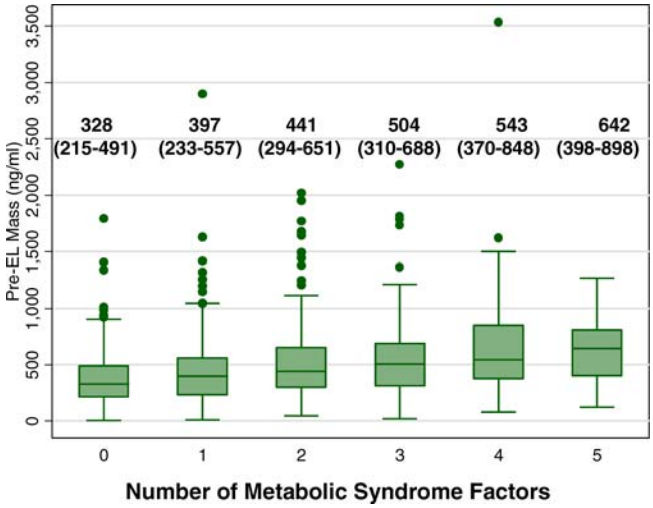

Figure 1. Pre-Heparin EL Mass Concentrations Were Determined in Subgroups According to the Presence of Increasing Numbers of Metabolic Syndrome Factors

There was an increase in median pre-heparin EL mass as the number of metabolic syndrome factors increased. Median values and IQR are listed above each box.

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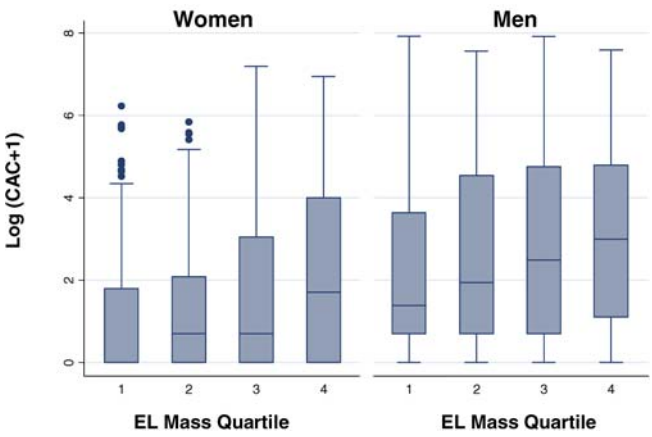

Figure 2. Coronary Artery Calcification Scores Were Compared across Quartiles of Pre-Heparin EL Mass in Both Men and Women

The box represents the 25th to 75th percentile, and the line represents the median CAC score within a given pre-heparin EL mass quartile. The whiskers represent the fifth and 95th percentiles. The diamonds are outliers above the 95th percentile. There was an increase in CAC scores as EL mass increased.

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High triglycerides and low HDL-C are two of the criteria used to diagnose metabolic syndrome. We examined the correlation between EL mass and HDL-C concentrations in participants with central obesity as defined by NCEP ATPIII metabolic syndrome waist circumference criteria (greater than 35 inches in women and greater than 40 inches in men). There were stronger negative correlations between post-heparin EL mass in both men and women, $r = -0.25$, $p = 0.03$ and $r = -0.31$, $p = 0.03$, respectively.

Since there were significant correlations between EL mass and each of the metabolic syndrome parameters, we examined differences in median post-heparin EL mass with increasing numbers of metabolic syndrome factors present (Figure 1). There was an additive effect of increasing numbers of metabolic syndrome factors, with median EL mass increasing from 328 ng/ml in individuals with no factors to 642 ng/ml in participants with all five factors present.

Association of EL Concentrations with Coronary Artery Calcification

CAC scores increased across quartiles of both pre- and post-heparin EL concentrations in men (for trend, $p < 0.001$ for both) and women (for trend, $p < 0.001$ for both) (Figure 2). Using multivariable ordinal regression analyses of the entire cohort, plasma concentrations of both pre- and post-heparin EL mass were significantly associated with CAC after controlling for age, gender, and established risk factors, and after further adjustment for plasma lipids, waist circumference, and vasoactive medications (Table 4). In stratified analyses, the fourth EL quartile compared to the first was associated with higher CAC scores for both pre-heparin EL mass, OR = 1.82 (confidence interval [CI] 1.02–3.24, $p = 0.043$) and post-heparin EL mass, OR = 7.63 (CI 2.44–23.9, $p < 0.001$) in women, while in men pre-heparin EL mass, OR = 1.7 (CI 1.0–2.9, $p = 0.05$) but not post-heparin EL mass, OR = 1.46 (CI 0.7–3.08, $p = 0.31$) was significantly associated with higher CAC scores.

Discussion

We report, to our knowledge for the first time, measurement of plasma concentrations of EL mass in routine, pre-heparin, and post-heparin plasma of human individuals. Using this newly developed sandwich ELISA, we demonstra-

Table 4. Multivariable Association of Plasma EL Concentrations with Coronary Artery Calcification

Variables	Total: OR (CI) *p*-Value		Men: OR (CI) *p*-Value		Women: OR (CI) *p*-Value	
	Pre ($n = 841$)	Post ($n = 366$)	Pre ($n = 459$)	Post ($n = 209$)	Pre ($n = 382$)	Post ($n = 157$)
Age, gender	2.57 (1.8–3.68) <0.001	3.44 (1.98–5.98) <0.001	2.44 (1.48–4.01) <0.001	1.71 (0.85–3.46) 0.132	3.0 (1.77–5.08) <0.001	10.42 (3.97–27.4) <0.001
Age, gender, RF	1.75 (1.19–2.56) 0.005	2.53 (1.14–4.54) 0.002	1.74 (1.03–2.96) 0.04	1.47 (0.7–3.08) 0.312	1.89 (1.07–3.36) 0.029	5.31 (1.85–15.3) 0.002
Age, gender, RF, BMI	1.67 (1.13–2.46) 0.01	2.42 (1.34–4.37) 0.003	1.7 (1.0–2.9) 0.05	1.46 (0.7–3.08) 0.312	1.82 (1.02-–3.24) 0.043	7.63 (2.44–23.9) <0.001

The ORs are the result of a comparison between the lowest EL quartile and the highest.

RF, risk factors: Total cholesterol, HDL-C, triglycerides, hypertension, smoking, exercise, and ethanol, glucose, waist circumference, and medication (niacin, fibrates, beta-blockers, statins, angiotensin-converting enzyme inhibitors, aspirin, and hormone replacement therapy [in women, $n = 115$]).

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