Comparison of the Outcomes between St.Thomas Cardioplegia and Modified del Nido Cardioplegia in on pump Coronary Bypass Surgery

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Abstract

Objective: Del Nido cardioplegic solution has become an option for the treatment of on pump arrested heart surgery. This study aims to compare the outcomes of on pump arrested heart CABG procedure, using modified del Nido cardioplegia versus St.Thomas cardioplegia.

Method: A retrospective review with prospective follow-up of 102 patients in elective cases of on pump arrested heart CABG from April 2019 to April 2020. Patient's demographic and early outcomes were analyzed.

Results: There were 68 patients underwent CABG using St.Thomas cardioplegia and 34 patients who underwent CABG using modified del Nido cardioplegia. The mean age of CABG patients using St.Thomas was 62.21+9.41 years old, and 63.12+10.38 years old for those using modified del Nido; (p-value > 0.51). There were no statistically significant differences in the two groups. There was no 30-day mortality case in both group. New neurological complications showed no statistically significant difference. Postoperative renal insufficiency was no different in either group (1.47% CABG using St.Thomas, 2.94% CABG using modified del Nido; p-value = 0.15). Prolonged intubation was not statistically different in either (0% CABG using St.Thomas, 2.94% CABG using modified del Nido; p-value = 0.61). Critical unit stay showed no difference between both groups (p-value = 0.25).

Conclusion: The on pump arrested heart CABG using modified del Nido cardioplegia solution did not have any difference in early outcome when compared to the elective, on pump arrest heart CABG using St.Thomas cardioplegia group.

Keyword: coronary artery bypass, del Nido cardioplegia, St. Thomas cardioplegia

Original Article

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Introduction

On pump CABG surgery is a worldwide procedure. In Thailand, there are many cardiac centers which can performed the CABG procedure. St.Thomas cardioplegia is the most frequently used in on pump arrested heart procedure. In late 2019, the distributor stopped importing St.Thomas cardioplegia from overseas. Some cardiac centers in Thailand continued using St.Thomas cardioplegia by producing it themselves using their pharmaceutical units. In our center policy, we decided to use modified del Nido cardioplegia (Our center using Ringer Lactate replace Plasma-Lyte A which is different from original formula) which was produced by our team to replace St.Thomas cardioplegia because some studies showed satisfactory outcomes in on pump arrest heart CABG[1-3] and valvesurgery.[2-4] In the first three months after initiation of modified del Nido cardioplegia solution, Preliminary observational data revealed no difference in early outcome results. The objective of this study was to compare the statistical outcomes of St.Thomas cardioplegia versus modified del Nido cardioplegia in elective on pump arrested heart CABG procedure. We excluded emergency cases, patients with stroke, chronic pulmonary disease and renal failure from the study in order to decrease confounding factors which might be affected the study results.

Methods

Patients

This study was granted the Institutional review board permission to collect and analyze clinical data from our prospectively maintained database. Between April 2019 through April 2020, 102 consecutive patients who diagnosed with triple coronary arteries disease or left main disease which were divided into two groups depending on the type of cardioplegia. Group A consisted of 68 patients who underwent on pump arrest heart CABG using St.Thomas cardioplegia (Composition of St. Thomas cardioplegia was showed in table 2)[2] Group B represented the other 34 patients who underwent on pump arrest heart CABG using modified del Nido cardioplegia(Composition of modified del Nido cardioplegia was showed in table 3)[5]. All of those in both groups were performed under cardiopulmonary bypass machine (CPB) using antegrade route cardioplegia. The ascending aorta was clamped in both groups.

Surgical Techniques

In the Andaman Heart Center at Vachira Phuket Hospital, on pump arrested heart CABG surgery was performed only by the cardiovascular thoracic team, which consisted of main surgeon who is first

assistant, two scrub nurses, two cardiac technicians and cardiac anesthesiologist. The processes combined with TEE in all surgical cases. After general anesthesia was performed, the patient was prepared in a supine position. Median sternotomy was performed. Vascular conduits (mostly IMA and SVGs) were harvested. Heparin 3-4 mg/ Kg was given. The patient was conducted to CPB using ascending aortic cannulation and two-staged venous cannula drainage via right atrial appendage. When ACT reached target (350-400). CPB was started and the patient was cooled down to 32 C. Antegrade cardioplegia was given. At this step, Patients Group A received St.Thomas cardioplegia 20 cc/kg initially and 10 cc/kg as a maintenance dose every 20 minutes. Patients group B received modified del Nido cardioplegia 20 cc/kg initially (maximal dose at 1000 ml) and 10 cc/kg as a maintenance dose every 90 minutes. Report from Smigla et al[8] showed that del Nido cardioplegia can re-dose every 45 minutes as compared with 90 minutes in our study. Modified del Nido cardioplegia will mixed with heparinized blood (1:1) for coronary perfusion test after finished each anastomosis **(Picture A)**. The heart was vented via aortic root. After that ascending aorta cross clamped was performed. Distal anastomosis of coronary arteries bypass was performed. Then the completion of aortocoronary bypass was performed under single or double clamp technique. The patient was rewarmed and CPB was weaned off. Decanulation and bleeding points were checked and drains were placed. The chest was closed and the patient was transferred to the cardiac critical unit.

Abbreviation

CABG: Coronary artery bypass graft , CPB cardiopulmonary bypass St.Thomas : Saint Thomas, TEE : transesophageal echocardiogram, IMA: inferior mammary artery, SVGs : saphenous vein grafts, Mg : milligram, Kg : kilogram, ACT : activated clotting time, CCU : cardiac critical unit, HTK : Histidine-tryptophan-ketoglutarate, LM : left main disease, DVD : double vessel disease, TVD : Triple vessel disease

Table 1 Demographics for patients who were used St.Thomas cardioplegia (n=68) versus modified del Nido cardioplegia (n=34)

Variables	Group A: St.Thomas	Group B: modified del Nido	p-value
Age	62.21 ± 9.41	63.12 ± 10.38	0.512
Sex			0.176
Male	51 (75.0)	21 (61.8)	
Female	17 (25.0)	13 (38.2)	
Underlying disease			0.941
Diabetic mellitus	41 (60.3)	21 (61.8)	
Hypertension	61 (89.7)	29 (85.3)	
Dyslipidemia	51 (75.0)	23 (67.7)	
Smoking status			0.263
Current smoker	7 (10.3)	1 (2.9)	
Never smoker	61 (89.7)	33 (97.1)	
Coronary artery lesions			0.784
TVD	41 (60.2)	22 (64.7)	
LM with DVD	4 (5.8)	1 (2.9)	
LM with TVD	23 (33.8)	11 (32.3)	
Mean preoperative LVEF	53.6%$\pm$7.12	51.1%$\pm$5.91	0.435
Mean Euroscore II	0.73$\pm$0.13	0.75$\pm$0.08	0.687
Aortic cross clamp time	58.46 ±14.33	61.18 ±19.61	0.637

Table 2 St.Thomas cardioplegia composition

1. Acetar 500 ml

2. St.Thomas cardioplegia 3 amp

St.Thomas cardioplegia	
Na^+	110 mmol/l
K^+	16 mmol/l
Mg^{2+}	16 mmol/l
Ca^{2+}	1.2 mmol/l
$NaHCO_3^-$	10 mmol/l

3. Sodium bicarbonate 25 ml

4. Insulin 0.05 ml

5. Glucose 25 ml

Table 3 Modified del Nido cardioplegia composition

1. Ringer lactate	1000 ml
2. 7.5% $NaHCO_3$	13 ml, 13 mEq
3. 50% $MgSO_4$	4 ml, 2 g
4. 20% Mannitol	16.3 ml, 3.26 g
5. 1% Lidocaine	13 ml, 130 mg
6. KCL (2mEq/ml)	13 ml, 26 mEq

Statistical analysis

Demographic, Perioperative details were abstracted from Andaman Heart Center Vachira Phuket Hospital database. Statistical analysis was performed using Prism – GraphPad. Quantitative data was compared between Group A and Group B using unpaired T-test. Qualitative data was compared between Group A and Group B using Chi- Square test. We used an alpha of 0.05 as a measure of statistical significance

Results

There were 102 elective patients who underwent on pump arrest heart CABG between April 2019 to April 2020. The patients were separated into two group determined by type of cardioplegia. Group A and Group B patients showed no statistically significant differences. The patient demographic data is showed in **table 1**.

Overall, 30-day and hospital mortality was 0%. There were no cerebrovascular events and perioperative myocardial infarction. There were no patients in group A who developed prolonged intubation for more than 96 hours and only one patient in group B who needed prolonged intubation for more than 96 hours (p-value = 0.155). Two patients needed temporary hemodialysis support, one patient (1.47%) from group A and another (2.94%) from group B (p-value = 0.613). Mean CCU night stays were 2.24±1.19 nights in group A and 2.56±1.44 in group B (p-value= 0.252). Overall perioperative results are shown in **table 4**.

Table 4. Early perioperative result (n=102)

Variables	Group A: St.Thomas	Group B: Modified del Nido	p-value
Mortality	0 (0.0%)	0 (0.0%)	-
Cerebrovascular events	0 (0.0%)	0 (0.0%)	-
Perioperative myocardial infarction	0 (0.0%)	0 (0.0%)	-
Prolong intubation > 96 hours	0 (0.0%)	1 (2.9%)	0.155
Acute kidney injuries	1 (1.5%)	1 (2.9%)	0.613
Cardiac critical unit stay (nights)	2.24 ±1.19	2.56±1.44	0.252

Discussion

In arrested heart CABG using cardiopulmonary bypass support, Cardioplegia solution is a cornerstone and necessary for myocardial protection. There are many types of cardioplegia solution have been developed[18]. In Thailand, St. Thomas cardioplegia and Histidine-tryptophan-ketoglutarate (HTK) cardioplegia solution are most popular and widely used in many cardiac centers. Because of St. Thomas cardioplegia has not been imported since late 2019 and HTK cardioplegia solution is much more expensive than St.Thomas formulation which is the reason why that del Nido cardioplegia is mentioned. There are many studies reveal that del Nido cardioplegia has been used successfully in pediatric cardiac surgery.[5, 13, 16] Some studies demonstrated that del Nido cardioplegia are also effectively been used in adult open cardiac surgery[8-10] and coronary artery bypass surgery[7] because it requires less interval dosing allowing the surgeon to operate uninterrupted and decrease the risk of myocardial acidosis which will affects the postoperative outcome adversely[11, 12] (St.Thomas cardioplegia re-dosing every 20 minute, del Nido cardioplegia re-dosing every 90 minute). Our study presents postoperative clinical outcomes which consist of mortality, cerebrovascular events, perioperative myocardial infarction, prolonged intubation time more than 96 hours, acute kidney injury and critical unit stay for the patients who underwent arrested heart CABG with CPB support using modified del Nido cardioplegia compare to the patients who received St.Thomas cardioplegia. Previous published studies have shown that the patients who underwent arrested heart CABG using del Nido cardioplegia have shorter aortic cross clamp time and CPB time.[2, 7, 8, 10, 15] Our study indicates that the patients who underwent CABG using St.Thomas cardioplegia seemed to have shorter aortic cross clamp time when compare to those using del Nido cardioplegia (58.46$\pm$14.33 min versus 61.1$\pm$19.61 min) but the difference did not reach statistical significance. This is because one of our surgeons who prefers St. Thomas cardioplegia is a nimble surgeon by nature. Because CPB time depended on many factors[6] such as body temperature, blood electrolyte level, acid-base condition, air bubble in cardiac chamber that why we didn't record CPB time into our study. Likewise, early postoperative complications and mortality were shown in the same direction.

There was no statistical difference in mortality and major complications in patients who using del Nido cardioplegia.[2, 15] However, the patients who using del Nido cardioplegia have improved LVEF during the early postoperative period.[2, 15] Rapid accumulation of intracellular calcium ion (Ca^{2+}) during myocardial ischemia causes the reperfusion injury which occurs during cardiac surgery[17] and which leads to increased myocardial energy requirement causing myocardial dysfunction. The del Nido cardioplegia is composed of Lidocaine, a membrane-stabilizing agent which increases Sodium ion (Na^{+}) channel blockade. In addition, magnesium content in del Nido cardioplegia will acts as a calcium ion antagonist. These are the mechanisms that the del Nido cardiolegia protect the myocytes from higher intracellular calcium ion.[13] Govindapillai et al[12], support that lower intracellular calcium ion in myocytes cause less reperfusion injury and improved cardiac function. Furthermore, Del Nido cardioplegic solution is more convenient to use, because this solution can be prepared by using the simple compositions which have already been available in our center. There are some limitations in our study which include its retrospective study and small sample size. There is limited reliable data which can be obtained from our patient clinical database because laboratory parameters (e.g. postoperative cardiac enzyme level) are not routinely collected from the patients. Finally, several patients have been lost to follow up due to Covid-19 pandemic situation which is consequent to lack of postoperative midterm echocardiographic parameters.Randomized control trails should be designed to compare del Nido cardioplegia versus another cardioplegia.

Conclusion

According to our study, there were no statistically differences of major postoperative complications between the use of St.Thomas cardioplegia and modified del Nido cardioplegia in the patients who underwent arrested heart CABG with CPB support. This mean that modified del Nido cardioplegia solution can be used safely in case of arrest heart CABG using CPB support comparable to St.Thomas cardioplegia.

Reference

1. Cayir MC, Yuksel A. The use of del Nido cardioplegia for myocardial protection in isolated coronary artery bypass surgery. Heart, Lung and Circulation. 2020;29(2):301-7.

2. Mishra P, Jadhav RB, Mohapatra CKR, Khandekar J, Raut C, Ammannaya GK, et al. Comparison of del Nido cardioplegia and St. Thomas Hospital solution–two types of cardioplegia in adult cardiac surgery. Kardiochirurgia i Torakochirurgia Polska= Polish Journal of Cardio-Thoracic Surgery. 2016;13(4):295.

3. Das S. Comparison of del Nido and St. Thomas Cardioplegia in adult cardiac surgery. Journal of Medical Science and Clinical Research. 2018;6:32-36.

4. Zwoliński R, Jaszewski R, Jander S, Zagórski M, Adamek-Kośmider A, Bednarski I, et al. Single Dose of Del Nido Cardioplegic Solution in Comparison with St Thomas Hospital Solution in Mitral Valve Surgery: A Propensity Matched Comparison. Clinics in Surgery. 2019;4:1-7.

5. Matte GS, Pedro J. History and use of del Nido cardioplegia solution at Boston Children's Hospital. The Journal of extra-corporeal technology. 2012;44(3):98–103.

6. Rubens FD. Cardiopulmonary bypass: Technique and pathophysiology. Sabiston ansd spensor surgery of the chest. 8th edition. Philadelphia. Saunders. 2010:957-971.

7. Yerebakan H, Sorabella RA, Najjar M, Castillero E, Mongero L, Beck J, et al. Del Nido Cardioplegia can be safely administered in high-risk coronary artery bypass grafting surgery after acute myocardial infarction: a propensity matched comparison. Journal of cardiothoracic surgery. 2014;9(1):141.

8. Smigla G, Jaquiss R, Walczak R, Bonadonna D, Kaemmer D, Schwimer C, et al. Assessing the safety of del Nido cardioplegia solution in adult congenital cases. Perfusion. 2014;29(6):554-8.

9. Sorabella RA, Akashi H, Yerebakan H, Najjar M, Mannan A, Williams MR, et al. Myocardial protection using del Nido cardioplegia solution in adult reoperative aortic valve surgery. Journal of Cardiac Surgery: Including Mechanical and Biological Support for the Heart and Lungs. 2014;29(4):445-9.

10. Mick SL, Robich MP, Houghtaling PL, Gillinov AM, Soltesz EG, Johnston DR, et al. del Nido versus Buckberg cardioplegia in adult isolated valve surgery. The Journal of Thoracic and Cardiovascular Surgery. 2015;149(2):626-36. e5.

11. Graffigna A, Nollo G, Pederzolli C, Ferrari P, Widesott L, Antolini R. Continuous monitoring of myocardial acid–base status during intermittent warm blood cardioplegia. European journal of cardio-thoracic surgery. 2002;21(6):995-1001.
12. Khuri SF, Healey NA, Hossain M, Birjiniuk V, Crittenden MD, Josa M, et al. Intraoperative regional myocardial acidosis and reduction in long-term survival after cardiac surgery. The Journal of Thoracic and Cardiovascular Surgery.2005;129(2) :372-81.
13. O'Brien JD, Howlett SE, Burton HJ, O'Blenes SB, Litz DS, Friesen CLH. Pediatric cardioplegia strategy results in enhanced calcium metabolism and lower serum troponin T. The Annals of thoracic surgery. 2009;87(5):1517-23.
14. 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. The Journal of thoracic and cardiovascular surgery. 2013;146(4):940-8.
15. Nardi P, Pisano C, Bertoldo F, Ruvolo G. New insights on the use of del Nido cardioplegia in the adult cardiac surgery. Journal of thoracic disease. 2018;10(Suppl 26):S3233–S3236.
16. Charette K, Gerrah R, Quaegebeur J, Chen J, Riley D, Mongero L, et al. Single dose myocardial protection technique utilizing del Nido cardioplegia solution during congenital heart surgery procedures. Perfusion. 2012;27(2):98-103.
17. Tsukube T, McCully JD, Federman M, Krukenkamp IB, Levitsky S. Developmental differences in cytosolic calcium accumulation associated with surgically induced global ischemia: optimization of cardioplegic protection and mechanism of action. The Journal of thoracic and cardiovascular surgery. 1996;112(1):175-84.
18. Dobson GP, Faggian G, Onorati F, Vinten-Johansen J. Hyperkalemic cardioplegia for adult and pediatric surgery: end of an era? Frontiers in physiology. 2013;4:228.