THE EFFECT OF CONTINUOUS ISOTHERMIC RETROGRADE CORONARY SINUS BLOOD CARDIOPLEGIA ON RIGHT VENTRICLE FUNCTIONS

E.AKINCI, M.D.
B. DAĞLAR, M.D.
E.EREN, M.D.
M. BALKANAY, M.D.
T.BERKİ, M.D.
Ö.IŞIK M.D.
and
C.YAKUT , M.D.

From: Koşuyolu Heart and Research Hospital, İstanbul

Adress for reprints:
Esat Akıncı, M.D.,
Koşuyolu Heart and Research Hospital, İstanbul,
TÜRKİYE

Isothermic aerobic arrest is a new alternative to hypothermochemical and anaerobic arrest techniques, depending on the suggestion that it provides more physiological and histobiochemical conditions. The nonhomogeneous distribution of the cardioplegic solution through the antegrade route is an important problem. Even-though retrograde perfusion provides more homogeneus distribution of the cardioplegic solution dispite critical coronary obstructions, still there is some suspect that the right ventricle is not adequately preserved. The main point for this argument is the venous blood drainage of the right ventricle.

A randomised, prospective clinical trial was conducted in Koşuyolu Heart and Research Center to investigate the effect of the "continuous isothermic retrograde blood cardioplegia" on the right ventricle functions in 30 selected patients of whom all had triple vessel disease and normal ventricle functions. Continuous retrograde isothermic blood cardioplegia was applied to group A (n=15). In group B, cardioplegic induction was made by antegrade route and maintainance was obtained by combined antegrade / retrograde aplication (n=15).

Parameters such as heart rate (HR), mean arterial pressure (MAP), right atrial pressure (RAP), pulmonary arterial pressure (PAP), pulmonary capillary wedge pressure (PCWP), cardiac index (CI), stroke index (SI), right and left ventricle stroke work index (SWI) were measured following the anesthetic induction, 10 minutes after weaning CPB, and at the postoperative 8th hour.

No significant differences were found between the two groups' values regarding the total perfusion time, aortic cross clamp time, and total number of mean distal anastomosis. There were no significance between the two groups' RAP, PAP, PCWP, CI values in all the 3 phases. When the LVSWI and RVSWI values recorded in the post induction and post perfusion phases were compared , a slight decrease was noted in the post perfusion phase values ($p<0.01$). However no significant difference was observed between the RVSWI values measured in the induction phase and postoperative 8th hour. Finally, there wasn't any significant difference between the 2 groups values recorded in all 3 phases.

As a consequence, we suggest that isothermic retrograde continuous blood cardioplegia administiration in coronary revascularisation operations can protect both the right and the left ventricle sufficiently.

***Key words:** Myocardial protection, retrograde blood cardioplegia, isothermic continuous cardioplegia*

One of the most important factors in the succes of open heart surgery adequate preservation of the myocardium during surgical procedure. The application of hypothermochemical anaerobic diastolic arrest technique has been initiated in 1950's, and it's been applied in comprehensive case series since 1970's. Because of the problems caused by the damage following the anaerobic arrest, hypothermia, and the inappropriate distribution of antegrade cardioplegia particularly in the coronary arterial disease; possible new techniques in this particular procedure have always been the focus of the releated research. Following the initiation of using retrograde sinus cardioplegia as an alternative technique to antegrade cardiople-gia, it's been a main discussion point whether the right ventricle can be protected or not during the surgical procedure, because of the particular anatomical status of its venous drainage. In this clinical trial, continuous retrograde coronary sinus blood cardioplegia administiration was compared with antegrade/retrograde isothermic blood cardioplegia in terms of their effects on the right ventricle functions under isothermic conditions and through the preoperative-postoperative hemodynamic parameters, so that the right ventricle protecting effect of this technique was discussed.

METHODS

Patients

30 patients who were hospitalised in Koşuyolu Heart and Research Center, and who had similar preoperative features, three vessel disseases as diagnosed by angiography, and who had normal left ventricle functions were selected and included in the trial. 15 randomised patients received only retrograde isothermic continuous blood cardioplegia (Group A) while the other 15 patients (Group B) received combined antegrade/ retrograde isotermic continuous blood cardioplegia. Preoperative characteristics of the patients are shown in Table I.

Hemodynamic Monitorization

In all patients, ECG, arterial pressure, right atrial pressure, pulmonary arterial pressure, cardiac output were monitorized. HR, MAP, RAP, MPAP, PCWP, CI were recorded after the anaesthetic induction (A-B), 10 minutes after weaning fram CPB (A1-B1), and at the postoperative 8th hour (A2-B2). SI, LVSWI, RVSWI values in all of the 3 phases were calculated by the classic formulas.

Surgical Procedure

Following median sternotomy left internal thoracic artery was prepared in all cases. After

Table 1. Patient characteristics

	Group A	Group B	p value
Number of Patients	15	15	
Sex			
Male	14	13	
Female	1	2	
Age	42-68	44-67	
Mean	57.6 ± 6.2	59.3 ± 6.9	>0.1
Body surface area(M2)	1.7 ± 0.2	1.75 ± 0.15	>0.1
Hypertension	3	2	>0.1
Unstable angina pectoris	6	7	>0.1
LMC disease	2	1	>0.1
Left ventricle performance score	9.6 ± 2.1	9.9 ± 2.4	>0.1
Left ventricle EDP	12.4 ± 2.5	13.1 ± 2.2	>0.1

heparinization, arterial cannulation throug ascending aorta and venous canulation throug right atrium by single two stage cannula wsa performed. Antegrade cardioplegic infusio cannula was placed in the aortic root, ad retroplegia cannula was placed in the coronay sinus by transatrial technique. These cannule were connected to the cardioplegia perfusio system. This system (is showed figure). includes a cardioplegia reservoir, a single 4/ line and antegrade/retrograde "Y" W/integra selector switch. This system enables th monitoring of the aortic root and coronary sinu pressures and the surgeon could direct th cardioplegia administiration route byselector switch. Left ventricle decompression from the aortic root was obtained by the venting lumen of the anteplegia cannula.

Centrifugal pump and membrane oxygenator were used in all cases. Systemic perfusion rate and systemic perfusion presure were not decreased below 2.4 L/m^2/min and 50 mmHg respectively. Body temperature was maintained within 30-32 °C, and Hct within 24-27% during CPB in both groups.

After the initiation of CPB, 1000 ml oxygenated blood was administered through the pump circuit while avoiding the fall in systemic perfusion pressure. The blood cardioplegia solution with high potassium concentration was prepared by adding 30 mEq/L potassium, 15 mEq/L $NaHCO_3$ and 10

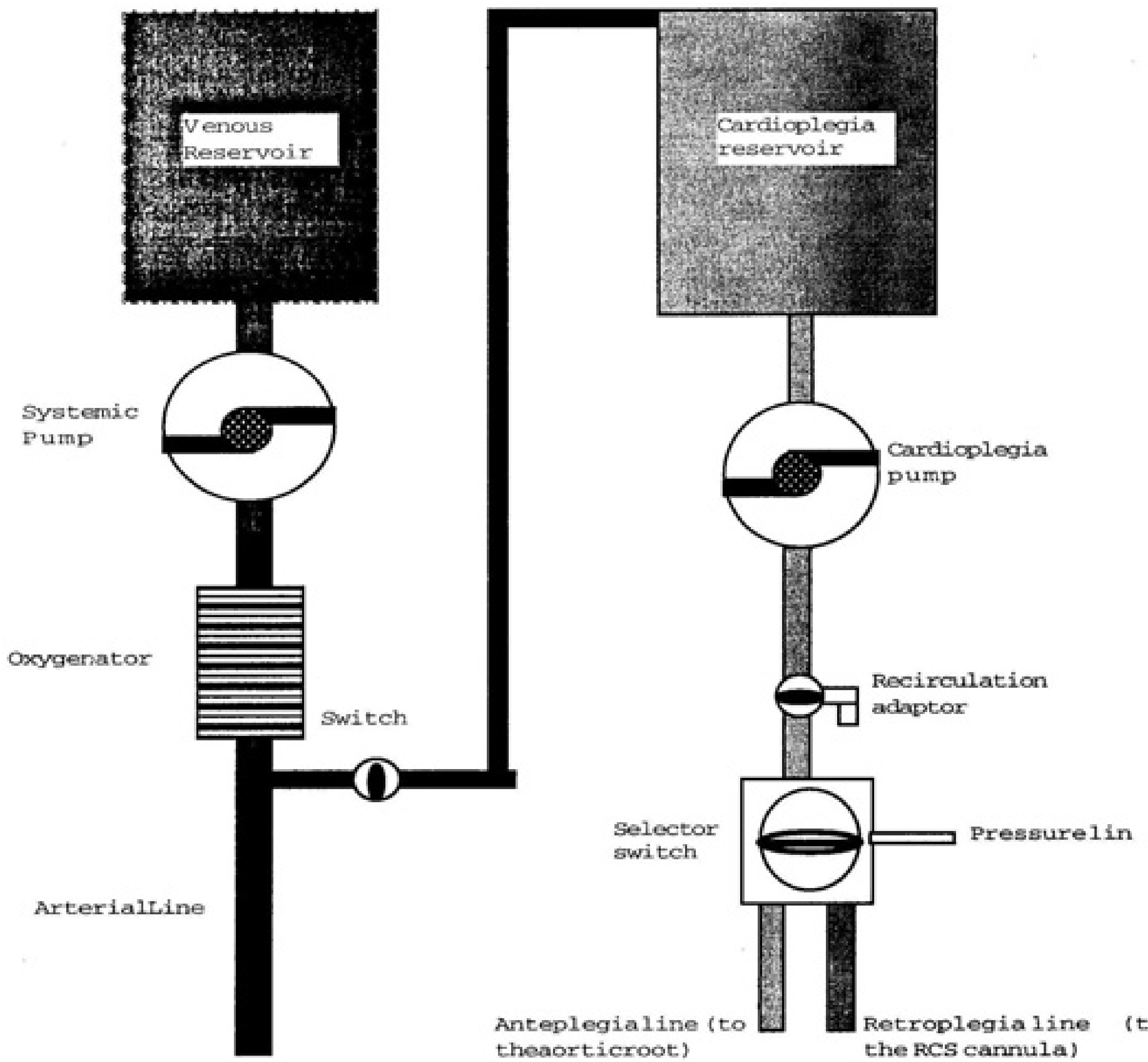

Figure 1. Cardioplegia perfusion system

ml CPD. The composition of this solution is shown in Table II.

Following cross-clamping of the aorta, this solution as the cardioplegic induction was administered continuously with an infusion rate of 100-200 ml at 15 ml/kg of body weight via the retrograde route in group A, while avoiding the coronary sinus pressure exceeding 40 mmHg. Cardioplegic solution with low K^+ concentration as the maintainance cardioplegia was given 80-100 ml/min rate at 30-32°C body temparature. Low potassium concentration cardioplegia solution is shown in Table III. Continuous venting from the aortic root was applied during the administration. In group B, same solution as the cardioplegic induction at 15 ml/kg of body weight was administered via the antegrade route while the aortic root pressure was maintained at 70 mmHg. The low potassium consantrated solution with an infusion rate of 80-100 ml/min was administered via the retrograde route while the coronary sinus pressure was taken care not to exceed 40 mmHg. After each anastomosis antegrade perfusion was applied for 3-4 minutes through the grefts and the aortic root. Total retrograde and antegrade perfusion times were recorded. When performing the distal anastomosis, the perfusion route was changed to retrograde. In order to obtain clear surgical areas, perfusion was withheld for 2-3 minute intervals when necessary. As the criteria for the effectivity of the retrograde perfusion, care was taken to provide the veins with being full of oxygenated blood, to continuously vent the desaturated blood from the aortic root.

The time between aortic cross-clamp and the absolute electromechanical arrest (mean arrest time), total perfusion time, aortic cross clamp time, total amount of cardioplegia solution, and the number of the anastomosis were recorded in all patients.

Immediately after placing the retrograde perfusion cannula, and immediately before taking of the cannula, coronary sinus blood samples were collected; CPK-MB levels were measured and malondialdehit presence were checked. CPK, CPK-MB and SGOT from the systemic blood samples were measured in the preoperative and postoperative 18th hour and recorded.

Table II. High potassium cardioplegic solution

PH	7.4
Temperature	isotermic
PCO2	35 mmHg
PO2	200 mmHg
O2	99.7 %
Hct	22-24%
Osmolarity	320 mOsm/L
Glucose	<400 mg/dl
Potassium	30 mEq/L

Table III. Cardioplegia administration

	Group A	Group B
Induction	retrograde	antegrade
Induction c.p.type	high potassium	high potassium
Maintenance	retrograde	retrograde/ antegrade
Maintainance c.p.type	low potassium	low potassium

RESULTS

No significant differences were observed between the two groups regarding the mean number of distal anastomosis, CPB times and aortic cross clamp times. LITA (Left Internal Thorasic Arter) was used as the arterial graft in all of the patients exept 1 group A patient whose LITA wasn't suitable. Coronary endarterectomy was performed to the right coronary artery in one patient of group A, and 2 of the group B patients. When the total amounts of blood cardioplegia were compared, group B demonstrated higher values. However, these differences were statistically significant. The amount of the cardioplegia was shown as graphics in Figure.2 The differences of mean arrest time between the groups (as shown in Figure 3) were found

Table IV. Hemodynamic results

	A	B	A1	B1	A2	B2
HR	65.5±8.2	63.2±7.6	83±12.6	81.7±10.5	83.3±8.6	81.3±10.1
MAP(mmHg)	78.3±7.8	81.3±9.3	71.3±9.8	74.5±9.7	81.7±9.4	84.4±9.2
RAP(mmHg)	6.8±2.1	7.1±1.7	8.4±2.2	7.8±1.7	8.1±1.3	8.4±1.1
MPAP(mmHg)	15.9±4.1	16.7±3.6	18.1±2.2	18.8±2.8	15.3±3.7	16.1±3.6
PCWP (mmHg)	8.7±2.6	8.9±2.1	10.3±1.8	9.9±2.3	9.1±2.3	8.9±2.3
CI (L/min/m2)	2.6±0.8	2.5±1.2	3.1±1.1	2.9±0.9	3.0±0.7	2.9±1.1
SI (ml/min/m2)	40.1±7.6	39.6±8.2	37.4±8.3	36.3±6.5	36.2±5.4	36.1±5.8
LVSWI (gm.m/m2)	37.9±7.9	38.9±7.7	30.7±9.5	31.9±5.3	35.4±8.7	36.9±9.3
RVSWI (gm.m/m2)	6.1±0.9	5.8±1.1	4.8±0.7	5.0±0.8	4.9±1.4	4.7±1.7

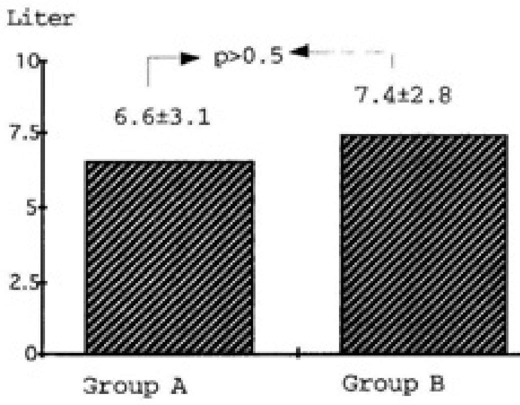

Figure 2. Amount of cardioplegia.

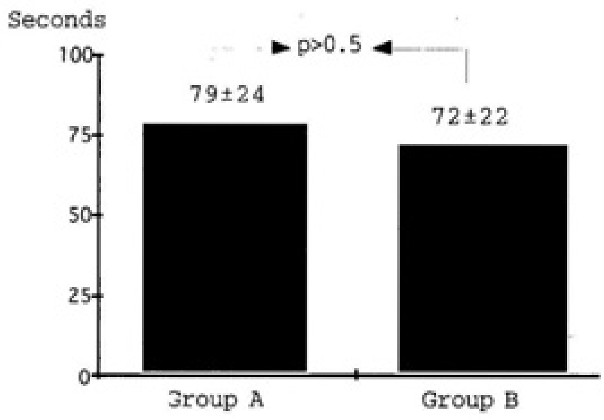

Figure 3. Mean arrest time.

significant.
The groups did not differ in terms of heart rate in all 3 phases, but each groups' own post perfusion and postoperative 8th hour values were higher then the postinduction values ($p<0.01$).The mean blood pressure values of the 3 phases didn't differ significantly among the groups. Post perfusion values of the mean right atrial pressure measurements were higher in both groups, but within normal limits as graphically shown in the Figure 4. When the changes in the mean pulmonar arterial pressure, the mean pulmonary capillary wedge pressure the mean cardiac index values were compared, no significant differense were observed between the groups.
Though both groups' LVSWI values were not different at each 3 phase as shown in Figure 2, post perfusion values were significantly decreased ($p<0.01$) when compared to the post induction values. However when the postoperative values were compared to the postinduction values, differences were not significant ($p<0.1$)
Both groups RVSWI values were not different at each 3 phase as shown in in Figure 5. However, postperfusion values were significantly decreased ($p<0.05$) when compared to the postinduction values. Postoperative 8th hour values were found to be decreased as well, when compared to the postinduction values
The CPK-MB enzym levels measured in the coronary sinus blood after weaning the aortic cross-clamping were within the normal limits

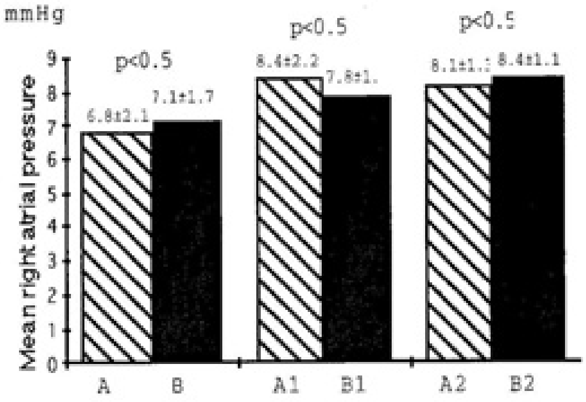

Figure 4. Right atrial pressure changes

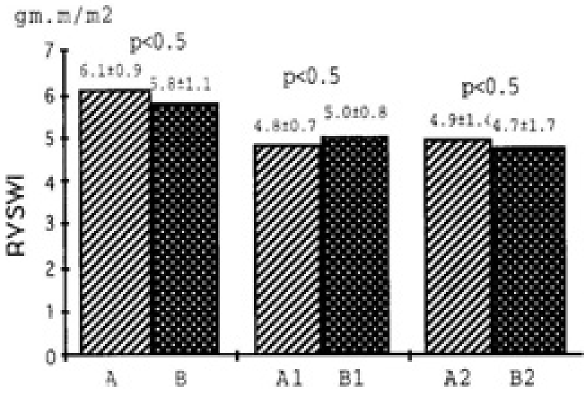

Figure 5. Changes in the RVSWI

and did not differ significantly among the groups as shown in Table V.

The mean CPK, CPK-MB, SGOT enzyme levels measured in the blood samples collected at the postoperative 18th hour were not significantly different as shown in Table VI.

One patient of the group B had anteroseptal perioperative MI in the postoperative follow-up period. Since low cardiac output symptoms and ventricular arrythmia were observed after weaning the CPB, hemodynamic stabilisation was achieved by inotropic and intraaortic baloon pump support. Postoperative patient characteristics were shown in Table VII.

DISCUSSION

Two main components of myocardial protection during the surgical procedure are supply and demand. The relationship between these three functions may be wich may be formulated as;

Myocardial protection= supply / demand

This formula indicates the importance of the balance between the O_2 and energy demand of the myocardium and the supply of these requirements. The succes of the myocardial protection is directly correleted with maintaining this ratio at least equal to 1. Therefore, the basic principle is to reduce the demand and to increase the O_2 and energy supply. Researchs related to myocardial protection has been based upon this supply/ demand concept. During the mid 70's the

Table V. The CPK-MB levels and the presence of malondialdehite in the coronary sinus blood after declamping the aorta.

	Group A	Group B
CPK-MB(U/L)	27±15	29±18
Malondialdehyte	(-)	(-)

Table VI. The enzyme values measured at the 18th postoperative hour.

	Group A	Group B	p
CPK (U/L)	680±346	725±310	>0.5
ÇPK-MB (U/L)	36±15	34±18	>0.5
SGOT (U/L)	81±27	76±31	>0.5

Table VII. Postoperative characteristics.

	Group A	Group B	p
Perioperative MI	(-)	1 pt	>0.5
Inotropics support	1 pt	2 pts	>0.5
IABP support	(-)	1 pt	>0.5
Atrial arrythmia	(-)	(-)	
Ventricular arrythmia	(-)	1 pt	>0.5
Mortality	(-)	(-)	

predominant approach has been towards reducing the demand, while the supply of this demand has been the focus of the recent years' research. The basic principle in reducing the O_2 and energy demand can be achieved by hypothermia and electromechanical arrest which are the components of the hypothermychemical arrest technique that's been used till to day.

Supplying the demands during the procedure can be achieved by delivering O_2, energy and the additional substrates such as glutamate, aspartat, creatinin phosphate and carnitene.

The normothermic aerobic arrest technique developed within the recent years as an alternative to the hypothermychemical anaerobic arrest. This technique has discarded the unfovorable effects of the hypothermia on the enzyme functions, membrane stability, calcium sequestration and glucose uptake [1-9], and this technique requires continuous and adequate administration of blood cardioplegia. However the apropriate, continuous and homogenous pefusion of the heart under normothermic conditions couldn't be adequately achieved particularly patients with critical or diffuse coronary obstructions. Because of the fact that vena cordis parva and vena cordis media which account for the veous drainage of the posterior septum and right ventricle are drained to the sinus coronarius just 0.5 cm before the ostium sinus coronarius; and that the inserted retroplegia cannula occludes the coronary sinus at a distal localisation of that site, same suspicion has born that the releted part of the heart couldn't be protected. Though Partington et al. determined the nutritive flow as 7±2 ml/100g/min at the right ventricle, they have observed the flow 82±11 ml/100g/min at the anterior wall of the left ventricle, and 23±9 ml/100g/min at the intervenricular septum. [10] Buckberg et al. found that myocardial O_2 consumption was 5.6 ml/100g/min in the empty beating heart, and 1.1 ml/100g/min in the arrested heart at 37 °C. Therefore the myocardial O_2 cosumption at the arrested heart has been considered to be 80% less than under normothermic condition, wich suggest that the perfusion of the posterior septum and the right ventricle by collateral flow could be sufficient [11]. Yau at al. demonstrated that the energy stores of the heart could be protected, the lactate production could be inhibited and the aerobic metabolism could exist when provided with a blood flow of 80 ml/min. [12] We didn't observe any anaerobic metabolism end products in the coronary sinus blood samples in our trial as well. (Table V)

Isothermic administration of the cardioplegic solution saves a lot of time and effort because of its basic rationale which means that it should be at the same temparature with the systemic circuit, and therefore warming and cooling isn't necessary.

The technique that we use for preparing the cardioplegic solution is free of an additional cristalloid solution and it's only 40 ml of potassium-bicarbonate-citrate combination that we add to every 1000 ml of blood from the systemic circuit. This volume of only 40 ml discards the volume loading effect of the formula which is achieved by the addition of the cristalloid as a ratio of 1/4. The total additional cardioplegia volume of our technique is approximately 250-300 ml while the other formula couses 1000-1500 ml aditional volume load during the procedure.

The RVSWI values regarding the right ventricle functions did not differ in the continuous retrograde perfusion group provided with the establishment of the right atrial filling pressures, which enables the optimal postperfusion cardiac output. Significant decreases in the postperfusion values of the both groups have been observed (Figure 12). Mullen et al. noted significant low post perfusion SWI values for both the right and the left ventricle in their study which the crystalloid and the blood cardioplegia were compared. [13] They postulated that the major factor was the increased heart rate. We found that the heart rate was increased and stroke index values were decreased in the post perfusion period, wich explain the decreases in the postperfusion SWI values.

We did not encounter any complications due the manupulation of coronary sinus catheter or high baloon pressure.

There were not any significant differences in both groups in achieving cardiac arrest times. Therefore we suggest that retrograde induction

is more effective, because;
1. It provides a more homogenous cardioplegic distribution,
2. Despite the high pressure at the aortic root and the left ventricle depending on the insertion of the cross-clamp against the beating heart in antegrade induction, and despite the left ventricle stress caused by the cardioplegic perfusion administred against that high pressure, continuous left ventricle decompression through the aortic root can be achieved during the retrograde induction.
3. The risk of the air influx to the system is higher during the cyclic antegrade/retrograde administration.

CONCLUSION

Because of the particular anatomic status of the venous drainage of the right ventricle, it's been the focus discussion in the recent years that whether the right ventricle could be protected or not during the surgical procedure. We observed that the right ventricle being predominantly perfused by the venous collateralisation was sufficently perfused, and showed no functional impairement in the arrested heart by this technique in isothermic condition.
In conclusion, advantages of "isothermic continuous retrograde blood cardioplegia";

-Provide a more homogenous cardioplegic distrubution,
-No LV strain at cardioplegic induction,
-Minimal air embolism,
-Easy and pratical,
-Time saving during cardioplegic infusion,
-Provides the flexibility of lenghtening the anoxic intervals,
-Minimal volume loading,
-Has no negative effect. It protects both the right and the left ventricle efficently, and it may be an alternative to other techniques.

REFERENCE

1- Martin DR, Scott DF, Downer GL, Belzer FO: Primary cause of unsuccessful liver and heart preservation: Cold sensitivity of the ATP-ase system. Ann Surg 1972; 175:111-115.
2- McMurchie EJ, Raison JK, Cairncross KD: Temperature induced phase changes in membranes of heart: a contrast between the termal response of poikilotherms an homeotherms. Comp Biochem Physiol 1973; 44B:1017-1026.
3- Sakai T,Kuihara S: Effect of rapid cooling on mechanical and electrical responses in ventricular muscle of the guinea pig. J Physiol 1985;361:361-378.
4- Fuhrman GJ, Furrman FA: Utilisation of the glucose by the hypothermic rat. Am J Physiol 1963;295:181-183.
5- Lyons JM,Raison JK: A temparature-induced transition in mitochondrial oxidation:contrast between cold and warm blooded animals. Comp Biochem Physiol 1970; 37:405-406.
6- Magovern GJ Jr, Flaherty JT, Gott VL, Bulkley BH, Gardner TJ: Failure of blood cardioplegia to protect myocardium at lower temperatures. Circulation 1982;66:160-162.
7- Rahn H, Reeves RB, Howell BJ: Hydrogen ion regulation temperature and evaluation. Am Rev Respir Dis 1975; 112:165-166.
8- MacKnight AC, Leaf A: Regulation of cellular volume. Physiol Rev 1977; 57:510-573.
9- Lichtenstein SV, Ashe KA, Dalati HE, Cusimano RJ, Panos A, Slutsky AS: Warm heart surgery. J Thorac Cardiovasc Surg 1991;101:269-274.
10- Partington MT, Acar C, Buckberg GD, Julia P, Kofsky ER, Bugyl HI: Studies of retrograd cardioplegia. 1. Capillary blood flow distribution to myocardium supplied by open and occluded arteries. J Thorac Cardivasc Surg 1989;97:605-606.

11- Buckberg GD, Brazier JR, Nelson RL, Goldstein SM, McConnel DH, Cooper N: Studies of the effects of hypothermia on regional myocardial blood flow and metabolism during cardiopulmonary bypass: The adequately perfused beating, fibrilating and arrested heart. J Thorac Cardiovasc Surg 1977;73:87-94.

12- Lichtenstein SV, Abel JG, Salerno TA: Warm heart surgery and results of operation for recent myocardial infarction. Ann Thorac Surg 1991;52:455-456.

13- Mullen JC, Christakis GT, Weisel RD: Late postoperative ventricular function after blood and cristalloid cardioplegia. Circulation 1986;74:89-90.