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Tepid Versus Cold Blood Cardioplegia in Patients with Low Preoperative Ejection Fraction

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Abstract: Patients undergoing aortocoronary bypass surgery were randomly assigned to receive cold (+10˚C, Group A, n: 36) or tepid (+29˚C, Group B, n: 47) blood cardioplegia. The preoperative ejection fraction of all the patients was under 40%. Cardioplegic solution was delivered in antegrade and retrograde fashion in both groups. The myocardial protective effects of these 2 different cardioplegic temperatures were compared in terms of the postoperative cardiac index and left ventricle stroke work index, dopamine and dobutamine requirements in the intensive care unit, intra aortic balloon pump requirement, intensive care unit stay length and mortality ratios. The daily mean cardiac index and left ventricular stroke work index values of Group B were significantly higher than those of Group A for the first and second postoperative days ($p<0.0001$). The daily mean dopamine and dobutamine requirements of the Group B were significantly lower than those of Group A for the first and second postoperative days ($p<0.0001$). The mean intensive care unit stay was 3.6±0.8 days for Group A and 2.9±0.7 days for Group B ($p<0.0001$). The postoperative intra aortic balloon pump requirement and mortality did not differ between the 2 groups. We concluded that tepid blood cardioplegia reduces the need for postoperative positive inotropic support and the required intensive care unit stay length. Therefore, it provides better myocardial function than cold blood cardioplegia in patients who undergo aortocoronary bypass surgery with low preoperative ejection fraction.

Key Words: Myocardial protection, tepid cardioplegia, aortocoronary bypass

Introduction

It is known that revascularization procedures on compromised myocardium are associated with high mortality and morbidity compared to those on normal myocardium [1,2]. Although cold blood cardioplegia prolongs the safe period of ischaemic arrest time by means of reducing oxygen demands, it puts the myocardium in an anaerobic condition during cross-clamping and prolongs the ischaemic damage so that reperfusion injury occurs [3-5]. As many studies have shown that tepid blood cardioplegia provides better myocardial protection than cold blood cardioplegia most surgeons prefer to deliver tepid cardioplegia in both of antegrade and retrograde fashion for better perfusion of the ischaemic regions beyond obstructed coronary arteries [6-10]. In this study we report our clinical experience with methods of myocardial protection which differed only with respect to cardioplegia temperature in patients who underwent aortocoronary bypass surgery with low preoperative ejection fraction (EF<40%).

Materials and Methods

Patient Population

Eighty-three patients with low preoperative ejection fraction (EF<40%) underwent aortocoronary bypass graft surgery during the period January 1992 to September 1997 in Izmir Ataturk State Hospital Thoracic and Cardiovascular Surgery Department. The preoperative ejection fraction and diseased vessels were estimated on the basis of preoperative 2-plane contrast ventriculography and coronary angiography. Table 1 describes the preoperative patient demographics.

Operative Technique

Cardiopulmonary bypass was established with a single 2-stage right atrial cannula and an ascending aorta cannula. During bypass, the hematocrit was maintained at 20%-25%, pump flows at 2.0-2.5 $L/min/m^2$ and the mean arterial pressure was kept at 50-60 mmHg. The systemic temperature was allowed to drop 29±1° C and topical cooling was achieved with ice slush. In all the

Table 1. Patient demographics.

Variable	Cold (Group A)	Tepid (Group B)	*p* value
Patients	36	47	
Age (years)	58±4	59±5	0.81 (NS)
Sex (M/F)	30/6	40/7	0.59 (NS)
Diabetes Mellitus	3	5	0.52 (NS)
Hypertension	11	16	0.59 (NS)
Smokers (M/F)	26/1	37/1	0.52 (NS)
NYHA class (II-III-IV)	4/18/14	6/25/16	0.65 (NS)
Left main disease	2	4	0.47 (NS)
Previous MI	28	36	0.73 (NS)
LVA	6	9	0.52 (NS)

Continuous variables are presented as the mean±standard deviation and were compared by "Independent-samples t test". x^2 or Fisher's exact test were used for categorical variables.
NYHA, New York Heart Association class
M, male
F, female
LVA, left ventricle aneurysm
MI, myocardial infarction

patients, a balloon-tipped coronary sinus retrograde cardioplegia cannula was placed into the coronary sinus through the right atrial wall for cardioplegia delivery. Rewarming of the patients was begun during the construction of the last anastomosis. The left internal thoracic artery was anastomosed to the left anterior descending artery as the last distal graft in all the patients. Proximal anastomosis of the vein grafts was completed with the placement of an aortic side clamp after removal of the aortic cross clamp. The operative data on the patients is shown in Table 2.

Cardioplegia Technique

The patients were divided randomly into 2 groups according to the cardioplegia temperature: cold (10°C, Group A: 36) or tepid (29°C, Group B: 47). Cardioplegia was given in both antegrade and retrograde fashion consecutively, and the temperature was maintained with a heat exchanger in both groups. All the patients received a blood cardioplegic solution that was prepared by mixing 4 parts oxygenated blood with 1 part crystalloid solution. Then it was delivered at a pressure of 50-70 mmHg. Cardiac arrest was obtained with an antegrade infusion of 10 ml/kg of high potassium cardioplegia (containing 18-20 meq/L of potassium) which was delivered into the aortic root at 10°C or 29°C and then a retrograde infusion of 5 ml/kg of the same solution via the retrograde coronary sinus cannula. For maintenance, 5 ml/kg of low potassium blood cardioplegia (containing 7-10 meq/L of potassium) was infused into the ascending aorta and coronary sinus sequentially after the completion of each vein graft.

Hemodynamic Measurements

Heart rate (HR), mean arterial blood pressure (MAP), mean pulmonary artery pressure (MPAP), mean right atrial pressure (RAP) and pulmonary capillary wedge

Table 2. Patients operative data.

	Group A	Group B	p value
No. of grafts per patient	3.2±0.2	3.4±0.2	0.42 (NS)
Cross-clamp time (min)	69.8±3.1	72.3±3.3	0.61 (NS)
CPB time (min)	89.5±2.5	91.2±2.4	0.30 (NS)
Grafts (2/3/4/5)	2/14/16/5	2/18/21/6	0.57
Left ventricle aneurysmectomy	6	9	0.52 (NS)

Continuous variables are presented as the mean ± standard deviation and were compared by "Independent-samples t test". x^2 or Fisher's exact tests were used for categorical variables.

pressure (PCWP) were measured. Cardiac output (CO) was measured by the thermodilution technique and the mean of the 4 measurements for each day was taken as the mean value of the day. Derived hemodynamic indices were calculated as follows:

Cardiac index (CI): CO/Body surface area (L/min/m^2);

Left ventricular stroke work index (LVSWI): CI/HRx(MAP-PCWP)x0.0136 (g.m/m^2).

These hemodynamic variables were calculated before the initiation of cardiopulmonary bypass, and for the first, the second and the third postoperative day in the ICU. The daily postoperative mean dopamine and dobutamine requirement was calculated as follows:

[Total dopamine (or dobutamine) dose required per day (µg)] / [Weight (kg) x Total inotropic support time per day (min)]

Despite adequate preload and appropriate afterload reduction, if CI was calculated to be under 2.0 L/min/m^2, MAP under 80 mmHg, and elevation of PCWP and low urine output occurred, it was proposed as an indication for dopamine or dobutamine support (or both).

The persistence of low CI despite positive inotropic support (dopamine and dobutamine) was considered an indication for IABP placement.

The mean intensive care unit stay length (ICUSL) and mortality, regardless of cause, occurring within the hospital stay were recorded in a prospective manner in both groups.

Data and Analysis

Statistical analysis was performed with the SPSS program (SPSS Inc., Chicago, IL). The data are presented as mean ± standard deviation of the mean. A X^2 or Fisher's exact test were used for categorical variables. The independent-samples t test was used in order to compare continuous variables. Significance was assumed at a probability level of less than 0.05.

Results

Hemodynamic Measurement

The hemodynamic measurements are summarized in Table 3. As shown in Figure 1, the CI values of Group B were significantly higher than those of Group A on the first and second postoperative days (p<0.0001). The LVSWI values of Group A were significantly lower than those of Group B on the same days, as shown in Figure 2 (p<0.0001). The dopamine and dobutamine requirements of Group A were significantly higher than those of Group B on the first and second postoperative days (p<0.05 and p<0.0001 respectively). On the third postoperative day, there were no statistically significant differences between the hemodynamic parameters and positive inotropic support requirements of the groups.

Clinical Outcome

Two patients in Group A and 1 patient in Group B required IABP support in the postoperative period. There was no statistically significant difference between the

Table 3. Hemodynamic measurements[a].

Variable	Group	Before CPB	1st day in the ICU	2nd day in the ICU	3rd day in the ICU
CI	Group A	1.8±0.1	1.9±0.2	2.0±0.1	2.4±0.1
(L/min/m^2)	Group B	1.8±0.1	2.1±0.2*	2.3±0.2*	2.4±0.1
LVSWI	Group A	29.9±0.8	32.8±0.7	37.7±0.8	45.1±0.9
(g.m/m)	Group B	30.0±0.6	35.8±0.9*	42.2±1.0*	46.5±1.1
Dopamin	Group A	None	7.7±1.3	5.2±1.2	2.8±0.3
(µg/kg/min)	Group B	None	6.2±1.3*	4.0±0.8*	2.7±0.3
Dobutamin	Group A	None	8.5±1.0	6.4±0.6	3.4±0.5
(µg/kg/min)	Group B	None	7.8±0.9**	5.8±0.5*	3.3±0.1

[a] Data are shown as the mean ± the standard error of the mean.
* Significance: p<0.0001 versus Group A
** Significance: p<0.05 versus Group A
CBP: Cardiopulmonary bypass
ICU: Intensive care unit
CI: Cardiac index
LVSWI: Left ventricle stroke work index

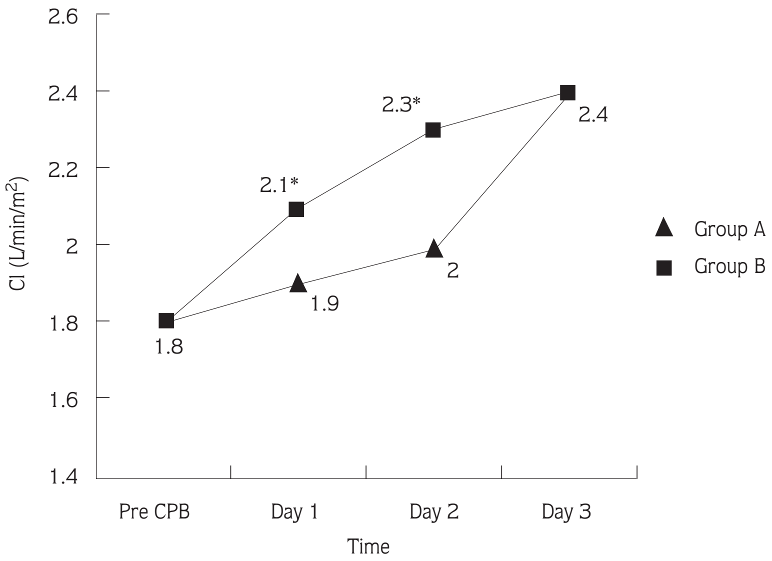

Figure 1. Cardiac index (CI) values of Group B were significantly higher than the Group A on the 1st and 2nd post-operative days. *p<0.0001
Pre CPB: Before cardiopulmonary bypass

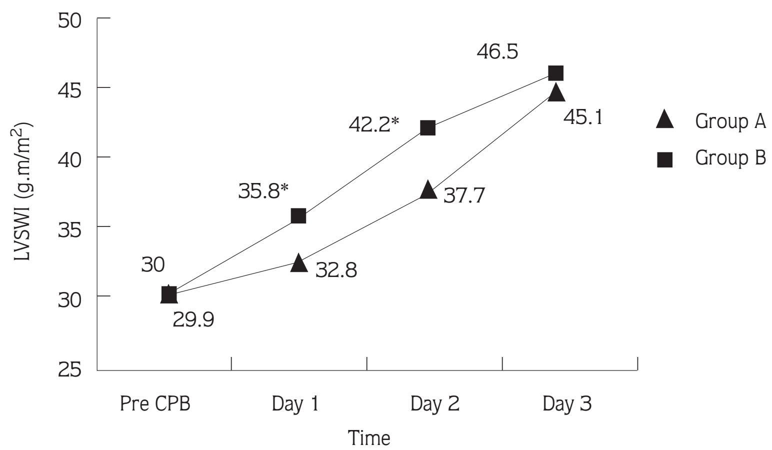

Figure 2. Left ventricle stroke work index (LVSWI) of Ggroup B was significantly higher than that of Group A on the 1st and 2nd postoperative days. *P<0.0001
Pre CPB: Before cardiopulmonary bypass.

groups (p=0.39). The mean ICUSL of Group B was significantly lower than that of Group A (p<0.0001) (Table 4). There were no operative deaths. Two patients in Group A and 3 patients in Group B died due to low cardiac output syndrome associated with multiorgan failure during the postoperative period (p=0.39).

Discussion

Improvements in myocardial protection have contributed to the reduction in the morbidity and mortality of cardiac operations [8,11]. The increasing proportion of patients with compromised myocardium means that better myocardial protection techniques are needed to prevent an increase in postoperative morbidity and mortality [3,12]. When the left ventricular preoperative ejection fraction is 40% or lower, there is a substantial increase in the risk of early postoperative morbidity and mortality in patients undergoing coronary artery bypass grafting [1,2]. Previous studies have shown the feasibility of tepid blood cardioplegia for rapid recovery of the myocardial functions after elective aortocoronary bypass operations in comparison with cold blood cardioplegia techniques. However, its possible protective effect in patients with low preoperative ejection fraction has not been fully determined [4,9,10,13]. Hayashida et al. reported that a tepid blood cardioplegia group was associated with better ventricular function 4 hours after the

Table 4. Clinical outcome.

	Group A	Group B	P value
ICUSL (days)	3.6±0.8	2.9±0.7	P<0.0001[a]
IABP (patients)	2	1	P=0.39°
Death (patients)	2	3	P=0.39°

[a] p value refer to the results of independent-samples t test.
° p value refer to the results of x- or Fisher's exact test.
ICUSL: Intensive care unit stay length
IABP: Intra aortic balloon pump

operation than was the case with a cold blood cardioplegia group because of the reduced metabolic demands of the myocardium [4]. In many papers, tepid blood cardioplegia has been reported to preserve coronary artery endothelial function in both the right and left ventricle and to reduce anaerobic myocardial lactate and acid release without inhibiting myocardial metabolic activity when compared with cold cardioplegia [4,6,7,10]. In our patients, we found that on the first and second postoperative days the CI and LVSWI values, which reflect left ventricular performance, were significantly higher in the tepid group than in the cold group. In parallel to the short myocardial recovery time, the tepid group required significantly less dopamine and dobutamine support in the early postoperative period and shorter ICUSL than the cold group. IABP use and the mortality and morbidity rates did not differ between the 2 groups. As reported previously, coronary artery obstructions limit antegrade cardioplegic delivery to ischaemic regions of the heart [8]. We used consequent antegrade and retrograde cardioplegia infusion to deliver cardioplegic solution beyond obstructed coronary arteries in order to provide better myocardial protection in both groups. Because our cardioplegic methods differed only with respect to temperature between the groups, we conclude that tepid blood cardioplegia preserves ventricular functions better than cold blood cardioplegia. It increases early postoperative CI and LVSWI, and, accordingly, reduces postoperative dopamine and dobutamine requirements and ICUSL in patients undergoing aortocoronary bypass operations with low preoperative ejection fraction.

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