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ORIGINAL ARTICLE

## Positive family history of coronary atherosclerosis and serum triglycerides may predict repeated coronary artery bypass surgery

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### Abstract

**Objective.** Cardiovascular risk factor profile of patients in need of repeated coronary artery bypass surgery (redo CABG) seldom differ from patients having only single coronary artery bypass surgery (CABG). The aim of this study was to analyse the influence of positive family history for coronary artery disease in respect to redo CABG vs CABG in a case-control setting. **Design.** One hundred and eighty four patients undergoing redo CABG between 1990–1998 were identified from the computed registry of the Department of Cardiothoracic Surgery in Tampere University Hospital. One hundred and eighty four age, gender and operation date matched patients with CABG were selected for control. **Results.** According to chi-square analysis, positive family history for coronary artery disease was more common in Study group, 60.4% versus 49.5% ( $p < 0.05$ ). Preoperative systolic blood pressure was  $135.5 \pm 1.4$  mmHg versus  $133.5 \pm 1.5$  mmHg (ns), preoperative diastolic blood pressure was  $81.2 \pm 0.8$  mmHg versus  $82.8 \pm 0.9$  mmHg (ns), serum total cholesterol was  $5.8 \pm 0.1$  mmol/L versus  $6.6 \pm 1.2$  mmol/L and preoperative blood glucose was  $5.6 \pm 0.2$  mmol/L versus  $5.3 \pm 0.2$  mmol/L (ns) in Controls and Study group, respectively. However, serum triglyceride level was significantly higher in Study group  $2.8 \pm 0.2$  mmol/L versus  $2.0 \pm 0.1$  mmol/L ( $p < 0.000$ ). In regression analysis, only positive family history (OR = 2.4; 95% CI = 1.1–5.1;  $p < 0.02$ ) and high serum triglyceride level ( $\geq 2$  mmol/L, OR = 1.6; 95% CI = 1.2–2.2;  $p < 0.02$ ) were independent predictors for redo CABG. **Conclusion.** According to this study, positive family history for coronary atherosclerosis at the presence of high serum triglyceride level is significantly predicting the need for future redo CABG as compared with age, gender and operation time matched controls of CABG.

**Key words:** Repeated coronary artery bypass surgery, family history

Morbidity and mortality during repeated coronary artery bypass grafting (redo CABG) is decreasing owing to meticulous surgical technique and improved myocardial preservation (1). Nevertheless, redo CABG poses technical challenges surgically and preoperative identification of patients at risk for redo CABG would be fundamental to choose right operational strategy for the individual patient and to understand the pathophysiology of coronary artery atherosclerosis itself (2,3).

Various studies indicate that preoperative risk factors for coronary atherosclerosis seldom differ among patients undergoing either single coronary artery bypass surgery (CABG) or redo CABG (2). Traditional risk factors include male gender, obesity,

smoking, hypertension, diabetes, high cholesterol and triglyceride levels, generalized atherosclerosis and myocardial infarct, to name but a few. These parameters alone questionably predict need for redo CABG.

Previously, positive family history of coronary artery disease has been shown as an independent predictor of poor late outcome after CABG (6). Asymptomatic twins of symptomatic counterparts may be in danger of considerable coronary artery disease (CAD) (7). Hereditary risk factors have been suspected to predispose to atherosclerotic graft occlusion after CABG (8). We hypothesized that redo CABG may be more frequent in patients with a positive family history of CAD. The aim of this study

was to analyse the influence of positive family history for CAD in respect to redo CABG vs CABG in a case-control setting.

## Materials and methods

### Patients

One hundred and eighty four patients experiencing redo CABG (Study group) between 1990–1998 were identified from our computed registry of Department of Cardiothoracic Surgery in Tampere University Hospital. Patients who experienced any additional cardiac operations or coronary artery interventions were excluded. One hundred and eighty four age, gender and operation date matched patients undergoing their first CABG, without any previous cardiac interventions were selected for control (Controls). Patient records were reviewed for background data. History of brain insult, diagnosis of atherosclerosis, diabetes and myocardial infarct were sought for. Positive family history for coronary artery disease was defined as CAD diagnosis found in at least one first grade relative. Preoperative blood pressure measurement, serum cholesterol and blood glucose values were recorded preoperatively. The study was approved by the local ethical committee. Patient characteristics are shown in Table I.

Evaluation of left ventricular ejection fraction was determined transthoracally and categorized into slightly diminished to normal ( $>30\%$ ) and low ( $\leq 30\%$ ) values. Coronary angiography was performed to investigate atherosclerotic coronary

arteries and localization of CAD was categorized into three main artery disease groups according to total number of the main three coronary arteries (left anterior descending artery, left circumflex artery and right coronary artery) involved. Left main artery stenosis was categorized as 2-main artery disease. CABG and redo CABG were performed according to surgical principles. The indication for redo CABG was unstable angina unresponsive to medical treatment.

### Statistical analysis

Chi-square analysis was used to detect the possible difference of frequencies in risk factors between the groups. Numeric values were expressed as mean (standard error of the mean) and possible difference between the groups was tested with t-test. Continuous variables are reported as mean  $\pm$  error of mean. Logistic regression analysis was used to create a model for repeated surgery as dependent variable and ejection fraction, serum triglyceride level, family history for coronary atherosclerosis, number of bypassed coronary arteries and arterial grafts as covariates. Forward selection was used to identify predictors for redo CABG. SPSS 11.5 statistical software (SPSS Inc., Chicago, IL, USA) was used for the statistical analyses.

## Results

Comparison of traditional coronary artery disease risk factors are shown in Table I. Positive family

Table I. Patient characteristics before initial coronary artery bypass grafting.

	Controls (N)	Study group (N)	p-value
No. of patients	184	184	
Mean age (years)	61.7 $\pm$ 0.5	61.7 $\pm$ 0.5	ns
Male/Female	157/27	157/27	ns
Body mass index (kg/m <sup>2</sup> )	27.4 $\pm$ 0.3 (184)	27.4 $\pm$ 0.4 (118)	ns
Family history of coronary artery disease	49.5% (184)	60.4% (184)	<0.05
Smoking	44.6% (184)	51.1% (159)	ns
Systolic blood pressure	135.5 $\pm$ 1.4 (178)	133.5 $\pm$ 1.5 (114)	ns
Diastolic blood pressure	81.2 $\pm$ 0.8 (178)	82.8 $\pm$ 0.9 (114)	ns
Diabetes	19.6% (184)	12.5% (160)	ns
B-Glucose (mmol/L)	5.6 $\pm$ 0.2 (171)	5.3 $\pm$ 0.2 (96)	ns
S-Cholesterol (mmol/L)	5.8 $\pm$ 0.1 (129)	6.6 $\pm$ 1.2 (93)	<0.000
S-Triglyceride (mmol/L)	2.0 $\pm$ 0.1 (122)	2.8 $\pm$ 0.2 (90)	<0.000
Brain insult	4.4% (182)	3.1% (162)	ns
Atherosclerosis	7.7% (183)	5.5% (163)	ns
Myocardial infarct	53.3% (184)	64.2% (173)	ns
Ejection fraction:	(184)	(184)	
>30%	97.4%	97.9%	
<30%	2.6%	2.1%	ns

Controls = patients undergoing a single coronary artery bypass operation.

Study group = patients undergoing a repeated coronary artery bypass operation.

N = number of cases.

history for coronary artery disease (CAD) was more common in Study group, 60.4% versus 49.5% in Controls ( $p < 0.05$ ). Obviously, as Controls were matched with Study group according to age, gender and date of operation, these parameters were statistically nonsignificant. Body mass index (BMI), smoking, systemic blood pressure, incidence of diabetes, brain insult, transient ischemic attack, myocardial infarct and generalised atherosclerosis were also nonsignificant. Glucose values were nonsignificant between Study group and Controls. However, serum triglyceride level (mmol/L) was significantly higher in Study group ( $2.8 \pm 0.2$  versus  $2.0 \pm 0.1$ ,  $p < 0.000$ ).

Preoperative left ventricular ejection fraction (EF) was more than 30% among 97.4% of Controls as compared with 97.9% of Study group (ns) (Table I). According to angiography, CAD was as prominent in Controls as in Study group. Emergency cases were equally distributed among patients (ns). Incidences of myocardial infarct and brain insult during initial CABG did not statistically differ among patients (Table II).

In regression analysis, only positive family history (OR = 2.4; 95% CI = 1.1–5.1;  $p < 0.02$ ) and serum triglyceride level ( $\geq 2$  mmol/L, OR = 1.6; 95% CI = 1.2–2.2;  $p < 0.02$ ) were predictors for redo CABG. Table III shows the relation between positive family history and serum triglycerides among Study group and Controls.

## Discussion

While a few studies have focused on postoperative morbidity after redo CABG (5,10,11), risk factors leading to redo CABG as compared with single CABG have rarely been studied (2). However, identifying patients at risk for redo CABG before

initial CABG would be most helpful in planning surgical strategy. As individual patients undergoing CABG may be stratified according to postoperative risk for complications on the basis of preoperative information (12), we speculated whether preoperative characteristics would analogically determine the need for redo CABG. In this study, technical bias for statistical analysis was minimized, as for each patient undergoing redo CABG, a control patient undergoing only a single CABG was randomly selected from our computed registry of Department of Cardiothoracic surgery in Tampere University Hospital by matching pair wise according to age, gender and time of operation.

Family history for CAD was more frequent among Study group as compared with Controls. Positive family history for coronary artery atherosclerosis is presumed to reflect hereditary predisposition (6). Therefore, the fate leading to redo CABG may not implicitly be determined by technical factors of impeccable surgery during initial CABG (2).

Traditional risk factors, such as male gender, obesity, smoking, hypertension, diabetes, generalized atherosclerosis and myocardial infarct, were statistically indistinguishable among investigated patients. Interestingly, serum triglyceride levels were significantly higher in Study group. Indeed, serum triglyceride level may reflect the degree of atherosclerotic involvement in coronary arteries (13) indicating the more diffuse state of stenoses in Study group as compared with Controls. This may explain, why patients in Study group experience redo CABG, though the degree of CAD as observed by number of stenosed vessels involved was similar initially in all patients. It may be speculated, that atherosclerotic lesions progressed more aggressively among Study group as compared with Controls (2).

Patients require redo CABG because of graft atherosclerosis or because of a combination of graft and native-vessel disease (11). As hereditary risk factors have been suspected to predispose to late graft occlusion after CABG (8), our study associates hereditary risk and serum triglycerides with the progression of atherosclerosis itself. Hence, family history and serum triglyceride level may be linked to each other (14) and predict redo CABG. It remains to be shown, whether decreasing serum triglyceride level with medication at the presence of positive family history would affect the incidence of redo CABG.

We acknowledge the small number of patients involved in our study. Further research for depiction of genetic profile of patients at risk for redo CABG is naturally warranted. We conclude that positive family history for CAD at the presence of high

Table II. Clinical status during initial coronary artery bypass grafting.

	Controls (N)	Study group (N)	p-value
Elective operation	96.7% (183)	96.7% (150)	ns
Emergency operation	3.3%	3.3%	ns
Target vessels involved:	(183)	(164)	
1- main artery disease	6.6%	4.3%	
2- main artery disease	24.1%	23.2%	
3- main artery disease	69.4%	72.6%	ns
Myocardial infarct	4.9%	7.2%	ns
Brain insult	0.6%	0.6%	ns

Controls = patients undergoing a single coronary artery bypass operation.

Study group = patients undergoing a repeated coronary artery bypass operation.

N = number of cases.

Table III. Interaction between positive family history for coronary artery disease and serum triglyceride level in patients undergoing single coronary artery bypass grafting (Controls) and subsequent operation (Study group).

S-Triglyceride	Negative family history		Positive family history	
	Control group	Study group	Control group	Study group
<1.9 mmol/L	60.7%	50.0%	57.1%	38.7%
≥2.0 mmol/L	39.3%	50.0%	42.9%	61.3%

serum triglyceride level may predict the need for future redo CABG as compared with age, gender and operation time matched controls of CABG.

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