Effect of Stenosis on Wall Motion

A Possible Mechanism of Stroke and Transient Ischemic Attack

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The mechanism by which atherosclerotic plaque causes stroke and transient ischemic attack is not fully understood. One possibility is that the plaque stenosis may set up hemodynamic conditions causing local arterial wall collapse. Arterial wall collapse may, in turn, affect the integrity of the plaque. This study was designed to define the effects of stenosis on the production of arterial wall collapse using a latex tube model. Stenoses ranging up to 81% by diameter were tested in a Starling resistor chamber under pulsatile pressure conditions upstream of the tube. Increasing the degree of stenosis progressively decreased the external pressure necessary to produce collapse, from 37 mm Hg with the 0% stenosis to 24 mm Hg for the 81% stenosis. The stenoses greater than 70% produced a new phenomenon of "systolic wall collapse" just distal to the stenosis. The maximum diameter decrease was 2.83 mm from the baseline diameter of 6.41 mm. Cyclic wall motion just downstream of the stenosis increased with the increased degree of stenosis from 0.34 mm at 0% stenosis to −1.28 mm at 75% stenosis. The phenomena are discussed in terms of simplified Bernoulli pressure drops. We conclude that local arterial stenosis can produce conditions favorable for wall collapse and increased wall motion at physiologic pressure and flow. This collapse may be important in the development of atherosclerotic plaque fracture and subsequent thrombosis or distal embolization. (Arteriosclerosis 9:842–847, November/December 1989)

Stroke is the third leading cause of morbidity and mortality in the United States and accounts for over 200 000 deaths a year. Extracranial atherosclerotic cerebrovascular disease localized within the carotid bifurcation is the cause of stroke and transient ischemic attack (TIA) in the majority of these patients.[1] The exact mechanism by which atherosclerotic plaque causes hemispheric stroke and TIA remains controversial and unresolved. However, recent evidence strongly favors a plaque fracture-embolization hypothesis.[2,3] One possible etiology is that the local stenosis produced by an atherosclerotic lesion may cause mechanical conditions favorable for plaque fracture and distal embolization.

This study was designed to investigate the effect of stenosis on wall motion and collapse in a latex tube model. Much work has been reported on the collapse of veins and other thin-walled tubes within Starling resistor chambers.[4–11] These articles identify the critical controlling factors such as transmural pressure, upstream and downstream pressure, and longitudinal tension. Additionally, they report choking, the waterfall phenomenon, and dynamic behavior such as flutter. Most of these articles address problems of flow limitation and instability in veins, airways, or ureters. The experimental setup or boundary conditions test an elastic tube of uniform diameter. None of these articles specifically address the problem of wall excursion and collapse distal to a high grade stenosis. However, Elad et al.[12] report on the increased likelihood of transition to supercritical flow with a local area constriction in a theoretical model of the pulmonary system, suggesting that stenoses may cause collapse.

Santamore and Walinsky[13] have presented radiographic evidence of a decrease in arterial diameter distal to a snare-type stenosis of approximately 97% of the diameter. In their in vitro tests, they created a decrease in the distal peripheral resistance, but they did not vary the external pressure. Developing a theoretical model of the compliant arterial stenosis, Santamore and Bove[14] described diameter and circumferential decreases, which may result from decreases in intraluminal pressure. Their analysis did not address the cases when the transluminal pressure becomes negative with collapse. Schwartz et al.[15] have also discussed the possibility of passive narrowing from decreases in lateral pressure when the distal pressure is lowered but did not present experimental evidence of diameter changes. In this article, we report physiologic conditions under which arterial wall collapse may occur distal to an atherosclerotic stenosis.

Methods

A drawing of the general experimental system is shown in Figure 1. The pulsatile continuous flow system was comprised of three constant pressure head reservoirs and a recirculating pump. This arrangement allowed for the precise and independent setting of the inlet and outlet pressures. The reservoirs consisted of partitioned chambers, which allowed one half of the chamber to contain a

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metabolism in perfused rat liver.Biochim Biophys Acta 1984;792:103-109
3. **Nestel PJ, Connor WE, Reardon MF, Connor S, Wong S, Boston R.** Suppression by diets rich in fish oil of very low density lipoprotein production inman. J Clin Invest 1984;74: 82-89
4. **Wong SH, Marsh JB.** Inhibition of apolipoprotein secretion and phosphatidate phosphohydrolase activity by eicosapentaenoic and docosahexaenoic acids in the perfused rat liver. Metabolism 1988;37:1177-1181
5. **Wong S, Nestel PJ.** Eicosapentaenoic acid inhibits the secretion of triacylglycerol and of apoprotein B and the binding of LDL in Hep G2 cells. Atherosclerosis 1987;64: 139-146
6. **Dole VP.** A relation between non-esterified fatty acids in plasma and the metabolism of glucose.J Clin Invest 1956;35:150-154
7. **Egusa G, Brady DW, Grundy SM, Howard BV.** Isopropanol precipitation method for the determination of apo B specific activity and plasma concentrations during metabolic studies of very low density lipoproteins and low density lipoprotein apolipoprotein B. J Lipid Res 1983;24:1261-1267
8. **Borchardt RA, Davis RA.** Intrahepatic assembly of very low density lipoproteins. Rate of transport out of the endoplasmic reticulum determines rate of secretion. J Biol Chem 1987;262:16394-16402
9. **White B, Bancroft F.** Cytoplasmic dot hybridization. J Biol Chem 1982;247:8569-8572
10. **Feinberg A, Vogelstein B.** A technique for radiolabelling DNA. Anal Biochem 1984;137:266-267
11. **Fisher E, Carroll R, Cortner J, Surrey S.** Transcriptional activity of the genes for apoproteins A-I and E in neonatal rat liver. Atherosclerosis 1987;68:249-253
12. **Chambaz J, Guillouzo A, Cardot P, Pepin D, Berezlat G.** Essential fatty acid uptake and esterification in primary culture of rat hepatocytes. Biochim Biophys Acta 1986;878:310-339
13. **Christensen E, Hagve T-A, Christophersen BO.** Mitochondrial and peroxisomal oxidation of arachidonic and eicosapentaenoic acids studied in isolated livercells. Biochim Biophys Acta 1986;879:313-321
14. **Rustan AC, Nossen JO, Christiansen EN, Drevon CA.** Eicosapentaenoic acid reduces hepatic synthesis and secretion of triacylglycerol by decreasing the activity of acyl-coenzyme A: 1,2-diacyl glycerol acyltransferase. J Lipid Res 1988;29:1417-1426
15. **Hagve T-A, Christophersen BO.** Effects of dietary fats on arachidonic acid and eicosapentaenoic acid biosynthesis and conversion to C22 fatty acids in isolated liver cells. Biochim Biophys Acta 1984;796:205-217
16. **Davis RA, Boogaerts JR.** Intrahepatic assembly of very low density lipoproteins. Effect of fatty acids on triacylglycerol and apolipoprotein synthesis. J Biol Chem 1982;257: 10908-10913
17. **Peters TJ, Peters JC.** The biosynthesis of serum albumin VI. Intracellular transport of albumin and rates of albumin and liver protein synthesis in vivo under physiological conditions. J Biol Chem 1972;247:3856-3863
18. **Nossen JO, Rustan AC, Gloppestad SH, Malbakken S, Drevon CA.** Eicosapentaenoic acid inhibits synthesis and secretion of triacylglycerols by cultured rat hepatocytes. Biochim Biophys Acta 1986;879:56-65
19. **Childs MT, King IB, Yamanaka WK.** Divergent lipoprotein lipid responses to fish oils enriched in eicosapentaenoic acid (EPA) or docosahexaenoic (DHA) [abstr]. FASEB J 1988;2:749
20. **Roach PD, Kambouris AM, Trimble RP, Topping DL, Nestel PJ.** Fish oil down-regulates the low-density lipoprotein receptor and up-regulates the high-density lipoprotein receptor of ratliver. FEBS Lett 1987;222:159-162
21. **Leaf A, Weber PC.** Cardiovascular effects of n-3 fatty acids. New Engl J Med 1988;318:549-557
22. **von Schacky C, Fischer S, Weber PC.** Long term effects of dietary marine w-3 fatty acids upon plasma and cellular lipids, platelet function, and eicosanoid formation in humans. J Clin Invest 1985;76:1626-1631
23. **Lee TH, Hoover RL, William JD, et al.** Effect of dietary enrichment with eicosapentaenoic and docosahexaenoic acids on in vitro neutrophil and monocyte leukotriene generation and neutrophil function. N Engl J Med 1985;312: 1217-1224

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