

## Improvement of Endothelium-Dependent Vasodilatation in Hypercholesterolemic Humans by Single LDL Apheresis

O.Tamai, H. Matsuoka, and T. Imaizumi, *Japanese Journal of Apheresis*. 1996;15:268-274

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**Summary:** The effects of a single LDL apheresis (LDL-A) on endothelium function in seven patients (6 men, 1 woman; 57.6±3.9 years; mean±SD, range 44 to 70 years) with hypercholesterolemia were examined. Forearm blood flow (FBF) was measured by strain-gauge plethysmography before and after single LDL-A while infusing acetylcholine (Ach; 4 to 24 μg/min) and sodium nitroprusside (SNP; 0.2 to 1.2 μg/min). Although Ach and SNP increased FBF dose-dependently before and after LDL-A, the endothelium-dependent vasodilatation responses were significantly (p<0.01) augmented only toward Ach after single session of LDL-A [1].

Total cholesterol, LDL cholesterol and oxidized LDL levels significantly decreased by 60.5±4.1% (p<0.0005), 76.5±3.0% (p<0.0005), and 67.3±8.9% (p<0.005), respectively, by LDL-A. Direct intra-arterial infusion of Ach and SNP increased FBF (p<0.01) dose-dependently without changes in blood pressure before and after LDL-A (Fig.1). After single LDL-A, vasodilatory responses to infusions of Ach were significantly augmented (p<0.01), with no changes in responses to SNP.

Production of NO<sub>x</sub> before and after LDL-A significantly increased (p<0.05) by intra-arterial infusion of Ach (24 μg/min, Table 1). Ach caused dose-dependent increases in FBF. LDL-A significantly augmented production of NO<sub>x</sub> in response to Ach (p<0.05, ANOVA). Increase in FBF to SNP were similar before and after single LDL apheresis. Plasma immunoreactive endothelin was significantly increased by LDL-A from 1.7±0.2 to 2.8±0.4 pg/mL (p<0.001).

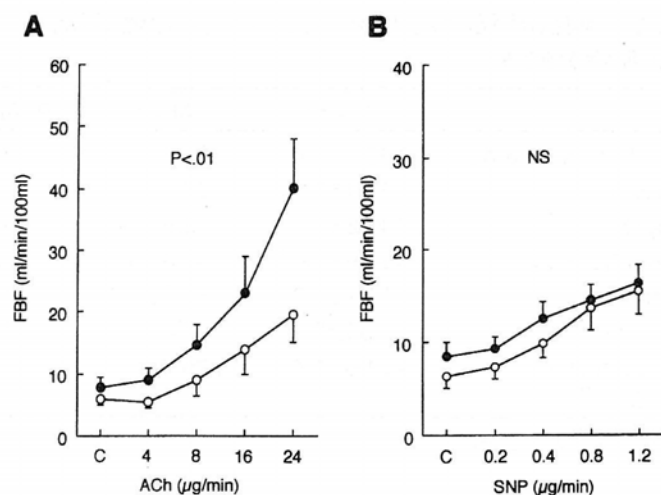


Fig. 1 A, Responses of forearm blood flow (FBF) to intra-arterially infused acetylcholine (Ach) before (□) and after (●) single LDL apheresis (n=7). B, Responses of FBF to intra-arterially infused sodium nitroprusside (SNP) before (□) and after (●) single LDL apheresis (n=7).

Table 1. Local Production at Baseline and During Acetylcholine Infusion Before and After LDL Apheresis

	Baseline Production	Acetylcholine-Induced Production	p value
NO <sub>x</sub> μmol/min/100mL			
Before	0.21±0.03	0.66±0.02	0.02
After	0.22±0.03	1.2±0.3*	0.02

Value are mean ± SEM.

\* p<0.05 vs before apheresis.

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The plasma level of total and oxidized LDL correlated with the degree of Ach-induced vasodilatation: there were significant correlations between the ratio of the maximal to baseline blood flow and the levels of total LDL ( $r = -.62$ ,  $p < 0.05$ ; Fig 2A) and oxidized LDL ( $r = -.67$ ,  $p < 0.01$ ; Fig 2B). Furthermore, there was a significant correlation between the ratio of the maximal to baseline production of NOx and the plasma level of total LDL and oxidized LDL.

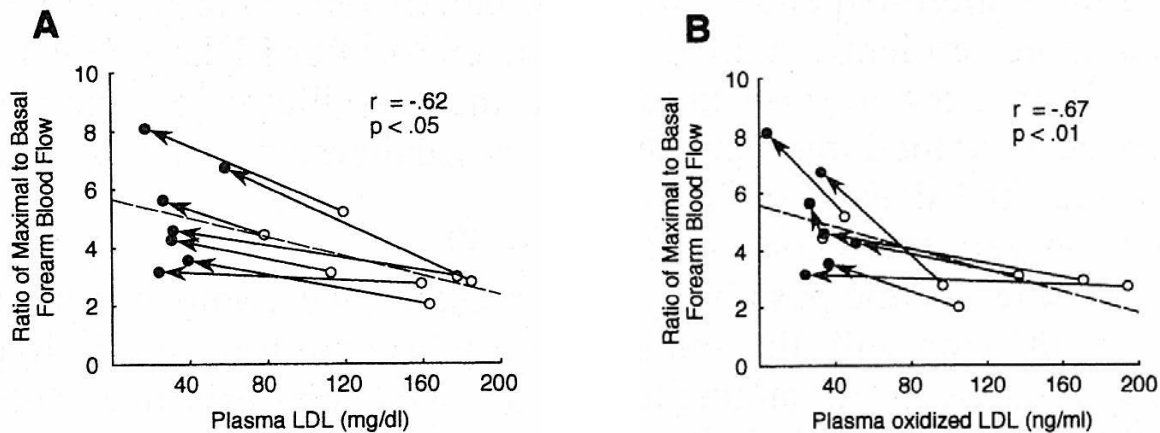


Fig. 2. A, Relation between ratio of maximal blood flow induced by acetylcholine to baseline FBF and level of plasma total LDL before (●) and after (○) single LDL apheresis (n=7). B, Relation between ratio of maximal blood flow induced by acetylcholine to baseline FBF and level of plasma oxidized LDL before (●) and after (○) single LDL apheresis (n=7).

The major findings of this study were as follows:

- (1) a single session of LDL-A augmented vasodilator responses to Ach but not to SNP in patients with hypercholesterolemia;
- (2) NOx production in response to Ach was significantly potentiated by a single session of LDL-A;
- (3) Plasma levels of oxidized LDL correlated significantly with the degree of Ach-induced vasodilation and with NOx production.

**Conclusion:** Endothelium function was improved even by a single session of LDL-apheresis with reduction in total LDL and oxidized LDL. It was suggested that total LDL and/or oxidized LDL may directly impair endothelium function in the human forearm vessel.

#### Reference:

- 1) O.Tamai, H.Matsuoka, H. Itabe, Y. Wada, K.Kohno, and T.Imaizumi, *Circulation*. 1997;95:76-82