Abstract

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Atherosclerosis and calcium signalling in endothelial cells.

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BAKGROUND: The link between atherosclerosis and regions of disturbed flow and low wall shear stress is now firmly established, but the causal mechanisms underlying the link are not yet understood. It is now recognised that the endothelium is not simply a passive barrier between the blood and the vessel wall, but plays an active role in maintaining vascular homeostasis and participates in the onset of atherosclerosis.

DISCUSSION: Calcium signalling is one of the principal intracellular signalling mechanisms by which endothelial cells (EC) respond to external stimuli, such as fluid shear stress and ligand binding. Previous studies have separately modelled mass transport of chemical species in the bloodstream and calcium dynamics in EC via the inositol trisphosphate (IP(3)) signalling pathway.

SUMMARY: We review existing models of these two phenomena, before going on to integrate the two components to provide an inclusive new model for the calcium response of the endothelium in an arbitrary vessel geometry. This enables the combined effects of fluid flow and biochemical stimulation on EC to be investigated and is the first time spatially varying, physiological fluid flow-related environmental factors have been combined with intracellular signalling in a mathematical model. Model results show that low endothelial calcium levels in the area of disturbed flow at an arterial widening may be one contributing factor to the onset of vascular disease.

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