# Intraoperative Risk Factors Associated with Heart Transplantation and Mechanical Circulatory Support-Special Considerations

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RESOLVING THE ORGAN SHORTAGE
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# Conflict of Interest Disclosure

- I have no relevant financial relationships to disclose

# Intraop Risk Factors for Heart Transplantation

- Redo
- coagulopathy
- Venous anatomy
- Endovascular wires/SVC
- Donor/Recipient Mismatch
- Prolong donor Ischemic Time
- PVR—RV Failure/Dysfunction
- Vasoplegia
- Hyperacute rejection
- Primary Graft Dysfunction

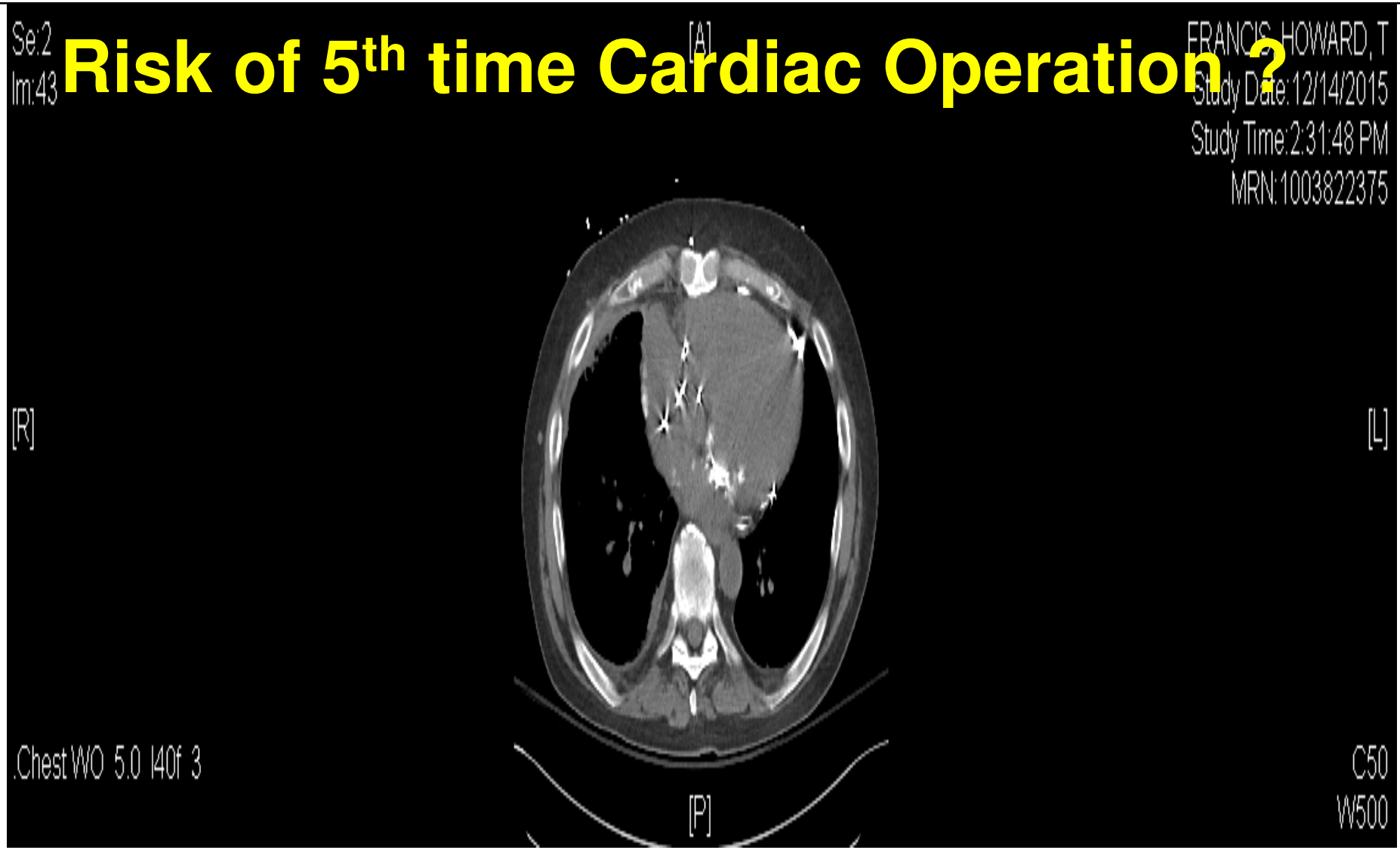
# Intraop Risk Factors at time of Heart Transplantation

- Redo
  - Re-entry
  - LVADs
  - Patent grafts
  - Congenital
    - Venous anatomy- anamalous LSVC/CS ; PAs; transposition; Fontan anatomy; atrial switch
  - CorCap

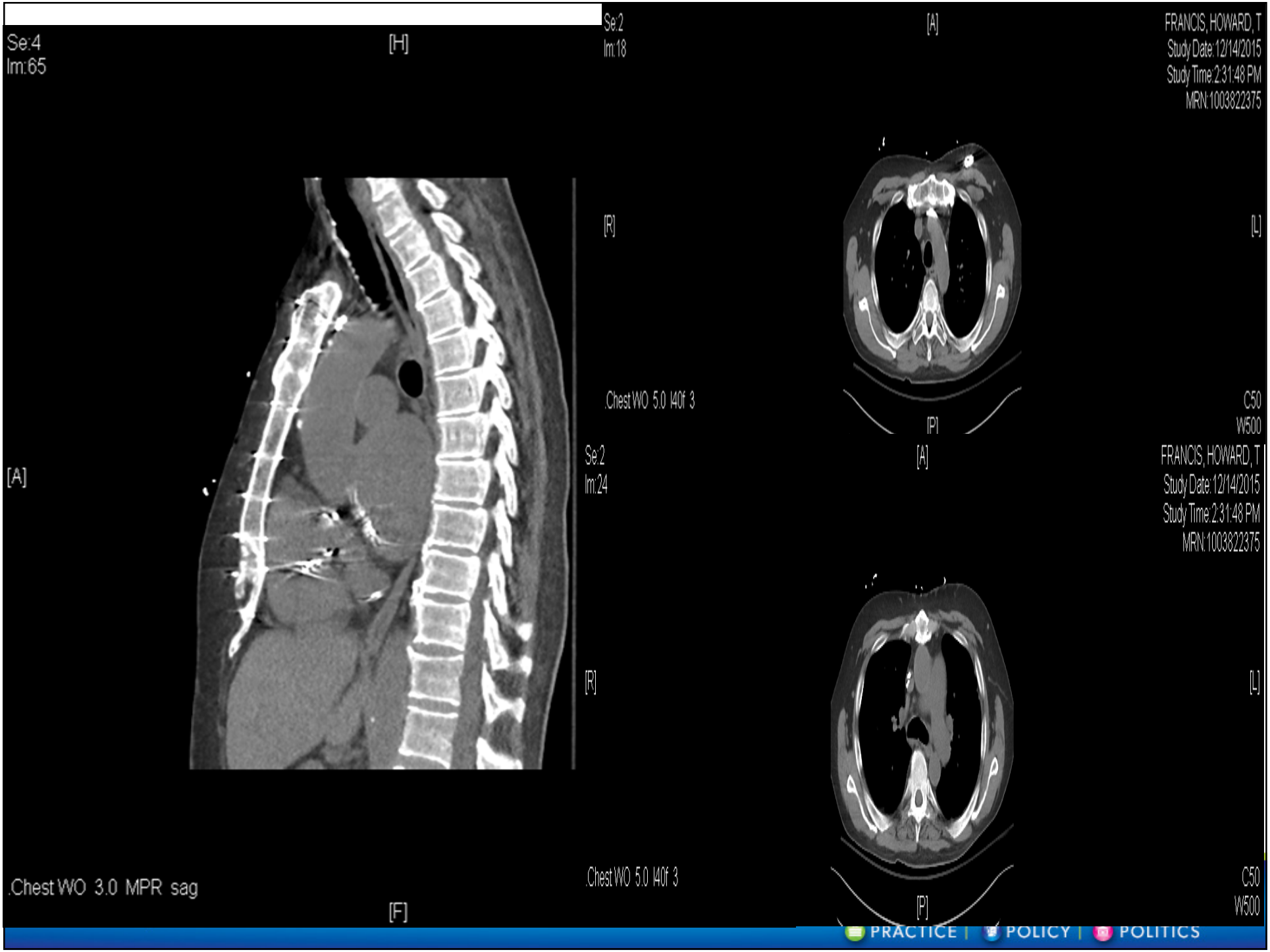
# Redo Strategies

- Pre-op non-contrast CT mandatory to plan re-entry and avoid disasters
- Groin access/cannulation depending on risk of re-entry
  - Rarely necessary to go on CPB prior to sternotomy
  - Cannulation strategy—aortic access; venous access
- Need to manage Donor XC to minimize ischemic time in redo
  - For BTT LVAD generally plan for maximum of 2 hours before ready to for donor heart
  - Must manage XC at donor hospital; depending on travel time

# Risk of 5th time Cardiac Operation ?




62 yo MVR 1983; redo MVR/TV repair 2000; redo,redo MVR 2013
Transapical amplatzer closure of paravalvular leak 2015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# Adult Congenital Heart Transplantation

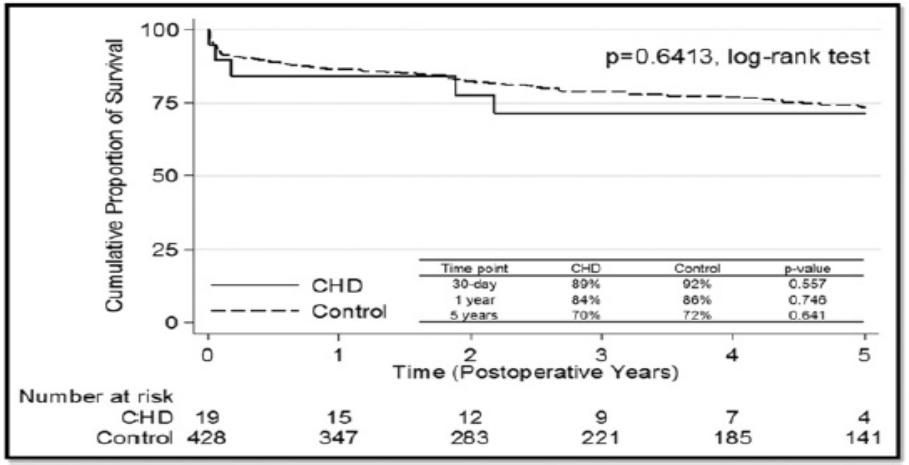



**Figure 1** Survival after HT in adults with CHD vs non-CHD indications.

**Table 5** Summary of Literature Regarding Heart Transplantation for Patients with Adult Congenital Heart Disease

| Investigators (year) | Era | Source | *n* | 30-day survival | 1-year survival | 5-year survival |
|---|---|---|---|---|---|---|
| Speziali et al[8] (1998) | 1991–1998 | SC | 16 | | 86% | 86% |
| Lamour et al[9] (1999) | 1985–1998 | SC | 24 | | 79% | 60% |
| Izquierdo et al[11] (2007) | 1991–2006 | SC | 8 | 75% | 75% | 75% |
| Coskun et al[10] (2007) | 1989–2005 | SC | 15 | | 80% | |
| Greutmann et al[12] (2009) | 1985–2006 | SC | 13 | 85% | 85% | 85% |
| Patel et al[13] (2009) | 1987–2006 | UNOS | 689 | 80% | 69% | 57% |
| Lamour et al[14] (2009) | 1990–2002 | CTRD[a] | 488 | | 80% | 70% |
| Irving et al[15] (2010) | 1988–2009 | SC | 37 | 70% | 68% | 58% |
| Karamlou et al[16] (2010) | 1990–2008 | UNOS | 575 | | 76% | 63% |
| Davies et al[17] (2011) | 1995–2009 | UNOS | 1,053 | ~80% | ~79% | ~60% |

SC, single center; UNOS, United Network of Organ Sharing.
[a]Cardiac Transplant Registry Database + Pediatric Heart Transplant Study.

Heart transplantation for adults with congenital heart disease: Results in the modern era.
Bhama JK et al. J Heart Lung Transplant 2013;32:499-504

# Adult Congenital Heart Transplantation

- Technically demanding
- Usually complex redos
- Must be familiar with Fontan anatomy; PA reconstruction; venous and situs variability
- Consider partnering with congenital heart surgeons

# Biatrial vs Bicaval

## Outcomes in Bicaval Versus Biatrial Techniques in Heart Transplantation: An Analysis of the UNOS Database

Eric S. Weiss, MD, Lois U. Nwakanma, MD, Stuart B. Russell, MD, John V. Conte, MD, and Ashish S. Shah, MD

**Background:** Despite 40 years of heart transplantation, the optimal atrial anastomotic technique remains unclear. The United Network for Organ Sharing (UNOS) database provides a unique and novel opportunity to address this question by examining survival in a large cohort of patients undergoing orthotopic heart transplantation (OHT). We hypothesized that, when examining the issue on a large scale, no difference in survival would exist between techniques.

**Methods:** We retrospectively reviewed first-time adult OHT in the UNOS database to identify 14,418 patients undergoing OHT between the years 1999 and 2005. Primary stratification was between those who underwent bicaval vs biatrial techniques. Baseline demographic and clinical factors were also recorded. The primary end-point was mortality from all causes during the study period. Secondary outcomes included length of hospital stay (LOS), and need for permanent pacemaker placement (PP). Post-transplant survival was compared between groups using a Cox proportional hazard regression model.

**Results:** Of the 11,931 patients who met inclusion criteria between 1999 and 2005, 5,207 (44%) underwent the bicaval anastomotic technique. Bicaval and biatrial groups were well matched for gender, donor age, ischemic time, pulmonary vascular resistance, transpulmonary gradient, cardiac index, body mass index and pre-operative creatinine. Technique was not associated with survival during the study period (hazard ratio 1.06, $p = 0.31$). On multivariate analysis, age, gender, donor age and ischemic time were independent predictors of mortality. The bicaval technique was associated with less need for post-operative PP (2.0% vs 5.3%, $p < 0.001$) and shorter LOS (19 vs 21 days, $p < 0.001$).

**Conclusions:** This study is the single largest series examining bicaval vs biatrial anastamotic techniques for OHT. We found no difference in survival between the two groups, although the bicaval technique was associated with shorter LOS and pacemaker placement. Both techniques lead to equivalent survival in OHT. J Heart Lung Transplant 2008;27:178-83. 

**Increase need for PPM and increase LOS with Biatrial vs Bicaval**

**(Biatrial for persistent LSVC to CS)**

**Table 3.** Bivariate and Multivariate Analysis of Secondary Outcome Variables

| | Outcome | Biatrial ($N$ = 6,724) | Bicaval ($N$ = 5,207) | $p$-value[a] |
|---|---|---|---|---|
| Bivariate | Permanent pacemaker placement[b] | 343 (5.3) | 103 (2.0) | <0.001 |
| | Length of hospital stay[c] | 20.9 (0.40) | 18.8 (0.28) | <0.001 |
| | | OR or regression coefficient (95% CI) | | |
| Multivariate (biatrial vs bicaval) | Permanent pacemaker placement[d] | 2.88 (2.10–3.94) | | <0.001 |
| | Length of hospital stay[d] | 2.44 (1.11–3.77) | | <0.001 |

OR, odds ratio for logistic regression; CI, confidence interval.

[a]$p$-value for bivariate analysis is based on either chi-square (pacemaker) or Student's $t$-test (LOS). $p$-values for multivariate analysis are based on either logistic (pacemaker) or linear (LOS) regression analysis. $p < 0.05$ was considered statistically significant.

[b]Data expressed as

[c]Data expressed as days (SEM).

[d]Data expressed as OR or regression coefficient (95% CI).

Outcomes in Bicaval Versus Biatrial Techniques in Heart Transplantation: An Analysis of the UNOS Database.
Weiss ES et al. J Heart Lung Transplant 2008;27:178-83.

# Coagulopathy

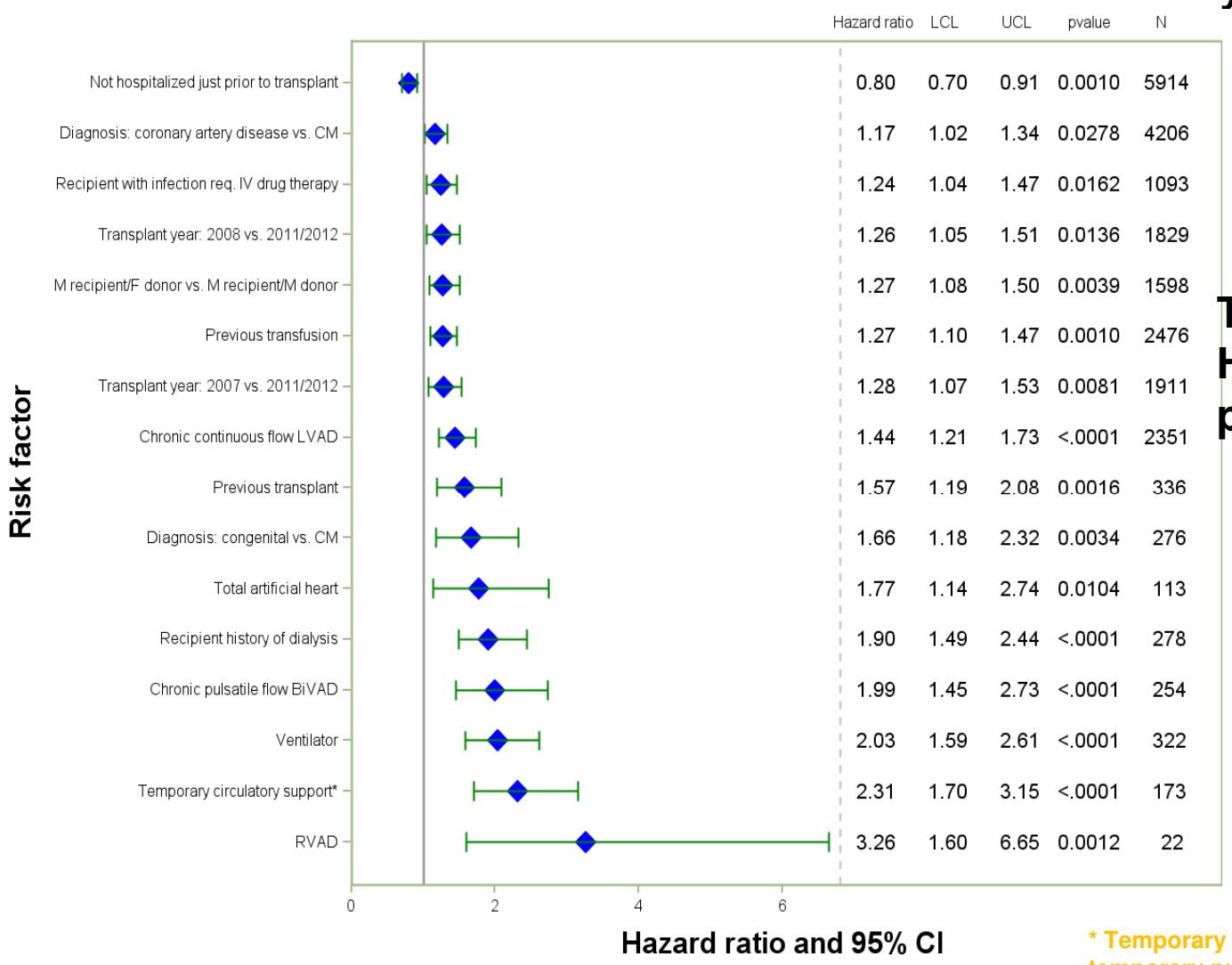
- Majority of heart transplant pts are anti-coagulated coming to OR
  - IV Vit K; prime pump with FFP
- Most intense in redos expecially LVAD patients
- Rx- FFP; cyroprecipitate; platelets; rarely factor 7

# Unique MCS Issues for Donor Selection

- Expect difficult dissection ( easier if covered with gortex)
  - Time donor XC to leave up to 2 hours for dissection to minimize ischemic time
- Will need blood products for expected coagulopathy
  - IV Vit K;FFP; Platelets; Cyro; Factor 7 rarely
- Be prepared for vasoplegia
  - Vasopressin; Methylene blue

# ADULT HEART TRANSPLANTS (2007-6/2012)

## Risk Factors For 1 Year Mortality

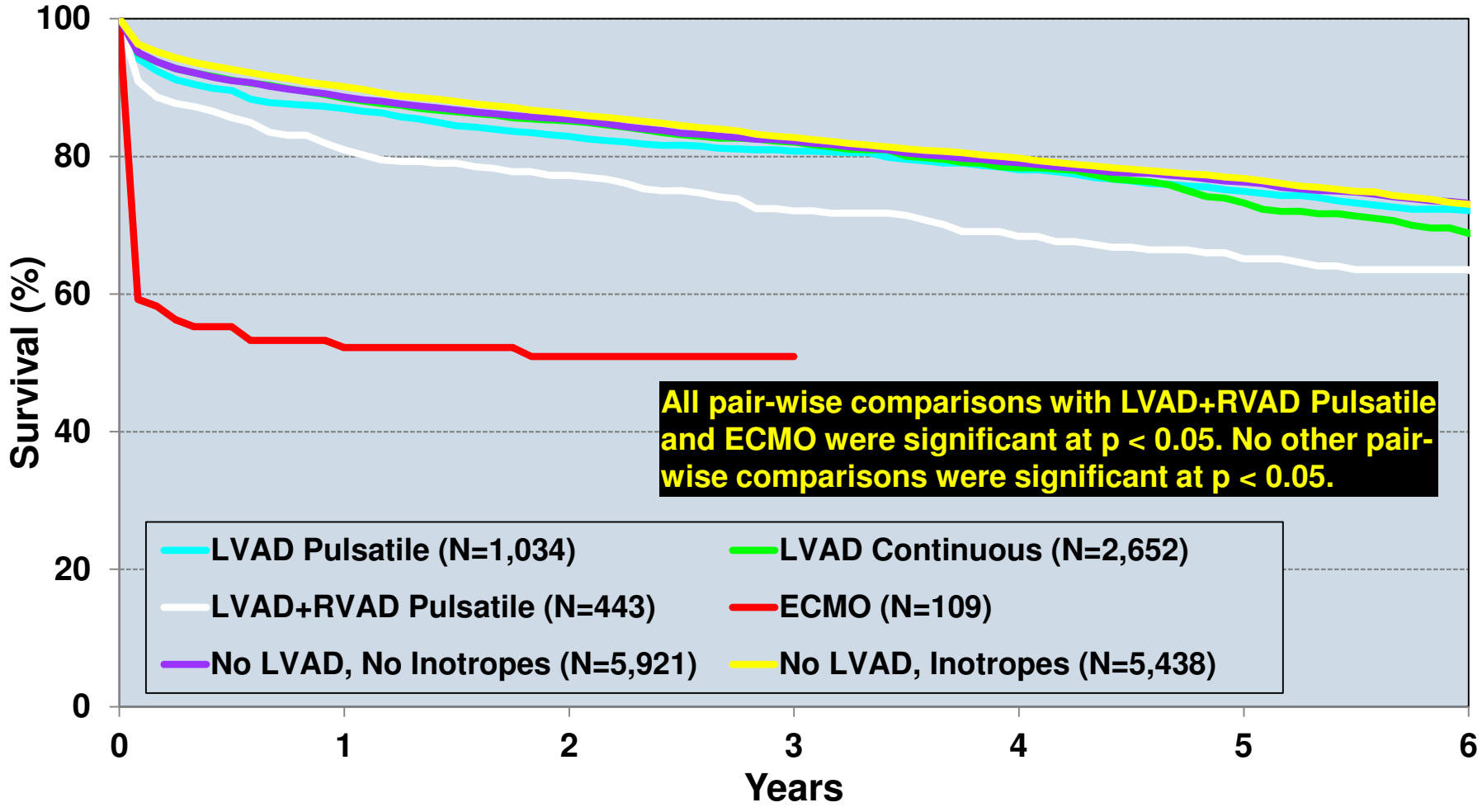



**Tempoarary MCS/ECMO Highest risk factor for post tx death**

**N = 10,739**

*** Temporary circulatory support includes ECMO and temporary pulsatile flow devices.**

# Adult Heart Transplants
## Kaplan-Meier Survival by VAD usage
(Transplants: January 2005 – June 2012)




ISHLT • INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION
2014
JHLT. 2014 Oct; 33(10): 996-1008

# Reoperative Sternotomy and Heart Transplantation (JHH and Wash U)

## Reoperative Sternotomy Is Associated With Increased Mortality After Heart Transplantation

Timothy J. George, MD, Claude A. Beaty, MD, Gregory A. Ewald, MD, Stuart D. Russell, MD, Ashish S. Shah, MD, John V. Conte, MD, Glenn J. Whitman, MD, and Scott C. Silvestry, MD

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*Background.* Although several studies have examined factors affecting survival after orthotopic heart transplantation (OHT), few have evaluated the impact of reoperative sternotomy. We undertook this study to examine the incidence and impact of repeat sternotomies on OHT outcomes.

*Methods.* We conducted a retrospective review of all adult OHT from 2 institutions. Primary stratification was by the number of prior sternotomies. The primary outcome was survival. Secondary outcomes included blood product utilization and commonly encountered postoperative complications. Multivariable Cox proportional hazards regression models examined mortality while linear regression models examined blood utilization.

*Results.* From January 1995 to October 2011, 631 OHT were performed. Of these, 25 (4.0%) were redo OHT and 182 (28.8%) were bridged to transplant with a ventricular assist device; 356 (56.4%) had undergone at least 1 prior sternotomy. On unadjusted analysis, reoperative sternotomy was associated with decreased 90-day (98.5% vs 90.2%, $p < 0.001$), 1-year (93.1% vs 79.6%, $p < 0.001$), and 5-year (80.4% vs 70.1%, $p = 0.002$) survival. This difference persisted on multivariable analysis at 90 days (hazard ratio [HR] 2.99, $p = 0.01$), 1 year (HR 2.98, $p = 0.002$), and 5 years (HR 1.62, $p = 0.049$). The impact of an increasing number of prior sternotomies was negligible. On multivariable analysis, an increasing number of prior sternotomies was associated with increased intraoperative blood product utilization. Increasing blood utilization was associated with decreased 90-day, 1-year, and 5-year survival.

*Conclusions.* Reoperative sternotomy is associated with increased mortality and blood utilization after OHT. Patients with more than 1 prior sternotomy do not experience additional increased mortality. Carefully selected patients with multiple prior sternotomies have decreased but acceptable outcomes.

(Ann Thorac Surg 2012;94:2025–32)



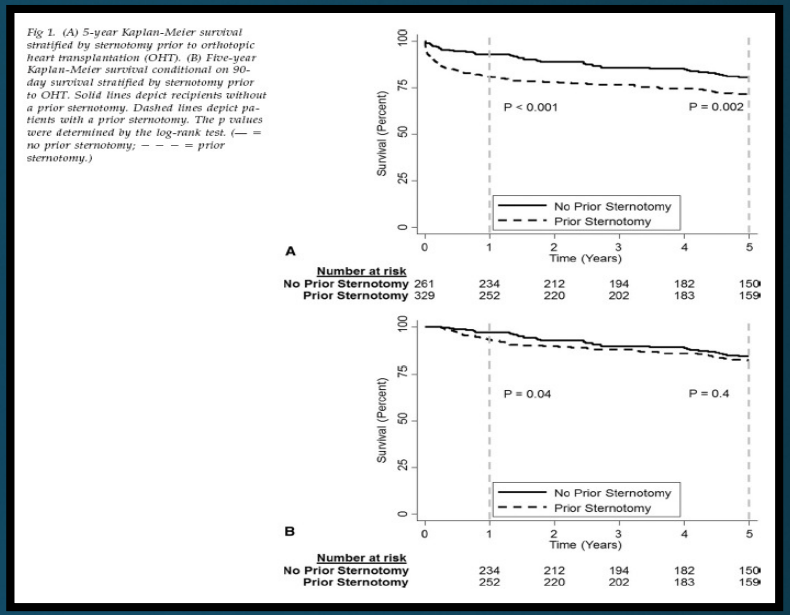


*Fig 1. (A) 5-year Kaplan-Meier survival stratified by sternotomy prior to orthotopic heart transplantation (OHT). (B) Five-year Kaplan-Meier survival conditional on 90-day survival stratified by sternotomy prior to OHT. Solid lines depict recipients without a prior sternotomy. Dashed lines depict patients with a prior sternotomy. The p values were determined by the log-rank test. (— = no prior sternotomy; – – – = prior sternotomy.)*

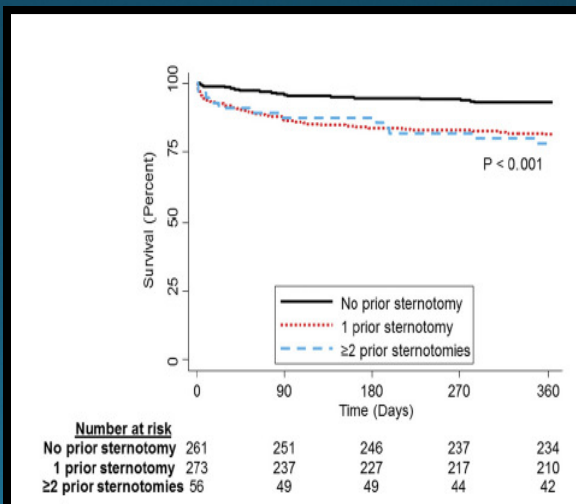


*Fig 2. One-year Kaplan-Meier survival stratified by number of sternotomies prior to orthotopic heart transplantation (OHT). Solid black line depicts recipients without a prior sternotomy, dashed red line 1 prior sternotomy, dashed-dotted blue line 2 prior sternotomies, and fine dotted green line ≥ 3 prior sternotomies. The p values were determined by the log-rank test.*

Reoperative Sternotomy Is Associated With Increased Mortality After Heart Transplantation.
George TJ et al. Ann Thorac Surg 2012; 94:2025-32.

# Reoperative Sternotomy and Heart Transplantation

*Table 2. Multivariable Cox Proportional Hazards Regression Model of 1-Year Mortality*

| Variable | Hazard Ratio | 95% Confidence Interval | *p* Value |
|---|---|---|---|
| Any prior sternotomy | 2.98 | 1.51–5.86 | 0.002 |
| Recipient age (per year) | 1.00 | 0.98–1.03 | 0.9 |
| Recipient creatinine (per mg/dL) | 1.80 | 1.33–2.44 | <0.001 |
| Recipient bilirubin (per mg/dL) | 1.15 | 1.04–1.27 | 0.005 |
| Congenital heart disease | 0.40 | 0.05–3.03 | 0.4 |
| No VAD | 1 (Reference) | | — |
| Older generation pulsatile VAD | 0.98 | 0.50–1.95 | 0.9 |
| Newer generation continuous flow VAD | 0.54 | 0.18–1.61 | 0.3 |
| Donor age (per year) | 1.03 | 1.01–1.05 | 0.01 |
| Redo OHT | 0.48 | 0.13–1.76 | 0.3 |
| Ischemic time (per hour) | 1.35 | 1.03–1.78 | 0.03 |

OHT = orthotopic heart transplantation; VAD = ventricular assist device.

1 year mortality associated
- any prior redo
- recipient Cr
- recipient Bili
- Donor age
- ischemic time (per hour)

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# Reoperative Sternotomy and Heart Transplantation

*Table 4. Complications Stratified by the Number of Prior Sternotomies*

| Variable | 0 Prior Sternotomies | 1 Prior Sternotomy | ≥2 Prior Sternotomies | *p* Value[a] |
|---|---|---|---|---|
| Length of stay (days) | 12 [9–17] | 14 [10–24] | 12 [9–25] | 0.001[b] |
| ICU LOS (days) | 4.2 [2.8–7.0] | 5.4 [3.3–9.9] | 7.5 [3.5–16.6] | 0.002[b,c] |
| Cardiac reoperation (%) | 19/159 (12.0%) | 75/187 (40.1%) | 12/35 (34.3%) | <0.001[b,c] |
| Drug-treated infection prior to discharge (%) | 13/257 (5.1%) | 41/263 (15.6%) | 5/58 (8.6%) | <0.001[b] |
| Drug-treated rejection prior to discharge (%) | 22/126 (17.5%) | 16/137 (11.7%) | 1/30 (3.3%) | 0.1 |
| Cerebrovascular accident (%)[d] | 11/275 (4.0%) | 25/295 (8.5%) | 6/61 (9.8%) | 0.049[b] |
| Renal replacement therapy (%) | 16/275 (5.8%) | 49/295 (16.6%) | 14/61 (23.0%) | <0.001[b,c] |
| Intraoperative blood products (units)[e] | 10 [6–14] | 14.5 [10–23] | 15 [10–22.5] | <0.001[b,c] |
| Postoperative blood products (units)[e] | 5.5 [2–12.5] | 8 [2–16] | 9 [6–20] | 0.3 |
| Total perioperative blood products (units)[e] | 18 [11–31] | 26.5 [17–44] | 34 [26–43] | 0.003[b] |

[a] The *p* values were determined by analysis of variance, $\chi 2$, or Fisher exact test. [b] Cohort 1 significantly different than cohort 2. [c] Cohort 1 significantly different than cohort 3. [d] Includes permanent and transient. [e] Includes packed red blood cells, fresh frozen plasma, and platelets.

ICU LOS = intensive care unit length of stay.

Reop assoc. -Increase incidence of:

- LOS and ICU LOS
- reoperation
- infection
- renal failure
- blood transfusion

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George TJ et al. Ann Thorac Surg 2012; 94:2025-32.

# Heart Transplantation for Redos/LVADs

## Prior Sternotomy and Ventricular Assist Device Implantation Do Not Adversely Impact Survival or Allograft Function After Heart Transplantation

Ann C. Gaffey, MD, Emily C. Phillips, BA, Jessica Howard, BS, George Hung, BA, Jason Han, BS, Robert Emery, BS, Lee Goldberg, MD, Michael A. Acker, MD, Y. Joseph Woo, MD, and Pavan Atluri, MD

Division of Cardiovascular Surgery, Department of Surgery, and Division of Cardiovascular Medicine, Department of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania, and Department of Cardiothoracic Surgery, Stanford University, Stanford, California

*Background.* Orthotopic heart transplantation (OHT) remains the gold standard for end-stage heart failure. However, donor availability is severely limited. With a median wait time of 6.6 months and more than 12% of patients waiting 5 or more years, the decision is often made to implant a left ventricular assist device (LVAD) as a bridge to transplantation for medical stabilization. Furthermore, the number of patients who have had at least one prior sternotomy while awaiting transplantation is increasing. Previous studies have indicated reoperative sternotomy as a risk factor for compromised survival. Concerns are specifically focused on perioperative, short-term, and long-term outcomes after LVAD explantation or redo sternotomy before OHT because of increasing operative complexity. We hypothesize that despite the greater technical difficulty caused by LVAD explantation or redo sternotomy, outcomes would not be compromised.

*Methods.* We retrospectively analyzed patients who underwent OHT at the University of Pennsylvania during a 5-year period (2008–2013; n = 253). All patients who underwent a bridge to transplantation LVAD (n = 72) or prior sternotomy (n = 65) were compared with those undergoing OHT with a virgin chest (n = 116). Preoperative, intraoperative, and postoperative variables were analyzed. Short- and long-term survival were studied (minimum follow-up, 6 months).

*Results.* Comorbidities were similar among the groups. There was no difference in donor allograft ischemic time ($p = 0.6$). However, cardiopulmonary bypass time was longer in both bridge to transplantation and prior sternotomy cohorts ($p < 0.00001$). The blood transfusion requirement was higher in bridge to transplantation (12.5 ± 13.7 units; $p = 0.0007$) and prior sternotomy groups (11.7 ± 12.9 units; $p = 0.02$) as compared with the virgin chest cohort (7.1 ± 10.7 units). For bridge to transplantation, both time to extubation (1.0 ± 1.6 versus 0.9 ± 1.0 days; $p = 0.03$) and intensive care unit length of stay (7.0 ± 7.0 versus 6.0 ± 7.0 days; $p = 0.06$) were longer compared with the virgin chest cohort. The same was true for prior sternotomy (extubation time, 1.9 ± 4.4 days; $p = 0.005$; intensive care unit length of stay, 8.0 ± 12.0 days; $p = 0.06$). There was no difference in hospital length of stay ($p = 0.2$). Overall, there was no difference in short- or long-term survival.

*Conclusions.* Implantation of an LVAD as a bridge to transplantation or prior sternotomy does not adversely impact allograft function, hospital length of stay, or long-term outcomes after OHT. The decision to manage a patient medically while awaiting transplantation versus an LVAD bridge strategy should not be limited by concerns of subsequent poor outcomes after transplantation.

(Ann Thorac Surg 2015;100:542–9)


*Table 2. Operative Patient Variables*

| Transplantation Variable | Virgin Chest (n = 116) | Bridge to Transplantation (n = 72) | Prior Sternotomy (n = 65) | *p* Value |
|---|---|---|---|---|
| Allograft ischemic time (min) | 203 ± 116 | 210.7 ± 50 | 205 ± 68 | 0.6 |
| Cardiopulmonary bypass time (min) | 154 ± 32 | 202 ± 68 | 194 ± 56 | <0.00001[a,b] |
| Cross-clamp time (min) | 108 ± 73 | 116 ± 29 | 123 ± 40 | 0.0001[a] |

[a] Cohort 1 significantly different from cohort 2. [b] Cohort 1 significantly different from cohort 3.

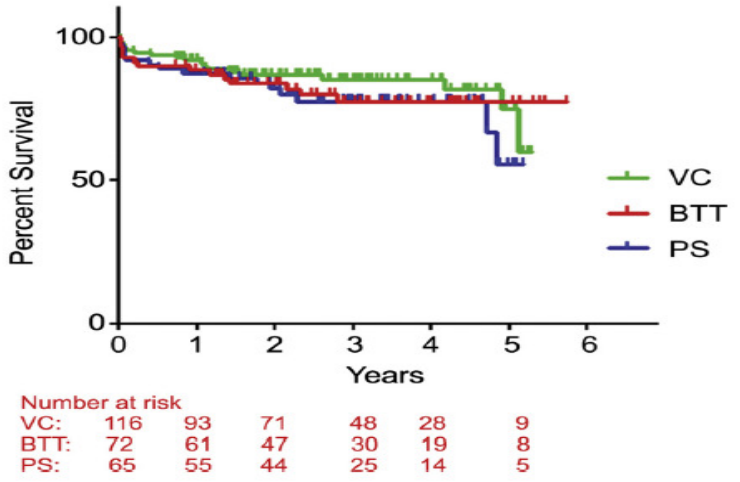



*Fig 2. Kaplan-Meier survival analysis for patients undergoing orthotopic heart transplantation grouped by virgin chest (VC; green line), bridge to transplantation (BTT; red line), and prior sternotomy (PS; blue line).*

**Increased CPB and XC times for redo/LVAD**
**No difference in survival**

Prior Sternotomy and Ventricular Assist Device Implantation Do Not Adversely Impact Survival or
Allograft Function After Heart Transplantation. Gaffey AC et al. Ann Thorac Surg 2015;100:542-9.

# Heart Transplantation for Redos/LVADs

*Table 3. Postoperative Outcomes*

| Outcome | Virgin Chest (n = 116) | Bridge to Transplantation (n = 72) | Prior Sternotomy (n = 65) | *p* Value |
|---|---|---|---|---|
| Postoperative ejection fraction | 0.58 ± 0.17 | 0.58 ± 0.19 | 0.58 ± 0.18 | 0.3 |
| Postoperative IABP support | 6/116 (5%) | 8/72 (11%) | 5/65 (8%) | 0.3 |
| Postoperative VAD support | 2/116 (2%) | 2/72 (3%) | 4/65 (6%) | 0.6 |
| Time to extubation (days)[e] | 0.9 ± 1.0 | 1.0 ± 1.6 | 1.9 ± 4.4 | 0.002[a,b] |
| ICU length of stay (days)[e] | 6.0 ± 7.0 | 7.0 ± 7.0 | 8.0 ± 12.0 | 0.06 |
| Complications | | | | |
| Stroke | 1/116 (0.9%) | 2/72 (2.8%) | 1/65 (1.5%) | 0.2 |
| Gastrointestinal bleed | 1/116 (0.9%) | 1/72 (1.4%) | 4/65 (6.2%) | 0.1 |
| Renal failure | 8/116 (6.9%) | 5/72 (7.5%) | 12/65 (18.5%) | 0.1 |
| Sepsis | 2/116 (1.7%) | 3/72 (4.3%) | 1/65 (1.5%) | 0.1 |
| Bleeding requiring transfusion | 86/116 (74.1%) | 66/72 (88.9%) | 56/65 (86.2%) | 0.03[a,b] |
| Reoperative exploration | 8/116 (6.9%) | 10/72 (13.9%) | 17 (26.6%) | 0.01[a,b,c] |
| Transfusion requirement (units) | 7.1 ± 10.7 | 12.5 ± 13.7 | 11.7 ± 12.9 | 0.0002[a,b] |
| Discharge ejection fraction | 0.69 ± 0.10 | 0.68 ± 0.13 | 0.68 ± 0.08 | 0.6 |
| Length of stay (days)[d] | 20 (24) | 24 (30) | 28 (24) | 0.2 |

[a] Cohort 1 significantly different from cohort 2. [b] Cohort 1 significantly different from cohort 3. [c] Cohort 2 significantly different from cohort 3. [d] Values reported as median (interquartile range).

IABP = intraaortic balloon pump; ICU = intensive care unit; VAD = ventricular assist device.

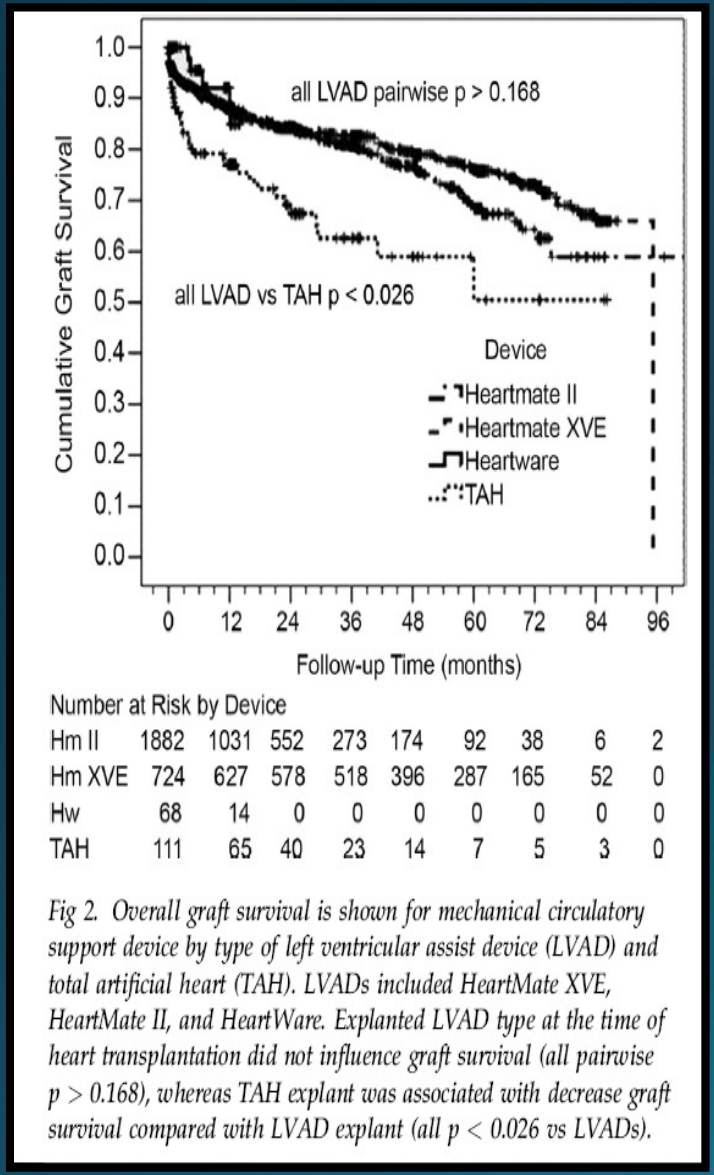
Reop/LVAD vs virgin chest:
- Increase blood transfusion
- Increase ICU stay
- Increase intubation time
- Increase reoperation for bleeding

LVAD vs Reop
NO Different from any other redo

But short and lonterm survival; allograft function; LOS no different than virgin chest

Prior Sternotomy and Ventricular Assist Device Implantation Do Not Adversely Impact Survival or
Allograft Function After Heart Transplantation. Gaffey AC et al. Ann Thorac Surg 2015;100:542-9

# MCS and Heart Transplantation: Donor and Recipient Factors Influencing Graft Survival




Number at Risk by Device

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Hm II | 1882 | 1031 | 552 | 273 | 174 | 92 | 38 | 6 | 2 |
| Hm XVE | 724 | 627 | 578 | 518 | 396 | 287 | 165 | 52 | 0 |
| Hw | 68 | 14 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| TAH | 111 | 65 | 40 | 23 | 14 | 7 | 5 | 3 | 0 |

*Fig 2. Overall graft survival is shown for mechanical circulatory support device by type of left ventricular assist device (LVAD) and total artificial heart (TAH). LVADs included HeartMate XVE, HeartMate II, and HeartWare. Explanted LVAD type at the time of heart transplantation did not influence graft survival (all pairwise $p > 0.168$), whereas TAH explant was associated with decrease graft survival compared with LVAD explant (all $p < 0.026$ vs LVADs).*

Worst early mortality of TAH Compared to LVADs

Mechanical Circulatory Support and Heart Transplantation: Donor and Recipient Factors Influencing Graft Survival. Maltais S et al. Ann Thorac Surg 2013;96:1252-8.

# MCS and Heart Transplantation: Donor and Recipient Factors Influencing Graft Survival

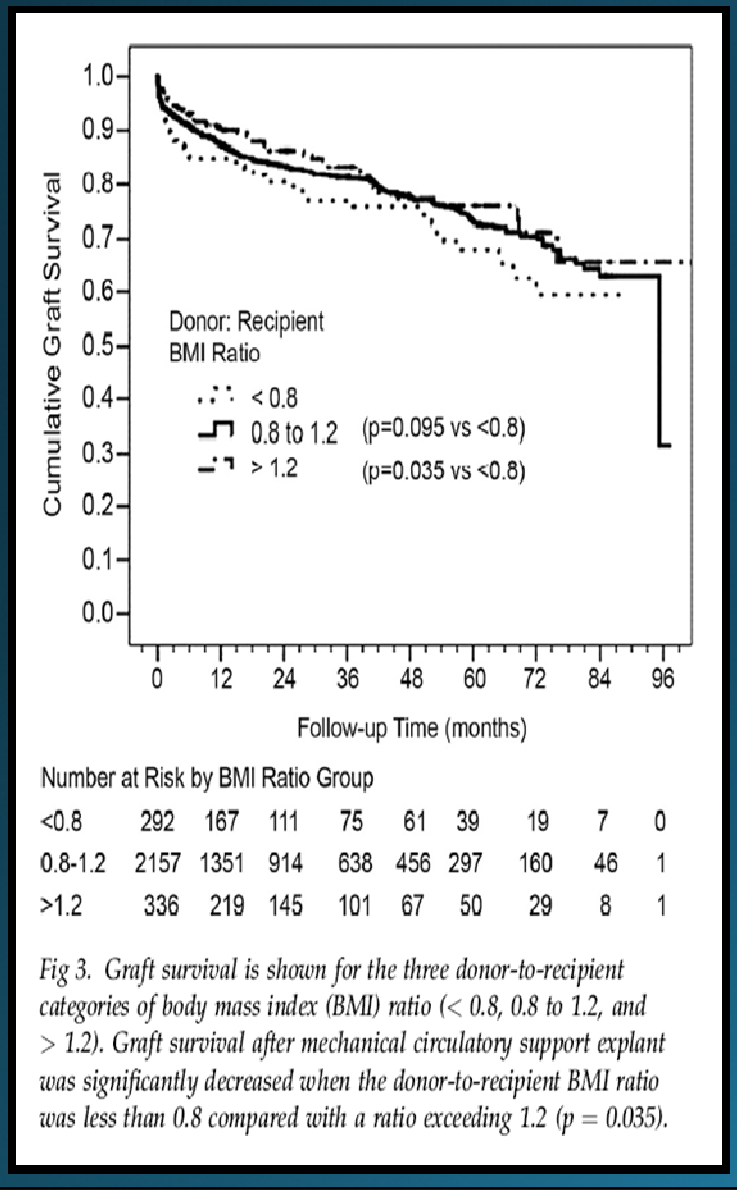



*Fig 3. Graft survival is shown for the three donor-to-recipient categories of body mass index (BMI) ratio (< 0.8, 0.8 to 1.2, and > 1.2). Graft survival after mechanical circulatory support explant was significantly decreased when the donor-to-recipient BMI ratio was less than 0.8 compared with a ratio exceeding 1.2 ($p = 0.035$).*

Donor to Recipient BMI ratio < .8
Increased early mortality

Mechanical Circulatory Support and Heart Transplantation: Donor and Recipient Factors Influencing Graft Survival. Maltais S et al. Ann Thorac Surg 2013;96:1252-8.

# MCS and Heart Transplantation: Donor and Recipient Factors Influencing Graft Survival

*Table 2. Multivariate Model of Donor, Recipient, and Technical Characteristics Associated With Graft Survival After Mechanical Circulatory Support Explantation*

| Donor/Recipient-Related Characteristics | β | *p* Value | HR | 95% CI of β |
|---|---|---|---|---|
| LVAD (ref = TAH) | −0.795 | <0.001 | 0.452 | 0.303–0.673 |
| Recipient PVR, Woods units | 0.045 | 0.013 | 1.046 | 1.010–1.084 |
| Ischemia time, min | 0.002 | 0.001 | 1.002 | 1.001–1.004 |
| Donor-recipient gender matched (ref = not matched) | −0.271 | 0.019 | 0.763 | 0.609–0.956 |
| Donor age, y | 0.016 | <0.001 | 1.016 | 1.007–1.024 |
| Donor-to-recipient BMI ratio | −0.523 | 0.023 | 0.593 | 0.377–0.932 |

BMI = body mass index; CI = confidence interval; HR = hazard ratio; LVAD = left ventricular assist device; PVR = peripheral vascular resistance; TAH = total artificial heart.

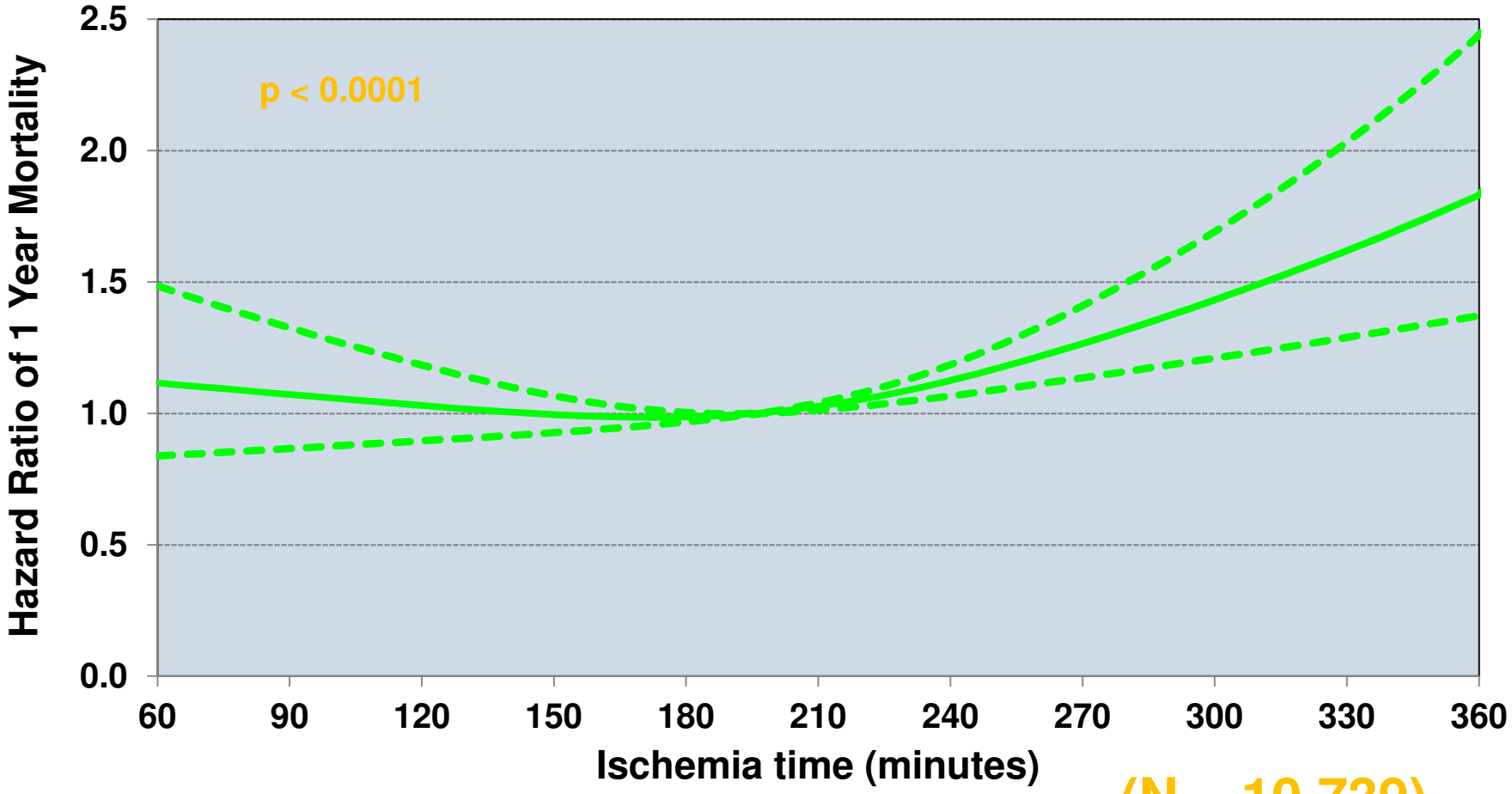
Decreased Survival: TAH; high PVR; Ischemic time; female to male; donor/recipient BMI ratio< .8; donor age

Mechanical Circulatory Support and Heart Transplantation: Donor and Recipient Factors Influencing Graft Survival. Maltais S et al. Ann Thorac Surg 2013;96:1252-8.

# ADULT HEART TRANSPLANTS (2007-6/2012)

## Risk Factors For 1 Year Mortality with 95% Confidence Limits

### Ischemia Time




(N = 10,739)

# Effect of Donor Extended Ischemic Time ( > 5 hours)

Table 9. Primary and Secondary Outcomes Based on Hourly Breakdown of Ischemic Time

| | <4 h | 4–5 h | *P* value | 5–6 h | *P* value[a] |
|---|---|---|---|---|---|
| Mortality, *n* (%) | 25 (14.3%) | 9 (13%) | .801 | 13 (28.9%) | .036 |
| Bypass time, median (range) | 83 (42–383) | 93 (45–190) | .026 | 102 (42–257) | .079 |
| Inotropic support, median (range) | 48 (0–840) | 24 (0–312) | .302 | 48 (0–1272) | .005 |
| Creatinine (mg/dL) | 1.4 (0.2–11.0) | 1.5 (0.7–6.5) | .216 | 1.6 (0.8–5.4) | .839 |
| Packed red blood cells | 8 (0–65) | 8 (0–40) | .706 | 10 (0–56) | .204 |
| Fresh frozen plasma | 6 (0–43) | 6 (0–40) | .744 | 6 (0–70) | .405 |
| Platelets | 30 (0–140) | 40 (0–130) | .889 | 40 (0–180) | .088 |
| Cryoprecipitate | 20 (0–120) | 20 (0–80) | .862 | 28 (0–180) | .055 |
| ICU (d) | 5 (2–64) | 5 (2–23) | .781 | 6 (2–58) | .057 |
| LOS | 20 (6–157) | 21 (2–111) | .639 | 25 (9–328) | .063 |
| Liver dysfunction | 127 (73%) | 58 (85.3%) | .043 | 35 (77.8%) | .305 |
| Renal failure | 51 (29.3%) | 20 (29.4%) | .988 | 14 (31.1%) | .814 |
| Prolonged ventilation support | 51 (29.7%) | 17 (25.8%) | .552 | 21 (51.2%) | .007 |
| Acute rejection | 126 (72.4%) | 49 (71%) | .827 | 30 (66.7%) | .448 |
| Transplant Coronary Artery Disease TCAD | 7 (4%) | 7 (10.1%) | .073 | 3 (6.7%) | .444 |

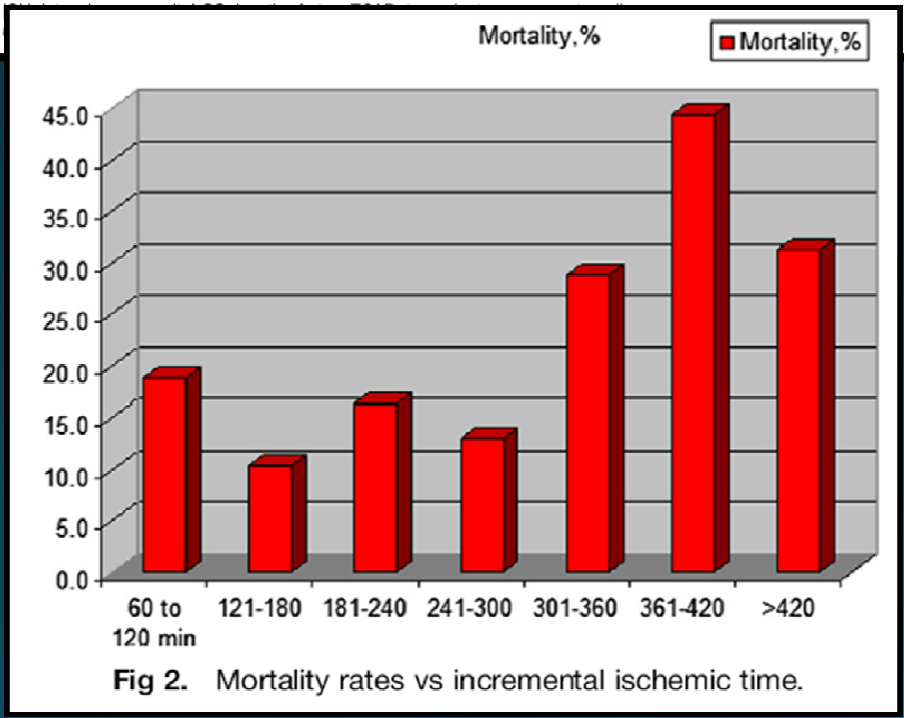



Fig 2. Mortality rates vs incremental ischemic time.

**Increased: mortality; inotropic support; Increased ICU and LOS Prolonged ventilation**

**Importance of being ready to sew of donor arrival to OR**

Outcomes of Adult Orthotopic Heart Transplantation with Extended Allograft Ischemic Time.
Yeen W et al. Transplantation Proceedings 2013;45:2399-2405.

# Effect of Ischemic time on 1 year post OHT Mortality

## Development of a quantitative donor risk index to predict short-term mortality in orthotopic heart transplantation

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**KEYWORDS:**
orthotopic heart transplantation;
outcomes;
database analysis;
UNOS;
organ donor;
risk analysis

**BACKGROUND:** No standard index based on donor factors exists for predicting mortality after orthotopic heart transplantation (OHT). We utilized United Network for Organ Sharing (UNOS) data to develop a quantitative donor risk score for OHT.

**METHODS:** We examined a prospectively collected open cohort of 22,252 patients who underwent primary OHT (1996 to 2007). Of the 284 donor-specific variables, those associated with 1-year (year) mortality (exploratory $p$-value $< 0.2$) were incorporated into a multivariate (MV) logistic regression model. The final model contained donor factors that improved the explanatory power (by pseudo-R2, area under the curve and likelihood ratio test). A quantitative donor risk score was created using odds ratios (ORs) from the final model. For external validity, a cross-validation strategy was employed whereby the score was generated using a randomly generated subset of cases ($n$ = 17,788) and then independently validated on the remaining patients ($n$ = 4,464).

**RESULTS:** A 15-point scoring system incorporated 4 variables: ischemic time; donor age; race mismatching; and blood urea nitrogen (BUN)/creatinine ratio. Derivation and validation cohort scores ranged from 1 to 15 and 1 to 12, respectively (mean 4.0 ± 2.1 for each). Each increase of 1 point increased the risk of 1-year death by 9% (OR = 0.09 [1.07 to 0.12]) in the derivation cohort and 13% (OR = 0.13 [1.08 to 0.18]) in the validation cohort (each $p < 0.001$). The odds of 1-year mortality by increments of 3 points were: 0 to 2 points (reference); 3 to 5 points (OR = 0.25 [1.12 to 0.40], $p < 0.001$); 6 to 8 pts (OR = 0.77 [1.56 to 2.02], $p < 0.001$); and 9 to 15 points (OR = 1.92 [1.54 to 2.39], $p < 0.001$). Donor risk score was predictive for 30-day mortality (OR = 0.11 [1.08 to 0.14], $p < 0.001$) and 5-year cumulative mortality (OR = 0.11 [1.09 to 0.13], $p < 0.001$).

**CONCLUSIONS:** We present a novel donor risk index for OHT predicting short- and long-term mortality. This donor risk score may prove valuable for donor heart allocation and prognosis after OHT.

J Heart Lung Transplant 2012;31:266–73



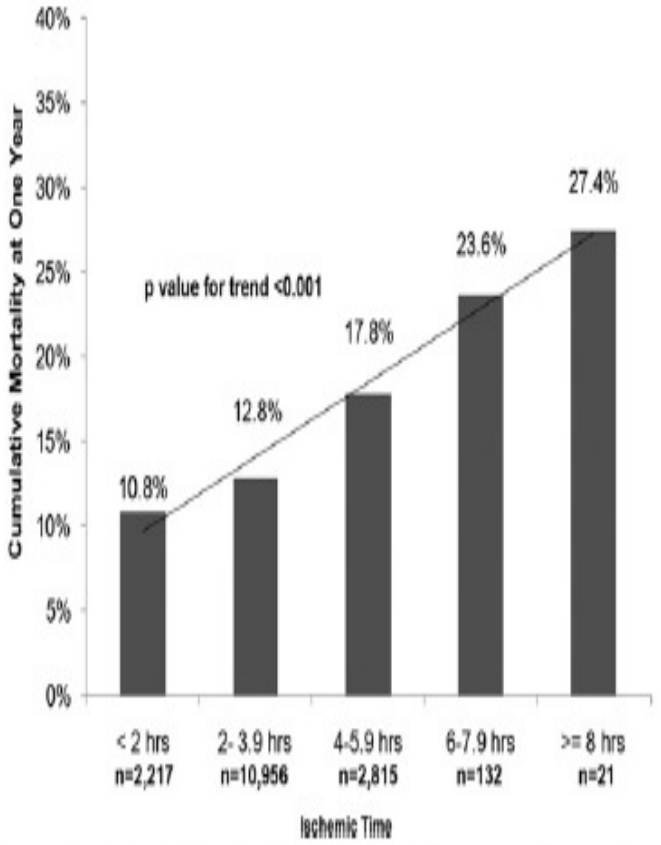


**Figure 1** Cumulative incidence of recipient mortality at 1-year post-OHT by categories of ischemic time.

Development of a quantitative donor risk index to predict short-term mortality in orthotopic heart transplantation..
Weiss ES et al. J Heart Lung Transplant 2012;31:266-73.

# Risk Factors for Early Death in BTT Continuous Flow VAD Patients (UNOS)

*Table 2. Results of Cox Regression Analysis*[a]

| Variable | HR (95% CI) | *p* Value |
|---|---|---|
| Age > 60 years | 1.70 (1.01–2.85) | 0.05 |
| GFR < 60 mL/min | 1.87 (1.15–3.06) | 0.01 |
| Infection requiring IV antibiotics | 1.14 (0.62–2.08) | 0.7 |
| Serum bilirubin > 4 mg/mL | 2.55 (1.08–6.30 | 0.02 |
| Mechanical ventilation pre-op | 4.91 (1.67–14.43) | 0.004 |
| HLA mismatch | 0.49 (0.30–0.81) | 0.005 |
| Donor age | 1.02 (1.01–1.04) | 0.03 |
| Ischemic time > 4 hours | 1.90 (1.16–3.12) | 0.01 |
| Average annual center volume | 0.92 (0.87–0.98) | 0.01 |
| Race | | |
| Caucasian | Reference | . . . |
| African American | 2.24 (1.23–4.07) | 0.008 |
| Hispanic | 2.60 (1.13–5.97) | 0.02 |
| Indication | | |
| Idiopathic cardiomyopathy | Reference | . . . |
| Ischemic | 1.48 (0.85–2.57) | 0.2 |

[a] Regression included transplant year as continuous variable to adjust for time trend.

CI = confidence interval; GFR = glomerular filtration rate; HLA = human leukocyte antigen; HR = hazard ratio; IV = intravenous.

**Increased mortality:**
**ischemic time > 4 hrs**
**Hazard ratio 1.9**

Risk Factors for Early Death in Patients Bridged to Transplant With Continuous-Flow Left Ventricular Assist Devices.
Arnaoutakis GJ et al. Ann Thorac Surg 2012;93-1549-55.

# Effect of Warm Ischemic Time on Early Mortality

## Sew heart in < 80 min

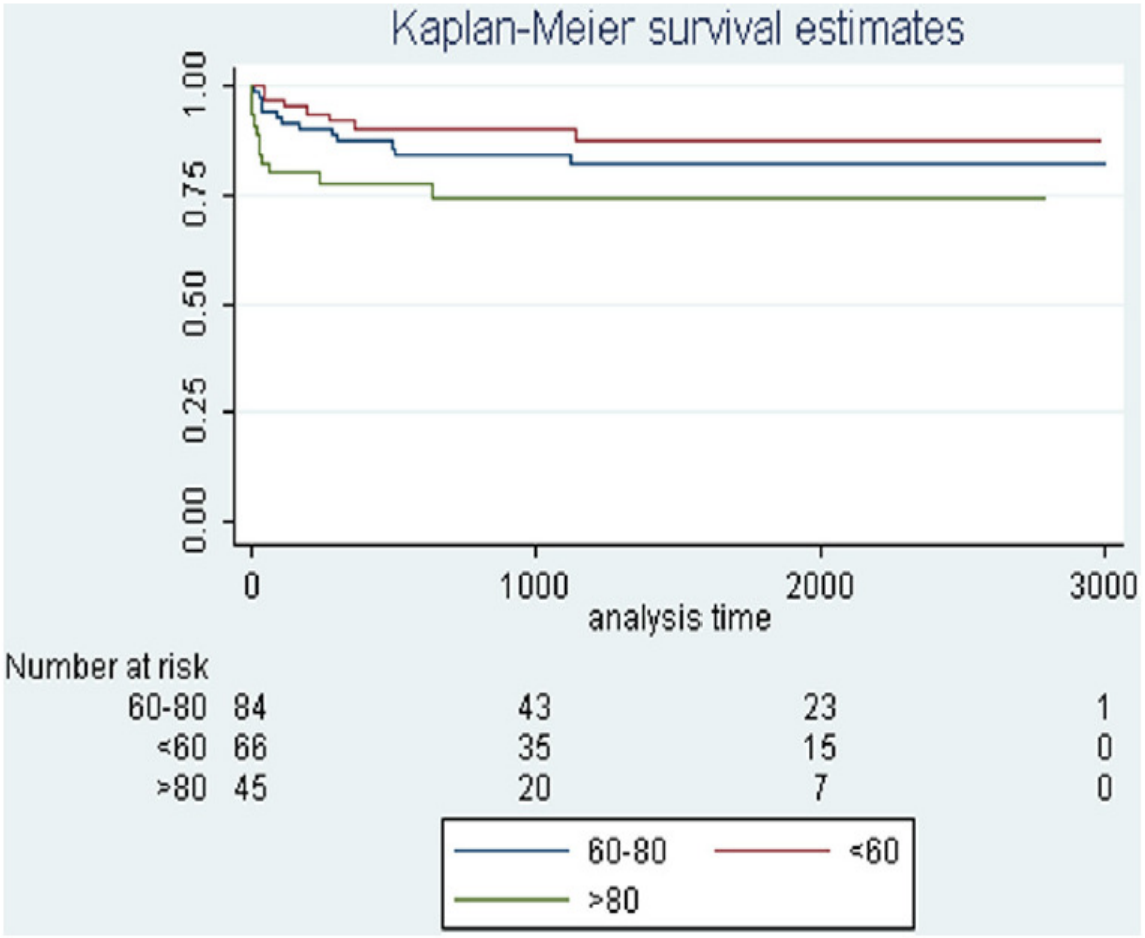


**Fig 1.** Kaplan-Meier survival for the three ischemia times (<60, 60–80, >80 min).

Impact of Warm Ischemia Time on Survival After Heart Transplantation.
Marasco SF et al.
Transplantation Proceedings, 44 (2012) 1385-1389

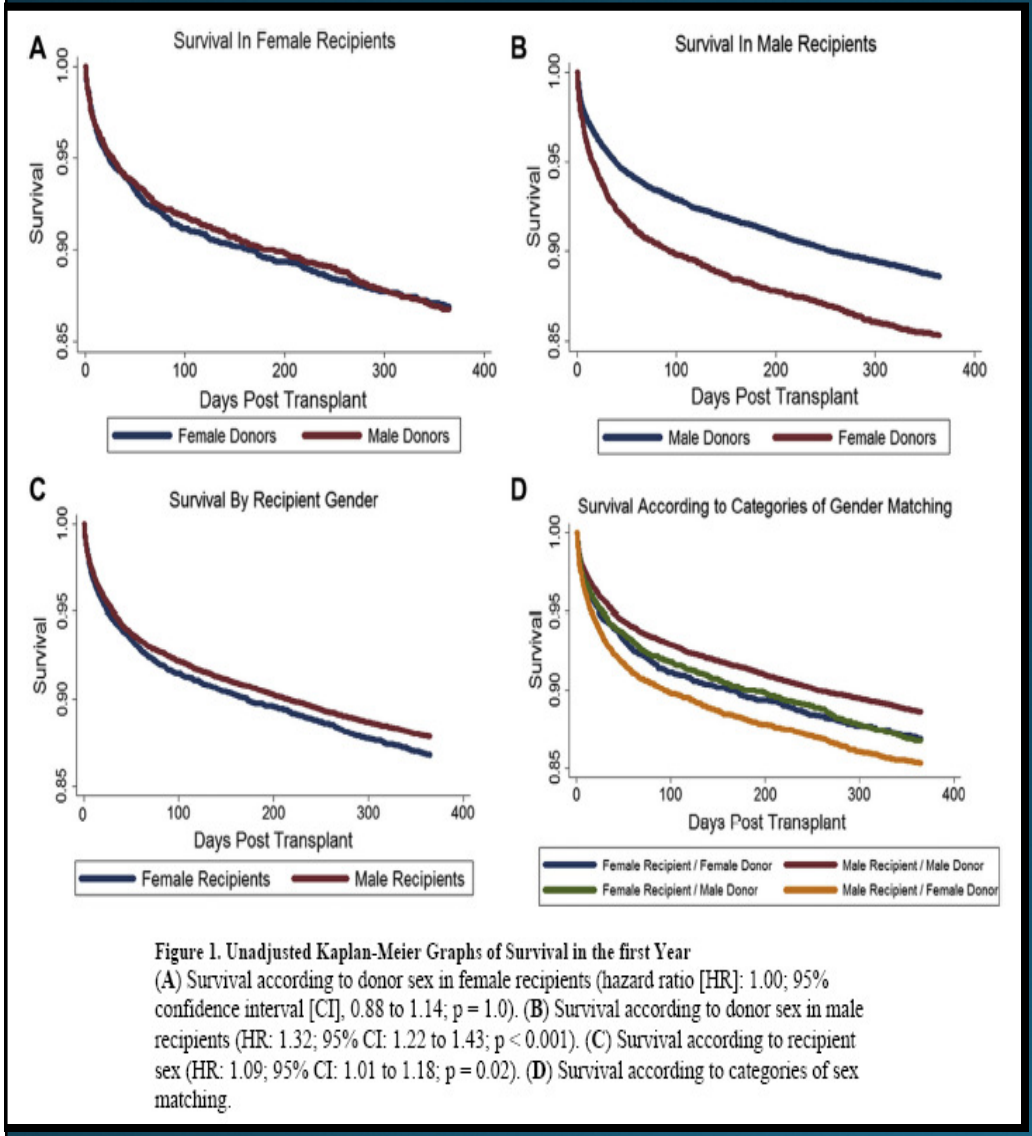


**Figure 1. Unadjusted Kaplan-Meier Graphs of Survival in the first Year**
(**A**) Survival according to donor sex in female recipients (hazard ratio [HR]: 1.00; 95% confidence interval [CI], 0.88 to 1.14; p = 1.0). (**B**) Survival according to donor sex in male recipients (HR: 1.32; 95% CI: 1.22 to 1.43; p < 0.001). (**C**) Survival according to recipient sex (HR: 1.09; 95% CI: 1.01 to 1.18; p = 0.02). (**D**) Survival according to categories of sex matching.

**Female donor into male recipient worst early survival**
**Effect magnified by weight discrepency**

Cardiac Size and Sex Matching in Heart Transplantation: Size Matters in Matters of Sex and the Heart. Reed RM et al. JACC Heart Fail. 2014 February 1; 2(1) 73-83.

# Vasoplegia Syndrome

## Pre-operative risk factors and clinical outcomes associated with vasoplegia in recipients of orthotopic heart transplantation in the contemporary era

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**KEYWORDS:**
heart transplantation;
vasoplegia;
risk factors

**BACKGROUND:** Patients who underwent orthotopic heart transplant (OHT) can develop vasoplegia, which is associated with high mortality and morbidity. Herein we examine the pre-operative risk in OHT recipients at our institution.

**METHODS:** We reviewed peri-operative data from 311 consecutive adult patients who underwent OHT between January 2003 and June 2008. Vasoplegia was defined as persistent low systemic vascular resistance, despite multiple intravenous pressor drugs at high dose, between 6 and 48 hours after surgery.

**RESULTS:** In our cohort of 311 patients, 35 (11%) patients developed vasoplegia syndrome; these patients were more likely to be UNOS Status 1A, with a higher body surface area (1.8 ± 0.25 vs 1.63 ± 0.36, $p = 0.0007$), greater history of thyroid disease (38.2% vs 18.5%, $p = 0.0075$) and a higher rate of previous cardiothoracic surgery (79% vs 48%, $p = 0.0006$). Pre-operatively, they were more frequently treated with aspirin (73% vs 48%, $p = 0.005$) and mechanical assist devices (ventricular assist devices [VADs]: 45% vs 17%, $p < 0.0001$; total artificial hearts: 8.6% vs 0%, $p < 0.0001$), and less treated with milrinone (14.7% vs 45.8%, $p = 0.0005$). Bypass time (118 ± 37 vs 142 ± 39 minutes, $p = 0.0002$) and donor heart ischemic time (191 ± 46 vs 219 ± 51 minutes, $p = 0.002$) were longer, with higher mortality (3.2% vs 17.1%, $p = 0.0003$) and morbidity in the first 30 days after transplant. In the multivariate analysis, history of thyroid disease (odds ratio [OR] = 2.7, 95% CI 1.0 to 7.0, $p = 0.04$) and VAD prior to transplant (OR = 2.8, 95% CI 1.07 to 7.4, $p = 0.03$) were independent risk factors for development of vasoplegia syndrome.

**CONCLUSIONS:** High body mass index, long cardiopulmonary bypass time, prior cardiothoracic surgery, mechanical support, use of aspirin, and thyroid disease are risk factors associated with development of vasoplegia syndrome.

J Heart Lung Transplant 2012;31:282–7

**Results in Increase mortality**

Increased incidence –
reop; MCS; prolonged CPB; hepatic dysfunction

??increased with continuous flow L VADs

Pre-operative risk factors and clinical outcomes associated with vasoplegia in recipients of orthotopic heart transplantation in the contemporary era. Patarroyo et al. J Heart Lung Transplant. 2012 Mar;31(3):282-7

# Vasoplegia Syndrome

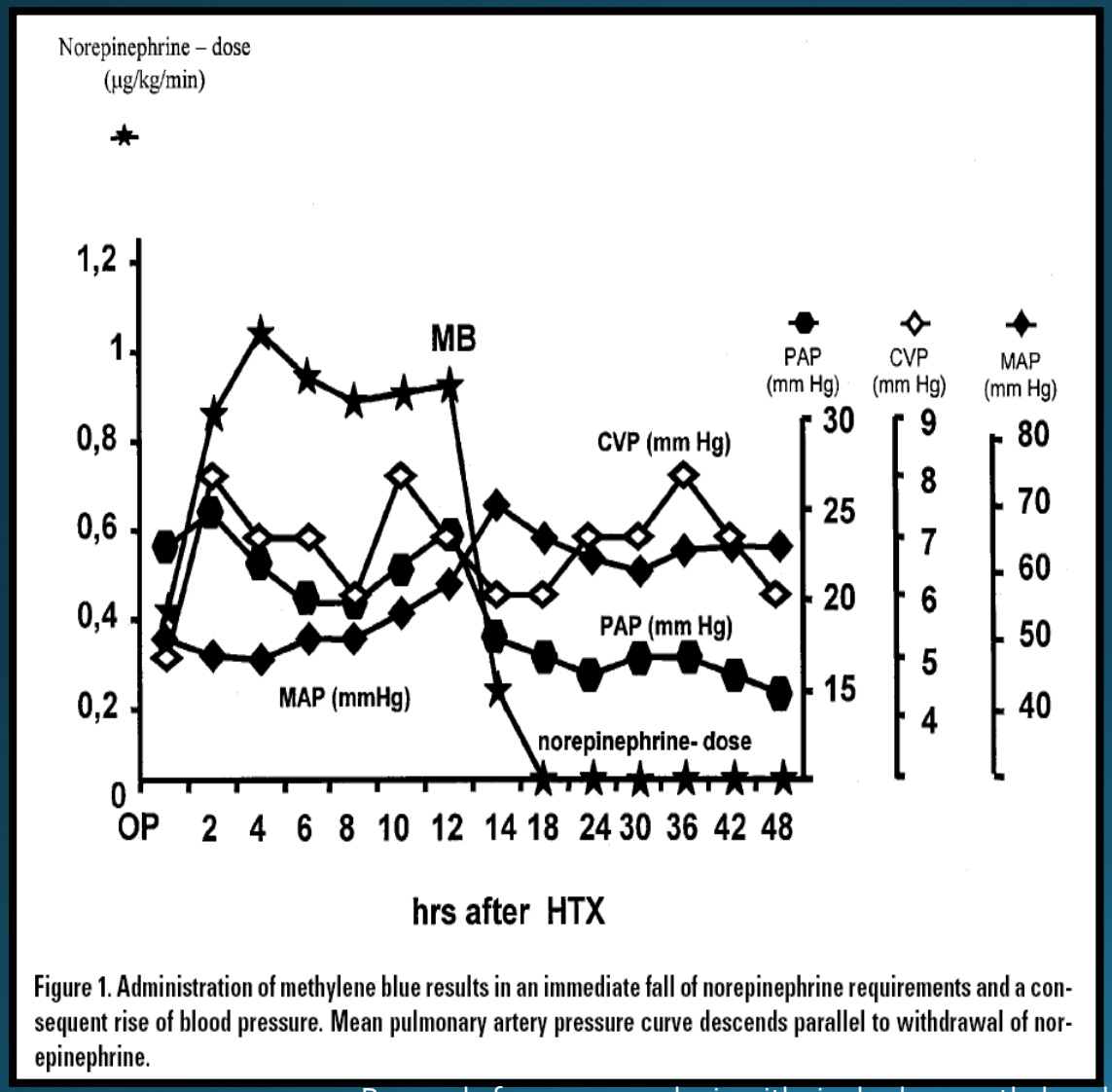


Figure 1. Administration of methylene blue results in an immediate fall of norepinephrine requirements and a consequent rise of blood pressure. Mean pulmonary artery pressure curve descends parallel to withdrawal of norepinephrine.

**Low dose vasopressin**
**Methylene blue-may need to be given prior to CPB**

Reversal of severe vasoplegia with single-dose methylene blue after heart transplantation.
Kofidis T et al. J Thorac Cardiovasc Surg. 2001 Oct;122(4):823-4

# Primary Graft Dysfunction

- Accounts for 36% of early deaths
- Inotropes-Epi; Milrinone; T4; Vaso/Neo/Levo
- NO vs Flolan
- IABP
- Temporary RVAD/LVAD/BVAD
- ECMO
  - Need to ensure the LV is vented and decompressed
  - Reverse anticoagulation
  - Chest left usually left open
  - Usually cardiac function improves within 2-3 days

# Primary Graft Dysfunction Requiring ECMO

*3.3. One-year mortality*

Overall 1-year mortality was 30% (120 patients). One-year mortality for patients, who did not experience PGF, was 21%

Table 3. Multivariate analysis.

| | OR | 95% CI | p |
|---|---|---|---|
| PGF occurrence | | | |
| Recipient | | | |
| Age ≥60 years | 2.11 | 1.16–3.87 | 0.01 |
| MCS dependent | 2.65 | 1.47–4.76 | <0.01 |
| Donor | | | |
| Cause of death: trauma | 2.45 | 1.44–4.16 | <0.01 |
| LVEF <55% | 2.72 | 1.19–6.22 | 0.02 |
| Mean norepinephrine dose[a] | 2.02 | 1.19–3.44 | <0.01 |
| Ischemic time[b] | 1.01 | 1.01–1.02 | <0.01 |
| PGF occurrence (sensitivity analysis)[c] | | | |
| Donor | | | |
| Cause of death: trauma | 3.21 | 1.61–6.37 | <0.01 |
| Mean norepinephrine dose[a] | 2.87 | 1.50–5.45 | <0.01 |
| Ischemic time[b] | 1.01 | 1.1–1.02 | <0.01 |

[a] OR unit = 1 mcg/kg/min.
[b] OR unit = 1 min.
[c] Sensitivity analysis carried on 253 patients with a known PVR value.

Recipient age > 60
MCS

Donor-death due to trauma
LVEF<55%; high NorEpi;
Ischemic Time

Predictive risk factors for primary graft failure requiring temporary extra-corporeal membrane oxygenation support after cardiac transplantation in adults.
D'Alessandro CD et al. European Journal of Cardio-thoracic Surgery 40 (2011) 962-970

# High PVR/RV Dysfunction

- Mortality increased if PVR > 3
  - Penn exclusion to listing
- Influences Choice of Donor
  - Oversize donor
  - Male into male
- NO vs Flolan
- Wean inotropes slowly
- Sidenafil
- ECMO/temporary RVAD

# Effect of Pre-LVAD PVR on Heart Transplant Outcome

**(presented AATS Seattle April 2015 --Columbia -Naka)**

- 256 potential OHT candidates underwent CF-LVAD implantation between March 2004 and December 2013 at NY-Presbyterian Hospital/Columbia University Medical Center.

- Pre-LVAD right heart catheterization data were available for 227 patients.

- Low PVR group (lPVR): PVR ≤ 3 Wood units (n = 106)
- Medium PVR group (mPVR): 3 < PVR < 5 Wood units (n = 76)
- High PVR group (hPVR): PVR ≥ 5 Wood units (n = 45)
- PVR used was after optimization

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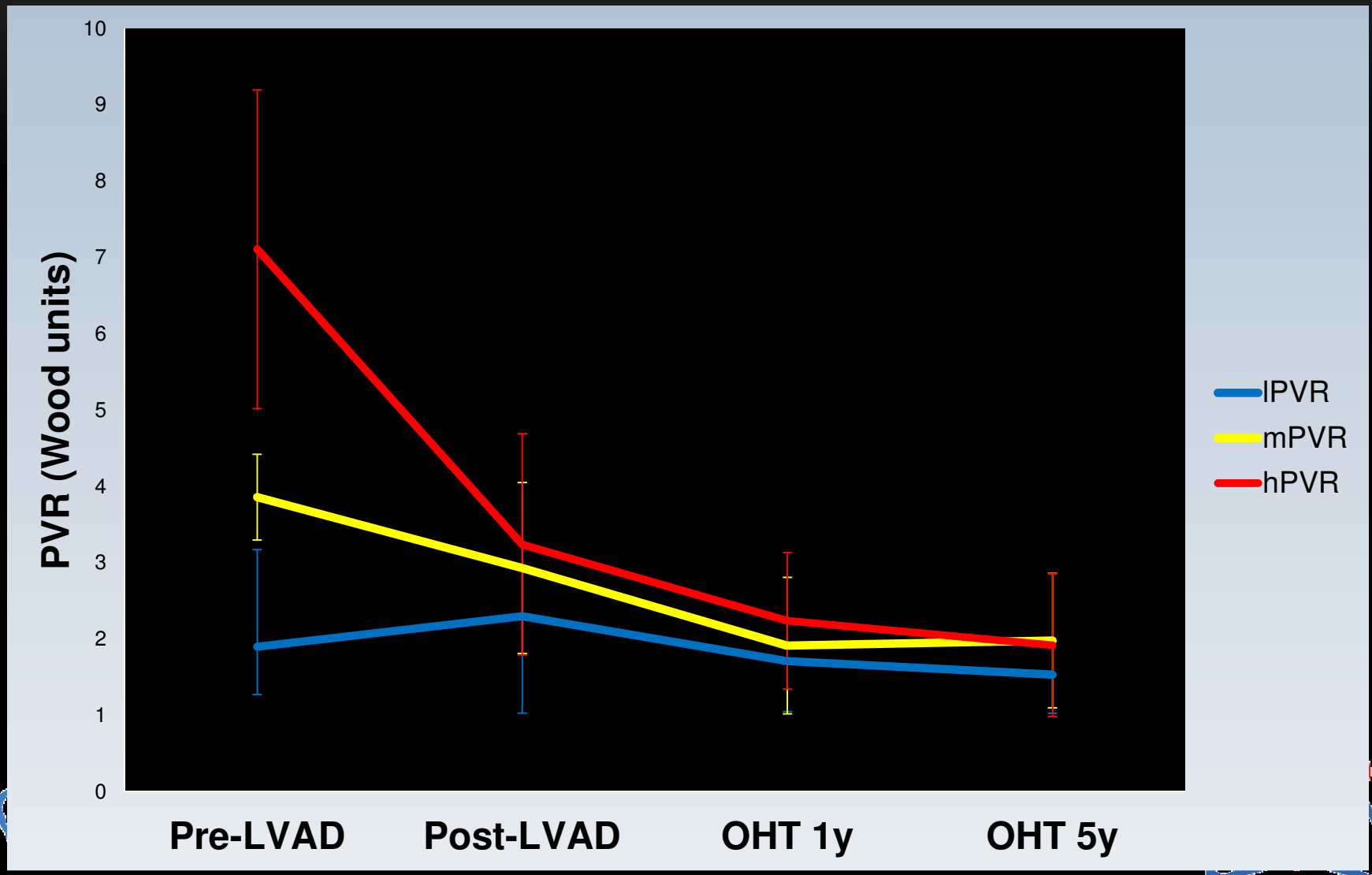
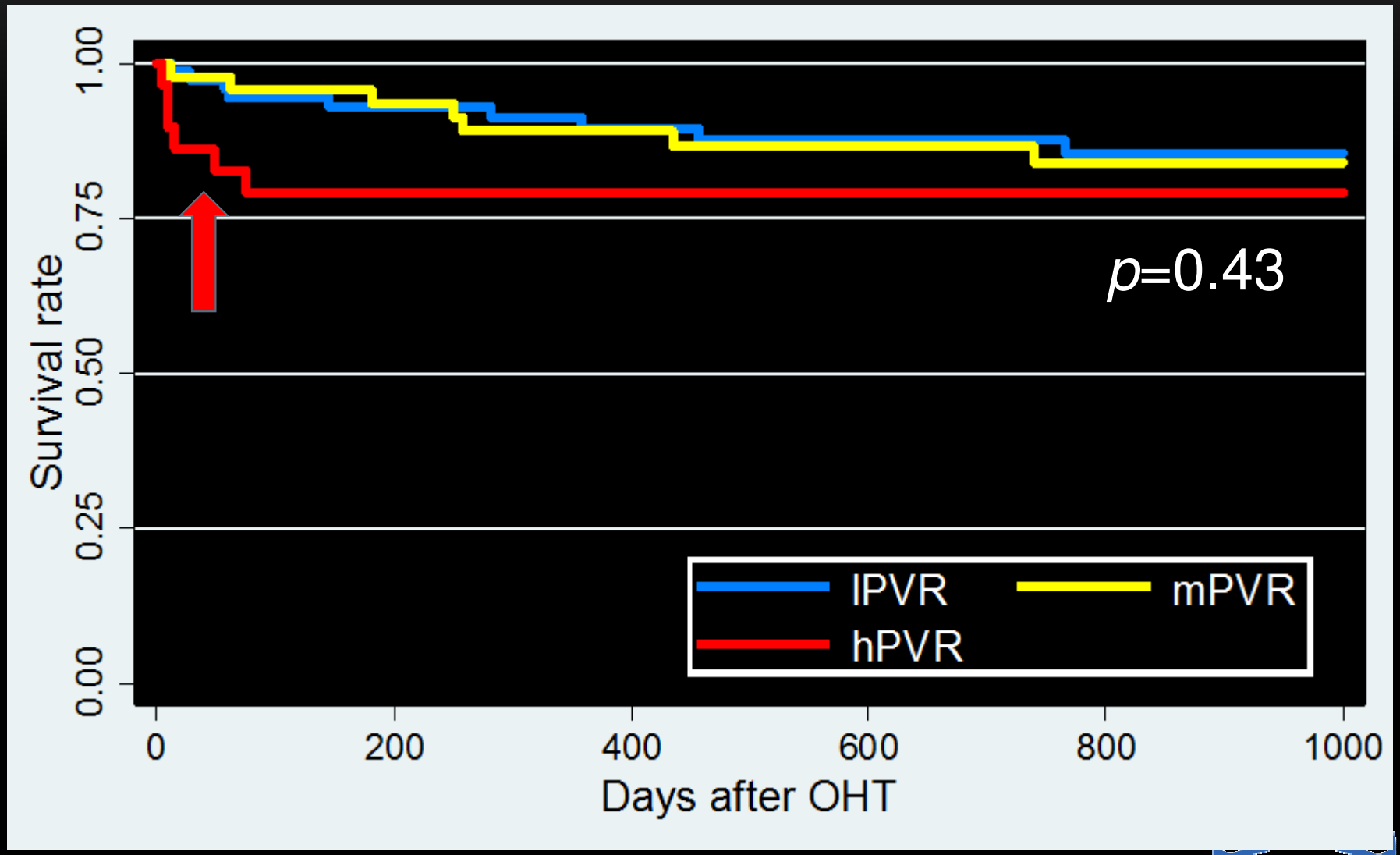
# Changes over time in pulmonary vascular resistance



# Intra- and postoperative data for OHT

| Variables | All patients (n = 148) | IPVR (n = 72) | mPVR (n = 47) | hPVR (n = 29) | p value |
|---|---|---|---|---|---|
| **Intraoperative data** | | | | | |
| **CPB time (min)** | 176 ± 54 | 175 ± 50 | 173 ± 43 | 184 ± 75 | 0.94 |
| **Ischemic time (min)** | 189 ± 51 | 187 ± 53 | 189 ± 46 | 195 ± 52 | 0.88 |
| **Postoperative data** | | | | | |
| **iNO usage** | 49 (33.6%) | 25 (35.2%) | 12 (25.5%) | 12 (42.9%) | 0.28 |
| **In-hosp mortality** | 13 (8.8%) | 5 (6.9%) | 2 (4.3%) | 6 (20.7%) | **0.036** |
| **HD/CVVH** | 24 (16.4%) | 8 (11.3%) | 11 (23.9%) | 5 (17.2%) | 0.20 |
| **Primary graft failure** | 12 (8.2%) | 7 (9.9%) | 1 (2.2%) | 4 (13.8%) | 0.16 |

# Kaplan-Meier survival curve after OHT



# Logistic regression of 30-day post-OHT mortality

| variables | Univariate analysis | | | Multivariate analysis | | |
|---|---|---|---|---|---|---|
| | OR | 95% CI | p Value | OR | 95% CI | p Value |
| **Age** | 1.03 | 0.96 to 1.10 | 0.44 | | | |
| **Sex (Male)** | 1.40 | 0.17 to 11.6 | 0.76 | | | |
| **BSA** | 0.72 | 0.036 to 14.6 | 0.83 | | | |
| **ICM** | 0.77 | 0.15 to 3.97 | 0.76 | | | |
| **HTN** | 2.98 | 0.58 to 15.4 | 0.19 | 2.70 | 0.52 to 13.96 | 0.24 |
| **HM II (vs. others)** | 0.46 | 0.09 to 2.39 | 0.36 | | | |
| **Pre-LVAD MCS** | 1.91 | 0.23 to 15.9 | 0.55 | | | |
| **Pre-LVAD PVR > 5** | **5.88** | 1.32 to 26.3 | 0.02 | **5.53** | 1.23 to 24.8 | **0.03** |
| **Post-LVAD PVR>3** | 0.58 | 0.05 to 6.35 | 0.65 | | | |

# CONCLUSION

- LVAD therapy significantly reduced PVR even in patients with severely elevated PVR.
- Early post-OHT mortality in LVAD patients with pre-existing high PVR was high.
- However, their long-term survival appeared comparable to that for patients with lower PVR.
- Need to oversize donors for VAD pts with initially HPVR ( > 5) even when PVR at time of Tx is <3 ?

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# Intraop Risk Factors for Heart Transplantation-Special Considerations

- Importance of management of redo operation
  - LVAD/adult congenital operation in efficient and safe fashion
  - Safe entry and cannulation
- Proper matching of donor with recipent-size; gender; PVR; extended donor criteria
- Minimize Ischemic Time < 4-5 hrs