OPEN PEER REVIEW

Open Peer Review (OPR)

As a new feature for progressing towards transparency, we decided to open a new window for all of our editors as well as authors titled "**Open Peer Review**". We hope by this new facility, our reviewers will be more motivated and authors will be more satisfied with the review process. We believe that publishing our peer review reports could make a transparent and clear environment for all our efforts within a journal, but not all reviewers tend to publish their comments.

What is "Open Peer Review" process?

An "Open Peer Review" process is making the details of all review process (including reviewers, associate editors, and EICs comments) as "Public" as it is agreed by EIC, Authors, and reviewers.

Advantages of "Open Peer Review" process

- More transparency, constructiveness and tactful comments of the peer review process: leads to an increase in the quality of reviews
- More motivations for all involved roles in the review process
- Authors' satisfactions from the review process: Increases honesty between authors and reviewers
- Education of both authors and new students
- Prevents reviewers from following their individual agendas and leading to the detection of reviewers' conflicts of interests

You can find out more at:
https://sites.kowsarpub.com/kowsar/knowledgebase/category/tree.html#opr.html

Multidisciplinary Cardiovascular Annals
Article DOI: 10.5812/mcardia.65154
Published in: Multidisciplinary Cardiovascular Annals: 9(1); e65154

Peer Review Report for "Impact of Different Prophylactic Antibiotic Regimen on Clinical Outcome of Coronary Artery Bypass Graft Surgery"

Author(s): Hassan Mirmohammadsadeghi, Nicholas Austine, Maryam Mirzaei, Farzaneh Shirnia, Alireza Alizadeh Ghavidel, Alireza Alizadeh Ghavidel, Hooman Bakhshandeh, Farzaneh Shirnia, Naser Hadavand

Review Timeline:

Submit Date: 14 Apr 2017
Revised Date: 19 May 2017
Accepted Date: 19 Feb 2018

Revision (0)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

REFEREE: Reviewer | **Revision** (0) 30 Dec 2017

Dear AE,
The English were good and the article is fluently written.
But please reconsider the following issues and make them correct;
1. In the abstract, the result section, it has been stated that There was no significant relationship between the administration of antibiotic prophylaxis and mean hospitalization time (P=0.04)
while in the result it has been said that Using a statistical t-test showed that the average duration of hospitalization in the intensive care unit in patients receiving cefazolin antibiotics was significantly lower than those who did not receive this antibiotic (p-value = 0.047). However, ICU stay was not affected by other prophylactic antibiotics. It has also been shown that the mean hospital stay was significantly higher in patients receiving ciprofloxacin (p-value = 0.049) than those who received other antibiotics. Please make it clear.
2. The references are not in numerical order in the introduction. E.g. the ref. 22 is after reference number 7. It can be seen in the following several other references (are highlighted in text) and there is no 14 in text.

3. In result paragraph 2 it has been said that Cefazolin was the most common prophylactic antibiotic (46.5%) while Cefezoline has been used in 46.5+24+0.5%= 71% of patients. Cefezolin as a single agent was used in 46.5%. This should be corrected

4. In table 2; why Old age (>70) and Morbid obesity do not have any values in their related cells?

5. Title of Table 6; “Clinical characteristics of mortality patients”, should be corrected. “Mortality patients” is wrong

6. There is a problem with a written discussion. The results are only compared to few other studies with mostly the same outcomes and nothing has been really discussed.

All the above-mentioned points are highlighted in grey in the main text.

Thanks.

REFEREE: Reviewer | **Revision** (0) 26 Jan 2018

Dear AE,

There are some comments which should be addressed by the author:

- Plagiarism is not detected
- Analysis method of the manuscript is good
- Results is accept
- Referencing and citations is correct.
- English writing is proper.

Thanks.

REFEREE: Associate Editor | **Revision** (0) 15 Feb 2018

Dear EIC,

This well written article after including the requested changes by reviewers can be published.

Best regards.

REFEREE: EIC | **Revision** (0) 17 Feb 2018

Dear Authors,

Thank you for submitting your research article.

Your potentially accepted article needs some revision based on the reviewers' comments.

Regards

OPEN PEER REVIEW

Revision (1)

Reply to Reviewers

Ideally, the reviewing process can significantly improve the submitted manuscripts by allowing the authors to take into account the advice of reviewers. Author(s) must reply to all reviewers' comments in a separate Word file, point by point. A "**Reply to Reviewers**" document is submitted along with revised manuscript during submission of revised files, summarizing the changes that the authors made in response to the reviewers' comments. The responses to reviewers' comments specifies how the authors addressed each comment the reviewers made.

You can read the authors' responses to the reviewers' comments in the next page.

Comparison of the Effects of Procaine Hydrochloride and Lidocaine in Cardioplegic Solution, on Arrhythmia after Opening of Aortic Valve in Coronary Artery Bypass Graft Surgery

Abstract

Background and aim of the research: The best way to reduce the occurrence of arrhythmias that generally occur after an open heart surgery is to improve the quality of myocardial protection against damages during the cross-clamp time. In this regard, different cardioplegic solutions play a key role. Differences in the types and contents of cardioplegic solutions may lead to different results of effective protection of the myocardium. The purpose of this study was to compare the effects of procaine hydrochloride and lidocaine in cardioplegic solution on arrhythmia after the opening of aortic valve in coronary artery bypass graft surgery.

Method of research: This study is a randomized clinical trial that was performed in Rajaie Cardiovascular, Medical and Research Center after obtaining permission from the Ethics Committee. A total of 100 patient candidates for coronary intervention in 2016 were divided into two groups and randomly assigned one of the two cardiopulmonary solutions that were only different in the antiarrhythmic solution contents of procaine hydrochloride and lidocaine. At the opening of the aortic valve, spontaneous sinus rhythm return, cases of arrhythmia, and the amounts of lidocaine, magnesium and inotropic drugs, or the use of defibrillator and pacemaker in the operating room or the intensive care unit have been investigated.

Results: After the opening of the aortic valve in the procaine hydrochloride group, the spontaneous return of heart rate was higher (P-value = 0.02, 64% for procaine hydrochloride and 42% for lidocaine group). Furthermore, the required values for lidocaine and magnesium (P = 0.02) and inotrope (P = 0.04) were also relatively lower, but in general, the percentage of arrhythmia occurred requiring defibrillator and pacemaker before and after operation between the two groups did not show any significant differences. Clinically, the required cardiopulmonary solution values were slightly higher in procaine hydrochloride.

Discussion and conclusion: Although the cardioplegic solution containing procaine hydrochloride is effective in protecting myocardial infarction, and it may be useful in spontaneous heartbeats in short-term surgeries to reverse the rhythm of spontaneous heartbeat, it does not have any significant effects on decreasing arrhythmia after opening of the aortic valve and is not preferable to the cardioplegic solution containing lidocaine. Obviously, the definitive result depends on the repetition of the results based on similar clinical studies, with more patients.

Key words: Coronary artery bypass, Cardioplegia solution, Arrhythmia, Cardiopulmonary bypass

Introduction

Coronary artery disease is associated with a high incidence of cardiac events, and drug therapy, dietary management and low-aggressive therapies are the mainstay of treatment. However if these methods were not responsive, to resolve problems coronary artery bypass graft surgery is done (CABG) in order to increase survival and improve the quality of patients' lives [1, 2]. Transplantation of coronary arteries has a number of complications during and after operation in spite of its favorable outcomes. . Cardiac arrhythmias is one of the most common and prevalent complications after open heart surgery, which is an important factor for mortality and morbidity [3, 4]. These arrhythmias often occur as ventricular and atrial fibrillation [5, 6]. Atrial fibrillation (AF) is the highest incidence of arrhythmias after CABG surgery [7]. Arrhythmia has a direct relationship with the onset of ischemic period after the opening of the aortic valve. Therefore, cardiopulmonary solution is used to prevent myocardial damage and develop its protection, and choosing a cardioplegic solution is important in this regard [3, 8]. The cardiopulmonary solution causes the heart to survive for longer ischemia and events during perfusion [9]. This solution uses different electrolyte and antiarrhythmic contents to stop the heart during distal anastomosis and protects the structure of the myocardium during the reperfusion period and its function after ischemia [10, 11]. In the cardioplegia solution, a lot of additives, such as beta-blockers, sodium blockers, and calcium blockers can be applied that affects arrhythmia after opening the clamp [12]. Topical lidocaine and procaine hydrochloride agents are two of the additives to cardioplegic solution that by decreasing the amount of extracellular sodium, cause cardiac arrest by removing substrate from the free sodium necessary for the potential for action and are supported by a small amount of extracellular charge of potassium, and with the stabilization of the cell membrane, it returns the rhythm after ischemia without reversible effect and has an antiarrhythmic effect [9, 10]. In this study, the effects of these two drugs in the cardioplegic solution on arrhythmia after declamp were analyzed and compared so that using a suitable cardioplegia could reduce the occurrence risk of arrhythmia after opening of the aortic valve and, consequently, the complications that follow It will be prevented.

Research Method

This is a randomized clinical trial that was conducted in the operating room of the Rajaie Cardiovascular, Medical and Research Center after obtaining permission from the Ethics Committee from October 2016 to March 2017. In this study, we selected patients who were candidates for coronary artery bypass graft surgery and consciously agreed to it. They also had no history of cardiac arrhythmia, mutagenic fraction of less than 30%, severe aortic failure, severe renal failure and the final stages of the disease, history of hypersensitivity to local hypertension and heart pacemaker, and their operation was not an emergency or recurrence. They also did not have a concomitant procedure, such as a valve replacement, and those of who returned to the operating room due to bleeding or surgery, died or had acute hypersensitivity to local anesthetic agents, were excluded from this study. The instrument used was a data collection form, which was based on the variables studied (demographic data and underlying illnesses, clinical information and arterial blood gas, intraoperative variables, variables related to arrhythmia in the operating room and intensive care unit, ...). Clinical data has been recorded and reviewed with direct observation by the use of continuous monitoring of electrocardiography, blood pressure and laboratory devices to measure arterial blood gases and echocardiography device of Rajaie Cardiovascular, Medical

and Research Center. These devices are calibrated daily by the personnel of the hospital and their accurate performance is tested.

Based on the previous study [11], considering 90% strength of the study and the significance level of 0.05, the number of patients required for study in each group was estimated to be 50.

The sampling method is non-random and using available samples based on entry and exit criteria. Afterwards, using a quadruple block, each patient was randomly (through balanced block randomization) assigned in either of the two groups of 1. The group of cardioplegic solution containing procaine hydrochloride and 2. The group of cardioplegic solution containing lidocaine. The cardioplegic solution was prepared according to the conditions and requirements under the supervision of the center's pharmacist and the pharmaceutical department, and then the drugs were numbered and blinded by seals envelopes method. Therefore none of the perfusionists, nurses, surgeons and researcher knew about the type of cardioplegic solution used. To evaluate the effect of these two drugs, the cardioplegic solution was prepared in such a way that, apart from the two antiarrhythmic drugs, there was no difference in electrolytes, osmolarity and their formulation. The composition and formulation of the cardioplegic solution are similar to the solution of ST.Thomas1, which is made and consumed in European countries by Martindale Pharmaceuticals Company with the registration number pl01883 / 0012. The latest drug review date was in February 2015, and is also being used in Australia under the name of DBL Sterile Cardioplegia Concentrate (https://www.medicines.org.UK) [13]. The Iranian sample is a cardioplegic solution prepared by Shahid Ghazi factory, which in terms of composition and content is exactly like the solution produced in Australia. This solution is in a volume of 50 ml; diluted in 1 liter of the ringer serum at 4℃. Each liter of diluted solution contains 44 milliequivalents of potassium, 64 milliequivalents of magnesium, 147 milliequivalents of sodium and 4.5 milliequivalents of calcium, and one millimole of procaine hydrochloride with osmolarity of 300 to 320 and a pH of about 7.4 to 7.6. This solution was used as the cardioplegic solution containing procaine hydrochloride and the other solution was prepared with the same formulation, osmolarity and PH, and only lidocaine 2% has been replaced instead of Procaine hydrochloride containing 5 cc (equivalent to 100 mg). Blood cardioplegia was used and electrolytes, especially potassium, were within the normal range and were given 1 to 1 cardioplegia and blood. At a rate of 300 cc per kg of patient's weight per minute, for three minutes or according to the instructions of the surgeon until a complete cardiac arrest, each of these solutions was administered at the root of the aorta. In order to homogenize the test, the method of induction and maintenance of anesthesia, surgical procedures, perfusion and the pump device, the model of the oxygenator, the method of priming, heparinization, the infusion method of cardioplegic solution (antegrade in the root of the aorta) and restoration of the effect of heparin by protamine were considered to be administered in the same way for all patients. Background data such as age, sex, weight, height, BSA, troponin levels and preoperative ejection fraction, history of hypertension, thyroid, smoking, history of MI and angioplasty and beta blocker drugs were recorded. These questions were completed through each patient's profile. At the opening of the aortic valve, if the rhythm returned in 3-5 minutes spontaneously, it would be recorded as a self-reversal rhythm, otherwise lidocaine and magnesium are injected (potassium values are checked to make sure they are in the normal range). Variables such as hemodynamic parameters and arterial blood gas parameters were measured at the entry to the

operating room, during the cross-clamp time, after the opening of the aortic valve, the end of the bypass pump, at the entrance to the ICU and after the extraction of the tracheal tube in the ICU. The amount of cardioplegic solution required and the number of injections, the minimum temperature during the bypass, the rate of spontaneous self-reversal of the heart rhythm, the frequency of arrhythmia after declamping, the duration of arrhythmia, the need for lidocaine, magnesium and potassium for rhythm return, the need for inotrope, the need for shock and pacemaker and stable strips of change in favor of ischemia were all recorded by perfusionists in the registered questionnaires. Also information about the need for inotrope or pacemaker, or the emergence of new dysrhythmic and AF attacks, troponin and electrocardiographic changes in favor of ischemia and EF decline have been collected by the researcher with the help of nurses in intensive care unit or extracted from medical records of patients and transferred to the questionnaires after the surgery in wards for as long as the patient had the tracheal tube and was under monitoring. Information was entered into SPSS 23 software and statistical analysis was performed. One-sample Kolmogorov Smirnov test and Student's t test (Mann Whitney U), Chi-square test and Fisher's exact test were used. Multivariate analysis was performed using logistic regression models. P value less than 0.05 was considered statistically significant. All stages of the plan were approved by the Ethiopic Committee of the Rajaie Cardiovascular, Medical and Research Center and the Code of Ethics was received from the committee (Code of Conduct: RHC.AC.IR.REC.1396.41). At all stages of the project, researchers were committed to protecting the patient's secrets and receiving informed consent. Research in the treatment of patients did not have an adverse effect. Research has not imposed any costs to the center or on patients. The two drugs used in the study have no known or uncontrolled side effects and are approved by the Food and Drug Administration. After approval, the design was registered at the Iranian Center for Clinical Trials (IRCT).

Findings

The two groups were similar in terms of demographic information and underlying illnesses, basic clinical data and during operation, and there were no differences between the two groups. As a result, the two studied populations with the same basic data in terms of the effect of procaine hydrochloride and lidocaine could be evaluated, and the difference in the type of cardioplegic solution was investigated.

As effective variables during the operation, the duration of the aortic valve cross clamp, potassium, magnesium, the temperature of the patient's body during the time of the aortic valve cross clamp and its opening, the volume and frequency of cardioplegia injection, the number of grafts and the use of internal mammary artery were investigated. All data is provided in Table 1.

Table 1: Comparison of the values of effective variables during surgery in the two studied groups

Variable	Procaine(n=50)	Lidocaine(n=50)	P value
Clamp time(minute)	41.5±14.5	41.2±9.5	0.89
Pump time(minute)	67.8±10.2	69.2±8.5	0.78
K(clamp)	4.06±0.6	3.8±0.28	0.03
Mg(clamp)	2.1±0.3	2.0±0.2	0.11
BT(clamp) (℃)	34.4±0.6	34.4±0.3	0.25
K(declamp)	4.8±0.75	4.6±0.57	0.17

Mg(declamp)	2.0±0.26	2.1±0.57	0.22
BT (declamp ¿(℃)	36.3±0.5	36.2±0.2	0.63
Cardio Dose)CC)	1406±312	1130±267	0.63
Cardio Number			0.59
1	25(%50)	27(%54)	
2	18(%36)	18(%36)	
3	6(%12)	5(%10)	
4	1(%2)	0(%0)	
Graft Number			0.12
1	0(%0)	0(%0)	
2	1(%2)	0(%0)	
3	29(%58)	38(%76)	
4	20(%40)	12(%24)	
Lima usage	45(%90)	47(%94)	0.46

Clamp time: Aortic crass clamp time ،Clamp: during Aortic crass clamp time; BT: Body Temperature; declamp: The opening of the aortic crass clamp time; Lima usage: Graft Lima to LAD

In this table, the average values of potassium during the aortic clamp time are statistically significant between the two groups, however since both values are within the normal range, they are not considered as clinically significant.

Considering the P value, there was no statistical difference in the amount of cardioplegia solution required and the frequency of injections between the two groups, but with a more detailed look, it can be seen that the injected solution and the number of injections were generally a little higher in the procaine hydrochloride group which is clinically remarkable.

Table 2 examines how the heart rhythm reverses as a consequence of the study

Table 2: Comparison of indicators related to arrhythmia and return of heart rhythm in the study groups

Variable	Procaine(n=50)	Lidocaine (n=50)	P value
Spontaneous sinus rhythm	32(%64)	21(%42)	0.02
Lidocaine + Mg*	18(%36)	29(%58)	0.02
Inotrope need			0.04
1-2 blues dose	5(%10)	6(%12)	
Low dose	7(%14)	15(%30)	
High dose	1(%2)	5(%10)	

Atrial Arrhythmias			0.58
PSVT	7(%14)	11(%22)	
AF	1(%2)	1(%2)	
Ventricular arrhythmias			0.10
VT	1(%2)	6(%12)	
VF	2(%4)	5(%10)	
Transient PVC	2(%4)	1(%2)	
Defibrillator	3(%6)	6(%12)	0.29
Pacemaker			0.40
Transit pacemaker	2(%4)	4(%8)	0.68
Permanent pacemaker	0(%0)	0(%0)	<0.99
Arrhythmia Time	6.2±4.59	6.5±5.79	0.76
New ST-T Change	1(%2)	0(%0)	>0.99

PSVT: Paroxysmal supra ventricular tachycardia; AF: Atrial Fibrillation; VT: Ventricular tachycardia: VF: Ventricular Fibrillation; Transient PVC: transient Premature Ventricular Complex; New ST: ST segment changes on ECG

*: Administration of a dose of lidocaine and magnesium if the normal sinus rhythm is not returned after 3-5 minutes after the opening of the clamp

A total of 64% of the patients in the procaine hydrochloride group and 48% of the patients in the lidocaine group experienced the spontaneous return of the heart rhythm at the time of the aortic valve opening. The amounts of lidocaine and magnesium required for returning to the normal sinus rhythm were comparatively lower in the procaine hydrochloride group (36% vs. 58%).

Inotropic drugs have been studied in three types in the two groups, which in general were lower in procaine hydrochloride group (P = 0.04). However, there was no statistically significant difference between the two groups in the incidence of atrial arrhythmias that were analyzed for both AF and PSVT and also for ventricular arrhythmias that were compared in three modes of VF, VT and Transient PVC.

In the procaine hydrochloride group, 3 patients required defibrillator due to arrhythmia after the opening of the aortic valve, of which 2 patients needed a pacemaker for having a sinus rhythm. Although, at the end of the operation, the heart had a sinus rhythm and the pacemaker has been stopped. However, in the lidocaine group, 6 patients needed a defibrillator, of which 4 of them needed a pacemaker afterwards. Among these four patients, two of them had a sinus rhythm at the end of the operation and the pacemaker has been stopped, and the two others were transferred to intensive care unit with a heart pacemaker.

In the intensive care unit, only one patient in the procaine hydrochloride group suffered from arrhythmia, where defibrillator and pacemaker were used, which eventually returned to sinus rhythm after a few hours and the heart pacemaker was stopped. In the two patients from lidocaine group, which had been transferred from the operating room with a pacemaker, the heart rhythm returned to normal

after a few hours and the pacemaker was stopped. There was no statistical difference in the results of the study between the two groups in intensive care unit.

In Tables 3 and 4, the effect of each of the variables of the studied groups including age, sex, history of myocardial infarction, potassium and magnesium, the opening time of the aortic valve and the duration of the aortic valve cross clamp have separately and with the removal of the effect of other confounding factors on the spontaneous return of heart rhythm and the need for inotropic drugs been investigated.

Table 3: Adjusted correlation between Spontaneous sinus rhythm and each of the variables

					95% C.I .for OR	
Variable	Coefficient	S.E.	P value	OR	Lower	Upper
GROUP	1.03	0.44	0.02	2.81	1.17	6.76
AGE	0.01	0.03	0.58	1.01	0.95	1.08
SEX	-0.17	0.44	0.68	0.83	0.35	1.98
History of MI	-1.06	0.55	0.05	0.34	0.11	1.02
K_declamp	-0.24	0.32	0.44	0.78	0.41	1.48
MG_declamp	-0.87	0.93	0.34	0.41	0.06	2.60
Clamp Time	-0.03	0.01	0.08	0.96	0.93	1.00

K_declamp: The amount of potassium at aortic valve opening time; MG_declamp: magnesium content at aortic valve opening time; Clamp Time: Aortic valve clamp time

Table 4: Adjusted correlation between Inotrope and each variable

					95% C.I .for OR	
Variable	Coefficient	S.E.	P value	OR	Lower	Upper
GROUP	-1.18	0.46	0.01	0.30	0.12	0.75
AGE	0.05	0.03	0.18	1.05	0.97	1.13
SEX	0.41	0.45	0.36	1.51	0.62	3.70
History of MI	0.86	0.54	0.11	2.37	0.81	6.93
K_declamp	0.18	0.34	0.58	1.20	0.61	2.36
MG_declamp	-0.03	0.96	0.97	0.96	0.14	6.40
Clamp Time	0.02	0.01	0.25	1.02	0.98	1.06

K_declamp: The amount of potassium at aortic valve opening time; MG_declamp: magnesium content at aortic valve opening time; Clamp Time: Aortic valve clamp time

These tables show that the studied groups and each of the cardioplegic solutions affect the spontaneous return of heart rhythm (P = 0.02) and the need for inotropic use (P = 0.01). Also, the history of MI is effective on the spontaneous return of the heart rhythm (P = 0.05).

Discussion and Conclusion

In the present study, there is a significant difference between two groups in the comparison of spontaneous sinus rhythm return after declamping according to the numerical P value of 0.02 and spontaneous return was higher in procaine hydrochloride group. The amount of lidocaine and magnesium and inotropic drugs required for sinus rhythm was lower in procaine hydrochloride group and the results are similar to those of Sellevold [(10)] study results where two cardioplegic solutions, one containing 1 mM Procaine hydrochloride have been compared to a cardioplegic solution containing 0.9% normal sodium in the control group, and the incidence of VF after opening of the aortic valve and the effect of procaine hydrochloride on the reduction of ventricular fibrillation after declamping have been investigated. In this study, the percentage of atrial arrhythmias in the two groups was 16-24% and the incidence of ventricular arrhythmias between the two groups was 10-24% and there was no significant difference between the two groups in regard to the occurrence of atrial and ventricular arrhythmias. In a similar study done by Peretto [(7)] in 2012, AF is referred to as usual and common early postoperative premature arrhythmia, with a 15 to 40% chance of occurrence in coronary procedures. Overall, in our study, the amount of required cardioplegia was higher for the solution containing procaine hydrochloride and lower for the solution containing lidocaine. Perhaps the amount of volume required for a solution containing Procaine hydrochloride may be related to its steric property. In two similar studies published by Mishra [(14)] and Buel [(15)] in 2016, the aortic valve clamp time and the required cardioplegic dose were relatively lower in the group using the del Nido cardioplegic solution (containing lidocaine) and EF after surgery was better than St.Thomas group.

References

1 Mozaffarian, D., Benjamin, E. J., Go, A. S., Arnett, D. K., Blaha, M. J., Cushman, M., De Ferranti, S., Després, J. P., Fullerton, H. J. & Howard, V. J. (2015) Executive summary: Heart disease and stroke statistics - 2015 update: a report from the American Heart Association. *Circulation*. 131 (4), 434-441.

-2 Preeshagul, I., Gharbaran, R., Jeong, K.H., Abdel-Razek, A., Lee, L.Y., Elman, E. & Suh, K.S. (2013) Potential biomarkers for predicting outcomes in CABG cardiothoracic surgeries. *Jornal of Cardiothoracic Surgery*. 8, 176.

-3 Chung, M., Asher, R., Yamada, D. & Eagle, K. (2001) Arrhythmias after cardiac and non cardiac surgey. In: Podrid, P. & Kowey, P. (eds.) *Cardiac arrhythmia*. Philadelphia, Lippincott Williams & Wilkins, pp. 631-638.

-4 Wu, Z-K., Iivainen, T., Pehkonen, E., Laurikka, J., Zhang, S. & Tarkka, M. R. (2003) Fibrillation in patients subjected to coronary artery bypass grafting. *The Journal of Thoracic and Cardiovascular Surgery*. 126 (5), 1477-1482.

-5 Braunwald, E., Zipes, D. & Libby, P. (2001) Heart Disease: A Textbook of Cardiovascular Medicine. Philadelphia, Saunders, 833-55.

-6 Alex, J., Bhamra, G. S., Cale, A. R., Griffin, S. C., Cowen, M. E. & Guvendik, L. (2003) Atrial fibrillation after coronary bypass surgery- pathophysiology, resource utilization and management strategies. *The British Journal of Cardiology*. 10, AIC 82-AIC 88.

-7 Peretto, G., Durante, A., Limite, L. R. & Cianflone, D. (2014) Postoperative arrhythmias after cardiac surgery: incidence, risk factors, and therapeutic management. *Cardiology Research and Practice*. 2014, ID 615987.

-8 Elankera, A. M. & Alawady, T. S. (2013) Continuous infusion of magnesium–lidocaine mixture for prevention of ventricular arrhythmias during on-pump coronary artery bypass grafting surgery. *Egyptian Journal of Anaesthesia*. 29, 419–425

-9 Ibrahim, M. F.,Venn, G. E., Young, C. P. & Chambers, D. J. (1999) A clinical comparative study between crystalloid and blood-based St Thomas' hospital cardioplegic solution. *European Journal of cardiothoracic surgery. 15(1), 75-83.*

-10 Sellevold, O. F., Berg, E. M. & Levang, O. W. (1998) Procaine hydrochloride in cardioplegia (CPL): An effective drug in reducing postischaemic ventricular fibrillation in man. *Journal of Cardiothoracic and Vascular Anesthesia*. 8 (3), 69.

-11 Aldemir, M., Karatepe, C., Bakı, E. D., Çarşanba, G. & Tecer, E. (2014) Comparison of plegisol and modified ST Thomas Hospital cardioplegic solution in the development of ventricular fibrillation after declamping of the aorta. *World Journal of Cardiovascular Surgery*. 4 (10), 159-166.

-12 Matte, G. S. (2012) History and use of del Nido cardioplegia solution at Boston Children's Hospital. *Journal of Extra Corpor Technol*. 44 (3), 98-103.

-13 Electronic Medicines Compendium (eMC). (2013) Sterile Concentrate for Cardioplegia Infusion.Availablefrom:https://www.medicines.org.uk/emcmobile/medicine/29886#PRODUCTIONFO [Accessed 15th October 2017].

-14 Mishra, P., Jadhav, R. B., Mohapatra, C. K. R., Khandekar, J., Raut, C., Ammannaya, G. K., Seth, H. S., Singh, J. & Shah, V. (2016) 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*. 13 (4), 295-299.

-15 Buel, S. T., Striker, C. W., O'Brien, J. E. (2016) del Nido versus St. Thomas cardioplegia solutions: a single-center retrospective analysis of post cross-clamp defibrillation rates. *The Journal of Extra-Corporeal Technology*. 48 (2), 67-70.

OPEN PEER REVIEW

Revision (1)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

REFEREE: EIC | **Revision (1)** 19 Feb 2018

Dear Author,
The final revision of the file meets the reviewers' comments and requirements and therefore can be accepted in the review process.
Thanks.