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ORIGINAL ARTICLE

Predictors of immediate and long-term outcomes of coronary bypass surgery in patients with left ventricular dysfunction

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Abstract Despite encouraging improvements, outcomes of coronary artery bypass grafting (CABG) in the presence of left ventricular (LV) dysfunction remain poor. In the present study, the authors' experience on this subject was reviewed to establish the predictors of immediate and long-term results of surgery. Out of 4383 consecutive patients with multivessel coronary artery disease who underwent primary isolated CABG at the authors' institution from January 1999 throughout September 2014, 300 patients (mean age 66.1 ± 9.6 years) suffered preoperatively from LV dysfunction (defined as LV ejection fraction ≤35 %). The mean expected operative risk (EuroSCORE II) was 10.3 ± 13 %. Hospital deaths and perioperative complications were analyzed retrospectively. Outcomes were evaluated during a mean follow-up of 6.2 ± 4 years. None, one or both internal thoracic arteries (ITAs) were used in 6.3, 29 and 64.7 % of cases, respectively. There were 16 (5.3 %) hospital deaths. Prolonged invasive ventilation (17.7 %), acute kidney injury (14.7 %) and multiple blood transfusion (21.3 %) were the most frequent major postoperative complications. The 10-year non-parametric estimates of freedom from all-cause death, cardiac death, and major adverse cardiac and cerebrovascular events (MACCEs) were 47.8 [95 % confidence interval (CI) 44.1–51.5], 65.3 (95 % CI 61.4–69.2), and 42.3 % (95 % CI 38.3–46.3), respectively. Shared predictors of decreased late survival and MACCEs were old age ($P < 0.04$), chronic lung disease ($P < 0.01$), chronic dialysis ($P < 0.0001$) and extracardiac arteriopathy ($P < 0.045$). After adjustment for corresponding risk factors, freedom from cardiac death was higher when both ITAs were used but only for patients with significant increase of LV ejection fraction early after surgery ($P = 0.04$). In patients with LV dysfunction, CABG may be performed with acceptable hospital mortality and long-term survival. Late outcomes depend mainly on preoperative characteristics of the patients. The use of both ITAs for myocardial revascularization may give long-term survival benefits but only for patients whose LV function improves significantly early after surgery.

Keywords Coronary artery bypass grafting · Cardiomyopathy · Outcomes

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Introduction

Coronary artery bypass grafting (CABG) is a well-established treatment for many patients with severe coronary artery disease and left ventricular (LV) dysfunction. In this difficult subset of patients, however, outcomes of surgery remain unpredictable and generally poor despite recent encouraging improvements [1–7]. Along the years, several authors have investigated very thoroughly on this matter. Selection criteria of the patients, preoperative tests of myocardial viability, the different impact of various cardioplegic solutions on myocardial protection, the value of complete myocardial revascularization with arterial grafts, the role of off-pump or beating heart on-pump techniques and a more extensive perioperative use of intra-aortic balloon pumping (IABP) or non-adrenergic inotropic agents are only part of the issues that have been taken into consideration [1–14].

In the present study, the authors reviewed retrospectively more than 15 years of their experience in CABG in the presence of LV dysfunction. The focus was placed on the predictors of early and late failure of surgery. The aim of the study was to analyze past results to improve hopefully future outcomes.

Patients and methods

Study patients

Between January 1, 1999 and September 30, 2014, 4383 consecutive patients with multivessel coronary artery disease underwent primary isolated CABG at the authors' institution. Out of these patients, 300 (6.8 %; mean age 66.1 ± 9.6 years, range 40–85) suffered preoperatively from LV dysfunction, which was defined as LV ejection fraction ≤35 %. The preoperative characteristics and risk profiles of the patients are listed in Table 1. Unless otherwise stated, definwitions were those employed for the European System for Cardiac Operative Risk Evaluation II (EuroSCORE II), which was used to evaluate the operative risk [15].

For those patients who were preoperatively in Canadian Cardiovascular Society class 1 or 2, dobutamine stress echocardiography demonstrated a viable myocardium in 20 % or more of the LV mass. To evaluate the suitability of both internal thoracic arteries (ITAs) to be used as coronary grafts, all patients had undergone bilateral selective angiography of the subclavian artery during preoperative coronary angiography.

Surgery

Surgery was carried out via a median sternotomy either with cardiopulmonary bypass, with or without cross-clamping the aorta, or the off-pump technique. When a period of myocardial ischemia was used, myocardial protection was usually achieved with multidose cold blood cardioplegia delivered both in an antegrade and retrograde mode. A single-dose crystalloid solution (Custodiol-HTK® solution; Essential Pharma, Newtown, PA, United States of America) was sometimes preferred, especially when longer ischemic times were expected [16]. Off-pump and beating heart on-pump techniques were adopted only in the presence of a diffusely calcified ascending aorta (confirmed by epiaortic ultrasonography scanning) to avoid the risk of cracking atherosclerotic plaques by the aortic crossclamp [17].

Both ITAs were harvested as skeletonized conduits with low-intensity bipolar coagulation forceps, extending from the inferior border of the subclavian vein distally to the bifurcation into the superior epigastric and musculophrenic arteries [18]. Both ITAs were used as in situ grafts whenever possible. When both ITAs were used simultaneously, the right ITA was preferentially directed to the left anterior descending coronary artery and the left ITA to the posterolateral cardiac wall. When one ITA was used, the left or (rarely) the right ITA was directed to the left anterior descending coronary artery. The anteaortic crossover right ITA bypass graft was protected by means of a pedicled thymus flap [19]. Additional coronary bypasses were performed with saphenous vein grafts (SVGs). Sometimes, the ITA was taken down and used as a free graft either from the in situ contralateral ITA (Y-graft) or the proximal (aortic) end of an SVG. Sometimes, SVGs alone were used. Revascularization of every stenotic coronary vessel of diameter ≥1 mm (complete myocardial revascularization) was always pursued [20–22].

All perioperative data were prospectively recorded for every patient in a computerized data registry (FileMaker Pro 6.0; FileMaker, Inc., Santa Clara, CA, United States of America). All discharged patients had an echocardiographic assessment within 2 months from discharge. Approval to conduct the study was acquired from The Hospital Ethics Committee, based on retrospective data retrieval, having waived the need for patients to provide their individual consent.

Follow-up

An up-to-date clinical follow-up was obtained by a telephonic interview with the patient or her/his family. The occurrence of at least one postoperative major adverse cardiac and cerebrovascular event (MACCE)—defined as any of the following complications from hospital discharge to follow-up: sudden death, recurrent angina, myocardial infarction, congestive heart failure needing hospital readmission, percutaneous coronary intervention, reoperation, cerebrovascular accident and pulmonary embolism—was recorded. For this study, follow-up was closed on December 31, 2014.

Statistical methods

Data were expressed as number of patients or mean ± standard deviation, with the percentage or the range between the first and the third quartile (interquartile range, IR) in brackets. Patients' clinical characteristics and operative data were compared using the χ^2, Fisher exact or McNemar test for dichotomous variables, and the Student's t or Mann–Whitney U test for continuous variables, as appropriate. The binary logistic and the Cox proportional-hazards regression analysis were performed to determine, respectively, the predictors of hospital death and the influence of patients' characteristics and operative data on late survival. All significant variables from univariable analysis

Table 1 Preoperative patients' characteristics and risk profiles ($N = 300$)

Characteristic	Patients
Age (years)	66.1 ± 9.6 (61–74)
<70	178 (59.3)
70–80	108 (36)
>80	14 (4.7)
Feminine gender	39 (13)
Former/current smoker	89 (29.7)/21 (7)
BMI (kg/m^2)	26.2 ± 3.4 (23.8–28.4)
<20	8 (2.7)
>30	46 (15.3)
Diabetes	113 (37.7)
Diabetes on insulin	45 (15)
Poor glycemic control[a]	26 (8.7)
Serum hemoglobin (g/l)	12.9 ± 1.7 (11.7–14)
<10	13 (4.3)
Poor mobility	4 (1.3)
Chronic lung disease	38 (12.7)
GFR (ml/min)[b]	69.8 ± 28 (51.5–87.6)
50–85	148 (49.3)
<50	65 (21.7)
Chronic dialysis	7 (2.3)
Extracardiac arteriopathy	88 (29.3)
Diffusely atherosclerotic ascending aorta[c]	28 (9.3)
Cardiac rhythm	
Paroxysmal/permanent AF	19 (6.3)/10 (3.3)
Pace-maker induced	12 (4)
NYHA class I, II, III, IV	119 (39.7), 59 (19.7), 71 (23.7), 51 (17)
CCS class 4	137 (45.7)
Silent myocardial ischemia	6 (2)
Recent myocardial infarction	96 (32)
Coronary artery disease	
Left main	103 (34.3)
Two-vessel	37 (13.3)
Three-vessel	243 (81)
LV ejection fraction (%)	30 ± 4.8 (28–34)
<20	23 (7.7)
Mitral regurgitation (mild-to-moderate)[d]	32 (10.7)
Pulmonary hypertension	11 (3.7)
Right ventricular dysfunction (severe)[e]	2 (0.7)
Cardiogenic shock[f]	10 (3.3)
Use of IABP	41 (13.7)
Previous PCI	7 (2.3)
Surgical priority	
Urgent	181 (60.3)
Emergency	19 (6.3)
Salvage	5 (1.7)

Table 1 continued

Characteristic	Patients
Expected operative risk (by EuroSCORE II) (%)[g]	10.3 ± 13 (2.5–11.5)
10–20	57 (19)
>20	70 (23.3)

Unless otherwise stated, definitions of variables were those employed for EuroSCORE II (Ref. [14])

Values are number of patients with percentages in brackets, or mean ± standard deviation with interquartile range in brackets

AF atrial fibrillation, *BMI* body mass index, *CCS* Canadian Cardiovascular Society, *EuroSCORE* European System for Cardiac Operative Risk Evaluation, *GFR* glomerular filtration rate, *IABP* intra-aortic balloon pumping, *LV* left ventricular, *NYHA* New York Heart Association, *PCI* percutaneous coronary intervention

[a] Defined as basal serum glucose >200 mg/dl at three consecutive measurements before surgery

[b] The creatinine clearance rate, calculated according to the Cockcroft-Gault formula, was used for approximating the GFR

[c] Confirmed by epiaortic ultrasonography scanning

[d] Confirmed by intraoperative echocardiography

[e] Defined as tricuspid annular plane systolic excursion <10 mm

[f] Defined as three consecutive cardiac index measurements <2.0 l/min/m^2 despite adequate preload, afterload and inotropic support, or IABP

[g] (Ref. [14])

were entered into multivariable models, which involved a stepwise backward elimination technique (of all variables with a *P* value >0.2) and only variables with a *P* value <0.1 were reported in the final model. The odds ratio (OR), or the hazard ratio (HR), with a 95 % confidence interval (CI), was given for each variable. Non-parametric estimates and curves of freedom from all-cause death (including hospital mortality), cardiac death (including hospital mortality), MACCEs, and heart failure hospital readmission were generated with the Kaplan–Meier method. The median value of changes between preoperative and early postoperative LV ejection fraction was calculated for patients who had received either one or two ITA grafts, respectively. For both groups of patients, non-parametric curves of freedom from cardiac death and survival curves at mean of all risk factors for cardiac death at follow-up (adjusted survival curves) were generated; survival and adjusted survival-free from cardiac death were compared separately in patients with an LV ejection fraction postoperative change greater and less than the corresponding median value. The first group of patients was arbitrarily defined "responder" while the second one "non-responder". Comparisons between survival curves were made by the log-rank test. A *P* value <0.05 was considered significant. Analyses were performed with IBM SPSS Statistics (IBM Software Group).

Results

Operative data

Complete myocardial revascularization was obtained in 100 % of cases, and the mean number of coronary anastomoses per patient was 3.8 ± 1.2 (IR 3–5). None, one or both ITAs were used in 19 (6.3 %), 87 (29 %) and 194 (64.7 %) patients, respectively. On-pump, beating heart on-pump, and off-pump techniques were adopted in 272 (90.7 %), 10 (3.3 %), and 18 (6 %) cases, respectively. When cardiopulmonary bypass was used, the mean time of bypass was 113 ± 77 min (IR 87–131). When a period of myocardial ischemia was used, the mean time of ischemia was 83 ± 28 min (IR 64–99). Blood or multidose crystalloid cardioplegia was used in 170 and 91 patients, respectively; the single-dose Custodiol-HTK solution was adopted in 11 cases. The mean duration of surgery was 283 ± 58 min (IR 241–320).

Immediate outcomes

Hospital mortality changed from 6.7 % (8/120) at the first 5-year period (1999–2003) to 7.1 % (6/85, $P = 0.92$) at the second 5-year period (2004–2008), up to 2.1 % (2/95, $P = 0.1$) at between 2009 and September 2014. Overall, there were 16 (5.3 %) hospital deaths: 15 patients died within postoperative day 30 (30-day mortality 5 %) and one patient later. Stroke = 1, pneumonia = 1, adult respiratory distress syndrome = 1, low cardiac output = 3, acute kidney injury = 3, mesenteric ischemia = 2, and multiorgan failure = 5 were the causes of death. Results from the risk factors analysis for hospital death are shown in Tables 2 and 3.

The mean hospital stay was 16.3 ± 44.8 days (IR 7–14). Prolonged invasive ventilation (17.7 %), acute kidney injury (14.7 %) and multiple blood transfusion (21.3 %) were the most frequent major postoperative complications (Table 4).

Table 2 Risk factors for hospital death (univariable analysis) (*N* = 300)

Variable	Dead *N* = 16	Alive *N* = 284	*P* value
Age >70 years	9 (56.3)	113 (39.8)	0.19
Diabetes on insulin	5 (31.3)	40 (14.1)	0.074
Poor glycemic control[a]	4 (25)	22 (7.7)	0.039
Chronic lung disease	2 (12.5)	36 (12.7)	0.67
GFR <50 ml/min[b]	7 (43.8)	58 (20.4)	0.036
Chronic dialysis	1 (6.3)	6 (2.1)	0.32
Extracardiac arteriopathy	5 (31.3)	83 (29.2)	0.53
NYHA class IV	8 (50)	43 (15.1)	0.0018
Recent myocardial infarction	9 (56.3)	87 (30.6)	0.033
LV ejection fraction <20 %	3 (18.8)	20 (7)	0.11
Cardiogenic shock[c]	3 (18.7)	7 (2.5)	0.012
Use of IABP	8 (50)	33 (11.6)	0.00035
Surgical priority: salvage	2 (12.5)	3 (1.1)	0.024
Crystalloid cardioplegia	8/15 (53.3)	94/257 (36.6)	0.19
Use of both ITAs	4 (25)	190 (66.9)	0.00064
Use of SVGs alone	5 (31.2)	14 (4.9)	0.0017

Unless otherwise stated, definitions of variables were those employed for EuroSCORE II (Ref. [14])

Values are number of patients with percentages in brackets

EuroSCORE European System for Cardiac Operative Risk Evaluation, *GFR* glomerular filtration rate, *IABP* intra-aortic balloon pumping, *ITA* internal thoracic artery, *LV* left ventricular, *NYHA* New York Heart Association, *SVG* saphenous vein graft

[a] Defined as basal serum glucose >200 mg/dl at three consecutive measurements before surgery

[b] The creatinine clearance rate, calculated according to the Cockcroft-Gault formula, was used for approximating the GFR

[c] Defined as three consecutive cardiac index measurements <2.0 l/min/m^2 despite adequate preload, afterload, and inotropic support, or IABP

Table 3 Risk factors for hospital death (multivariable analysis) (*N* = 300)

Variable	Hospital death		
	OR	95 % CI	*P* value
Poor glycemic control[a]	3.66	0.84–16	0.084
GFR <50 ml/min[b]	3.94	1.16–13.4	0.028
NYHA class IV	3.2	0.98–10.4	0.054
Use of IABP	5.14	1.49–17.7	0.0096
Surgical priority: salvage	6.39	0.75–54.4	0.089
Use of both ITAs	0.27	0.08–0.94	0.039

Unless otherwise stated, definitions of variables were those employed for EuroSCORE II (Ref. [14])

Variables with a *P* value >0.2 (recent myocardial infarction, cardiogenic shock, and use of SVGs alone) were not included in the model

EuroSCORE European System for Cardiac Operative Risk Evaluation, *GFR* glomerular filtration rate, *IABP* intra-aortic balloon pumping, *ITA* internal thoracic artery, *NYHA* New York Heart Association, *SVG* saphenous vein graft

[a] Defined as basal serum glucose >200 mg/dl at three consecutive measurements before surgery

[b] The creatinine clearance rate, calculated according to the Cockcroft-Gault formula, was used for approximating the GFR

Time-related survival

The follow-up was 100 % complete. A total of 1873 cumulative patient-years were reviewed. The mean follow-up was 6.2 ± 4 years (IR 3.1–9.4). There were 52 cardiac or cerebrovascular deaths and 48 non-cardiac non-cerebrovascular deaths. The causes of death were myocardial infarction = 5, congestive heart failure = 36, sudden death = 6, pulmonary embolism = 5, malignancy = 20, pneumonia = 12, chronic renal failure = 12, trauma = 2, mesenteric ischemia = 1, and sepsis following abdominal surgery = 1. The 1-, 5- and 10-year non-parametric estimates of freedom from all-cause death were 90.3 (95 % CI 88.6–92), 77.1 (95 % CI 74.5–79.7) and 47.8 % (95 % CI 44.1–51.5), respectively (Fig. 1a). The 1-, 5- and 10-year non-parametric estimates of freedom from cardiac death were 91 (95 % CI 89.3–92.6), 85.4 (95 % CI 83.2–87.6) and 65.3 % (95 % CI 61.4–69.2), respectively (Fig. 1b). The independent risk factors for decreased freedom from all-cause death and cardiac death at follow-up are listed in Table 5.

Functional status

During the follow-up, the New York Heart Association class was improved from 2.3 ± 0.8 preoperatively to 2 ± 1 ($P = 0.001$) postoperatively, and the Canadian Cardiovascular Society class from 3 ± 0.8 to 1.3 ± 0.6 ($P < 0.0001$). A total of 181 MACCEs were recorded from hospital discharge to follow-up: sudden death = 6, recurrent angina = 32, myocardial infarction = 18, congestive heart failure = 113, percutaneous coronary intervention = 2, reoperation = 2 (CABG and heart transplantation), cerebrovascular accident = 3, and pulmonary embolism = 5. Of the two patients who underwent percutaneous coronary intervention during follow-up, coronary angiography had showed a critical lesion of the SVG in one case and a new critical lesion of the right coronary artery in the other one. Coronary angiography had showed a critical lesion of the left anterior descending coronary artery distally to the previous anastomotic site with the right ITA in the patient who underwent redo CABG, and a diffuse and terminal coronary artery disease in the patient who underwent transplantation. There was no disease of ITA grafts. The 1-, 5- and 10-year non-parametric estimates of freedom from MACCEs were 92.6 (95 % CI 91–94.2), 77.3 (95 % CI 74.6–79.9) and 42.3 % (95 %

Table 4 Perioperative complications and management ($N = 300$)

Complication	Patients
Stroke	5 (1.7)
Prolonged (>48 h) invasive ventilation	53 (17.7)
Pneumonia	27 (9)
AF, new-onset	74/278 (26.6)[a]
Myocardial infarction[b]	10 (3.3)
Low cardiac output[c]	22 (7.3)
Use of adrenergic agonists	216 (72)
Use of calcium-sensitizing agent (levosimendan)	7 (2.3)
Intra- and postoperative use of IABP	15 (5)
Use of ECMO	2 (0.7)
Acute kidney injury[d]	44 (14.7)
Renal replacement therapy	14 (4.7)
Mesenteric ischemia	4 (1.3)
Multiorgan failure	16 (5.3)
Sepsis	7 (2.3)
Blood transfusion	162 (54)
Multiple blood transfusion (>2 RBCs)	64 (21.3)
Mediastinal re-exploration for bleeding or tamponade	20 (6.7)
Deep sternal wound infection[e]	9 (3)
Leg wound complication	6/251 (2.4)[f]

Values are number of patients with percentages in brackets

AF atrial fibrillation, *ECMO* extracorporeal membrane oxygenator, *IABP* intra-aortic balloon pumping, *RBCs* red blood cells, *SVG* saphenous vein grafts

[a] Patients in preoperative stable sinus rhythm or paroxysmal AF

[b] Defined as the development of new Q-waves, or significant loss of R-wave forces, in two or more contiguous leads on a 12-lead electrocardiogram together with congruent regional wall motion abnormalities at the echocardiographic assessment, or creatine kinase enzyme peak values >400 IU/l with creatine kinase-MB enzyme peak values >40 IU/l, or cardiac troponin *I* >12 ng/ml 10 h after release of the aortic clamp

[c] Defined as three consecutive cardiac index measurements <2.0 l/min/m^2 despite adequate preload, afterload, and inotropic support, or IABP

[d] Defined as postoperative serum creatinine >2.0 mg/l in the patients without preoperative renal impairment, and postoperative increase in serum creatinine of at least 1.0 mg/l above baseline in the patients with preoperative renal impairment

[e] Defined according to The Centers for Disease Control and Prevention classification of surgical site infections (Ref. [23])

[f] Patients who received concomitant SVGs

CI 38.3–46.3), respectively (Fig. 1c). In 92 patients, there was at least one hospital readmission due to congestive heart failure, and the 1-, 5- and 10-year non-parametric estimates of freedom from heart failure hospital readmission were 94.3 (95 % CI 92.9–95.7), 82.4 (95 % CI 80–84.8) and 52.2 % (95 % CI 47.9–56.5), respectively (Fig. 1d). The independent risk factors for MACCEs and heart failure hospital readmission are listed in Table 5.

The impact of the use of both ITAs on the freedom from cardiac death at follow-up

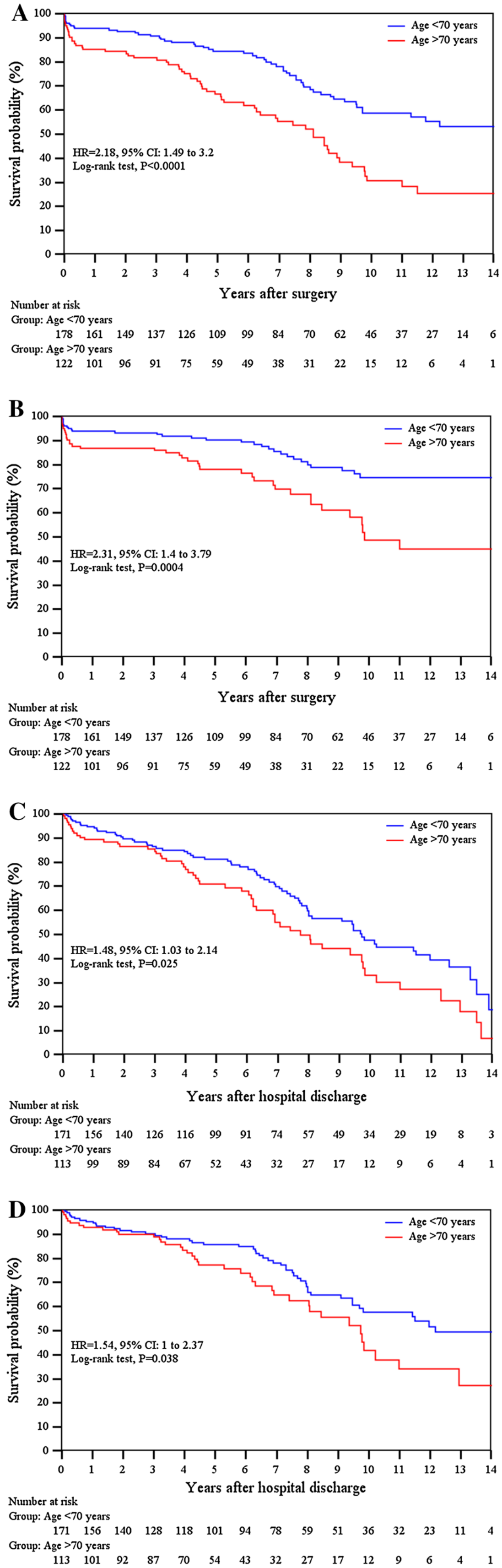
Postoperative echocardiographic assessment showed an early improvement in LV ejection fraction in 86.3 % of the 80 hospital discharged patients who had undergone single ITA grafting, and in 80 % of the 190 discharged patients who had undergone bilateral ITA grafting ($P = 0.22$). The median value of the LV ejection fraction postoperative changes for patients who had received either one or two ITA grafts was +22.5 and +24 %, respectively. Between these two groups of patients, there were no differences in freedom from cardiac death ($P = 0.51$) and adjusted survival-free from cardiac death ($P = 0.66$) for the non-responder patients (Fig. 2a, b). Instead, for the responder patients, there were higher freedom from cardiac death ($P = 0.051$) and adjusted survival-free from cardiac death ($P = 0.04$) when both ITAs were used (Fig. 2c, d).

Discussion

Although great efforts have been made to establish the best treatment for patients with severe coronary artery disease and LV dysfunction, the management of these patients remains individualized and relies on currently available, and sometimes conflicting, information [1–14]. In the present study, a 15-year period and more of the authors' experience in CABG were reviewed retrospectively to improve knowledge about the causes and mechanisms of immediate and late failure of surgery in the presence of LV dysfunction.

A total of 300 consecutive patients with multivessel coronary artery disease and LV dysfunction were enrolled in the study. As for many reports of the Literature for this study as well, LV dysfunction was arbitrarily defined as LV ejection fraction of 35 % or less. Previous cardiac surgery and any operation other than isolated CABG were the sole exclusion criteria that were adopted. Thus, as patients who have undergone concomitant operations such as mitral valve surgery or LV reconstruction were excluded from the analysis, all postoperative changes in heart failure symptoms or LV ejection fraction could be attributed exclusively to CABG combined with the optimized medical therapy.

The preoperative characteristics of the patients of the present study were equivalent to those of studies conducted on populations of patients with advanced ischemic heart disease and LV dysfunction [1–14]. The high-risk profile was due mainly to the high rates of heavy comorbidities and risk factors for atherosclerotic disease. However, despite the high expected operative risk according to EuroSCORE II [15], there were a limited number of hospital deaths and the operative mortality was comparable with the



◀ **Fig. 1** Non-parametric curves according to age (Kaplan–Meier model) of freedom from **a** all-cause death (including hospital mortality), **b** cardiac death (including hospital mortality), **c** major adverse cardiac and cerebrovascular events, and **d** heart failure hospital readmission. The number of patients remaining at risk is reported. *CI* confidence interval, *HR* hazard ratio

best results of the Literature [1–14]. Glomerular filtration rate <50 ml/min and the preoperative use of IABP identified the patients at risk for hospital death according to the multivariable analysis. Since 1999, the authors of the present study have been prospectively recording all perioperative data for every patient in a computerized data registry, the rate of use of both ITAs being increased from about 60 % in 1999 to over 80 % in the last 3 years. All patients with multivessel coronary artery disease needing left-sided myocardial revascularization were potential candidates for bilateral ITA grafting. The exceptions have been the rare cases where one or both ITAs were unsuitable as coronary grafts, when there was an unexpected operative finding of severe cardiac dysfunction, or when a rapid ischemic worsening of hemodynamics needed immediate institution of cardiopulmonary bypass. Thus, the rate of use of both ITAs was very high (65 %) even in the patients with LV dysfunction of the present study [20–22]. Furthermore, in this study, the use of both ITAs resulted to be an independent protective factor for hospital death. This was not an entirely unexpected result. Although many published series [21, 24–28] and a randomized controlled trial as well [29] have shown no significant differences in the early mortality between bilateral and single ITA grafting, in many out of these studies, however, hospital (or 30-day) mortality was lower (albeit not significantly) in bilateral than in single ITA grafting. Moreover, almost none of these studies discriminate between patients with and without LV dysfunction. In the only study (at the best of the present authors' knowledge) where this discrimination has been performed, operative mortality between propensity-matched patients was lower (of about 30 % and more) in bilateral than in single ITA group, both for patients with and without LV dysfunction, even though the difference was not significant or almost significant, respectively [14]. It is possible that the higher hospital mortality in single ITA patients of the present study is due to more frequent occurrence of stronger risk factors and comorbidities in these patients than in bilateral ITA patients. It is also possible that the multivariate analysis has not been able to cancel the different impact of these variables on the two groups of patients, namely the potential selection bias, though no selection of patients for either bilateral or single ITA grafting based on the expected operative risk has been performed (according to the authors' institutional policy) [20–23]. Certainly,

Table 5 Cox proportional-hazards regressions for all-cause death, cardiac death, MACCEs and HF hospital readmission at follow-up ($N = 284$)

Variable	All-cause death[a]			Cardiac death[b]			MACCEs[c]			HF hospital readmission[d]		
	HR	95 % CI	*P* value	HR	95 % CI	*P* value	HR	95 % CI	*P* value	HR	95 % CI	*P* value
Age (years)	1.06	1.03–1.09	<0.0001	1.04	1–1.07	0.027	1.02	1–1.04	0.031	1.03	1–1.05	0.036
Feminine gender	–	–	–	–	–	–	–	–	–	0.34	0.16–0.73	0.0058
Diabetes	1.82	1.18-2.82	0.0073	–	–	–	–	–	–	–	–	–
Chronic lung disease	2.25	1.26–4.01	0.0063	3.31	1.6–6.85	0.0013	2.14	1.31–3.52	0.0027	2.16	1.21–3.83	0.0091
GFR <50 ml/min	–	–	–	–	–	–	–	–	–	1.58	0.94–2.66	0.086
Chronic dialysis	14	4.76–41.1	<0.0001	17.4	4.91–61.4	<0.0001	7.74	3.06–19.6	<0.0001	13.9	3.98–48.6	<0.0001
Extracardiac arteriopathy	1.63	1.08–2.44	0.02	2.36	1.35–4.11	0.0027	1.47	1.01–2.13	0.044	1.62	1.05–2.52	0.032
Paroxysmal/permanent AF	–	–	–	–	–	–	1.57	0.93–2.64	0.091	1.71	0.93–3.12	0.084
Recent myocardial infarction	1.79	1.16–2.77	0.0093	–	–	–	–	–	–	–	–	–
Right ventricular dysfunction (severe)[e]	16.5	3.81–71.5	0.0002	12.2	1.59–93.8	0.017	–	–	–	–	–	–
Preoperative use of IABP	1.53	0.87–2.68	0.14	2.16	1.02–4.58	0.045	–	–	–	–	–	–

Unless otherwise stated, definitions of variables were those employed for EuroSCORE II (Ref. [14])

AF atrial fibrillation, *CI* confidence interval, *EuroSCORE* European System for Cardiac Operative Risk Evaluation, *GFR* glomerular filtration rate, *HF* heart failure, *HR* hazard ratio, *IABP* intra-aortic balloon pumping, *MACCEs* major adverse cardiac and cerebrovascular events, *NYHA* New York Heart Association

[a] Variables with a *P* value >0.2 (feminine gender and GFR <50 ml/min) were not included in the model

[b] Variables with a *P* value >0.2 (recent myocardial infarction) were not included in the model

[c] Variables with a *P* value >0.2 [feminine gender, diabetes, GFR <50 ml/min, NYHA class IV, mitral regurgitation (mild-to-moderate), right ventricular dysfunction (severe), and use of IABP] were not included in the model

[d] Variables with a *P* value >0.2 [NYHA class IV, mitral regurgitation (mild-to-severe), and right ventricular dysfunction (severe)] were not included in the model

[e] Defined as tricuspid annular plane systolic excursion <10 mm

this is an important limitation of the present retrospective study, which is not even supported by more sophisticated statistical methods such as the propensity-matched analysis. Perhaps, however, a more important goal was achieved, to show that the use of both ITAs for myocardial revascularization is not a risk factor for increased early mortality even for patients with LV dysfunction, as the long-term survival benefits derived from their use are well accepted now. Although the patients undergoing CABG using SVGs alone had a higher expected operative risk according to EuroSCORE II ($P < 0.0001$), the use of SVGs alone for myocardial revascularization was a risk factor for hospital death according to the univariable but not the multivariable analysis. Neither the various solutions for myocardial protection nor the various surgical strategies (off-pump, beating heart on-pump, and on-pump technique) that have been used had a different impact on hospital mortality [3, 11, 16]. Actually, according to the present authors' institutional policy, off-pump and beating heart on-pump techniques were used rarely (9 %) and only in the presence of an unclampable ascending aorta; the single-dose Custodiol-HTK solution was sometimes adopted to reduce the duration of surgery [20–23]. Prolonged invasive ventilation, acute kidney injury and multiple blood transfusion were the most frequent major postoperative complications. Despite LV dysfunction and frequent preoperative symptoms of heart failure, low cardiac output was a relatively uncommon perioperative complication (7 %). This was due probably to the complete myocardial revascularization, which was reflected in a relatively high number of coronary anastomoses, the extensive use of IABP (19 %) and, more recently, the practice of using calcium-sensitizing agents from the day before surgery for patients with LV ejection fraction of 20 % or less (hospital mortality decreased consistently in the last period of the present experience, $P = 0.1$) [3, 12, 13]. Delayed intensive care unit and hospital discharges were due mainly to prolonged invasive ventilation and careful weaning from the pharmacological and mechanical support (ventilator, IABP and extracorporeal membrane oxygenator).

During the follow-up, there were significant improvements in heart failure symptoms for patients, and long-term actuarial survival was free from MACCEs or heart failure hospital readmission [30] in 40 and 50 % of cases, respectively. Intermediate and long-term survival compared favorably with the late outcomes of many series of CABG patients with preoperative LV dysfunction that have been reported in the Literature [1–14]. Old age and comorbidities

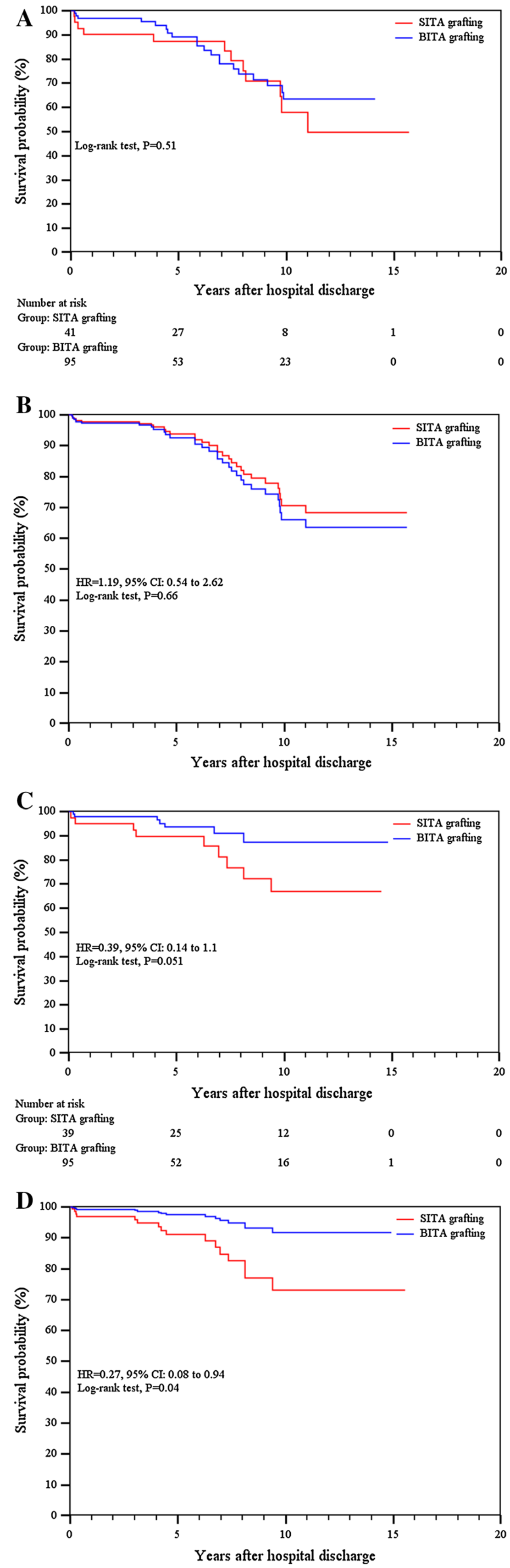


Fig. 2 Non-parametric curves according to the use of one or both ▸ ITA grafts (Kaplan–Meier model) of: **a** freedom from cardiac death and **b** adjusted survival-free from cardiac death in patients with an LV ejection fraction postoperative change less than the corresponding median value (non-responder group); **c** freedom from cardiac death and **d** adjusted survival-free from cardiac death in patients with an LV ejection fraction postoperative change greater than the corresponding median value (responder group). The number of patients remaining at risk is reported. *BITA* bilateral ITA, *CI* confidence interval, *HR* hazard ratio, *ITA* internal thoracic artery, *LV* left ventricular, *SITA* single ITA

such as chronic lung disease, chronic dialysis and extracardiac arteriopathy were shared predictors of all-cause death, cardiac death, MACCEs and heart failure hospital readmission. Interestingly, according to the multivariable analysis, severe right ventricular dysfunction was a predictor both of all-cause and cardiac death but mild-to-moderate ischemic mitral regurgitation was not a predictor of poor late outcomes [3, 31, 32]. In the authors' opinion, complete myocardial revascularization, which has been obtained for every patient [3], the choice of ITA to bypass the left anterior descending coronary artery in 94 % of cases [31] and the extensive use of both ITAs, which achieved totally arterial myocardial revascularization in over 16 % of patients [10, 14, 21], may explain these satisfactory results. Actually, the hypothetical long-term survival benefits from bilateral versus single ITA grafting were confirmed only for the patients who experienced a significant improvement in LV ejection fraction early after surgery (responder patients). Indeed, this improvement identified all the patients with a significant amount of viable myocardium that has been successfully revascularized and that might be jeopardized in the future by an earlier failure of venous with respect to arterial grafts.

This study is subject to the limitations inherent to retrospective analyses of observational data. Although statistical models were used to adjust for treatment selection bias, the results might have been affected by unmeasured confounders, procedure bias and detection bias. In particular, subgroup analyses of patients according to surgical strategies (pump strategies, the use of one or both ITAs) are more likely to be affected by such bias even with the rigorous statistical adjustments. Only a relatively small number of patients operated on in a single Institution over a 15-year period and more were evaluated at different times after surgery. Along the years, there were some changes in the perioperative management of these difficult patients with LV dysfunction, and the outcomes were affected inevitably by these changes. No postoperative echocardiographic results other than LV ejection fraction measured immediately after surgery were reported. Coronary angiography was performed only in strongly symptomatic patients, and there was no direct information about patency of coronary grafts in all the remaining patients. Consequently, the results obtained can, in no way, be considered conclusive, and should be verified in larger patient populations by means of prospective controlled trials that include echocardiographic and angiographic evaluations.

In conclusion, in the patients with multivessel coronary artery disease and LV dysfunction of the present study, CABG was performed with frequent perioperative complications. Hospital mortality was satisfactory despite the high expected operative risk according to EuroSCORE II. Late outcomes were encouraging and depended mainly on preoperative characteristics of the patients. The use of both ITAs for myocardial revascularization is not a risk factor for hospital death, and give long-term survival benefits but only for patients whose LV function improves significantly early after surgery.

Compliance with ethical standards

Conflict of interest None declared.

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