Two-Year Experience with Integrated Myocardial Management

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BÜTÜNLENMİŞ MİYOKARD KORUNMASINDA İKİ YILLIK KLİNİK DENEYİM

Kalp cerrahisinde uzun süreli yarar sağlayacak teknik açıdan mükemmel bir ameliyatı gerçekleştirmek için intraoperatif hasarı sınırlayacak çeşitli teknikleri bilmek ve kullanmak gerekmektedir. Bu yazımızda son iki yılda bütünlenmiş miyokard korunması kullanılarak ameliyat edilen ardışık bir dizi olgudaki deneyimlerimizi aktardık. Yapılan bir ön çalışmada, bütünlenmiş miyokard korunmasının kristalloid kardiyoplejiyle karşılaştırıldığında hasta morbiditesini anlamlı şekilde düşürdüğü saptandı. Bütünlenmiş miyokard korunması uygulanan 214 olgunun 162 (%75.7) sine izole koroner bypass cerrahisi, 13 (%6.1) üne koroner bypass cerrahsi ile birlikte ilavegirişim ve 39 (%18.2) una ise kapak replasmanı uygulandı. Her olgu için ortalama beklenen yaklaşık mortaliteyi saptamak için Parsonnet risk strafikasyonu skorlama sistemi kullanıldı. 23 olguda (%10.7) 30 majör komplikasyon gözlendi. Bu olguların 19 u yüksek risk (risk skoru >4) grubundaydı. Koroner bypass olguları için hastanede kalış ortalama süresi 8.6 gün iken, bu süre kapak hastaları için 8.8 gün olarak belirlendi. Skorları 0 ile 4 arasında olan (düşük risk) 86 koroner bypass olgusunda beklenen mortalite 1.3±1.6 iken gözlenen mortalite 1 olgu ile %1.2 olarak gerçekleşti. Koroner bypass olgularında genel mortalite %4.57, kapak olgularında ise %0 olarak saptandı. Tüm olgular ele alındığında ise beklenen ve gerçekleşen mortalite oranları sırasıyla 7.1±6.5 ve 3.7 idi. Sonuç olarak, bütünlenmiş miyokard korunması birçok farklı miyokard koruma tekniklerinin kısıtlamaları ve dezavantajlarını çözüp bu tekniklerin yararlı bölümlerini birleştirerek maksimum yararı sağlayan bir yöntem olarak karşımıza çıkmaktadır.

Anahtar kelimeler: *Kalp cerrahisi, kardiyoplejik solüsyonlar.*

There is a trend toward fewer elective and more urgent operations, increasing age, and a decreasing ejection fraction in patients undergoing cardiac surgery in recent years (1). Blood cardioplegic strategies have been shown to increase myocardial oxygen uptake, repay depleted energy stores, and improve myocardial function and survival in high-risk subset of patients (ie, cardiogenic shock, extending myocardial infraction, hemodynamic instability) undergoing cardiac surgery (2). Cardioprotective strategies, like cardiac operations, have evolved to the point that it is essential to underst and use various techniques to obtain the desired result of limitation of intraoperative damage during completion of a technically perfect operation that offers the best long-term benefit. Integrated myocardial management (IMM), first described by Buckberg and associates (3), combines the advantages of various techniques which compensates for their individual shortcomings. It incorporates the strategies of warm/cold blood cardioplegia, antegrade/retrograde delivery, continuous/intremittent infusion, and blood/blood cardioplegic perfusion during a single period of aortic clamping. The overriding principle is the marriage of cardioprotective strategies to conduct the operation so that the surgeon can work without interrupting the continuity of the operation. This procedure (1) provides unimpaired vision, (2) avoids unnecessary ischemia and cardioplegic overdose, (3) allows aortic clamping as soon as cardiopulmonary bypass is begun, (4) permits aortic unclamping and discontinuation of bypass shortly after the technical aspects of the operation are complated, (5) minimizes the duration of ischemia and cardiopulmonary bypass, (6) allows single aortic crossclamping in coronary artery bypass graft (CABG) operations and (7) maximizes the positive attributes of the strategies available currently.

Based on a recent survey of 1413 surgeons in the United States (4), blood cardioplegic solution is preferred by the great majority (72.2%), and of the major cardioplegic solution types, the Buckberg formulation is the most frequently chosen among blood cardioplegia users. In this report we present our two-

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year experience in a consecutive series of patients in whom IMM was undertaken.

PATIENTS and METHODS

In a preliminary study we compared IMM with cold crystalloid cardioplegia in patients undergoing CABG (Table 1-3). After this study a total of two hundred fourteen patients underwent cardiac operations by one surgical team in Siyami Ersek Thoracic and Cardiovascular Surgery Center from February 1994 through March 1996. Patient characteristics, operative data, and operative procedures are summarized in Table 4 and Table 5. The Parsonnet risk stratification scoring system was used to determine the approximate predicted mortality for each patient [5].

Operative Procedure

Unless there is a contraindication, all coronary patients receive ß- blockers, Ca-antagonists and nitrates and all valve patients receive digoxin and diuretics until the date of the operation. After anesthetic induction, patients are intubated and hemodynamic monitoring lines including a flow directed thermodilution cathater are established. After internal thoracic artery long saphenous veins are harvested in CABG patients heparin is administered. A retrograde cardioplegia cannula is inserted to the coronary sinus using a right atrial technique after aortic and venous cannulation. An antegrade cannula containing a port for venting, and delivering cardioplegic flow is used routinely. This cannula is placed in the high right corner of the aorta, just proximal to the proposed site of the aortic clamp. This site is not used for construction of the proximal anastomosis. Then the patients are placed on cardiopulmonary bypass. Centrifugal pumps and membrane oxygenators are used in all operations. The aorta is crossclamped as soon as cardiopulmonary bypass is established. Systemic temperature is allowed to drift to ~ 32°C. Cold blood cardioplegic solution is delivered antegrade and retrograde intermittantly with the use of continuous cold blood (without cardioplegia) where applicable. Warm induction is used in high-risk patients (i.e. cardiogenic shock, evolving myocardial infarction). A warm terminal reperfusate followed immediately by warm retrograde noncardioplegic blood infusion is delivered in all patients. Cardiopulmonary bypass is usally discontinued a few minutes after aortic unclamping. In CABG operations, a single aortic crossclamp period is used in all patients. The distal and proximal anastomoses are constructed sequentially with aorta fully clamped.

Definitions

Diabetes was considered to be present if the patient was being treated with oral medication or insulin. Hypertensive patients were included if the patient had a history of high blood pressure frequently exceeded 140/90 mmHg. or if the patient was taking antihypertensive medications. Left ventricular ejection fraction was determined from the angiographic ventriculogram and confirmed with echocardiography and/or radionuclide multigated acquisition when it was than 0.40. A stress thallium scan was also obtained in patients with left ventricular ejection fraction less than 0.40, to look for reversible myocardial ischemia. Reoperative cases were defined as patients who had undergone an open heart procedure previously. The priority of operation was assesed by the cardiothoracic surgeon using previously described definitions [6]. Briefly, emergent means that medical factors relating to the patient's cardiac disease dictated that operation should be performed within hours to prevent morbidity or death; urgent means that medical factors required the patient to stay in the hospital for an operation before discharge; and elective means that medical factors indicated the need for operation, but the clinical situation allowed discharge from the hospital with readmission at a later date. Low cardiac output syndrome was defined as a cardiac index of 2 $L \cdot min^{-1} \cdot m^{-2}$ or less or the need of positive inotropic agents or use of an intraaortic balloon pump to maintain a cardiac index of $2L \cdot min^{-1} \cdot m^{-2}$ higher or a systolic blood pressure of 90 mmHg or higher. Inotropic support was defined as any inotropic infusion other than digoxin or calcium. Inotropic support was used in patients with unstable hemodynamic parameters and intra aortic balloon counterpulsation was used in patients requiring increasing doses or more than two inotropic agents. Perioperative myocardial infarctions were diagnosed if the creatine kinase myocardial isoenzyme level was greater than 60 IU, or appearance of electrocardiographic changes including new Q waves or loss of R waves (more than 25 % reduction in at least two contiguous leads). Respiratory distress was defined as the need for ventilatory support exceeding 48 hours or the need for reintubation, or pulmonary infection. Cerebral injury was defined as a new focal central nervous system deficit postoperatively that persisted for more than 24 hours. Length of stay was calculated from the time of operation to time of discharge. Mortality includes all patients who died within 30 days of operation or within the same hospitalization.

RESULTS

In the preliminary study the IMM group of patients had slightly higher clinical risk scores than crystalloid cardioplegia group (Table 2). However, IMM reduced patient morbidity by decreasing myocardial infarction, respiratory distress and wound infection rates significantly in patients with higher risk (Table 3). Length of hospital stay was also less in patients operated on with IMM compared with crystalloid cardioplegia. This preliminary study has led us to the intensive use of IMM especially in patients with higher risk. Also, it seemed to us that it was impossible to go further with this study for ethical reasons. After obtaining the results of the preliminary study, all patients with high risk scores had been operated on with IMM.

Of the 214 patients operated with IMM. 162 (75.7 %) had undergone isolated CABG, 13 (6.1 %) had CABG and additional procedures, and 39 (18.2 %) had valve replacements (Table 4). 13 patients who

Table 1. Patient characteristics

	IMM (n=74)	CC (n=61)	p value*
Patient characteristics			
Mean age ± SD (yr)	56±9	58±10	NS
Women	10 (13.5 %)	13 (21.3 %)	NS
Diabetes	12 (16.2 %)	17 (27.9)	NS
Hypertension	20 (27 %)	25 (41 %)	NS
Left main trunk ≥ 60 % occlusion	3 (4 %)	0	NS
EF < 0.30	14 (18.9 %)	5 (8.2 %)	0.08

* Student's t test

CC = Crystalloid cardioplegia, IMM = integrated myocardial management, NS = not significant

Table 2. Clinical risk scores

	IMM (n = 74)	CC (n = 61)	p value *
0-4 (lower risk)	46	35	NS
median	1.1 ± 1.6	0.9 ± 1.4	NS
5-10 + (higher risk)	28	26	NS
median	10.1 ± 4.9	8.4 ± 3.8	NS

* Student's t test

CC = Crystalloid cardioplegia, IMM = integrated myocardial management, NS = not significant

did not have CABG or valve operations included 5 congenital cases (0% mortality), 3 patients operated for acute aortic arch dissection (67 % mortality), 3 patients for acute dissection of ascending aorta (0% mortality), and 1 patient operated for post infarction VSD (100 % mortality).

Nearly, one third of the patients undergoing CABG had severe left ventricular dysfunction, and almost 20 % had their operations on the urgency and emergency basis (Table 5). 91 % of the CABG patients received internal mammary artery grafts solely to their left anterior descending artery. Overall, the CABG patients had a mean crossclamp time of 72+22 minutes for a mean of 3.1+1 distal anastomosis per patient and valve patients occur by necessity

Table 4. Operative procedures

Operative procedures	n (%)
CABG	**175 (81.8 %)**
Isolated CABG	162 (75.7 %)
CABG and additional procedures	13 (6.1 %)
+ peripheral vascular surgery	4 (1.9 %)
+ AVR	6 (2.8 %)
+ MVR	2 (0.9 %)
+ AVR + MVR	1 (0.5 %)
Valve	**39 (18.2 %)**
MVR	25 (11.7 %)
AVR	7 (3.3 %)
AVR + MVR	7 (3.3 %)
Total	**214 (100 %)**

AVR = Aortic valve replacement; CABG = Coronary artery bypass grafting; MVR = Mitral valve replacement.

with the single clamp method because the proximal anastomoses for vein grafts are performed with the aorta fully occluded. In the beginning of our practice cardiopulmonary bypass time tended to be higher, however, with the experience gained by the surgical team, cardiopulmonary bypass time rarely exceeds crosslamp time more then ten minutes, currently.

Table 6 shows the prevalance of major morbidity and arrhytmia in CABG and valve patients. Overall, 23 patients (10.7 %) had 30 major complications. 19 of these patients were in the high-risk (>4) group. Stroke was encountered in two patients, and one of these patients was in the low-risk group who constituted the only death in this subset of patients. Indeed, this patient awakened without any neurologic deficit. However at the sixth postoperative hour, a massive bleeding occured resulting from a suture dehiscence of a side branch of a saphenous graft during an hypertensive attack. The patient was resuscitated in the intensive care unit, but developed right sided hemiplegia and died at eighth postoperative day. Among those with clinical scores of 0 to 4 (lower

Table 3. Results of integrated myocardial management and crystalloid cardioplegia adjusted for clinical risk score

	Risk score 0 - 4			Risk score 5 - 10 +		
	IMM (n=46)	CC (n=35)	p value *	IMM (n=28)	CC (n=26)	p value *
Hospital death (%)	0	0	NS	3.6	7.7	NS
Patient morbidity (%)	8.7	2.9	NS	0	34.6	0.0006
Myocardial infarction /IABP use (%)	4.3	0	NS	0	19.2	0.004
Stroke (%)	0	0	NS	0	3.8	NS
Return for bleeding (%)	4.3	0	NS	0	0	NS
Respiratory distress (%)	0	2.9	NS	0	19.2	NS
Wound infection (%)	2.2	0	NS	0	15.4	0.04
Renal failure (%)	0	0	NS	0	3.8	NS
Length to hospital stay (days)	8.8±2.5	9.3±1.7	NS	9.2±2.4	11±3.1	0.02

* Fisher's exact test

CC = Crystalloid cardioplegia, IABP = intraaortic balloon pump, IMM = integrated myocardial management, NS = not significant

Table 5. Patient characteristics and operative data

	CABG (n = 175)	Valve (n = 39)
Patient characteristics		
Mean age ± SD (yr)	57.5 ± 8.5 (33-74)	43.1 ± 13 (10-65)
Age≥70	24 (13.7 %)	-
Women	23 (13 %)	19 (48.7 %)
Diabetes	45 (26 %)	-
Hypertension	72 (41 %)	2 (5.1 %)
Left main trunk ≥ 60 % occlusion	27 (15.4 %)	-
EF < 0.30	56 (32 %)	56 (32 %)
EF = 0.30-0.40	8 (4.6 %)	4 (10.3 %)
EF > 0.40	111 (63.4 %)	30 (77 %)
Operative data		
Emergent	11 (6.3 %)	3 (7.7 %)
Urgent	23 (13.1 %)	0
Elective	141 (80.6 %)	36 (92.3)
Reoperation	2 (1.1 %)	4 (10.3 %)
Distal anastomosis/patient (mean±SD)	3.1 ± 1 (-5)	-
Use of internal mammary artery	159 (91 %)	-
Cross clamp time (min.) (mean±SD)	72 ± 22 (20-120)	86 ± 27 (46-149)
CBP time (mean+SD)	99 ± 21 (30-190)	107 ± 32 (60-213)

CABG = Coronary artery bypass grafting; CPB = Cardiopulmonary bypass; EF = Ejection fraction; SD = Standard deviation.

Table 6. Patient morbidity

Patient morbidity	CABG (n = 175)	Valve (n = 39)
Major morbidity		
Low cardiac output	11 (6.3 %)	0
Inotropic support	11 (6.3 %)	0
IABP	9 (5.1 %)	0
Perioperative myocardial infarction	1 (0.6 %)	0
Respiratory distress	5 (2.9 %)	0
Cerebral injury	2 (1.1 %)	0
Wound infection	5 (2.9 %)	0
Return for bleeding	4 (2.3 %)	1 (2.6 %)
Renal failure	1 (0.6 %)	0
Arrhythmia		
Atrial arrhythmia	6 (3.4 %)	2 (5.1 %)
Ventricular arrhythmia	4 (2.3 %)	1 (2.6 %)

IABP = intraaortic balloon pump

Table 7. Overall predicted and observed mortality

Risk score	(n)	Predicted Mortality (%)	Observed Mortality %
CABG			
(0-4) low risk	86	1.3 ± 1.6	1.2
(5+)	89	11.6 ± 5.7	7.9
Valve	39	9.9 ± 4.8	0
Total	214	7.1 ± 6.5	3.7

CABG = Coronary artery bypass grafting

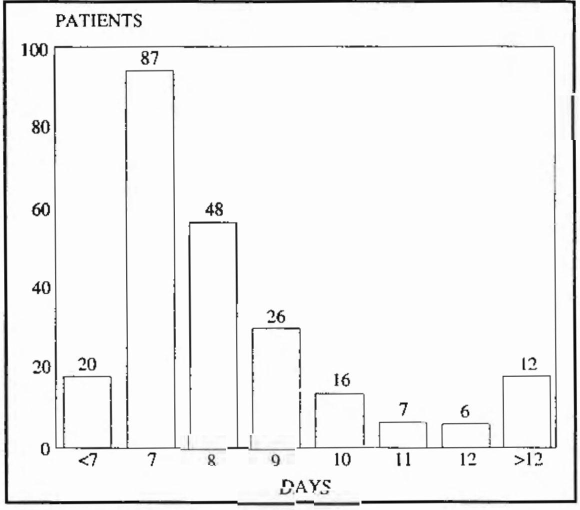

Figure 1. Length of hospital stay

risk) in whom the predicted mortality was 1.3±1.6, 1 of 86 (1.2 %) patients undergoing CABG died (Table 7). For those with severity scores of >5 (higher risk) in whom the predicted mortality was 11.6±5.7, the observed mortality was 7.9 % (7 of 89 patients). Overall mortality was 4.57 % for the CABG patients, and 0 % for the valve patients.

The median lenght of hospital stay was 8.6 days for the CABG patients, and 8.8 days for the valve patients. A great majority of the patients were discharged at 7th or 8th postoperative day (Figure 1)

DISSCUSSION

In myocardial revescularization, the limitations of antegrade delivery of cardioplegia for myocardial protection result in inadequate and inconsistent distribution of cardioplegia distal to coronary artery obstructive lesions (7-9). The study of specific markers in circulating blood samples of myocardial suffering observed during ischemia-reperfusion phenomena have been shown that myocardial protection offered by antegrade/retrograde cardioplegia was significantly better than that observed with antegrade cardioplegia alone (10). Retrograde cardioplegia affords more homogenous distribution of the cardioplegic solution to the left ventricular microcirculation especially in case of obstructive coronary lesion (7,10,11,12), and endocavitary cooling of the right ventricle by the cardioplegic solution diverted from the arterial network through the thebesian veins and arteriorvenous shunts (13).

Continuous warm blood cardioplegia as described by Litchenstein and associates (14), has become extremely popular in a very short time, with the hope of being the "perfect" from of myocardial protection. However, there are disadvantages to the warm blood technique. Dislodgement of coronary sinus catheter leads to inadequate or even absent delivery of blood to the myocardium with resultant warm ischemic arrest. Difficulties in obtaining and maintaining complete electromechanical arrest, difficulty in visualizing the distal coronary anastomoses, increased incidence of peripheral vasodilation [15,16], and increased rate of neurologic damage [17] are the other drawbacks of warm heart surgery.

However, cold blood cardioplegia, lower myocardial oxygen demands and the rate and development of ischemic damage when blood supply must be interrupted to provide the technical advantages of a quiet, dry operative field, or becomes maldistributed due to coronary obstruction and/or retrograde routes of administration. Peripheral vasodilation is not encountered frequently because of the use of mild hypothermia.

The conventional way of constructing CABGs, consisting of the differential application of a totally occluding clamp to construct the distal anastomoses and a partially occluding clamp to construct the proximal anastomoses, is the one widely practiced by most surgeons today. The routine use of an aortic to myocardial and cerebral protection. This is especially true for elderly patients. Quantitative ultrasonic techniques in an elderly cardiac surgical population have revealed atherosclerotic disease of the ascending aorta in half of the patients [18]. Recently Blauth and associates [19] in a postmortem study identified embolic disease in 69 adults having cardiac surgery. Atheroemboli were more common in patients undergoing coronary artery procedures (26%) than in those undergoing valve procedures (9%), and more so with advanced age, peripheral vascular disease, and ascending aortic atherosclerosis. An alternative technique was described by Salerno [20], in which the distal and proximal anastomoses are constructed during a single period of total aortic occlusion. This technique has been shown to decrease stroke rates secondary to atheroembolism resulting from manipulation of and trauma to the ascending aorta [21,22]. The advantages of the single cross-clamp in terms of myocardial protection may be related to the more homogenous cardioplegia delivery and myocardial cooling associated with its use, and to the synchronized rewarming and maximal reperfusion that take place upon removal of the clamp. This reduces the incidence of reperfusion injury and allows for better myocardial recovery [22]. Myocardial protection with IMM allows safe time for this single-clamp strategy.

IMM has also been shown to decrease the time in the intensive care unit and length of hospitalization and reduce myocardial infarction, and respiratory and wound complications [21].

Another advantage of the IMM is its versatility. The surgeon can work without interrupting the continuity of the operation and the principles are similar for all cardiac procedures.

In a recent study [23], we have documented that in elective first time coronary artery bypass grafting where overall ventricular function is good, crystalloid cardioplegia and intermittent aortic crossclamping techniques afford good myocardial protection, and can be performed with very low mortality, morbidity, and acceptable length of hospital stay. However, as the risk profile for patients undergoing open heart surgery changed in recent years (ie, increased age, poor left ventricular function, increased number of emergency operation) we deviated from above mentioned techniques to IMM in these subgroup of patients. Our preliminary study, comparing IMM and crystalloid cardioplegia has also showed that in low risk patients undergoing CABG IMM was not superior to crystalloid cardioplegia. However, in high risk patients IMM reduced patient morbidity and length of hospital stay, significantly.

A recent survey of more than 1400 surgeons in the United States, showed that 72 % of the respondents use blood cardioplegia and 60 % use a combination of antegrade and retrograde route as the primary method of cardioplegia delivery [24].

In summary, IMM combines the advantages various techniques which compensates for their individual shortcomings. It is associated with a demonstrable and favorable effect on outcome, especially in high risk patients. However, prospective, randomized studies comparing clinically defined end points, morbidity and cost effectiveness in larger series of patients are still lacking.

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