Risk factor control five years after coronary bypass grafting

ABSTRACT—The prevalence of three major coronary risk factors, hyperlipidaemia, hypertension and cigarette smoking, and the change in lipid fractions were assessed five years after coronary bypass surgery and compared to pre-operation in 353 consecutive patients undergoing elective first time surgery at a single centre. Five years after surgery 309 patients were alive without further cardiac surgery, questionnaire follow-up was available in 291 (94%). Lipid profile measurements were made in 255 (83%) of these five-year survivors and 100 (34%) had a history of hypertension.

Five years after surgery, 146 (50%) of the 291 patients thought they had high cholesterol, of whom 92 (63%) were following a diet, 36 (25%) were also taking lipid-lowering drugs and 18 (12%) were taking no measures; 141 (48%) of them did not think they had high cholesterol, and four (2%) did not know. There had been a favourable change in all lipid fractions compared with pre-operation, including total serum cholesterol, particularly in patients taking lipid-lowering drugs. However, total serum cholesterol was above 5.2 mmol/l in 203 (80%) patients and low-density lipoprotein (LDL) cholesterol was above 3.4 mmol/l in 180 (71%). Only 30% of patients taking lipid-lowering drugs had an LDL cholesterol of 3.4 mmol/l or less.

Blood pressure was recorded in 257 (83%) of the 309 five-year survivors: 82 (28%) were taking antihypertensive medication; 32 (12%) and 87 (34%) patients had a diastolic blood pressure above 95 mmHg and 90 mmHg, respectively, and 49 (19%) had a systolic blood pressure above 160 mmHg. There were 22 (9%) regular cigarette smokers. Corroboration of non-smoking with exhaled carbon monoxide measurements confirmed an accurate history of non-smoking in nearly all patients.

The benefits of risk factor reduction after coronary artery bypass grafting (CABG) have gained general acceptance. Hypercholesterolaemia, hypertension and cigarette smoking are all modifiable risk factors which are important in isolation and may also act synergistically. The benefit of lowering high serum cholesterol levels to reduce clinical events in patients with established coronary artery disease is now proven [1], and similar effects are likely from lowering serum cholesterol in patients after CABG. Dyslipidaemia predicted vein graft disease seven [2] and ten [3] years after surgery. The incidence of new lesions in vein grafts detected angiographically was reduced by the aggressive therapeutic reduction of cholesterol after two [4] and four [5] years of follow-up. Patients with a history of hypertension had an increased risk of death [6,7] and of re-operation [8], and patients who continued to smoke cigarettes after coronary artery surgery had a greater risk of recurrent angina, admission to hospital, re-operation and death [9].

Guidelines published by the British Hyperlipidaemia Association (BHA) for the management of serum cholesterol levels in patients with coronary artery disease, including those who have had CABG surgery, state that lipid-lowering drug therapy should be instituted if total serum cholesterol levels remain above 5.2 mmol/l and low-density cholesterol (LDL) above 3.4 mmol/l despite dietary treatment [10]. Similarly, guidelines have been suggested for the initiation of antihypertensive therapy. In these high-risk patients, treatment should be considered when their diastolic blood pressure remains above 90 mmHg [11].

We have prospectively studied 353 consecutive patients who underwent surgery at the Freeman Hospital five years ago and have recently determined their current risk factor status; in particular we assessed to what extent the BHA guidelines are being met.

Patients and methods

Between 24 October 1988 and 4 December 1989, of the 368 patients with chronic stable angina admitted consecutively for elective, first time CABG surgery, 355 (297 men, 56 women, mean age, 57.2 years (standard deviation, 7.31)), were recruited to a prospective study. Patients were excluded if they lived outside the Northern Region (8), if they had valve surgery performed at the time of surgery (3) or if they refused to participate (3); one patient had his operation cancelled because he continued to smoke. The protocol for the study was approved by the Newcastle Joint Ethics Committee.

Immediately prior to CABG, blood was taken for total serum cholesterol, high-density lipoprotein (HDL) cholesterol and triglyceride measurements after a 12-hour fast. Thereafter, patients were seen at...
intervals until one year after surgery when lipid profiles were again measured. Both the patient and the general practitioner (GP) were informed if the total cholesterol at one year was greater than 6.5 mmol/l.

Five years after surgery, patients were seen in a morning clinic by a single investigator and asked whether they thought they had 'high cholesterol or fats in the blood'. Those who thought they had, were asked whether they took any measures to control it. They were also asked if they had a history of 'high blood pressure or hypertension' and, if so, whether they took antihypertensive medication. Current smoking status was assessed and corroborated by measurement of exhaled carbon monoxide (Smokerlyzer; Bedfont Scientific Ltd, Kent, UK) as a measure of carboxyhaemoglobin. Patients who were unable to attend were asked to complete a questionnaire at home.

Blood pressure was measured to the nearest 2 mmHg with a mercury sphygmomanometer after 10 minutes rest (phase V diastolic). Blood for total serum cholesterol, HDL cholesterol and triglycerides was taken after a 12-hour fast. Standard enzymatic methods were used to measure serum cholesterol (cholesterol oxidase, interassay coefficient of variation (cv) 1.3–2.1%) and triglycerides (lipase-glycerol kinase (GK/GPO) interassay cv 2.7–9.4%). HDL cholesterol was measured after precipitation of apolipoprotein B-containing lipoproteins with heparin and manganese, or with phosphotungstate and magnesium, and assayed by the cholesterol oxidase method (interassay cv 8.8–14.6%). Values obtained using the phototungstate and magnesium method were adjusted to be equivalent to those with the heparin and manganese method using the regression equation, phototungstate and magnesium method = 0.99 x heparin and manganese method — 0.07. LDL cholesterol was calculated from the Friedewald equation [12].

Statistics

Categorical variables are expressed as the number (%) and continuous variables as the mean (standard deviation). Lipid fractions before and five years after surgery were compared using a paired t-test. HDL cholesterol and triglycerides before and five years after surgery, stratified by beta-blocker therapy, were compared using an unpaired t-test.

Results

Lipid profiles were measured in 324 (92%) of the 353 patients prior to surgery. Five years after surgery 309 patients were assessed (265 men, 44 women; mean age, 61.8 years (standard deviation, 7.33); 41 patients had died and three had undergone further surgery and left the study. Of the 309, 257 patients were seen as outpatients, 34 completed a questionnaire at home, and 18 failed to respond although they were known to be alive. Questionnaire follow-up was available for 291 (94%) patients. Blood pressure was measured in 257 (83%) patient, and 255 (83%) patients had blood samples taken. Blood was not taken from two patients, one because there was no peripheral venous access and the other because he had leukaemia and had been transfused within the preceding week.

**Cholesterol status**

Of 291 patients completing a questionnaire five years after surgery, 146 (50%) thought they had high cholesterol, 141 (48%) did not think so and (2%) did not know. Of those who thought they had high cholesterol, 92 (63%) were following a diet, 36 (25%) were also taking lipid-lowering drugs and 18 (12%) were taking no measures.

Table 1 shows the number of patients grouped by target levels of total serum cholesterol and LDL cholesterol for all patients before and five years after surgery. Table 2 shows the number of patients five years after surgery according to patient awareness and current treatment. The numbers of patients with serum HDL cholesterol less than 1.0 mmol/l and of those with serum triglyceride level above 2.0 mmol/l are also shown. Among the 255 patients whose serum lipid profile had been measured, ten (4%) had a total serum cholesterol level greater than 7.8 mmol/l; seven of them thought they had high cholesterol and two were taking lipid lowering drugs. In the 146 patients who thought they had high cholesterol, the level was above 6.2 mmol/l in 67 patients; 8 (12%) taking no measures; 48 (72%) taking dietary measures only and 11 (16%) patients taking both lipid lowering drugs and dietary measures. In 25 patients the serum

| Table 1. Number and percentage of patients whose lipid measurements deviated from target levels [10] before and after coronary artery bypass graft (CABG) surgery |
|----------------------------------------------------------|
| **Before CABG** | **Five years after CABG** |
|-----------------|--------------------------|
| n = 353         | n = 309                  |
| Total cholesterol |                          |
| ≤ 5.2 mmol/l     | 324 (92%)                |
| > 5.2 mmol/l     | 269 (83%)                |
| LDL cholesterol |                          |
| ≤ 3.4 mmol/l     | 317 (91%)                |
| > 3.4 mmol/l     | 255 (80%)                |
| HDL cholesterol |                          |
| < 1.0 mmol/l     | 317 (91%)                |
| ≥ 2.0 mmol/l     | 137 (42%)                |
| Triglycerides    |                          |
| n / 324         | 255 (75%)                |

HDL = high-density lipoprotein
LDL = low-density lipoprotein

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Table 2. Number and percentage of patients five years after surgery with total and LDL cholesterol above and below the target levels published by the British Hyperlipidaemia Association [10] according to patient awareness and treatment

|                          | Cholesterol high (n = 146) | Diet and lipid lowering drugs (n = 36) | Cholesterol not high (n = 141) |
|--------------------------|-----------------------------|----------------------------------------|--------------------------------|
| Total cholesterol        |                             |                                        |                                |
| ≤ 5.2 mmol/l             | n = 14 (100%)               | n = 32 (91%)                          | n = 121 (87%)                  |
| > 5.2 mmol/l             | n = 14 (100%)               |                                        |                                |
| LDL cholesterol          |                             |                                        |                                |
| ≤ 3.4 mmol/l             | n = 12 (86%)                | n = 30 (83%)                          | n = 117 (82%)                  |
| > 3.4 mmol/l             | n = 12 (86%)                |                                        |                                |
| HDL cholesterol          |                             |                                        |                                |
| < 1.0 mmol/l             | n = 12 (86%)                | n = 30 (83%)                          | n = 117 (82%)                  |
| > 1.0 mmol/l             | n = 12 (86%)                |                                        |                                |
| Triglycerides            |                             |                                        |                                |
| > 2.0 mmol/l             | n = 14 (71%)                | n = 32 (91%)                          | n = 121 (86%)                  |
|                          | n = 32 (91%)                |                                        |                                |

HDL = high-density lipoprotein
LDL = low-density lipoprotein

cholesterol level was above 7.2 mmol/l; five (20%) taking no measures, 17 (68%) taking dietary measures and three (12%) both lipid lowering drugs and diet.

Figure 1 shows the overall distribution of total cholesterol five years after surgery in patients who thought they did not have high cholesterol. There was a significant fall in mean total serum cholesterol five years after surgery compared to before surgery (6.1 mmol/l versus 6.5 mmol/l, mean difference 0.4 mmol/l, p < 0.001). Figure 2 shows the mean change in the different lipid parameters before and five years after surgery stratified by patient awareness and treatment at five years. In patients taking beta blockers before surgery, there was no significant difference five years after surgery in the mean increase in serum HDL cholesterol between patients who continued to take beta blockers and those who no longer did so (0.23 mmol/l versus 0.30 mmol/l, p = 0.11). Similarly, there was no significant difference in the mean reduction in serum triglycerides between patients who continued to

**Fig 1.** Distribution of total serum cholesterol in 121 patients who thought their cholesterol was not high
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take beta blockers and those who no longer did so (0.04 mmol/l versus 0.25 mmol/l, \( p = 0.16 \)).

**Hypertension**

Of the 100 (34%) with a history of hypertension, 82 (82%) were taking antihypertensive medication. Blood pressure was measured in 257 (83%) of the 309 surviving patients; 92 (12%) and 87 (34%) of these patients had a diastolic blood pressure above 95 mmHg and 90 mmHg, respectively, and 49 (19%) a systolic blood pressure above 160 mmHg.

**Smoking**

Twenty-two (8%) of the 291 patients admitted that they regularly smoked cigarettes. Exhaled carbon monoxide measurements confirmed that nearly all patients gave an accurate history of non-smoking, but two (0.8%) patients had a borderline level for non-smoking (10ppm).

**Discussion**

The prevalence of three major risk factors was assessed five years after coronary artery surgery. Compared to pre-operation, there was a favourable improvement in lipid levels five years after CABG surgery, but three-quarters of patients still have cholesterol above the level at which drug therapy should be considered; 45% of these patients thought they did not have high cholesterol. Only 19% of patients who thought their cholesterol was high were adequately treated and only 12% were taking lipid-lowering agents. One-third of patients had a history of hypertension and 82% of them were taking antihypertensive therapy but despite that, 12% had a diastolic blood pressure above 95 mmHg. A smaller proportion continued to smoke cigarettes.

A high prevalence of untreated hyperlipidaemia after CABG surgery has also been reported by Northridge et al [13] in the UK and by Simons et al [14] in Australia. A number of factors may have contributed to this high prevalence:

- serum cholesterol may never have been measured except as part of the research protocol,
- patients may never have been told their cholesterol level, or
- if they were told the level, the significance of the result may have been misinterpreted.

One year after surgery, patients and their GPs were telephoned with the result only if total cholesterol was...
greater than 6.5 mmol/l. More recent guidelines [10], strongly supported by the results of the Scandinavian Simvastatin Survival Study [11], indicate that the threshold for initiating lipid-lowering therapy in patients with established coronary artery disease is a total cholesterol level above 5.2 mmol/l. However, although our relatively high threshold for informing GPs of the level one year after surgery may be considered inappropriate according to recent guidelines, results obtained as part of the research protocol were not a substitute for the usual clinical care of the patients in our study.

The fact that potential gains from treating patients with overt coronary artery disease are much greater than those from treating otherwise low-risk patients may not always be recognised. Early after surgery, there may be uncertainty about the responsibility of the different hospital doctors and the GPs for initiating lipid-lowering therapy; later, patients who are well may have been discharged from hospital care and be only infrequently in contact with their GP. However, being aware of high serum cholesterol and taking measures to control it did not ensure adequate treatment. Diet alone in patients who thought their cholesterol was high had little impact, with a mean fall of only 0.2 mmol/l over five years. In patients in whom lipid-lowering medication had been instituted there was a mean fall of 1.0 mmol/l over the five years since surgery—but even then only 30% reached the recommended therapeutic goal.

Before surgery, 46% of the patients had unfavourable serum HDL levels; five years after surgery this had fallen to 14%. Long-term beta-blocker therapy has an adverse impact on lipid profiles, resulting in a reduction in serum HDL cholesterol and an increase in serum triglycerides [15]. However, discontinuing beta-blockers in patients after successful revascularisation does not fully explain the increase in serum HDL cholesterol and the reduction in serum triglycerides but may have contributed. Pre-operative serum HDL cholesterol levels, particularly in combination with elevated serum triglyceride levels, were important prognostic indicators of 10-year survival after CABG surgery [16]. In our study, 84 (26%) patients had the particularly unfavourable pre-operative combination of serum HDL cholesterol less than 1.0 mmol/l and serum triglycerides above 2.0 mmol/l. Five years after surgery, fewer patients had serum HDL levels of less than 1.0 mmol/l, but 12 (5%) of five-year survivors still had this unfavourable combination.

Simons et al [14] reported a higher prevalence of history of hypertension in their patients (54%) than we found in ours (34%), but a much lower prevalence of raised diastolic blood pressure (>95 mmHg) (3% vs 12%). Taking a diastolic blood pressure of 90 mmHg as the threshold for the diagnosis of hypertension increases its prevalence in our patients from 12% to 34%. Nevertheless, there seems to be less reluctance to initiate adequate antihypertensive medication than to initiate lipid-lowering medication. Some patients may have been taking drugs for reasons other than hypertension (eg to treat angina) but which also have an antihypertensive action. This may have masked otherwise untreated, undetected hypertension.

Limitations of the study

We have reported here the prevalence of hyperlipidaemia from a single measurement of the lipid profile, but there is biological variability in lipid profiles. However, although we may have mislabelled some patients as hyperlipidaemic, some may also have been misdiagnosed as normal. Similarly, blood pressure is labile and subject both to diurnal and to day-to-day variation. Patients with diastolic blood pressures between 90 and 95 mmHg may have been erroneously diagnosed as hypertensive. Some of our borderline cases may have been under surveillance by GPs, and hence should not be considered as ‘untreated’, but as ‘under surveillance’ whilst awaiting confirmation of the need or otherwise for specific treatment. Although patient awareness of cholesterol status was reported, we cannot differentiate inadequate assessment of risk factors from inadequate treatment once measurements have been made. The differentiation of these two possibilities may help when planning future strategies to improve risk factor management after CABG surgery.

Conclusions

Coronary risk factors five years after CABG surgery often remain undetected and/or untreated. This is particularly true of hypercholesterolaemia, but there is also room for improvement in the detection and treatment of hypertension. Patients are honest about their smoking habits, and some patients continue to smoke cigarettes; however, it may be difficult to make a major impact on this. Heightened awareness of the benefits of treating hypercholesterolaemia in high-risk patients may make their management more effective. The Scandinavian Simvastatin Survival Study [1] has recently reported an important reduction in clinical events in patients with coronary artery disease treated with simvastatin and this may influence doctors’ attitude to treating hyperlipidaemia.

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