Comparison between single and double internal mammary artery grafts: results over ten years

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Key words:
Coronary artery bypass graft; Coronary artery surgery; Ischemic heart disease.

Background. **In view of the superior patency of the internal mammary artery (IMA), grafting of this vessel to the left anterior descending artery is advantageous in terms of survival and quality of life; the benefits of using both the mammary arteries remain unproved.**

Methods. **Among the patients operated upon during the period 1988-1990, we randomly selected 150 patients in whom one IMA (group 1) was grafted and 150 patients in whom both IMAs (group 2) were grafted. The survival and event free curves of these two groups of patients were designed using the Kaplan-Mayer method; the log-rank test was used to assess the statistical difference between the curves and to determine whether, in the long term, benefits were superior in patients in whom both IMAs were grafted.**

Results. **Patients in group 1 were older (p = 0.002). In this group there were more patients with diabetes (p = 0.004) and with peripheral vascular disease (p = 0.047). There were more female patients in group 2 (p < 0.02) and more coronary vessels were grafted (p = 0.03). Follow-up was complete (100%) and equivalent in duration for both groups (109 ± 30 months for group 1 and 110 ± 33 months for group 2, p = NS). The survival rate at 10 years was equal for both groups (82.5 ± 3.4% for group 2 vs 82.9 ± 3.2% for group 1, p = NS) and so was the freedom from cardiac death. The provocative test for myocardial ischemia was more frequently positive in group 1 than in group 2 (21 vs 10 cases, p = 0.054). Freedom from new myocardial infarction (p = NS), angina recurrence (p = NS) and reoperation (p = NS) was equally distributed during follow-up. Group 2 patients more frequently necessitated coronary angioplasty but the difference was not significant (p = 0.17). Survival free from angina recurrence, new myocardial infarction, coronary angioplasty and reoperation was more frequent in group 2 (respectively 74.6 ± 3.8 vs 70.7 ± 4.1%) but the difference was not statistically significant (p = NS).**

Conclusions. **After 12 years of follow-up, patients submitted to grafting of a single IMA more frequently presented with inducible myocardial ischemia, but neither survival nor the quality of life were superior in the patients in whom both IMAs were grafted.**

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Introduction

In 1986 Loop et al.[1] reported the advantages of coronary revascularization performed by the internal mammary artery (IMA) on the left anterior descending artery. The use of this conduit modified the patient's prognosis and the advantages were independent of the number of the diseased vessels. This report changed the strategy of coronary surgery.

In 1974 Barner[2] reported the use of both IMAs for coronary revascularization: 25 years later the advantage of using the second IMA is still subject of debate.

In this study we compared the results obtained in two groups of patients operated on in the same institution by the same surgeons and during the same period. Either one or both IMAs were grafted. The aim of this study was to verify whether the use of both IMAs was advantageous in terms of survival and quality of life compared to grafting of only one IMA.

Methods

During the period 1988-1990 in the Cardiac Surgery Unit at the Varese Hospital, 992 patients were operated on for isolated coronary artery revascularization. Either one or two IMAs were grafted. In 651 cases one

IMA was used and other venous grafts were employed when necessary. In 341 cases both IMAs were used. Each IMA was used to revascularize a single coronary vessel. In 95.6% of these patients one IMA was grafted to the left anterior descending coronary artery. In most cases, the second IMA was anastomosed to the obtuse marginal branch: a mammary artery graft on a large first diagonal branch or on a ramus intermedius supplying the lateral wall was used in 53 patients; the right coronary artery was revascularized by a mammary artery only in 4 cases.

Patients with single vessel disease, patients without an IMA graft on the left anterior descending coronary artery and patients with a ventricular aneurysm were excluded from this study; among the survivors, at hospital discharge, of each of these two groups we randomly selected 150 patients. The long-term results obtained after a mean follow-up of 110 months are the object of this study.

Ten preoperative variables (age, gender, a history of diabetes mellitus, obesity defined as Quatelet's index > 28, peripheral vascular disease, left main stem stenosis, left ventricular ejection fraction, history of acute myocardial infarction graduation of priority, first or redo operation), and three operative variables (number of coronary anastomoses, extracorporeal circulation time and aortic cross clamping time) were compared to assess the differences between the two populations studied.

Follow-up information was obtained between January 1999 and January 2000 either in an outpatients setting or by telephone interview. In case of death, we checked and recorded the cause and the date of this event in the Community Death Registry.

The occurrence of acute myocardial infarction, recurrence of angina pectoris or ischemia (tested by means of stress electrocardiography), re-operation, coronary angioplasty and coronary angiography performed during the follow-up period were recorded together with the time intervals from the date of surgery.

Statistical analysis. All statistical analysis were completed using Stat view 5.0 Mc (SAS Inst. Inc., Cary, NC, USA). Continuous variables with normal distribution were analyzed using the unpaired Student's t-test; otherwise the Mann-Whitney U-test was used. Discrete variables were analyzed using the χ^2 method with Fisher's exact test.

The survival and event-free curves were designed using the Kaplan-Mayer method and the log-rank test was used to investigate their statistical differences.

Results are expressed as mean values ± SD (± SE in case of survival estimates).

A p value < 0.05 was considered statistically significant.

Results

Patients operated on using a single IMA (group 1) were older (p = 0.002), were more frequently female (p = 0.013), had a higher incidence of diabetes (p = 0.004) and of peripheral vascular disease (p = 0.047), had a smaller number of grafted coronary vessels (p = 0.03) and were operated in an emergency setting more frequently (p = 0.052) than patients in whom both IMAs (group 2) were grafted. In all patients included in group 2, the second IMA was anastomosed either to the obtuse marginal branch or to a ramus intermedius supplying the lateral wall of the left ventricle. All the other preoperative and intraoperative characteristics taken into consideration were equally distributed in the two groups (Table I). Data regarding the long-term follow-up were obtained in all patients (100%). The mean duration of follow-up was similar for both groups (110 ± 33 months for group 2 vs 109 ± 30 months for group 1, p = NS) (Table II). There were 23 deaths in group 2 and 25 deaths in

Table I. Comparison of variables for patients operated on using one internal mammary artery (group 1) vs both internal mammary arteries (group 2).

Variable	Group 1 (n=150)	Group 2 (n=150)	p
Preoperative			
Gender (M/F)	124/26	139/11	0.013
Age (years)	59.3 ± 8.3	56.5 ± 8.2	0.002
Diabetes mellitus	37	17	0.004
Obesity	49	52	NS
Peripheral vascular disease	33	19	0.047
Left main stenosis	21	22	NS
LVEF (%)	54.5 ± 13.5	57.2 ± 13.6	NS
Prior AMI	47	56	NS
Emergency surgery	41	26	0.052
Redo operation	6	13	NS
Operative			
No. coronary grafts	2.9 ± 0.5	3.0 ± 0.6	0.03
Bypass time (min)	88 ± 30	85 ± 24	NS
Cross-clamp time (min)	55 ± 22	55 ± 16	NS

AMI = acute myocardial infarction; LVEF = left ventricular ejection fraction.

Table II. Results: follow-up, patient survival, ischemic events, diagnostic and interventional management by group.

Event	Group 1 (n=150)	Group 2 (n=150)	p
Follow-up (months)	109 ± 30	110 ± 33	NS
Death (overall)	25	23	NS
Cardiac death	13	14	NS
Acute myocardial infarction	23	17	NS
Angina	23	21	NS
Coronary angiography	17	20	NS
Positive stress ECG	21	10	~ 0.05
Re-operation	2	4	NS
Coronary angioplasty	4	10	NS

group 1: the overall survival at 12 years of follow-up (same values at 10 years for both groups; 82.5 ± 3.4% for group 2 vs 82.9 ± 3.2% for group 1, p = NS) or at any of the observed periods (Fig. 1) was not different in the two groups. A cardiac death occurred in 14 cases in group 2 and in 13 cases in group 1: freedom from cardiac death was not significantly different in the two groups.

Seventeen patients in group 2 and 23 patients in group 1 had acute myocardial infarction during follow-up. Acute myocardial infarction-free survival was similar in both groups of patients (Fig. 2).

Recurrence of angina pectoris was observed in 21 patients in group 2 and in 23 patients in group 1; angina-free survival was similar in both groups of patients (Fig. 3).

One hundred and twenty-nine patients of each group were submitted to an exercise test; in 10 patients in group 2 and in 21 patients in group 1 this test was positive for cardiac ischemia without angina; this difference was significant at analysis performed using only the χ^2 test (p = 0.035), but this value was not confirmed by more sophisticated analyses: p = 0.055 at continuity correction analysis and p = 0.054 with the Fisher's exact test.

Twenty patients in group 2 and 17 patients in group 1 underwent a coronary angiography during follow-up to investigate the cause of cardiac ischemia (p = NS).

Four patients in group 2 and 2 patients in group 1 were submitted to repeat coronary bypass graft surgery; the difference was not significant (Fig. 4).

Ten patients in group 2 and 4 patients in group 1 underwent a coronary angioplasty; the difference was not significant (p = 0.17) (Fig. 5).

With regard to the quality of life, there was no significant difference between the two groups: after 10 years 74.6 ± 3.8% of patients in group 2 and 70.7 ± 4.1% in group 1 (p = 0.52) were alive and free from ischemic events (angina and acute myocardial infarction) and invasive therapies (re-operation and coronary angioplasty) (Fig. 6).

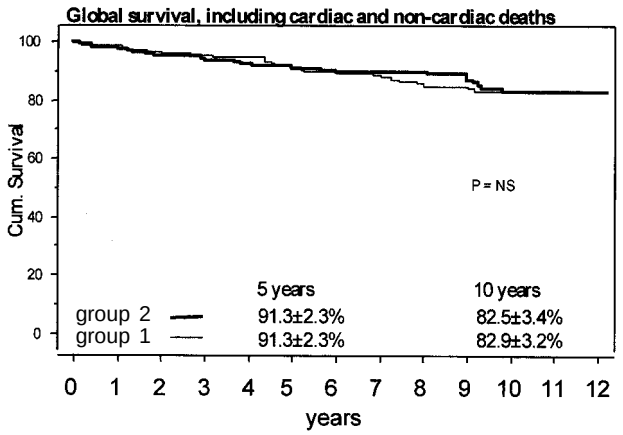

Figure 1. *Overall survival for patients revascularized using both internal mammary arteries (group 2) and one internal mammary artery (group 1).*

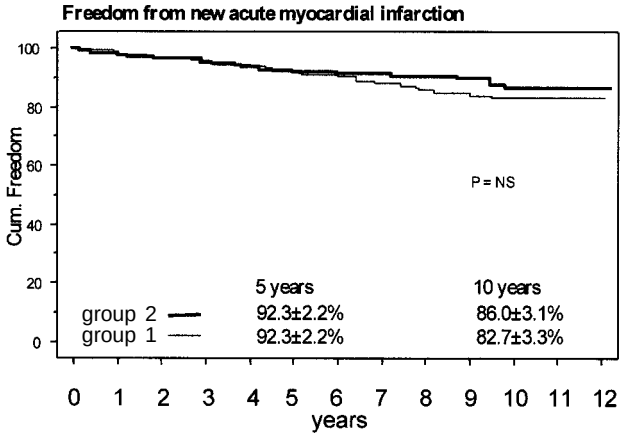

Figure 2. *Freedom from acute myocardial infarction for patients revascularized using both internal mammary arteries (group 2) and one internal mammary artery (group 1).*

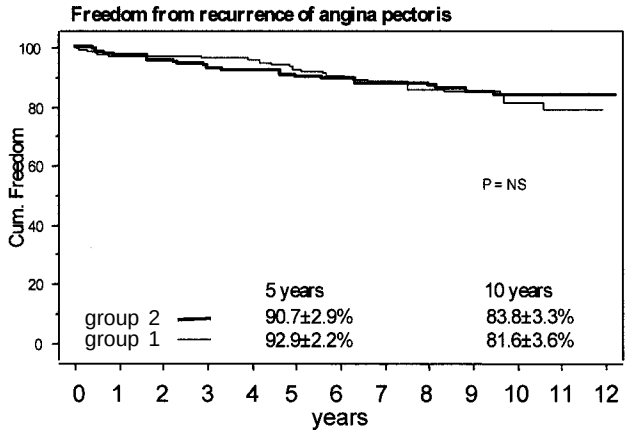

Figure 3. *Angina-free survival for patients revascularized using both internal mammary arteries (group 2) and one internal mammary artery (group 1).*

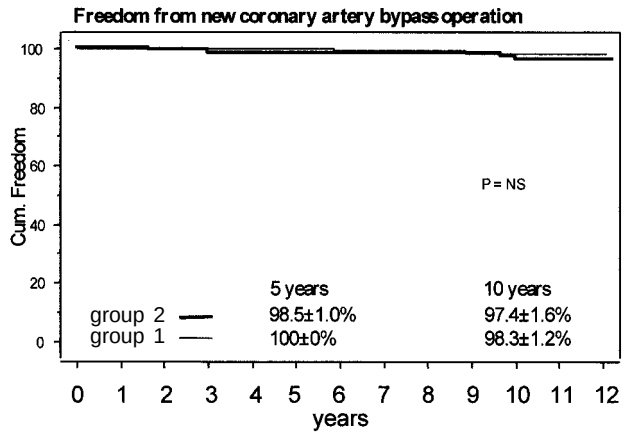

Figure 4. *Re-operation-free survival for patients revascularized using both internal mammary arteries (group 2) and one internal mammary artery (group 1).*

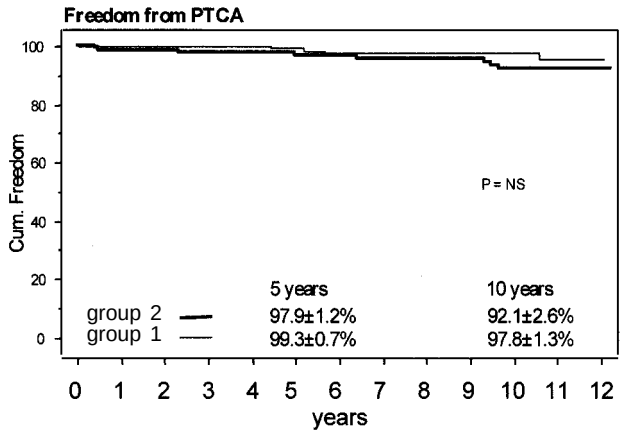

Figure 5. *Coronary angioplasty (PTCA)-free survival for patients revascularized using both internal mammary arteries (group 2) and one internal mammary artery (group 1).*

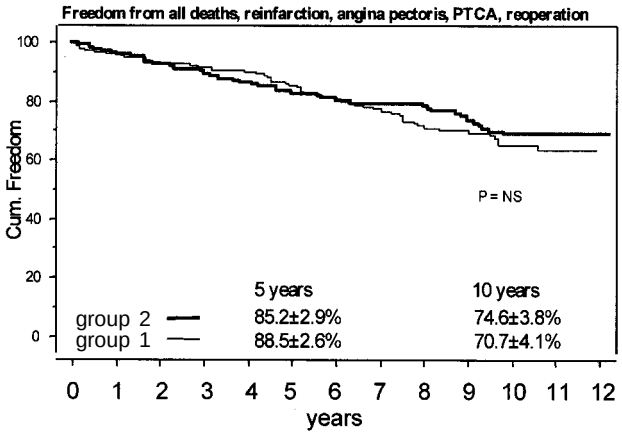

Figure 6. *Ischemic event (angina and myocardial infarction) and intervention (re-operation and coronary angioplasty-PTCA)-free survival for patients revascularized using both internal mammary arteries (group 2) and one internal mammary artery (group 1).*

Discussion

The enthusiastic use of the left IMA in coronary revascularization started in 1984 when Grondin et al.[3] demonstrated that, 10 years following surgery, while nearly half of the saphenous vein grafts were occluded, 95% of the IMA grafts were still patent. In 1986 Loop et al.[1] demonstrated that survival in patients in whom the IMA was grafted on the left anterior descending coronary artery was better than in vein-only patients and that this advantage was independent of the number of the diseased coronary arteries.

These and later reports led to the widespread use of the IMA graft.

The resistance of the IMA to atherosclerosis, its functional endothelium and its capability for flow regulation in response to the myocardial demand seem to be the reasons of its prolonged patency[4,5].

The first report about bilateral IMA grafting was published by Barner[2] in 1974. Since then, many surgeons recommended the widespread use of both IMAs but, even today, it is difficult to prove the real survival benefit of this technique.

With regard to this topic, two studies recently published by Lytle et al.[6] (Cleveland Clinic) and by Sergeant et al.[7] (Gasthuisberg University Hospital) compared the results obtained in two very large populations (more than 9000 patients each) with the use of either one or two IMAs after more than 10 years of follow-up. The conclusions reached in these two studies are different. The reason for this discrepancy might be that (due to the variable preoperative selection criteria used by the surgeons when they decide whether to use one or both IMAs), the populations compared within each study, like in our and other studies[6-10], are different.

Moreover, the study performed at the Cleveland Clinic[6] reported that, using both IMAs, the survival advantage after 15 years of follow-up was only 3% (67 vs 64%). The authors considered that this difference was large enough to conclude: "the strategy of bilateral internal thoracic artery grafting decreases the risk of death, re-operation and coronary angioplasty when compared to a strategy of single internal thoracic artery grafting", but probably it is too small to be considered definitive.

We started using both IMAs in 1982, and we have a large population of patients with a follow-up lasting more than 10 years and in whom either one or both IMAs were grafted. In 97% of these patients one IMA was used on the left anterior descending artery. The second IMA was used on the coronary artery supplying the lateral wall of the left ventricle in all except 11 cases[11]. This strategy seems to be the most effective[12]. Starting from 1987 we had the same early mortality (2.1% for single IMA and 1.5% for double IMA patients, $p = 0.5$) and the same incidence of early postoperative myocardial infarction using either one or both IMAs[11]. The aim of this study was to compare the results we obtained using both IMAs versus one after a mean follow-up of 110 months.

Due to the inherent difficulty in performing a follow-up evaluation for almost 1000 patients, we restricted our study to two groups, each composed of 150 patients. We considered this to be a consistent sample. The entire group of patients in whom both IMAs were grafted was different to that of the patients in whom one IMA was utilized. We could choose to select the patients of each group in such a way as to make the two groups comparable with respect to some preoperative variables. Since it was not possible to have two groups completely equivalent and, at the same time, big enough to reach statistical significance for the end points of this study, we chose to analyze two groups of randomized patients and to consider them as being representative of our whole experience. Like our whole populations the two studied groups were not equal: in group 1 diabetes mellitus, peripheral vascular disease, surgery in an emergency setting and female gender were more frequent. The issue of age at the time of surgery is of course very important when comparing the long-term survival: group

1 patients were significantly older (59 vs 56 years). This makes the absence of any advantage in terms of survival in group 2 even more striking. On the basis of the hypothesis that the longer life expectancy of female in the general population could affect our results, we have analyzed the effect of gender on survival: no intra or intergroup differences were noted. With the exception of the number of grafted vessels (group 2 superior to group 1, $p = 0.03$) (Table I), all other preoperative and operative characteristics were similar.

Data regarding the patients' follow-up were complete in both groups of patients: the overall survival and myocardial infarction-free, angina-free, re-operation-free and coronary angioplasty-free survivals were not different.

The 10-year survival rates in the two groups (82.5% for group 2 and 82.9% for group 1 respectively) are similar to those reported by other authors[4,6,9,10]. Other studies[7-10,13] failed to show any survival benefit for the use of both IMAs.

According to some studies, the quality of life was better in patients in whom both IMAs were grafted[6,9,13]. However, the reported advantages differ according to the study: Naunheim et al.[13] and Pick et al.[9] found better results for recurrence of angina and of myocardial infarction, but no significant difference for re-operation and coronary angioplasty. Lytle et al.[6] found that a double IMA graft produced better outcomes for all adverse events (re-operation, death, coronary angioplasty). On the other hand, Farinas et al.[10] found that patients with double IMA graft had a higher rate of angina recurrence and of coronary angioplasty.

In our study the provocative test for myocardial ischemia was more frequently positive in group 1. This difference almost reached statistical significance ($p \sim 0.05$). In view of the better performance of the IMA conduit compared to the saphenous vein and considering that group 1 had worse preoperative characteristics which could have influenced the short- and long-term outcomes (these patients were older, more often had diabetes or peripheral vascular disease), we expected increased benefits for group 2. This, however, was not the case. The myocardial infarction-free, the angina-free, the coronary angioplasty-free and the re-operation-free survivals were similar in both groups.

In conclusion, in view of its renowned properties which make the IMA more durable, we still think that this vessel is the best available conduit for coronary revascularization. Nevertheless, similar to other authors, we were not able to demonstrate any striking advantage for the use of both IMAs. Some reasons may be speculated: if there is any advantage, this is probably small; the preoperative selection of the patients and the surgical strategy employed render comparison of the two populations difficult. Moreover, some conditions cannot be reliably analyzed (for instance, the differences in the arborization of the coronary arteries) but they could interfere with the prognosis of the operated patient and result in increased benefits for one of the two studied populations.

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