The impact of obesity on late patency of left internal mammary artery grafts

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Abstract

Background: Arterial conduits having long-term patency rates have been increasingly used for bypass of coronary arteries although some risk factors for their occlusion such as recipient vessel size, older age, and hyperlipidaemia have been described. Obesity, on the other hand, has been well established as a coronary risk factor. However, the effects of obesity on patency of arterial conduits, especially the internal mammary artery, have not been studied previously.

Aim: To assess the long-term effects of obesity on left internal mammary artery (LIMA) patency.

Methods: Angiograms of all patients with a LIMA conduit only were analysed. Two groups were formed according to the LIMA patency: group 1 – patients with occluded LIMA (n = 59), and group 2 – patients with patent LIMA (n = 68). Baseline demographic, haemodynamic, and laboratory characteristics of patients in both groups were compared. Obesity was defined as body mass index ≥ 30 kg/m^2.

Results: The mean BMI value in group 1 was significantly higher than in group 2 (30.4 ± 3.1 vs. 28.7 ± 4.7, p = 0.025). The two groups differed in time from surgery, drug use, and HDL cholesterol level. In addition, patients in both groups were categorised by BMI, and obese and non-obese groups were formed. Higher BMI was significantly associated with LIMA occlusion such that 71% of patients in group 1 had increased BMI, compared with 25% of patients in group 2 (p < 0.001). Multivariate analysis showed that multiple adjusted OR of the risk of LIMA occlusion was 7.41 (95% CI 3.38-16.28) for patients with increased BMI.

Conclusions: Obesity (≥ 30 kg/m^2) has a significant and independent negative effect on the patency of the LIMA graft.

Key words: obesity, body mass index, left internal mammary artery, patency

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Introduction

Internal mammary arteries, especially the left one, are the most suitable arterial conduits for surgical revascularisation of the left coronary circulation, especially the left anterior descending (LAD) coronary artery, due to its long-term patency and mortality benefit [1-3]. During the postoperative period following coronary artery bypass graft (CABG) some patients may develop angina. Causes of angina include incomplete revascularisation at the time of surgery, progression of atheromatous disease or occlusion of the grafts.

Obesity is a well known risk factor for coronary artery disease (CAD), and increased body mass index (BMI) has been found to be negatively associated with operative and long-term outcomes following CABG using venous or arterial conduits [4, 5]. Some risk factors such as metabolic syndrome, smoking, and diabetes mellitus have been described as independent risk factors for early saphenous vein graft stenosis [6]. However, obesity alone has not been extensively studied in patients undergoing CABG. In addition, to our best knowledge, the effect of obesity on patency of arterial conduits has not been studied previously. Therefore, the aim of the present study was to demonstrate the impact of obesity on the late patency of the left internal mammary artery (LIMA) graft following CABG.

Methods

Study population

A total of 127 patients with a LIMA as a single graft used for revascularisation of LAD were included in the study. Inclusion criteria were a time period of at least 6 years after CABG and LIMA as the only graft used for

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revascularisation. Exclusion criteria were a time period of ≤ 5 years after surgery, graft use other than LIMA, refusal to participate in the study, unstable angina, and chronic liver and kidney diseases. All patients were asked about any cardiovascular drug use and the time from CABG in years, and underwent transthoracic echocardiography for left ventricular ejection fraction assessment. In addition, type of surgical procedure, CABG/OPCABG and skeletonised/pedicled LIMA were determined from the surgical files. All the patients were divided into two groups according to the LIMA patency. Patients with occluded LIMA formed group 1 (n = 59), and others with patent LIMA formed group 2 (n = 68).

Cardiac catheterisation

All patients in the study underwent selective coronary artery and LIMA angiography after standard patient preparation. The femoral artery and, in some patients, the left radial artery were used for the arterial access site and the Judkins system was used for cannulating the left and right coronary arteries. In the majority of patients, the right Judkins catheter was used for selective angiography of LIMA. The LIMA catheter was also used in the case of failed selective cannulation, and the sphygmomanometer was used if the LIMA could not be visualised. The LAD diameters were measured by quantitative angiography via an automated computer system. The mid-LAD region was used for the measurement. All angiograms were evaluated by two experienced physicians blinded to the patients' characteristics.

Anthropometric measurements

Height and weight of patients were measured, and BMI was calculated by dividing weight in kilograms by height in square meters and described as kg/m^2.

Laboratory data

Fasting peripheral venous blood samples were obtained from all patients for the measurement of fasting plasma glucose, total cholesterol, LDL cholesterol, HDL cholesterol, triglyceride, and fibrinogen levels. Blood samples were centrifuged and plasma was obtained. Fasting blood glucose, total cholesterol, HDL cholesterol and triglyceride levels were measured enzymatically by an autoanalyser (Hitachi 911, Japan). The LDL cholesterol level was calculated using the formula described by Friedewald et al. [7].

Statistical analysis

Data were analysed with the SPSS software version 15.0 for Windows (SPSS Inc., Chicago, Illinois, USA). Continuous variables are presented as mean ± SD and categorical variables as numbers and percentages. The Kolmogorov-Smirnov test was used to assess the distribution of continuous variables. Student's t-test was used to compare normally distributed continuous variables, and the Mann-Whitney U test was used for variables without normal distribution. A two-tailed p value of < 0.05 was considered statistically significant. Multiple logistic regression analysis was used to evaluate the independent predictors of patency of LIMA. In addition, multivariate Cox regression analysis was performed to estimate associations between obesity groups and patency rates. The odds ratios (OR) and 95% confidence intervals (CI) were calculated.

Results

The mean age of the study population was 66 ± 10 years (range, 46-84 years). Demographic and clinical characteristics of both groups are compared in Table I. The mean time from CABG in group 1 was longer than in group 2. Male/female ratio was significantly higher in group 2 than in group 1. The calcium channel blocker usage was higher in group 2 than in group 1, whereas angiotensin II receptor blocker, aldosterone antagonist, and digoxin use were higher in group 1 than in group 2. In addition, the mean HDL cholesterol level was lower in group 1 than in group 2. There was no significant difference between group 1 and 2 as far as the type of surgery is concerned. Off-pump CABG was the most preferred procedure (78% in both groups). Mammary arteries were harvested with skeletonisation technique in all patients.

There was a significant difference between the two groups in the BMI values. Group 1 had higher BMI values than group 2 (30.4 ± 3.1 vs. 28.7 ± 4.7, p = 0.025). Individual values of BMI are depicted in Figure 1.

Patients in both groups were then categorised in terms of obesity, based on BMI. A cut-off point of 30 kg/m^2 was used for obesity definition, and the patients divided into two groups as obese (≥ 30 kg/m^2) and non-obese (< 30 kg/m^2). Increased BMI was significantly associated with the fate of LIMA such that 71% of patients in group 1 had elevated BMI, compared with 25% of patients in group 2 (p < 0.001) (Figure 2). The presence of BMI ≥ 30 kg/m^2 increased the risk of LIMA occlusion by 9.26-fold (95% CI 3.81-22.54) (p < 0.001). After adjustment for age, sex, time from surgery, BMI, the presence of hypertension, diabetes mellitus, smoking, serum levels of total, LDL and HDL cholesterols, triglycerides, current use of calcium channel blocker, angiotensin II receptor blocker, aldosterone antagonist, digoxin, and statins, the multiple adjusted OR of the risk of LIMA occlusion was 7.41 (95% CI 3.38-16.28) (p < 0.001) for the increased BMI.

Lastly, in the multivariate Cox regression analysis, there was a significant difference between obese and non-obese patients according to adjusted cumulative patency rates (HR 0.43, 95% CI 0.29 to 0.64, p < 0.001) (Figure 3).

Discussion

We found that patients with occluded LIMA had significantly increased BMI compared to patients with

Table I. Demographic, laboratory, and haemodynamic characteristics of patient groups

	Group 1 (n = 59) occluded LIMA	Group 2 (n = 68) patent LIMA	p
Age [years]	66 ± 9	66 ± 11	0.790
Male sex, n (%)	41 (70)	65 (96)	< 0.001
Hypertension, n (%)	25 (42)	30 (44)	0.843
Diabetes mellitus, n (%)	4 (7)	9 (13)	0.231
Smoking, n (%)	10 (17)	8 (12)	0.403
Family history of CAD, n (%)	27 (46)	24 (35)	0.230
Time after CABG [years]	14 ± 4	12 ± 2	< 0.001
Type of surgery, CABG/OPCABG	13/46	15/53	0.997
Acetylsalicylic acid, n (%)	57 (97)	67 (99)	0.478
Beta blocker, n (%)	49 (83)	56 (82)	0.917
Calcium channel blocker, n (%)	2 (3)	9 (13)	0.049
Nitrate, n (%)	42 (71)	48 (71)	0.941
Statin, n (%)	35 (59)	36 (53)	0.470
ACE inhibitor, n (%)	35 (59)	40 (59)	0.955
ARB, n (%)	10 (17)	3 (4)	0.020
Aldosterone antagonist, n (%)	4 (7)	0 (0)	0.029
Digoxin, n (%)	7 (12)	1 (2)	0.016
Body mass index [kg/m^2]	30.4 ± 3.1	28.7 ± 4.7	0.025
Fasting plasma glucose [mg/dl]	99 ± 16	105 ± 33	0.148
Cholesterol [mg/dl]			
Total	199 ± 24	205 ± 34	0.237
LDL	136 ± 22	133 ± 34	0.646
HDL	33 ± 7	42 ± 12	<0.001
Triglyceride [mg/dl]	148 ± 65	147 ± 58	0.869
Fibrinogen [mg/dl]	3.28 ± 0.86	3.56 ± 1.51	0.211
LV ejection fraction [%]	49 ± 9	49 ± 7	0.754
Heart rate [beats/min]	74 ± 10	72 ± 8	0.377
Blood pressure [mmHg]			
Systolic	130 ± 22	131 ± 18	0.947
Diastolic	80 ± 11	82 ± 12	0.204
LAD diameter during angiography [mm]	1.92 ± 0.62	2.05 ± 0.50	0.211

Abbreviations: ACE – angiotensin-converting enzyme, ARB – angiotensin II receptor blocker, CABG – coronary artery bypass grafting, CAD – coronary artery disease, HDL – high-density lipoprotein, LAD – left anterior descending coronary artery, LDL – low-density lipoprotein, LV – left ventricle, OPCABG – off--pump coronary artery bypass grafting

patent LIMA. In addition, this significant and positive relationship was independent of risk factors for CAD.

Interestingly, the ratio of female patients in the occluded LIMA group was significantly higher than in the patent LIMA group. This finding might result from the relatively small vessel size of female patients. Small recipient vessel size is associated with lower patency rates, and 10-year patency was 100% for vessels > 2.0 mm versus 82% for vessels ≤ 2.0 mm [8], although there was no significant difference between the two groups for LAD diameter in our study.

Time from CABG is also an independent predictor for LIMA patency. As expected, we found that time from surgery to angiography was longer in the occluded LIMA group than the patent LIMA group.

Another factor affecting graft patency is aspirin use. The use of aspirin is predictive for patency status when all types of grafts are taken into account [8]. The majority of patients in our study have used acetylsalicylic acid. Although the use of angiotensin II receptor blocker, aldosterone antagonist, and digoxin was significantly higher, and the use of calcium channel blocker was lower in the occluded LIMA group, they

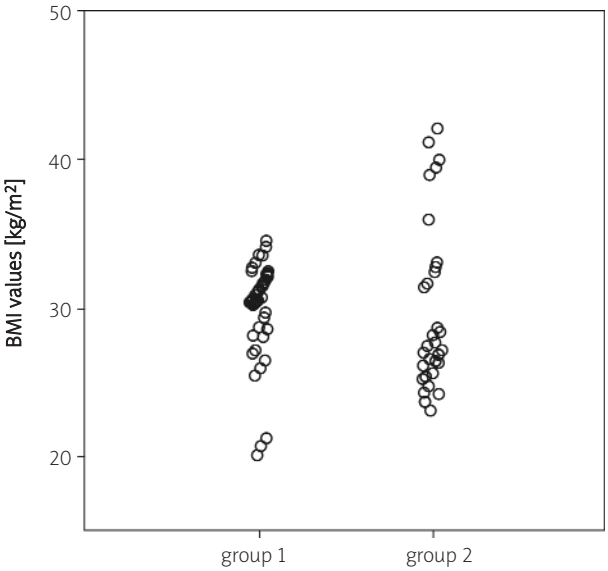

Figure 1. Distribution of BMI values in both groups

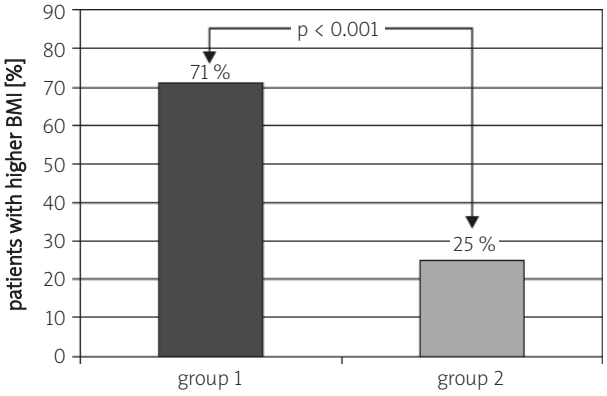

Figure 2. Proportion of patients with increased BMI values (≥ 30 kg/m^2) in the occluded LIMA (group 1) and patent LIMA (group 2) groups

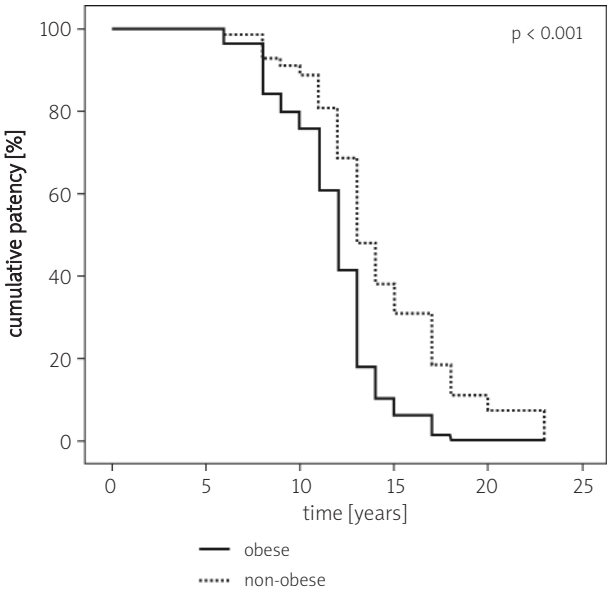

Figure 3. Adjusted* patency curves for obese (≥ 30 kg/m^2) and non-obese (< 30 kg/m^2) patients

**Adjusted for age, sex, presence of hypertension, diabetes mellitus, and smoking, serum levels of total, LDL and HDL cholesterol, and triglycerides, and current use of calcium channel blocker, angiotensin II receptor blocker, aldosterone antagonist, digoxin, and statins*

lost their significance in multivariate analysis. We also found that the occluded LIMA group had lower mean HDL cholesterol level than the patent LIMA group. A lower HDL cholesterol level may affect the patency rate of LIMA [8]. However, after being adjusted for HDL cholesterol, the BMI value remained an independent predictor of LIMA patency.

Obesity is a well known risk factor for hypertension, diabetes mellitus, dyslipidaemia, and coronary atherosclerosis morbidity and mortality [9]. Coronary artery bypass surgery with the use of LIMA has also been used in obese patients. Previous studies showed conflicting results on the effects of obesity on outcomes after CABG. Habib et al. showed that obesity was independently associated with increased postoperative morbidity and decreased long-term survival [4]. On the other hand, Perrotta et al. showed that obesity was negatively related to perioperative outcomes other than postoperative survival [5]. Furthermore, obesity did not increase the risk of perioperative death and other adverse outcomes in patients undergoing CABG in another study [10]. However, the above-mentioned studies included patients with saphenous vein grafts. For IMA grafts, the 10 year patency is 85% [8]. Some independent predictors for patency have been described for coronary grafts including LIMA. The most powerful ones are recipient vessel size, age, aspirin use, and dyslipidaemia.

Obesity as a risk factor for occlusion of the LIMA has not been studied previously. In our study, for the first time, we found obesity to be an independent and significant risk factor for occlusion of the LIMA in the long-term follow-up.

Study limitations

Although quite a large study population was used in our study, we believe it is still too limited in number to generalise the results to all patients because only patients with referral indications for cardiac catheterisation were included. The invasive nature of the study was another reason for the relatively small sample size. In addition, the data are only from the survivors who, by definition, may have had better graft patency than the non-survivors.

Conclusions

We have demonstrated for the first time that obesity, defined by BMI, in patients with occluded LIMA was significantly and independently higher than in patients with patent LIMA. The BMI values above 30 kg/m^2 increased risk of LIMA occlusion in the long term. Prospective studies with large sample sizes using multivariate survival analysis are needed to confirm our findings.

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Związek pomiędzy otyłością a drożnością tętniczych pomostów wieńcowych w obserwacji odległej

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Wstęp: Z uwagi na wysoki odsetek zachowanej po wielu latach drożności pomosty tętnicze są preferowanym sposobem wykonywania operacji rewaskularyzacyjnych (CABG). Istnieją pewne czynniki zwiększające ryzyko zamknięcia, do których należą przekrój naczynia chorego, wiek oraz hiperlipidemia. Z kolei otyłość jest dobrze udokumentowanym czynnikiem ryzyka choroby wieńcowej. Dotychczas związek pomiędzy otyłością a drożnością pomostów tętniczych, szczególnie z wykorzystaniem tętnicy piersiowej wewnętrznej (LIMA), nie był badany.

Cel: Ocena związku pomiędzy otyłością a drożnością pomostów tętniczych w obserwacji długoterminowej.

Metody: Poddano analizie angiogramy wszystkich chorych z LIMA. Biorąc pod uwagę drożność LIMA, utworzono dwie grupy chorych: grupa 1 – chorzy z zamkniętym pomostem (n = 59), oraz grupa 2 – chorzy z drożną LIMA (n = 68). Porównano dane demograficzne, hemodynamiczne i laboratoryjne obu grup. Otyłość zdefiniowano jako indeks masy ciała (BMI) ≥ 30 kg/m^2.

Wyniki: Średnia wartość BMI w grupie 1 była istotnie wyższa niż w grupie 2 (30,4 ± 3,1 *vs* 28,7 ± 4,7, p = 0,025). Obie grupy różniły się również pod względem czasu, który upłynął od zabiegu chirurgicznego, stosowanych leków i stężenia HDL-cholesterolu. Dodatkowo chorych podzielono na otyłych i nieotyłych. Otyłość wiązała się ze zwiększonym ryzykiem zamknięcia LIMA: stwierdzono ją u 71% chorych z grupy 1 wobec 25% z grupy 2 (p < 0,001). Analiza wieloczynnikowa wykazała, że ryzyko zamknięcia LIMA było 7,41 razy wyższe u chorych otyłych (95% CI 3,38–16,28).

Wnioski: Otyłość jest istotnym i niezależnym czynnikiem ryzyka zamknięcia pomostu tętniczego w obserwacji odległej.

Słowa kluczowe: otyłość, pomostowanie aortalno-wieńcowe, drożność

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