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Lipolysis of emulsion models of triglyceride-rich lipoproteins is altered in male patients with abdominal aorta aneurysm

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Abstract

Disorders of the lipid metabolism may play a role in the genesis of abdominal aorta aneurysm. The present study examined the intravascular catabolism of chylomicrons, the lipoproteins that carry the dietary lipids absorbed by the intestine in the circulation in patients with abdominal aorta aneurysm. Thirteen male patients (72 ± 5 years) with abdominal aorta aneurysm with normal plasma lipid profile and 13 healthy male control subjects (73 ± 5 years) participated in the study. The method of chylomicron-like emulsions was used to evaluate this metabolism. The emulsion labeled with ^{14}C-cholesteryl oleate and ^{3}H-triolein was injected intravenously in both groups. Blood samples were taken at regular intervals over 60 min to determine the decay curves. The fractional clearance rate (FCR) of the radioactive labels was calculated by compartmental analysis. The FCR of the emulsion with ^{3}H-triolein was smaller in the aortic aneurysm patients than in controls (0.025 ± 0.017 *vs* 0.039 ± 0.019 min^{-1}; $P < 0.05$), but the FCR of ^{14}C-cholesteryl oleate of both groups did not differ. In conclusion, as indicated by the triglyceride FCR, chylomicron lipolysis is diminished in male patients with aortic aneurysm, whereas the remnant removal which is traced by the cholesteryl oleate FCR is not altered. The results suggest that defects in the chylomicron metabolism may represent a risk factor for development of abdominal aortic aneurysm.

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- Abdominal aortic aneurysm
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- Chylomicrons
- Emulsions

Abdominal aorta aneurysms (AAA) are mostly of atherosclerotic origin (1) and the classical plasma lipid risk factors for coronary artery disease are involved. However, the metabolism of chylomicrons, lipoproteins that carry dietary fats absorbed by the intestine in the circulation, has not been investigated. Once in the bloodstream, chylomicron triglycerides are degraded by lipoprotein lipase and the resulting chylomicron remnants are then taken-up by the liver. Diminished chylomicron triglyceride breakdown and the accumulation of remnants are linked to coronary artery disease (2-5). However, evaluating this metabolism in human subjects is difficult. Plasma kinetic determi-

nation of double-labeled chylomicron-like emulsions is a practical method for the study of chylomicron metabolism: 1) the plasma decay curves of the emulsion triglycerides trace the lipolysis process, and 2) the cholesteryl ester curve traces the remnant removal from plasma.

The study was conducted on 13 patients with AAA (72.1 ± 5.0 years) and 13 healthy control subjects (72.9 ± 4.9 years) confirmed by computed tomography. The protocol was approved by the Ethics Committee of the Hospital of the University of São Paulo Medical School and a written informed consent was obtained from all participant subjects. Body mass index, that has been previously shown to correlate with the plasma kinetics of chylomicrons (6), was similar in the two groups (controls: 25.2 ± 2.5; AAA: 24.3 ± 3.2 kg/m^2). The emulsion was prepared by sonication of constituent lipids followed by ultracentrifugation and labeled with ^{14}C-cholesteryl oleate and ^{3}H-triolein. The emulsion was then injected intravenously in the fasting subjects and radioactivity was counted in plasma samples collected over a period of 1 h for plasma fractional clearance rate (FCR) calculation.

There were no differences between groups regarding plasma concentrations of HDL (AAA: 50 ± 13; controls: 50 ± 9 mg/dL), LDL (133 ± 18; 131 ± 16 mg/dL), total cholesterol (203 ± 23; 201 ± 20 mg/dL), and triglyceride (96 ± 33; 106 ± 43 mg/dL), or in plasma concentrations of apolipoprotein A1 (1.40 ± 0.26 and 1.38 ± 0.15 g/L) and apolipoprotein B (1.08 ± 0.14 and 1.05 ± 0.12 g/L). None of the subjects had diabetes mellitus according to the Standards of Medical Care in Diabetes - 2006, American Diabetes Association (7), and plasma glucose levels were similar for the AAA and control groups (96 ± 12 and 99 ± 4 mg/dL, respectively).

Although the frequency of smokers was higher in AAA (3/13) than in controls (0/13), the frequency of arterial hypertension was similar (5/13 and 3/13).

FCR of ^{3}H-triolein was smaller in AAA (0.025 ± 0.017 min^{-1}) than in controls (0.039 ± 0.019 min^{-1}, $P < 0.05$, Mann-Whitney test), but the ^{14}C-cholesteryl oleate FCR did not differ between groups (0.011 ± 0.011 and 0.018 ± 0.009 min^{-1}). This implies that lipolysis of the emulsion triglycerides is diminished, but the remnant removal is not altered in AAA.

Modification of risk factors for atherosclerosis is a priority in the clinical management of aortic aneurysms (8). In a recent study (9), arterial hypertension and classic lipid risk factors were not determinants of aneurysmal growth, whereas smoking and aneurysm baseline diameter were, highlighting our finding of a novel lipid marker.

In coronary artery disease patients submitted to secondary prevention, diminished lipolysis was an independent predictor of severe angina while remnant removal was not (10). The postprandial increase in plasma triglycerides should impair arterial vasodilator capacity and enhance procoagulant factors. Reduced lipolysis decreases free fatty acids, the natural activator ligands to α subclass peroxisome proliferator-activated receptors. Decreased peroxisome proliferator-activated receptors should increase endothelial production of the proinflammatory tumor necrosis factor-α and vascular cell adhesion molecule-1 (11,12). In conclusion, a disturbance of triglyceride-rich lipoprotein lipolysis and not remnant clearance is related to AAA.

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