ELSEVIER

European Journal of Cardio-thoracic Surgery 16 (1999) 331–336

EUROPEAN JOURNAL OF CARDIO-THORACIC SURGERY

www.elsevier.com/locate/ejcts

Non-cardioplegic coronary surgery in patients with severe left ventricular dysfunction

Pedro E. Antunes, J. Ferrão de Oliveira, Manuel J. Antunes*

Cardiothoracic Surgery. University Hospital, Coimbra, Portugal

Received 22 February 1999; received in revised form 25 May 1999; accepted 9 June 1999

Abstract

Objectives: Although most surgeons use cardioplegia for myocardial protection during coronary artery bypass grafting (CABG), some still use non-cardioplegic methods with very good early and long-term outcome. However, the results in patients with severe left ventricular dysfunction remain unproved. This study evaluates the perioperative mortality and morbidity in patients with severe left ventricular dysfunction submitted to CABG using non-cardioplegic methods. **Methods**: From April 1990 through December 1997, 3,180 patients were consecutively subjected to isolated CABG using non-cardioplegic methods, for construction of the distal anastomoses. This prospective study is based on the 107 (3.4%) patients with severe impairment of the left ventricular function (ejection fraction $< 30\%$). The mean age at operation was 57.0 ± 9.2 years and 95.3% of patients were male. Fifty three patients (49.5%) were in class CCS III / IV and 12 (11.2%) were subjected to urgent surgery. A history of previous myocardial infarction was recorded in 99 (92.5%) patients. Ninety seven (90.6%) patients had triple vessel and 17 (15.9%) left main stem disease, and 77 (71.9%) had a left ventricular end-diastolic pressure > 20 mmHg. Cardiopulmonary bypass time was 73.1 ± 21.7 min. The mean number of grafts per patient was 3.2. At least one internal mammary artery was used in all cases and 16 patients (14.9%) had bilateral internal mammary artery grafts (1.2 arterial grafts/patient). Endarterectomies were performed in 23 (21.5%) patients. **Results**: Perioperative mortality was 2.8% (respiratory-1; cardiac-2). Forty one (38.3%) patients required inotropes, but for longer than 24 h in only 12 (11.2%), and two (1.9%) needed intra-aortic conterpulsation. The incidence of myocardial infarction was 2.8%. Two (1.9%) patients had reintervention for haemorrhage and another five (4.6%) for sternal complications. The incidences of supraventricular arrhytmias, renal failure and cerebrovascular accident were 16.8%, 3.6% and 2.8%, respectively. The mean time of hospital stay was 9.3 ± 6.4 days. **Conclusion**: These results appear to demonstrate that non-cardioplegic methods afford good myocardial protection and operating conditions with excellent applicability, even in patients with severe left ventricular dysfunction.

Keywords: Coronary surgery; Left ventricular dysfunction; Myocardial protection; Intermittent aortic cross-clamping; Fibrillatory arrest

1. Introduction

Revascularization of ischemic myocardium in patients with severe left ventricular function still constitute a surgical challenge. Despite advances in the surgical technique and myocardial protection, perioperative morbidity and mortality remain high [1–3]. There is no consensus as to the optimal method of myocardial protection during CABG. Although most surgeons use cardioplegia for myocardial protection in any of its numerous variations during CABG, some still use non-cardioplegic methods. These include intermittent aortic cross-clamping and ventricular fibrillation with local control of coronary blood flow.

The safety and efficacy of non-cardioplegic methods have been demonstrated during elective primary and reoperative CABG, as well as in higher risk patients [4–14], and are further endorsed by some prospective randomised clinical trials [15–17]. Despite the continued use of non-cardioplegic methods since the early days of coronary surgery, in the last two decades there has been, to our knowledge, no report specifically addressing its results in patients with severe left ventricular dysfunction.

In this paper, we report the experience that we have obtained with these methods in 107 such patients.

2. Material and methods

2.1. Patient's data

Between April 1990 and December 1997, 3180 patients

* Corresponding author. Cirurgia Cardiotorácica, Hospitais da Universidade, 3049 Coimbra Codex, Portugal. Tel.: +351-39-400-418; fax: +351-39-829-674.

E-mail address: antunes.cct.huc.@mail.telepac.pt (M.J. Antunes)

1010-7940/99/$ - see front matter
PII: S1010-7940(99)00213-4

were consecutively subjected to isolated CABG using non-cardioplegic methods, i.e. intermittent aortic cross-clamping (initial 540 patients) or ventricular fibrillation (last consecutive 2640 patients). This prospective study is based on the 107 (3.4%) patients with severe impairment of the left ventricular function, i.e. with an ejection fraction of less than 30%(range 14–29%), as assessed by ventriculography or gated blood pool scintigraphy. All patients had angina or demonstrable ischemia and significant lesions in bypassable vessels. Patients undergoing associated procedures, such as valvular surgery, closure of ventricular septal defects or excision of ventricular aneurysms were not included in this series. A database comprising 38 perioperative variables for each patient was analysed. There were no cases of reoperation among these patients.

Preoperative clinical and angiographic data are summarised in Table 1. The mean age at operation was 57.0 ± 9.2 years and 95.3% of the patients were male. Ninety five patients (88.8%) underwent elective operations and twelve (11.2%), who had unstable symptoms with maximal medical therapy, including intravenous nitrates, required urgent operation. As to the extent and severity of the coronary disease, 97 patients (90.6%) had triple and 10 (9.4%) double vessel disease, and 17 (15.9%) had left main disease. A left ventricular end-diastolic pressure >20 mmHg was observed in 77 patients (71.9%).

Table 1
Preoperative clinical data[a]

	No.	%
Mean age (years)	57.5 ± 9.2	
Sex (male)	102	95.3
Coronary risk factors		
Diabetes mellitus	32	29.9
Smoking	71	66.3
Hypertension	52	48.6
Dislipidemia	51	47.6
Family history of CAD	25	23.4
History of MI		
Old	93	86.9
Recent (<30 days)	6	5.6
Peripheral vascular disease	4	3.7
Angina (CCS class)		
I/II	42	39.2
III/IV	53	49.5
Unstable angina	12	11.2
Extent of disease		
Two vessels	10	9.4
Three vessels	97	90.6
Left main disease	17	15.9
LVEDP >20 mmHg	77	71.9
IABP support	1	0.9

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

2.2. Surgical technique

Cardiopulmonary bypass was conducted with non-pulsatile flow and mild hypothermia (32°C). On cardiopulmonary bypass the systemic perfusion pressure was electively maintained at 55–65 mmHg. A left ventricular vent was always used, introduced through the right superior pulmonary vein into the left atrium. No topical cooling was used. In the first 17 patients of this series we used intermittent aortic cross-clamping, a technique described in detail in a previous report. In the remaining cases, ventricular fibrillation without clamping was used for construction of the distal anastomoses. The technique used was essentially that previously described by Akins, and we detail here only some aspects related to the method. Although ventricular fibrillation occurred spontaneously in some patients, as the heart cooled down or with manipulation, frequently a brief application of a direct electrical current was necessary to initiate ventricular fibrillation.

The choice of the territory to be revascularized first depended on several factors. Generally speaking, the most ischemic area and occluded arteries were addressed first, with the exception of the anterior wall, in order to avoid excessive traction on the internal mammary artery pedicle, after anastomosis to the left anterior descending artery. If there was no clear indication of a significant ischemic area, we generally constructed first the anastomoses to the right coronary artery and/or branches of the inferior surface of the heart. Next were the anastomosis to the vessels of the circumflex system and last were those to the anterior descending artery and its diagonal branches. Control of the residual and/or collateral blood flow is, obviously, an important aspect of these techniques and was achieved by a variety of methods. Commonly, we could obtain a dry field with the use of the coronary occluders and a soft jet of oxygen. Occasionally, however, we would also slow down the pump flow transiently or, if necessary, even cross-clamp the aorta. Early in the series, the proximal anastomosis of each vein graft was generally constructed immediately after the distal one with a side-biting clamp. Currently, all distal anastomosis are constructed first, followed by all proximal anastomoses in a single partial clamping period during which the heart is defibrillated and allowed to beat. Systemic rewarming was begun during the performance of the last distal anastomosis. In order to measure the filling pressures in the post-operative period, a catheter was placed into the left atrium, through the ventricular venting site, and left in place for 24 to 48 h.

The left internal mammary artery was grafted to the anterior descending artery in all patients, in 9 cases with sequential anastomoses to its diagonal branches. The right mammary artery was used in 16 cases, in all but one as a free graft, essentially to branches of the circumflex system. Double mammary artery grafting was used, as a rule, in patients younger than 60 years with a favourable coronary anatomy, i.e. a single large obtuse marginal branch. The

Table 2
Operative data[a]

	No.	%
Surgical priority		
Elective	95	88.8
Urgent/emergent	12	11.2
No. of grafts/patient	3.1	
Arterial conduits		
LIMA	107	100.0
RIMA	16	14.9
Endarterectomy	23	21.5
Perfusion time (min)	73.0 ± 21.7	
Aortic crossclamp (min)[b]	19.9 ± 9.1	
Crossclamp/graft (min)[b]	6.4	

[a] LIMA and RITA: left and right internal mammary artery.
[b] Population: 17 patients in whom intermittent aortic cross-clamping was used.

proximal anastomoses of free arterial grafts were usually constructed over the aortic anastomosis of a venous graft.

Bloodless prime was used in more than 90% of the cases, whenever the haematocrit was greater than 40%, and blood was not given unless the haematocrit dropped bellow 25% during cardiopulmonary bypass. Patients were actively vasodilated, both during and after the procedure to keep the mean arterial blood pressure at 55–65 mmHg, for cardiac outputs at normal or above normal levels. Towards the end of the procedure, all blood remaining in the oxygenator and tubing was given back to the patient. Collected mediastinal blood shed during the first 6 postoperative hours was reinfused.

3. Results

Internal mammary grafts were used in all patients, including 16 (14.9%) in whom both left and right internal mammary arteries were used, for a total of 132 arterial anastomoses (1.2 per patient). Additionally, 208 venous anastomoses (1.9 per patient) were constructed. Hence, an average of 3.1 coronary artery branches were bypassed per patient. Endarterectomies were performed in 23 patients (21.5%), 18 of the right and 5 of the left coronary system. In the intermittent aortic crossclamp group (17 patients) the average crossclamp time per graft was 6.4 min., adding to a global clamp time of 19.9 ± 9.1 min (range 7–34 min). The cardiopulmonary bypass time for all patients was 73.0±21.7 min (range 39–147 min) (Table 2).

3.1. Mortality

There were three (2.8%) perioperative deaths (defined as deaths in the hospital or within 30 days if the patient was discharged sooner). The first of the three patients was a 67-year old man who died of respiratory failure on the 33rd postoperative day. The second was a 44-year old man who died of acute cardiac failure on the 3rd postoperative day. The third was a 46-year old man who developed severe bilateral pneumonia and acute mediastinitis and died of chronic cardiac failure on the 67th postoperative day. This was the only patient operated on under ventricular fibrillation, without aortic clamping. Because there were only three deaths, predictors of operative mortality could not be derived from the current series.

3.2. Morbidity

Forty one patients (38.3%) required inotropic support (defined as the use of any inotropic agent after the patient left the operating room), but for longer than 24 h in only 12 cases (11.2%). An intra-aortic balloon was used in two patients (1.9%) to assist weaning from cardiopulmonary bypass, including that which had already been inserted preoperatively. There were ECG criteria of perioperative myocardial infarction in three patients (2.8%). Two patients (1.9%) were returned to the operating room because of haemorrhage and five (4.6%) had reoperation for sternal complications, including 3 with the diagnosis of acute mediastinitis (presence of pus or bacterial growth in the mediastinal tissues sampled during surgical re-exploration). Supraventricular arrhythmias necessitating medical and/or electrical treatment occurred in 18 patients (16.8%). One patient (0.9%) had an episode of ventricular fibrillation, and 3 (2.8%) transient complete AV block. Four patients (3.6%) developed acute renal failure (creatinine >2.5 mg/dl) that did not require dialysis. Three patients (2.8%) had a cerebrovascular accident and another 3 delirium (Table 3). The mean time of hospital stay was 9.3 ± 6.4 days for the whole group and 8.4 ± 1.8 days for survivors.

Table 3
Perioperative mortality and morbidity

	No.	%
Mortality	3	2.8
Morbidity		
Inotropic support		
< 12 h	16	14.9
12–24 h	13	12.2
> 24 h	12	11.2
IABP support	2	1.9
Perioperative MI	3	2.8
Acute renal failure	4	3.6
Respiratory failure	1	0.9
Reoperation for bleeding	2	1.9
Reoperation for sternal complications	5	4.6
Stroke	3	2.8
Delirium	3	2.8
Arrhytmias		
Supraventricular tachycardia	18	16.8
Ventricular fibrillation	1	0.9
Complete heart block	3	2.8

4. Discussion

4.1. Surgical technique and myocardial protection

Hypothermic ventricular fibrillation, with or without intermittent aortic cross-clamping, was used in the earliest days of coronary surgery for ischemic heart disease but most surgeons now use one of several forms of cardioplegia for myocardial protection during CABG.

There is no doubt that cardioplegia affords good protection to the myocardium. An unlimited number of reports dealing with cardioplegia in any of its numerous variations showed it unequivocally. However, this does not mean that non-cardioplegic methods, which are still used by some, result in a lesser protection. The safety and efficacy of these methods have been demonstrated in primary and reoperative CABG as well in higher risk patients [4–13]. In fact, three recent prospective randomised clinical trials have demonstrated that intermittent aortic cross-clamping provides equivalent, if not better protection than blood cardioplegia. In 1994, Anderson et al. [15] performed a study using either blood cardioplegia or fibrillatory arrest with intermittent ischemia in the context of elective CABG and found lower post-operative serum levels of CK-MB and troponin T in the group of intermittent ischemic arrest. In the same year, Gerola et al. [16] found no significant difference in the release of cardiac enzymes between the same two techniques. Finally, in 1998, Musumeci et al. [17] found that intermittent ischemic arrest was associated with lower release of the cardiac-specific enzymes CK-MB, Troponin T and Troponin I.

There is also some evidence that non-cardioplegic methods preserve LV diastolic function better. In a recent comparative study conducted in patients subjected to elective CABG, Casthely et al. [18] found that impairment in LV diastolic function in the immediate perioperative period was minimal when ventricular fibrillation and intermittent cross-clamping was used, while it was highly significant when retrograde and anterograde blood cardioplegia were used.

We have used cardioplegia for myocardial protection during CABG until about 9 years ago. Since then, we have continuously used intermittent aortic cross-clamping and later ventricular fibrillation without aortic occlusion. There was no major reason to move to non-cardioplegic techniques, other than, in our opinion, their simplicity. We now prefer non-cardioplegic methods, not only because they are safe and efficient but also because they are more versatile and allow greater operative flexibility. In a previous report [8], we have discussed the basic operative principles and technical aspects related to the method of intermittent aortic cross-clamping. In that work, we had found that patients operated on with intermittent cross-clamping had better clinical outcome and lower requirements for inotropic support, when compared with those operated on under cardioplegia immediately before the change of the myocardial protection strategy, using otherwise identical techniques.

Since the middle of 1992, we have been using ventricular fibrillation, without aortic occlusion, with success for primary and reoperative CABG, as well as for resection of left ventricular aneurysms and for closure of ischemic ventricular septal defects. The main reason to change from intermittent aortic cross-clamping to ventricular fibrillation without aortic occlusion was that we found it even simpler, as we learnt to obtain good local control and operating conditions. But, besides the patient with an atherosclerotic aorta, in whom there is an obvious disadvantage in clamping the aorta, in routine cases these two non-cardioplegic techniques have basically the same advantages. Hence, the option to clamp the aorta is mainly a matter of convenience and exposure, and is still occasionally made.

The basic principles of the technique were developed in the late 1960s and early 1970s, supported by numerous research studies, and since then only minor modifications have been added. The technique which we have used was essentially that previously described by Akins [11]. Nevertheless, there were some differences and probably the most important is that which relates to the systemic perfusion pressure during the period of fibrillatory arrest. Supported by some experimental animal works, Akins advised the maintenance of an aortic root pressure of 80 to 100 mmHg [9]. Based on our own clinical experience, we believe that a perfusion pressure around 60–65 mmHg is safe to maintain an adequate perfusion gradient across the coronary vascular bed and good subendocardial perfusion, even in hypertrophied hearts. Additionally, active peripheral vasodilatation, improves tissue perfusion and decreases the afterload when the heart beating is resumed. We have found that with this policy the requirement for inotropic support was markedly reduced.

4.2. Results

The results reported here confirm those of other surgeons in that non-cardioplegic techniques are safe and effective in preserving the myocardium during CABG. Although the number of patients included is limited, a major relevance of this report lies in that it includes all cases with severe LV dysfunction who underwent CABG during an 8-year period in one department, all operated on by one surgeon (MA). On the other hand, and in the absence of other secure indicators of myocardial lesion, clinical performance is an acceptable way of assessing the adequacy of the myocardial protection, and this may be particularly true in this group of patients with severe left ventricular dysfunction.

Although this study was not designed to compare different techniques of myocardial protection, the perioperative clinical results provide suitable hard points to allow comparison with other series. Table 4 summarises studies of CABG performed with cardioplegic techniques in patients with severe LV dysfunction published since 1990 [1–3,19–22]. The operative mortality ranged from 4.8 to 15.0%. Our peri-

Table 4
Studies published since 1990 of CABG in patients with severe left ventricular dysfunction performed with cardioplegic techniques

First Author	No. of patients	Years	EF	30-day mortality (%)
Milano [1]	118	1981–91	≤ 0.25	11.0
Christakis [2]	487	1982–90	≤ 0.20	9.8
Kaul [3]	210	1987–92	≤ 0.20	10.0
Lansman [19]	42	1986–90	≤ 0.20	4.8
Sanchez [20]	23	1982–89	Mean 0.28	9.0
Blakeman [21]	20	1984–88	Mean 0.18	15.0
Wong [22]	22	1986–89	Mean 0.25	9.0

operative mortality of 2.8% compares favourably with these, even considering that some of the studies were conducted in patients with an ejection fraction of 20% or less.

As occurred with other studies [1–3,19], we have had a higher (38.3%) requirement for inotropic support than in our patients without LV dysfunction (7.6%), although only 11.2% of the patients required it for longer than 24 h. Besides the LV dysfunction, per se, one additional possible reason for this difference may be related to the fact that in this group of patients we may have had a greater tendency for 'prophylactic' use of inotropic agents, i.e. their use may not have been directly related to the presence of low-cardiac output in many instances. By contrast with other studies [1–3,19], we report a much lower use of IABP; it was utilised to assist weaning from cardiopulmonary bypass in only two patients, but in one it had already been inserted preoperatively.

The incidence of perioperative myocardial infarction, which is also a good clinical indicator of myocardial protection, was 2.8% in our series; this result is quite acceptable and even compares favourably with those of some other studies [2,22]. Although the incidence of cerebrovascular accidents was somewhat high, at 2.8%, we did not find any significant difference between the two techniques of myocardial preservation used (with or without aortic cross-clamping). Finally, the low incidence of other causes of morbidity, as well as the mean time of hospital stay (9.3 ± 6.4 days), also constitute good clinical benchmarks for a relatively smooth perioperative period and, presumably, are an index of good myocardial performance.

In conclusion, the results in this series appear to demonstrate that non-cardioplegic methods afford good myocardial protection and operating conditions with excellent applicability, even in patients with severe left ventricular dysfunction. They remain very usefully alternative techniques of myocardial preservation, and should be known to everyone who does coronary surgery.

References

[1] Milano CA, White WD, Smith R, Jones RH, Lowe JE, Smith PK, Jones RH, Lowe JE, Smith PK, Trigt PV. Coronary artery bypass in patients with severely depressed ventricular function. Ann Thorac Surg 1993;56:487–493.

[2] Christakis GT, Weisel RD, Fremes SE, Ivanov J, David TE, Goldman BS, Salerno TA. Coronary artery bypass grafting in patients with poor ventricular function. J Thorac Cardiovasc Surg 1992;103:1083–1092.

[3] Kaul TK, Agnihotri AK, Fields BL, Riggins LS, Wyatt DA, Jones CR. Coronary artery bypass grafting in patients with an ejection fraction of twenty percent or less. J Thorac Cardiovasc Surg 1996;111:1001–1012.

[4] Bonchek LI, Burlingame MW, Vazales BE, Lundy EF, Gasmann CJ. Applicability of non-cardioplegic coronary bypass to high-risk patients: selection of patients, technique, and clinical experience in 3000 patients. J Thorac Cardiovasc Surg 1992;103:230–237.

[5] Akins CW, Carroll DL. Event-free survival following non-emergency myocardial revascularization during hypothermic fibrillatory arrest. Ann Thorac Surg 1987;43:628–633.

[6] Flameng W. Intermittent ischemia. Semin Thorac Cardiovasc Surg 1993;5:107–113.

[7] Taggart DP, Bhusari S, Hooper J. Intermittent ischemic arrest and cardioplegia in coronary artery surgery: coming full circle? Br Heart J 1994;72:136–139.

[8] Antunes MJ, Bernardo JB, Oliveira JM, Fernandes LE, Andrade CM. Coronary artery bypass surgery with intermittent aortic cross-clamping. Eur J Cardio-thorac Surg 1992;6:189–194.

[9] Akins CW. Hypothermic fibrillatory arrest for coronary artery bypass grafting. J Card Surg 1992;7:342–347.

[10] Bonchek LI, Burlingame MW. Coronary artery bypass without cardioplegia. J Thorac Cardiovasc Surg 1987;93:261–267.

[11] Akins CW. Non-cardioplegic myocardial preservation for coronary revascularization. J Thorac Cardiovasc Surg 1984;88:174–181.

[12] Akins CW. Early and late results following emergency isolated myocardial revascularization during hypothermic fibrillatory arrest. Ann Thorac Surg 1987;43:131.

[13] Bonchek LI. Technical considerations for coronary artery bypass without cardioplegia. J Card Surg 1992;7:333–341.

[14] Tagart DP, Atari C, Wong P, Paul EA, Wright JE. Applicability of intermittent global ischemia for repeat coronary artery operations. J Thorac Cardiovasc Surg 1996;112:501–507.

[15] Anderson JR, Hossein-Nia M, Kallis P, Pye M, Holt DW, Murday AJ, Treasure T. Comparison of two strategies for myocardial management during coronary artery operations. Ann Thorac Surg 1994;58:768–773.

[16] Gerola LR, Oliveira SA, Moreira LP, Dallan LO, Delgado P, Luz PL, Jatene AD. Blood cardioplegia with warm reperfusion versus intermittent aortic cross clamping in myocardial revascularization. J Thorac Cardiovasc Surg 1993;106:491–496.

[17] Musumeci F, Feccia M, MacCarthy PA, Ellis GR, Mammana L, Brinn F, Penny WJ. Prospective randomized trial of single clamp technique versus intermittent ischemic arrest: myocardial and neurological outcome. Eur J Cardio-thorac Surg 1998;13:702–709.

[18] Casthely PA, Shah C, Mekhjiam H, Swistel D, Yoganathan T, Komer C, Miguelino RA, Rosales R. Left ventricular diastolic function after coronary artery bypass grafting: a correlative study with three different myocardial protection techniques. J Thorac Cardiovasc Surg 1997;114:254–260.

[19] Lansman SL, Cohen M, Galla JD, Machac J, Quintana CS, Ergin MA, Griepp RB. Coronary bypass with ejection fraction of 0.20 or less using centigrad cardioplegia: long term follow-up. Ann Thorac Surg 1993;56:480–486.

[20] Sanchez JA, Smith CR, Drusin RE, Reison DS, Malm JR, Rose EA. High risk reparative surgery, a neglected alternative to heart transplantation. Circulation 1990;82 (suppl 4):302–305.

[21] Blakeman BM, Pifarre R, Sullivan H, Constanzo-Nordin MR, Zucker MJ. High risk heart surgery in the heart transplant candidate. J Heart Transplant 1990;9:468–472.

[22] Wong JW, Tong MC, Ong KK. Coronary artery bypass in patients with impaired left ventricular function. Ann Acad Med Singapore 1990;103:1083–1092.