Coronary Artery Bypass Grafting for Multi-Vessel Coronary Disease on the Beating Heart: Comparative Study of 500 Patients

Antonis A. Pitsis, Nikolaos E. Mezilis, Petros S. Dardas, Dimitris D. Tsikaderis, Andreas I. Mpakas, Despina B. Deliaslani, Sola Z. Olalere, George D. Ioannidis, Emmanouel E. Diarmisakis

Cardiosurgical Institute of Thessaloniki, "Agios Loukas" Clinic, Thessaloniki

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Introduction: We present the mid-term results of coronary artery bypass grafting for multi-vessel disease on the beating heart in comparison to conventional surgery with the use of cardiopulmonary bypass.

Methods: We studied a total of 500 patients over a period of 14 months. Group A (on-pump) consisted of 240 pts, whereas Group B (off-pump) consisted of 260 pts. The following parameters were investigated: mortality, incidence of acute myocardial infarction and stroke at day 30, intubation time, blood transfusions, biochemical markers and the duration of hospitalization.

Results: There was a significant difference in the incidence of stroke, as well as in the increase of serum creatinine between group A and B (3% vs. 0% and 1 ± 0.4 vs. 0.9 ± 0.3 respectively). Patients operated on the beating heart had less need of inotropic support (62% in group A vs. 17% in group B), less transfusions (88% vs. 58%), spent less time in the Intensive Care Unit (2.21 days vs. 2) and in the Hospital (6.97 vs. 5.93).

Conclusions: Coronary artery bypass grafting on the beating heart is safer than on-pump surgery. Off-pump surgery is associated with fewer post-operative complications and quicker mobilization of patients when compared with conventional surgery.

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Correspondence:
Antonis Pitsis

Cardiosurgical Institute of Thessaloniki, "Agios Loukas" Clinic, 552 36 Panorama, Thessaloniki
e-mail:
apitsis@hotmail.com

The development of cardiac surgery in the last 30 years is directly related to the improvement of the techniques of Cardio-Pulmonary Bypass (CPB). However, CPB utilization constitutes one of the primary causes of perioperative complications[1]. These complications relate to hypoperfusion, cardioplegia administration with the potential of inefficient maintenance of left ventricular contractility and mainly to the interruption of normal blood flow to the aorta, with potential complications to the brain and the kidneys[2-5]. In an attempt to avoid the above-mentioned complications, there was recently a renewal of interest in the performance of Coronary Artery Bypass Grafting (CABG) without using CPB ("off-pump"), i.e. on the beating heart[6-8]. This technique, although was performed for the first time in the early days of coronary artery bypass surgery in the 60s, remained out of use in the following decades due to the development of the CPB and the use of cardioplegia. Certain important studies in recent years, however, have focused on this old technique[9] again. However, the access to deep areas that have to be revascularized remains problematic, as does the possibility of complete revascularization of the heart using arterial grafts. In this study, we present the mid-term results of CABG on patients with multi-vessel coronary artery disease (≥2 vessels) on the beating heart, in comparison to the results of "on pump" surgery. For this purpose, a comparative analysis was carried out on

various clinical and laboratory parameters of the patients during the first 30 postoperative days. The operations were carried out at our Institute during the last two years and, in a significant percentage of patients, the operation was performed with the use of a new technique of complete revascularization with arterial grafts only[10].

Material and methods

Patients and inclusion criteria

The study covers a period of 14 months (January 1999 - March 2000). During this period, CABG surgery was performed on 500 patients. During the first 6 months of the study, all patients were operated on with the use of CPB and administration of intermittent warm blood cardioplegia (Group A, n = 240). In the following 8 months of the study, all patients were operated off-pump on the beating heart (Group B, n = 260) and they represent 90% of the total number of patients operated on for coronary artery disease during the second period. Apart from the standard inclusion criteria for revascularization on the beating heart (appropriate coronary anatomy and coexistent pathological conditions that potentially increase mobility and mortality following the use of CPB)[11,12], we have extended such criteria to include a) older patients (>70 years old), b) patients with atheromatous aorta, c) reoperations and d) patients with severely depressed left ventricular function (ejection fraction <30%). Exclusion criteria initially included the presence of extensive atheromatous disease of the coronary vessels, moderate degree of aortic or mitral valve insufficiency and tachyarrythmias. Then, all patients that participated in the study had a CABG on the beating heart, regardless of the coronary anatomy.

Method of Anesthesia

The anesthesia protocol applied was the same for all patients. Following the placement of the patient on the operating table with a heating blanket underneath at 37˚C and with preheated gel pillows, induction to anesthesia was performed with the administration of bolus Midazolam 10-15mg and a maintenance dose of 0.1-0.3mg/Kg/h. Fentanyl was administered in a bolus intravenous dose 7.5-15μg/Kg and supplemented accordingly during the operation. Neuromuscular block was accomplished with the administration of Pancuronium bromide 0.1-0.15mg/Kg and continuous ventilation was maintained at a ratio of air/ oxygen 30:70. Heparin was intravenously administered at a dose of 100 IU/Kg to achieve an ACT between 290 to 340. Rotating the operating table to Trendelenburg position helped in certain cases (anastomosis of the circumflex artery) to maintain hemodynamic parameters.

Surgical Technique

For Group A, the operations were performed through a median sternotomy using intermittent hyperkalemic and hypermagnesemic warm blood cardioplegia according to an established protocol[12]. The temperature of the patient during CPB was maintained at 34˚C.

The revascularization technique of the circumflex coronary artery system (Figure 1) that we applied and we have already published,[13] was the following: the operating table was placed at a 20˚ Trendlenburg position and was rotated as much as possible to the right, towards the surgeon. Two folded umbilical tapes (2cm wide and 80cm long) were sutured with 0 silk suture, one at the border between the posterior and septal pericardium and the other at the level of the left upper pulmonary vein between the phrenic nerve and the midline. One of the ends of each tape was used to raise the posterior pericardium as much as possible and then it was fixed on the surgical field towards the assistant's side. In this way, the apex of the heart was turned to the midline and upwards. A mechanical stabilizer (Abbey Surgical, Surrey, UK) fixed directly to the sternal dilator

Figure 1. Revascularisation of the circumflex artery with the aid of a stabiliser.

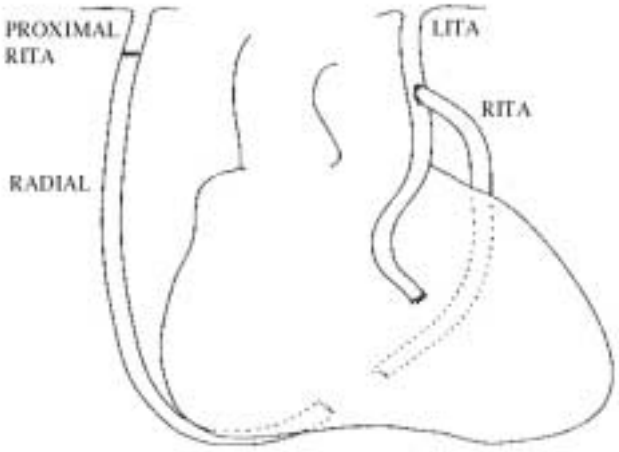

Figure 2. Schematic presentation of the technique of total revascularisation with the use of arterial grafts.
RITA: right internal thoracic artery.
LITA: left internal thoracic artery.

was used to support the heart in this position and to reduce the movement of the area in which the anastomosis was to be performed. Then, the arteriotomy was performed without using coronary snares. Instead, we introduced intraluminal shunts of appropriate size with the help of a carbon dioxide blower/humidifier. Anastomosis was performed in the usual fashion and the shunts were removed before tying the sutures.

In a significant percentage of patients, complete revascularization of the heart was accomplished with the use of arterial grafts only. One of the techniques used has been published in the past[10] and is shown schematically in figure 2.

Clinical and Biochemical Parameters

The main objectives of the study were to evaluate the mortality during the first 30 post-operative days as well as the in-hospital morbidity. In order to comparatively evaluate the morbidity of both methods, several clinical parameters were analyzed, a) the intubation time, b) the administration of inotropic drugs, c) the amount of blood transfusions, d) the incidence of acute perioperative myocardial infraction (MI) and e) the incidence of stroke. The postoperative diagnosis of MI was based on the presence of two out of three standard criteria: a) increase of the creatine kinase myocardial fraction (CK-MB) value by more than 30% of the total value of CK, and b) development of a new pathological Q-wave. The development of a local or atypical precordium pain was not considered an MI criterion. The biochemical markers that were included in the analysis were a) creatinine kinase myocardial fraction (CK-MB) value, and b) serum creatinine value (Cr). During the intensive care unit (ICU) stay, blood and plasma transfusions, intubation time and hospitalization days both in ICU and in the hospital in total, were also studied.

Statistical analysis

The data is presented as a mean value ± standard deviation (mean ± SD). The values were compared using Student's t-test and the qualitative characteristics were compared using a chi-square test. Comparisons between the two groups were made in the basic clinical characteristics such as gender, age, number of diseased vessels and left ventricular ejection fraction. A limit of statistical significance was considered the value of 5% ($p < 0.05$).

Results

Table 1 shows the basic clinical characteristics of the two groups. There were no differences between the two groups as regards gender, age, severity of the coronary artery disease, ejection fraction and preoperative biochemical parameters. The total number of grafts used in Groups A and B was 2.7 ± 0.4 and 2.6 ± 0.5 respectively, while the number of arterial grafts was 1.6 ± 0.5 and 1.7 ± 0.8 respectively, hence such differences were not statistically significant.

Table 2 summarizes the results regarding the main objectives of the study. There were no significant statistical differences in mortality at 30 days, or the time of acute MI incidence between the two

Table 1. Characteristics of patients.

	CPB CABG Group A (n=240)	OP CABG Group B (n=260)	p value
Men	205 (85%)	210 (80%)	NS
Age	63,7±7,9	64,0±10,1	NS
Unstable angina	148 (62%)	166 (64%)	NS
Ejection fraction			
Good (EF > 50%)	165 (69%)	170 (65%)	NS
Moderate (EF 30% - 50%)	60 (25%)	75 (29%)	NS

CPB CABG = cardiopulmonary bypass coronary artery bypass surgery
OP CABG = off pump coronary artery bypass surgery
EF = ejection fraction.

Table 2. Clinical and laboratory parameters of patients during and after surgery.

	CPB CABG Group A (n=240)	OP CABG Group B (n=260)	p value
Inotropic	148 (62%)	45 (17%)	< 0,0001
CK-MB	37 ± 78	18 ± 23	< 0,0001
Serum Creatinine	1 ± 0.4	0,9 ± 0,3	< 0,009
AMI	6 (2,5%)	3 (1,1%)	NS
Stroke	7 (3%)	0	< 0,03
30-day mortality	5 (2%)	1 (0,4%)	NS

CPB CABG = cardiopulmonary bypass coronary artery bypass surgery
OP CABG = off pump coronary artery bypass surgery.

groups. Significant differences were observed in the biochemical markers of the study, such as the increase of CK-MB and serum creatinine levels. A significant clinical finding was the absence of strokes in Group A and less inotrope utilization than Group B patients.

During the stay in the intensive care unit (ICU), intubation time and blood and plasma transfusion requirements were less for Group B patients (Table 3). Finally, both the stay in the ICU and the stay in the hospital were significantly reduced for Group B patients.

For 55% of the patients, total arterial revascularization was achieved using arterial grafts only. Figure 3 illustrates radial artery anastomosis at the right

Table 3. Comparison of parameters during treatment in the Intensive Care Unit.

	CPB CABG Group A (n=240)	OP CABG Group B (n=260)	p value
Intubation time (hours)	9,96 ± 6,48	6,10 ± 2,3	< 0,01
Erythrocytes transfusions (units)	1,13 ± 1,28	0,13 ± 0,35	< 0,001
Plasma transfusions (units)	1,1 ± 1,68	0,07 ± 0,37	< 0,01
Patients without transfusion	51 (22%)	110 (42%)	< 0,01
Treatment in ICU (days)	2,21 ± 0,41	2,00 ± 0,00	<0,01
Hospitalization days	6,97 ± 1,92	5,93 ± 1,53	< 0,0001

CPB CABG = cardiopulmonary bypass coronary artery bypass surgery
OP CABG = off pump coronary artery bypass surgery.

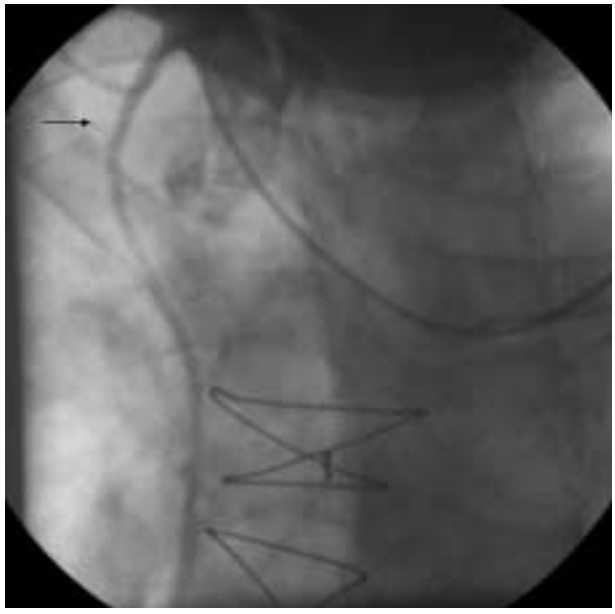

Figure 3. Angiography of a patient post revascularisation: the arrow shows the point of the anastomosis of the radial artery with the proximal part of the right internal thoracic artery.

internal mammary artery stump from a patient's coronary arteriogram in the context of an angiographic study for the evaluation of graft patency on the beating heart, that is in progress in our Laboratory.

Discussion

Off-pump CABG on the beating heart tends to become a routine operation for most cardiosurgical centers[11,14-16]. The development of mechanical stabilizers that stabilize the field to be revascularized, now enables the anastomosis to be performed with excellent precision, avoiding any complications of CPB. However, up to now, one of the main disadvantages of the technique is the difficulty of its application in bypassing arteries of the inferior and posterior wall of the left ventricle.

In this study, we have included patients that were operated on following the new technique without excluding patients with right and circumflex coronary artery disease. We have shown in the past that the revascularization of these areas is possible with excellent immediate results[13]. The quality of the anastomosis using the technique of "verticalization" of the heart, i.e. its displacement towards the midline and upwards, has been evaluated angiographically by Cartier et al[15] on 12 patients and the graft blood flow

was found to be excellent according to standard criteria.[17]

Our results show that the immediate post-operative mortality for the two techniques and the incidence of MI during the first 30 post-operative days did not differ significantly (2% vs 0.4%, and 2.5% vs 1.1%, respectively), although there was a decreasing trend for Group B possibly due to the need for a larger sample in order to demonstrate such differences. These findings are in accordance with other large studies[11,14], although the rates differ, perhaps due to the presence of differences as regards the basic clinical characteristics of the patients studied. It is worthwhile mentioning that in our study we included patients consecutively and excluded only those patients for whom it was impossible to collect and record any post-operative data.

It is important to point out the significant difference of the two techniques regarding the incidence of post-operative stroke. Other studies have demonstrated differences in the incidence of cerebral events, but without reaching any statistically significant differences[11]. Since the appearance of such events is directly related to the presence of extensive atheromatosis of the ascending aorta and the carotids, larger multi-center studies may be needed to demonstrate such differences, although most researchers would agree upon the fact that the ischemic attacks are rather rare for operations on the beating heart.

The differences in the administration of inotropic drugs, intubation time and transfusion requirements were significant. Group B patients clearly needed less inotropic solutions and blood transfusions after the operation, a finding that is consistent with that of other researchers[11].

As regards the biochemical parameters, we observed a significant difference in CK-MB values for patients operated on the beating heart. Although this finding is directly related to the number of perioperative MIs, it seems that the cardioplegia administered to patients on whom CPB is used, greatly affects the post-operative increase of myocardial enzymes. The difference in post-operative creatinine values of the patients of two groups is also significant. There are several causes of the post-operative renal dysfunction, including the use of CPB, the hypoperfusion of the kidneys and the release of substances with a toxic effect on kidneys[18]. The renal function is a parameter that has been recently studied and the data to-date show a clear superiority of off-pump surgery on the beating heart versus CPB surgery with respect to maintenance of normal creatinine clearance values[19].

In conclusion, our study shows that off-pump surgery on the beating heart can be safely performed on the majority of patients. Compared to the use of CPB, patients develop fewer complications and have a better post-operative biochemical profile. In particular, the beating heart is related to a dramatic decrease in the development of post-operative ischemic attacks and the length of stay of the patients in the ICU and in the hospital in total. During the last 2 years, the technique has been applied in our hospital to 94% of our patients and 1250 subjects had been operated on the beating heart by December 2000. What remains to be confirmed is the quality of the anastomoses and the long-term patency of the grafts, i.e. two parameters that are the subject of reserch for many centers, including our own.

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