December 15, 2015 ; Service de Cardiologie, Centre Hospitalier Universitaire Vaudois ;

Pre-transplant Patient Characteristics and Early Post-transplant Mortality

Schmidhauser M[1], Regamey J[1], Yerly P[1], Pilon N[2], Pascual M[2], Rotman S[4], Tozzi P[3], Antonietti JP[5], Meyer P[6], Hullin R[1]

[1]Service de Cardiologie, Département de Médecine ; [2]Centre de Transplantarion d'Organes solides, Département de ; [3]Service de Chirurgie cardiaque, Département de Chirurgie Thoracique ; [4]Insitute of Pathology ; Centre Hospitalier Universitaire Vaudois ; Université de Lausanne ; Rue du Bugnon 46, 1011 Lausanne , Switzerland ; [5]Institute of Psychology, Bâtiment Géopolis, Quartier UNIL-Dorigny, University of Lausanne, CH-1015 Lausanne; .

Word count (text + references) : 4223 words

Key words : Heart transplantation – recipient characteristics - early mortality

Corresponding author :
Roger Hullin M.D.
Cardiology
Department of Internal Medicine
Centre Hospitalier Universitaire Vaudois (CHUV)
University of Lausanne
Rue du Bugnon 46
1011 Lausanne
Switzerland
phone : +41.21.314.00.12
e-mail : roger.hullin@chuv.ch

Disclosure

The corresponding author receives support from Swiss National Science Foundation (320030_147121/1) and SWISSHEART Foundation. No other disclosures.

SUMMARY

Background:

In 2007, the University Hospital of Lausanne established the multi-disciplinary Heart Transplantation (HTx) team to improve quality of peri-transplant care. Comparison of the period 2000-2007 and 2008-2014 showed a decrease of in-hospital mortality from 22.2 to 16.2% and a reduction of 1-year all cause mortality (ACM) from 25.8% to 18.9% (p=0.612). This study investigates whether decreased mortality early post-transplant is associated with pre-transplant characteristics of HTx recipients.

Methods and Results:

A total of 140 patients were included with HTx recipients operated between the years 2000 to 2007 (n=66) and 2008 to 2014 (n=74). Mean age of all patients was 53.5 years (IQR 47.3-59.8), 112 males, donor/recipient mismatch was present in 38.3% of patients, length of in-hospital stay was 34 days (IQR 26-61 days); donor age was 41 years (IQR 26-51 years). There was no respective difference between patients operated 2000-2007 and 2008-2014. HTx recipients operated between the years 2008-2014 less often had dilated cardiomyopathy of non-ischemic origin (43.2 vs 63.6%; p=0.024), received more often resynchronization therapy (66.2 vs. 33.3%; p=0.0002), AICD treatment (60.8 vs. 21.2%; p<0.0001), or assist device treatment (24.3 vs. 9.1%; p=0.030). Mean stay on the waiting list was longer (177 vs. 110 days; p=0.04). Baseline hemodynamic data, echocardiographic parameters, cardiovascular risk factors, comorbidity load, and baseline clinical parameters were not different between groups. Diabetes mellitus was a predictor of in-hospital and 1-year ACM in patients operated between 2000 and 2007.

Conclusion:

Characteristics of HTx recipients and donors were not significantly different between HTx recipients operated between the years 2000 to 2007 and 2008 to 2014 suggesting that establishment of a HTx team improved early outcome after HTx.

INTRODUCTION:

The care of heart transplant (HTx) patients is complex requiring a finely orchestrated effort to improve outcome after transplant. Given the chronic and often complex nature of HTx recipients, various disciplines are involved in their care in the early and the late post-transplant phases. Recognizing the increasing difficulties with post-transplant care, the University Hospital of Lausanne established in 2008 a medical care team in order to improve efficiencies in pretransplant listing process, operative care, post-transplant inpatient and outpatient care, and in the collaboration with heart failure specialist of the University Hospital of Geneva. This HTx team consisting of transplant cardiologists with a particular focus on heart failure and heart transplantation works as an integral part of the team for solid organ transplantation consisting of specialists in cardiac surgery, anesthesiology, intensive care, cardiac pathology, infectious diseases, immunology, and nurses trained in pre- and post-transplant care. Recognizing the difficulty to maintain communication among team members and striving for improved efficiencies in our pretransplant listing process, our inpatient care, our team meets at regular intervals to assure improved communication to enhance quality of patient care.

To identify the clinical impact of the establishment of the HTx team in 2008, we compared in our local HTx population in-hospital mortality and 1-year all-cause mortality between HTx recipients with operation in the years 2008 to 2014 and patients who benefited from HTx in the years 2000 to 2007. Several reason prompted us to limit the inclusion of HTx recipients to the time interval 2000 to 2014 : first, during this period of time at our institution the selection criteria for HTx candidates did not change (Mehra et al., Banner et al.), and pharmacological and device-based treatment remained always based on respective guidelines (Gronda et al; Jessup et al.; McMurray et al.); second, immunosuppressive therapy was guided always by regularly scheduled endomyocardial biopsy with drug treatment applied in accordance with recommendations of guidelines in heart transplantation (Costanzo et al.) ; third, the time-interval of 1 year was chosen because pre-transplant co-morbidity may have impact on outcome within the first year post-transplant whereas transplant-associated co-morbidity becomes increasingly relevant thereafter (Lund et al.). This study investigates whether pre-transplant characteristics of HTx recipients explain the decreased mortality observed for the period 2008 to 2014.

METHODS :

This study includes all patients who benefited from HTx at the University Hospital of Lausanne from the 01.01.2000 to the 31.08.2014. This retrospective analysis was approved by the local ethics committee and complies with the Declaration of Helsinki.
Demographic, clinical, and laboratory data derive from the admission day for HTx and were obtained retrospectively from the electronic medical record at the University Hospital of Lausanne (M.S.). Donor data were retrieved from the Swiss Organ Allocation System (S.O.A.S.) data bank (N.P.). Regarding the graft rejection, the average rejection grade was calculated based on myocardial biopsies obtained during the first year after heart transplant. All biopsies were graded in accordance using the ISHLT working formulation 2004 (Stewart et al.). Echocardiographic data derive from standard transthoracic studies signed by a board-certified cardiologist at our institution; all exams were performed during index hospitalization. Physicians' diagnosis of co-morbidity followed the respective guidelines (Russo et al. ; ESC Working group; WHO). A random sample of 20 patients was chosen for control of data quality (R.H.).

Statistical analysis :

Continuous variables are presented as mean (±SD) or median (±interquartile range; IQR). Categorical variables are presented as numbers and percentages. Analysis of variance compared continuous variables ; and chi^2-statistic compared categorical variables.
The computer software we use was « R », version 3.1.2 (2014-10-31).
The outcome variables of this study were in-hospital mortality and 1-year all-causes mortality. Association between the explanatory variables and the two outcome parameters were analyzed for the whole study population and the two study groups. Variables predicting in-hospital and one-year mortality were identified from parameters associated with the outcome in univariate analysis with a threshold of 10% using the « stepwise backward-forward » analysis applying the Akaike Information Criteria (AIC) to increase the likelihood of the model. The final model was adjusted for age of the donor and the recipient. Survival curves were calculated using the Kaplan-Meier method ; comparison of survival curves used the log-rank test. All tests were two-sided and used a significance level of $p<0.05$. Analyses were performed using the R statistical software (version R 3.1.0, R development core team).

RESULTS:

A total of 140 patients were included into this retrospective analysis of a local cohort of HTx recipients. Patients had a mean age of 53.5 years and were predominantly male (80%). The length of stay post-transplant was about 34 days without respective differences between groups. Time on the waiting list was significantly longer in patients with HTx between the years 2008 and 2014 (177 vs. 109 days ; p=0.04). Mean rejection grade of all biopsies obtained within the first year post-transplant was 0.4 in the entire cohort and significantly different between groups (0.65 vs. 0.20 ; p<0.0001). Mean donor age was about 41 years in the entire cohort and not different between the two groups.

More patients in the first period suffered from dilated cardiomyopathy of non-ischemic origin (63.6 vs. 43.2% ; p=0.0249), more patients in the second period were treated with resynchronization (66.2 vs. 33.3% ; p=0.0002), AICD (60.8 vs. 21.2% ; p<0.0001), or ventricular assist devices (24.3 vs. 9.1% ; p=0.0306).

Mean LVEF was 20%, mean PVR 2.3 Woods Units, mean BMI 24.3 without difference between groups. The prevalence of the various cardiovascular risk factors was not significantly different between the two periods (entire cohort : HTA : 31.4%, diabetes mellitus : 15.7%, history of tobacco use : 45.3%, dyslipidemia : 43.8%, BMI : 24.3 kg/m^2). Likewise, the rate of co-morbidities such as chronic obstructive pulmonary disease (COPB) and thyroid disease were not significantly different between the two groups.

Drug treatment was not significantly different between the two periods except for the use of eplerenone which was administered more often in patients of the second period (25.7 vs. 1.5% ; p=0.0001). Furthermore, laboratory values were not different between groups except for the serum iron, which was higher in the second period (12.5 vs. 10.2 umol/l ; p=0.048). The prevalence of positive serologies for CMV, EBV, and toxoplasma gondii was not different between the two periods both for the recipients and the donors, and the prevalence of respective serologies between donor and recipient serologies was not significantly different. The number of biopsies procured during the first and second period did not differ (587 vs. 575 biopsies) whereas the mean rejection grade of patients with HTx during the first period was significantly higher when compared to the second period, as calculated by the sum of the grade of biopsies with rejection (Stewart et al.) divided the number of successfully procured biopsies within the first year (0.70 vs. 0.20, p<0.0001). Histological grading of the EMB ≥2R (Stewart et al.) was associated with increased in-hospital in both periods (Chi-square 4.39 ; p=0.0361 for the first period, Chi-square 3.92 ; p=0.0476 for the second period)

but not with 1-year ACM (Chi square 1.97 ; p=0.16 and Chi-square 2.65 ; p=0.1032 respectively).

In hospital-mortality and 1-year ACM was 21.2% and 22.7% respectively in the first period, and 15.1% and 16.4 % respectively in the second period (p=0.4711 and p=0.4708, respectively). Univariate analysis showed associations between first-period in-hospital mortality and LVEF (OR 1.04 (1.01-1.08 ; p=0.0262), diabetes mellitus (OR 9 (2.07-39.14) ; p=0.0034), leucocyte count (OR 0.63 (0.46-0.88) ; p=0.0065), and length of stay (OR 0.91 (0.86-0.96), p=0.0012).

These associations were not observed in the second period where pre-transplant spironolactone treatment was associated with increased in-hospital mortality (OR 10 (1.21-82.9); p=0.0329). The associations of LVEF, diabetes, mellitus, leucocyte count, and length of stay were maintained for 1-year all-cause mortality but not for spironolactone. Multivariate statistical analysis controlled for donor and recipient age retained in the first period diabetes and length of stay as predictors of in-hospital mortality and 1-year ACM while in the second period pre-transplant medication with spironolactone was a predictive for in-hospital mortality but not for 1-year ACM.

DISCUSSION

This study shows that establishment of a multidisciplinary HTx team with dedicated transplant cardiologists is associated with an increase of the number of HTx recipients, a not significant decrease of in-hospital mortality and 1-year all causes mortality, and a significant decrease of the mean acute cellular rejection (ACR) grade. The decrease of in-hospital and 1-year mortality and the mean ACR grade was not associated with different pre-transplant characteristics of HTx recipients or distinct donor characteristics.

Various studies have shown that the multidisciplinary team approach increases quality of care and decreases length of stay of patients at the intensive care unit (Kim and al.), with heart failure (McMurray et al., Wensing et al.), or after HTx (Costanzo et al., Roussel et al.). In 2008, the University Hospital of Lausanne established a multidisciplinary team for the care of severe heart failure patients and HTx recipients. With regard to heart transplantation, this team is part of the multidisciplinary team of the solid organ transplant center combing expertise from specialties involved in the complex care of the transplant patient. Pertaining to heart transplantation, the multidisciplinary team approach starts with a multidisciplinary review committee for the listing process and continues with regular multidisciplinary in-hospital rounds and an integrated care service for ambulatory follow-up. Roussel et al. have already shown that this intervention decreases the time to listing of HTx candidates as well as the length of stay and the readmission rate after HTx. However, it remains unclear whether the multidisciplinary team approach for in-hospital and integrated ambulatory care after discharge decreases the incidence of hard endpoints, in particular in-hospital and early mortality after HTx - as reported for patients hospitalized with heart failure (Philbin et al., Mc Allister et al.).

In order to investigate the effect of the multidisciplinary care team on outcome after HTx, this study compares the in-hospital and 1-year all causes mortality of HTx recipients with operation in the period 2000-2007 (n=66) and 2008 to August 2014 (n=74), assuming a strong impact of the multidisciplinary approach on the selection of HTx candidates and the immediate and early postoperative outcomes. Basic for this retrospective analysis investigating the effect of establishment of a multidisciplinary team approach in HTx is an unmodified strategy for guiding immunosuppression after transplant and selecting of HTx candidates. In fact, guidance of immunosuppression on the basis of histological grading of endomyocardial biopsies procured at regular intervals after HTx had not been modified between the two periods. In addition, there was no significant difference in immunosuppressive drug treatment between the two groups despite of the advent of everolimus after 2003 (Eisen and al.). However, everolimus was administered to only few

patients of the period 2008 to 2014. In this group, mortality was similar to mortality in the group of patients who benefited from an immunosuppressive treatment with cyclosporine and mycophenolate mofetil (Eisen et al.).

Comparison of the pre-transplant clinical characteristics of HTx recipients showed that more patients in the period 2000-2007 had dilated cardiomyopathy of non-ischemic origin, otherwise there were no significant differences between groups for recipient age or gender, donor age, as well as biological variables, LVEF, pulmonary vascular resistance, BMI, cardiovascular risk factors, or co-morbidities. Furthermore, the prevalence of donor/recipient mismatch for gender, age, or CMV /EBV serology status was not different, suggesting that the profile of patients accepted for HTx listing did not change significantly since the establishment of the multidisciplinary team approach.

We observed a higher in-hospital and 1-year ACM in HTx recipients operated in the period 2000-2007 when compared with the later period despite of the higher prevalence of dilated cardiomyopathy, which has been associated with increased early survival after HTx (Stehlik et al.; Zielinski et al.). However, log-rank analysis did not reveal a significant difference of survival between the two groups ($p=0.612$), suggesting nonetheless that the multidisciplinary team approach with a specialized HTx team more than compensated the increased risk for mortality associated with HTx of patients with ischemic cardiomyopathy. Multivariable analysis identified diabetes and length of stay as predictors for mortality in the first period while these risk factors were not retained for the second period despite of a similar prevalence of diabetes. Various studies show that a multidisciplinary approach for care of diabetic patients improves outcome (Norris and al.), therefore, we hypothesize that taking care of diabetes by the multidisciplinary team improved outcome in HTx recipients with diabetes in the second period. So far, it remains unclear why spironolactone is a predictor of in-hospital mortality in the second period despite of almost similar pre-transplant administration of this drug in both groups. It could be interesting to investigate more this possible relationship in the future.

A total of 587 EMBs were procured within the first period while 575 biopsies were obtained during the second period despite of more patients with HTx during the second period. Presence of a histological grade of acute cellular rejection ≥2R was associated with in-hospital mortality in the early and the late period but not with 1-year ACM despite of a higher mean grade of acute cellular rejection in the years 2000-2007. Data from a retrospective single-center study show that ≥1 moderate acute cellular rejection is associated with a decrease of 10 years survival (Soederlund et al.) suggesting that our follow-up limited to 1 year post-transplant may have missed the effect of a higher mean acute cellular rejection

grade on survival. However, the number of biopsies per patient within the first year post-transplant as well as the individual mean rejection grade was lower in the later period, suggesting that timely executed EMB with subsequent optimal tailoring of therapy was facilitated by the multidisciplinary approach. Nevertheless, we cannot exclude that less stringent adherence to immunosuppressive drug treatment may have increased the incidence of acute cellular rejection in the early period because HTx recipients were repetitively trained for comprehensive appreciation of their individual therapy during hospitalization and rehabilitation, and outpatient care.

Limitations of the study

As a limitation to the present study, it should be noted that this single-center study investigates retrospectively the effect of a change in patient care without prospectively stratified outcome parameters at the time of intervention. The study includes only a small number of patients operated in a medium-sized European center, therefore, it is not clear whether results also apply to non-European centers. Another weakness of our research is that this study does not quantify the change introduced by single action of the multidisciplinary approach, but instead focuses on the secondary change such as the number of HTx per year, mean acute cellular rejection grade of the individual patient, and survival.

CONCLUSION

Care of the HTx recipient by a multidisciplinary team increases the number of HTx, decreases the number of biopsies procured during the first year after HTx, decreases the mean rejection grade of the individual patient, and has the potential to reduce both in-hospital and all cause mortality within the first year after HTx. It remains to be shown whether the multidisciplinary team approach may also reduce medium-term and late mortality after HTx.

LITERATURE:

1. Costanzo MR, Dipchand A, Starling R, Anderson A, Chan M, Desai S, et al. The International Society Heart and Lung Transplantations guidelines for the care of heart transplantation recipients. J Heart Lung transplant 2010; 29:914-956.
2. Roussel MG, Gorham N, Wilson L, Mangi AA. Improving recovery time following heart transplantation: the role of the multidisciplinary health care team. J Multidisciplinary Healthcare 2013;6:293-302.
3. Mehra MR, Kobashigawa J, Starling R, Russell S, Uber PA, Parameshwar J, Mohacsi P, Augustine S, Aaronson K, Barr M. Listing criteria for heart transplantation: International Society for Heart and Lung Transplantation guidelines for the care of cardiac transplant candidates--2006. J Heart Lung Transplant. 2006 ;25:1024-42.
4. Gronda E, Bourge RC, Costanzo MR, Deng M, Mancini D, Martinelli L, Torre-Amione G, O'Hara ML, Chambers S. Heart rhythm considerations in heart transplant candidates and considerations for ventricular assist devices: International Society for Heart and Lung Transplantation guidelines for the care of cardiac transplant candidates--2006. J Heart Lung Transplant. 2006;25:1043-56.
5. McMurray JJ, Adamopoulos S, Anker SD, Auricchio A, Böhm M, Dickstein K, Falk V, Filippatos G, Fonseca C, Gomez-Sanchez MA, Jaarsma T, Køber L, Lip GY, Maggioni AP, Parkhomenko A, Pieske BM, Popescu BA, Rønnevik PK, Rutten FH, Schwitter J, Seferovic P, Stepinska J, Trindade PT, Voors AA, Zannad F, Zeiher A; ESC Committee for Practice Guidelines. ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012: The Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association (HFA) of the ESC. Eur Heart J. 2012;33:1787-847.
6. Banner NR, Bonser RS, Clark AL, Clark S, Cowburn PJ, Gardner RS, Kalra PR, McDonagh T, Rogers CA, Swan L, Parameshwar J, Thomas HL, Williams SG. UK guidelines for referral and assessment of adults for heart transplantation. Heart. 2011 Sep;97(18):1520-7.
7. Lund LH, Edwards LB, Kucheryavaya AY, Benden C, Christie JD, Dipchand AI, Dobbels F, Goldfarb SB, Levvey BJ, Meiser B, Yusen RD, Stehlik J; International Society of Heart Lung Transplantation. The registry of the International Society for Heart and Lung Transplantation: thirty-first official adult heart transplant report-2014; focus theme: retransplantation. J Heart Lung Transplant 2014;33(10):996-1008.

8. Russi EW, Karrer W, Brutsche M, Eich C, Fitting JW, Frey M, et al. Diagnosis and management of chronic obstructive pulmonary disease. Respiration 2013;85:160-74.
9. ESC task force for the management of arterial hypertension. 2013 practice guidelines for management of arterial hypertension of the European Society of Hypertension (ESH) and the European Society of Cardiology (ESC): ESH/ESC task force for the management of arterial hypertension. J Hypertens 2013;31:1925-38.
10. World Health Organization. (WHO) consultation: Definition and diagnosis of diabetes mellitus. Geneva: World Health Organisation; 1999, Rapport 99.2. http: //whqlibdoc.who.int/hq/1999/who_ncd_ncs_99.2pdf
11. Stewart S, Winters GL, Fishbein MC, Tazelaar HD, Kobashigawa J, Abrams J, Andersen CB, Angelini A, Berry GJ, Burke MM, Demetris AJ, Hammond E, Itescu S, Marboe CC, McManus B, Reed EF, Reinsmoen NL, Rodriguez ER, Rose AG, Rose M, Suciu-Focia N, Zeevi A, Billingham ME. Revision of the 1990 working formulation for the standardization of nomenclature in the diagnosis of heart rejection. J Heart Lung Transplant 2005;24:1710- 20.
12. Kim MM, Barnato AE, Angus DC, Fleisher LA, Kahn JM. The effect of multidisciplinary care teams on intensive care unit mortality. Arch Intern Med. 2010 Feb 22;170:369-76.
13. Wensing M, Wollersheim H, Grol R. Organizational interventions to implement improvements in patient care: a structured review of reviews. Implement Sci. 2006;1:2.
14. Philbin EF. Comprehensive multidisciplinary programs for the management of patients with congestive heart failure. J Gen Int Med 1999; 14:130-135.
15. McAlister FA, Lawson FME, Teo KK, Armstrong PW. A systematic review of randomized trials of disease management pro- grams in heart failure. Am J Med 2001, 110:378-84.
16. Roussel MG, Gorham N, Wilson L, Mangi AA. Improving recovery time following heart transplantation: the role of the multidisciplinary health care team. J Multidisciplinary health care 2013; 6:293-302.
17. Eisen HJ, Tuzcu EM, Dorent R, Kobashigawa J, Mancini D, Valantine-von Kaeppler HA, Starling RC, Sørensen K, Hummel M, Lind JM, Abeywickrama KH, Bernhardt P; RAD B253 Study Group. Everolimus for the prevention of allograft rejection and vasculopathy in cardiac-transplant recipients. N Engl J Med. 2003;349:847-58.
18. Eisen HJ, Kobashigawa J, Starling RC, Pauly DF, Kfoury A, Ross H, Wang SS, Cantin B, Van Bakel A, Ewald G, Hirt S, Lehmkuhl H, Keogh A, Rinaldi M, Potena L, Zuckermann A, Dong G, Cornu-Artis C, Lopez P. Everolimus versus mycophenolate mofetil in heart transplantation: a randomized, multicenter trial. Am J Transplant. 2013 May;13(5):1203-16.
19. Zielinski T, Kurjata P, Korewicki J, on behalf of the participants of POLKARD-HF. Prognosis in patients with severe heart failure referred for heart transplantation –

POLKARD-HF 2003-2007. Int J Cardiol 2009 ; doi:10.1016/j.ijcard.2009.08.026.

20. Stehlik J, Edwards LB, Kucheryavaya AY, Aurora P, Christie JD, Kirk R, Dobbels F, Rahmel AO, Hertz MI. The Registry of the International Society for Heart and Lung Transplantation: twenty-seventh official adult heart transplant report--2010. J Heart Lung Transplant 2010;29:1089-103.
21. Norris SL, Nichols PJ, Caspersen CJ, Glasgow RE, Engelgau MM, Jack L, Isham G, Snyder SR, Carande-Kulis VG, Garfield S, Briss P, McCulloch D. The effectiveness of disease and case management for people with diabetes. A systematic review. Am J Prev Med 2002, 22:15-38.Söderlund C1, Öhman J, Nilsson J, Higgins T, Kornhall B, Johansson L, Rådegran G.
22. Acute cellular rejection the first year after heart transplantation and its impact on survival: a single-centre retrospective study at Skåne University Hospital in Lund 1988-2010. Transpl Int. 2014;27:482-92.
23. Weiss ES, Allen JG, Arnaoutakis GJ, George TJ, Russell SD, Shah AS, Conte JV. Creation of a quantitative recipient risk index for mortality prediction after cardiac transplantation (IMPACT). *Ann Thorac Surg*. 2011;92:914 –921.
24. Singh TP, Almond C, Givertz MM, Piercey G, Gauvreau K. Improved survival in heart transplant recipients in the united states: racial differences in era effect. *Circ Heart Fail*. 2011;4:153–160.
25. Lloyd-Jones DM, Leip EP, Larson MG, D'Agostino RB, Beiser A, Wilson PW, Wolf PA, Levy D. Prediction of lifetime risk for cardiovascular disease by risk factor burden at 50 years of age. *Circulation*. 2006;113:791–798.
26. Ridker PM, Paynter NP, Rifai N, Gaziano JM, Cook NR. C-reactive protein and parental history improve global cardiovascular risk prediction: the Reynolds Risk Score for men. *Circulation.* 2008;118:2243–2251.
27. Ridker PM, Buring JE, Rifai N, Cook NR. Development and validation of improved algorithms for the assessment of global cardiovascular risk in women: the Reynolds Risk Score. *JAMA*. 2007;297:611– 619.
28. Aaronson KD, Schwartz JS, Chen TM, Wong KL, Goin JE, Mancini DM. Development and prospective validation of a clinical index to predict survival in ambulatory patients referred for cardiac transplant evaluation. *Circulation*. 1997;95:2660 –2667.
29. Gupta PK, Gupta H, Sundaram A, Kaushik M, Fang X, Miller WJ, Esterbrooks DJ, Hunter CB, Pipinos II, Johanning JM, Lynch TG, Forse RA, Mohiuddin SM, Mooss AN. Development and validation of a risk calculator for prediction of cardiac risk after surgery. *Circulation*. 2011;124:381–387.

30. Nashef SA, Roques F, Michel P, Gauducheau E, Lemeshow S, Salamon R. European System for Cardiac Operative Risk Evaluation (EuroSCORE). *Eur J Cardiothorac Surg*. 1999;16:9 13.
31. Nativi JN, Drakos SG, Kucheryavaya AY, Edwards LB, Selzman CH, Taylor DO, Hertz MI, Kfoury AG, Stehlik J. Changing outcomes in patients bridged to heart transplantation with continuous- versus pulsatile-flow ventricular assist devices: an analysis of the Registry of the International Society for Heart and Lung Transplantation. *J Heart Lung Transplant*. 2011;30:854–861.

Disclosure:

Roger Hullin receives grant support from NOVARTIS, the SWISSHEART foundation, and the Swiss National Science Foundation (320030_147121/1); RBvH received grant support from the Emma Muschamp Foundation.

LEGENDS :

TABLE 1

[IQR] = Inter quartile range ; LoS = length of stay ; CMP = cardiomyopathy ; ARVD = arrythmogenic right ventricular dysfunction ; HCM = hypertrophic cardiomyopathy ; LVEF = left ventricular ejection fraction ; PVR = pulmonary vascular resistance ; PM = pacemaker ; AICD = automated internal cardio-defibrillator ; VAD = ventricular assistant device ; BSA = body surface area ; BMI = body mass index ; HTA = arterial hypertension ; COPD = chronic obstructive pulmonary disease.

TABLE 2

ACE = angiotensin converting enzyme ; AT_1= angiotensin II receptor type 1.

TABLE 4

ASAT = alanie-serine transferase; ALAT = alanine-aspartate transferase ; CMV = cytomegalo virus; EBV = Ebstein-Barr virus.

TABLE 1 RECIPIENTS AND DONOR CHARACTERISTICS :

	all (n=140)	2000-2007 (n=66)	2008-2014 (n=74)	p-value
RECIPIENT DEMOGRAPHICS :				
Age	53.52 [47.33, 59.8]	53.52 [47.29, 59.57]	53.2 [47.78, 59.6]	0.6637
Female	28 (20%)	15 (22.7%)	13 (17.6%)	0.5821
Male	112 (80%)	51 (77.3%)	61 (82.4%)	0.5821
Time on waiting list (d)	152 [62.75, 386.5]	109.5 [50.25, 313.5]	177 [88.25, 425.75]	0.04
Mean rejection grade	0.43	0.7	0.1964	<0.0001
LoS (d)	34 [25.75, 60.5]	32 [25.25, 53]	36 [27.25, 62]	0.2169
DONOR DEMOGRAPHICS				
Age	41 [26, 51]	40.5 [26, 51]	43 [29, 51.9]	0.8856
ETIOLOGY of CMP				
Ischemic CMP	49 (35.0%)	20 (30.3%)	29 (39.2%)	0.3561
Dilated CMP	74 (52.9%)	42 (63.6%)	32 (43.2%)	0.0249
Congenital CMP	18 (12.9%)	9 (13.6%)	9 (12.2%)	0.9942
ARVD	5 (3.6%)	1 (1.5%)	4 (5.4%)	0.4342
HCM	14 (10.0%)	7 (10.6%)	7 (9.5%)	1
Doxocyclin-induced CMP	2 (1.4%)	0 (0%)	2 (2.7%)	0.5275
Myocarditis	2 (1.4%)	0 (0%)	2 (2.7%)	0.5275
DEVICE TREATMENT				
PM	71 (50.7%)	22 (33.3%)	49 (66.2%)	0.0002
AICD	59 (42.1%)	14 (21.2%)	45 (60.8%)	<0.0001
VAD	24 (17.1%)	6 (9.1%)	18 (24.3%)	0.0306
CLINICAL PARAMETERS				
LVEF	20 [15, 25]	20 [15, 25]	22 (15, 30]	0.3883
PVR	2.3 [1.4, 3.2]	2.63 [1.46, 3.63]	2.15 [1.4, 3.12]	0.3889
BSA	1.86 [1.7, 2]	1.86 [1.7, 2]	1.88 [1.7, 2]	0.9036
Size	1.72 [1.65, 1.78]	1.72 [1.64, 1.78]	1.71 [1.65, 1.78]	0.754
Weight	73.8 [61.9, 83]	71.8 [61.25, 83]	74 [63, 84.25]	0.655
BMI	24.27 [21.81, 28.07]	23.62 [21.64, 28.07]	24.73 [21.88, 28]	0.596

RISK FACTORS / COMORBIDITIES				
Previous thoracic surgery	53 (37.9%)	20 (30.3%)	33 (44.6%)	0.1174
HTA	44 (31.4%)	17 (25.8%)	27 (36.5%)	0.2369
Diabetes	22 (15.7%)	10 (15.2%)	12 (16.2%)	1
History of tobacco abuse	63 (45.3%)	25 (38.5%)	38 (51.4%)	0.1762
Dyslipidemia	60 (43.8%)	28 (43.8%)	32 (43.8%)	1
Thyroid disease	18 (12.9%)	5 (7.6%)	13 (17.6%)	0.131
COPD	12 (8.6%)	4 (6.1%)	8 (10.8%)	0.484

TABLE 2 PRE-TRANSPLANT DRUG TREATMENT

	all	**2000-2007**	**2008-2014**	**p-value**
DRUGS				
Metoprolol	31 (22.1%)	10 (15.2%)	21 (28.4%)	0.0934
Bisoprolol	7 (5.0%)	4 (6.1%)	3 (4.1%)	0.8765
Carvedilol	37 (26.4%)	20 (30.3%)	17 (23.0%)	0.4296
Nebivolol	8 (5.7%)	1 (1.5%)	7 (9.5%)	0.0976
ACE Inhibitors	68 (48.6%)	37 (56.1%)	31 (41.9%)	0.1323
AT_1-Receptors Blockers	37 (26.4%)	16(24.2%)	21 (28.4%)	0.7173
Spironolactone	80 (57.1%)	38 (57.6%)	42 (56.8%)	1
Eplerenone	20 (14.3%)	1 (1.5%)	19 (25.7%)	0.0001
Torasemide	111 (79.3%)	49 (74.2%)	62 (83.8%)	0.2373
Hydrochlorthiazid	22 (15.7%)	12 (18.2%)	10 (13.5%)	0.5996

TABLE 3 MORTALITY

	all	2000-2007	2008-2014	p-value
1 year-ACM	27 (19.4%)	15 (22.7%)	12 (16.4%)	0.4708
In-hospital mortality	25 (18%)	14 (21.2%)	11 (15.1%)	0.4711

Figure 1

Kaplan Meier Survival curves for all patients, and HTx recipients from period 2000-2007 and 2008-8/2014

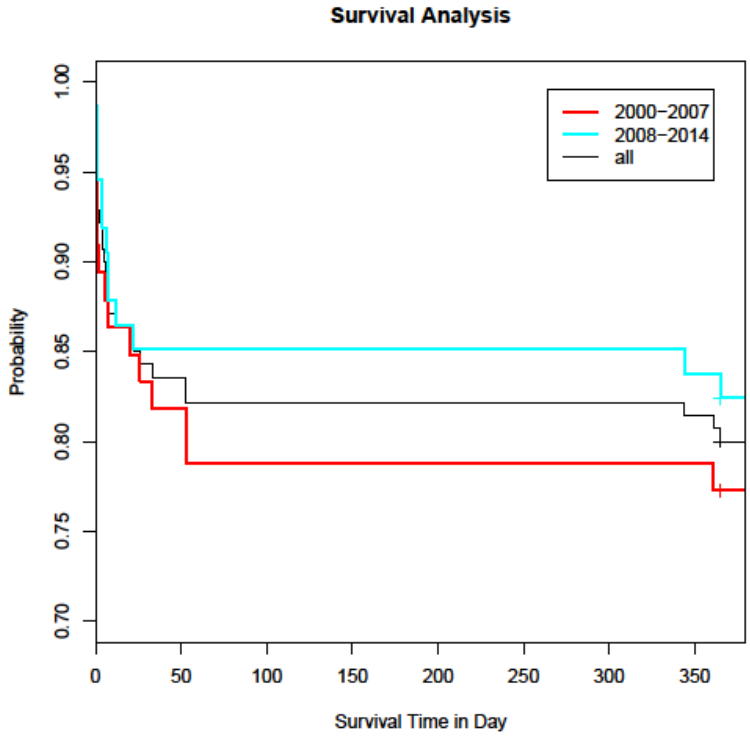

TABLE 4 PRE-TRANSPLANT RECIPIENT LABORATORY FINDINGS

	all	2000-2007	2008-2014	p-value
Bicarbonate	22.3 [20.7, 23.6]	22.45 [20.95, 24.6]	21.4 [20.25, 23.4]	0.0488
Creatinine (mmol/l)	111.5 [91.5, 135]	112.5 [90.75, 136,7]	109 [93, 135]	0.6264
Blood urea nitrogen (mmol/l)	8.95 [6.8, 12.35]	9.05 [6.93, 13.75]	8.65 [6.65, 11.32]	0.4044
Bilirubin (mg/l)	<6.5 [<10, 15]	11 [<10, 17]	<10 [<10, 14]	0.1384
ASAT (U/l)	31 [23, 41.5]	31 [23, 38]	31 [23,43]	0.7073
ALAT (U/l)	27 [19, 44.5]	27.5 [20, 46]	27 [19, 42]	0.7338
CRP (mg/l)	6 [2,14]	13 [0.5, 26.5]	6 [2, 12.5]	0.3399
Iron (/l)	11.95 [8.4, 17.03]	10.2 [7.7, 14.4]	12.5 [9.15, 18]	0.0479
Albumin (mg/l	28 [24.75, 34.25]	28 [26,32]	28 [25, 34]	0.9417
Hemoglobin (g/l)	130 [115, 141.5]	129 [113, 142]	131 [116, 141]	0.4966
Leucocytes (G/l)	8.1 [6.3, 10]	8.5 [6.4, 9.9]	7.6 [6.12, 10.07]	0.4055
Thromocytes (G/l)	212 [170, 258]	213.5 [171.5, 239.2]	209 [167.75, 265.75]	0.8964
TSH (U/l)	1.64 [0.62, 2.92]	3.01 [2.18, 3.4]	1.42 [0.62, 2.28]	0.4159
Free T4 (ug/L)	13 [11.75, 16.25]	13 [12.5, 17.5]	13 [11, 16]	0.786
SEROLOGICAL DATA :				
Anti-CMV antibodies	81 (58.7%)	34 (53.1%)	47 (63.5%)	0.2879
Anti-EBV antibodies	123 (90.4%)	56 (90.3%)	67 (90.5%)	1
Anti-Toxoplasmosis antibodies	87 (63%)	39 (60.9%)	48 (64.9%)	0.7643
DONORS SEROLOGICAL DATA :				
Anti-CMV antibodies	69 (56.6%)	33 (59%)	36 (64.3%)	0.1606
Anti-EBV antibodies	111 (91%)	60 (90.9%)	51 (91.1%)	1
Anti-Toxoplasmosis antibodies	87 (63%)	39 (60.9%)	48 (64.9%)	0.7643

TABLE 5 DONOR / RECIPIENT MATCH

	all	2000-2007	2008-2014	p-value
Gender mismatch	49 (39.84%)	29 (43.9%)	20 (32.2%)	0.2393
Age mismatch	53 (43.4%)	34 (51.51%)	20 (35.71%)	0.1169
CMV mismatch	29 (22.3%)	18 (27.27%)	11 (17.19%)	0.2419
EBV mismatch	9 (6.71%)	5 (7.94%)	4 (5.63%)	0.8526
Toxoplasmose mismatch	29 (21.32%)	15 (22.73%)	14 (20.0%)	0.8582

TABLE 6

Univariate analysis for 1 year-ACM

	ALL		2000-2007		2008-2014	
	OR	**p-value**	**OR**	**p-value**	**OR**	**p-value**
RECIPIENT DEMOGRAPHICS						
Age	1 (0.97-1.03)	0.84	1 (0.95-1.05)	0.971	1 (0.96-1.04)	0.897
Gender	0.66 (0.25-1.76)	0.406	0.76 (0.2-2.84)	0.679	0.59 (0.13-2.56)	0.48
Time on waiting list (d)	1 (1-1)	0.98	1 (1-1)	0.109	1 (1-1)	0.331
Mean biopsy grade		0.1602		0.1032		0.6872
LoS	0.99 (0.98-1)	0.17	0.92 (0.87-0.97)	0.0013	1 (0.99-1.01)	0.985
DONOR DEMOGRAPHICS						
Donor age	1 (0.97-1.03)	0.847	1 (0.96-1.03)	0.808	1.01 (0.97-1.06)	0.573
ETIOLOGY of CMP						
Ischemic CMP	1.62 (0.69-3.81)	0.268	2.56 (0.78-8.44)	0.123	1.1 (0.31-3.87)	0.881
Dilated CMP	0.97 (0.42-2.24)	0.938	0.57 (0.18-1.84)	0.348	1.44 (0.42-4.98)	0.565
Congenital CMP	1.73 (0.56-5.36)	0.341	1.87 (0.41-8.62)	0.419	1.54 (0.28-8.53)	0.619
Recipient ARVD	1.04 (0.11-9.68)	0.974	0 (0-Inf)	0.992	1.76 (0.17-18.49)	0.639
Recipient HCM	0.67 (0.14-3.17)	0.61	1.42 (0.25-8.16)	0.697	0 (0-Inf)	0.991
DEVICE TREATMENT						
PM	0.74 (0.32-1.73)	0.494	1 (0.29-3.39)	1	0.68 (0.19-2.42)	0.555
AICD	0.76 (0.32-1.8)	0.527	1.49 (0.39-5.68)	0.558	0.56 (0.16-1.96)	0.368
VAD	0.8 (0.25-2.57)	0.708	0.66 (0.07-6.1)	0.712	1.02 (0.24-4.27)	0.976
CLINICAL PARAMETERS						
LVEF	1.02 (0.99-1.05)	0.132	1.04 (1-1.08)	0.0336	0.99 (0.94-1.04)	0.682
PVR	0.99 (0.66-1.48)	0.958	0.96 (0.53-1.75)	0.89	1.01 (0.58-1.75)	0.969
BSA	1.09 (0.36-3.29)	0.875	1.96 (0.53-7.18)	0.311	0.34 (0.06-1.75)	0.196
Size	0.09 (0.01-1.48)	0.0911	0.02 (0-7.94)	0.209	0.1 (0-2.29)	0.151
Weight	0.98 (0.96-1.01)	0.172	0.98 (0.94-1.02)	0.283	0.99 (0.96-1.02)	0.369
BMI	0.95 (0.87-1.05)	0.313	0.94 (0.82-1.08)	0.416	0.96 (0.85-1.09)	0.545
RISK FACTORS/ COMORBIDITIES						
Previous thoracic surgery	1.15 (0.49-2.7)	0.756	1.76 (0.53-5.86)	0.356	0.84 (0.24-2.95)	0.788
HTA	1.1 (0.45-2.69)	0.835	1.06 (0.29-3.92)	0.927	1.27 (0.36-4.47)	0.714
Diabetes	2.45 (0.88-6.84)	0.0872	7.83 (1.83-33.47)	0.00547	0.46 (0.05-4)	0.485
History of tobacco abuse	0.43 (0.17-1.06)	0.0669	0.5 (0.14-1.8)	0.29	0.4 (0.11-1.46)	0.164
Dyslipemia	1.97 (0.83-4.68)	0.125	1.66 (0.52-5.3)	0.395	2.52 (0.67-9.53)	0.173
Thyroid.disease	0.81 (0.22-3.02)	0.752	0 (0-Inf)	0.993	1.7 (0.39-7.41)	0.48
COBP	0.82 (0.17-3.96)	0.801	0 (0-Inf)	0.993	1.83 (0.32-10.41)	0.494

	ALL		2000-2007		2008-2014	
	OR	**p-value**	**OR**	**p-value**	**OR**	**p-value**
PRE-TRANSPLANT TREATMENT						
Metoprolol	1.28 (0.49-3.39)	0.615	0.83 (0.16-4.39)	0.823	2.01 (0.56-7.24)	0.286
Bisoprolol	1.71 (0.31-9.34)	0.535	3.77 (0.48-29.37)	0.205	0 (0-Inf)	0.994
Carvedilol	0.42 (0.13-1.3)	0.131	0.5 (0.12-2.01)	0.329	0.26 (0.03-2.14)	0.208
Nebivolol	0.68 (0.08-5.89)	0.726	20974889.71 (0-Inf)	0.991	0 (0-Inf)	0.992
ACE Inhibitors	0.96 (0.42-2.23)	0.929	0.87 (0.27-2.75)	0.809	0.96 (0.27-3.37)	0.951
AT_1-Receptors Blockers	0.57 (0.2-1.63)	0.293	0.41 (0.08-2.04)	0.273	0.8 (0.19-3.29)	0.753
Spironolactone	1.37 (0.58-3.26)	0.475	0.56 (0.18-1.8)	0.334	4.84 (0.98-23.94)	0.0533
Eplerenone	0.42 (0.09-1.92)	0.262	20974889.7 (0-Inf)	0.991	0.22 (0.03-1.81)	0.158
Torasemide	0.9 (0.33-2.5)	0.847	0.62 (0.18-2.16)	0.448	2.42 (0.28-20.75)	0.42
Hydrochlorthiazid	0.61 (0.17-2.24)	0.458	0.63 (0.12-3.26)	0.582	0.53 (0.06-4.58)	0.56
PRE-TRANSPLANT LABORATORY FINDINGS						
Bicarbonate	1.03 (0.88-1.22)	0.693	0.97 (0.79-1.18)	0.735	1.15 (0.86-1.54)	0.35
Creatinine	1 (0.99-1)	0.299	0.99 (0.98-1.01)	0.379	1 (0.98-1.01)	0.512
BUN	0.99 (0.93-1.06)	0.833	0.98 (0.9-1.07)	0.71	1 (0.9-1.11)	0.989
Bilirubin	1.01 (0.98-1.04)	0.395	1 (0.96-1.04)	0.88	1.03 (0.98-1.08)	0.193
ASAT	1 (1-1.01)	0.335	1 (0.98-1.01)	0.525	1.01 (1-1.01)	0.185
ALAT	0.99 (0.97-1.01)	0.211	0.98 (0.95-1.01)	0.179	1 (0.97-1.02)	0.773
CRP	0.99 (0.97-1.02)	0.593	0.93 (0.83-1.04)	0.176	1.01 (0.98-1.04)	0.373
Iron	0.94 (0.86-1.03)	0.198	0.91 (0.79-1.04)	0.166	0.99 (0.88-1.11)	0.86
Albumin	0.91 (0.76-1.09)	0.309	0 (0-Inf)	1	0.97 (0.82-1.14)	0.693
Hemoglobin	1.01 (0.99-1.03)	0.499	1.01 (0.98-1.04)	0.38	1 (0.97-1.04)	0.908
Leucocyte	0.78 (0.65-0.95)	0.0147	0.62 (0.45-0.86)	0.00456	0.94 (0.75-1.17)	0.565
Platelets	1 (0.99-1)	0.569	0.99 (0.99-1)	0.131	1 (1-1.01)	0.287
TSH	0.66 (0.26-1.67)	0.377	1 (0-Inf)	1	0.7 (0.26-1.85)	0.468
Free T4	0.89 (0.66-1.22)	0.477	1 (0-Inf)	1	0.92 (0.7-1.21)	0.563
RECIPIENTS SEROLOGICAL DATA						
Anti-CMV antibodies	1.27 (0.53-3.02)	0.591	2.08 (0.62-6.99)	0.235	0.79 (0.22-2.79)	0.714
Anti-EBV antibodies	1.35 (0.28-6.48)	0.71	1.51 (0.16-14.13)	0.717	1.2 (0.13-10.98)	0.872
Anti-toxopl. antibodies	0.57 (0.24-1.33)	0.193	0.95 (0.29-3.1)	0.932	0.32 (0.09-1.15)	0.081
Anti-HBC antibodies	0 (0-Inf)	0.989	0 (0-Inf)	0.992	0 (0-Inf)	0.994
Anti-HCV antibodies	1 (0.11-9.33)	1	1.64 (0.14-19.5)	0.694	0 (0-Inf)	0.993
Anti-HSV antibodies	1.16 (0.4-3.42)	0.783	1.11 (0.2-6.05)	0.908	1.07 (0.26-4.44)	0.929

	ALL		2000-2007		2008-2014	
	OR	**p-value**	**OR**	**p-value**	**OR**	**p-value**
DONOR SEROLOGICAL DATA						
Anti-CMV antibodies	0.66 (0.27-1.59)	0.355	0.59 (0.18-1.91)	0.381	0.83 (0.2-3.37)	0.792
Anti-EBV antibodies	1.19 (0.24-5.89)	0.831	0.55 (0.09-3.36)	0.52	10636203.07 (0-Inf)	0.993
Anti-toxopl. antibodies	0.9 (0.37-2.21)	0.819	0.82 (0.25-2.67)	0.739	1 (0.25-4.05)	1
Anti-HBC antibodies	0.6 (0.07-5.25)	0.646	0 (0-Inf)	0.993	4.78 (0.27-83.71)	0.284
Anti-VZV antibodies	0.29 (0.08-1.05)	0.0593	0.52 (0.09-3.2)	0.482	0.14 (0.02-1.01)	0.0515
Anti-HSV antibodies	1.61 (0.49-5.3)	0.433	1.19 (0.28-4.98)	0.813	2.91 (0.31-27.07)	0.348

TABLE 7

Univariate analysis for in-hospital mortality

	ALL		2000-2007		2008-2014	
	OR	**p-value**	**OR**	**p-value**	**OR**	**p-value**
RECIPIENT DEMOGRAPHICS						
Age	1.01 (0.98-1.05)	0.409	1 (0.95-1.04)	0.857	1.03 (0.98-1.09)	0.256
Gender	0.76 (0.27-2.12)	0.596	0.67 (0.18-2.55)	0.558	0.97 (0.18-5.13)	0.972
Time on waiting list (d)	1 (1-1)	0.993	1 (1-1)	0.191	1 (1-1)	0.48
Mean biopsy grade		0.03612		0.04761		0.2482
LoS	0.99 (0.97-1)	0.0929	0.91 (0.86-0.96)	0.00123	1 (0.99-1.01)	0.81
DONOR DEMOGRAPHICS						
Donor age	1 (0.97-1.03)	0.946	0.99 (0.95-1.03)	0.548	1.01 (0.97-1.06)	0.573
ETIOLOGY of CMP						
Ischemic CMP	1.28 (0.53-3.12)	0.584	2.04 (0.6-6.92)	0.255	0.85 (0.22-3.19)	0.805
Dilated CMP	0.97 (0.41-2.32)	0.954	0.49 (0.15-1.61)	0.237	1.78 (0.49-6.46)	0.383
Congenital CMP	1.36 (0.41-4.55)	0.617	2.09 (0.45-9.7)	0.346	0.68 (0.08-6)	0.724
Recipient ARVD	1.15 (0.12-10.71)	0.905	0 (0-Inf)	0.992	1.97 (0.19-20.84)	0.574
Recipient HCM	0.74 (0.15-3.53)	0.705	1.57 (0.27-9.09)	0.617	0 (0-Inf)	0.991
DEVICE TREATMENT						
PM	0.89 (0.37-2.12)	0.794	1.14 (0.33-3.94)	0.831	0.9 (0.24-3.41)	0.872
AICD	0.72 (0.29-1.76)	0.473	1.02 (0.24-4.29)	0.982	0.71 (0.19-2.58)	0.6
VAD	0.9 (0.28-2.89)	0.853	0.72 (0.08-6.75)	0.776	1.17 (0.28-5)	0.827
CLINICAL PARAMETERS						
LVEF	1.02 (0.99-1.05)	0.109	1.04 (1.01-1.08)	0.0262	0.99 (0.93-1.04)	0.674
PVR	0.99 (0.65-1.49)	0.947	0.96 (0.51-1.84)	0.912	1.01 (0.58-1.75)	0.969
BSA	1.57 (0.54-4.57)	0.406	1.66 (0.48-5.81)	0.425	1.18 (0.16-8.7)	0.874
Size	0.43 (0.03-6.34)	0.54	0 (0-1.36)	0.0626	2.48 (0.02-274.33)	0.706
Weight	0.99 (0.96-1.01)	0.326	0.96 (0.92-1)	0.0791	1 (0.97-1.04)	0.83
BMI	0.97 (0.88-1.07)	0.537	0.92 (0.8-1.06)	0.259	1.02 (0.89-1.15)	0.809
RISK FACTORS/ COMORBIDITIES						
Previous thoracic surgery	1.35 (0.56-3.24)	0.505	2.04 (0.6-6.92)	0.255	1.01 (0.28-3.67)	0.986
HTA	1.27 (0.51-3.15)	0.607	1.2 (0.32-4.49)	0.786	1.52 (0.41-5.54)	0.53
Diabetes	2.78 (0.98-7.83)	0.0534	9 (2.07-39.14)	0.00339	0.52 (0.06-4.53)	0.554
History of tobacco abuse	0.5 (0.2-1.24)	0.135	0.57 (0.16-2.07)	0.394	0.47 (0.12-1.77)	0.265
Dyslipemia	2.01 (0.82-4.91)	0.126	1.38 (0.42-4.53)	0.595	3.45 (0.81-14.64)	0.0927
Thyroid.disease	0.9 (0.24-3.38)	0.876	0 (0-Inf)	0.993	1.95 (0.44-8.65)	0.38
COBP	0.9 (0.19-4.41)	0.901	0 (0-Inf)	0.993	2.07 (0.36-11.91)	0.413

	ALL		2000-2007		2008-2014	
	OR	**p-value**	**OR**	**p-value**	**OR**	**p-value**
PRE-TRANSPLANT TREATMENT						
Metoprolol	1.12 (0.41-3.12)	0.822	0.37 (0.04-3.18)	0.363	2.4 (0.64-8.93)	0.193
Bisoprolol	1.9 (0.35-10.38)	0.461	4.17 (0.53-32.65)	0.174	0 (0-Inf)	0.994
Carvedilol	0.47 (0.15-1.47)	0.192	0.56 (0.14-2.28)	0.42	0.29 (0.03-2.43)	0.252
Nebivolol	0.75 (0.09-6.52)	0.794	23031251.44 (0-Inf)	0.991	0 (0-Inf)	0.992
ACE Inhibitors	1.16 (0.49-2.76)	0.734	1.06 (0.32-3.48)	0.927	1.15 (0.32-4.19)	0.828
AT_1-Receptors Blockers	0.64 (0.22-1.85)	0.411	0.45 (0.09-2.28)	0.336	0.92 (0.22-3.85)	0.905
Spironolactone	1.44 (0.59-3.53)	0.426	0.47 (0.14-1.55)	0.215	10 (1.21-82.9)	0.0329
Eplerenone	0.46 (0.1-2.14)	0.325	23031251.44 (0-Inf)	0.991	0.24 (0.03-2.05)	0.194
Torasemide	1.07 (0.36-3.14)	0.907	0.54 (0.15-1.92)	0.341	25442734.32 (0-Inf)	0.993
Hydrochlorthiazid	0.68 (0.19-2.51)	0.565	0.7 (0.13-3.64)	0.671	0.59 (0.07-5.18)	0.633
PRE-TRANSPLANT LABORATORY FINDINGS						
Bicarbonate	0.96 (0.81-1.14)	0.649	0.86 (0.69-1.06)	0.161	1.18 (0.86-1.61)	0.302
Creatinine	1 (0.99-1)	0.412	0.99 (0.98-1.01)	0.373	1 (0.99-1.01)	0.693
BUN	1 (0.94-1.07)	0.922	0.99 (0.91-1.08)	0.833	1.01 (0.92-1.12)	0.777
Bilirubin	1.02 (0.99-1.05)	0.282	1 (0.96-1.04)	0.874	1.03 (0.98-1.08)	0.193
ASAT	1 (1-1.01)	0.319	1 (0.98-1.01)	0.542	1.01 (1-1.01)	0.185
ALAT	0.99 (0.97-1.01)	0.246	0.98 (0.95-1.01)	0.217	1 (0.97-1.02)	0.773
CRP	1 (0.97-1.02)	0.712	0.93 (0.83-1.04)	0.176	1.02 (0.99-1.05)	0.258
Iron	0.94 (0.86-1.03)	0.201	0.9 (0.77-1.04)	0.148	0.99 (0.88-1.11)	0.86
Albumin	0.91 (0.76-1.09)	0.309	0 (0-Inf)	1	0.97 (0.82-1.14)	0.693
Hemoglobin	1 (0.98-1.03)	0.669	1.01 (0.98-1.04)	0.56	1 (0.97-1.04)	0.931
Leucocyte	0.79 (0.64-0.96)	0.019	0.63 (0.46-0.88)	0.00652	0.94 (0.74-1.18)	0.578
Platelets	1 (0.99-1)	0.604	0.99 (0.99-1)	0.143	1.01 (1-1.01)	0.272
TSH	0.66 (0.26-1.67)	0.377	1 (0-Inf)	1	0.7 (0.26-1.85)	0.468
Free T4	0.89 (0.66-1.22)	0.477	1 (0-Inf)	1	0.92 (0.7-1.21)	0.563
RECIPIENTS SEROLOGICAL DATA						
Anti-CMV antibodies	1.33 (0.54-3.27)	0.53	1.8 (0.53-6.13)	0.347	1.03 (0.27-3.91)	0.963
Anti-EBV antibodies	2.79 (0.34-22.54)	0.336	1.36 (0.15-12.81)	0.786	8508962.43 (0-Inf)	0.991
Anti-toxopl. antibodies	0.58 (0.24-1.39)	0.221	0.82 (0.25-2.72)	0.742	0.4 (0.11-1.46)	0.164
Anti-HBC antibodies	0 (0-Inf)	0.989	0 (0-Inf)	0.992	0 (0-Inf)	0.994
Anti-HCV antibodies	1.1 (0.12-10.33)	0.931	1.81 (0.15-21.54)	0.64	0 (0-Inf)	0.993
Anti-HSV antibodies	1.43 (0.45-4.58)	0.549	0.99 (0.18-5.45)	0.988	1.7 (0.33-8.68)	0.524

	ALL		2000-2007		2008-2014	
	OR	**p-value**	**OR**	**p-value**	**OR**	**p-value**
DONOR SEROLOGICAL DATA						
Anti-CMV antibodies	0.73 (0.3-1.79)	0.495	0.69 (0.21-2.28)	0.548	0.83 (0.2-3.37)	0.792
Anti-EBV antibodies	1.13 (0.23-5.58)	0.885	0.5 (0.08-3.06)	0.453	10636203.07 (0-Inf)	0.993
Anti-toxopl. antibodies	0.83 (0.33-2.05)	0.681	0.71 (0.21-2.35)	0.57	1 (0.25-4.05)	1
Anti-HBC antibodies	0.64 (0.07-5.56)	0.683	0 (0-Inf)	0.993	4.78 (0.27-83.71)	0.284
Anti-VZV antibodies	0.27 (0.07-0.98)	0.0471	0.47 (0.08-2.89)	0.414	0.14 (0.02-1.01)	0.0515
Anti-HSV antibodies	1.5 (0.45-4.96)	0.506	1.05 (0.25-4.46)	0.945	2.91 (0.31-27.07)	0.348

TABLE 8 MULTIVARIATE ANALYSIS FOR THE PERIOD 2000-2007 :

	2000-2007	
IN-HOSPITAL MORTALITY (WITHOUT CONTROLLING AGE AND GENDER OF THE RECIPIENT AND DONOR)	**z value**	**Pr(>|z|)**
Recipient LVEF	2.068	0.03869
Recipient weight	-2.231	0.02570
Diabetes mellitus	2.698	0.00697
Los	-2.449	0.01433
IN-HOSPITAL MORTALITY (WITH CONTROLLING AGE AND GENDER OF THE RECIPIENT AND DONOR)		
Recipient LVEF	1.772	0.0764
Recipient weight	-2.188	0.0287
Diabetes mellitus	2.551	0.0107
Los	-2.413	0.0158
1-YEAR ACM (WITHOUT CONTROLLING AGE AND GENDER OF THE RECIPIENT AND DONOR)		
Recipient leucocytes	-1.881	0.5992
Diabetes mellitus	1.977	0.04801
LoS	-2.690	0.00716
1-YEAR ACM (WITH CONTROLLING AGE AND GENDER OF THE RECIPIENT AND DONOR)		
Recipient leucocytes	-1.909	0.5626
Diabetes mellitus	2.044	0.04095
LoS	-2.703	0.00687

TABLE 9 MULTIVARIATE ANALYSIS FOR THE PERIOD 2008-2014 :

	2000-2007	
IN-HOSPITAL MORTALITY (WITHOUT CONTROLLING AGE AND GENDER OF THE RECIPIENT AND DONOR)	**z value**	**Pr(>|z|)**
Spironolactone	2.134	0.032863
IN-HOSPITAL MORTALITY (WITH CONTROLLING AGE AND GENDER OF THE RECIPIENT AND DONOR)		
Spironolactone	1.604	0.1087
1-YEAR ACM (WITHOUT CONTROLLING AGE AND GENDER OF THE RECIPIENT AND DONOR)		
Spironolactone	1.933	0.053290
1-YEAR ACM (WITH CONTROLLING AGE AND GENDER OF THE RECIPIENT AND DONOR)		
Spironolactone	1.604	0.1087