REPERFUSION STRATEGY AFTER REGIONAL ISCHEMIA. CLINICAL APPLICATION:EXPERIENCE IN 37 EVOLVING PHASE MYOCARDIAL INFARCTION

N. T. OĞUŞ, MD,
M.H. US, MD,*
T. YILDIRIM, MD,
V. ERENTUĞ, MD,***
H. OĞUŞ, MD,**
Ö. IŞIK, MD

From:
Maltepe University Faculty of Medicine Cardiovascular Surgery Department
*GATA Haydarpaşa Research Hospital Cardiovascular Surgery Department
**Koşuyolu Heart Research and Education Hospital Anesthesia and Reanimation Department
***Koşuyolu Heart Research and Education Hospital Cardiovascular Surgery Department, Türkiye

Adress for reprints:
Dr. Noyan Temuçin Oğuş
Nuhkuyusu C. Pişkinler S.
Aykent Sitesi D Blok D.20
Altunizade
Üsküdar-İstanbul
Tel: 0216 3431827
Fax: 0212 4145111
e-mail:
togus@superonline.com

Provision of suitable reperfusion conditions may prevent the reperfusion injury in the emergency revascularization of patients with evolving myocardial infarction (EMI). Our previous experimental studies showed that ensuring low reperfusion pressure in the first two minutes of reperfusion is the main effective component of controlled reperfusion and even integrated cardioplegia application. Initially applied low reperfusion pressure may prevent the stunning of the myocardium.

In this clinical study; we present the preliminary results of 37 emergency revascularization cases in which reperfusion period pressure was controlled only in the first two minutes of reperfusion. The time between the onset of EMI and the beginning of operation was between 3-6,5 hours. Four patients had cardiac failure, 6 had life threatening rhythm disturbances, 9 had inotropic or mechanical cardiac support, and 3 patients were being mechanically ventilated because of pulmonary edema.

Following completion of the revascularization procedures, pressure controlled tepid reperfusion (PCTR) was applied. Spontaneous sinus rhythm could be maintained in 31 (83.7 %) patients. Recovery time was 9±2,3 minutes. CK-MB levels of the patients decreased from the preoperative values of 74±17 to 65±16 IU within the first 24 hours of the operation. We didn't observe any reperfusion-related arrhythmia or any ECG change suggesting infarct expansion. Seven patients required additional inotropic and 2 patients required mechanical support postoperatively. No hospital mortality occurred and all patients were discharged between 7-13 days. During follow-up, echocardiographic assessments revealed that wall motion of infarcted areas was almost totally preserved.

In this study we concluded that, PCTR technique is successful in the prevention of the reperfusion injury; it is easy to establish, and it does not require any additional equipment and it allows direct anastomosis of the left internal thoracic artery to the left anterior descending artery.

Key Words: Pressure Controlled Tepid Reperfusion, Emergency, Revascularization, LITA

In the current era, advancement in myocardial protection and better understanding of the underlying mechanisms of reperfusion injury allows us to operate high risk emergency cases in the evolving phase of myocardial infarction (EMI) successfully, even after 8 hours of myocardial infarction (1) Modifying the composition and delivery conditions of cardioplegia and reperfusion have been investigated in severely energy depleted hearts, such as in patients EMI, with congestive heart failure, in patients who undergo multiple procedures, who require prolonged aortic cross clamping time and who has severely cyanotic congenital heart disease (1,2,3). Buckberg et collegues and other investigators have done large numbers of studies on prevention of reperfusion injuries since late 1970s. New surgical strategies are still being investigated. The substrate enriched (modified) blood solutions that are used for cardioplegia and reperfusion have been experimentally and clinically shown to be beneficial (3,4,5). However technical difficulties encountered in practice and problems related to the availability of some components limited worldwide utilization of these techniques and protocols.

In this preliminary report, we are presenting the clinical results of a simplified reperfusion technique, in which only the reperfusion pressure of the first 2 minutes is controlled in order to prevent reperfusion injury.

MATERIAL AND METHOD

In the past, cases with evolving myocardial infarction were operated in our clinic with the similar technique described by Buckberg and colleagues (5). Figure 1 shows schematically this technique. In order to obtain warm controlled aortic root perfusion, a blood reservoir (R), two additional pumps (one for venting and one for the delivery of the antegrade/retrograde cardioplegia and final reperfusate), two lines that were connected to a transducer for pressure monitoring of antegrade and retrograde perfusate (P1, P2), and a heat exchanger were utilized. We constructed a systemically closed aortic root reperfusion technique, thus we performed a saphenous vein anastomosis between ascending aorta and left anterior descending artery and anastomosed the left internal thoracic artery (LITA) to the distal part of the saphenous vein graft. Controlled aortic root reperfusion was performed while there is a bulldog clamp on LITA and following completion of controlled aortic root reperfusion we interrupted the vein graft with ligation and allowed the LITA to perfuse the LAD via a short vein graft. The reperfusate composition was as described in our previous study; it was enriched with glucose, citrate, glutamate and aspartate.

Our first application of this modified and simplified technique was in April 1996. The first practice was an obligatory application due to the absence of Glutamate-Aspartate solution in the hospital. Between April 1996 and April 2000, 40 patients with evolving myocardial infarction were operated by the use of this simplified technique. Following the initial 3 successful operations, a prospective clinical study was carried out in 37 consecutive patients. Preoperative characteristics of patients are presented in Table 1. In one patient the left main coronary artery; and in 36

Table I. Preoperative Characteristics of Patients.

Age	66±5,6 (range: 47 -73)
Gender	
Male	27 (73%)
Female	10 (27%)
Time interval between AMI and emergency operation	4,8h (range: 3-6,5h)
Hemodynamic Status in Operating Room	
Stable	16 (43%)
Unstable	21 (57%)
Cardiogenic shock	4 (10,8)
LTRD	6(16,2%)
IABP support	4 (10,8%)
Inotropic support	5 (13,5%)
Intubated (APE)	3 (8,1%)
Diseased vessels	
One vessel disease	3 (8,1%)
Two vessel disease	3 (8,1%)
Triple vessel disease	31(83,7%)
LMCAS	4(10,8)
Left ventricular ejection fraction	39,4 % (range: 33-51%)

AMI: Acute myocardial infarction, LTRD: life treating rhythm disturbances. IABP: Intra-aortic balloon pump. APE: Acute pulmonary edema. LMCAS: Left main coronary artery stenosis

patients the left anterior descending artery was occluded.

Patients who were operated in a stable or unstable condition did not differ in terms of the utilisation of midazolam, fentanyl, etomidate or vecuronium bromide in the induction of anesthesia. For all patients, following the midline sternotomy, immediate cannulation, establishment of cardiopulmonary bypass (CPB) and subsequent cooling was performed. Aortic cross clamp (XC) was placed and initial antegrade warm cardioplegic blood was administered with 75-100 mmHg aortic root pressure and at an induction dose of 10ml/kg. After completion of the initial warm cardioplegia, consecutive retrograde (30-35 mmHg) and antegrade (75-100 mmHg) tepid blood cardioplegia were infused intermittently. Maintenance cardioplegia was prepared from the circulating oxygenated tepid blood. Cardioplegia components of the warm induction and tepid blood cardioplegia are shown in Table 2.

Table II. Characteristics of cardioplegics

	Induction	Maintenance
Temperature	Warm	Tepid
Amount	10ml/kg	20-70ml/kg
Potassium	30mEq/L	6-10mEq/L
Sodium bicarbonate	5mEq/L	5mEq/L
Diltiazem	10mg/L	5mEq/L

A 1000 ml crystalloid cardioplegia bag was used as a reservoir and to fill this bag with blood; a Y shaped polyvinyl set was attached to the aortic cannula. A stopcock was placed on the entrance of the bag for adding the cardioplegia components. Antegrade induction of the warm cardioplegia was performed with the aid of a pressure bag. Finger palpation of the aortic root was used to estimate the pressure (75-100 mmHg) applied. Retrograde coronary sinus cannulation was made with a transatrial coronary sinus cannula (Baxter RC2014-USA). Retrograde coronary sinus cardioplegia bag was placed 50 cm above the sternum and then retrograde cardioplegia was applied without pressure monitorization. Our cardioplegia composition and delivery system (Bıçakçılar " cardioplegia line) are shown schematically in Figure 2. Aortic root decompression during retrograde coronary sinus cardioplegia application was done with the aid of gravity; a clamp was placed on this line when antegrade cardioplegia delivery was initiated.

After diastolic cardiac arrest, LITA was harvested for LAD and for the other diseased coronary arteries saphenous vein grafts were

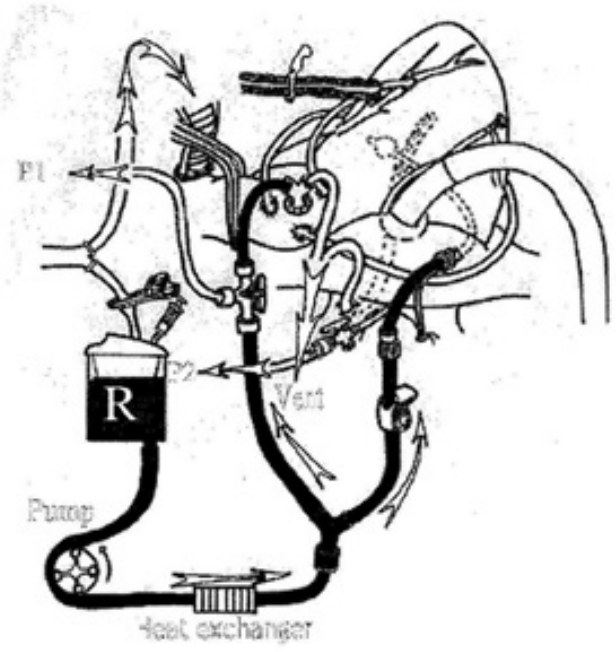

Figure 1: Our previous cardioplegia delivery reperfusion system (closed to systemic circulation) and its application, which was abondoned due to the development of the new open technique

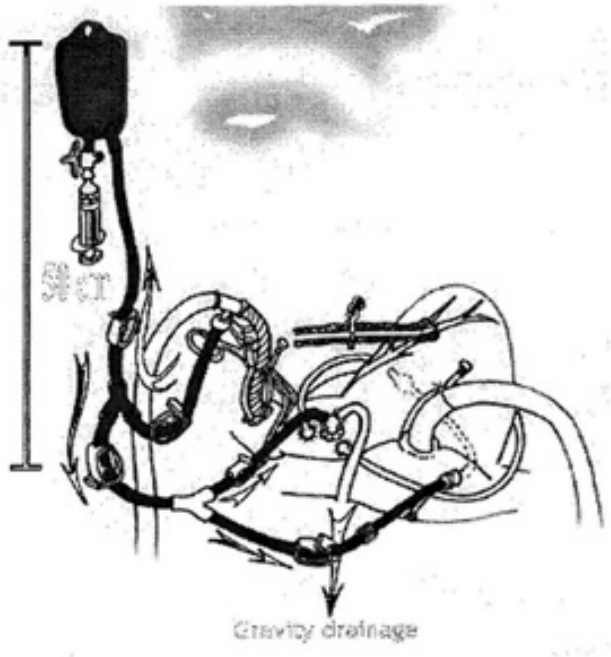

Figure 2: Simplified cardioplegia delivery system and reperfusion (simple releasing cross clamp to open the coronary flow to systemic aortic cannulae circulation)

prepared. 28°C systemic hypothermia and whole body pulsatile (occlusive) perfusion was applied in all patients. Distal and proximal anastomoses were performed with conventional continuous polypropylene suture technique. LITA to LAD anastomosis was always performed with direct end-to-side anastomosis, without interposing the saphenous vein graft between the ascending aorta and the LAD and creating an additional anastomosis of LITA at the distal part of this saphenous vein graft.

When all distal and proximal anastomoses were completed under XC, the pump flow was decreased in order to keep the systemic pressure between 20 - 25 mmHg and XC was released at 28°C. At this pressure, the mean pump flow varied between 400 - 800 ml/min, according to the patient's vascular resistance and body surface area. We waited for "two" minutes at this perfusion pressure, and then rewarming was started and systemic perfusion pressure was raised gradually to reach the calculated pump flow within two minutes. Weaning from CPB and the remainder of the operation was as usual.

Table III. Intraoperative and postoperative variables

XC time	45±11 min (range: 24 -76 min)
CPB time	76±20 min (range 46 - 110 min)
VF in the first two min of PCTR	2 (5,4%)
VF in rewarming phase of CPB	4 (10,8%)
Spontaneous sinus rhythm	31 (83,7%)
Recovery time	9±2,3 min (range: 7-14 min)
LCO	
Inotropic requirement	12 (32%)
Preoperative requirement	5 (13%)
Postoperative requirement	7 (19%)
IABP requirement	6 (16,2%)
Preoperative requirement	4 (10,8)
Postoperative requirement	2 (5,4%)
Mortality	- 0
Stay in intensive care unit	2,9±2,2 days (1-7)
Stay in hospital	10,4±1,7 days (7-13)

XC: Aortic cross clamp. CPB: Cardiopulmonary bypass. VF: Ventricular fibrillation. PCTR: Pressure controlled tepid reperfusion. LCO: Low cardiac output. IABP: Intra-aortic balloon pump.

Outcome Measures:

Preoperative and postoperative low cardiac output (LCO) conditions, inotropic support and intra-aortic counterpulsation need at the end of CPB were noted. Serum CK-MB levels were measured preoperatively and at postoperative 2nd, 24th, 48th hours and 4th day. Time necessary for restoration of sinus rhythm and optimal contractility (recovery period), and the first cardiac rhythm following reperfusion was noted during the operation.

As a sign of reversibility of ischemia-reperfusion injury to myocardium and conduction system, preoperative and postoperative ECG changes were also investigated.

RESULTS

Intraoperative variables are presented in Table III. Seven patients who didn't receive preoperative inotropic support needed inotropic support postoperatively; and in 2 of them, intra-aortic balloon counterpulsation (IAB) was required.

Atrial fibrillation developed in 2 patients without previous experience of atrial fibrillation, between 2nd and 8th postoperative days. Sinus rhythm was restored with medical cardioversion in these patients.

None of the patients had any ECG sign suggesting expansion of myocardial infarction. In 6 patients that had Q formation with accompanying ST segment elevation, this ECG sign changed postoperatively and ST segment returned to the isoelectric level. In 5 of these patients an rS pattern was observed in V 1-4 derivations during the first 6 postoperative months. In one patient the Q generation remained and echocardiography showed severe anterolateral hypokinesia. Figure 3 shows CK-MB serum level changes during the perioperative period. Mean duration of hospitalization was 10.4±1.7 days (range: 7 - 13 days). None of the patients had extracardiac complications.

Patients were followed-up postoperatively 14 to 30 months, a total of 54.0 patient years. All followed patients were New York Heart Association (NYHA) Class I, no recurrence of angina was seen and echocardiographic examinations (Table III) revealed that wall motion in LAD area were almost totally preserved.

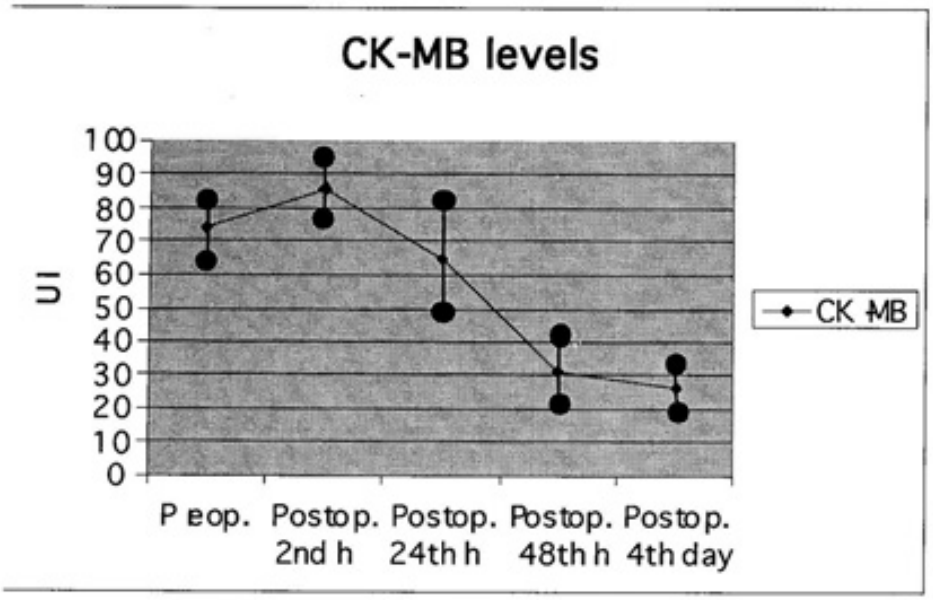

Figure 3: Perioperative CK-MB levels

DISCUSSION

Following are the three main purposes of the controlled reperfusion in AMI surgery: to minimize myocardial stunning seen in patients after XC and CPB (6,7); to create a suitable condition for the potentially reversible myocyte injury and to restore the optimal contractility at the end of CPB; and to resuscitate the myocytes that would otherwise die without intervention. We tried to reach these goals in our study technique. In order to generate a systemic tepid hypothermia, we applied isothermic consecutive antegrade and retrograde modified (but not enriched) blood cardioplegia, which we believe to be an appropriate method of myocardial protection and resuscitation and as successful as substrate enriched warm cardioplegia.

If the reperfusion conditions are inadequate and uncontrolled, reperfusion may result in cellular necrosis (8). Injury caused by reperfusion begins earlier in endothelial cells than myocytes, and it is as early as the induction of reperfusion and leads to capillary occlusions (9). It is reported that reperfusion should be initiated with a low pressure in order to prevent endothelial cell injury and myocyte edema due to the hyperemia following a prolonged ischemic interval (10,11,12). It is recommended that the pressure should be kept between 20-30 mmHg in the first 2-3 minutes of reperfusion and it should then be increased to 50-75 mmHg (12).

We diminished the arterial pressure to 20-25 mmHg after completion of and before removal of XC and the bulldog clamp on LITA. Thus we provided the recommended low aortic root reperfusion pressure via the grafts, as stated in Buckberg's controlled aortic root reperfusion technique. The major difference between these two techniques was that our technique is open to systemic circulation. It may be suggested that cerebral functions would be affected in this hypotensive interval of the initial reperfusion. In human subjects and in normothermic conditions, the upper limit for circulatory arrest to preserve normal neurologic function and histology is 5 minutes (13). Animal studies suggest that time required for a permanent brain injury may be several fold longer than 5 minutes with anesthesia and hypothermia. A dog model study showed, with moderate hypothermia (28-32oC) and hemodilution, even 17 minutes of circulatory arrest could be well tolerated without any cerebral injury (14). Protection of hypothermia against brain damage during hypoxia has been demonstrated in many studies. Hypothermia and hemodilution is accepted as major means of protection against hypoxia in human brain, if they are induced prior to hypoxic insult (15). We did not see any sign of cerebral hypoxia in the postoperative period. This is probably due to the which pressure controlled tepid reperfusion lasted only two minutes under hypothermic conditions (28°C) and circulation of oxygenated blood was continued at diminished levels (400-800cl/min). At the end of this hypotensive two minutes, we didn't observe acidosis in arterial blood gas analysis and mixed venous blood sample analysis

didn't show significant PO_2 fall indicating organ ischemia.

High blood pressure at the early reperfusion period create flow forces that injure endothelial cells and create a reperfusion injury cascade, and this may result in perivascular, interstitial, myocyte edema and/or cellular damage, as was observed in our previous experimental studies. Clinically, reperfusion damage is seen as myocardial dysfunction and/or arrythmias. In our study, it was not possible to observe endothelial cell function directly. Parameters reflecting myocardial injury (serum enzyme levels) left ventricular function, ECG changes suggesting infarct expansion and arrhythmias were recorded during the study.

The elevation of CK-MB levels during the operation may well be explained by the release of cumulated enzymes due to cellular disruption into the coronary circulation following reestablishment of coronary perfusion in the totally obstructed artery. Reperfusion didn't cause remarkable secondary cell injury, because CK-MB levels fell below preoperative values at 24th postoperative hour.

Incidence of left ventricular dysfunction and rhythm disturbances in the postoperative period may be considered as low for a high-risk patient population. Preoperatively, ventricular malign arrhythmias were observed in 12 (32%) patients. In 4 patients, these rhythm disturbances were associated with left ventricular failure and these patients were transferred to the operating room with extracardiac massage, two patients were stabilized with IAB counterpulsation and the remainder required multiple cardioversions. After the operation, no patient of this group showed any ventricular rhythm disturbance. Transient LCO was seen in 12 patients (32%) after emergent revascularization procedures; 5 of them were patients who were receiving inotropic support preoperatively and only 2 patients required IAB counterpulsation postoperatively. In all patients IABP was removed in the postoperative 3rd day suggesting a fast recovery of heart and reversal of myocardial injury. Except one patient who had persistent Q waves, no ECG sign that shows an increase in the infarcted area size was recorded postoperatively.

It is important to have an electromechanical quiscence in the first 2 or 3 minutes of reperfusion in order to get a fast energy charge with homogenous distribution of blood in the fully relaxed heart. It is important whether that energy consumption by contractile forces begin only after a significant restoration of ATP reserves is completed (16).

For this purpose, for 2 or 3 minutes during XC, pressure controlled aortic root reperfusion with "warm blood" supplemented with potassium was used as the reperfusate. There after during XC, a second stage of controlled reperfusion was initiated with unmodified blood, aortic root pressure was augmented, the left ventricle was vented and the heart was allowed to beat till the optimal contractility was reached and than XC was released. In this technique, which is close to systemic blood circulation, use of "additives" is recommended for the faster recovery of the heart (17).

This technique requires two additional pumps, one for controlled aortic root perfusion, and the second for venting the left ventricle. It also requires additional monitoring of the aortic root in order to regulate pressure accurately and many lines for connecting the aortic root, left ventricle, pumps and the monitor. This complex technique is difficult to establish, requiring components that is not easily available in our country and is too expensive for routine use in high risk patients. On the other hand, benefits of enriched reperfusion solutions are still debated. In our previous experimental study, like some others (18,19), we didn't observe any superiority of enriched solutions to unmodified blood reperfusion. In this simplified reperfusion technique, we didn't use XC at any time of reperfusion. When the systemic arterial pressure was between 20-25 mmHg, XC was released and pressure controlled reperfusion was started at 28°C. Also, during the first two minutes electromechanical quiscence was observed in the majority of patients (83,7%). This lack of activity or severely depressed automatism may be explained by hypothermia and the effect of diltiazem and potassium included in cardioplegic solution that was given during

XC. In 6 patients (16,3%) ventricular fibrillation occured in the first reperfusion and in the subsequent rewarming period. One or two cardioversions were done and a slow regular rhythm was achieved. In this first stage of reperfusion, generally atrio ventricular blocks and intraventricular conduction delays are seen. Any manipulation of the ventricles in this stage may cause ventricular arrythmias and should be avoided. Regular spontaneous sinusal rhythm emerges within 6-15 (mean 9±2.3) minutes of the rewarming period, contractions become stronger and reach to the maximum. These are the clinical markers for the termination of the recovery phase (20). For this reason, we can propose that the shorter recovery period indicate a more successfull reperfusion technique. In patients with PCTR technique although recovery phase covered the rewarming period, the total duration of the recovery phase was similar to that reported for the technique closed to systemic circulation in the literature (20).

This indicates that in our patients capillary perfusion is maintained and effective cellular preservation is achieved, although reperfusion was done with unmodified blood and started at 28°C.

PCTR technique provides a surgical advantage for the patient. LITA can be used directly as a graft for LAD without the need of an additional saphenous vein graft bypass procedure. In the controlled aortic root reperfusion technique closed to systemic circulation, saphenous vein graft is needed for pressure-controlled reperfusion (1) that is performed via aortic root or directly via saphenous graft.

Conclusion

We report the satisfactory clinical results of emergency revascularization performed by using pressure controlled unmodified tepid blood reperfusion technique in patients with evolving myocardial infarction. As confirmed clinically, by echocardiographically, and by serum enzyme level studies, controlling only the reperfusion pressure at the initial reperfusion can prevent an additional reperfusion injury due to revascularization procedure. This simplified technique does not require specialized equipment, does not have an additional cost and does not necessitate additional surgical modification. It is routinely used in our institution during emergency revascularizations, in patients who undergo multiple procedures and need prolonged XC time, and in surgical interventions for cyanotic congenital heart defects. Slight or mild aortic insufficiency negligible by operative intervention, may preclude these integrated cardioplegia and reperfusion techniques application. In such cases a left ventricular venting may be helpful.

REFERENCES

1. Allen BS, Buckberg GD, Schwaiger M, et al. Studies of controlled reperfusion after ischemia. XVI. Early recovery of regional wall motion in patients following surgical revascularization after 8 hours of acute coronary occlusion. J Thorac Cardiovasc Surg 1986 ; 92:636-648
2. Battist G, Merserau W, Malashenko BA, Chiu RCJ. Response to ischemia-reperfusion injury in hypertrophic heart. Role of free-radical metabolic pathways. Circulation 1987;80 (suppl III):10-19.
3. Julia PL, Buckberg GD, Acar C, Partington MT, Sherman MP. Studies of controlled reperfusion after ischemia XXI. Reperfusate composition: Superiority of blood cardioplegia over crystalloid cardioplegia in limiting reperfusion damage: Importance of endogenous oxygen free-radical scavengers in red blood cells. J Thorac Cardiovasc Surg 1991;101:303-313
4. Follette DM, Fey KH, Steed DL, Foglia RP, Buckberg GD. Reducing reperfusion injury with hypocalcemic, hypercalemic, alcalotic blood during reoxygenation Surg Forum 1978 ; 29:284-286
5. Allen BS, Okamoto F, Buckberg GD, et al. Immediate functional recovery after six hours of regional ischemia by careful control of conditions of reperfusion and

composition of reperfusate. J Thorac Cardiovasc Surg 1986;92:621-635
6. Passini E, Ferrari G, Cremonta G, Ferrari M. Revascularization of severe hybernating myocardium in the beating heart: early hemodynamic and metabolic features. Ann Thorac Surg 2001;7:176-179.
7. Eberhardt F, Mehlhorn U, Larose K, De Vivie ER, Dhein S. Structural myocardial changes after coronary artery surgery. Eur J Clin Invest 2000;30:938-946
8. Ambrosio G, Weisman HF, Mannisi JA, Becker LC. Progressive impairment of regional myocardial perfusion after initial restoration of postischemic blood flow. Circulation 1989; 80:1846-1861.
9. Quillen JE, Sellke FW, Brooks LA, Harrison DG. Ischemia -reperfusion impairs endothelium dependent relaxation of coronary microvessels but does not affect large arteries. Circulation 1990; 82:586-594.
10. Okamoto F, Allen BS, Buckberg GD, Bugyi H, Leaf J. Studies of controlled reperfusion after ischemia XIV. Reperfusion conditions: Importance of ensuring gentle versus sudden reperfusion during relief of coronary occlusion. J Thorac Cardiovasc Surg 1986; 92:613-620.
11. Sawatari K, Kadoba K, Bergner KA, Mayer JE JR. Influence of initial reperfusion pressure after hypothermic cardioplegic ischemia on endothelial modulation of coronary tone in neonatal lambs: Impaired coronary vasodilator response to acetylcholine. J Thorac Cardiovasc Surg 1991; 101:777-782.
12. Digerness SB, Kirklin JW, Naftel DC, Blackstone EH, Kirklin JK, Samuelson PN; Coronary and systemic vascular resistance during reperfusion after global myocardial ischemia. Ann Thorac Surg 1988; 46:447-454.
13. Gisvold SE, Sterz F, Abramson NS, et al. Cerebral resuscitation from cardiac arrest: treatment potentials. Crit Care Med 1996;24(2Suppl):69-80.
14. Safar P, Sterz F, Leonov Y, Radovsky A, Tisherman S, Oku K. Systematic development of cerebral resuscitation after cardiac arrest. Three promising treatments: cardiopulmonary bypass, hypertensive hemodilution and mild hypothermia. Acta Neurochir Suppl 1993;57:110-121.
15. Ping FC, Jenkins LC. Protection of the brain from hypoxia: a review. Can Anaesth Soc J 1978;25:468-473
16. Follette DM, Steed DL, Foglia RP, Fey KH, Buckberg GD. Reduction of postischemic myocardial damage by maintaining arrest during initial reperfusion. Surg Forum 1977;28:281-283
17. Rosenkranz ER, Okamoto F, Buckberg GD, Robertson JM, Vinten-Johansten J, Bugyi HI. Safety of prolonged aortic cross clamping with blood cardioplegia. III. Aspartate enrichment of glutamate-blood cardioplegia in energy depleted hearts after ischemic and reperfusion injury. J Thorac Cardiovasc Surg 1986;91:428-435
18. Frierson JH, Penn MS, Lafont AM, et al. Effect of Buckberg cardioplegia and peripheral cardiopulmonary bypass on infarct size in the closed chest dog. J Am Coll Cardiol 1992;20:1642-1649
19. Edwards R, Treasure T, Nia HM, Murday A, Kantidakis GH, Holt DW. A controlled trial of substrate enhanced warm reperfusion ("hot shot") versus simple reperfusion. Ann Thorac Surg 2000;69:551-555.
20. Rosenfeldt FL, Rabinov M, Newman M. Coronary blood flow and myocardial metabolism during reperfusion after hypothermic cardioplegia in the dog. Eur J Cardiothorac Surg 1987;1:91-97