Statin Treatment Equalizes Long-Term Survival Between Patients With Single and Bilateral Internal Thoracic Artery Grafts

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Background. **The use of 2 internal thoracic artery (ITA) grafts increases survival 10 years after coronary artery bypass grafting (CABG) compared with single ITA grafting. Statin treatment was also shown to decrease development and progression of saphenous vein graft atherosclerosis. This study examined the effect of statin treatment on long-term survival after CABG.**

Methods. **Operative, survival, and pharmacologic data of 6655 patients who underwent CABG with ITAs between 1995 and 2007 in our institution were obtained.**

Results. **Patients with bilateral ITA grafts had an average 10-year-survival rate of 83% ± 2% compared with 67% ±1% in patients with single ITA grafts ($p = 0.0001$). Statin treatment caused a significant decrease in the long-term risk of death among patients who underwent single ITA grafting (hazard ratio [HR], 0.735, $p = 0.0001$). However, statin treatment had no effect on the risk of long-term death among patients who underwent bilateral ITA grafting (HR, 1.053; $p = 0.7806$).**

Conclusions. **Statin treatment initiated early after grafting improved long-term survival in patients with a single ITA graft but not in those with bilateral ITA grafts. Survival of statin-treated patients with single ITA grafts was similar to bilateral ITA patients.**

(Ann Thorac Surg 2009;88:789–95)

At first, single then bilateral internal thoracic artery (ITA) grafting was shown to improve patient survival at 10 years compared with the use of saphenous vein grafts [1–9]. The bilateral ITA grafts for arterial grafting became the procedure of choice for patients undergoing multiple coronary artery bypasses grafting (CABG) [10, 11]. Because most studies supporting these recommendations were obtained from patients operated on in the 1980s and 1990s, before the use of statin treatment to control lipid levels after CABG, most patients did not receive treatment with proven measures of secondary prevention after significant coronary clinical events.

The Post Coronary Artery Bypass Graft (Post CABG) trial studying 1351 patients at 1 to 11 years after CABG demonstrated a clear benefit of an aggressive lowering of low-density lipoprotein cholesterol (LDL-C) to below 100 mg/dL with lovastatin on the angiographic progression of atherosclerosis in saphenous vein grafts [12]. Treatment with aspirin, β-blockers, and especially a statin, must have a significant effect on long-term survival and complication rates that needs to be studied in addition to the simple definition of the surgical technique in single and bilateral ITA grafts.

The objective of the present study is to analyze the benefit of secondary prevention with medication, including statin treatment, and single and bilateral ITA grafts on long-term survival after CABG. We hypothesized that statin treatment initiated early after CABG provides a significant long-term protection against death and coronary events. We also tested the hypothesis that the protection effect of statin treatment on long-term coronary events causes a substantial modification of the effect of using a single ITA graft.

Material and Methods

Between January 1995 and December 2007, 9980 consecutive adult patients underwent primary and isolated CABG with ITA grafting at the Montreal Heart Institute. All patients undergoing CABG with at least one ITA graft were included in the present analysis. Patients undergoing a concomitant valve or other cardiac surgical procedures were excluded, as well as patients undergoing reoperation.

The indication for myocardial revascularization was based on standard angiographic and clinical criteria. The left ITA was harvested with its pedicle and usually grafted on the left descending artery or a diagonal

Accepted for publication April 24, 2009.

Presented at the Forty-fifth Annual Meeting of The Society of Thoracic Surgeons, San Francisco, CA, Jan 26–28, 2009.

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Published by Elsevier Inc

0003-4975/09/$36.00
doi:10.1016/j.athoracsur.2009.04.097

Table 1. Patient Characteristics

Variable	Type of Insurance		
Mean ± SD or No (%)	Public	Private	*p* Value
Patients	6655	3220	
Age, y	67 ± 9	58 ± 8	<0.0001
Female gender	1778 (27)	439 (14)	<0.0001
Diabetes	1950 (29)	763 (24)	<0.0001
Hyperlipidemia	3139 (47)	1571 (49)	0.1328
Hypertension	3388 (51)	1379 (43)	<0.0001
Unstable angina	2366 (36)	986 (31)	<0.0001
Prior recent MI ≤ 30 days	1250 (19)	621 (19)	0.5507

MI = myocardial infarction; SD = standard deviation.

branch; when used, the right ITA was mostly harvested pedicle aiming at the circumflex or the right coronary territory or used as a free graft [7]. Sequential ITA grafts were used occasionally. Patients underwent single and bilateral ITA grafting depending on the preference of the attending surgeon.

Demographic variables (gender and age) and risk factors for coronary artery disease and major comorbidities were obtained by retrospective review of the institutional discharge summary.

Patient survival during follow-up and the occurrence of cardiac reoperation and percutaneous coronary interventions (PCI) were recorded. Follow-up data were obtained by matching the patients' health insurance number in the institutional database with the corresponding files in a governmental centralized health care database (*Régie de l'Assurance Maladie du Québec*), where all episodes of health care (in and out of the hospital) are recorded. Deaths were obtained from the national index of the provincial government.

The drug insurance program covered all unemployed and also elderly persons in the province before 1997. After this date, all citizens had to register with a private or with the government drug insurance program. All drugs prescribed under the public system were recorded and the data were available for our analysis.

Patients were separated in three subgroups according to the use of specific classes of medication after CABG: (1) no use of the medication, (2) the prescription starting after the first 30 postoperative days, and (3) prescription of the medication starting within 30 days of the operation and continuing until the last year of follow-up. The decision to use the 30-day cutoff was arbitrary considering the hypothesis that medical treatment initiated early after the operation might give better long-term results after CABG.

Four classes of medication were studied: antiplatelet agents, β-blockers, statins, and angiotensin-converting enzyme (ACE) inhibitors. A prescription of one agent in each class was considered as present or absent, irrespective of the doses and the trade names of the particular drug.

Permission to use the denominated database was obtained from the Information Access Board of the Quebec government and from the Ethics Committee of the Montreal Heart Institute. Follow-up was complete except for 81 patients, who were mostly foreign, where the health insurance number was unavailable (9880 [99%] of 9918 of complete data). All information, clinical follow-up, and vital status was obtained until October 2007, the closing interval for our cohort of patients.

Statistical Analysis

Data were expressed as means ± standard deviation for continuous variables and frequencies and percentages for categoric variables. Demographic data were compared between groups using χ^2 test for categoric variables, and continuous variables were compared using the *t* test. Mortality at 30 days was analyzed for the entire cohort of 9875 patients. Long-term survival was studied with hospital survivors followed up under the public insurance program, thus including 6655 patients. Mortality, PCI, cardiac reoperation, and the combination of all adverse events were studied using survival analysis.

Survival curves were computed using the Kaplan-Meier formulas and compared between groups with the log-rank test. Cox proportional hazard multivariate regression model was used to analyze the effect of ITA graft techniques and the use of a statin on long-term mortality rates and the combination of all adverse events adjusted for demographic, clinical, and medication covariates. All analyses were done with SAS 9.1 software (SAS Institute Inc, Cary, NC) and conducted at a significance level of 0.05.

Results

Patient Characteristics

Patients registered in the public drug program were significantly older, a larger percentage were women, and

Table 2. Medications After Coronary Artery Bypass Grafting in Patients Participating in the Drug Public Insurance Program

Medication, No. (%)	Public Insurance
Patients	6655
Antiplatelet agents	
None	233 (3)
Started after 30 days from CABG	1786 (27)
Started within 30 days after CABG	4636 (70)
β-Blockers	
None	1292 (19)
Started after 30 days from CABG	2041 (31)
Started within 30 days after CABG	3322 (50)
ACE inhibitors	
None	2028 (30)
Started after 30 days from CABG	2840 (43)
Started within 30 days after CABG	1787 (27)
Statins	
None	654 (10)
Started after 30 days from CABG	2923 (44)
Started within 30 days after CABG	3978 (46)

ACE = angiotensin converting enzyme; CABG = coronary artery bypass grafting.