2012 Los Angeles
scientificsessions.org
Exhibits Nov. 4–6
Scientific Sessions Nov. 3–7
Resuscitation Science Symposium Nov. 3–4
Cardiovascular Nursing Symposium Nov. 6–7
American Heart Association. SCIENTIFIC SESSIONS 2012

Control/Tracking Number: 2012-SS-A-13127-AHA
Activity: Abstract
Current Date/Time: 6/10/2012 2:29:35 AM

Expression of the Highly Electronegative LDL Receptor LOX-1 Is Increased in Thrombi of STEMI Patients

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Abstract:

Background: L5 is highly electronegative low-density lipoprotein (LDL) that exhibits atherogenic properties in vitro and is significantly increased in the plasma of patients with acute myocardial infarction (AMI). L5 is the only naturally occurring LDL capable of inducing expression of the lectin-like oxidized LDL receptor-1 (LOX-1), which is the receptor through which L5 transmits signals in endothelial cells and platelets. To determine whether L5 plays a pathogenic role in AMI, we semiquantitatively measured LOX-1 and apolipoprotein (apo) levels in intra-arterial tissues of acutely occluded coronary arteries.

Methods and Results: Intracoronary tissues were removed by thrombectomy from patients (age, 52±13 years) with ST-elevation MI (STEMI; n=34) or non-STEMI (NSTEMI; n=10). Fresh lytic tissues were identified in 79% and organized tissues in 21% of all samples. In 26% of all samples, the thrombus contained soft plaque constituents consisting of foam cells and cholesterol crystals. LOX-1 and apo levels were immunochemically quantified in thrombi by measuring the fluorescence intensity. LOX-1 was more robustly expressed in STEMI than in NSTEMI thrombi (17.8±4.0 vs. 6.4±2.3 au, P=0.016). In STEMI thrombi, LOX-1 expression strongly correlated with apoB100 content (r=0.69, P=0.001, n=20) but not apoA1, apoA2, or apoC3 content or any conventional cardiometabolic risk factor (see Table). ApoB100 is the main protein in L5 and L1 (the least electronegative LDL). Using deconvolution microscopy, we observed that L5 but not L1 particles quickly formed aggregates, suggesting that L5 was favored over L1 for retention in lesions.

Conclusions: LOX-1 expression was increased in the intracoronary thrombi of patients with AMI, particularly those with STEMI, and significantly correlated with the content of apoB100 in tissue. Because L5 is the only LDL that can induce expression of and signal through LOX-1, our evidence is consistent with a pathogenic role of L5 in AMI.

Table. Correlation of cardiometabolic factors with LOX-1 expression

	DM	T-chol	TG	HDL	LDL	hs CRP	Apo B100	Apo A1	Apo A2	Apo C3
r	0.06	0.08	0.13	0.16	0.03	0.04	0.69	0.36	0.29	0.31
P-value	0.72	0.64	0.44	0.34	0.87	0.85	0.001	0.12	0.22	0.37

DM, diabetes mellitus; T-chol, total cholesterol; TG, triglyceride; HDL, high-density lipoprotein; LDL, low-density lipoprotein; hsCRP, high-sensitivity C-reactive protein; Apo, apolipoprotein

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Author Disclosure Information: K. Chang: None. Y. Wang: None. S. Chang: None. P. Lo: None. J. Lu: None. T. Sawamura: None. Y. Lee: None. A. Burns: None. C. Chen: None.
Category (Complete): 715. Unstable Angina, NSTEMI and STEMI: Diagnosis and Pathophysiology
Keyword (Complete): Acute coronary syndromes ; Lipoproteins ; Receptor-mediated signaling ; Apolipoproteins ; Arteriosclerosis
Presentation Preference (Complete): Oral or Poster
Additional Info (Complete):
*: E. Have Submitted in the Past
*: No
*Disclosure: There are no unlabeled/unapproved uses of drugs or products.
*: Yes

Payment (Complete): Your credit card order has been processed on Monday 4 June 2012 at 1:27 PM.
Status: Complete