Original Article

Comparison Between Beating and Non–Beating-Heart Pump Approaches Among Patients Undergoing Pulmonary Valvar Surgery: A Randomized Clinical Trial

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ABSTRACT

Background: Open-heart surgery is usually done in 2 ways. The first and most common method is done with cardiac arrest after aortic clamping and the perfusion of the cardioplegic solution into the coronary arteries. The second method is the on-pump beating heart, done usually for the right-heart chambers. In this study, we sought to compare these 2 methods concerning cardiac muscle damage, kidney and liver parameters, and clinical outcomes in patients with isolated pulmonary valve repair.

Methods: Forty-three patients that underwent cardiopulmonary bypass were randomly assigned to 2 on-pump non-beating (n=20) and beating (n=23) heart groups. We assessed between-group hemodynamics and arterial blood gasses.

Results: The operation time was shorter in the beating-heart group than in the non-beating heart group (*P*=0.003). The ejection fraction (EF) at discharge in the non-beating group was significantly lower than that in the beating-heart group (44.25±6.12 vs 50.00±5.56). Cardiac troponin I and creatine phosphokinase levels showed significant decreases at the preoperative time in both groups; the levels were better in the beating-heart group. No changes were observed in arterial blood gasses before surgery, postoperatively, at intensive care unit admission, and 24 hours after surgery in the 2 groups. The potassium level after the operation was significantly lower in the beating-heart group (4.18 [± 0.85]).

Conclusions: The beating-heart surgical procedure conferred a better EF at discharge. Additionally, cardiac troponin I and creatine phosphokinase levels decreased after the preoperative time. ***(Iranian Heart Journal 2023; 24(1): 22-30)***

KEYWORDS: On-pump, Beating and Non-Beating, Heart surgery, Cardiopulmonary bypass, Pulmonary valve repair and replacement

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Cardiovascular diseases (CVDs) constitute one of the leading causes of death worldwide, with an estimated 17.9 million lives lost per year. [1] The burden of CVDs is exponentially increasing, along with the aging of the world's population. [2] In the past decade, heart valve surgeries and other related diseases have saved thousands of lives. [3] Most surgical procedures cannot be performed without cardiopulmonary bypass (CPB). [4] Cardiac and pulmonary pumps are usually performed in 2 ways. During the first approach, which is the traditional one, the perfusionist, in collaboration with the surgeon, injects the cardioplegic solution into the coronary arteries, causing cardiac arrest. [5] The second method is the on-pump beating-heart technique, during which the heartbeat is maintained. [6]

Off-pump coronary artery bypass grafting (CABG), which avoids the use of CPB with cardioplegic arrest and aortic cross-clamping, has attracted the interest of an increasing number of cardiac surgeons and patients scheduled for surgical revascularization. [7,8] On-pump beating-heart CABG, which uses CPB without either cardioplegic arrest or aortic cross-clamping, has recently been applied in high-risk patients. [9]

Myocardial protection is an essential component of cardiac surgery. [10] The basic principles of this protection include reducing myocardial metabolism by cooling down and interrupting myocardial electrical and mechanical activity. Cooling the whole body down to 32 °C reduces total oxygen consumption by 45%. [11] The use of cardioplegia provides additional degrees of myocardial protection during cardiac surgery. Cardiac surgery with the aid of the beating-heart pump, instead of cardioplegia injection, is a valid and feasible method in cardiac surgery. [4] Previous studies have shown that the use of the beating-heart technique can be extended to valve surgery with satisfactory outcomes. [12-14] Common strategies in myocardial protection, such as hypothermia, cause postoperative left ventricular dysfunction. [15] This problem is more significant among patients with preoperative left ventricular dysfunction, necessitating hot anterograde and retrograde injections to reduce the injury. In pulsed heart surgery (without cardioplegia injection) with an empty heart, the workload of the heart is significantly reduced. [11] Continuous perfusion-derived feeding in this method reduces the development of hypoxemia and arrhythmia. Evidence from clinical studies has shown that pulsatile heart surgery has several advantages, such as no reperfusion injury, reduced cardiac workload, reduced CPB duration, convenience in finding a ventricular septal defect, and residual leakage. However, this method has disadvantages, such as the inability to access a blood-free environment in the area of surgery, greater damage to blood cells, and the need for technical capabilities other than cardioplegia. [2,16] The advantage of this method of surgery is still debatable. The present study aimed to compare these 2 methods concerning cardiac muscle damage, kidney and liver parameters, and clinical outcomes.

METHODS

Study Design and Sample

This randomized clinical trial randomly assigned 43 patients to groups: the conventional del Nido cardioplegia (n=20; non-beating heart surgery) and on-pump beating-heart surgery (n=23). Random sampling was performed in the surgical rooms, intensive care unit (ICU), and inpatient ward of Rajaie Cardiovascular Medical and Research Center between June 2017 and April 2018.

Inclusion and Exclusion Criteria

The study included patients who underwent open-heart surgery with either primary or secondary pulmonary valve problems and

could read and understand Farsi. Written informed consent was obtained from the study population after the provision of comprehensive explanations regarding the study design and objectives. The screening process was done by 2 trained nurses, who were blind to the study groups. Patients were excluded if they had a history of patent foramen ovale, atrial septal defect, ventricular septal defect, congenital heart lesions requiring combined surgery, cardiopulmonary arrest during surgery, and emergency surgery.

Data Collection

Data were collected in 2 steps. First, information was gathered on the patients' demographics, including age, weight, and sex, disease diagnoses, and the type of surgery. Next, data were collected regarding the CPB process registration form and associated clinical implications, including the CPB time, peripheral cannulation, the left ventricular ejection fraction, cardiac troponin I, creatine phosphokinase, aspartate aminotransferase, and alanine transaminase. Additionally, blood pressure, pulse oximetry, and heart rate were monitored in the operating room after noninvasive blood pressure (NIBP) monitoring. All the patients received a crystalloid ringer solution of 10 mL/kg before open-heart surgery. They were then mechanically ventilated with anesthesia machines at a respiratory volume of 7-8 mL/kg body weight adjusted for age. Moreover, $PaCO^2$ was maintained between 30 and 35 mm Hg. Heart rate, systolic and diastolic blood pressures, and central venous pressure were recorded before the induction of anesthesia, on admission to the ICU, and then every 2 hours until 48 hours after ICU admission.

Outcomes

The left ventricular ejection fraction (preoperatively and at discharge) was estimated by a specialist physician using echocardiography. In addition, before surgery and at discharge, cardiac troponin I, creatine phosphokinase, aspartate aminotransferase, alanine transaminase, blood urea nitrogen, and creatinine levels were measured. The need for inotropic drugs, such as epinephrine, norepinephrine, milrinone, dopamine, and dobutamine, was also evaluated according to medication orders recorded by the physician in the patient's record in the operating room and during the ICU care period. Arterial blood gas analysis was performed preoperatively, postoperatively, on admission to the ICU, and 24 hours postoperatively with the patient's blood samples and detailed laboratory examinations.

Statistical Analysis

Categorical variables were treated as proportions while continuous variables were reported as means and standard deviations. First, the normality of the data was examined using the Kolmogorov–Smirnov test. Then, the groups were compared using the Student *t* test for parametric data and the Mann–Whitney *U* test for nonparametric data concerning the continuous variables. The categorical variables were presented as numbers or frequencies (%) and were analyzed using the χ^2 or Fisher exact test as appropriate. The data were analyzed using the SPSS 23.0 statistical software, and a significant level was set at an α of 0.05.

RESULTS

One hundred patients were eligible for the study. Forty-five patients did not meet the inclusion criteria, 5 patients refused to participate, and 7 patients were excluded for other reasons. Hence, 43 patients were enrolled and randomly allocated to 2 groups: 23 patients in the beating-heart group and 20 patients in the non–beating-heart group (Fig. 1).

As is shown in Table 1, 75% (n=15) of the beating-heart group and 25% (n=5) of the

non–beating-heart group were males. No significant differences were observed between the 2 groups regarding demographic information and physical assessments (P>0.05).

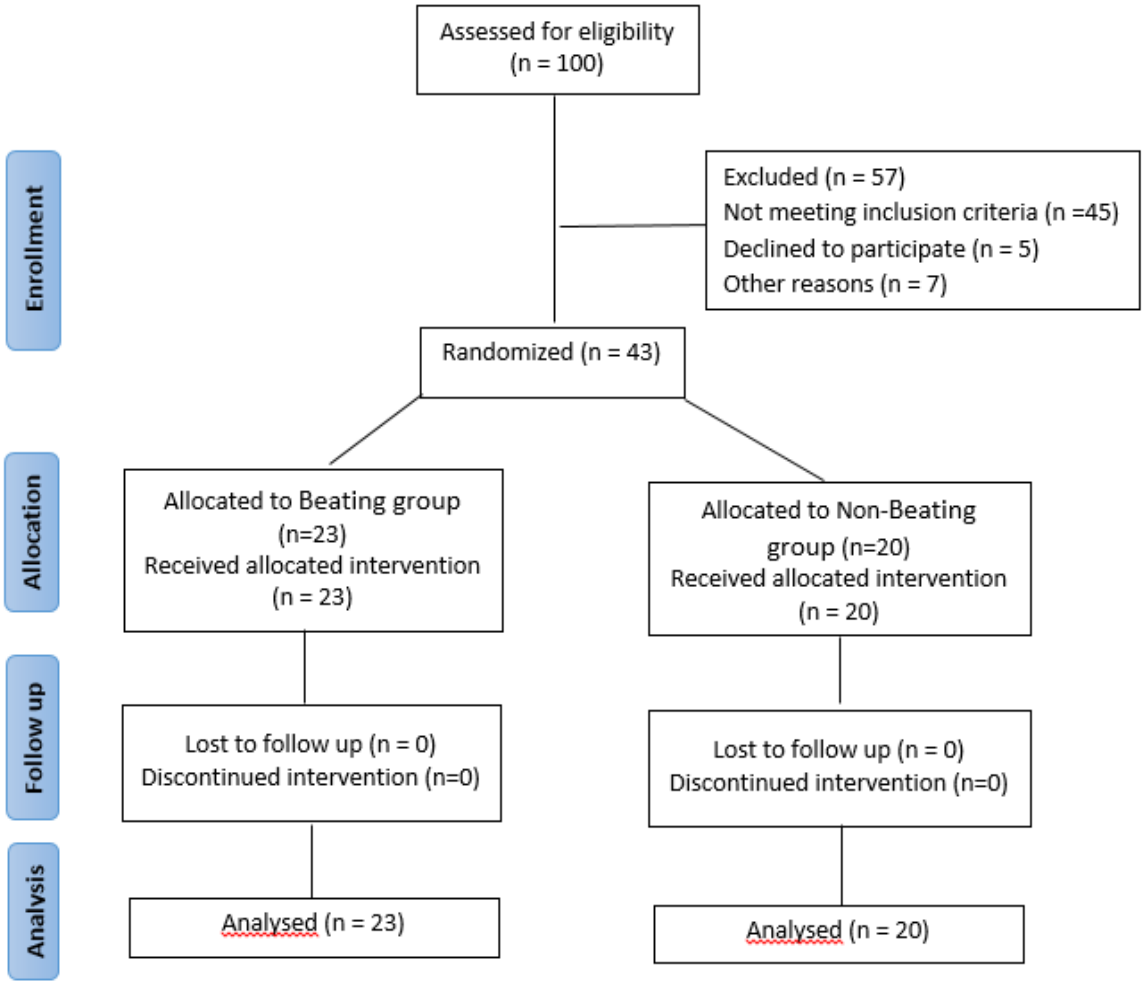

Figure 1: The image depicts the flow diagram of the participants through each stage of the randomized trial.

Table 1: Baseline characteristics of the patients in the beating and non–beating-heart groups

Variables	Non–Beating-Heart Group	Beating-Heart Group	*P* value**
Age, y (mean±SD)	22.35(±11.31)	19.78(±7.57)	0.382
Sex, N (%) Female Male	 5(%25) 15(%75)	 7(%30.4) 16(%6.69)	0.745
Height, cm (mean±SD)	163.90(±19.02)	163.00(±15.48)	0.865
Weight, kg (mean±SD)	63.10(±24.73)	54.13(±17.74)	0.175
Body surface area, m (mean±SD)	1.74(±0.43)	1.54(±0.30)	0.093

The *P* values listed represent differences between the beating and non–beating-heart groups.
** The italic rows indicate estimates with borderline *P* values, while the bold rows indicate estimates with significant *P* values at a 5% level.

As is displayed in Table 2, the duration of surgery was significantly different between the 2 groups: it was lower in the beating-heart group (*P*=0.003). The ejection fraction was significantly increased in the beating-heart group (*P*=0.003). A decrease in the output fraction was observed at discharge in the beating-heart group, with the difference between the 2 groups being significantly greater in the beating-heart group (*P*=0.003). As is shown in Table 3, the cardiac troponin I level was significantly decreased in the beating-heart group preoperatively (*P*=0.023). The level of creatine phosphokinase decreased significantly in the beating-heart group in the preoperative period (*P*=0.038). Figure 2 illustrates changes in the levels of potassium, sodium, hemoglobin, and lactate preoperatively, postoperatively, on admission to the ICU, and 24 hours after surgery. For potassium, sodium, and hemoglobin, both groups had a similar pattern, while the mean lactate level was higher at all times in the beating-heart group. Epinephrine, milrinone, and dobutamine were also prescribed in the operating room and during the ICU care period. The beating-heart group received significantly more milrinone (*P*=0.026).

Table 2: Cross-clamp time, cardiopulmonary bypass time, length of surgery, mechanical ventilation, and length of stay in the intensive care unit in the beating and non–beating-heart groups

Variables	Non–Beating-Heart Group	Beating-Heart Group	*P* value**
Duration of Surgery			
Cross-clamp time, min	43.85±20.30	-*	-
Cardiopulmonary bypass time, min	86.55 ±41.16	70.69 ±29.57	0.151
Surgery time, min	267.25 ±47.55	218.47 ±53.73	**0.003**
Length of Stay in the Intensive Care Unit			
Mechanical ventilation time, h	9.06 ±4.09	9.78 ±5.55	0.634
Length of stay in the intensive care unit, h	93.60 ±33.85	100.17 ±45.56	0.599

The *P* values listed represent differences between the beating and non-beating groups.
* Cross-clamping was not performed in this group.

Table 3: Changes in the ejection fraction, cardiac troponin I, and other inflammatory markers in the beating and non-beating groups

Variables		Non–Beating-Heart Group	Beating-Heart Group	*P* value*
Ejection fraction	Preoperative	46.85 ±8.64	46.08 ±7.37	0.756
	Discharge time	44.25 ±6.12	50.00 ±5.56	**0.003**
Troponin I	Preoperative	0.027 ±0.024	0.016 ±0.010	*0.081*
	Discharge time	23.41 ±82.12	2.67 ±1.77	**0.023**
Creatine phosphokinase	Preoperative	15.82 ±8.12	15.82 ±4.11	0.506
	Discharge time	73.69 ±27.28	33.43 ±21.72	**0.038**
Aspartate aminotransferase	Preoperative	22±8.59	21.50±6.40	0.873
	Discharge time	73.93±15.23	57.58±27.41	0.313
Alanine aminotransferase	Preoperative	21.09±9.23	17.91±8.75	0.407
	Discharge time	24.06±10.65	22.23±16.15	0.705
Blood urea nitrogen	Preoperative	14.15±3.68	12±3.48	**0.057**
	Discharge time	13.30±3.52	13.82±7.02	0.766
Creatinine	Preoperative	0.73±0.22	0.82±0.24	0.211
	Discharge time	0.73±0.21	0.77±0.23	0.605

** The italic rows indicate estimates with borderline *P* values, while the bold rows indicate estimates with significant *P* values at a 5% level.

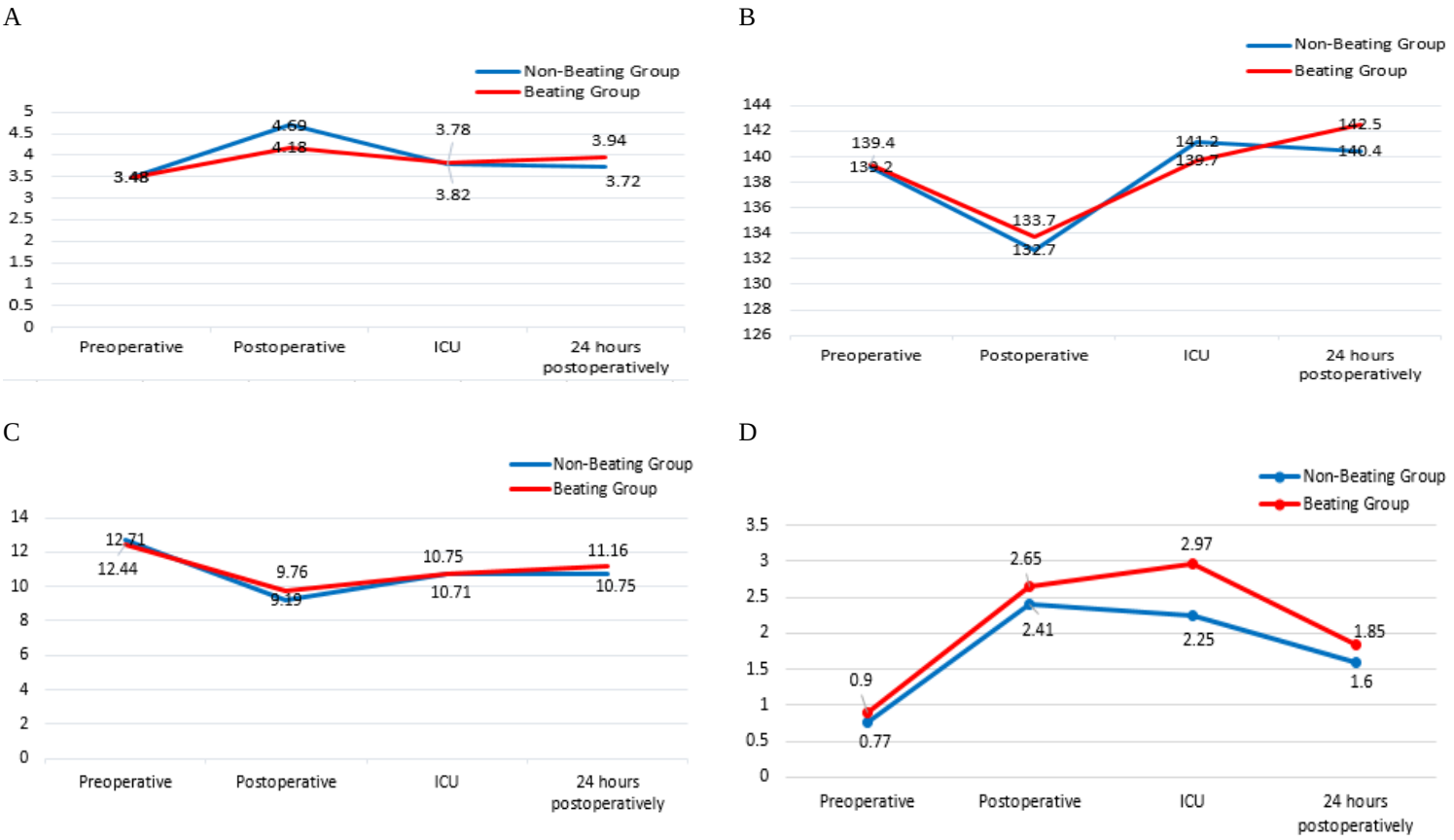

Figure 2: The images illustrate changes in the mean of the parameter K of arterial blood gas (ABG) (A), sodium (Na) (B), hemoglobin (Hb) (C), and lactate (D) in the beating and non–beating-heart groups.

DISCUSSION

Cardiac troponin I is a protein specifically expressed in the cardiac muscle; therefore, measuring its level is deemed specific in the study of myocardial injury. In line with a previous study, [17] we found that the level of troponin I was significantly decreased at discharge in the beating-heart group compared with the non–beating-heart group. This decrease may be due to the better protection of the myocardium during bleeding surgery, less myocardial injury, and non-reperfusion injury due to the type of surgical technique in this group. Nevertheless, some other reports have demonstrated that biomarkers of cardiac injury, such as creatine phosphokinase and cardiac troponin I, are similar between beating and non–beating-heart groups. [18,19]

In our study, the marker of cardiac muscle creatine phosphokinase injury was significantly decreased in the beating group after surgery. Matsumoto et al [17] also showed that the rate of myocardial creatine phosphokinase marker was significantly lower in the beating-heart group than in the arrest group with the cardioplegia solution. This decrease could also be due to the better protection of the myocardium and its continued perfusion during surgery, resulting in less damage to the myocardium and less reperfusion injury due to the type of surgical technique in this group. Another significant marker that we measured was the preoperative ejection fraction and the discharge-time ejection fraction in the 2 study groups. At discharge, the rate was significantly higher in the beating-heart group than in the non–beating-heart group. The increase can be

explained by the ischemia time, a better blood supply to the heart muscle during surgery, the non-use of cardioplegia injection, and consequently the non-use of potassium injection in the beating-heart group.

The results of several studies have shown that patients with reduced ejection fractions can benefit from beating-heart surgery. [20-22] The on-pump beating-heart technique for heart valve surgery is possible if myocardial perfusion is maintained and particulates and air emboli are avoided. [12,23] A prior study revealed that the off-pump procedure was superior to the on-pump beating-heart procedure vis-à-vis the length of hospital stay, blood product transfusion, and atrial fibrillation development. [18]

We measured the levels of creatinine and blood urea nitrogen before and after surgery and 24 hours after surgery. We observed no significant differences between the 2 groups, with the measurements showing that patients had a relatively similar status in renal function. Therefore, renal function in these patients could be independent of the type of surgery; and in both perfusion groups, the use of the heart and lungs could confer a good protective effect on these organs. In contrast, in 2015, Baraki et al [24] showed that the rate of renal failure was significantly higher in the beating-heart group than in the non–beating-heart group.

We measured liver markers, aspartate aminotransferase and alanine transaminase, preoperatively, postoperatively, and 24 hours postoperatively, with no significant differences between the 2 groups. This could be explained by a good protective effect and proper perfusion of the liver using the artificial heart and lung system. [25] Postoperative milrinone in the ICU was significantly lower in the beating-heart group. Matsumoto et al [17] showed that in terms of drug use, the dopamine inotropic of the beating-heart group was significantly lower than that of the non–beating-heart group. This indicates that myocardial injury was less in the beating heart group than in the non–beating-heart group and that the right ventricle was significantly better in this group.

The 2 groups received blood and blood products, such as packed cells and fresh frozen plasma in the operating room. We found no significant differences between the 2 groups in this regard. In 2015, Baraki et al [24] reported no significant differences in mortality and clinical outcomes between their 2 study groups; however, the survival rate was insignificantly lower in 1, 5, and 10 years in the beating-heart group. Badr et al [12] reported that beating-heart mitral valve replacement was a safe alternative to the conventional method with comparable outcomes. Dayan et al [26] showed that although some differences were noted between both techniques in the immediate postoperative period, operative mortality and long-term survival were similar. Our results demonstrated no significant differences between the 2 groups apropos of the length of stay in the ICU and the duration of mechanical ventilation in the operating room and the ICU. A previous investigation found that the beating technique was effective for revascularization and myocardial function and was associated with low postoperative morbidity and mortality. [20]

Matsumoto et al [17] found no significant differences between their study 2 groups in clinical factors, such as postoperative low cardiac output syndrome, the return to the operating room to control bleeding, neurological disorders, the duration of mechanical ventilation, and hospitalization in the ICU. Thus, they concluded that non-cardioplegic and beating injections due to proximity to physiologic status could be a good option for cardiac valve bypass surgery.

The current study has several limitations. Firstly, the low sample size may have influenced the generalizability of the results. Secondly, the short postoperative follow-up evaluation might have impacted the

findings. Thirdly, the single-center design of this clinical trial is a limitation.
Further prospective studies with more participants and longer study times are required to elucidate the effects of the types of heart surgery procedures on long-term clinical outcomes in patients.

CONCLUSIONS

The current study compared the markers of cardiac muscle injury and clinical outcomes in patients undergoing pulmonary valve surgery using CPB between pulsatile and non-pulse cardiac procedures. In pulmonary valve surgery using pulsed heart, heart rate, and artificial pulmonary devices, the discharge time was better, and there was a significant decrease in cardiac markers, troponin and creatine phosphokinase, postoperatively. The duration of surgery in this group was shorter than that in the non–beating-heart group, but there was a significant difference in clinical outcomes between the 2 groups. Accordingly, we recommend that the surgical method be based on the type of surgery and the preference of the surgeon and the perfusionist.

Authors' Note

All the procedures performed in the present study were in keeping with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. This study was approved by the Ethics Committee of Iran University of Medical Sciences (RHC.AC.IR.REC.1396.86).

Conflict of Interest

The authors hereby declare that they have no potential conflicts of interest.

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REFERENCES

1. Khan DT. Cardiovascular diseases (CVDs) 2017 [Available from: https://www.who.int/en/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds).
2. Iranagh JA. Effectiveness of health education intervention based on health belief model among elderly women in urmia, iran. 2015.
3. Tofield AJEHJ. Novel TAVI presented at South Africa Heart Congress 2016. 2017; 38(16):1181-2.
4. Taegtmeyer H, Young ME, Lopaschuk GD, Abel ED, Brunengraber H, Darley-Usmar V, et al. Assessing cardiac metabolism: a scientific statement from the American Heart Association. Circulation research. 2016; 118(10):1659-701.
5. Paal P, Gordon L, Strapazzon G, Maeder MB, Putzer G, Walpoth B, et al. Accidental hypothermia–an update. Scandinavian journal of trauma, resuscitation and emergency medicine. 2016; 24(1):1-20.
6. Xia L, Ji Q, Song K, Shen J, Shi Y, Ma R, et al. Early clinical outcomes of on-pump beating-heart versus off-pump technique for surgical revascularization in patients with severe left ventricular dysfunction: the experience of a single center. 2017; 12(1):1-8.
7. Godinho AS AA, Pereira AJ, Pereira TS. On-pump versus off-pump coronary-artery bypass surgery: a meta-analysis. Arq Bras Cardiol. 2016; 98:87–94.
8. Lemma MG CE, Tritto FP, Centofanti P, Fondacone C, Salica A, et al. On-pump versus off-pump coronary artery bypass surgery in high-risk patients: operative results of a prospective randomized trial (on-off study). Thoracic Cardiovascular Surgery. 2012; 143:625–31.
9. Darwazah AK BV, Isleem I, Helwa K. Myocardial revascularization using on-pump beating heart among patients with left ventricular dysfunction. J Cardiothorac Surg. 2016; 5:109.
10. Harjola VP, Mebazaa A, Čelutkienė J, Bettex D, Bueno H, Chioncel O, et al. Contemporary management of acute right ventricular failure: a statement from the Heart Failure Association and the Working Group on Pulmonary Circulation and Right

Ventricular Function of the European Society of Cardiology. European journal of heart failure. 2016; 18(3):226-41.

11. Cappabianca G, Rotunno C, Schinosa LdLT, Ranieri VM, Paparella D. Protective effects of steroids in cardiac surgery: a meta-analysis of randomized double-blind trials. Journal of cardiothoracic and vascular anesthesia. 2011; 25(1):156-65.

12. Badr A-A, Yousef E, Kotb M, Deebis A. Beating-heart versus conventional mitral valve replacement; a randomized clinical trial. The Egyptian Cardiothoracic Surgeon. 2020; 2(3):90-8.

13. Walter KN, Wagner JA, Cengiz E, Tamborlane WV, Petry NM. The need for research addressing alcohol use disorder and diabetes. Addiction. 2015.

14. Pasic M, Sündermann S, Unbehaun A, Kempfert J, Jacobs S, Falk V. Beating heart mitral valve surgery: results in 120 consecutive patients considered unsuitable for conventional mitral valve surgery. Interactive cardiovascular and thoracic surgery. 2017; 25(4):541-7.

15. Harjola VP, Mebazaa A, Čelutkienė J, Bettex D, Bueno H, Chioncel O, et al. Contemporary management of acute right ventricular failure: a statement from the Heart Failure Association and the Working Group on Pulmonary Circulation and Right Ventricular Function of the European Society of Cardiology. heart failure. 2016; 18(3).

16. XIAO Y-b, CHEN L, WANG X-f, ZHONG Q-j, CHEN J-j, CHENG B-c. On-Pump Beating-Heart Intracardiac Procedures in 2100 Cases [J]. Chinese Journal of Extracorporeal Circulation. 2006; 4.

17. Matsumoto Y, Watanabe G, Endo M, Sasaki H, Kasashima F, Kosugi I. Efficacy and safety of on-pump beating heart surgery for valvular disease. The Annals of thoracic surgery. 2002; 74(3):678-83.

18. Velioglu Y, Isik M. Early-Term Outcomes of Off-Pump versus On-Pump Beating-Heart Coronary Artery Bypass Surgery. The Thoracic and cardiovascular surgeon. 2019; 67(07):546-53.

19. Rastan AJ, Bittner HB, Gummert JF, Walther T, Schewick CV, Girdauskas E, et al. On-pump beating heart versus off-pump coronary artery bypass surgery—evidence of pump-induced myocardial injury. European journal of cardio-thoracic surgery. 2005; 27(6):1057-64.

20. Wang W, Wang Y, Piao H, Li B, Wang T, Li D, et al. Early and medium outcomes of on-pump beating-heart versus off-pump CABG in patients with moderate left ventricular dysfunction. Brazilian journal of cardiovascular surgery. 2019; 34(1):62-9.

21. Xia L, Ji Q, Song K, Shen J, Shi Y, Ma R, et al. Early clinical outcomes of on-pump beating-heart versus off-pump technique for surgical revascularization in patients with severe left ventricular dysfunction: the experience of a single center. Journal of cardiothoracic surgery. 2017; 12(1):1-8.

22. Erkut B, Dag O, Kaygin MA, Senocak M, Limandal HK, Arslan U, et al. On-pump beating-heart versus conventional coronary artery bypass grafting for revascularization in patients with severe left ventricular dysfunction: early outcomes. Canadian Journal of Surgery. 2013; 56(6):398.

23. Hasde Aİ, Özçınar E, Çakıcı M, Baran Ç, İnan MB, Yazıcıoğlu L, et al. Comparison of aortic cross-clamping versus beating heart surgery in tricuspid valve repair. Turkish Journal of Thoracic and Cardiovascular Surgery. 2018; 26(4):519.

24. Baraki H, Saito S, Al Ahmad A ,Fleischer B, Haverich A, Kutschka I. Beating heart versus arrested heart isolated tricuspid valve surgery. International heart journal. 2015; 56(4):400-7.

25. MarcoRanieriMD†DomenicoPaparellaMD GCLLTSV. Protective Effects of Steroids in Cardiac Surgery: A Meta-Analysis of Randomized Double-Blind Trials. Journal of Cardiothoracic and Vascular Anesthesia. 2011; 25(1).

26. Dayan V, Paganini JJ, Marichal A, Brusich D. On-pump beating/non-beating CABG in stable angina have similar outcomes. Brazilian Journal of cardiovascular surgery. 2018; 33(2):183-8.