SCIENTIFIC LETTER

Hypertriglyceridaemia is associated with early non-patency of coronary bypass grafts

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Heart 2006;92:536–538. doi: 10.1136/hrt.2005.068593

Coronary artery bypass grafting (CABG) has prognostic benefit in patients with severe coronary disease and left ventricular dysfunction. It is particularly important in diabetic patients where CABG confers greater long term protection against coronary events than percutaneous angioplasty. However, up to 32% of saphenous vein grafts (SVGs) and 31% of radial artery grafts (RAGs) may be non-patent by one year.¹ Hypertriglyceridaemia is associated with increased mortality after CABG, particularly among diabetics, but its relation to early graft patency is unknown.^{2–3} We investigated the association between metabolic risk factors and early graft occlusion by using non-invasive computed tomography (CT) angiography.

METHODS

The study was approved by the institutional review board ethics committee. All patients attending a preoperative clinic for elective CABG between October 2002 and January 2004 in sinus rhythm with normal serum creatinine, but without a history of intravenous contrast allergy, were invited to participate. Written informed consent was obtained. Of 94 consecutive participants, 14 were subsequently excluded: two died postoperatively, one had a stroke, three developed renal impairment, and eight withdrew from the study.

Recorded baseline characteristics were age, sex, history of smoking, hypertension (blood pressure > 140/90 mm Hg or pharmacological treatment for hypertension), hypercholesterolaemia (fasting cholesterol > 5.5 mmol/l or taking a cholesterol lowering agent), diabetes, and body mass index (BMI). Fasting preoperative total, low density lipoprotein, and high density lipoprotein cholesterol, triglycerides, glucose, insulin, C reactive protein, haemoglobin A_{1c}, fibrinogen, activated partial thromboplastin time, and white cell count were measured at a government certified laboratory. Insulin resistance and pancreatic β cell secretory capacity were calculated by means of the homeostasis model assessment for insulin resistance (HOMA-R) and for β cell function (HOMA- β), according to the formulas $\text{HOMA-R} = \text{fasting glucose (mmol/l)} \times \text{fasting insulin (mU/l)} / 22.5$, and $\text{HOMA-}\beta = \text{fasting insulin (mU/l)} / [\text{fasting glucose (mmol/l)} - 3.5]$.⁴

Graft patency was assessed by multislice computed tomographic (CT) angiography (Lightspeed Plus, GE Medical Systems, Waukesha, Wisconsin, USA) at 4–6 weeks postoperatively. Forty three patients were given oral metoprolol to achieve an average (SD) scan heart rate of 62 (9) beats/min. The scan parameters were 4 × 2.5 mm collimation, 1.3–1.5 pitch, 0.5 seconds rotation time, 120 kV, 270 mA, and 150 ml of intravenous non-ionic contrast medium (Ultravist 300, Schering AG, Berlin, Germany) at 3.5 ml/s. The mean breath hold was 27 seconds (range 22–32 s). Two analysers independently assessed each graft for patency (Card IQ, Advantage Workstation 4.0, GE Medical Systems) and, as there was complete agreement, consensus evaluations were not required. The reference diameter and

the target native artery stenosis were measured from the preoperative conventional coronary angiograms by quantitative vessel analysis. All analysers were blinded to other results and clinical information.

Data were statistically analysed with SPSS for Windows 10.0 (SPSS Inc, Chicago, Illinois, USA). χ^2 , Fisher's exact, Mann-Whitney, and independent *t* tests were used to compare parameters in patients with non-patent grafts versus those without. Stepwise binary logistic regression multivariate analysis included all parameters with *p* < 0.10 on univariate analyses plus diabetes, BMI, and fasting insulin.

RESULTS

Eighty patients, 67 men and 13 women, had CT at a mean (SD) of 35 (8) days postoperatively. The mean (SD) age was 63 (11) years, 35 (44%) were diabetic, 44 (55%) had hypertension, 17 (21%) were obese (BMI > 30), 49 (61%) were former smokers, and none were current smokers. All were taking aspirin, 56 (70%) were taking β blockers, 42 (53%) were taking angiotensin converting enzyme inhibitors, 10 (13%) were taking angiotensin receptor antagonists, 30 (38%) were taking calcium antagonists, 67 (84%) were taking statins, and 38 (48%) were taking nitrates. The mean (SD) fasting total cholesterol was 4.1 (0.9) mmol/l (157 mg/dl) and triglycerides 1.5 (0.7) mmol/l (136 mg/dl).

Fifteen of the 80 patients had occluded grafts. Clinical risk factors and metabolic parameters were compared in patients with patent versus those with non-patent grafts (table 1). The groups did not differ in age, smoking, hypertension, hypercholesterolaemia, diabetes, or obesity. However, patients with non-patent grafts had higher preoperative serum triglycerides (2.0 (0.8) v 1.4 (0.6) mmol/l or 180 (70) v 127 (55) mg/dl, *p* = 0.002) and had trends towards higher white cell counts (7.9 (1.4) v 7.0 (1.7) × 10⁹/l, *p* = 0.06) and shorter activated partial thromboplastin time (31.6 (2.7) v 33.6 (4.0) seconds, *p* = 0.07). Diabetic control (haemoglobin A_{1c}, fasting glucose), HOMA-R, HOMA- β , fibrinogen, C reactive protein, and usage of medications (all *p* > 0.10), including statins (83% and 87%, *p* = 1.0), did not differ significantly.

On multivariate analysis incorporating triglycerides, total cholesterol, non-HDL cholesterol, white cell count, activated partial thromboplastin time, age, diabetes, fasting insulin, and BMI, the preoperative triglyceride concentration (*p* = 0.009) and the white cell count (*p* = 0.03) were the only significant independent predictors of graft non-patency.

Abbreviations: BMI, body mass index; CABG, coronary artery bypass grafting; CT, computed tomography; HOMA- β , homeostasis model assessment for β cell function; HOMA-R, homeostasis model assessment for insulin resistance; RAG, radial artery graft; SVG, saphenous vein graft

Table 1 Univariate analysis between clinical factors and the presence of graft non-patency

	All grafts patent (n = 65)	Non-patent graft (n = 15)	p Value
Clinical data			
Age (years)	64 (11)	59 (13)	0.09
Men	86%	73%	0.25
Former smoker (<5 years)	22%	13%	0.72
Hypertension	51%	73%	0.15
Hypercholesterolaemia	89%	93%	1.0
Diabetes	43%	46%	1.0
Body mass index (kg/m)	28.1 (3.5)	29.0 (3.6)	0.37
Laboratory data			
Total cholesterol (mmol/l)	4.0 (0.8)	4.4 (0.9)	0.10
LDL cholesterol (mmol/l)	2.1 (0.7)	2.4 (0.9)	0.32
HDL cholesterol (mmol/l)	1.20 (0.31)	1.17 (0.18)	0.70
Non-HDL cholesterol (mmol/l)	3.2 (0.9)	2.8 (0.8)	0.06
Triglycerides (mmol/l)	1.43 (0.62)	2.03 (0.79)	0.002*
Fasting glucose (mmol/l)	7.0 (2.1)	7.3 (2.5)	0.64
Fasting insulin (mU/l)	10.3 (7.0–16.8)	9.7 (6.8–12.5)	0.37
HOMA-R (mmol/l)	2.6 (1.5–5.1)	3.1 (2.0–5.4)	0.47
HOMA-β	3.3 (2.2–6.1)	3.0 (2.1–4.9)	0.34
Haemoglobin A _{1c} (%)	6.6 (1.3)	6.6 (1.1)	0.95
Fibrinogen (mmol/l)	4.1 (0.7)	4.3 (0.8)	0.22
APTT (s)	33.6 (4.0)	31.6 (2.7)	0.07
C reactive protein (mg/l)	23 (13–40)	24 (11–63)	0.66
White cell count ($\times 10^9/l$)	7.0 (1.7)	7.9 (1.4)	0.06

Continuous variables are expressed as mean (SD) for parametric data and median (interquartile range) for non-parametric data. Categorical values are expressed as %.

* $p \leq 0.05$.

APTT, activated partial thromboplastin time; HDL, high density lipoprotein; HOMA-β, homeostasis model assessment for β cell function; HOMA-R, homeostasis model assessment for insulin resistance; LDL, low density lipoprotein.

Post hoc subgroup analysis by graft type

There were 190 grafts (2.4/patient) requiring 281 distal anastomoses (3.5/patient). All 74 left internal thoracic artery grafts, 76 of 84 (90%) SVGs, 22 of 28 (79%) RAGs, and three of four (75%) right internal thoracic artery grafts were patent on CT. SVG and RAG patency rates were not statistically different ($p = 0.10$). On multivariate analysis of RAGs, incorporating triglycerides, total cholesterol, target artery diameter, and target artery stenosis severity, the preoperative triglyceride concentration was the only significant independent predictor of RAG non-patency ($p = 0.027$). For SVGs, the clinical or laboratory measured risk factors did not differ significantly between patients with patent and those with non-patent SVGs.

DISCUSSION

Our finding that mild preoperative hypertriglyceridaemia increases the risk of graft non-patency may provide a mechanism for the increased mortality conferred by hypertriglyceridaemia after CABG.^{2–3} This association was observed despite the high usage of aspirin (all patients) and statins (84% of patients) and therefore is relevant to contemporary patient populations. If confirmed in larger interventional studies, this may also provide a modifiable target to improve graft patency. A causal link between mildly increased serum triglycerides and graft occlusion is plausible, as triglyceride-rich particles stimulate factor VII activity, endothelial expression of adhesion molecules, and the prothrombotic plasminogen activator inhibitor 1. Triglyceride rich particles also directly impair endothelial function and increase oxidative stress in monocytes and polymorphonuclear cells; increased triglyceride concentrations have also been associated with coronary events, peripheral arterial thrombosis, and arterial spasm. Alternatively, fasting plasma triglycerides may be an indirect marker of other features of the metabolic syndrome or that postprandial hypertriglyceridaemia itself is pathogenic (as fasting triglycerides predict the area under the curve of the postprandial response to a fatty meal). Our

analyses indicate that the association of triglycerides with graft non-patency is independent of insulin concentrations or HOMA scores and obesity as assessed by BMI; however, we cannot exclude a relation with waist to hip ratio, which we did not record for our patients.

Although conventional risk factors such as hypercholesterolaemia compromise long term SVG patency, the role of metabolic factors mediating short term graft patency are unknown. This is, in part, related to the invasiveness of conventional coronary angiography. With a sensitivity of 89–100% and specificity of 97–100% for detecting non-patency of arterial and venous coronary grafts compared with conventional coronary angiography, CT affords a low risk strategy for patency assessment.⁵ It cannot, however, discriminate between occluded grafts and grafts with minimal flow and severe stenosis or between occluded grafts and arterial graft spasm. Nevertheless, non-patency is likely to be clinically significant, as it entails severe lumen loss and coronary blood flow restriction.

Preoperative hypertriglyceridaemia is independently associated with early non-patency of coronary bypass grafts. Larger, controlled intervention studies are required to investigate a potential causal relation between preoperative hypertriglyceridaemia and graft non-patency.

The work was supported by the National Heart Foundation of Australia (LK, GL) and a Pfizer Cardiovascular Lipid research grant.

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Accepted 11 August 2005

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doi: 10.1136/hrt.2005.070896

No reflow during carotid stenting

An 82 year old man with severe bilateral (90% on the right side, 80% on the left side) stenosis at the origin of the internal carotid artery (ICA), demonstrated by ultrasound, and recurrent transient ischaemic attacks causing weakness of the left arm was referred for stenting of the right ICA. The patient was pre-treated with aspirin and clopidogrel and the activated clotting time following unfractionated heparin administration was 280 seconds. The right ICA lesion (panel A) was easily passed with a filter-emboli protection system and the device was deployed in the cervical part of the vessel. Thereafter, balloon pre-dilatation and self expanding stent deployment were performed. Following balloon post-inflation of the stent, no flow was detectable in the ICA (panel B). On the assumption that the no reflow was caused by thrombus/debris in the filter, the ICA blood column was aspirated with a catheter to catch possible suspended particles. Subsequently, the filter was retrieved. Control angiography demonstrated normal carotid flow with no evidence of either local vessel complications such as dissection or spasm (panel C) or intracranial vessel cut-offs suggesting distal embolisation. The patient remained asymptomatic throughout the procedure. Inspection of the retrieved filter showed a large amount of debris trapped in the device (panel D).

No reflow during carotid stenting occurs typically following post-inflation

Digital subtraction angiography of the right common carotid artery demonstrating severe stenosis at the origin of the internal carotid artery (ICA) (panel A). Panel B shows the absence of flow in the right ICA (black arrows). The white arrow demonstrates the position of the filter-emboli protection system. The final angiographic result is shown in panel C.

of the stent. This phenomenon has to be recognised and properly treated (that is, with aspiration of the blood column in the internal carotid) before filter retrieval in order to prevent distal embolisation.

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Retrieved filter-emboli protection system showing large amount of debris.