages) and three key chemicals (vascular endothelial growth factors, extracellular matrix and matrix metalloproteinase) are involved in the intraplaque angiogenesis model, and described by the reaction-diffusion partial equations. The hemodynamic calculation of the microcirculation on the generated microvessel network is carried out by coupling the intravascular, interstitial and transvascular flow. The plasma concentration in the interstitial domain is defined as the description of IPH area according to the diffusion and convection with the interstitial fluid flow, as well as the extravascular movement across the leaky vessel wall. The simulation results demonstrate a series of pathophysiological phenomena during the progression of an atherosclerotic plaque, including the high microvessel density (MVD) region at the shoulder areas, the transvascular flow through the capillary wall and the intraplaque hemorrhage. The hemodynamic results show significant consistency with both the histology data and the MR imaging data in quality and quantity. In addition, the sensitivity analysis of IPH to model parameters reveals that the decreased MVD and the vessel permeability may reduce the IPH area dramatically.

Keywords: Numerical model of vulnerable atherosclerosis, intraplaque angiogenesis and hemorrhage, microcirculation inside the plaque lesion, plaque microenvironmental dynamics.

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