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Cardioprotective effect of propofol in cardioplegia compared to systemic propofol in heart valves surgery; a randomized controlled trial

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Abstract

Background Myocardial protection is still a focus of ongoing research. Propofol is used widely during the induction of anaesthesia in cardiac surgery. So, this triggers us to investigate the cardioprotective effect of the propofol when added to the cardioplegia compared to systemic propofol by measuring the troponin T level.

Methods This clinical randomized controlled trial was carried out on 150 patients operated for elective valvular heart surgery. Patients were assigned into three equal groups: Group 1: received propofol in the cardioplegia, Group 2: received propofol injection in the aortic line before and after the aortic cross-clamp, and Group 3 (control group): patients without propofol in the cardioplegia or aortic line. All patients were subjected to full medical histories, physical examinations, routine tests, and echocardiography. Cardiac troponin T was measured before surgery and 4 times postoperatively.

Results In group 1, there was a significant improvement in troponin T level at the last reading compared with the control group (mean ± SD. of group 1 was 246.4 ± 131.4, mean ± SD. of group 3 was 317.0 ± 117.9, $p = 0.031$), denoting propofol's cardioprotective effect when added as a cardioplegia additive. In group 2, there was a significant improvement of troponin T level at the last reading compared with the group 1 and control group (mean ± SD. of group 2 was 202.54 ± 156.03, mean ± SD. of group 3 was 317.0 ± 117.9, $p < 0.001$), denoting propofol's more cardioprotective effect when used systemically during cardiopulmonary bypass than when added as a cardioplegia additive.

Conclusions In valvular cardiac surgery, propofol has an additional cardioprotective effect and a superior cardiac outcome when administered systematically during cardiopulmonary bypass rather than added to cardioplegia.

Trial registration Pan African Clinical Trials Register PACTR201907764652028. Registered on 01 July 2019, retrospectively registered, https://pactr.samrc.ac.za/TrialDisplay.aspx?TrialID=5726.

Keywords Heart Valves Surgery, Cardioplegia, Propofol, Cardioprotective Effect

Background

Myocardial protection is still a focus of ongoing research, and cardioplegia is still the most appropriate way for cardiac arrest during cardiac surgery with cardiopulmonary bypass. In cardiac surgery, myocardial protection is performed to prevent damage to the heart from cardiopulmonary bypass or from surgically-caused ischemia,

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enabling the surgeon to perform the procedure with high precision in a silent, bloodless area [1, 2].

Cardioplegia has a crucial function in preserving the myocardium, enabling the induction and maintenance of diastolic collapse. Several additives have been added to the cardioplegia to enhance myocardial protection, but the ideal cardioplegia composition has not been reached yet [3].

Propofol is used widely during the induction of anaesthesia in cardiac surgery [4]. Several animal studies proved the propofol's cardioprotective effect by improving the tissue's antioxidant capacity in addition to it's anaesthetic effect [5]. However, its benefits when used as a cardioplegia additive are not fully studied, and it is not known whether the cardioprotective effect of propofol is different depending on the route of administration, either with cardioplegia or systemically [6, 7].

Cardiac troponin T is a good indicator of the cardioprotective effect of propofol, and it was used in several studies to predict clinical outcomes. Measuring postoperative highly sensitive cardiac troponin T, is an index for the adequacy of cardiac protection and is a prognostic index of clinical outcomes [8].

This study aimed to investigate the impact of propofol on outcomes after valvular heart surgery when added to cardioplegia compared to systemic propofol and control groups.

Methods

This clinical randomized controlled trial was conducted on 150 patients operated for elective valvular heart surgery at the Cardiothoracic Surgery department in Tanta University Hospital for 24 months, started at 11 November 2018, aged 18 to 70 years old, both sexes, subjected to valve replacement or repair due to rheumatic affection.

The ethical committee of the Faculty of Medicine, Tanta University Hospital, Tanta, Egypt, has approved the study (approval code 32,679/11/18). Then, registration was done on Pan African Clinical Trials Register (PACTR201907764652028). Before enrolment, informed written consent was taken from patients.

Exclusion criteria

were patients younger than 18 years old and over 70 years old, coronary artery disease, emergency cardiac surgery, redo cardiac surgery, minimally invasive cardiac surgery, non-rheumatic valve pathology, and patients experiencing end stage kidney disease.

Randomization

Patients were randomized by the computer-generated method in parallel method into three equal groups by sealed opaque envelopes and only participants were blinded; Group 1: including 50 patients with propofol in the cardioplegia; Group 2: including 50 patients with propofol injection in the aortic line before and after the aortic cross-clamp and Group 3 (control group): including 50 patients without propofol in the cardioplegia or aortic line.

Preoperative

All patients were subjected to full medical histories and physical examinations, complete blood count, liver and kidney function tests and echocardiography. Cardiac troponin T was measured before surgery, after first hour of arrival to the intensive care unit (ICU), 12 h, 24 h, and 3 days postoperatively.

Intraoperative

Propofol cardioplegia was administered through the antegrade cannula in group 1, and injection use of propofol systemically during cardiopulmonary bypass in group 2. The composition of the cold crystalloid cardioplegia were: ringer bottle 500 ml, 3 ml lidocaine (20 mg/ml), 10 ml HCO3, 30 ml mannitol 20% and 50 ml glucose 25%. The dosage of the propofol in the cardioplegia was 10 μg/ml, which is a small dose to produce any side effects, and the dose when injected in the aortic line during cardiopulmonary bypass, was 1 mg/kg titrated according to the blood pressure. Moderate hypothermia and cardioplegia every 25 min were used in all patients.

Operative data including cardiopulmonary bypass (CPB) time (minutes), cross clamp time (minutes), and reperfusion time (minutes) were recorded. Every case was sent to the ICU in our hospital, and full monitoring was done.

Postoperative

Echocardiography was done before discharge of the patients. Duration of mechanical ventilation, ICU, and hospital stay was mentioned. Postoperative investigations as renal and liver functions and complete blood picture were also done.

Primary outcome was troponin T level and secondary outcomes were postoperative echocardiography (EF%), hospital and ICU stay, and postoperative complications.

Sample size calculation

Sample size calculation to detect the superiority of propofol administration versus control group was 150 patients. Three groups were created, and the measurement of the troponin T was performed at baseline and repeated four times postoperatively. A study of 150 patients was required to detect 0.05 effect variance between groups with study power of 80%, alpha error

0.05 and 0.7 correlation (rho) between the repeated measures were assumed.

Statistical analysis

IBM's statistical analysis program, SPSS, version 20, was used to process the data (Armonk, NY: IBM Corp). The normality of the distribution was tested using the Shapiro–Wilk procedure. Parametric quantitative variables were presented as mean and standard deviation (SD) and were compared by paired Student's t-test for the same group and by F-test (ANOVA) for different groups. Chi-square test was used for categorical variables to compare between different groups. Fisher's Exact or Monte Carlo correction used for chi-square when more than 20% of the cells have expected count less than 5.

Non-parametric quantitative variables were compared by the Kruskal Wallis test between more than two studied groups and Post Hoc (Dunn's multiple comparisons test) for pairwise comparisons. Comparison of effect size mean values between groups was performed using one way analysis of variance. Comparison of effect size mean values within each group was done using repeated measurement analysis of variance. Pairwise analysis of significant difference was performed using least significant difference test (LSD). F test (ANOVA) with repeated measures, significance between periods was done using Post Hoc Test (adjusted Bonferroni). A two-tailed P value < 0.05 was considered significant.

Results

In this study, 181 patients were assessed for eligibility, 20 patients did not meet the criteria (younger than 18 years, or over 70 years old, coronary artery disease, emergency cardiac surgery, redo cardiac surgery, minimally invasive cardiac surgery, non-rheumatic valve pathology, and patients experiencing end stage kidney disease), and 11 patients refused to participate in the study. The remaining 150 patients were randomly allocated into three equal groups (50 patients in each). All allocated patients were followed-up for 3 days and analyzed statistically. Figure 1

There was no statistically significant difference between the three groups as regard demographic data, preoperative risk factors, and preoperative echocardiography. Table 1

As regard the comparison between preoperative and postoperative echocardiography in the three groups, ejection fraction was insignificantly different between preoperative and postoperative readings in the three groups. LA diameter, LVEDD, and LVESD significantly declined in postoperative measurements in the three groups. Table 2

As regard the comparison between preoperative and postoperative laboratory investigations in the three groups, in group 1: urea was significantly higher postoperatively, and Hb was significantly lower postoperatively. In group 2: serum albumin and Hb were significantly lower postoperatively, and SGOT was significantly higher postoperatively. In group 3: serum albumin, platelet, and Hb were significantly lower postoperatively. Table 3

As regard the intraoperative data, group 2 had a lower total cardiopulmonary bypass time than the other two groups with statistical significance. There was an insignificant difference regarding other parameters between the three groups. Table 4

Regarding the comparison between the three groups according to Troponin-T, during preoperative (the baseline troponin T level), the three groups showed no significant difference. During the first hour postoperatively, all groups showed rapid ascent in the troponin T level with no significant difference. After 12 h postoperatively, the troponin T level decreased in all groups with no significant difference. After 24 h postoperatively, the descent of troponin T level in group 2 was significantly than the same descent in groups 1 and 3. Also, we noticed that the decline in group 1 was more significant than in group 3. After 3 days postoperatively, the troponin T level continued to decrease in all groups, but group 2 showed a more powerful decline in the troponin T level than the other two groups. Also, we noticed that the descent in group 1 was more significant than in group 3. Collectively and comparing the troponin T level in all groups, the troponin T level of group 2 changed more significantly in contrast with those in groups 1 and 3. Overall, the p value of the whole curve in Fig. 2 was significant ($p = 0.040$). Table 5, Fig. 2

As regard the comparison between the three groups according to hospital outcome, group 2 had lower times in the ICU and hospital stay in contrast with the other groups with statistical significance. All patients in the three groups did not suffer postoperatively from respiratory failure, hepatic failure, renal failure, or stroke. Postoperative complications were statistically insignificant between the three groups. Table 6

Discussion

Myocardial protection with cardioplegia remains the most popular technique during cardiac surgery with cardiopulmonary bypass [1, 2].

During cardiac surgery, propofol is commonly used to induce and maintain anaesthesia. In addition to its anaesthetic effect, extensive animal studies have demonstrated that direct coronary perfusion with propofol is cardioprotective during coronary reperfusion. This protection is mediated by an increase in tissue antioxidant capacity and a decrease in lipid peroxidation [4–7].

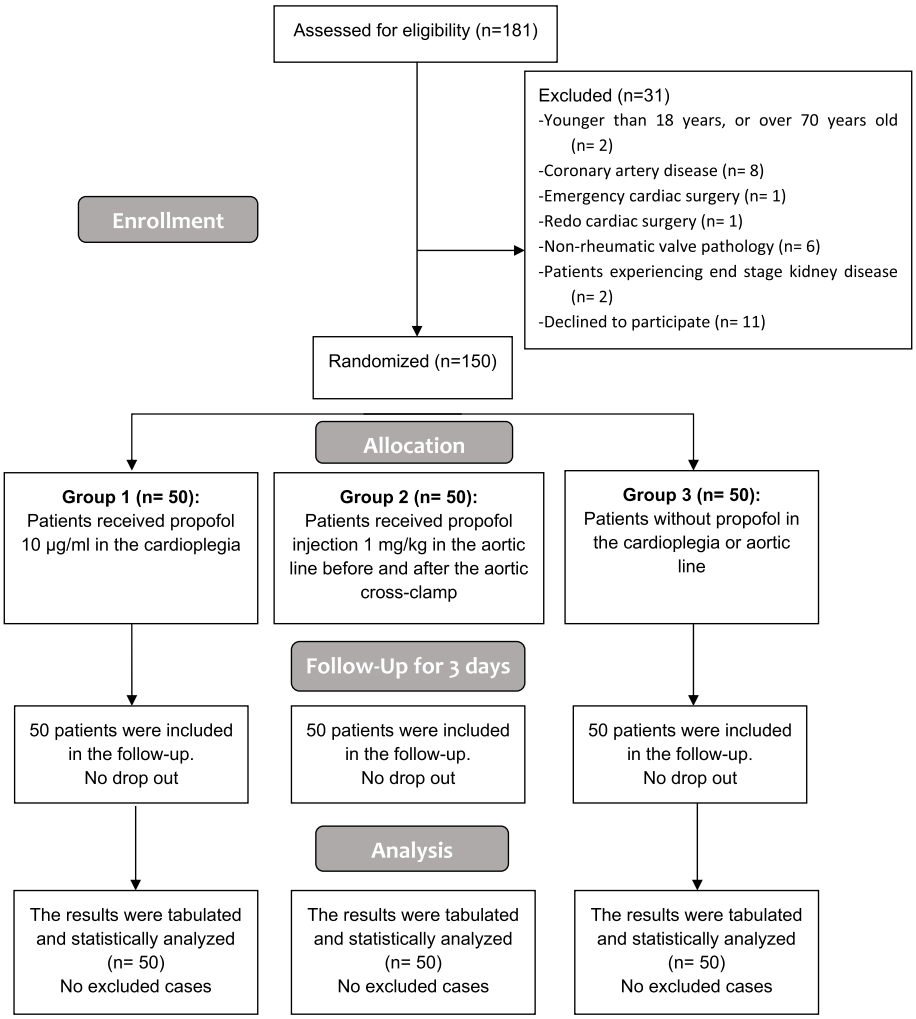

Fig. 1 CONSORT flowchart of the enrolled patients

We research the effect of propofol on outcomes after valvular heart surgery when added to cardioplegic solution compared to systemic propofol and control groups. Our motive is to determine if there is a statistical correlation between troponin T changes and propofol when added to cardioplegia or systemically during cardiopulmonary bypass, as our research deals with limited other centers studies and weak multi-analytic data.

Previous studies have reported that troponin release is predictive of outcome. Soraas and colleagues [9] demonstrated that the long-term mortality risk increases by 31% for every 1 mg/L rise in troponin T.

Numerous experimental studies have demonstrated the advantages of multiple pharmacologic additives to conventional cardioplegic solutions; however, it is uncommon for these experimental studies to be followed by clinical research. In addition, Yamamoto [10] typically failed to demonstrate the expected benefits observed in experimental studies.

There was no statistically significant difference between the three groups as regard demographic data, preoperative risk factors, preoperative echocardiography, laboratory investigations, and postoperative complications.

We compared echocardiography preoperative and postoperative in each group, including ejection fraction, left atrial diameter, left ventricular end-diastolic, and end-systolic diameters. Our finding revealed that the three groups' left ventricular ejection fraction didn't change significantly in postoperative than preoperative reading. Regarding left atrial diameter, left ventricular end-diastolic, and end-systolic diameters, all three groups declined in the postoperative parameters compared to the preoperative readings without a statistically significant difference.

Table 1 Comparison between the three groups according to demographic data, preoperative risk factors, and echocardiography

Demographic data		Group 1 ($n=50$) No. %	Group 2 ($n=50$) No.%	Group 3 ($n=50$) No.%	*P*- value
Sex	Male	28 (56%)	26 (52%)	35 (70%)	0.157
	Female	22 (44%)	24 (48%)	15 (30%)	
Age (years)		53.88 ± 9.60	50.52 ± 11.06	49.46 ± 9.09	0.071
Risk factors					
HTN		11 (22%)	9 (18.0%)	7 (14.0%)	0.582
DM		6 (12%)	7 (14.0%)	6 (12.0%)	0.942
NYHA	2	24 (48%)	14 (28%)	29 (58%)	0.645
	3	26 (52%)	27 (54%)	21 (42%)	
	4	0 (0%)	9 (18%)	0 (0%)	
Smoking	No	41 (82%)	40 (81%)	44 (88%)	0.548
	Smoker	6 (12%)	4 (8.2%)	5 (10%)	
	Ex-smoker	3 (6%)	5 (10%)	1 (2%)	
Euro Score	0	7 (14%)	3 (6%)	3 (6%)	0.627
	1	30 (60%)	33 (66%)	35 (70%)	
	2	8 (16%)	7 (14%)	9 (18%)	
	3	5 (10%)	7 (14%)	3 (6%)	
	Mean ± SD	1.22 ± 0.82	1.36 ± 0.80	1.24 ± 0.66	
AF	No	35 (70%)	36 (72%)	37 (74%)	0.906
	Yes	15 (30%)	14 (28%)	13 (26%)	
Echocardiography					
Mitral Valve					
Normal		12 (24%)	5 (10%)	14 (28%)	0.416
Mild stenosis		1 (2%)	0 (0%)	3 (6%)	
Moderate stenosis		3 (6%)	2 (4%)	2 (4%)	
Severe stenosis		13 (26%)	14 (28%)	12 (24%)	
Mild regurge		4 (8%)	3 (6%)	3 (6%)	
Moderate regurge		4 (8%)	5 (10%)	5 (10%)	
Severe regurge		13 (26%)	21 (42%)	11 (22%)	
Aortic Valve					
Normal		21 (42%)	28 (56%)	14 (28%)	0.087
Mild stenosis		0 (0%)	0 (0%)	0 (0%)	
Moderate stenosis		5 (10%)	1 (2%)	1 (2%)	
Severe stenosis		8 (16%)	5 (10%)	9 (18%)	
Mild regurge		4 (8%)	2 (4%)	4 (8%)	
Moderate regurge		5 (10%)	4 (8%)	4 (8%)	
Severe regurge		7 (14%)	10 (20%)	18 (36%)	
Tricuspid Valve					
Normal		21 (42%)	18 (36%)	24 (48%)	0.639
Mild regurge		6 (12%)	11 (22%)	6 (12%)	
Moderate regurge		15 (30%)	12 (24%)	10 (20%)	
Severe regurge		8 (16%)	9 (18%)	10 (20%)	
LA Thrombus					
No		48 (96%)	48 (96%)	49 (98%)	1.000
Yes		2 (4%)	2 (4%)	1 (2%)	
SPAP		24.64 ± 6.87	30.60 ± 14.58	28.90 ± 11.39	0.279

Data are presented as mean ± SD or frequency (percentage). *HTN* Hypertension, *DM* Diabetes Mellitus, *NYHA* New York Heart Association, *AF* Atrial fibrillation, *LA* Left Atrial, *SPAP* Systolic Pulmonary Artery Pressure

Group 1: Patients with propofol in the cardioplegia, Group 2: Patients with propofol injection in the aortic line, Group 3 (control group): Patients without propofol in the cardioplegia or aortic line

Table 2 Comparison between preoperative and postoperative echocardiography in the three groups

	Echocardiography	Preoperative ($n=50$)	Postoperative ($n=50$)	*P*
Group 1	**EF %**	58.16 ± 4.61	57.92 ± 4.38	0.767
	LA diameter (cm)	3.82 ± 0.85	3.68 ± 0.77	< 0.001*
	LVEDD (cm)	5.31 ± 0.57	5.13 ± 0.57	< 0.001*
	LVESD (cm)	3.50 ± 0.58	3.43 ± 0.50	0.017*
Group 2	**EF %**	59.77 ± 9.19	57.74 ± 3.98	0.058
	LA diameter (cm)	4.29 ± 0.93	4.02 ± 0.82	< 0.001*
	LVEDD (cm)	5.52 ± 0.85	5.32 ± 0.80	0.001*
	LVESD (cm)	3.58 ± 0.79	3.44 ± 0.80	0.010*
Group 3	**EF %**	59.52 ± 3.97	58.40 ± 4.12	0.162
	LA diameter (cm)	3.83 ± 1.03	3.72 ± 0.97	< 0.001*
	LVEDD (cm)	5.28 ± 0.63	5.11 ± 0.61	< 0.001*
	LVESD (cm)	3.40 ± 0.61	3.30 ± 0.52	< 0.001*

Data are presented as mean ± SD. *EF* Ejection Fraction, *LA* Left Atrial, *LVEDD* Left ventricular end-diastolic diameter, *LVESD* Left ventricular end-systolic diameter.
* $p < 0.05$ is statistically significant

Group 1: Patients with propofol in the cardioplegia, Group 2: Patients with propofol injection in the aortic line, Group 3 (control group): Patients without propofol in the cardioplegia or aortic line

Table 3 Comparison between preoperative and postoperative laboratory investigations in the three groups

	Laboratory investigations	Preoperative ($n=50$)	Postoperative ($n=50$)	*P*
Group 1	**Creatinine**	0.88 ± 0.22	0.92 ± 0.17	0.302
	Urea	18.18 ± 5.24	21.48 ± 5.72	0.001*
	S. albumin	3.91 ± 0.34	3.79 ± 0.40	0.097
	SGPT	29.16 ± 11.72	24.26 ± 5.73	0.068
	SGOT	26.56 ± 8.98	28.54 ± 5.45	0.068
	Hb	12.38 ± 1.33	10.17 ± 0.94	< 0.001*
	Platelet	263.18 ± 62.13	257.24 ± 61.62	0.648
	TLC	6724 ± 1603	6961 ± 1820.8	0.432
Group 2	**Creatinine**	0.90 ± 0.23	0.93 ± 0.16	0.425
	Urea	21.48 ± 5.72	23.40 ± 6.30	0.060
	S. albumin	4.13 ± 0.38	3.84 ± 0.33	< 0.001*
	SGPT	28.80 ± 12.11	29.06 ± 9.57	0.348
	SGOT	26.66 ± 10.45	28.86 ± 10.10	0.043*
	Hb	13.15 ± 1.19	10.13 ± 0.97	< 0.001*
	Platelet	253.10 ± 59.07	237.68 ± 56.03	0.181
	TLC	6834 ± 1703.6	6609 ± 1776.14	0.545
Group 3	**Creatinine**	0.89 ± 0.22	0.88 ± 0.22	0.822
	Urea	20.40 ± 4.69	21.48 ± 5.72	0.382
	S. albumin	3.93 ± 0.33	3.77 ± 0.41	0.039*
	SGPT	29.16 ± 11.72	28.80 ± 12.11	0.811
	SGOT	26.56 ± 8.98	26.66 ± 10.45	0.608
	Hb	12.38 ± 1.33	10.17 ± 0.87	< 0.001*
	Platelet	263.18 ± 62.13	237.12 ± 58.16	0.029*
	TLC	6890 ± 1657.7	6834 ± 1703.6	0.831

Data are presented as mean ± SD. *SGPT* Serum glutamic pyruvic transaminase, *SGOT* Serum glutamic oxaloacetic transaminase, *Hb* Hemoglobin, *TLC* Total leucocytic count. * $P < 0.05$ is statistically significant

Group 1: Patients with propofol in the cardioplegia, Group 2: Patients with propofol injection in the aortic line, Group 3 (control group): Patients without propofol in the cardioplegia or aortic line

Table 4 Comparison between the three groups according to intraoperative data

Intraoperative data	Group 1 ($n=50$)	Group 2 ($n=50$)	Group 3 ($n=50$)	*P*
CPB (min.)				
Min. – Max	57.0 – 210.0	50.0 – 180.0	60.0 – 175.0	0.049*
Mean ± SD	98.78 ± 34.16	87.06 ± 31.87	100.42 ± 36.16	
Median (IQR)	90.0 (76.0–110.0)	75.0 (65.0–100.0)	93.50 (75.0–130.0)	
Significance between groups	$p_1=0.033^*$, $p_2=0.972$, $p_3=0.036^*$			
Cross clamp time (min.)				
Min. – Max	46.0 – 130.0	40.0 – 135.0	52.0 – 140.0	0.147
Mean ± SD	75.0 ± 21.47	69.74 ± 24.90	79.58 ± 28.10	
Median (IQR)	70.0 (59.0–90.0)	61.50 (50.0–85.0)	73.0 (60.0–100.0)	
Reperfusion time (min.)				
Min. – Max	11.0 – 20.0	10.0 – 30.0	8.0 – 25.0	0.743
Mean ± SD	12.04 ± 2.96	12.38 ± 5.76	14.42 ± 14.70	
Median (IQR)	10.50 (10.0–14.0)	11.50 (10.0–15.0)	12.0 (10.0–15.0)	
Number of patients needed for defibrillation	4	3	4	0.885

Data are presented as min. – max., mean ± SD, Median (IQR), or frequency (percentage). CPB: Cardiopulmonary bypass. P1: *p* value for comparing between group1 and group2, P2: *p* value for comparing between group1 and group3, P3: *p* value for comparing between group2 and group3. * $P<0.05$ is statistically significant

Group 1: Patients with propofol in the cardioplegia, Group 2: Patients with propofol injection in the aortic line, Group 3 (control group): Patients without propofol in the cardioplegia or aortic line

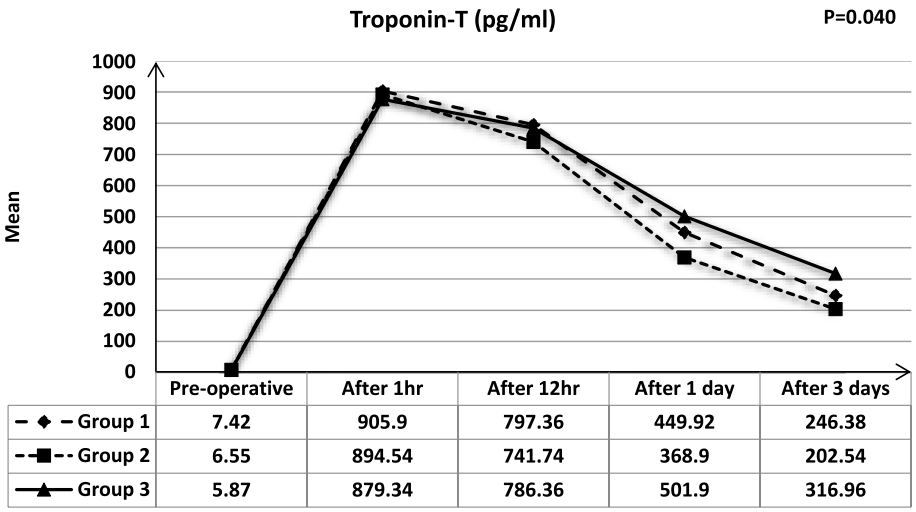

Fig. 2 Comparison between the three groups according to Troponin-T

We also tested and compared operative data and hospital outcomes between the three groups: total bypass time, cross-clamp time, reperfusion time, need for defibrillation, mechanical ventilator/hours, ICU days, and hospital days.

Finally, the most important issue was detecting the cardioprotective effect of propofol in cardioplegia compared to systemic propofol by measuring troponin T level at preoperative, the first hour of arrival to the intensive care unit, 12 h postoperatively, 24 h postoperatively and lastly, 3 days postoperatively.

Our research showed that group 2 had a lower total cardiopulmonary bypass time than the other two groups with statistical significance. Our study had no significant difference between the three groups regarding cross-clamp time, reperfusion time, and the need for defibrillation. Moreover, Rogers et al. [11] agreed with us as they studied the cardioprotective effect of the propofol when added to the cardioplegia through 101 participants subjected to elective cardiac surgery in this study (51 in the propofol group and 50 in the control group). They found no significant difference

Table 5 Comparison between the three groups according to Troponin-T

Troponin-T (pg/ml)	Group 1 ($n=50$)	Group 2 ($n=50$)	Group 3 ($n=50$)	*p*
Pre-operative				
Range	2.47 – 31.60	0.90 – 14.0	0.90 – 10.0	
Mean ± SD	7.42 ± 4.41	6.55 ± 3.01	5.87 ± 2.30	0.072
After 1 h				
Range	412.0 – 4391.0	417.0 – 1430.0	412.0 – 1553.0	
Mean ± SD	905.9 ± 552.1	894.5 ± 212.2	879.3 ± 249.7	
Mean effect size	898.47 ± 552.27	887.99 ± 211.83	873.47 ± 249.68	0.944
After 12 h				
Range	385.0 – 4138.0	305.0 – 1380.0	360.0 – 1300.0	
Mean ± SD	797.4 ± 518.6	741.7 ± 228.1	786.4 ± 222.9	
Mean effect size	789.93 ± 518.74	735.19 ± 227.66	780.49 ± 222.92	0.708
After 1 day				
Range	126.0 – 2178.0	104.0 – 992.0	280.0 – 900.0	
Mean ± SD	449.9 ± 289.3	368.90 ± 239.56	501.9 ± 152.7	
Mean effect size	442.49 ± 289.80	362.35 ± 240.39	496.03 ± 152.56	0.018*
Significance between groups	$p1=0.257$, $p2=0.806$, $p3=0.015$*			
After 3 days				
Range	76.0 – 870.0	50.0 – 710.0	140.0 – 790.0	
Mean ± SD	246.4 ± 131.4	202.54 ± 156.03	317.0 ± 117.9	
Mean effect size	238.96 ± 132.13	195.99 ± 156.31	311.09 ± 117.69	< 0.001*
Significance between groups	$p1=0.328$, $p2=0.031$*, $p3<0.001$*			
F	40.781	464.261	182.196	
p	< 0.001*	< 0.001*	< 0.001*	

Data are presented as range, mean ± SD. and mean effect size. P1: *p* value for comparing between group1 and group2, P2: *p* value for comparing between group1 and group3, P3: *p* value for comparing between group2 and group3 * $P<0.05$ is statistically significant

Group 1: Patients with propofol in the cardioplegia, Group 2: Patients with propofol injection in the aortic line, Group 3 (control group): Patients without propofol in the cardioplegia or aortic line

Table 6 Comparison between the three groups according to hospital outcome and postoperative complications

Hospital outcome	Group 1 ($n=50$)	Group 2 ($n=50$)	Group 3 ($n=50$)	*P*
Duration of Ventilation (hrs.)	11.04 ± 7.62	11.72 ± 7.59	15.86 ± 9.63	0.002*
Significance between groups	$p_1=0.033^*$, $p_2=0.972$, $p_3=0.036^*$			
ICU days	5.04 ± 1.35	3.42 ± 1.34	4.54 ± 1.13	< 0.001*
Significance between groups	$p_1<0.001^*$, $p_2=0.161$, $p_3<0.001^*$			
Hospital days	11.02 ± 2.43	8.04 ± 2.21	12.26 ± 2.38	< 0.001*
Significance between groups	$p_1<0.001^*$, $p_2=0.016^*$, $p_3<0.001^*$			
Postoperative complications				
Pericardial tamponade	2 (4%)	1 (2%)	0 (0%)	$^{MC}p=0.773$
Reintubation	1 (2%)	2 (4%)	3 (6%)	$^{MC}p=0.872$
Arrythmias	14 (28%)	10 (20%)	6 (12%)	0.873

Data are presented as mean ± SD. or frequency (percentage). ICU: intensive care unit. p1: p value for comparing between group1 and group2, p2: *p* value for comparing between group1 and group3, p3: *p* value for comparing between group2 and group3. * $p<0.05$ is statistically significant

Group 1: Patients with propofol in the cardioplegia, Group 2: Patients with propofol injection in the aortic line, Group 3 (control group): Patients without propofol in the cardioplegia or aortic line

between the two groups regarding total bypass and cross-clamp times.

Contrasted to our results, Samir et al. [12] studied the anti-inflammatory effects of systemic propofol during cardiopulmonary bypass through 23 participants subjected to CABG surgery (12 in the propofol group and 11 in the control group). They reported a decrease in the total bypass time and cross-clamp time in the propofol group than in the control group without significant differences.

Our research showed that group 2 takes less time in the ICU and hospital stay than the other groups with statistical significance. Rogers et al. [11] disagreed with our results as they found no significant difference between the propofol cardioplegia group and the control group regarding hospital outcomes.

In our research, we detected the cardioprotective effect of the propofol either when added to cardioplegia in group 1 or systemically during cardiopulmonary bypass in group 2 by measuring troponin T level and comparing them with the control group 3. In group 1, the dose of propofol in the cardioplegia was 10 µg/ml. We noticed a significant improvement in troponin T level at the last reading compared with the control group denoting the cardioprotective effect of the propofol when added as a cardioplegia additive.

In group 2, the dose of propofol when injected in the aortic line during cardiopulmonary bypass was 1 mg/kg. We noticed a significant improvement in troponin T level at the last reading compared with the group 1 and control group, denoting propofol's more cardioprotective effect when used systemically during cardiopulmonary bypass than when added as a cardioplegia additive.

Rogers et al. [11] were parallel with our results as they involved 101 participants in their study subjected to elective cardiac surgery (51 in the propofol group and 50 in the control group). They added the propofol to the cardioplegia at the dose of 6 µg/ml, and they depended on the troponin T level six times to assess the cardioprotective effect of the propofol (preoperative, 1 h postoperative, 6 h postoperative, 12 h postoperative, 24 h postoperative and 48 h postoperative). They found that the propofol group had lower results of troponin T than the control group indicating the cardioprotective effect of the propofol when added to cardioplegia.

Conversely, Samir et al. [12] involved 23 participants in their study subjected to CABG surgery (12 in the propofol group and 11 in the control group). They used propofol systemically at a rate of 120 mcg/kg/minute immediately after starting the cardiopulmonary bypass. They were maintained throughout the surgery and for 6 h in the intensive care unit. The control group in the study also received propofol systemically with a dose of 30–50 mcg/kg/minute which was started at chest closure and continued for the next 6 h in the intensive care unit. They found that the propofol group's anti-inflammatory markers were less than the control group without significant differences.

Corcoran et al. [13] agreed with our findings; they noticed that the propofol had an anti-inflammatory effect by measuring inflammatory markers, which were decreased in the propofol group than the control group with statistical significance.

Limitations of the research

short-term follow-up, single-center study, and cardiac surgery team are not unified. Further prospective studies are needed with larger sample size and long term follow up, using different doses of propofol to explore dose–response relationship and to generalize our results.

Conclusions

From this research, we concluded that: propofol has an additional protective effect on the myocardium. Propofol is more cardioprotective when used systemically during cardiopulmonary bypass in valvular cardiac surgery than when added to cardioplegia.

Abbreviations

AF	Atrial fibrillation
CPB	Cardiopulmonary bypass
CABG	Coronary artery bypass grafting
DM	Diabetes mellitus
EF	Ejection fraction
HTN	Hypertension
ICU	Intensive care unit
LA	Left atrium
LVEDD	Left ventricular end-diastolic diameter
LVESD	Left ventricular end-systolic diameter
NYHA	New York Heart Association
SPAP	Systolic pulmonary artery pressure
SD	Standard deviation

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Authors' contributions

AA, EW, and AT conceived and supervised the study. AA and MT were responsible for the data collection. AA and MA analyzed and interpreted the data. All authors provided comments on the manuscript at various stages of development. All authors read and approved the final manuscript.

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Availability of data and materials

Data and materials are available on a reasonable request from the authors.

Declarations

Ethics approval and consent to participate

The ethical committee of the Faculty of Medicine, Tanta University Hospital, Tanta, Egypt, has approved the study. Before enrolment, informed written consent was taken from the patients.

Consent for publication
All authors give their consent for publication in the journal.

Competing interests
The authors declare that they have no competing interests.

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