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Coronary artery bypass surgery in patients with impaired left ventricular function. Predictors of hospital outcome

M. A. Soliman Hamad (*), K. Peels (**), A. Van Straten (*), A. Van Zundert (***) and J. Schönberger (*)

Abstract : This prospective study evaluates the surgical outcome of 75 consecutive patients with impaired left ventricular function, including an analysis of predictors of the short-term outcome following coronary artery bypass grafting (CABG). Seventy-five patients (mean age 64 ± 13 years) with coronary artery disease and impaired left ventricular function (left ventricular ejection fraction [EF] ≤ 40%) who underwent a coronary artery bypass surgery were prospectively studied. Echocardiography and thallium-201 myocardial scintigraphy were preoperatively performed to measure the left ventricular function and to assess myocardial viability. Postoperative echocardiography was done before discharge and six months later to evaluate recovery of left ventricular function. Five patients (6.7%) died in total : three deaths were cardiac related (4%) and two patients (2.7%) died due to other causes. The left ventricular ejection fraction improved immediately after the operation (from 32.2 ± 6% to 39.5 ± 8%, $p = 0.01$) and showed a sustained improvement at later follow-up (mean = 16.3 ± 4.5 months) (44.0 ± 4.0%, $p = 0.01$). The left ventricular wall motion score improved significantly only at later follow-up (from 12.2 ± 1.8 to 9.4 ± 2.0, $p = 0.03$). In 43 patients of whom a preoperative thallium-201 scintigraphy was available, the presence of extensive reversible defects was correlated with significant improvement in EF. On the other hand, a poor outcome was correlated with the presence of pathological Q waves in the preoperative ECG and with an increased left ventricular endsystolic volume index (> 100 ml/m^2). Patients with marked left ventricular dysfunction can safely undergo CABG with a low mortality and morbidity. The presence of extensive reversible defects on preoperative thallium-201 scintigraphy is a strong predictor of postoperative recovery of myocardial function. A poor outcome of surgery can be expected in the presence of pathological Q waves on the preoperative ECG or when the left ventricular endsystolic volume index exceeds 100 ml/m^2.

Key words : Cardiac surgery ; impaired left ventricle function ; outcome.

Introduction

Traditionally, it has been assumed that persistent left ventricular dysfunction in patients with coronary artery disease results from previous myocardial infarction and irreversible myocardial damage. With the emergence of the concept of hibernating myocardium, however, this assumption has been challenged. It has become clear that chronic myocardial asynergy is not necessarily due to infarction and, therefore, is not always irreversible (1). Medical therapy for patients with severe left ventricular dysfunction has often been unsatisfactory in controlling angina pectoris and carries a poor long term survival (2). Although the recent advances in myocardial protection and surgical techniques have resulted in a major improvement of the results of coronary artery bypass grafting (CABG) in selected patients with ischemic cardiomyopathy, there is no uniform agreement regarding improvement in left ventricular performance following CABG procedures (3, 4). In view of the lack of sufficient data regarding the outcome of patients with left ventricular dysfunction after CABG, the present study was designed to evaluate the serial changes of left ventricular performance throughout the early and midterm postoperative period. This prospective study evaluates the surgical outcome of 75 consecutive patients with angiographic and echocardiographic evidence of moderate to severe left ventricular dysfunction, including an analysis of predictors of the outcome following CABG.

M. A. Soliman Hamad, M.D. ; K. Peels, M.D. ; A. Van Straten, M.D. ; A. Van Zundert, M.D., Ph.D, F.R.C.A. ; J. Schönberger, M.D., Ph.D.
(*) Cardiac Surgeon, Department of Cardio-Thoracic Surgery, Catharina Hospital Eindhoven, The Netherlands.
(**) Cardiologist, Department of Cardiology, Catharina Hospital, Eindhoven, The Netherlands.
(***) Professor of Anaesthesiology, Department of Anaesthesiology, ICU & Pain Therapy, Catharina Hospital, Eindhoven, The Netherlands.
Correspondence address : Prof. Dr. André van Zundert, Catharina Hospital – Brabant Medical School, Department of Anaesthesiology, ICU & Pain Therapy, Michelangelolaan 2, NL-5623 EJ Eindhoven, The Netherlands.
Tel. : ++ 31 40 239.91.11. Fax : ++ 31 40 246.39.78. E-mail : zundert@iae.nl.

METHODS

This study includes 75 patients (66 males and 9 females) who underwent an isolated CABG operation in our hospital. The mean age of the patients was 64 ± 13 years (range : 44-84 years). Inclusion criteria for this study consisted of a global left ventricular ejection fraction (EF) of 40% or less, a regional wall motion score of 10 or more, and a left ventricular enddiastolic pressure (LVEDP) of 15 mmHg or more as measured by angiography. Patients were excluded from the study if they had to undergo an emergency operation, concomitant procedures such as valve operation or left ventricular aneurysmectomy ; if they were in cardiogenic shock or if they were selected for an off-pump CABG procedure (OPCAB).

In the analysis of the left ventriculogram, emphasis was placed upon the left ventricular wall motion score and measurement of the left ventricular enddiastolic pressure (LVEDP). An LVEDP $\geq$ 15 mmHg has been reported to be indicative of depression of left ventricular function (1, 5, 6). The echocardiographic examination in patients at rest focused on the following data : left ventricular EF, left ventricular enddiastolic dimension (LVEDD), left ventricular endsystolic dimension (LVESD), left ventricular enddiastolic volume (LVEDV), left ventricular endsystolic volume (LVESV). The left ventricular function was evaluated by regional wall motion analysis after dividing the left ventricle into 16 segments (7). Global ejection fraction was measured with 2-D Echocardiography using the biplane apical method. EF was calculated using the modified Simpson's rule (8).

Data of preoperative thallium-201 scintigraphy to detect the presence of reversible ischemic defects and to evaluate myocardial viability were available in 43 patients (57.3%). The myocardium was divided into 19 segments. Reversible defects were considered extensive if they were found in $\geq$ 5 segments (9).

Postoperative evaluation consisted of detailed analysis of hospital and short term (16.3 ± 4.5 months) mortality and morbidity. All patients underwent an echocardiographic examination one week, three months and six months postoperatively to trace the serial changes in left ventricular function.

In an attempt to screen for predictors of a favourable outcome of myocardial revascularisation, the hospital survivors (n = 72) were included in a multivariate analysis at six months. The patients were divided into two groups : group A, the favourable outcome group (n = 54), defined as patients who survived the operation and showed an improvement in EF of 5% or more, and group B, the poor outcome group (n = 18), defined as either hospital mortality or survival with a postoperative decrease of EF, no change or increase of less than 5% compared to the preoperative value. The following preoperative variables were analyzed : age, severity of angina classification according to the Canadian Cardiovascular Society (CCS class III & IV) , heart failure classification according to New York Heart Association (NYHA class III or IV), the presence of pathological Q waves in the preoperative electrocardiogram (ECG), a left ventricular endsystolic volume index (LVESVI) of more than 100 ml/m^2, and the presence of extensive reversible perfusion defects on myocardial thallium-201scintigraphy (arbitrarily more than 5 of 19 segments) (9).

Statistical analysis

All data were collected prospectively and stored in a computer data bank. The Number Cruncher Statistical System was used for analysis of the data. Continued data were expressed as mean ± SD. Clinical data were compared by one-way analysis of variance. Univariate analysis of discrete variable comparisons was performed with the χ^2 test and the Fisher exact test when appropriate. In all survivors, the correlation between preoperative, operative, and postoperative data, and recovery of left ventricular function was tested by univariate analysis. In a multivariate analysis of selected variables, based on recent correlative studies in the literature, the best predictors of a favourable outcome were determined (9). A p value of less than 0.05 was considered statistically significant.

RESULTS

Tables 1 and 2 illustrate the distribution of the angina class as defined by the CCS and the functional class as defined by the NYHA. Severe angina (classes III and IV) was the primary presenting symptom in 44 patients (58.7%). Twenty-eight patients (37.3%) had congestive heart failure as their main symptom and three patients presented with arrhythmias. Table 3 summarizes the coexisting morbidities. Forty-six patients (61.3%) had a previous myocardial infarction and eight patients (10.6%) had a previous CABG.

Table 1

Distribution of Angina Classification (CCS)

Angina class (CCS)	Number	%
II	8	10.7
III	31	41.3
IV	36	48

CCS = Canadian Cardiovascular Society.

Table 2

Distribution of NYHA Classification

NYHA Class	Number	%
I	15	20
II	13	17.3
III	19	25.3
IV	28	37.4

NYHA = New York Heart Association.

Table 3

Incidence of Coexisting Morbidities

Comorbidity	Number	%
Hypertension	16	21.4%
Diabetes	19	25.3%
Hyperlipidemia	12	16%
Previous myocardial infarction	46	61.3%
Redo Surgery	8	10.6%
Renal failure	4	5.3%

Table 4 summarizes the extent and distribution of coronary artery disease and left ventricular function parameters. Critical stenosis of the left main stem coronary artery (> 70%) was present in 11 patients (14.7%), three-vessel disease in 53 patients (70.7%) and two-vessel disease in 22 patients (29.3%). Evaluation of preoperative angiography was done by an in dependent heart team (a cardiac surgeon and a cardiologist). The mean left ventricular ejection fraction was 32.2 ± 6%. Twelve patients (16.0%) had an ejection fraction below 25%. The mean left ventricular wall motion score was 12.2 ± 1.8 ; in 26 patients (34.6%), the wall motion score was more than 15. The mean LVEDP was 22.7 ± 4 mmHg. Out of the 43 patients who were subjected to preoperative thallium-201 scintigraphy, 28 patients (65.1%) showed extensive reversible myocardial perfusion defects.

The mean cardiopulmonary bypass (CPB) time was 73.7 ± 13.5 min, the mean aortic cross clamp time was 55.3 ± 9.2 min, the mean number of distal anastomoses per patient was 3.6 ± 1.2. In 65 patients (85.8%), the left internal mammary artery (LIMA) was used for revascularization of the left anterior descending (LAD) coronary artery in

Table 4

Preoperative Catheterization Data

Variable	Number	%
Left main stenosis (> 70%)	11	14.7
No. of stenosed vessels		
three vessel disease	53	70.7
two vessel disease	22	29.3
Mean ejection fraction (%)		
0.25-0.4	63	84.0
< 0.25	12	16.0
Wall motion score		
10-15	49	65.4
> 15	26	34.6

combination with venous graft or radial artery to the other coronary targets. In two patients, both internal mammary arteries were used. In six patients, only venous grafts were used and in two patients, only the radial artery was used.

Inotropic agents to support ventricular function were instituted in 39 patients (52.0%), all of them had a postoperative cardiac index (CI) of less than 2.0 L/min./m^2. An intraaortic balloon pump (IABP) was intraoperatively inserted in six patients (8.0%).

Hospital mortality : Three patients (4.0%) died either during the hospital stay or within 30 days after the operation. A 71 year-old man with a preoperative EF of 22%, a wall motion score of 16, and impaired renal function (hemodialysis dependent), underwent a repeat CABG. Despite insertion of IABP, he developed hemodynamic instability and oliguria, and died on the fourth postoperative day. The second patient, also a 71 year-old man with an EF of 33% underwent successful revascularisation of the LAD and the circumflex (Cx.) artery. The patient developed mediastinal infection 2 weeks postoperatively. He was treated with an open drainage technique. However, he gradually deteriorated and died 4 weeks postoperatively of septic shock. The third patient, a 71 year-old man with an EF of 25%, underwent repeat CABG. According to the operating surgeon, all coronary arteries were of very small diameter and of poor quality. The patient had myocardial infarction immediately postoperatively and despite the insertion of IABP, the patient died a few hours later.

Follow-up (mean 16.3 ± 4.5 months) : Two patients (2.7%) had perioperative myocardial infarction, one of whom died immediately. Low cardiac output syndrome was encountered in eleven patients (14.7%), six of whom received IABP. Ventricular arrhythmias including premature ventricular complexes, ventricular tachycardia or

Table 5

Postoperative Complications

Complication	Number	%
Acute myocardial infarction	2	2.7
Low cardiac output	11	14.7
Ventricular arrhythmia	9	12.0
Pneumonia	4	3.0
Resternotomy for bleeding	3	4.0
Stroke	2	2.7
Renal dysfunction	3	4.0
Sternal wound complications	3	4.0

ventricular fibrillation were documented in nine patients (12.0%) and required antiarrhythmic drugs for more than 24 hours. Further postoperative complications are summarized in table 5.

Analysis of left ventricular function : The postoperative left ventricular function parameters are summarized in Table 6. The mean EF significantly improved from 32.2 ± 6% preoperatively to 39.5 ± 8% ; $p = 0.01$. Further improvement was also noted during follow-up reaching a mean of 44.0 ± 4% ; $p = 0.01$ (compared to the immediate postoperative value). On the other hand, we noted a significant improvement in WMS only during follow up from 12.2 ± 1.8 to 9.4 ± 2.0 ($p = 0.03$). The immediate postoperative value was 11.1 ± 1.5, reaching no statistical significance.

Late Mortality (6-21 months) : Two patients (2.78%) died during follow-up. One patient died of massive pulmonary embolism 14 months postoperatively. The other patient died suddenly at home 9 months postoperatively.

Incidence of cardiac events : Recurrent angina pectoris was demonstrated in seven patients (9.3%), three of whom (4.0%) were successfully treated by PTCA of the native coronary system. No patients required a reoperation during the follow-up period. Three patients were rehospitalized : two for congestive heart failure and one for complete heart block necessitating a pacemaker implantation.

With regard to the quality of life at follow-up, the number of patients in functional class IV is significantly decreased from 28 (37.3%) preoperatively to 8 (10.7%) postoperatively ($p = 0.03$). The number of patients in functional class II is significantly increased from 13 (17.3%) preoperatively to 29 (38.7%) postoperatively ($p = 0.02$). The changes in the numbers of patients in functional class I and III were not statistically significant.

In an attempt to detect predictors of postoperative prognosis, patients were divided into two groups according to the outcome (9) :

Group A : patients with favourable outcome : These are patients who survived the operation and showed a postoperative increase in the EF of ≥ 5% ;

Group B : patients with poor outcome : These are patients who didn't survive the operation or showed a postoperative increase of EF of < 5%, no change or even worsening of the EF.

Multivariate analysis (table 7) demonstrated a significant correlation of pathological Q waves in the ECG and a LVESVI of more than 100 ml/m^2 with patients who had a poor outcome (adjusted ratio of 12). Reversely, there was a significant correlation between patients with a favourable outcome and reversibility of perfusion defects on thallium-201 scintigraphy (adjusted ratio of 15). None of the other clinical variables showed any predictive value in terms of outcome.

Discussion

This study demonstrates the safety of CABG in patients with impaired left ventricular function (EF ≤ 40%) as shown by the low short term mortality and morbidity. Our patients showed significant postoperative improvement in echocardiographic parameters of left ventricular function.

With the emergence of the concept of hibernating myocardium, it has become clear that

Table 6

Changes in Echocardiographic parameters of Left Ventricular Function

Variable (mean)	Preoperative	Postoperative	Short term (16 ± 4.5 months)
Ejection fraction (%)	32.2 ± 6.0	39.5 ± 8.0*	44.0 ± 4.0*
Left ventricular enddiastolic dimension(mm)	57.4 ± 13.0	55.2 ± 7.0	50.1 ± 8.0*
Left ventricular endsystolic dimension (mm)	44.7 ± 5.0	42.4 ± 5.0*	39.9 ± 5.0**
Wall motion score	12.2 ± 1.8	11.1 ± 1.5	9.4 ± 2.0**
Left ventricular enddiastolic volume (ml)	162.8 ± 14	147.5 ± 11	138.1 ± 17**
Left ventricular endsystolic volume (ml)	102.1 ± 15	95.6 ± 15	78.5 ± 9.0*

Data are expressed as mean ± SD.
* : p < 0.01 ; ** : p < 0.05.

Table 7

Comparison of preoperative variables between patients with favourable and poor outcome after myocardial revascularisation

Preoperative variables	Favorable outcome (n = 54)	Poor outcome (n = 18)
Age, years	63 ± 8	68 ± 8
Severe angina pectoris, n	27 (50%)	8 (44.4%)
CHF symptoms, n	37 (68.5%)	11 (61.1%)
Pathological Q waves, n	29 (53.7%)	15 (83.3%)*
LVESVI > 100 ml/m^2, n	19 (35.2%)	13 (72.3%)*
Extensive reversible defects on Thallium-201 scintigraphy	22/27 (81.4%)*	6/16 (37.5%)

CHF = congestive heart failure ; LVESVI = left ventricular endsystolic volume index.
* : $p < 0.05$.

chronic myocardial asynergy is not necessarily due to infarction, and therefore, might be reversible (10). With advances in surgical techniques and myocardial protection, the safety of CABG in selected patients with impaired left ventricular function has been demonstrated. However, clinical reports about improvement of left ventricular function following CABG have not been in uniform agreement (11-15). Moreover, information concerning the course of recovery of wall motion abnormalities during the immediate postoperative period has not been readily available. In this perspective, the present study was designed to evaluate the short-term serial changes in left ventricular performance in patients with impaired left ventricular function after CABG. This study includes patients operated with the use of extracorporeal circulation and no off-pump patients. Myocardial ischemia during aortic cross-clamp and possible post-ischemic reperfusion injury (stunning) can influence the perioperative changes in function (12). This factor is excluded in patients operated with off-pump technique.

Recovery of LV function : With echocardiography of our patients in the early postoperative period (one week after the operation), we were able to demonstrate a significant improvement in the left ventricular EF. Moreover, during short term follow-up (minimally 6 months postoperatively), the left ventricular EF continued to show a significant increase. This continued improvement of EF in our patients is in agreement with the findings described in other reports (1, 6, 9, 14, 16, and 17). The underlying mechanism for this steady improvement of the left ventricular function may be the gradual functional recovery of hibernating myocardium. In contrast to this phenomenon, it was described by GHODS *et al.* (14) that recovery is unlikely to occur in patients with left ventricular dysfunction caused by myocardial fibrosis (14). JACOBSON and co-workers (18) reported that only 40% of the patients showed an early postoperative improvement of the left ventricular EF without further late improvement. In this regard, 72% of our patients showed a significant improvement of EF at short term follow-up.

We believe that the left ventricular dimensions and volumes deserve more attention as indicators of impairment of left ventricular function and predictors of postoperative functional recovery of the myocardium. Louie *et al.* (19) have demonstrated that reversibility of left ventricular volume enlargement is a predictor of the presence of hibernating myocardium. In this regard, we measured the left ventricular dimension and volumes in our patients and demonstrated a significant decrease in the end-diastolic left ventricular volume in comparison to the preoperative value. This decrease was already detectable the first week after the operation and it was even further decreased six months later. In addition, we demonstrated a significant decrease in the endsystolic left ventricular volume at six months follow up, which is in agreement with several other reports (19-22). According to WOLF and colleagues (23), the immediate decrease in the left ventricular volume is most likely due to the effect of shortening of the period of diastolic filling secondary to postoperative tachycardia. In our patient population, the pericardium was widely opened at the time of surgery and not re-approximated. Thus, the enddiastolic volume was not affected by the confines of a closed pericardial space. A decrease in left ventricular compliance secondary to intraoperative myocardial ischemia is also unlikely to be a causative factor in the decrease of the enddiastolic volume because such changes tend to be resolved within a few hours postoperatively (24). In this regard, our earliest postoperative echocardiographic measurement was obtained in the first postoperative week.

Regional wall motion score analysis is considered an excellent method for the detection of functional impairment of myocardial contractility and

for the documentation of its recovery after revascularisation (4, 25). Improvement of wall motion score in our patients was only statistically significant at short term follow-up. This improvement is the result of gradual recovery of hibernating hypokinetic and akinetic myocardial segments. In recent reports it is suggested that the structural abnormalities as observed in hibernating myocardium are responsible for the delayed return of contractile performance after revascularisation (7, 22, 26, 27). Shivalkar and co-workers (28) demonstrated that only patients with no or minimal structural myocardial abnormalities invariably show early recovery of myocardial function after revascularisation.

With regard to the time course of recovery of left ventricular wall motion abnormalities, we noted considerable controversy in the available reports (7, 29, 26). Functional recovery of akinetic and dyskinetic segments may occur early or late postoperatively, and we could confirm in our study the possibility of different responses to revascularisation. It seems that recovery of segmental function in asynergic regions after CABG does not depend only on early restoration of myocardial function by an increase of myocardial perfusion, but also on the late recovery of functionally damaged yet viable myocytes. Bashour and Wason (30) characterized the latter process with the term 'embalment'.

Predictors of outcome : We found a significant correlation between poor outcome and the presence of a Q wave on the preoperative ECG, and an increased LVESVI (> 100 ml/m^2). Only in 43 patients, preoperative thallium-201 scintigraphy was available. We noticed a significant correlation between a good outcome and the presence of extensive reversible perfusion defects. KAUL and coworkers (31) also reported that an enlarged left ventricle (enddiastolic dimension > 70 mm) and advanced age were predictors of a poor outcome after CABG. HAMER *et al.* (20) and YAMAGUCHI *et al.* (21) found that, among all parameters of left ventricular function, the LVESVI was the only independent measurement being predictive of survival and improvement of left ventricular function. We agree with them that the left ventricular EF alone is not a strong predictor of operative outcome based on the fact that a low EF does not differentiate between hibernation and infarction as the cause of a poor contractile function. We confirm that an increased left ventricular volume may be a more specific indicator of the presence of myocardial fibrosis and a more specific predictor of unfavourable outcome than the left ventricular EF under resting conditions.

Reversible defects on stress thallium-201 scintigraphy represent regions of ischemic viable myocardium secondary to hypoperfusion during stress. These regions are capable of further thallium-201 uptake at rest during redistribution imaging. This procedure is able to identify intact cellular membrane function, which is a good marker of myocardial viability (32). In this respect, our findings are in agreement with other studies (32, 33). In addition, preoperative positron emission tomography and low-dose dobutamine echocardiography are described by several investigators to be predictive of a favourable postoperative outcome (34). This observation supports the use of these imaging modalities for the purpose of risk stratification of CABG in patients with poor left ventricular function.

In our patients, the presence of extensive reversible perfusion defects on myocardial scintigraphy (arbitrarily > 5 of 19 segments) appeared to be a significant predictor of postoperative improvement in left ventricular EF. In patients with this finding we also noticed an increased tendency toward improvement of congestive heart failure during follow-up. The role of preoperative rest-reinjection thallium-201 scintigraphy in myocardial viability assessment and prediction of postoperative outcome was documented in a number of studies (9, 35, 36).

Quality of life : Although the follow-up period of our patient cohort was rather short (mean of 16 ± 4.2 months), it was evident that the patients showed a significant improvement in angina class and functional status. In 77.4% of the patients, angina was improved by one or two classes and in 33.0%, the symptoms of congestive heart failure were improved by one or two classes. These results are in agreement with the results described in earlier reports (6, 37, 38).

In conclusion, our study confirms the safety of CABG in patients with impaired left ventricular function. The majority of patients showed significant improvement of left ventricular function. This favourable outcome can be predicted by the presence of considerable amount of viable myocardial segments in preoperative thalium scan. A poor outcome is predicted in case of the presence of Q waves on the preoperative ECG and in patients with a preoperative LVESVI of more than 100 ml/m^2.

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