Plasma Leptin Levels and Coronary Heart Disease

To the Editor:

In the West of Scotland Coronary Prevention (WOSCOP) study, Wallace et al.1 show that plasma leptin levels predict coronary heart disease (CHD), and they interpret this finding on the basis of the known relationships between leptin and several facets of the metabolic syndrome, including high body mass index (BMI), insulin resistance, arterial hypertension, and of the relationship between leptin and C-reactive protein, a marker of inflammation and a predictor of CHD events.1 Other interpretations are possible. We analyzed BMI, serum leptin levels, and the QT interval (QTc) in 45 morbidly obese subjects, and we found that loss of weight obtained through laparoscopic adjustable gastric banding (from 44.6±1.01 kg/m² to 35.6±0.89 kg/m² in one year) is accompanied by a significant decrease of leptin levels (from 36.9±2.94 ng/mL to 19.7±2.04 ng/mL) and of the QTc (from 407.7±3.69 ms to 391.9±3.57 ms). Considering basal values, as well as values registered under basal conditions and after one year, we found significant relationships between BMI and leptin (r=0.63, P<0.001; r=0.72, P<0.001, respectively), and between leptin and QTc (r=0.57, P<0.001; r=0.52, P<0.001, respectively).

A long QTc, frequent in obese and in hypertensive subjects, is a risk factor for ventricular arrhythmia and sudden death;2 in addition, leptin levels correlate with heart rate in healthy individuals,3 in heart-transplant recipients,4 and with blood pressure.5 Indeed, in the WOSCOP study, subjects with CHD events had higher systolic and diastolic blood pressure than subjects without events; however, no data were given for their heart rate, nor whether cases were fatal or nonfatal. Leptin acts in the central nervous system, via interaction with several neuromediators in the hypothalamus, and may represent a partial link between excess weight gain and increased sympathetic activity; in turn, increased sympathetic activity can lead to increased heart rate and long QTc. In summary, it is tempting to speculate that leptin can be involved in increased heart rate and in long QTc, thus amplifying the risk for CHD and sudden death.

Antonio E. Pontiroli, MD
Pierluigi Pizzocri, MD
Franco Folli, MD
Università degli Studi di Milano
Cattedra di Medicina Interna
Ospedale San Paolo
Divisione di Medicina 2°
Ospedale San Raffaele
Divisione di Medicina
Milano, Italy


Response

We thank Pontiroli and colleagues for their interesting comments in relation to our paper1 on leptin as a novel risk factor for coronary heart disease (CHD). We accept that mechanisms other than those proposed in our article, including increased heart rate and long QTc, may link leptin to CHD. Fortunately, such parameters were measured at baseline in the West of Scotland Coronary Prevention Study (WOSCOPS) and we have therefore examined the relationship between leptin and the above parameters. In the 783 control subjects with leptin measurements, log leptin did not correlate with heart rate (r=0.03, P=0.39) but did so positively with QTc (r=0.10, P=0.005). However, body mass index (BMI) also correlated with QTc (r=0.15, P<0.001) and the association of leptin with QTc was lost with adjustment for BMI (r=0.018, P=0.62). This observation contrasts with findings for established risk factors such as C-reactive protein and triglyceride that do correlate with leptin independently of BMI. These data suggest that total adiposity rather than fat mass per se is linked to increased QTc.

Naveed Sattar, MD, PhD
Peter W. Macfarlane, PhD
Chris J. Packard, DSc
Anne Kelly, MIBiol
James Shepherd, PhD
Allan Gaw, MD
A. Michael Wallace, PhD
Departments of Pathological Biochemistry, Cardiology, Clinical Trials Unit Glasgow Royal Infirmary
Glasgow, Scotland, UK

Alex D. McMahon, PhD
Robertson Center for Biostatistics
University of Glasgow
Glasgow, Scotland, UK

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Antonio E. Pontirolì, Pierluigi Pizzocri and Franco Folli

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