INTERVENTIONAL CARDIOLOGY AND SURGERY

Coronary surgery with non-cardioplegic methods in patients with advanced left ventricular dysfunction: immediate and long term results

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Heart 2003;**89**:427–431

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Accepted 20 November 2002

Objective: To evaluate perioperative results and long term survival in patients with severe left ventricular (LV) dysfunction undergoing coronary artery bypass grafting (CABG) using non-cardioplegic methods.

Methods: From April 1990 through December 1999, 4100 consecutive patients underwent isolated CABG using hypothermic ventricular fibrillation. Of these, 141 (3.4%) had severe LV dysfunction (ejection fraction < 30%). Mean age was 58.3 (9.6) years. 64 patients (45.4%) were in Canadian Cardiovascular Society class III or IV and 16 (11.3%) were subjected to urgent or emergent surgery. A previous myocardial infarction was recorded in 127 (90.1%). The majority (89.4%) had triple vessel and 26 (18.4%) had left main disease. The mean number of grafts per patient was 3.1. At least one internal thoracic artery was used in all patients and 21 (14.8%) had bilateral internal thoracic artery grafts (1.2 arterial grafts per patient).

Results: Perioperative mortality was 2.8% (4 patients) and the incidence of acute myocardial infarction 2.8%. 50 (35.5%) patients required inotropes but only 16 (11.3%) required it for longer than 24 hours; 5 patients (3.5%) needed mechanical support. The incidence of renal failure was 3.5%. Mean duration of hospital stay was 9.6 (8.3) days. Follow up was 95% complete and extended for a mean of 57 (30) months. Late mortality was 11.5%. Actuarial survival rates at 1, 3, and 5 years were 96%, 91%, and 86%, respectively.

Conclusions: Non-cardioplegic techniques are safe and effective in preserving the myocardium during CABG in patients with coronary artery disease and poor LV function, with low operative mortality and morbidity, and encouraging medium to long term survival rates.

Coronary artery bypass grafting (CABG) in patients with advanced left ventricular (LV) dysfunction has been regarded as a high risk procedure.[1 2] However, because alternative surgical treatments (such as transplantation and cardiomyoplasty) have considerable limitations and the results of medical treatment are often unsatisfactory, revascularisation should always be considered as a treatment option.[3 4] In addition, advances in surgical technique, perioperative care, and myocardial protection have enhanced the safety of CABG in this cohort of patients.[5–9]

Effective myocardial preservation is essential for successful CABG when the myocardium is handicapped. However, there is still controversy over the optimal technique of myocardial protection and a variety of safe and effective methods, which involve the use of either crystalloid or blood cardioplegia, are available and routinely used by most surgeons. Nonetheless, non-cardioplegic methods have gained in popularity. For the past 10 years, we have routinely opted to perform CABG under hypothermic ventricular fibrillation. The present study was undertaken to assess the results achieved by this approach in patients with severe LV dysfunction.

PATIENTS AND METHODS

Demographic, clinical, operative, perioperative, and in-hospital outcome data were collected prospectively and entered into a computerised database comprising all patients undergoing CABG at our institution. From this database, the records of 4100 patients undergoing isolated CABG with non-cardioplegic methods between April 1990 and December 1999 were retrieved for analysis. Data for 141 (3.4%) patients (group 1) with severe impairment of LV function (ejection fraction (EF) < 30%), determined semiquantitatively by contrast ventriculography, were analysed. Echocardiography and nuclear ventriculography were carried out in a minority of patients and, when these additional data were available, the highest EF value was used for subsequent analysis. All patients had angina or evidence of ischaemia.

Patients

Table 1 details the perioperative clinical and angiographic data. The mean age of the 133 male (94.3%) and eight female patients was 58.3 (9.6) years. Forty (28.6%) patients had diabetes and 72 (51.1%) had dyslipidaemia. Sixty four (45.4%) were in Canadian Cardiovascular Society class III or IV. Twelve (8.5%) patients had been on intravenous antianginal medication in the last two days before the operation (unstable angina). A previous myocardial infarction was recorded in 127 patients (90.1%), 11 (7.8%) of which had occurred in the 30 days preceding coronary surgery. The majority (88.7%) of the patients were operated on electively.

One hundred and twenty six patients (89.4%) had triple and 14 (9.9%) had double vessel coronary disease. Twenty six (18.4%) had left main disease. There was only one case of repeat CABG among these patients. By definition, the EF was < 30% in all cases (range 12–29%).

Surgical technique and operative data

Cardiopulmonary bypass was instituted using a bubble or membrane oxygenator and non-pulsatile flow. Patients were

Abbreviations: CABG, coronary artery bypass grafting; EF, ejection fraction; ITA, internal thoracic artery; LV, left ventricular

Table 1 Preoperative clinical data in 141 patients with left ventricular dysfunction

	Number
Mean age (years)	58.3 (9.6)
Sex (male)	133 (94.3%)
Coronary risk factors	
Diabetes mellitus	40 (28.6%)
Smoking	92 (65.2%)
Hypertension	70 (49.6%)
Dyslipidaemia	72 (52.2%)
Family history of CAD	33 (23.6%)
History of MI	
Old	116 (82.3%)
Recent (<30 days)	11 (7.8%)
Peripheral vascular disease	22 (15.6%)
Cerebrovascular disease	5 (3.5%)
Angina (CCS class)	
I	14 (9.9%)
II	63 (44.7%)
III	46 (32.6%)
IV	18 (12.8%)
Unstable angina	12 (8.5%)
Cardiomegaly	64 (45.4%)
Anaemia	10 (7.1%)
Extent of disease	
One vessel	1 (0.7%)
Two vessels	14 (9.9%)
Three vessels	126 (89.4%)
Left main disease	26 (18.4%)
LVEDP >20 mm Hg	107 (75.8%)
Prior IABP support	1 (0.7%)

CAD, coronary artery disease; CCS, Canadian Cardiovascular Society; IABP, intra-aortic balloon pump; LVEDP, left ventricular end diastolic pressure; MI, myocardial infarction.

cooled to an oesophageal temperature of 30–32°C. An LV vent was always placed through the right superior pulmonary vein and left atrium. No topical cooling was used.

The method predominantly used during the construction of the distal anastomoses was ventricular fibrillation, without clamping of the aorta. This method has been described in detail in a previous report, and we refer here to only some aspects.[8]

Generally, the anastomoses to the right coronary artery or its branches on the inferior surface of the heart were constructed first, followed by the anastomoses to the branches of the circumflex system. Bypasses to the anterior descending artery and its diagonal branches were performed last. Very early in the series, the proximal anastomoses of each vein graft was usually constructed immediately after the distal one, but now all distal anastomoses are constructed first, followed by all proximal anastomoses in a single partial clamping period. In the case of ongoing ischaemia, the coronary artery branch that was likely to be involved was grafted first followed immediately by the proximal anastomosis. Control of residual and collateral blood flow was achieved by a variety of methods, mainly with the use of the coronary occluders and a gentle jet of oxygen.

Internal thoracic artery (ITA) grafts were used in all patients. In 21 (14.8 %) patients both left and right ITAs were used, for a mean of 1.2 (0.4) arterial anastomoses per patient. Additionally, a mean of 1.9 (0.8) venous anastomoses were constructed per patient. Hence, an average of 3.1 (0.7) coronary artery branches were bypassed per patient. Endarterectomies were performed in 26 cases (18.4 %), 19 of the right coronary and seven of the left system. Perfusion time was 69.4 (20.2) minutes.

Statistical methods

Data were collected prospectively on standard forms and entered into a computerised database. All data were retrospectively analysed with the assistance of Systat statistical software (Systat Software Inc). All data are expressed as mean (SD) or as proportions. For univariate analysis of categorical data, the χ^2 test (2×2 contingency tables) or Fisher's exact test were used. Univariate analysis of continuous variables was carried out using Student's *t* test. Long term actuarial survival rates were calculated using the Kaplan-Meier method.

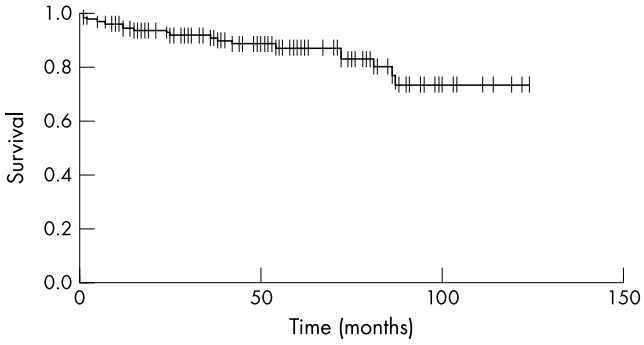

Figure 1 Kaplan-Meier survival curve of the 141 patients in the study.

RESULTS

There were four (2.8%) perioperative deaths (defined as deaths in the hospital or within 30 days if the patient was discharged sooner). Three patients died of cardiac failure and one of respiratory failure. Fifty patients (35.5%) required inotropic support (defined as the use of any inotropic agent after the patient left the operating room) but only 16 (11.3%) for periods longer than 24 hours. Mechanical support (intra-aortic balloon or LV assist device) was used in five patients (3.5%). Five patients (3.5%) developed acute renal failure (creatinine > 220 μmol/l) but none required dialysis. Four patients (2.8%) had ECG criteria of perioperative myocardial infarction. Supraventricular arrhythmias necessitating medical or electrical treatment occurred in 24 patients (17.0%). Three patients (2.1%) had an episode of ventricular fibrillation, successfully converted, and another three had transient complete atrioventricular block. Three patients (2.1%) required re-exploration because of haemorrhage and seven (4.9%) were reoperated for sternal dehiscence, including three with the diagnosis of acute mediastinitis (presence of pus or bacterial growth in the mediastinal tissues sampled during surgical re-exploration). Five patients (3.5%) had a cerebrovascular accident, all with at least partial recovery. The mean length of hospital stay was 9.6 (8.3) days.

Follow up was conducted by mail or telephone and was 95% complete. The mean follow up time of the 130 survivors (seven patients were lost) was 57 (30) months (range 9–124 months). Fifteen patients (11.5%) had died. The actuarial survival at one, three, and five years was 96%, 91%, and 86%, respectively (fig 1).

To place the immediate results into perspective, results for group 1 were compared with the clinical, angiographic, and operative data, as well as of the mortality and in-hospital events, of 3557 patients with normal LV function or only mild dysfunction (EF $\geq$ 40%) who had undergone isolated CABG during the same time period (group 2; tables 2 and 3).

Compared with group 2 patients, those in group 1 were younger and had higher incidences of peripheral vascular disease, anaemia, cardiomegaly, and prior myocardial infarction. There were no significant differences in the angina symptoms or in the preoperative use of intra-aortic balloon pump.

On the other hand, patients with severe LV dysfunction had more extensive coronary artery disease (mean number of vessels involved was 2.9 *v* 2.7 in group 2; $p < 0.001$). This difference results essentially from a larger number of patients with single vessel disease in group 2. Hence, as would be expected,

Table 2 Comparison of clinical and operative data between groups 1 and 2

Variable	Group 1	Group 2	p Value
Number of patients	141	3557	
Mean age (years)	58.3 (9.6)	60.1 (9.2)	0.032
Sex (female) (%)	5.7	11.7	0.027
Coronary risk factors (%)			
Diabetes mellitus	28.6	20.3	0.017
Smoking	65.2	53.9	0.008
Hypertension	49.6	56.9	NS
Dyslipidaemia	52.2	55.5	NS
Family history of CAD	23.6	22.2	NS
History of MI (%)			
Old	82.3	45.1	<0.001
Recent (<30 days)	7.8	4.9	NS
Peripheral vascular disease (%)	15.6	11.1	0.023
Cerebrovascular disease (%)	3.5	4.8	NS
Angina (CCS class III/IV)	46.1	42.0	NS
Cardiomegaly (%)	45.4	7.9	<0.001
Anaemia (%)	7.1	4.2	0.042
Number of diseased vessels (mean)	2.9 (0.3)	2.7 (0.6)	<0.001
Left main disease (%)	18.4	15.8	NS
Surgical priority (elective) (%)	89.3	92.1	NS
Number of grafts/patient (mean)	3.1 (0.7)	2.8 (0.8)	<0.001
Number of arterial grafts/patient (mean)	1.2 (0.5)	1.3 (0.5)	NS
Number of venous grafts/patient (mean)	1.9 (0.8)	1.5 (0.8)	<0.001
Arterial conduits (%)			
LITA	100.0	99.2	NS
RITA	14.8	24.1	<0.001
Endarterectomy (%)	18.4	9.2	<0.001
Perfusion time (min) (mean)	69.4 (20.2)	6 3.2 (26.0)	<0.001

LITA, left internal mammary artery; RITA, right internal mammary artery.

Table 3 Comparison of results (%) between groups 1 and 2

Variable	Group 1	Group 2	p Value
Mortality	2.8	0.9	0.025
Morbidity			
Inotropic support	35.5	5.5	<0.001
Mechanical support	3.5	0.6	<0.001
Perioperative MI	2.8	4.1	NS
Acute renal failure	3.5	2.8	NS
Reoperation for bleeding	2.1	2.5	NS
Reoperation for sternal complications	4.9	2.1	0.022
Stroke	3.5	2.1	NS
Arrhythmias	19.1	23.3	NS
Hospital stay (mean time in days)	9.6(8.3)	7.9(5.6)	0.002

there was a significant difference in the number of coronary artery grafts constructed per patient (3.2 *v* 2.8, respectively; $p < 0.0001$). The mean number of arterial grafts per patient was similar in the two groups.

Mortality was higher in group 1 (2.8%) than in group 2 (0.9%; $p = 0.025$). The use of inotropes or mechanical support and the number of sternal complications were also higher in group 1. There were no significant differences in the incidences of myocardial infarction, stroke, acute renal failure, arrhythmias, and reoperation for bleeding. Finally, patients in group 1 had a longer hospital stay (1.7 days longer; $p = 0.002$) but there was no difference if only survivors were counted.

DISCUSSION

Patients with coronary disease and advanced LV dysfunction have a poor prognosis when treated only medically. They have a limited survival and usually die of cardiac causes. On the other hand, several studies have shown that they respond better to coronary surgery.[1 2 4 10] Although transplantation is an effective treatment option, it is limited by availability of donor organs and by the implications of immunosuppression. Therefore, revascularisation should always be considered as an option in these patients. It has been shown that CABG increases survival, improves functional status, provides better control of angina symptoms, and reduces the prevalence of sudden cardiac death caused by arrhythmias.[1 3 4 7 9 11]

Case selection and myocardial protection

One important question to be addressed is which patients with severe coronary artery disease and low EF would derive most benefit. It has been suggested that symptoms of angina (versus symptoms of heart failure) are associated with a more favourable outcome.[12] Some groups require evidence of reversible ischaemia or viability of hibernating myocardium by radioisotopic scanning, positron emission tomography, or dobutamine echocardiography to select patients for this approach.[13 14] We have not excluded patients because of lack of significant angina, nor have we routinely used viability studies to select candidates for grafting. Patients were considered to be unsuitable for grafting only if they had angiographic evidence of diffuse distal disease, particularly of the anterior descending artery, or in the presence of comorbidities that significantly increase operative risk.

We concur with others in that, in patients with little functional reserve, favourable results can only be achieved

with optimal myocardial protection. An unending series of reports dealing with cardioplegia in any of its numerous variations have shown this unequivocally. However, this evidence does not mean that non-cardioplegic methods result in less protection. In fact, several randomised clinical studies have shown that intermittent aortic cross clamping provides protection that is equivalent to, if not better than, blood cardioplegia and preserves LV diastolic function better.[15–18] We and others have previously shown the safety and efficacy of these methods, even in higher risk patients, possibly because during the operation the myocardium is continuously perfused with the patient's unaltered blood.[8 19–21]

The use of off-pump coronary bypass in this subgroup of patients has recently been studied with respect to early outcomes. Two recent retrospective studies have reported similar results when comparing off-pump coronary bypass with cardioplegic techniques and concluded that this method is safe and efficacious.[22 23] The question may also be raised about non-cardioplegic methods. Nonetheless, anatomical factors, which were frequently found in our patients, such as cardiomegaly and, more important, heavily calcified vessels requiring endarterectomy, may preclude off-pump coronary bypass in many of these patients. We believe that longer follow up is required before a conclusion can be reached.

Perioperative results and survival

Recent reports indicate that the perioperative mortality after CABG in patients with advanced LV dysfunction varies between 2.5–8%.[5–8] In the present series, the perioperative mortality was 2.8%. As others have experienced, we have had a higher requirement for inotropic support than in our patients with an EF > 40%. However, in contrast with other studies, in our study very few patients (3.5%) required mechanical support in the early postoperative period, and the incidence of myocardial infarction was 2.8%.[5 9 12] Considering the characteristics of the group, these results are quite acceptable and compare favourably with those of series where cardioplegic methods were used. The relatively low incidence of other causes of morbidity and the short hospital stay also constitute good clinical benchmarks for a relatively smooth perioperative period.

However, the incidence of sternal complications was somewhat higher (4.9%) than those reported by others, which may be related to the fact that all of our patients received ITA grafts, including 14.8% in whom both ITAs were used.[6] The use of ITA grafts in this cohort of patients is an important issue because the reports are conflicting. Concerns about the short term limitations of ITA grafts may have made surgeons more likely to use venous conduits in these high risk patients. Eventual problems of the ITA include lower initial flow than with vein grafts, the potential for spasm, the time required for harvesting in unstable patients, and, eventually, the inability to deliver the cardioplegic solution down a pedicled arterial graft. Additionally, the reduced late survival usually associated with LV dysfunction, advanced age, and significant comorbidities in these patients may offset the survival advantage generally associated with ITA use.

Despite these concerns, we follow a more liberal approach. We used left ITA grafts in all patients of the study group and, additionally, right ITA grafts in 21 (14.8%) patients. Some similar studies reported left ITA use in 76–86% of patients with LV dysfunction, with excellent initial results.[7 11] Anderson and colleagues[24] reported the use of left ITA in 70% of patients with ventricular dysfunction presenting with chronic congestive heart failure and concluded that its use enhanced late survival. By contrast, others have used ITA in as few as 41% of patients, and some question the survival benefit of the use of the left ITA conduit in these patients.[25 26] In any case, early outcomes have not been adversely affected by the use of arterial grafts in the setting of ventricular dysfunction.

In a previous publication, we had already shown this favourable immediate outcome. Apart from increasing the number of patients studied, we have now been able to complete the medium term follow up (mean 57 (30) months).[8] Our five year survival of 86% compares favourably with those reported by others after CABG in patients with severe LV dysfunction of between 60–80%.[7 9 11 27–29] However, it is important to note that some of these studies included only patients with an EF of ⩽ 20%. Another possible reason for this difference may be related to our population being somewhat younger and with fewer female patients, which are two important clinical factors positively correlated with early and late death. Compared with the dismal outcome generally observed with medical treatment alone, these survival rates have to be considered excellent.

The present study has some limitations. These include the definition of severe LV dysfunction as EF of < 30% determined semiquantitatively by contrast ventriculography, which is not very precise. In fact, assessing ventricular function on contrast ventriculography is not entirely satisfactory. In some cases this study was done after the coronary arteriogram, which could have overestimated the incidence of LV dysfunction. However, in many cases where there was doubt, other methods of indirect measurement of the EF helped to clarify the situation. Additionally, because the long term survival results in the group with EF ⩾ 40% are not available yet, it is not possible to put into perspective these results by comparison with those here reported for patients with ventricular dysfunction. Finally, although some of the significant differences found between groups 1 and 2 may have little clinical relevance, it is quite evident that the higher incidence of diabetes and the more extensive vessel disease, requiring a higher number of grafts, may have had an impact in the early and long term results.

In conclusion, the results reported herein confirm that non-cardioplegic techniques are safe and effective in preserving the myocardium during CABG, including in patients with poor LV function, in whom low operative mortality and morbidity rates were achieved. This study also confirmed an encouraging medium to long term survival in this high risk population.

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ELECTRONIC PAGES

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Successful radiofrequency catheter ablation of "clockwise" and "counterclockwise" bundle branch re-entrant ventricular tachycardia in the absence of myocardial or valvar dysfunction without detecting bundle branch potentials

K Matsuoka, E Fujii, F Uchida

A case is reported of a patient with only isolated conduction abnormalities of the His-Purkinje system with no identifiable myocardial or valvar dysfunction, leading to "clockwise" and "counterclockwise" bundle branch re-entrant ventricular tachycardias (BBRVTs). The electrophysiological study showed infra-Hisian conduction system disease and two different inducible wide QRS complex tachycardias. Neither right bundle branch nor left bundle branch potentials were recorded despite extensive catheter manipulation. However, these tachycardias were diagnosed as BBRVTs by using entrainment manoeuvres and comparing the HV intervals during both sinus rhythm and the tachycardias. These tachycardias were eliminated by catheter ablation of the right bundle branch, using the morphology of the local electrograms and anatomical findings.

(*Heart* 2003;**89**:e12) www.heartjnl.com/cgi/content/full/89/4/e12

Concordance for hypoplastic left heart syndrome in a monochorionic twin pregnancy

R E Andrews, A C Cook, R W M Yates

The risk of structural heart disease is significantly higher in twin pregnancies than in singleton pregnancies, but the concordance rate has been found to be relatively low, even in monochorionic pregnancies. This is the first report of a monochorionic twin pregnancy concordant for hypoplastic left heart syndrome (HLHS), the diagnosis having been made by fetal echocardiography at 15 weeks' gestation. The findings were confirmed at necropsy at 17 weeks' gestation, following termination of pregnancy. Both twins had mitral and aortic atresia, with severely hypoplastic aortic arches. This report adds weight to there being a genetic component to the cause of HLHS in some cases and illustrates how the findings from early fetal echocardiography with postmortem follow up can help to extend the understanding of the aetiology of this condition.

(*Heart* 2003;**89**:e13) www.heartjnl.com/cgi/content/full/89/4/e13

Toad venom poisoning: resemblance to digoxin toxicity and therapeutic implications

R M Gowda, R A Cohen, I A Khan

A healthy man developed gastrointestinal symptoms after ingesting purported aphrodisiac pills. He had severe unrelenting bradycardia, hyperkalaemia, and acidosis. He rapidly developed severe life threatening cardiac arrhythmias and died after a few hours. He was found to have positive serum digoxin concentrations, although he was not taking digoxin. Toad venom poisoning is similar to digitalis toxicity and carries a high mortality. Cardiac glycoside poisoning can occur from ingestion of various plants and animal toxins, and the venom gland of cane toad (*Bufo marinus*) contains large quantities of cardiac glycosides. Toad venom, a constituent of an aphrodisiac, was considered responsible for the development of clinical manifestations and death in this patient. Digoxin specific Fab fragment has been reported to be beneficial in the treatment of toad venom poisoning. This report alerts physicians to the need to be aware of a new community toxic exposure, as prompt treatment with digoxin specific Fab fragment may be life saving. The treatment approach to patients with suspected toad venom poisoning is described

(*Heart* 2003;**89**:e14) www.heartjnl.com/cgi/content/full/89/4/e14