

# The effects of St. Thomas I and St. Thomas II Cardioplegia Solutions on Coronary Sinus Lactate in Mitral Valve Surgery; A Randomized, Double-blinded, Clinical Trial

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## Abstract

**Background:** Cardiac protection strategies in different methods are challenging and crucial, affecting postoperative morbidity and mortality.

**Objectives:** We compared the cardio-protective effect of two cardioplegia solutions based on coronary sinus lactate levels.

**Methods:** This randomized, double-blinded clinical trial study was performed on 46 candidates for mitral valve replacement between June 2020 and January 2021. The patients were categorized via block randomization method: 1) St. Thomas I cardioplegia (n=23) and St. Thomas II cardioplegia (n=23). The coronary sinus lactate levels at different times were measured. In addition, some intra-operative and clinical characteristics after cardiac surgery were recorded. Data were analyzed in SPSS software (version 26.0) using paired and independent t-tests, repeated measure ANOVA, and Pearson correlation test at a significance level of  $P < 0.05$ .

**Results:** In the time trend, the lactate levels in patients with St. Thomas II cardioplegia solution had a significantly lower rate than in St. Thomas I ( $P=0.001$ ). The two groups displayed no statistical difference between the aortic cross-clamp time ( $P=0.069$ ) and the CPB time ( $P=0.091$ ). Furthermore, the weaning from mechanical ventilation ( $P=0.078$ ) and ICU stay ( $P=0.061$ ) demonstrated no statistical difference between the study groups.

**Conclusion:** Based on significantly lower measures of the coronary sinus lactate, the St. Thomas II cardioplegia solution showed a better cardio-protective effect in patients undergoing mitral valve surgery.

**Keywords:** Cardio-pulmonary Bypass, Coronary Sinus, Mitral Valve, St. Thomas' Hospital cardioplegic solution

## 1. Background

Cardio-protection strategies during cardiac surgeries are the composition of all measures and interventions to prevent and attenuate myocardial injury from myocardial ischemia and reperfusion (1). Due to the fact that these cardiac surgeries should be done safely, the cardiac protection induced cardiac arrest by the infusion of cardioplegia solution into the myocardium. Nevertheless, the infusion of cardioplegia causes a cessation of myocardial contractions; ischemia occurs in myocardial tissue (2).

This event increases free radicals and reactive oxygen species and enhances inflammatory response. Meanwhile, one of the most critical consequences of myocardial ischemia is altering the axis of cell metabolism and proton ( $H^+$ ) production due to anaerobic glycolysis (3-6). On the other hand, a shred of evidence has illustrated changes within the metabolic status of the myocardium throughout the aortic cross-clamp and reperfusion process. Also, accumulation of the lactate caused by prolonged ischemia correlated with depletion of adenosine triphosphate myocardial reserve, leading to myocardial contractility alterations (7-8).

Myocardial protection tends to prevent or attenuate cardiac dysfunction as a complication of myocardial ischemia/ reperfusion injury (I/R Injury). This phenomenon is caused by suboptimal myocardial protection during aortic cross-clamping (9). Many cardioplegia formulations were evaluated to achieve optimal myocardium protection by preserving myocardial energy, inhibiting cellular destruction during cardiac surgery, minimizing I/R injury after restoring blood flow in the coronary arteries, and inducing diastolic arrest (3). Nevertheless, no reliable evidence illustrates a superiority between cardioplegia solutions and other methods (10).

Also, evaluating and maintaining the acid-base balance of coronary sinus blood during aortic cross-clamping would allow a reasonable strategy to assess the myocardial protection quality.

## 2. Objectives

The present study aimed to evaluate the cardioprotective effects of St. Thomas I and St. Thomas II cardioplegia solutions in mitral valve surgery.

### 3. Methods

This study is a registered double-blinded, randomized clinical trial (IRCT20140519017756N47). All patients were enrolled in the study for elective mitral valve replacement or repair surgery with Cardiopulmonary Bypass (CPB) between June 2020 to January 2021.

The patients included if they were aged 20 - 70 years, had a preserved left ventricular function (LVEF)  $\geq 40\%$ , and signed the informed consent form. The exclusion criteria included all the patients with a history of previous cardiac surgery, patients in a Low Cardiac Output State (LCOS) before the surgery, patients with pulmonary arterial hypertension (PAP  $\geq 45$  mmHg), and those requiring intra-aortic balloon pump (IABP) after cardiac surgery.

All included in the study were assigned to St. Thomas I or St. Thomas II based on block randomization with a four-block size. In this way, the patients were allocated to each block as A for St. Thomas I group and B for the St. Thomas II group until each group included 23 participants. Then, a nurse not informed about the study groups determined the related cardioplegia solution group for each patient. Also, the participants were unaware of the study group and the randomization (Figure 1).

The CPB system and strategy for patients in the St. Thomas I and the St. Thomas II groups were standard

and uniform. The oxygenator in all of them was Fusion®.

The prime solution was considered crystalloid (isotonic saline) for all the patients. The patients' temperature was reduced to normothermia or mild hypothermia (30-33 °C) based on the surgical procedure and the bypass length.

Cardiopulmonary bypass (CPB) was initiated after the cardiac surgeon, anesthesiologist, and perfusionists confirmed favorable conditions. All patients underwent median sternotomy. Cannulation was performed after administration of three mg/kg heparin and when the activated coagulation time (ACT) was greater than 480 seconds.

Non-pulsatile perfusion was used to maintain tissue perfusion between 2 and 2.8 L/m<sup>2</sup>/min. The alpha-stat strategy was administrated during CPB to evaluate arterial blood gasses to maintain PaCO<sub>2</sub> and PaO<sub>2</sub> at 35-45mmHg and 150-250 mmHg, respectively.

In the patients of the first group, 10 ml/ kg ST I cardioplegia solution was injected at pH 5.5 at 8°C for 3 minutes by the antegrade method. Also, in group two patients, ten cc/ kg St. Thomas I cardioplegia solution with normal concentration was infused in the aortic root as a standard method and same temperature and time as group 1. The compositions of the St. Thomas I and the St. Thomas II cardioplegia solutions have been illustrated in Table 1. Blood samples were taken from the coronary sinus at predetermined times.

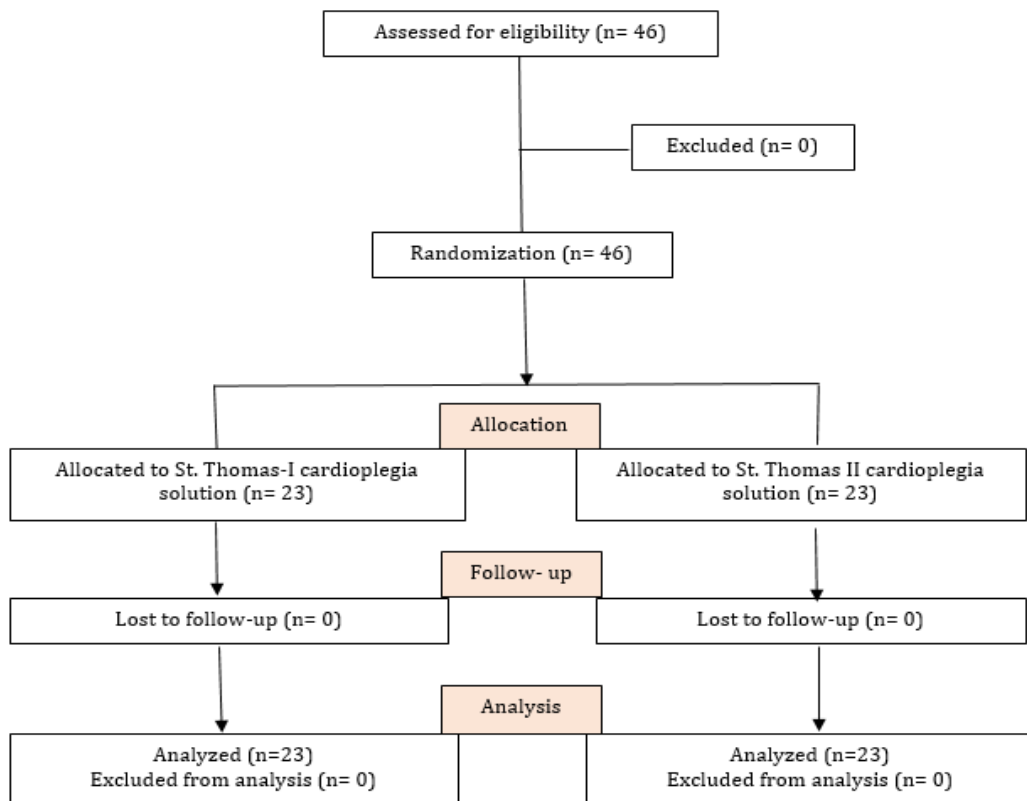


Figure 1. CONSORT diagram presenting the flow of participants in each stage of the randomized trial

**Table 1. The composition of St. Thomas I and the St. Thomas II cardioplegia solutions**

Cardioplegia solution content	St. Thomas I (Content in 1000 ml)	St. Thomas II (Content in 1000 ml)
sodium chloride (Mmol/l)	144	110
Potassium chloride (Meq/l)	20	16
Magnesium sulfate (Mg/dl)	16	16
Calcium chloride (Mmol/l)	2.4	1.2
Lidocaine (Mg)	100	-
Sodium bicarbonate (mmol/l)	-	10

The primary outcome was the Lactate levels that were measured immediately after weaning from the cardiopulmonary bypass (T0), 15 minutes after CPB (T1), and 30 minutes after that time (T2). Also, the bypass and cross-clamp time, weaning time from mechanical ventilation, and ICU stay was recorded as the secondary outcome.

All patients signed the informed consent form approved by the Institutional Committee on Human Research after the approval of the Board of Ethics of Mashhad University of Medical Sciences (IR.MUMS.MEDICAL.REC.1400.008). The protocol of the study was consistent with the guidelines in the Declaration of Helsinki.

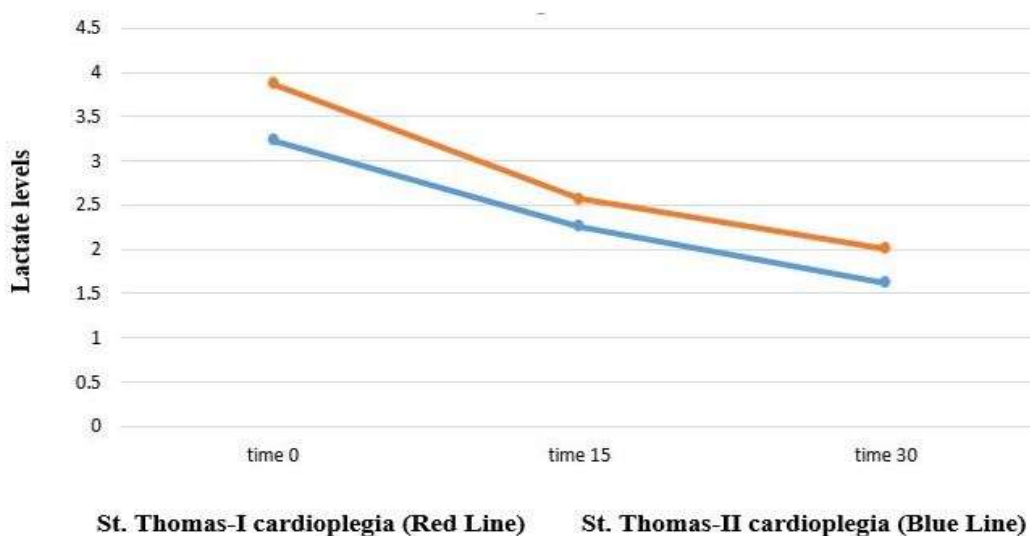
Statistical analysis was performed using SPSS version 26.0 (Chicago, IL, USA), paired and independent t-test, repeated measure ANOVA, and Pearson correlation test at a significance level of  $P < 0.05$ .

## 4.Result

The main finding of the present study demonstrated no statistical differences between the coronary sinus lactate levels immediately after aortic cross-clamp in St. Thomas I and the St. Thomas II cardioplegia solutions groups. Nevertheless, after 15 min, the mean value of the coronary sinus lactate in the St. Thomas-I cardioplegia group was significantly higher than the St. Thomas II group. These values dramatically differed in the last sample, 30 min after the aortic cross-clamp (Table 2). The statistical models with repetitive measurements were used to examine the effect of different times in coronary sinus lactate values in the St. Thomas-I and St. Thomas-II cardioplegia groups. This analysis displayed no significant differences between the mean lactate levels of the two groups at different times (Lact T0 ( $P=0.091$ ), Lact T1 ( $P=0.065$ ), and Lact T2 ( $P=0.041$ )). (Figure 2).

**Table 2. The comparison between coronary sinus lactate levels in St. Thomas-I and St. Thomas II groups. (Lact (T0): Coronary sinus lactate level immediately after aortic cross-clamp, Lact (T1): Coronary sinus lactate level 15 minutes after aortic cross-clamp, and Lact (T2): Coronary sinus lactate level 30 minutes after aortic cross-clamp). (\*= significant)**

Lactate (Time)	Groups	Mean± Std. Deviation	P-value
Lact (T0)	St. Thomas II group	3.2304± 0.57083	0.691
	St. Thomas-I group	3.8739± 0.56183	
Lact (T1)	St. Thomas II group	2.2609± 0.51939	0.0374*
	St. Thomas-I group	2.5783± 0.58072	
Lact (T2)	St. Thomas II group	1.6261± 0.31940	0.001*
	St. Thomas-I group	2.0130± 0.46934	



**Figure 2. The coronary sinus lactate levels at different times of measurement. (Time 0= Coronary sinus lactate level immediately after aortic cross-clamp, Time 15= Coronary sinus lactate level 15 minutes after aortic cross-clamp, and Time 30= Coronary sinus lactate level 30 minutes after aortic cross-clamp).**

The comparison of the aortic cross-clamp time between St. Thomas I and the St. Thomas II cardioplegia solutions groups ( $24.52 \pm 1.33$  versus  $27.48 \pm 9.21$ , respectively,  $P=0.069$ ) and CPB time ( $36.48 \pm 3.24$  versus  $34.5 \pm 9.32$ , respectively;  $P=0.091$ ) revealed no statistical differences. There were no statistical differences between the mean time of the mechanical ventilation in St. Thomas-I versus St. Thomas-II cardioplegia groups ( $515.15 \pm 23.40$  min versus  $502.1 \pm 20.15$  min, respectively;  $P=0.078$ ) and ICU stay ( $50 \pm 7$  hours versus  $56 \pm 4$  hours, respectively;  $P=0.061$ ).

## 5. Discussion

Cardioplegic solutions protect the heart from myocardial injury during mitral valve surgery (11,12). Initially, the St. Thomas solution was invented as crystalloid cardioplegia, which provided reliable cardiac arrest and desirable levels of myocardial protection. However, the amount of cardioplegia used caused much hemodilution and many challenges in managing complications (13).

As the investigation in myocardial protection techniques has progressed, the additives vary in temperature and content of different cardiac solutions. Despite these developments, no technique fully protects myocardial function (14). Refinement and formulations of cardioplegia were followed, and more complex strategies for prescribing cardioplegia were described so that, based on further research and experiences, several formulations of this solution became common in different centers (15).

Myocardial recovery depends on myocardial protection; therefore, it is imperative to monitor its effectiveness (9). Also, there are shreds of evidence that the most sensitive marker of myocardial ischemia is lactate measured directly in the coronary sinus blood since it can precisely reveal alteration within the myocardial metabolic status (16).

The changes in lactate levels caused by inadequate myocardial protection showed the progression of anaerobic metabolism, myocardial tissue acidosis, and lactate production. Although, myocardial necrosis, detected with the release of specific myocardial enzymes, may occur later (17,18).

In our study, the primary blood sample immediately after aortic cross-clamp was not different in lactate content in St. Thomas-I and St. Thomas-II cardioplegia groups. Nevertheless, this measure dramatically differed at 15 minutes and 30 minutes after aortic cross-clamp in St. Thomas-I and St. Thomas-II cardioplegia groups. These findings revealed that the cardio-protective effect of the St. Thomas-II cardioplegia solution might be

superior to the St. Thomas-I group. Also, the different content in cardioplegic solutions and sodium bicarbonate in St. Thomas-II may affect the lactate levels after ischemic event initiation induced by aortic cross-clamp (19).

A study states that serum lactate levels were significantly elevated in groups of Del-Nido (DN) cardioplegic solution and St. Thomas-II cardioplegia as Modified St. Thomas solution (MST) (20). As well as in a study compared two widely used crystalloid Cardioplegic Bret-schneider (Custodiol®) versus St. Thomas II in patients who underwent Right Mini-thoracotomy Mitral Valve Surgery. They concluded that using St. Thomas II cardioplegia solution was associated with higher myocardial protection based on cardiac markers, such as troponin- I, compared to other cardioplegia solutions (21).

Although, other studies showed different results in myocardial protection in patients undergoing cardiopulmonary bypass cardiac surgeries (3, 22).

The aortic cross-clamp time and CPB time between the two groups of our study had no statistical differences. It is worth mentioning that the results of this study may be more precise because a single surgeon operated on all of the patients for mitral valve replacement.

The main benefit of this item is that the time of ischemia induced by aortic cross-clamp directly affects the alteration of ischemia and reperfusion myocardial injury parameters (23).

Our results showed no statistical difference between weaning from mechanical ventilation and ICU stay in St. Thomas-I and St. Thomas-II cardioplegia groups. These findings paralleled with other studies (23-24).

Albeit our findings seem trivial next, some studies showed that the patients with St. Thomas-II cardioplegia solution had a higher rate or even lower times of mechanical ventilation and ICU stay (25-26).

These controversial results may be due to the heterogeneity of the patients' groups in terms of the time of the ischemia as well as the CPB time. Also, it seems that the patients were not placed in groups of their studies as a programmed method, such as block randomization methods. So, this item can affect the final results of their studies.

## 6. Conclusion

Regarding the myocardial protection effect of St. Thomas-I and St. Thomas-II cardioplegia solution, the St. Thomas-II showed the optimal cardio-protective effect based on lactate in the coronary sinus. Moreover, our results recommended that lactate level in the coronary sinus is a valid measurement and may be considered a good prognostic value in myocardial preservation in

valvular heart surgical patients.

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## Conflicts of interest

The authors declare no conflict of interest in this study.

## References

- Heusch G. Myocardial ischemia-reperfusion injury and cardioprotection in perspective. *Nat Rev Cardiol.* 2020;**17**(12): 773-89. doi: [10.1038/s41569-020-0403-y](https://doi.org/10.1038/s41569-020-0403-y). [PubMed: [32620851](https://pubmed.ncbi.nlm.nih.gov/32620851/)].
- Hamad R, Nguyen A, Laliberté É, Bouchard D, Lamarche Y, El-Hamamsy I, et al. Comparison of del Nido cardioplegia with blood cardioplegia in adult combined surgery. *Innovations (Phila).* 2017;**12**(5): 356-62. doi: [10.1097/IML.0000000000000403](https://doi.org/10.1097/IML.0000000000000403). [PubMed: [29016380](https://pubmed.ncbi.nlm.nih.gov/29016380/)].
- Mousavizadeh M, Ghanbari A, Zirak N, Ghadrdooost B, Yaghubi M, Hosseini S. Comparative myocardial protection effects of Buckberg and del Nido in Mitral Valve Surgery: A Prospective Randomized Trial. *Int Cardio Res J.* 2021;**15**(4): e117124.
- Kim WH, Park JY, Ok SH, et al. Association between the neutrophil/lymphocyte ratio and acute kidney injury after cardiopulmonary surgery: a retrospective observational study. *Medicine (Baltimore).* 2015;**94**(43): e1867. doi: [10.1097/MD.0000000000001867](https://doi.org/10.1097/MD.0000000000001867). [PubMed: [26512598](https://pubmed.ncbi.nlm.nih.gov/26512598/)].
- Pearse RM, Wijesundera DN. Steroids for cardiac surgery: has the story finally ended?. *Lancet.* 2015;**386**: 1215-16. doi: [10.1016/S0140-6736\(15\)00303-7](https://doi.org/10.1016/S0140-6736(15)00303-7). [PubMed: [26460640](https://pubmed.ncbi.nlm.nih.gov/26460640/)].
- Floh AA, Manlihot C, Redington AN, McCrindle BW, Clarizia NA, Caldaroni CA, et al. Insulin resistance and inflammation are a cause of hyperglycemia after pediatric cardiopulmonary bypass surgery. *J Thorac Cardiovasc Surg.* 2015;**150**(3):498-504.e1. doi: [10.1016/j.jtcvs.2015.06.028](https://doi.org/10.1016/j.jtcvs.2015.06.028). [PubMed: [26190660](https://pubmed.ncbi.nlm.nih.gov/26190660/)].
- Chowdhury UK, Sheil A, Kapoor PM, Narang R, Gharde P, Malik V, et al. Short-term prognostic value of perioperative coronary sinus-derived-serum cardiac troponin-I, creatine kinase-MB, lactate, pyruvate, and lactate-pyruvate ratio in adult patients undergoing open heart surgery. *Ann Card Anaesth.* 2016;**19**(3):439-53. doi: [10.4103/0971-9784.185526](https://doi.org/10.4103/0971-9784.185526). [PubMed: [27397448](https://pubmed.ncbi.nlm.nih.gov/27397448/)].
- Healey CM, Kumbhani DJ, Healey NA, Crittenden MD, Gibson SF, Khuri SF. Impact of intraoperative myocardial tissue acidosis on postoperative adverse outcomes and cost of care for patients undergoing prolonged aortic clamping during cardiopulmonary bypass. *Am J Surg.* 2009;**197**(2):203-10. doi: [10.1016/j.amjsurg.2008.01.023](https://doi.org/10.1016/j.amjsurg.2008.01.023). [PubMed: [18722580](https://pubmed.ncbi.nlm.nih.gov/18722580/)].
- Raicea V, Kovacs J, Moraru L, Suci H. Coronary Sinus Lactate as Marker of Myocardial Ischemia in Cardiac Surgery: Correlation with Morbidity and Mortality after Cardiac Surgery / Lactatul din sinusul coronarian - marker al ischemiei miocardice în chirurgia cardiacă: corelații cu morbiditatea și mortalitatea postoperatorie. *RJLabMed.* 2015;**23**(2): 189-197. doi: [10.1515/rjlm-2015-0019](https://doi.org/10.1515/rjlm-2015-0019).
- Yamamoto H, Yamamoto F. Myocardial protection in cardiac surgery: a historical review from the beginning to the current topics. *Gen Thorac Cardiovasc Surg.* 2013;**61**(9):485-96. doi: [10.1007/s11748-013-0279-4](https://doi.org/10.1007/s11748-013-0279-4). [PubMed: [23877427](https://pubmed.ncbi.nlm.nih.gov/23877427/)].
- Ghasemi F, Azarfarin R, Salahi S, Baharestani B, Alizadeh Ghavidel A. The Effects of Cold Blood Cardioplegia with and without Adenosine on Hemodynamic Status of Patients Undergoing Mitral Valve Surgery. *Multidiscip Cardio Annal.* 2020;**11**(1):e96919. doi: [10.5812/mca.96919](https://doi.org/10.5812/mca.96919).
- Vaidya S, Adhikari AB, Karmacharya R, Rai K. Comparative study between the use of St. Thomas' II cardioplegia and del Nido cardioplegia in patients who underwent open-heart surgery. *Nepal heart j.* 2020;**17**(1):23-7. doi: [10.3126/njh.v17i1.28802](https://doi.org/10.3126/njh.v17i1.28802).
- Sharma A, Dixit S, Mittal S, Sharma M, Sharma D, Mawar KK. DelNido cardioplegia versus St Thomas cardioplegia solution in double valve replacement: a single centre experience. *Perfusion.* 2021;**36**(5):476-481. doi: [10.1177/0267659120961921](https://doi.org/10.1177/0267659120961921). [PubMed: [33203307](https://pubmed.ncbi.nlm.nih.gov/33203307/)].
- Moktan Lama PB, Khakural P, Sigdel S, Raj Bhatta M, Sah Teli R, Baral RK, et al. Del Nido Cardioplegia in Coronary Artery Bypass Grafting Surgery: A safe, efficacious and economic alternative to St. Thomas solution; an experience from a developing nation. *Perfusion.* 2021;**36**(5):470-475. doi: [10.1177/0267659121991033](https://doi.org/10.1177/0267659121991033). [PubMed: [33509043](https://pubmed.ncbi.nlm.nih.gov/33509043/)].
- Mohammed S, Menon S, Gadhinglajkar SV, Baruah SD, Ramanan SV, Gopalakrishnan KA, Suneel PR, Dharan BS. Clinical outcomes of del nido cardioplegia and st thomas blood cardioplegia in neonatal congenital heart surgery. *Ann Card Anaesth.* 2022;**25**(1):54-60. doi: [10.4103/aca.aca.220\\_20](https://doi.org/10.4103/aca.aca.220_20). [PubMed: [35075021](https://pubmed.ncbi.nlm.nih.gov/35075021/)].
- Onorati F, Cristodoro L, Caroleo S, Esposito A, Amantea B, Santangelo E, et al. Troponin I and lactate from coronary sinus predict cardiac complications after myocardial revascularization. *Ann Thorac Surg.* 2007;**83**(3):1016-23. doi: [10.1016/j.athoracsur.2006.10.103](https://doi.org/10.1016/j.athoracsur.2006.10.103). [PubMed: [17307451](https://pubmed.ncbi.nlm.nih.gov/17307451/)].
- White HD. Pathobiology of troponin elevations: do elevations occur with myocardial ischemia as well as necrosis? *J Am Coll Cardiol.* 2011;**57**(24):2406-8. doi: [10.1016/j.jacc.2011.01.029](https://doi.org/10.1016/j.jacc.2011.01.029). [PubMed: [21658560](https://pubmed.ncbi.nlm.nih.gov/21658560/)].
- Fathi M, Valaei M, Ghanbari A, Ghasemi R, Yaghubi M. Comparison of Patient's Kidney Function Based on Kidney Disease Improving Global Outcomes (KDIGO) Criteria and Clinical Parameters in Isolated Coronary Artery Bypass Graft (CABG) Surgery in On-Pump and Off-pump Methods in Patients with Low Cardiac Output Syndrome (LCOS) After Surgery. *Anesth Pain Med.* 2020;**10**(2):e100517. doi: [10.5812/aapm.100517](https://doi.org/10.5812/aapm.100517). [PubMed: [32754433](https://pubmed.ncbi.nlm.nih.gov/32754433/)].
- Buel ST, Striker CW, O'Brien JE. del Nido versus St. Thomas Cardioplegia Solutions: A Single-Center Retrospective Analysis of Post Cross-Clamp Defibrillation Rates. *J Extra Corpor Technol.* 2016;**48**(2):67-70. [PubMed: [27578896](https://pubmed.ncbi.nlm.nih.gov/27578896/)].
- Mishra P, Jadhav RB, Mohapatra CK, 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. *Kardiochir Torakochirurgia Pol.* 2016;**13**(4):295-299. doi: [10.5114/kitp.2016.64867](https://doi.org/10.5114/kitp.2016.64867). [PubMed: [28096823](https://pubmed.ncbi.nlm.nih.gov/28096823/)].
- Barbero C, Pocar M, Marchetto G, Cura Stura E, Calia C, Dalbesio B, et al. Single-Dose St. Thomas Versus Custodiol® Cardioplegia for Right Mini-thoracotomy Mitral Valve Surgery. *J Cardiovasc Transl Res.* 2023;**16**(1):192-198. doi: [10.1007/s12265-022-10296-z](https://doi.org/10.1007/s12265-022-10296-z). [PubMed: [35939196](https://pubmed.ncbi.nlm.nih.gov/35939196/)].
- Talwar S, Bhoje A, Sreenivas V, Makhija N, Aarav S, Choudhary SK, et al. Comparison of del Nido and St Thomas Cardioplegia Solutions in Pediatric Patients: A Prospective Randomized Clinical Trial. *Semin Thorac Cardiovasc Surg.* 2017;**29**(3):366-374. doi: [10.1053/j.semtcvs.2017.08.017](https://doi.org/10.1053/j.semtcvs.2017.08.017). [PubMed: [29055711](https://pubmed.ncbi.nlm.nih.gov/29055711/)].
- Kim JS, Jeong JH, Moon SJ, Ahn H, Hwang HY. Sufficient myocardial protection of del Nido cardioplegia regardless of ventricular mass and myocardial ischemic time in adult cardiac surgical patients. *J Thorac Dis.* 2016;**8**(8):2004-10. doi: [10.21037/jtd.2016.06.66](https://doi.org/10.21037/jtd.2016.06.66). [PubMed: [27621853](https://pubmed.ncbi.nlm.nih.gov/27621853/)].
- Mork C, Koechlin L, Schaeffer T, Schoemig L, Zenklusen U, Gahl B, et al. Bretschneider (Custodiol®) and St. Thomas 2 Cardioplegia Solution in Mitral Valve Repair via Anterolateral Right Thoracotomy: A Propensity-Modelled Comparison. *Mediators Inflamm.* 2019;**2019**:5648051. doi: [10.1155/2019/5648051](https://doi.org/10.1155/2019/5648051). [PubMed: [31885497](https://pubmed.ncbi.nlm.nih.gov/31885497/)].
- Ali I, Hassan A, Shokri H, Khorshed R. Efficacy of Histidine-Tryptophan-Ketoglutarate Solution Versus Blood Cardioplegia in Cardiac Surgical Procedures: A Randomized Controlled | Parallel Group Study. *Heart Surg Forum.* 2021;**24**(1):E170-E176. doi: [10.1532/hfsf.3495](https://doi.org/10.1532/hfsf.3495). [PubMed: [33635238](https://pubmed.ncbi.nlm.nih.gov/33635238/)].
- Lin YZ, Huang JB, Li XW, Tang XM, Lu WJ, Wen ZK, et al. Clinical comparative analysis of histidine-tryptophan-ketoglutarate solution and St. Thomas crystalloid cardioplegia: A 12-year study from a single institution. *Exp Ther Med.* 2017;**14**(3):2677-2682. doi: [10.3892/etm.2017.4814](https://doi.org/10.3892/etm.2017.4814). [PubMed: [28962211](https://pubmed.ncbi.nlm.nih.gov/28962211/)].