July 2019, Volume 4, Issue 3 (85-88)

Impact of Cardiopulmonary Resuscitation on Cardiac Transplantation Outcome

Meysam Mojtabaee [1], Farah Naghashzadeh [1], Fariba Ghorbani [2], Shahrzad Ghafarian [1], Shagin Shahryari [1], Farahnaz Sadegh Beigee [1,*]

[1] Lung Transplantation Research Center (LTRC), National Research Institute of Tuberculosis and Lung Diseases (NRITLD), Shahid Beheshti University of Medical Sciences, Tehran, Iran
[2] Tracheal Diseases Research center (TDRC), National Research Institute of Tuberculosis and Lung Diseases (NRITLD), Shahid Beheshti University of Medical Sciences, Tehran, Iran

** Corresponding author: Farahnaz Sadegh Beigee, MD, Assistant Professor of Thoracic Surgery. Lung Transplantation Research Center(LTRC), National Research Institute of Tuberculosis and Lung Diseases (NRITLD), Shahid Beheshti University of Medical Sciences, Darabad, Shahid Bahonar St., Tehran, Iran. Tel: +98-2127212032; Fax: +98-2127122032. E-mail: Beigeef@hotmail.com*

DOI: 10.29252/ijcp-26340

Submitted: 11-07-2019
Accepted: 03-08-2019

Keywords:
Cardiopulmonary Resuscitation
Heart
Tissue Donors
Transplants

Abstract

Introduction: Donor heart shortage limits heart transplantations programs while the number of patients waiting for cardiac transplant continues to increase. Optimizing the use of all available donor hearts is a vital key to reduce waiting list mortality. Among different extended criteria, prolong cardiopulmonary resuscitation (CPR), i.e. more than 20 min, has been considered under doubt to be a selection criterion in donor selection. The aim of this study was to compare the outcomes of heart transplantation from cardiopulmonary-resuscitated donors to those who received hearts from donors who did not require cardiopulmonary resuscitation.

Methods: This study was a retrospective analysis of adult heart transplantation program in Masih Daneshvari Hospital in Tehran, Iran from 2010 to 2019. Donors and recipients' demographics, cause of end-stage heart disease and brain death, duration of hospitalization for both donors and recipients and also the duration of cardiopulmonary resuscitation and other factors related to it were investigated. Qualitative variables were compared using Chi-square test. Quantitative variables were compared using T-test. Patient and graft survival rates were calculated using the actuarial method and compared using Wilcoxon's test.

Results: Among 92 recipients, 39 were transplanted with cardiac grafts from CPR-suffering donors. There were no significant differences regarding sex, age, donor and recipient hospitalization periods, early rejection and 1-year-survival rate considering CPR and non-CPR grafts. However, we detected a strong negative correlation between the duration of CPR and 3-year-survival rate (P = 0.02 and R-value = -0.62) and also its association with post-transplant arrhythmias (P = 0.04).

Conclusion: There is a negative possible influence of long-lasting CPRs (especially more than 20 minutes) in midterm survival and post-transplant complications.

INTRODUCTION

For end-stage cardiac diseases, heart transplantation is the last therapeutic option with promising results. In this regard organ shortage limits this treatment; according to the Eurotransplant standards only 67% of allocated hearts were eventually used for transplantation [1]. Now, there is a dramatic increase in the number of heart transplant centers and lack of standardized donor selection criteria, lead to extend donor criteria [2, 3]. Likewise, pretransplant mortality has been reduced. However, along with reducing waiting list time, patient

survival is challenging. Recently change in acceptable heart donor age, virology profile and other risk factors are some strategies for organ shortage [4-6]. Besides, successful animal model of heart transplantation from cardiac death along with cardiac tissue engendering are other approaches in the future but now the only available treatment for patients on the waiting list is transplantation [7].

Generally, long cardiopulmonary resuscitation (CPR), (more than 30 min) [3], induces myocardial injury and may affect graft survival. Although in a study published in 2014, Kevin W. Southerland et al. showed no adverse effect regarding CPR on cardiac transplantation. In their study among almost 20000 cardiac recipients, 4.2% obtained CPR-suffered heart and 10-year survival rate between CPR and non-CPR heart groups was not considerably different [8]. Likewise in another study, the rate of CPR donor heart was 4.7% among 29240 recipients and recipient graft survival was the same over 5-year follow-up [9].

Moreover, regarding CPR duration, Cheng et al. stated that it does not affect transplant survival according to UNOS database of more than 1700 recipients [10]. However, more than 30% of the experts in the field of cardiac donor selection, agree with excluding a donor heart with a history of CPR duration more than 30 minutes [3].

The first heart transplantation in Iran was performed in 1994. Now there are 10 active heart transplant centers and more than 120 transplants were performed in 2018. The acceptance rate of offered heart was 21.32% in 2011 and reached 36% in 2018 [11]. Hence, the aim of this study was to compare the outcomes of heart transplantation from cardiopulmonary-resuscitated donors to those who received hearts from donors who did not undergo cardiopulmonary resuscitation before.

METHODS

This study was a retrospective analysis of adult heart transplantation program in Masih Daneshvari Hospital in Tehran, Iran from 2010 to 2019. In our Organ Procurement Unit (OPU) after final confirmation of brain death using ancillary tests, the quality of organs for transplant is assessed according to the protocols established by the authorities of the Iranian Ministry of Health. In case of ideal or acceptable marginal heart, cardiac allocation would be performed to identify the proper recipient.

Study Population

Patients who underwent cardiac transplantation from both genders and in any age were included in the study. The recipient population was divided into 2 groups; CPR donor group and non-CPR donor group. Re-transplant participants, kidney-heart transplants and mortalities at operating room were excluded from the analysis. Donors and recipients' demographics, cause of end stage heart disease and brain death, duration of hospitalization for both donors and recipients and also duration of cardiopulmonary resuscitation and other factors related to it were compared. Immediate and medium-term (up to 3 years after transplant) survival rates were calculated. All procured hearts were harvested and preserved by a uniform method. This study was approved by the ethical committee of National Institute of Tuberculosis and Lung Diseases (IR.SBMU.NRITLD.REC.1398.034).

Statistical Analysis

Data was gathered and analyzed using SPSS 22 (Statistical Package for the Social Sciences, Chicago, IL, The USA). Continuous variables were expressed as a mean ± standard deviation and analyzed using a 2-sample T-test. Qualitative variables were presented as percent and analyzed using Chi-square test. Significance level was considered as P value less than 0.05. Survival rates of recipients were compared at 1 to 3 years post-transplant using Kaplan-Meier and log-rank test.

RESULTS

From 2010 to 2019, 1720 brain death donors were transferred to our OPU with different brain dead cause. Seven hundred and twenty-two (42%) of donors were trauma induced brain death. In total, 24% of procured hearts were suitable for donation and 42.3% of them had the history of CPR. The Average number of times that the donors underwent CPR in CPR-positive group was 1.2 with the range of one to 5 times, and accumulative time was 38 minutes. In total, 13.43% of CPR donors required cardiogenic shock to be stable.

In total, 92 recipients were followed, of which 39 were transplanted with cardiac grafts from CPR-suffering donors. There were no significant differences regarding sex, age, donor and recipient hospitalization periods, early rejection and 1-year-survival rate considering CPR and non-CPR grafts. However, we detected a strong negative correlation between duration of CPR and 3-year-survival rate (P = 0.02 and R-value = -0.62) and also its association with post-transplant arrhythmias (P = 0.04) (Table 1).

DISCUSSION

Our study indicated no statistical difference in one-year survival between CPR and non-CPR grafts. Although 3-year graft survival was significantly lower in CPR donor group. Due to recent efforts to improve donor hearts usage and to standardize what should be considered as extended criteria donor, some researches have used the UNOS database to examine the impact of donor CPR duration on transplant survival and outcomes. Their analysis indicated no adverse effects of presence and duration of donor CPR even more than 30 minutes on either short-term or long-term survival rates [12, 13].

Our donors were procured from one single center while heart recipients were from four different heart transplant centers. In our study long ischemic time (more than 4

hours in heart transplantation) [14] was correlated with lower 3-year patient survival. Therefore, it seems that along with expansion of our donor criteria, in case of history of long CPR (more than 20 minutes), [3] we should justify our allocation policy to pass over comorbidities such as long ischemic time.

Also, in CPR donors, in addition to CPR duration, the number of resuscitation occurred for a donor is important. In Iran brain dead donors are transferred from other hospitals to our OPU to undergo ethical and legal procedures related to donation. Adverse events of intra-hospital transfer including transient ventilator disconnection, decrease of PaO_2 to FIO_2 ratio and poor donor management in the primary hospital before transferring the donor, are some confounding factors [15]. Consequently, performing some strategies to reduce the risk factors related to heart donation including biomarkers assessment to evaluate potential CPR positive donors, reducing ischemic time or ex-vivo perfusion of hearts for transport might improve cardiac transplantation outcomes [16].

Table1. Donor and Recipient Characteristics and Transplantation Outcome

	Control Group (N = 53)	CPR Group (N = 39)	P Value
Donor age, y	29.7 ± 11.2	31.7 ± 7.4	NS
Recipient age, y	32.5 ± 8.7	37.3 ± 7.5	NS
Male sex	32 (60.3)	29 (56.4)	NS
Brain death Caused by trauma	30 (56.6)	23 (58.9)	NS
Intubation days	4.8 ± 6.2	4.6 ± 5.3	NS
Smoking history, PY	1 ± 0.5	1.1 ± 0.7	NS
Arterial Blood pressure, mmHg	92.2 ± 7.3	89.9 ± 6.9	NS
Central Venous Pressure	9.7 ± 3.4	10.8 ± 3.1	NS
Early rejection episode	30 (56.6)	18 (46.1)	NS
Duration of CPR (altogether), min	-	38 ± 28	-
1-year-survival	47 (88.6)	34 (87.1)	NS
3-year-survival	40 (77.3)	26 (66.6)	P = 0.04
Post-transplant arrhythmias	34 (64.1)	24 (61.5)	NS

Data in table are presented as Mean ± SD or No. (%)

NS = not significant; PY: peak per year; CPR: cardiopulmonary resuscitation

In the study conducted by Quad et al. the mean duration of CPR was 20 minutes [9] while our donors experienced longer CPR (38 min) with 3-year survival rate of 66.6%. In the report from the American Society of Transplantation Conference in 2017, 20% of cardiac transplant scientists believe to exclude heart donors with CPR duration more than 20 minutes [3]. Now, heart-donor selection is based on numerous factors including hemodynamic status, echocardiographic parameters, catheterization results, pressor requirements, gross evaluation at operating room, etc. We suggest more data analysis to compare transplant outcomes donated from extended criteria and cost-benefit studies regarding this strategy to increase the number of transplant organs. We hypothesize that our pre-transplant mortality is superior to post-transplant mortality in CPR group.

Our study had some limitations corresponded to pre-transplant condition and waiting time on the transplant waiting list. Sometimes recipient teams accept marginal donors for patients in an urgent condition. So, from this point of view, CPR heart recipients are in a poor condition at the time of transplant. Moreover, the study lacks the doses of inotropes used to stabilize hemodynamic status of donors.

In conclusion, beyond international standardized criteria, the final decision for donor selection should be based on local conditions.

Conflict of Interest

There is no conflict of interests with this article.

REFERENCE

1. Samuel U. Annual Report 2017 Eurotransplant International Foundation 2017 [updated 2019; cited 2017]. Available from: https://www.eurotransplant.org.
2. Smits JM, De Pauw M, de Vries E, Rahmel A, Meiser B, Laufer G, et al. Donor scoring system for heart transplantation and the impact on patient survival. J Heart Lung Transplant. 2012;31(4):387-97. doi: 10.1016/j.healun.2011.11.005 pmid: 22177692
3. Kobashigawa J, Khush K, Colvin M, Acker M, Van Bakel A, Eisen H, et al. Report From the American Society of Transplantation Conference on Donor Heart Selection in Adult Cardiac Transplantation in the United States. Am J Transplant. 2017;17(10):2559-66. doi: 10.1111/ajt.14354 pmid: 28510318
4. Khush KK. Donor selection in the modern era. Ann Cardiothorac Surg. 2018;7(1):126-34. doi: 10.21037/acs.2017.09.09 pmid: 29492390
5. Van Cleemput JJA, Verbelen TOM, Van Aelst LNL, Rega FRL. How to obtain and maintain favorable results after heart transplantation: keys to success? Ann Cardiothorac Surg. 2018;7(1):106-17. doi: 10.21037/acs.2017.12.03 pmid: 29492388
6. Reich HJ, Kobashigawa JA, Aintablian T, Ramzy D, Kittleson MM, Esmailian F. Effects of Older Donor Age and Cold Ischemic Time on Long-Term Outcomes of Heart Transplantation. Tex Heart Inst J. 2018;45(1):17-22. doi: 10.14503/THIJ-16-6178 pmid: 29556146
7. Grant A, Gonzalez RR, Klima A, Badiye A, Gardiner A, Thomas M, et al. In Vivo Resuscitation, Perfusion and Transplantation of a Porcine Cardiac Allograft Donated after Cardiac Death. J Heart Lung Transplant. 2019;38(4):S182-S3. doi: 10.1016/j.healun.2019.01.441
8. Southerland KW, Castleberry AW, Williams JB, Daneshmand MA, Ali AA, Milano CA. Impact of donor cardiac arrest on heart transplantation. Surgery. 2013;154(2):312-9. doi: 10.1016/j.surg.2013.04.028 pmid: 23889957

9. Quader MA, Wolfe LG, Kasirajan V. Heart transplantation outcomes from cardiac arrest-resuscitated donors. J Heart Lung Transplant. 2013;32(11):1090-5. doi: 10.1016/j.healun.2013.08.002 pmid: 23994219
10. Cheng A, Schumer EM, Trivedi JR, Van Berkel VH, Massey HT, Slaughter MS. Does Donor Cardiopulmonary Resuscitation Time Affect Heart Transplantation Outcomes and Survival? Ann Thorac Surg. 2016;102(3):751-8. doi: 10.1016/j.athoracsur.2016.02.034 pmid: 27173071
11. Sadegh Beigee F, Ghorbani F, Shahryari S, Mojtabaee M. Demographic Differences Between Two 7-Year Periods of Organ Donation in Iran: A Single-Center Experience. Exp Clin Transplant. 2019;17(Suppl 1):242-5. doi: 10.6002/ect.MESOT2018.P106 pmid: 30777566
12. L'Ecuyer T, Sloan K, Tang L. Impact of donor cardiopulmonary resuscitation on pediatric heart transplant outcome. Pediatr Transplant. 2011;15(7):742-5. doi: 10.1111/j.1399-3046.2011.01565.x pmid: 21883750
13. Wang Y, Cai J, Sun Y, Zhang J, Xie F, Alshirbini MH, et al. Extended donor criteria in heart transplantation: a retrospective study from a single Chinese institution. J Thorac Dis. 2018;10(4):2153-65. doi: 10.21037/jtd.2018.03.149 pmid: 29850119
14. Russo MJ, Chen JM, Sorabella RA, Martens TP, Garrido M, Davies RR, et al. The effect of ischemic time on survival after heart transplantation varies by donor age: an analysis of the United Network for Organ Sharing database. J Thorac Cardiovasc Surg. 2007;133(2):554-9. doi: 10.1016/j.jtcvs.2006.09.019 pmid: 17258599
15. Najafizadeh K, Ghobadi O, Ghorbani F, Shafaghi S, Radpei B, Shojaei SP, et al. Transfer protocol of brain-dead patients to specialized donor management unit. Transplantation. 2012;94(1):e6-8. doi: 10.1097/TP.0b013e31825a7cf6 pmid: 22766731
16. Ozeki T, Kwon MH, Gu J, Collins MJ, Brassil JM, Miller MB, Jr., et al. Heart preservation using continuous ex vivo perfusion improves viability and functional recovery. Circ J. 2007;71(1):153-9. doi: 10.1253/circj.71.153 pmid: 17186994