QUANTITATIVE INVERSE CORRELATION OF WALL SHEAR STRESS WITH EXPERIMENTAL INTIMAL THICKENING

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BOTH HIGH and low wall shear stress have been implicated as important hemodynamic determinants in the pathogenesis and localization of early atherosclerotic plaques (1,2). The purpose of this study was to create a wide variation in wall shear stress, both high and low, and to quantitatively correlate the development of intimal thickening with the level of wall shear stress. Shear stress variation was achieved by constricting the thoracic aorta in atherosclerotic monkeys, and wall shear stress was measured in an analogous model of stenosis under controlled conditions.

MATERIALS AND METHODS

Moderate stenoses of the mid-descending thoracic aorta were created in 13 cynomolgus monkeys fed an atherogenic diet containing 2% cholesterol and 25% peanut oil. The degree of stenosis was determined using biplanar thoracic aortography and aortic pressure gradient measurements prior to sacrifice six months later. Each aorta was pressure perfusion fixed and eight transverse histologic sections were obtained proximal, through, and distal to the stenosis in order to sample sites exposed to wide variations in shear stresses. Intimal thickness was quantified at each level using computer-assisted morphometric techniques. An analogous scaled Plexiglas flow model was constructed from averaged diameter measurements of the monkey thoracic aortograms. Pulsatile flow conditions that were physiologically realistic and reflected the in vivo hemodynamics were used (volume flow = 350 mL/min, kinematic viscosity = 0.04 poise, mean diameter = 7 mm). Under these flow conditions the derived Reynolds number was 600. Time-averaged centerline and near-wall velocity gradients were used to construct cyclic wall shear stress at axial levels corresponding to the histologic sections. Wall shear stress magnitude was quantitatively correlated with intimal thickness using linear regression analysis.

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RESULTS

The mean aortic pressure gradient at death was $6.5 \pm 1.9$ mm Hg. Thoracic aortic stenoses ranged from 32% to 75% cross-sectional area reduction (mean, $58\% \pm 4.3\%; n = 13$). Proximal to the stenosis, maximum shear was 29 dynes/cm² and increased to 323 dynes/cm² within the stenosis. Distal to the stenosis, shear stress became negative ($-33$ dynes/cm²). Proximal to the stenosis, intimal thickness was $0.06 \pm 0.02$ mm and decreased $66\%$ to $0.02 \pm 0.02$ mm within the stenosis ($P < 0.05$). Two diameters distal to the stenosis, shear stress decreased to $-14.9$ dynes/cm² and intimal thickness increased twofold to $0.12 \pm 0.03$ mm ($P < 0.05$ vs. proximal aorta). There was a strong inverse linear relationship between the absolute magnitude of shear stress and intimal thickness at all eight axial locations about the stenosis, irrespective of shear stress direction (linear regression of $1/\text{max. shear}$ and intimal thickness: $r = 0.97$, $P < 0.001$).

CONCLUSIONS

The hemodynamic effects of arterial stenoses have been investigated in pulsatile flow models and have demonstrated increased centerline velocity within and distal to the stenosis with flow separation, reattachment and reversal occurring in the poststenotic region (3,4). Previous quantitative correlative flow studies of nonstenotic human carotid bifurcations have suggested that atherosclerotic plaques develop in areas of low shear stress and not in areas of high shear stress (2,5). The findings of this study are consistent with these observations and indicate that the magnitude of shear stress in arterial stenoses may be an important determinant of intimal thickness. The inverse relationship between shear stress magnitude and intimal thickness appears to persist over a wide range of shear stress levels, irrespective of shear stress direction.

REFERENCES