Acute elevation of serum triglycerides increases left ventricular contractility measured by 2D strain and strain rate

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Background

Chronic elevation of circulating lipids is a potent risk factor for cardiovascular disease and there is growing evidence implicating the specific role of raised triglyceride levels in the development of coronary artery disease and left ventricular hypertrophy (LVH). Despite this, an independent, causal relationship remains uncertain. There is an abundance of data pertaining to the risk of chronically elevated blood lipids, but to our knowledge, there are no data available on the combined myocardial and vascular effects in response to an acute elevation of circulating triglycerides. Previous reports demonstrate endothelial dysfunction and decreased vasoreactivity possibly suggesting that repeated acute elevations of triglycerides, as occurs in the post-prandial metabolic response, may contribute to increased cardiovascular risk.

Considering the widely reported adverse effects associated with the post-prandial response, we hypothesized that acute elevation of serum triglycerides would impair vascular function and have secondary effects on myocardial function, resulting in a deterioration of the V-V relationship.

Aim

To assess the effect of acutely elevated serum triglycerides on myocardial and vascular function

Methods

Patient selection. We recruited 12 healthy men (aged 30-65) who were free of cardiac or metabolic conditions and medications.

Study protocol. This study was conducted in a randomized, double-blind fashion. All subjects attended the laboratory after an overnight fast (>9 hours, water allowed) on two separate occasions, separated by approximately one week.

Figure 1 depicts the study protocol. In brief, we randomly assigned subjects to receive either an intravenous fat emulsion (IFE) or saline. Blood samples and measurements of arterial stiffness (pulse wave velocity), central blood pressure and echocardiography were taken at baseline and after 60 minutes of substrate infusion.

Vascular. Arterial waveforms were acquired in duplicate at the radial artery by hand-held applanation tonometry and calibrated to brachial BP. The central pressure waveform was used to measure central end-systolic pressure (ESP) derived from the radial pulse using a generalized transfer function and commercial software. Arterial stiffness was estimated by duplicate measures of aortic and brachial PWV and peripheral vascular resistance was calculated by mean arterial pressure/cardiac output expressed in peripheral resistance units.

Myocardial. Diastolic assessment was made by conventional criteria; with diastolic transit flow measured by E and A wave velocities in early and late diastole, respectively. Pulsed-wave tissue Doppler was used to measure myocardial velocities in systole, late diastole, and early and late (a) diastole. LV filling pressure was estimated by the E/E' ratio. LV volumes were calculated, as were left atrial area and volume. Stroke volume (SV) was calculated as the difference between end diastolic (EDV) and end systolic volumes (ESV). Myocardial deformation was measured by global longitudinal strain and strain rate (SR) using frame-by-frame speckle tracking in three standard apical views and averaged over 18 segments.

Results

Biochemistry. Infusion of the IFE solution resulted in a significant increase in triglycerides (P<0.001), whereas there was a decrease in increase to saline. IFE induced a significant decrease in LDL and an increase in VLDL cholesterol and the total cholesterol/HDL ratio with respect to the saline infusion (P<0.001 for both). IFE also induced significant changes in platelets and eosinophils.

Vascular response. There were no significant differences for any BP variable after infusion of saline or IFE (P>0.05 for all). There were no associations between the biochemical response to IFE and brachial BP (P>0.05 for all), and no difference in peripheral vascular resistance between groups (P>0.05 for all).

Myocardial response. IFE resulted in a decrease (improvement) in global strain (P=0.007) and SR (P=0.005) from baseline, accompanied by a decrease in mean ESP (P=0.005). The changes in ESP, strain and SR with IFE were also significantly different to the change in the saline group (P>0.02 for all). There were no changes in diastolic function with IFE (P>0.05 for all).

Ventricular-Vascular response. We found a significant increase in SV and E /Lv. after the IFE infusion, compared to saline. IFE also resulted in a significant decrease in the E /Lv. ratio. The change in LDL cholesterol was inversely associated with changes in both E /Lv. (r=-0.642; P=0.033) and E /Lv. (r=-0.674, P=0.001). The change in VLDL cholesterol held similar associations. Importantly, there were associations between V-V coupling and global SR with IFE: E /Lv. (r=-0.033; P=0.037) and SV/PE (r=-0.629; P=0.038), which were not apparent with saline.

Conclusions

Intravenous fat emulsion increased myocardial contractility measured by myocardial deformation and changes in V-V interaction, independent of LV load and arterial function. These findings are very different to those in chronic hyperlipidaemia and may be due to shifts in myocardial substrate utilization. This action may provide support for the use of IFE infusions in the management of complications associated with lipid-soluble drugs.