A Retrospective Comparative Study of Del Nido Versus Intermittent St Thomas Hospital Blood Cardioplegia Solutions in Aortic-Mitral Double Valve Replacement

Kallol Dasbaksi[1], Mohammad Zahid Hossain[2], Suranjan Haldar[3], Plaban Mukherjee[4]

ABSTRACT

Introduction: It is not uncommon in patients, having rheumatic mitral and aortic valve disease, to undergo mitral valve replacement with aortic valve replacement that is, double valve replacement (DVR) operation who often have severe cardiac dysfunction optimized with medical management before surgery. In this retrospective study we investigated 60 such patients, who underwent DVR operation with either conventional cold blood cardioplegia with St Thomas 2 solution (STH), or del Nido cardioplegia (DN) over five years and compared the effects of the two types of cardioplegia during perioperative and postoperative period with simultaneous comparative study between changes of cardiac performances in the patients with larger left ventricle as compared to those with less enlarged ones.

Material and methods: For this retrospective study, the data of 60 patients of DVR over five years, in Medical College, Kolkata, India, were retrieved for study. The cases were placed into 2 groups: STH and DN according to cardioplegia used during DVR. Demographic, echocardiographic, and several perioperative and postoperative data of the two groups of patients, were collected. Differences between perioperative behaviour between STH and DN groups and post operative changes in the echocardiographic parameters between predominantly mitral stenosis (MS) and mitral regurgitation (MR) patients, were analyzed.

Results: The aortic cross clamp (CC) and cardiopulmonary bypass (CPB) time in both predominant MS and MR patients was shorter in the DN than the STH groups. There was less arrhythmia, less inotropic and ventilator support in the DN group. There was 10% mortality in the series with majority being in the STH and MR predominant patients. Postoperative improvement of LVEF, reduction of LVIDS and LVIDD were also observed in MS predominant in comparison to MR predominant patients after DVR in both STH and DN groups.

Conclusion: Use of DN has been found to have a better outcome and survival when compared to STH cardioplegia solution. DVR could reversely remodel depressed hearts with relatively smaller LV volume and restore LV function of relatively smaller LV of predominant MS patients better in comparison to MR predominant patients with relatively dilated hearts.

Keywords: del Nido (DN) Cardioplegia Solution, St Thomas 2 (STH) Cardioplegia Solution, DVR, Predominant Mitral Stenosis (MS), Predominant Mitral Regurgitation (MR)

INTRODUCTION

Myocardial protection during open heart surgery has been the focus of clinical research for many decades, but the debate regarding the ultimate cardioprotective strategy and the search for the ideal cardioplegic solution are still ongoing.[1] Cardioplegic solutions should improve tolerance to ischemia and reperfusion by preserving myocardial energy reserves, preventing osmotic and electrolyte imbalances and offer buffering for acid- base disturbances.[2] Some other important factors that needs to be considered for myocardial protection are the myocardial reserve and contractile state of the myocardial tissue, the temperature of the tissue, and the composition of the coronary blood at the onset of ischemia by aortic cross clamp (CC) during cardiopulmonary bypass (CPB).[3]

St. Thomas' Hospital solution no 1 (STH1) was introduced clinically by Braimbridge in 1975.[4] Later St Thomas hospital solution 2 (STH) was formulated and was found to be superior in comparison to STH1 in terms of less ischemic reperfusion injury.[5] The composition of STH solution, which is now used in our hospital, was slightly different from STH1 and contained less calcium (1.2 mm).[6,7] It was used earlier as a crystalloid cardioplegia in our hospital but since 2000, it is being used as blood cardioplegia (4 parts of blood to one part of the crystalloid solution) either warm (35-37° C) or cold at 4° C. Blood in cardioplegia solution serves as a bicarbonate donor.

del Nido cardioplegic solution (DN), a modified depolarizing solution, was developed by Dr Pedro J del Nido, a pediatric cardiac surgeon and his team at University of Pittsburgh, USA during early 1990s. It contains low sodium and low

[1]Associate Professor, [2]Assistant Professor, [3]Assistant Professor, [4]Professor and HOD, Department of Cardiothoracic Surgery, Medical College Kolkata, 88, College Street, Kolkata-700073, India

Corresponding author: Dr. Kallol Dasbaksi, Associate Professor, epartment of Cardiothoracic Surgery, Medical College Kolkata, 88, College Street, Kolkata-700073, India

How to cite this article: Kallol Dasbaksi, Mohammad Zahid Hossain, Suranjan Haldar, Plaban Mukherjee. A retrospective comparative study of del nido versus intermittent st thomas hospital blood cardioplegia solutions in aortic-mitral double valve replacement. International Journal of Contemporary Medical Research 2020;7(1):A1-A7.

DOI: http://dx.doi.org/10.21276/ijcmr.2020.7.1.29

calcium solution with low sugar and added potassium chloride, magnesium sulphate, lidocaine and mannitol in fixed doses. It induces long depolarizing arrest during aortic cross clamp (CC) period.[8] DN is more dilute (1 : 4, as blood : crystalloid) as compared to the traditional 4:1 STH blood cardioplegia. Addition of polarizing agents like lidocaine and calcium-competing ions like magnesium in optimum concentration was presumed to prevent intracellular concentration of calcium, thus preventing myocardial injury. Apart from pediatric cardiac surgery, use of DN was extended gradually, initially with some hesitancy, to adult cardiac surgery.[9]

The aim of this study was to evaluate the efficacy and safety of DN as compared to STH in adults who needed long CC time undergoing elective DVR. The following parameters were evaluated and compared between each group and also between mitral stenosis (MS) and mitral regurgitation (MR) predominant patient groups. They included (1) duration of CC and CPB in STH and DN groups, perioperative and post-operative performances of cardiac function, arrhythmias and need for defibrillation, (2) postoperative inotropic and ventilator support, stay in intensive therapy unit (ITU), recovery and mortality, (3) changes in the echocardiographic parameters of left ventricular ejection fraction (LVEF) and left ventricular internal diameter in end systole (LVIDS), and Left ventricular internal diameter in end diastole (LVIDD) before and after DVR.

MATERIAL AND METHODS

This retrospective study was conducted at the Department of Cardiovascular and Thoracic Surgery of Medical College, Kolkata, India. Records of 60 consecutive patients undergoing elective DVR for rheumatic mitral and aortic valve disease were retrieved for the study from 1st January 2013 to 31st December, 2017. Those patients of DVR, due to degenerative pathology and with additional coronary artery bypass grafting were excluded from this study. Our patient population as retrieved from the records, were placed into two groups based on the type of cardioplegia administered during surgery: (1) intermittent STH blood cardioplegia (n = 30), and (2) del Nido (DN) cardioplegia (n = 30). 36 patients (60%) were found to have predominant mitral stenosis (MS) (mitral valve area less than 1.5 cm^2) while 24 patients (40%) were found to have predominant mitral regurgitation (without MS) as the principal mitral valve disease. Aortic pathology was either aortic stenosis (AS) or aortic regurgitation (AR). All procedures were performed using a standard general anesthesia protocol, median sternotomy, CPB with bicaval cannulation and moderate systemic hypothermia (30 to 31 °C). After the aorta was cross clamped, antegrade cold cardioplegia at 4°C with STH (4:1 dilution as blood : STH crystalloid) or DN (1:4 dilution as blood : DN solution) was infused by cardioplegia delivery system at a rate of 20 ml/kg. STH was repeated 15 to 20 ml/kg at intervals of 20 to 23 minutes. A second dose (800 to 1000 ml) of DN was infused whenever the cross clamp time exceeded 90 min in the DN group. Both were run mostly antegradely. Retrograde cardioplegia was used in cases when there was RV enlargement (> 30 mm at base) or LV hypertrophy.

MVR was done after completing chordal preservation wherever feasible and next AVR was done using interrupted # 2-0 polyester sutures. Rewarming, de-airing, aortic declamping and weaning off bypass were done in the usual manner. Rest of the procedures of decannulation and chest closure were performed in standard fashion. Surgery was done by five surgeons and their experiences were also shared.

The base line information about the cardioplegia used, patient's demography, presence of AF, RV dimension are summarized in Table-1. Intraoperative and postoperative data are summarized in Table 2. Changes in several cardiac parameters like LVEF, LVIDS, LVIDD were assessed between the STH and DN groups and are summarized in Table-3. Table-4 shows the differences between the changes in LVEF, LVIDS, LVIDD after DVR in MS and MR predominant lesions irrespective of STH and DN groups.

This retrospective study, was approved by the ethics committee of our institution and being it retrospective in nature, patient consent was not required. The cardiac procedures performed using different cardioplegic solutions

Variables	Total	STH	DN	p
Total No of patients	60	30	30	
Age (years,mean ± SD	38.50 ± 10.33	37.68±8.25	39.32±11.30	-
Male, n (%)	19 (31.67%)	8 (13.33%)	11(18.33%)	-
Female, n (%)	41(68.33%)	22 (36.673%)	19(31.67%)	-
BSA m^2 (mean ± SD)	1.38 ± 0.23	1.36 ±0.17	1.39 ± 0.13	0.88
AF	52 (86.673%)	27(45.00%)	25(41.67%)	0.96
PASP mm Hg mean± SD	50 (60mm ± 12)			
RV basal diameter >39 mm	n=12	5(8.33%)	7(11.6%)	0.78

Values are presented as mean mm, ± SD =mean±standard deviation, number (%), EF= Left ventricular ejection fraction in %, LVIDS= left ventricular internal diameter in mm in end systole, LVIDD= Left ventricular internal diameter in end diastole in mm, STH= St Thomas 2 cardioplegia group, DN= del Nido cardioplegia group, MS predominant = mitral stenosis being predominant lesion in patients with Aortic and Mitral valve disease, MR predominant = mitral regurgitation being predominant lesion in patients with Aortic and Mitral valve disease, AF=atrial fibrillation, PASP= Pulmonary artery systolic pressure, RV= right ventricle

Table-1: Distribution of base line characteristics of patients with predominantly MS or MR who underwent DVR using STH or DN

were in accordance with the routine standard of care being followed at the institution during 2013-2017.

STATISTICAL ANALYSIS

Data were checked for normality before statistical analysis. Categorical variables were analyzed using either the χ^2 test or Fisher's exact test. Normally distributed continuous variables were compared using the unpaired *t* test. The Mann- Whitney *U* test was used for those variables that were not normally distributed. Differences between study groups were considered statistically significant when *p* was less than or equal to 0.05.

RESULTS

The mean age of the patients was 38.50 years± 10.33. The aortic CC time and CPB time were significantly longer, in STH group in comparison to DN in groups (Table-2). Spontaneous electrical activity was found to be higher in STH (n=12,20%) than in DN (n=5,8.33%) group during CC period. Time taken for return of steady spontaneous cardiac impulse after CC removal was significantly early in cases of STH when compared to DN groups (34±5.09 sec vs 70±12.06 sec respectively, p=0.01). Incidence of post CPB ventricular tachycardia (VT), ventricular fibrillation (VF), and defibrillation were significantly higher in STH than in the DN groups. Higher inotropic support in ITU was required more in STH and ventilator support was slightly more in STH (25 hours ±4.7) than the DN group (21 hours ±5.6) in the survivors. Reintubation rate was more in STH than the DN group. ITU stays were not significantly different between the two groups being slightly higher in STH (5 days± 2.7) than the DN group (3.5 days ± 2.5) (Table-2).

There were 6 deaths in the study group. Cause of death was low cardiac output syndrome (LCOS) during post operative period between 7th to 10th day in 5 patients with MR as predominant lesion being 4 (6.67%) in STH and 1 in DN group. There was one death in MS predominant in STH group (mitral restenosis after previous TVMC 8 years back) which occurred due to post operative CVA and hazards of prolonged ventilation.

DISCUSSION

Incidence rheumatic heart valve disease (RHD): In RHD, the order of involvement of valves has been reported as mitral (60.2%), followed by aortic, tricuspid and pulmonary

Groups		STH	DN	p
MS predominant Variables				
CC min	(mean mm, ± SD)	136.10±5.14	127.6± 3.6	0.05
CPB min	(mean mm, ± SD)	162.6 6±6.23	150.3 ±9.3	0.05
MR predominant Variables				
CC min		144.58±8.14	131.83± 4.36	0.04
CPB min		166.6 7±14.23	158.16 ±9.69	0.05
MS and MR predominant patients combined				
Time taken for cardioplegic arrest		24.5 ±4.07 sec	32.5± 7.85 sec	0.05
Spontaneous electrical activity during CC period (n)		12 /60(20.0%)	5/60(8.33%)	
Time taken for return of steady cardiac impulse		34±5.09 sec	70±12.06 sec	0.01
Arrhythmias n (%)	VT/VF	14(23.33)	6(10.0)	0.01
Defibrillation n(%)		5(8.33%)	3(5%)	0.12
Postoperative variables in ITU in both MS and MR predominant patients combined				
Variables	Values	STH	DN	P
Mechanical ventilation	(hours)	29±7.7	26 ±5.6	0.21
Reintubation rate	n (%)	4(6.67%)	2 (3.33%)	0.13
High inotropic support	n (%)	17 (28.3%)	10 (16.67%)	0.05
Mean ITU stay days	n (%)	5 ± 2.7	3.5 ± 2.5	0.21
LCOS	n (%)	8(13.33%)	4(6.67%)	0.07
Hospital stay in days		10 ± .80	8 ± 7.5	0.17
30 day mortality	6 (10.0%)	5 (8.33%)	1(0.17%)	0.09
n	MR 5	4	1	
n	MS	1	0	

Values are presented as mean mm, ± SD (standard deviation), number (%),STH= St Thomas 2 cardioplegia group, DN= delNido cardioplegia group, MS predominant = mitral stenosis being predominant lesion in patients with Aortic and Mitral valve disease, MR predominant = mitral regurgitation being predominant lesion in patients with Aortic and Mitral valve disease, CC= aortic cross clamp time in minutes, CPB= total cardiopulmo -nary bypass time in minutes, High inotropic support= A dose of dobutamine more than 5 µg/kg/min, epinephrine 1.0 µg/kg/min, LCOS= Low output cardiac failure or persistent hypotension defined as systolic blood pressure < 90 mmHg or mean arterial pressure (MAP) 30 mmHg below baseline or requirement of vasopressors to achieve a sys-tolic blood pressure ≥ or 90 mmHg; and (2) signs of impaired organ perfusion (e.g., central nervous system abnormalities including confusion or lack of alertness, or even loss of consciousness; oliguria; cold, clammy skin and extremities, tachypnea , ITU= intensive care unit.

Table-2: Distribution of intraoperative and postoperative profiles in STH and DN groups in both MS/MR predominant patients

Cardiac parameters	Variables	Preoperative	Post operative	p
MS predominant STH	EF	54.72±2.49	57.94±2.78	0.02
MS predominant DN	EF	53.06±2.41	56.18±1.85	0.05
MS predominant STH	LVIDS	34.78±2.02	33.44 ± 2.83	0.82
MS predominant DN	LVIDS	36 ± 2.41	34.53±2.22	0.21
MS predominant STH	LVIDD	48.06±5.92	45.53±2.54	0.43
MS predominant DN	LVIDD	49.78 ± 7.8	45.89±3.12	0.23
MR predominant STH	EF	49.80±1.39	45.41±2.71	0.04
MR predominant DN	EF	50.17±0.2.79	47.25±4.86	0.05
MR predominant STH	LVIDS	39.50±1.31	42.56 ± 2.83	0.09
MR predominant DN	LVIDS	38.17±2.51	42.42±3.52	0.13
MR predominant STH	LVIDD	52.58±2.06	55.67±2.90	0.07
MR predominant DN	LVIDD	51.83±2.69	54.75±2.20	0.21

Values are presented as mean ± SD= mean±standard deviation, number (%), EF= Left ventricular ejection fraction in %, LVIDS= left Ventricular internal diameter in mm in end systole, LVIDD= Left ventricular internal diameter in end diastole in mm, STH= St Thomas 2 cardioplegia group, DN= delNido cardioplegia group, MS predominant = mitral stenosis being predominant lesion in patients with Aortic and Mitral valve disease, MR predominant = mitral regurgitation being predominant lesion in patients with Aortic and Mitral valve disease, LCOS= low cardiac output state, Post operative echocardiography was done in 21 patients in STH and 20 patients in DN groups. The echocardiographic data of the patients who expired has not been included in the above table but discussed in results section.

Table-3: Distribution of changes after DVR between preoperative and postoperative profiles in STH and DN groups in both MS/MR predominant patients

Parameters	Preoperative	Postoperative	p
EF in MS predominant in STH and DN	53.89%± 4.39	55.62±2.23	0.03
EF in MR predominant in STH and DN	49.98±2.56	45.38±1.45	0.04
LVIDS in MS Predominant in STH and DN	35.24±2.34	33.46±1.32	0.12
LVIDD in MS predominant in STH and DN	48.92±6.38	46.93±2.38	0.22
LVIDS in MR Predominant in STH and DN	38.66±1.47	40.48±1.32	0.14
LVIDD in MR predominant in STH and DN	52.74±2.98	54.67±1.35	0.16

Values are presented as mean±standard deviation, number (%), EF= Left ventricular ejection fraction in %, LVIDS= left ventricular internal diameter in mm in end systole, LVIDD= Left ventricular internal diameter in end diastole in mm, STH= St Thomas 2 cardioplegia group, DN= delNido cardioplegia group, MS predominant = mitral stenosis being predominant lesion in patients with Aortic and Mitral valve disease, MR predominant = mitral regurgitation being predominant lesion in patients with Aortic and Mitral valve disease

Table-4: Distribution of changes after DVR between preoperative and postoperative cardiac profiles in STH and DN groups in predominant MS and MR patients

valves. Mitral stenosis, predominantly seen in females, is almost exclusively of rheumatic etiology (97.4%) in India. The predominant form of isolated MR is also rheumatic (41.1%). While MR + AR was commoner than MS + AR in the pediatric age group (< 19 years of age), the reverse was true in the adult age group reflecting the natural progression of valve lesions leading to MS due to chronic rheumatic pathology.[10] This is agreeable to our findings as MS+AR/AS (60%) was more common than (MR+AR/AS) (40%) and the average age was also more than 30 in our present study for surgical DVR. AS was also less than AR in our series of DVR (not shown in table). Female patients formed 68.33% while males formed 31.67% in our series similar to those reported by others.[10]

Single dose del Nido cardioplegia: DN which was originally developed for pediatric cardiac surgery.[8,9,11,12] and was gradually extended to adult cardiac surgery.[9,13] The benefit of this solution is to maintain arrest for long period of time, generally 90 minutes before redosing and avoidance of repetitive interruption of operation unlike multiple doses of standard cardioplegia. It has been claimed to sustain myocardial viability for 3 hours without redosing during aortic CC[14] which leads to shorter CC times and CPB duration.[15,16,17] Though DN cardioplegia can give adequate myocardial protection in for 3 hours after a single dose[14] and has been confirmed by our experience in cases of aortic arch replacement for arch aneurysm with normal cardiac function, with aortic CC of 3 hours, we have noted cardiac dysfunction in hypertrophied heart for AVR after CC of 2 hours. There was on an average 2 cardioplegia doses in DN in our patients at intervals of 90 minutes as opposed to an average 5 to 6 doses in STH group. This is in agreement with other reports.[8,9,18]

CC and CPB times and role of preexisting myocardial function: The CC and CPB duration in the present study were, however, longer than those reported in previously published studies about DVR in adult patients.[18] The plausible explanation for this may be preponderance of often deformed calcified valves, slower surgical procedures of using interrupted sutures for valve replacement, chordal

preservation, difficult dissection and hemostasis for patients with history of trans ventricular mitral commissurotomy (TVMC), presence of thrombus in LA, post cross clamp RV and LV dysfunction, arrhythmia etc. There was also significant difference between the CC and CPB duration in respect of STH and DN (table-2) with the greater CC and CPB times in STH than in DN groups as observed in our study. The CC time for MS predominant patients in both STH and DN group (136.10 min±5.14 in STH and 127.6 min ± 3.6 in DN) was shorter than that in the MR group (144.58 min± 8.14 in STH and 131.83 min ± 4.36 in DN). Preoperatively more compromised LV with larger LVIDS (>38 mm), lower LVEF (<50%) and consequent less contractile reserve may have resulted in more time taken to come off CPB in MR (166.6 7 min ±14.23 in STH and 158.16 min ±9.69 in DN) in comparison to MS predominant patients (162.6 6 min ±6.23 in STH and 150.3 min ±9.3 in DN groups). LV contractility was better preserved with LVIDS<38mm. AR with MR were often the patients with longer CPB duration due to more LV dilatation.

Dilated RV which is associated with right ventricular dysfunction (RVD) is also a surrogate for LV dysfunction due to interdependence. Both ventricles, are bound together with spiral muscle bundles originating from interventricular septum (IVS) that encircle them in a complex interlacing fashion to form a highly interdependent functional unit.[19] RVD may occur in mitral valve disease and is more due to long standing pulmonary hypertension and thus may lead to prolonged CPB duration in both the MS and MR predominant patients after long CC time due to inadequate preservation of inter ventricular septum (IVS) viability. Gerald D Buckberg advocated routine antegrade combined with retrograde cardioplegia apart from other measures, for proper conservation of IVS to prevent RVD.[19] and prolongation of CPB. In our series, retrograde perfusion was not routine affair but used only when required due to unfavorable coronary anatomy during antegrade cardioplegic infusion or when the RV diameter was more than 30 mm. In 12 of our patients with RV>39mm, such retrograde perfusion probably mitigated RV dysfunction. In fact, during retrograde cardioplegia, soon after antegrade osteal cardioplegia, dark blood was seen oozing retrogradely through the coronary ostea as seen through incised aorta. This also indicates that there must have been areas of nonperfused myocardium after antegrade cardioplegia delivery. This fact was reported by Buckberg[19] and we also confirm it.

Spontaneous electromechanical activity during CC and reperfusion arrhythmia after CC release: Occasional wide complex beats seen on the electrocardiogram with accompanying weak mechanical activity was sometimes observed during the arrest period in 40% hearts in the STH group 8 to 12 minutes after reinfusion of cardioplegia well ahead of the subsequent dose. It was less in the DN group, 16.67%, (table-2). Inadvertent rewarming by noncoronary collateral myocardial flow might have been a reason for such activity which has also been corroborated by others.[20,21] Apart from rewarming and cardioplegic washout, a higher plasma potassium concentration (>5.5 mmol/liter) has also been implicated.[21,22] Other biochemical alterations such as low magnesium concentration can also cause membrane potential to be less polarized raising intracellular sodium accumulation resulting in Na+- K+ pump inhibition. This change in membrane potential has also been hypothesized as a potential mechanism for causing such arrhythmias.[22,23] But since both STH and DN have equivalent magnesium concentration as 16 mmol/L, the presence of lidocaine in DN may have resulted in membrane stabilization effect and prevented inappropriate rise of action potential during CC period.[8,9,12] But on the other hand presence of lidocaine may also have delayed the reappearance of spontaneous return of steady cardiac impulse after CC release in DN group. After CC release, VT or VF developed in 20 of 60 patients (23.33%) being significantly higher in the STH group (p=0.01) (Table-2). The patients with AF mostly had these arrhythmia and mostly had delayed weaning from CPB in both the groups. This finding of ours corroborates those of others.[18,20,24,25] However, defibrillation was required in 8 patients, more in the STH group (n=5) than the DN group (n=3) due to persistent VT or VF with hypotension despite correction of electrolytic abnormalities and anti arrhythmic medications. Inability to prevent mitochondrial calcium (Ca) uniporter, (MCU) by STH, in mediating reperfusion-induced arrhythmias was an explanation for an increased incidence in the STH group.[26] MCU inhibition prevents mitochondrial Ca^{2+} uptake and reactive oxygen species (ROS) production and preserves the mitochondrial membrane potential to protect the cells from apoptosis.[27] MCU inhibition might have been an additional factor in the DN group due to its ability to inhibit the intracellular Ca accumulation. However, the absence of Ca^{2+} increased the risk of inducing a "calcium paradox", as envisaged by certain investigators. But traces of contaminant Ca^{2+in} in blood, hypothermia, low Na, and high Mg^{2+} may have counteracted this risk in DN cardioplegia.[28] Delay in redosing STH could also have resulted in myocardial dysfunction triggering arrhythmias.[29]

Magnesium: Investigators[30] observed during their animal experiments, that an optimal magnesium concentration of 20-25 mmol/l was associated with improved ATP availability and reduced ATP utilisation and reduced ischaemic contracture development when compared to hyperkalaemia in STH. Magnesium inhibits L-type calcium channels, sodium-calcium exchange, sarcoplasmic reticulum calcium release and is likely to be associated with direct reduction in intracellular calcium accumulation. Such effects may have influenced the benefit seen with DN compared to STH with relatively more calcium. It has been observed that the diseased senescent myocardium with increasingly elderly cardiac surgery patients which is more sensitive to ischemia, has a 30% more rapid rise in intracellular calcium in contrast to normal mature myocardium. So, magnesium based cardioplegia have advocated for relatively magnesium rich low calcium solutions in preference to STH in this elderly

group of patients.[30]

Post operative period: Postoperatively in the ITU the cohorts with preoperative class 3 or 4 NYHA had longer intubation in both the groups. Significantly higher inotropic support (p=0.05) was observed in STH group (Table-2). Similarly low cardiac output state (LCOS) and longer ITU stay were also observed in STH group. Mortality was also higher in STH group with MR predominant patients (Table-2) in comparison to DN group. The overall mortality was 10% in our series which was higher than reported by others.[18,31] This may have been due to inclusion of more symptomatically sick patients with inherent LV dysfunction with LV dilatation and high PASP for DVR when they were referred for DVR.

Post operative changes of LV function: Number of patients with pre operative LVEF > 50% was more in the MS predominant group than the MR predominant groups in both the STH the DN group (Table-3). There was a general trend toward improvement of LVEF after DVR in MS predominant patients with LVIDS < 38 mm after DVR in STH and DN combined (Table-4) and also significantly in both DN (p=0.05) and STH (p= 0.02) groups separately (Table-3). There was a trend toward decrease of LVEF in the MR predominant cases, most of which had LVIDS > 38 mm, in STH and DN combined patients (vide Table No.4) and in both the DN (p=0.05) and STH (p=0.04) groups separately (Table 3) though symptomatic improvement was noted in such patients during follow up. This finding was in agreement with observations of others.[31] There was decrease in LVIDS and LVIDD after DVR in MS predominant patient. In our predominant MR patients in both STH and DN groups, both the LVIDS and LVIDD increased. Investigators from Japan reported that postoperative decrease of 2 to 3 mm from preoperative LVIDS of 61.2 mm ± 6 in dilated cardiomyopathy patients was noted after MVR or MV repair.[32] But such patients had preoperative PASP <40 mm Hg which is distinctly lower than the average PASP (of >50 mm Hg) in our patients with rheumatic pathology, and that that too, after pretreatment with sildenafil in addition to diuretics. Preoperative additional sildenafil (25 mg TDS) has shown in our experience to decrease PASP from 90 to 60 mmHg in patients with severe MS or MR. Others have also reported use of sildenafil for high PASP and RVD[24]

Our patients had symptomatically improved with higher LVEF in the MS predominant patients to NYHA class II or I, from preoperative class III or class IV disability status. But in in the MR predominant patients (both the STH and DN groups) the improvements in symptoms were also noted but not so marked as in the MS predominant patients. MR predominant patients experienced decreased postoperative LVEF and increased chamber dilatation and needed more diuretic and angiotensin inhibitor support. This was also observed by others.[19,31] Such patients after DVR in our series also were prescribed additional sildenafil (25 mg TDS) and continued postoperatively indefinitely and improvement in disability status was observed on follow up.

Our data demonstrate that reverse remodeling occurs following surgery with LV mass regression and LV ejection fraction recovery in patients of predominant MS. This implies that the ventricular remodeling process imparts less reversible changes, particularly as patients develop chamber dilatation and ventricular dysfunction which is more prevalent in MR predominant patients. These findings indirectly support a growing body of evidence suggesting earlier surgical intervention for patients having mitral regurgitation[31] who need MVR or DVR.

CONCLUSION

The best cardioplegia with optimal re-dosing interval is likely to vary with different patients having different pathologies and risk factors. When the clamp time is less than 60 min, one can actually use whatever cardioplegia or myocardial protection available and still can still get to the shore.[28] But with long cross clamp time, we observed less CC and CPB duration, less arrhythmias, less use of defibrillation, less ventilator and inotropic support, less ITU stay in DN as compared to STH group.

Limitations of the study

There are certain limitations of our study. Firstly it is a single-institution retrospective study, which limits its generalizability, is descriptive in nature and small cohort size. Secondly, only pre and postoperative hemodynamic parameters were used to assess myocardial protection, while biochemical parameters such as changes in cardiac enzymes compared to their pre operative values could have enabled better analysis of direct cardiac injury. Finally, no long-term follow-up of myocardial protection was done. More prospective longterm studies must be designed to explore the applications of DN cardioplegia and to validate our current findings.

REFERENCES

1. Hearse DJ, J Physiol (Paris). 1980;76:751-68
2. Gunnes S., Jynge P. (2011) Fundamentals of the Past: Cardioplegia: The First Period Revisited. In: Podesser B., Chambers D. (eds) New Solutions for the Heart. Springer, Vienna
3. Qiu Y, Galifianes M, Haddock PS, Hearse DJ. Continuous warm versus intermittent cold cardioplegic infusion: a comparison of energy metabolism, sodium-potassium adenosine triphosphatase activity, and postischemic functional recovery in the blood-perfused rat heart, J Thorac Cardiovasc Surg 1996;112:797-805
4. Cankovic-Darracott S, Braimbridge MV, Williams BT, Bitensky L, Chayen J. Myocardial preservation during aortic valve surgery. Assessment of five techniques by cellular chemical and biophysical methods. J Thorac Cardiovasc Surg. 1977;5:699-706
5. Ledingham SJ et al. The St Thomas Hospital Cardioplegic Solution. A comparison of the efficacy of the two formulations, J Thorac Cardiovasc Surg, 1987;93: 240-6
6. Jynge P, Hearse DJ, Braimbridge MV et al. The St. Thomas' hospital cardioplegic solution: a characterization in two species, Scand J Thorac

Cardiovasc Surg Suppl. 1981;30:1-28
7. Chambers DJ, Haire K, MD, Morley N, Fairbanks L, et al. St. Thomas' Hospital Cardioplegia: Enhanced Protection With Exogenous Creatine Phosphate Ann Thorac Surg, 1996;61:67-75
8. Matte GS, del Nido PJ. History and use of del Nido cardioplegia solution at Boston Children's Hospital. JECT 2012; 44: 98-103.
9. Mongero LB. Del Nido Cardioplegia—Not Just Kids Stuff, JECT. 2016;48:25–28
10. Manjunath CN, Srinivas P, Ravindranath KS, Dhanalakshmi C. Incidence and patterns of valvular heart disease in a tertiary care high-volume cardiac center: a single center experience. Indian Heart J. 2014;66:320-6.
11. Kim K, Ball C, Grady P, Mick S. Use of del Nido Cardioplegia for Adult Cardiac Surgery at the Cleveland Clinic: Perfusion Implications. J Extra Corpor Technol. 2014;46:317–323
12. O'Brien JD, Howlett SE, Burton HJ, O'Blenes SB, Litz DS, Friesen CL. Pediatric, cardioplegia strategy results in enhanced calcium metabolism and lower serum troponin T. Ann Thorac Surg 2009; 87: 1517-1523
13. Smigla G, Jaquiss R, Walczak R, Bonadonna D, Kaemmer D, Schwimer C, Lodge A. Assessing the safety of del Nido cardioplegia solution in adult congenital cases. Perfusion 2014; 29: 554-558.
14. Spratt JR, Guleserian KJ, Shumway SJ, Historical perspectives of The American Association for Thoracic Surgery: Pedro J. del Nido, J Thorac Cardiovasc Surg 2017;153:225-7
15. Sorabella RA, Akashi H, Yerebakan H, Najjar M, Mannan A, Williams MR, Smith CR, George I. Myocardial protection using del Nido cardioplegia solution in adult reoperative aortic valve surgery. J Card Surg 2014; 29: 445-449.
16. Yerebakan H, Sorabella RA, Najjar M, Castillero E, Mongero L, Beck J, Hossain M, Takayama H, Williams MR, Naka Y, Argenziano M, Bacha E, Smith CR, George I. Del Nido cardioplegia can be safely administered in high-risk coronary artery bypass grafting surgery after acute myocardial infarction: a propensity matched comparison. J Cardiothorac Surg 2014; 9: 141.
17. Mick SL, Robich MP, Houghtaling PL, Gillinov AM, Soltesz EG, Johnston DR, Blackstone EH, Sabik JF 3rd. Del Nido versus Buckberg cardioplegia in adult isolated valve surgery. J Thorac Cardiovasc Surg 2015; 149: 626-634.
18. Mishra P, Ranjit B. et al. Comparison of del Nido cardioplegia and St. Thomas Hospital solution – two types of cardioplegia in adult cardiac surgery, Kardiochirurgia i Torakochirurgia Polska, 2016; 13: 295–299
19. Buckberg GD, Athanasuleas CL. Cardioplegia: solutions or strategies? Eur J Cardiothorac Surg 2016; 50: 787–91
20. Govindapillai A, Hua R, Rose R, Friesen CH, O'Blenes SB. Protecting the aged heart during cardiac surgery: use of del Nido cardioplegia provides superior functional recovery in isolated hearts. J Thorac Cardiovasc Surg 2013; 146: 940-948.
21. Lake CL, Sellers TD, Nolan SP, Crosby IK, Wellons HA, Jr, Crampton RS. Determinants of reperfusion cardiac electrical activity after cold cardioplegic arrest during coronary bypass surgery. Am J Cardiol. 1984; 54: 519–525.
22. Walter A. Parham, Ali A. Kurt M, Carey S, et al. Hyperkalemia Revisited, Tex Heart Inst J. 2006; 33: 40–47
23. Yeatman M, Caputo M, Narayan P, et al. Magnesium-Supplemented Warm Blood Cardioplegia in Patients Undergoing Coronary Artery Revascularization, Ann Thorac Surg 2002;73:112– 8
24. Lindqvist P, Henein MY. Right ventricular function in pulmonary hypertension, Imaging Med. 2012;4:657–665
25. Buckberg GD. Controlled reperfusion after ischemia may be the unifying recovery denominator. J Thorac Cardiovasc Surg 2010;140:12–8, 18
26. H Clements-Jewery. Mitochondria, the calcium uniporter, and reperfusion-induced ventricular fibrillation, Br J Pharmacol. 2006;149: 811–813.
27. Sebag SC, Koval OM, Paschke JD, Winters CJ, Comellas AP, Grumbach IM. Inhibition of the mitochondrial calcium uniporter prevents IL-13 and allergen-mediated airway epithelial apoptosis and loss of barrier function, Exp Cell Res. 2018;362:400-411
28. Chambers DJ, Mechanisms and Alternative Methods of Achieving Cardiac Arrest Ann Thorac Surg 2003;75:S661–6
29. Durandy YD. Is there a rationale for short cardioplegia re-dosing intervals? World J Cardiol. 2015;7: 658–664
30. Maruyama Y, Chambers DJ,Myocardial protection: efficacy of a novel magnesium-based cardioplegia (RS-C) compared to St Thomas' Hospital cardioplegic solution, Interact Cardiovasc Thorac Surg, 2008;7:745-9.
31. Quintana E, Suri RM, Thalji NM, Daly RC, Dearani JA, Burkhart HM et al. Left ventricular dysfunction after mitral valve repair-the fallacy of 'normal' preoperative myocardial function. J Thorac Cardiovasc Surg 2014; 148: 2752–60.
32. Horii T, Suma H, Isomura T, Nomura F, Hoshino H, Left Ventricle Volume Affects the Result of Mitral Valve Surgery for Idiopathic Dilated Cardiomyopathy to Treat Congestive Heart Failure, Ann Thorac Surg 2006;82:1349 –55

Source of Support: Nil; **Conflict of Interest:** None

Submitted: 16-12-2019; **Accepted:** 22-012020; **Published:** 26-01-2020