Intact Capillaries Sensitive to Rate, Magnitude, and Pattern of Shear Stress Stimuli as Assessed by Hydraulic Conductivity (Lp)

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Abstract

Magnitude of abrupt changes in fluid shear stress ($\Delta\tau$) correlates with capillary hydraulic conductivity (L_p). Cultured endothelial cells differentiate between rate of change in and pattern of fluid stimulation; however, neither rate nor pattern sensitivity has been evaluated in individual capillaries. We hypothesized that L_p would be greater following abrupt compared to slow $\Delta\tau$ and that magnitude of $\Delta\tau$ would correlate with L_p regardless of rate. Mesenteric venular capillaries (VC, $n = 41$) located in pithed North American leopard frogs *(Rana pipiens)* were cannulated either above or at in situ pressure to induce abrupt (<0.1 s) or slow (1-5 min.) $\Delta\tau$. L_p was assessed always at the same pressure (30 cm H_2O) using the modified Landis technique. Mean ± SE L_p was sixfold higher (P= 0.005) following abrupt (19.0 ± 3,9 × 10^{-7}) compared to slow (2.7 ± 0,9×10^{-7} cm/s/cm H_2O) $\Delta\tau$ after accounting for stimulus pattern variability. Linear relationships between L_p and $\Delta\tau$ existed for both abrupt [L_p= 0.026($\Delta\tau$) – 1.6, R^2 = 0.90, P = 0.0001] and slow [L_p = 0.005($\Delta\tau$) – 0.3, R^2 = 0.82, P, = 0.03] stimuli. These results suggest that frog mesenteric VC sense unique characteristics of $\Delta\tau$ and respond by altering L_p.

Key-words: Microcirculation, Filtration, Frog, Mesentery, Endothelial cell.

Preanalytic and Analytic Sources of Variations in C-reactive Protein Measurement: Implications for Cardiovascular Disease Risk Assessment

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Background: C-reactive protein (CRP) is a widely recognized indicator of inflammation and is known to play an important role in atherogenesis. Recent prospective studies have demonstrated that increased CRP concentrations within the reference interval are a strong predictor of myocardial infarction, stroke, sudden cardiac death, and peripheral vascular disease in apparently healthy adults. On the basis of available evidence, the American Heart Association and the CDC have issued guidelines for the utility of CRP in the primary prevention of coronary heart disease and in patients with stable coronary disease or acute coronary syndromes. Nevertheless, there remains considerable work to optimize the utility of this marker for risk assessment.

Issues: Most traditional CRP tests designed to monitor acute and chronic inflammation have inadequate sensitivity for risk stratification of coronary disease. Thus, manufacturers have had to develop tests with higher sensitivity. Because an individual's CRP concentration will be interpreted according to fixed cut-points, issues related to the preanalytic and analytic components of CRP measurement must be considered and standardized where possible to avoid potential misclassification of cardiovascular risk.

Conclusions: Efforts to define performance criteria for high-sensitivity CRP applications coupled with growing awareness of the physiologic aspects of CRP most likely will lead to refinements in standardization, improved performance in quality-assessment schemes, and enhanced risk prediction.