Practical Technique

Perfusion

Perfusion
1–7

DOI: 10.1177/0267659119886717
journals.sagepub.com/home/prf
SAGE

Myocardial protection technique structured on cardiac mass

Ignazio Condello[1], Patrizio Lancellotti[2] and Giuseppe Speziale[1]

Abstract

Objective: Myocardial protection is crucial in cardiac surgery: quantification is often difficult as there is a significant mismatch between body weight and heart weight as per geometric remodeling. This study has the objective to compare two groups of patients on the administration of myocardial protection in valvular pathologies: the first group has indexed the administration with left ventricular mass index; the second has indexed it on the body weight or on the body surface area. The primary endpoint of double-blind case-control study is to detect the difference in incidence in terms of post-operative low cardiac output syndrome.

Methods: A single-center double-blind case-control study in a specialized regional tertiary cardiac surgery center in Italy. Between March 2017 and September 2018, 200 adults (100 per Group A vs. Group B) were scheduled for elective procedures: Group A (50 aortic valve replacement-50 mitral valve repair in minimally invasive cardiac surgery) used blood cardioplegic solution with Saint Thomas I solution, with calculation of left ventricular mass index with echocardiographic measures (Formula Group A); Group B (50 aortic valve replacement-50 mitral valve repair in minimally invasive cardiac surgery) used blood cardioplegic solution with Saint Thomas I solution, with calculation indexed on the body surface area, Du Bois Method (Formula Group B).

Results: A statistically significant difference was found for Student's t-test in patients who used myocardial indexed protection on left ventricular mass index versus control: aortic valve replacement procedures in aortic valve stenosis—ejection fraction (24 hours, p-value = 0.046), TnT (24 hours, p-value = 0.047), stroke volume shift (24 hours, p-value = 0.043), and infusion of epinephrine after cardiopulmonary bypass (p-value = 0.033); aortic valve replacement procedures in aortic valve insufficiency—ejection fraction (24 hours, p-value = 0.044), TnT (24 hours, p-value = 0.047), stroke volume shift (24 hours, p-value = 0.046), and infusion of Epinephrine after cardiopulmonary bypass (p-value = 0.029). No statistically significant differences in patients undergoing mitral valve repair surgery.

Conclusion: The study group in the aortic valve surgery that administered myocardial protection indexed for the left ventricular mass index and showed a statistically significant lower incidence for post-operative low cardiac output syndrome compared to the control group.

Keywords

myocardial protection solution volume; cardiopulmonary bypass; echocardiographic patterns; cardiac surgery; cardiac mass index

Introduction

Between March 2017 and September 2018, 200 adults (100 per Group A vs. Group B) were scheduled for elective procedures (Table 1); the study protocol was approved by the local ethics committee. This study analyzed patients aged >28-80 years (n = 200). EuroSCORE II calculated for the 200 adults scheduled for elective surgery in the absence of coronary heart disease was 2.7-5.6%. The patients were divided into two groups, where the 100 blood myocardial protection was administered on the basis of the characteristics of the echocardiographic calculations, and 100 were treated with indirect calculation of the heart mass of cardioplegia indexed on the body surface. The cardiac

[1]Department of Cardiovascular Surgery, Anthea Hospital, GVM Care & Research, Bari, Italy
[2]Department of Cardiology, University of Liège, Heart Valve Clinic, CHU Sart Tilman, Liège, Belgium

Corresponding author:
Ignazio Condello, Department of Cardiovascular Surgery, Anthea Hospital, GVM Care & Research, Perfusion service, Anthea Hospital, Via Camillo Rosalba 35/37, Bari 70124, Italy.
Email: ignicondello@hotmail.it

Table 1. Samples characteristics.

	Group A (n = 100)	Group B (n = 100)
Age in years (mean)	69 (69.7)	66 (66.7)
Body surface area (m^2)	1.85	1.86
NYHA class (median)	2	2
EuroSCORE II	3.8	3.1
Pre-CPB hematocrit (%, mean ± SEM)	33.6 ± 1.3	33.8 ± 2.1
Pre-CPB Hg (g/dl)	10.4 ± 1.1	10.8 ± 1.2
CPB time (minutes)	62 ± 15.2	57 ± 8.37
Aortic cross-clamp time (minutes)	42 ± 9	41 ± 7
FE Biplane Simpson (%)	47.5 ± 3	48.9 ± 4

NYHA: New York Heart Association; SEM: standard error of the mean; CPB: cardiopulmonary bypass; Hg: hemoglobin; FE: ejection fraction.
Group A represents cardiac mass index and Group B represents body surface area.

Table 2. Operation.

	Group A CMI (n = 100)	Group B BSA (n = 100)	Echocardiographic characteristics
AVR			
AVR stenosis	25	25	AVA < 1 cm^2 MG > 45 mmHg
AVR insufficiency	25	25	EROA > 0.29 cm^2
MVR with minimally invasive approach			
Mitral valve insufficiency in minimally invasive cardiac surgery	50	50	Rvol > 59 mL/beat

CMI: cardiac mass index; BSA: body surface area; AVR: aortic valve replacement; MVR: mitral valve repair; EROA: effective regurgitant orifice area; MG: mean gradient; AVA: aortic valve area; Rvol: regurgitant volume.
Values show the number of patients who underwent each procedure.

surgery procedures that have been analyzed for this study are aortic valve replacement (AVR) and mitral valve repair (MVR) with minimally invasive approach (Table 2). Procedures with coronary artery disease (CAD) were excluded to make the samples not preconditioned by the ischemic insult. The study protocol was approved by the local ethics committee. The primary endpoint of double-blind case-control study is the relationship between cardioplegia volume, left ventricular mass index, and ischemia time by means of the infused cardioplegia index and its relationship with post-operative low cardiac output syndrome.

We prospectively selected patients according to the following criteria:

- Elective, primary cardiac surgery: complete cardiopulmonary bypass (CPB) and cardioplegic arrest had to be foreseen.
- We excluded patients with CAD, renal or liver failure, obesity, uncompensated diabetes, autoimmune disease, active infection, any immunosuppressant therapy, or coagulation disorder. Patients undergoing surgery with circulatory arrest and/or more than mild systemic hypothermia or having preoperative hematocrit (Hct) < 27% were also excluded.

Materials and methods

Procedures: 100 AVR for treatment of 25 aortic stenosis and 25 aortic insufficiency (50 per Group A vs. Group B), 100 MVR in minimally invasive approach for treatment of severe mitral insufficiency (50 per Group A vs. Group B) (see Table 2)—myocardial protection with intermittent cardioplegia, single-shot cardioplegia, multidose cardioplegia, and blood cardioplegia. They have been analyzed in two groups: the difference in posology results—volume myocardial protection (mL), time of ischemia (minutes), and temperature (°C); and the difference in results after procedures—ejection fraction at 24 hours Simpson biplane ejection fraction, VAM (mechanical ventilation) in intensive care unit (ICU) (hours), TnT (ng/L) levels (24 hours), stroke volume shift (L/min) (24 hours) with continuity equation through transthoracic echocardiography, and patients with infusion of epinephrine after CPB.

- Group A (50 AVR-50 MVR) used blood cardioplegic solution with Saint Thomas I (Yves D Durandy) anterograde and retrograde technique of administration (Table 3), with calculation of left ventricular mass index with echocardiographic measures (Formula Group A), on induction and

Table 3. Administration site and pressure.

Administration sites	Aortic root 120 mmHg	Selective coronary 80 mmHg	Coronary venous sinus 35-40 mmHg
Valvulopathy			
Aortic stenosis	Induction	Maintenance	
Mitral value insufficiency	Induction maintenance		
Aortic insufficiency		Maintenance	Induction

maintenance of cardiac arrest, on the volume of the solution, temperature, and time of ischemia.
- Group B (50 AVR-50 MVR) used blood cardioplegic solution with Saint Thomas I (Yves D Durandy) anterograde and retrograde technique of administration (Table 3), with calculation indexed on the body surface area (BSA), Du Bois Method (Formula Group B) on induction and maintenance of cardiac arrest, on the volume of the solution, temperature, and time of ischemia.

The system components are listed below:

- The RemoweLL oxygenator (Eurosets, Medolla, Italy): this is characterized by low priming volume (190 mL), limited (1.35 m^2) contact surface area, and separation of the pericardial blood from the intracavitary suction blood. The pericardial blood is collected separately and can be processed or re-injected, if needed. The oxygenating module is treated with phosphorylcholine.
- Philips iE33 Ultrasound Machine.
- The HARMONY Smart Suction System (Haemonetics, Braintree, MA). This automatically regulates the flow rate and pressure of aspiration of extracavitary blood. The flow rates may vary between 0.5 and 4 L/min.
- A pumpless, vacuum-assisted venous drainage (VAVD) system: this module is managed by an Amvex 100 digital controller, which regulates both the venous return flow and the intracavitary vent flow (pressures ranging between −20 and −45 mmHg).
- Heparin-coated circuits.
- Roller pumps: no roller pumps are used for the suckers.

A Stockert S5 (LivaNova, Italy) heart/lung machine and the same cannulae was employed in both groups. The priming volume was 1,000 mL in Group A, and 700 ± 50 mL in Group B ($p < 0.001$). Mild hypothermia was employed in patients with carotid stenosis. Heparin reversal was obtained with 0.5-0.75 mg of protamine for every 100 units of heparin.

Anesthesia was obtained by fentanyl, midazolam, and rocuronium. Concentrated red cells were transfused whenever hemoglobin (Hg) concentrations fell below 6 g/dL during surgery or below 8 g/dL during the ICU stay. For the administration of myocardial protection a closed circuit for cardioplegia with heat exchanger, with infusion syringe pump in series and Saint Thomas solution with procaine has been used. LANDING Eurosets monitoring system was used for DO2 management during cardiopulmonary bypass.

Methods and perfusion technique in Group A

This methodology refers to the rational of the study hypothesis on volume of intermittent cardioplegia, especially that of maintenance, and should probably be individualized, adjusting for ischemia time and left ventricle mass index:[1–3]

- The study group (Group A) calculated myocardial protection with echocardiographic computation (LVMI) left ventricular mass index, in perfusate volume, pharmacological volume, temperature, ischemia times, and administration site, based on the geometry of the left ventricle.
- The control group (Group B) calculated myocardial protection with calculation indexed on the BSA (Du Bois Method) in perfused volume, pharmacological volume, temperature, ischemia times, and administration site.

The group a has been subdivided into sub-groups based on reference ranges and partition values for left ventricular mass indexed to BSA (g/m^2):

- Normal: Female = 43-95; Male = 49-115;
- Mildly abnormal: Female = 96-108; Male = 116-131;
- Moderately abnormal: Female = 109-121; Male = 132-148;
- Severely abnormal: Female ⩾ 122; Male ⩾ 149.

Formula Group A: calculated myocardial protection volume. Left ventricular mass and left ventricular mass indexed to BSA estimated by left ventricular cavity dimension and wall thickness at end-diastole. Relative wall thickness (RWT) allows further classification of left ventricular mass increase as either concentric hypertrophy (RWT > 0.42) or eccentric hypertrophy (RWT ⩽ 0.42) (Image 1)

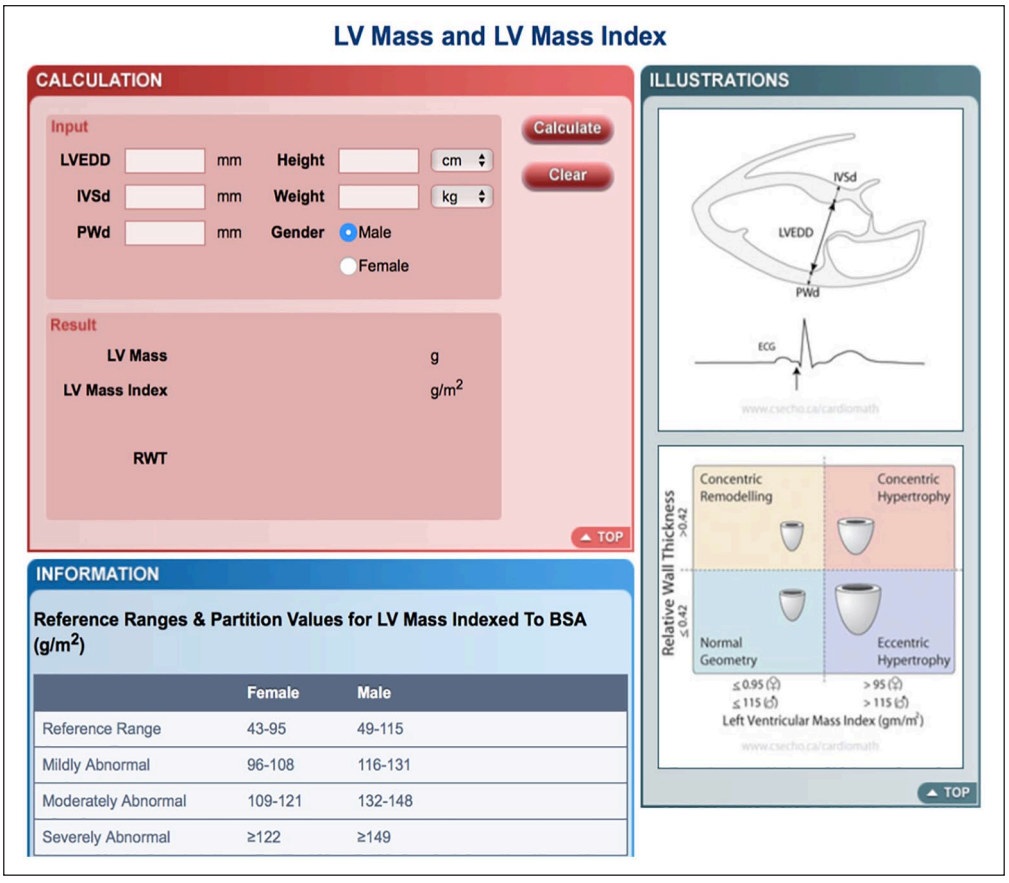

Image 1. Formula LV mass computer calculation.
Source: http://www.csecho.ca/wp-content/themes/twentyeleven-csecho/cardiomath/?eqnHD=echo&eqnDisp=lvmlvmi

$$\text{Left Ventricular Mass}\,(\text{g}) \times 0.7\ \text{mL solution} = 0.8\left\{1.04\left(\left[\text{LVEDD} + \text{IVSd} + \text{PWd}\right]^3 - \text{LVEDD}^3\right)\right\} + 0.6 \times 0.7 \times 10$$

where LVEDD is the left ventricular end-diastolic dimension (mm); IVSd is the interventricular septal thickness at end-diastole (mm); Pwd is the posterior wall thickness at end-diastole (mm); 1.04 is the specific gravity of the myocardium (g/cm^3); weight is expressed in kg or lb; height is expressed in cm or in.[1,2,4–10]

$$\text{RWT}\,(\text{Relative wall thickness}) = 2 \times \frac{\text{Pwd}}{\text{LVEDD}}$$

- Formula Group A: Administration pharmacological perfused volume, temperature (°C), interval of ischemia (minutes) (Table 4).[4,5,11]

Methods and perfusion technique in Group B

This method of administration it refers to from myocardial protection studies, where the volume is indexed and compared to body weight, is known as protocol and AM Calafiore technique.[1–3,10]

Formula Group B: calculated myocardial protection volume. Protocol for intermittent antegrade warm blood cardioplegia acquired some popularity for its simplicity and effectiveness. The possibility to deliver the warm blood cardioplegia intermittently using the antegrade route attracted the attention of the scientific world, as the surgical procedure was less complicated.

In Group B, the volume of myocardial protection solution was indexed for the BSA, the calculation is from the formula of Du Bois and Du Bois

$$\text{Myocardial protection blood volume}\,(\text{mL}) = \text{BSA}\left(\text{W}^{0.425} \times \text{H}^{0.725}\right) \times 0.007184 \times 5.2 \times 100$$

or

$$\text{Simplified formula} = 15\ \text{mL}\,(\text{of solution}) \times \text{kg}\,(\text{body weight})$$

where the weight is in kilograms and the height is in centimeters

- Group B: Administration pharmacological perfused volume, temperature (°C), and interval of ischemia (minutes) (Table 5).

Table 4. Relative wall thickness in administration pharmacological perfused volume, temperature (°C), and interval of ischemia.

Classification mass	Relative wall thickness	Pharmacologic solution (solution mEq/1,000 mL blood solution)	Perfused temperature (°C)	Interval of ischemia (minutes)
Normal ventricle	0.32-0.42	30 mEq K^+Cl^-	34	25
Concentric remodeling	>0.42	35 mEq K^+Cl^-	28	18
Concentric hypertrophy	>0.42	40 mEq K^+Cl^-	20	18
Mixed hypertrophy	>0.42	40 mEq K^+Cl^-	20	18
Physiologic hypertrophy	0.32-0.42	40 mEq K^+Cl^-	18	15
Eccentric hypertrophy	<0.32	35 mEq K^+Cl^-	20	18
Eccentric remodeling	<0.32	35 mEq K^+Cl^-	20	18

Table 5. BSA index for administration pharmacological perfused volume, temperature (°C), and interval of ischemia.

Myocardial protection blood volume (mL)	BSA $(W^{0.425} \times H^{0.725}) \times 0.007184 \times 5.2 \times 100$
Pharmacologic solution (solution mEq/1,000 mL blood solution)	35 mEq K^+Cl^-
Interval of ischemia	25 minutes
Perfused temperature (°C)	30

BSA: body surface area.

Table 6. AVR stenosis correlation results (mean values).

Posology results	AVR stenosis Group A (n = 25) (cardiac mass)	AVR stenosis Group B (n = 25) (BSA)	p-value
Volume myocardial protection (mL)	1,830	975	0.043
Ischemia time	15	25	0.048
Temperature (°C)	18	30	0.046
Results after procedures			
FE% at 24 hours	45	39	0.046
VAM in ICU (hours)	8	17	0.063
TnT ng/L (24 hours)	9.5	18.9	0.047
Stroke volume + shift L/min (24 hours)	2.1	1.4	0.043
Patient with infusion of epinephrine after CPB	2	8	0.037

AVR: aortic valve replacement; BSA: body surface area; FE: ejection fraction; VAM: mechanical ventilation; ICU: intensive care unit; CPB: cardiopulmonary bypass.

The temperature of the perfusate of 30° centigrade was maintained and the cardioplegia was administered for a time of ischemia every 25 minutes[4–7,11] and the concentration of K^+ was 35 mEq/L with Mg^{++}.

Results

Student's t-test was used to compare continuous variables between groups. A p-value of <0.05 was considered significant. Different myocardial geometries have been found for valvular pathologies; however, the two groups in comparison are homogeneous for geometric variability. A statistically significant difference was found in patients who used myocardial indexed protection on left ventricular mass index versus control: AVR procedures in aortic valve stenosis (Table 6)—ejection fraction (24 hours, p-value = 0.046), TnT (24 hours, p-value = 0.047), stroke volume shift (24 hours, p-value = 0.043), infusion of epinephrine after CPB (p-value = 0.033); AVR procedures in aortic valve insufficiency (Table 7)—ejection fraction (24 hours, p-value = 0.044), TnT (24 hours, p-value = 0.047), stroke volume shift (24 hours, p-value = 0.046), infusion of epinephrine after CPB (p-value = 0.029). No statistically significant differences in patients undergoing mitral valve repair surgery (Table 8).

Low cardiac output syndromes (n%) for Group A is 8% and Group B is 23%; reduction left ventricular ejection fraction after CPB is −10% (Group A: 7 patients, Group B: 29 patients).

Table 7. AVR insufficiency correlation results (mean values).

Posology results	AVR insufficiency Group A (n = 25) (cardiac mass)	AVR insufficiency Group B (n = 25) (BSA)	p-value
Volume myocardial protection (mL)	1,715	876	0.046
Ischemia time	18	25	0.051
Temperature (°C)	28	30	0.054
Results after procedures			
FE% at 24 hours	44	37	0.044
VAM in ICU (hours)	7.3	14	0.072
TnT ng/L (24 hours)	8.3	19.9	0.047
Stroke volume + shift L/min (24 hours)	1.6	1.1	0.046
Patient with infusion of Epinephrine after CPB	2	9	0.029

AVR: aortic valve replacement; BSA: body surface area; CPB: cardiopulmonary bypass; FE: ejection fraction; VAM: mechanical ventilation; ICU: intensive care unit.

Table 8. Mitral valve repair correlation results (mean values).

Posology results	Mitral valve repair Group A (n = 50) (cardiac mass)	Mitral valve repair Group B (n = 50) (BSA)	p-value
Volume myocardial protection (mL)	1,250	1,125	0.083
Ischemia time	23	25	0.067
Temperature (°C)	29	30	0.054
Results after procedures			
FE% at 24 hours	44	42	0.044
VAM in ICU (hours)	9.3	12	0.072
TnT ng/L (24 hours)	9.1	11.3	0.074
Stroke volume + shift L/min (24 hours)	1.84	1.79	0.085
Patient with infusion of epinephrine after CPB	4	5	0.084

BSA: body surface area; CPB: cardiopulmonary bypass; FE: ejection fraction; VAM: mechanical ventilation; ICU: intensive care unit.

Discussion

In this study, a calculation formula for the volume of myocardial protection solution is proposed. There is a different degree of myocardial remodeling in every heart valve disease, we observed in the cardiac structures a dimensional mismatch between cardiac mass and body surface in particular on the aortic valve pathology, volume of the solution was calculated on the cardiac mass calculated through the measurements of transesophageal and transthoracic echocardiography. A statistically significant difference in efficacy in protection in the study group emerged in patients undergoing aortic valve replacement, who indexed the solution volume on the cardiac mass, compared to the control group that used the BSA, no variation was shown in terms of statistically significant superior protection in mitral repair procedures. However, many studies dealing with myocardioprotection, in particular, have been centered on the type of solution, single dose or multidose, and often the volume is indexed on the body weight; many European and international surveys in different centers have shown there is a wide individual variability in the posology of administration in cardiac surgery for adults and children. The limitations of this study are that it was performed on patients in elective procedure, with a good performance of cardiac function, and is a limited sample of subjects needed for a larger sample to validate these preliminary results.

Conclusion

This single-center double-blind case-control study shows that the Study Group A that used the myocardial protection technique indexed on cardiac mass reported a mismatch in the volume of the solution, in aortic valve pathology, in aortic valve stenosis, and insufficiency 50% more on average compared to the Control Group B that indexed myocardial protection on the BSA. The increase in posology showed in this subgroup a statistically significant correlation in cardiac systolic and

diastolic performance with echocardiography, in terms of stroke volume (continuity equation L/min), after the procedures and in ejection fraction (Simpson biplane %) in reduction of markers (TnT ng/L) of ischemic damage at 24 hours, in using of epinephrine in aortic valve replacement, and in duration of mechanical ventilation, better in the Study Group A than in the Control Group B. However, numerous studies are needed to strengthen the state of research.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

ORCID iD


Ignazio Condello https://orcid.org/0000-0003-1192-1908

References

1. Maloney JV, Nelson RL. Myocardial preservation during cardiopulmonary bypass: an overview. *J Thorac Cardiovasc Surg* 1975; 70: 1040–1050.
2. Jimenez Rivera JJ, Llanos Jorge C, Iribarren Sarrias JL, et al. Infused cardioplegia index: a new tool to improve myocardial protection. *Med Intensiva* 2019; 43: 337–345.
3. Calafiore AM, Pelini P, Foschi M, et al. Intermittent antegrade warm blood cardioplegia: what is next? *Thorac Cardiovas Surg* 2019. Epub ahead of print 5 March 2019. DOI: 10.1055/s-0039-1679925.
4. Kwiecinski J. Adverse prognosis associated with asymmetric myocardial thickening in aortic stenosis. *Eur Heart J Cardiovasc Imaging* 2018; 19: 347–356.
5. Aranki SF, Nathan M, Shekar P, et al. Hypothermic circulatory arrest enables aortic valve replacement in patients with unclampable aorta. *Ann Thorac Surg* 2005; 80: 1679–1686.
6. Durandy Y. Warm pediatric cardiac surgery: European experience. *Asian Cardiovasc Thorac Ann* 2010; 18: 386–395.
7. Durandy Y, Hulin S. Intermittent warm blood cardioplegia in the surgical treatment of congenital heart disease: clinical experience with 1400 cases. *J Thorac Cardiovasc Surg* 2007; 133: 241–246.
8. Sakata J, Morishita K, Ito T, et al. Comparison of clinical outcome between histidine-triptophan-ketoglutalate solution and cold blood cardioplegic solution in mitral valve replacement. *J Card Surg* 1998; 13: 43–47.
9. Matte GS, del Nido PJ. History and use of del Nido cardioplegia solution at Boston children's hospital. *J Extra Corpor Technol* 2012; 44: 98–103.
10. Allen BS. Pediatric myocardial protection: where do we stand. *J Thorac Cardiovasc Surg* 2004; 128: 11–13.
11. Durandy YD. Is there a rationale for short cardioplegia re-dosing intervals. *World J Cardiol* 2015; 7: 658–664.