# Composite risk factors predict survival after transplantation for congenital heart disease

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**Objective(s):** Previous studies have shown that individual risk factors are poor predictors of mortality after heart transplantation in patients with congenital heart disease. We developed composite risk factor groups to better predict mortality after cardiac transplantation.

**Methods:** We conducted a cross-sectional retrospective analysis of all heart transplants performed for congenital heart disease at a single congenital heart transplant center between 1996 and 2011. Patient, procedural, and hospital course data were obtained through a review of medical records. Univariate analyses were performed using the Fisher exact test for categorical data and the Mann-Whitney *U* test for continuous variables. Overall mortality was examined using Kaplan-Meier estimates for univariate analysis and Cox regression analysis for multivariate analysis. A comparison of patients with functional single ventricles (SVs) versus biventricular (BV) hearts was performed. Mean follow-up duration for the whole group was 51 ± 43 months (median, 43 months).

**Results:** Forty-six patients underwent heart transplantation during the study period. Mean age at transplant was 9.0 ± 9.1 years; 45% (n = 21) were in the SV group and 55% (n = 25) were in the BV group. The SV group had significantly more previous sternotomies ($P = .006$) and longer bypass times (266 ± 78 vs 207 ± 64 minutes; $P = .001$). High panel-reactive antibody levels (>10%) were also more common in the SV group (38% vs 13%; $P = .08$). Overall hospital mortality was 4.3% (n = 2, both SVs). There was no significant difference in operative mortality (10% SV vs 0% BV; $P = .20$) or major morbidity (33% SV vs 44% BV; $P = .51$) between the 2 groups. High-risk groups identified by univariate analysis were patients with an SV diagnosis + dialysis ($P < .0005$), SV + mechanical assist device (VAD)/extracorporeal membrane oxygenation (ECMO) ($P = .026$), or VAD/ECMO + renal insufficiency ($P = .006$)/VAD/ECMO + dialysis ($P < .0005$), and SV + reoperation ($P = .016$). By multivariate analysis, preoperative renal insufficiency ($P = .038$) and the composite SV + dialysis ($P = .005$) were predictors of overall mortality. Although survival at 2 years was lower in the SV cohort (73% vs 96%; $P = .16$), this benefit was not apparent (63% vs 69%) at late follow-up.

**Conclusions:** Preoperative renal insufficiency and SV + dialysis are strong predictors of overall mortality and identify high-risk congenital heart transplant recipients. Although individual risk factors may not predict survival, a composite of factors may be more useful in identifying the high-risk recipient. (J Thorac Cardiovasc Surg 2013;146:888-93)



Rapid strides have been made in the surgical reconstruction and postoperative care of patients with congenital heart disease (CHD), particularly neonates with complex defects.[1] Despite these advances, many children with complex CHD develop end-stage heart failure. For some of these patients, heart transplantation is the only therapeutic option. These patients have commonly undergone multiple procedures and are known to be at a higher risk for postoperative death and complications after transplantation.[2,3] The supply of pediatric organ donors is limited by strict donor-recipient weight criteria, and is steadily decreasing,[4] which makes optimal organ allocation critical for the maintenance of viable pediatric heart transplant programs.

The ability to reliably identify patients at high risk is essential to optimize pediatric donor heart allocation. Individual risk factors that are associated with poor outcomes after heart transplant have been identified.[5] However, it has been demonstrated that risk factors taken individually are unable to reliably predict mortality after heart transplant.[6] A combination of risk factors may be more accurate predictors of mortality after pediatric heart

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**Abbreviations and Acronyms**
BIVAD = biventricular assist device
BV = biventricular
CHD = congenital heart disease
ECMO = extracorporeal membrane oxygenation
PRA = panel-reactive antibody
SV = single ventricle
UNOS = United Network of Organ Sharing
VAD = ventricular assist device

transplant.[6] Also, risk factors shown to be predictive of outcome in multicenter studies do not seem to be accurate predictors in single-center studies.[2]

We evaluated the outcomes of patients receiving a heart transplant at a single center with the diagnosis of CHD. We assessed established risk factors both individually and in combination for their association with and ability to predict outcome.

## METHODS

### Study Population

We conducted a cross-sectional retrospective analysis of all heart transplants performed for congenital heart disease at the Medical University of South Carolina (Charleston) Congenital Heart Transplant Center between 1996 and 2011. This study received approval for exemption from the Institutional Review Board of the Medical University of South Carolina. Patient, procedural, and hospital course data were obtained through a review of medical records.

*Renal insufficiency* was defined as a preoperative creatinine level of 1.5 mg/dL or higher and/or a need for preoperative dialysis. To identify recipients who had a significant postoperative inotrope requirement, *postoperative inotropic support* was defined as inotropes other than milrinone and dopamine more than 48 hours posttransplant and was quantified in days posttransplant for comparison between single-ventricle (SV) and biventricular (BV) groups. This definition was selected because many heart transplant recipients in our program remain on low-dose dopamine for 3 to 4 days and milrinone for the first postoperative week. *Postoperative bleeding* was defined as the need for re-exploration. *Postoperative infection* was defined as a positive blood culture or deep sternal wound infection requiring operative intervention. *Postoperative renal failure* was defined as a creatinine level increase of 1.5 mg/dL or higher, with or without renal replacement therapy required in the first postoperative week.

To compare morbidity rates in the SV versus BV group, we defined *major postoperative morbidity* as a composite of postoperative cerebrovascular accident, important postoperative bleeding, renal failure, postoperative infection, or grade 3 rejection. Mechanical support patients received extracorporeal membrane oxygenation (ECMO) and/or ventricular assist device (VAD) support before transplantation.

### Data Analysis

Univariate analyses were performed using the Fisher exact test for categorical data and the Mann-Whitney *U* test for continuous variables. Mortality was examined at 1 month, 1 year, 3 years, 6 years, and overall using Kaplan-Meier estimates for univariate analysis and Cox regression analysis for multivariate analysis. A comparison of patients with functional SVs versus BVs was performed. Mean follow-up duration for the whole group was 51 ± 43 months (median, 43 months).

## RESULTS

Forty-six patients underwent heart transplantation during the study period. Preoperative risk factors were evaluated for the whole group (Table 1), and a comparison was performed between SV and BV groups (Table 2). Mean age at transplant was 9.0 ± 9.1 years.

A total of 45% (n = 21) were in the SV group and 55% (n = 25) were in the BV group. High panel-reactive antibody (PRA) levels (>10%) were more common in the SV group (38% vs 13%; $P = .08$). The SV group had significantly more previous sternotomies ($P = .006$) and longer bypass times (266 ± 78 vs 207 ± 64 minutes; $P = .001$). Eight patients received preoperative mechanical support. Three patients in each group had ECMO. Two patients in the BV group had Abiomed BVS 5000

**TABLE 1. Patient demographics and risk factors in single-ventricle versus biventricular congenital heart transplant patients**

| Variable | SV (n = 21) | BV (n = 25) | *P* value |
|---|---|---|---|
| Age, y | | | |
| Mean ± SD | 8 ± 9 | 10 ± 9 | .208 |
| Median | 3 | 9 | |
| Range | 0.05-28 | 0.42-35 | |
| Male sex | 13 (62) | 15 (60) | 1.000 |
| Race | | | |
| White | 12 (57) | 14 (56) | .403 |
| Black | 9 (43) | 9 (36) | |
| Other | 0 (0) | 2 (8) | |
| Recipient weight, kg | | | |
| Mean ± SD | 26 ± 23 | 31 ± 24 | .396 |
| Median | 12 | 30 | |
| Range | 4-69 | 3-95 | |
| Donor weight, kg | | | |
| Mean ± SD | 27 ± 21 | 41 ± 27 | .060 |
| Median | 18 | 32 | |
| Range | 6-63 | 7-88 | |
| Donor/recipient weight ratio | | | |
| Mean ± SD | 1.5 ± 0.5 | 1.6 ± 0.6 | .308 |
| Median | 1.5 | 1.8 | |
| Range | 0.8-2.5 | 0.7-3.0 | |
| Previous cardiac procedure | 20 (95) | 15 (60) | .006 |
| Total bilirubin, mg/dL | | | |
| Mean ± SD | 1.6 ± 1.3 | 1.7 ± 2.7 | .365 |
| Median | 1.1 | 0.9 | |
| Range | 0.3-4.8 | 0.4-13.4 | |
| Creatinine, mg/dL | | | |
| Mean ± SD | 0.7 ± 0.8 | 0.7 ± 0.5 | .602 |
| Median | 0.5 | 0.6 | |
| Range | 0.3-3.8 | 0.1-1.7 | |
| Ventilator dependent | 6 (29) | 8 (32) | 1.000 |
| Inotrope dependent | 14 (67) | 14 (56) | .551 |
| ECMO/VAD dependent | 3 (14) | 6 (24) | .478 |
| Dialysis dependent | 2 (10) | 1 (4) | .585 |
| PRA >10% | 8 (38) | 3 (13) | .081 |

Data are given as number (%) unless otherwise indicated. *SV*, Single ventricle; *BV*, biventricular; *ECMO*, extracorporeal membrane oxygenation; *VAD*, ventricular assist device; *PRA*, panel-reactive antibody; *SD*, standard deviation.

**TABLE 2. Intraoperative and postoperative events in single-ventricle and biventricular congenital heart transplant patients**

| Variable | SV (n = 21) | BV (n = 25) | *P* value |
|---|---|---|---|
| Bypass time, min | | | |
| Mean ± SD | 266 ± 78 | 207 ± 64 | .001 |
| Median | 239 | 190 | |
| Range | 172-511 | 140-375 | |
| Donor ischemic time, min | | | |
| Mean ± SD | 266 ± 42 | 262 ± 47 | .749 |
| Median | 272 | 263 | |
| Range | 175-338 | 151-360 | |
| ICU length of stay, d | | | |
| Mean ± SD | 24 ± 47 | 10 ± 7 | .492 |
| Median | 9 | 8 | |
| Range | 3-195 | 3-25 | |
| Hospital length of stay, d | | | |
| Mean ± SD | 40 ± 48 | 27 ± 29 | .309 |
| Median | 16 | 14 | |
| Range | 8-195 | 10-107 | |
| Follow-up, mo | | | |
| Mean ± SD | 48 ± 50 | 54 ± 37 | .251 |
| Median | 30 | 45 | |
| Range | 0.5-169 | 3-136 | |
| Postoperative inotropes | 15 (71) | 16 (64) | .754 |
| Postoperative bleeding | 4 (19) | 2 (8) | .390 |
| Postoperative infection | 2 (10) | 5 (20) | .428 |
| Postoperative CVA | 1 (5) | 1 (4) | 1.000 |
| Postoperative renal failure | 4 (19) | 6 (24) | .735 |
| Operative mortality | 2 (10) | 0 (0) | .203 |
| Postoperative major morbidity | 7 (33) | 11 (44) | 1.000 |

Data are given as number (%) unless otherwise indicated. *SV*, Single ventricle; *BV*, biventricular; *ICU*, intensive care unit; *CVA*, cerebrovascular accident; *SD*, standard deviation.

**TABLE 3. Univariate and multivariate analyses of preoperative variables with overall mortality**

| Variable | Univariate *P* value |
|---|---|
| SV and dialysis | <.0005 |
| Creatinine >1.5 mg/dL | .005 |
| Dialysis | <.0005 |
| Ventricular assist and dialysis | <.0005 |
| Ventricular assist and creatinine >1.5 mg/dL | .006 |
| SV and reoperation | .016 |
| Previous operations >2 | .043 |
| SV and ventricular assist | .026 |
| Bypass >3 h | .068 |
| Female sex | .147 |
| Single ventricle | .224 |
| SV and PRA >10 | .395 |
| Ventricular assist | .396 |
| Ventilator dependent | .547 |
| Donor/recipient weight ratio | .603 |
| PRA >10 and ventricular assist | .636 |
| PRA >10 | .716 |
| Age | .805 |
| Recipient weight | .940 |

In multivariate analysis, for SV and dialysis, the odds ratio was 16.1 (95% confidence interval, 2.3-112.1; $P = .005$); and for creatinine >1.5 mg/dL, the odds ratio was 4.8 (95% confidence interval, 1.1-20.7; $P = .038$). *SV*, Single ventricle; *PRA*, panel-reactive antibody.

biventricular assist devices (BIVAD) placed, and 1 patient received a Berlin Heart BIVAD after initial ECMO support. Overall hospital mortality was 4.3% (n = 2). Although there were more deaths in the SV group, there was no statistically significant difference in operative mortality (10% SV vs 0% BV; $P = .2$) or major morbidity (33% SV vs 44% BV; $P = .55$) between the 2 groups.

Risk factors associated with overall mortality by univariate analysis (Table 3) were creatinine level higher than 1.5 mg/dL ($P = .005$), dialysis ($P < .0005$), and 3 or more previous sternotomies ($P = .043$). High-risk groups identified by univariate analysis were patients with an SV diagnosis + dialysis ($P < .0005$) (Figure 1, *A*), SV diagnosis + reoperation greater than 2 ($P = .016$) (Figure 1, *B*), SV diagnosis + VAD ($P = .026$) (Figure 1, *C*), or VAD/ECMO + renal insufficiency ($P = .006$)/VAD/ECMO + dialysis ($P < .0005$) (Figure 2, *A* and *B*) (Table 3). By using multivariate analysis, the composite of SV + dialysis was a predictor of overall mortality ($P < .0005$) (Figure 2). Although survival at 2 years was lower in the SV cohort (73% vs 96%; $P = .16$), this benefit was not apparent (63% vs 69%) at late follow-up (Figure 3).

## DISCUSSION

Complex congenital heart disease has been an independent predictor of mortality after heart transplantation.[2,3] Improved operative technique and postoperative care has resulted in more children surviving complex neonatal repairs.[1] Several of these patients, particularly the complex SV group, develop end-stage ventricular dysfunction. Within this group of complex CHD recipients, certain subgroups are at a particularly high risk of death after heart transplant.

Recipients who require complex pulmonary artery reconstructive procedures concomitant with transplant have been at a particularly higher risk.[6] Heart transplant recipients with preexisting renal insufficiency are intuitively at a high risk of postoperative renal failure from nephrotoxic immunosuppressive therapy. Preoperative renal insufficiency has been consistently associated with increased posttransplant morbidity and mortality.[6,7] In our study, we found that renal insufficiency and the composite SV + dialysis were independent predictors of overall mortality. Concomitant heart-renal transplant in carefully screened and selected recipients may help improve outcomes in patients with end-stage heart disease from CHD and significant preoperative renal insufficiency.[8,9] Combined heart-kidney transplant should, therefore, be considered a viable therapeutic option in this high-risk subgroup.

Elevated PRA levels in these high-risk recipients contribute to a prolonged time on the waiting list and

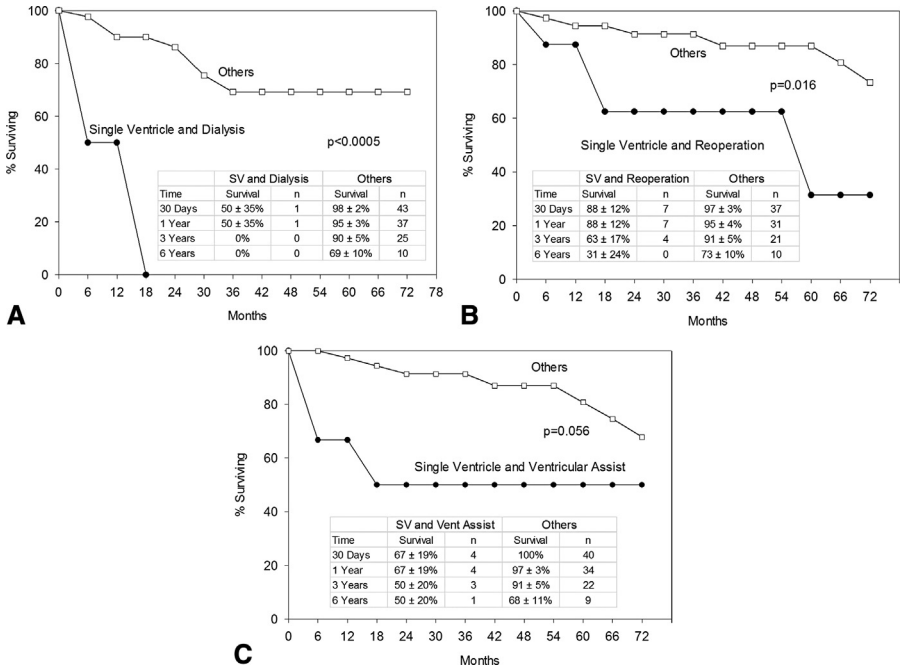


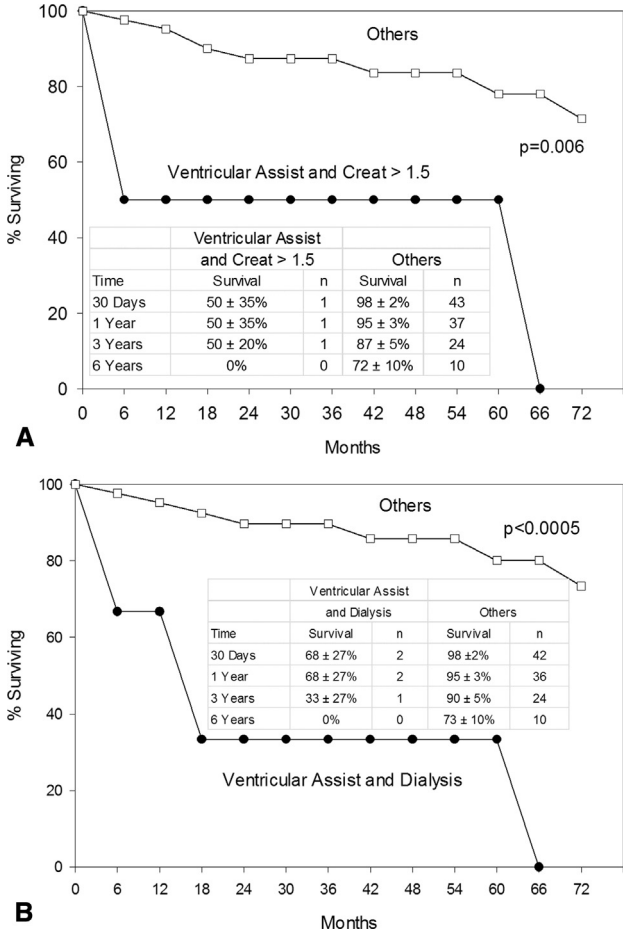

**FIGURE 1.** A, Survival in patients with single-ventricle *(SV)* diagnosis and preoperative dialysis. B, Survival in patients with SV diagnosis and reoperation (>2). C, Survival in patients with SV diagnosis and mechanical support. *Vent Assist*, Ventricular assistance.

have been associated with poor outcome.[10,11] As in a previous multicenter study from the United Network of Organ Sharing (UNOS) database, our analysis did not find elevated PRA levels to be predictive of mortality. In addition, other individual risk factors (ie, need for preoperative mechanical support or SV diagnosis) were not predictive of mortality.

Previous studies have found that SV diagnosis is associated with poor outcomes.[12] Multicenter studies from the Pediatric Heart Transplant Study group found that a previous Fontan procedure was a risk factor for reduced survival, particularly early after heart transplant.[13,14] However, contrary to these reports, others have found comparable outcomes within the SV subgroup and Fontan patients.[15,16] In our recipients with CHD undergoing heart transplant, we did not find SV diagnosis, previous bidirectional Glenn, or previous Fontan procedure to be associated with mortality. Both operative deaths in our series were in the SV group (10% vs 0%). However, the differences noted in early and 2-year mortality were less apparent at late follow-up. This could reflect the steady attrition observed with heart transplant recipients, regardless of their initial diagnosis. We found that, although SV diagnosis alone was not associated with poor outcomes, the combination of SV patients with 3 or more prior sternotomies, SV patients who required preoperative dialysis, or those who required preoperative mechanical support were strongly associated with mortality. SV patients who required preoperative dialysis were specifically predictive of mortality by multivariate analysis.

The need for mechanical support before transplant has been associated with poor posttransplant outcomes.[17,18] However, most patients in these studies received ECMO as mechanical support, which is an established predictor of mortality.[19] In a UNOS database study, children requiring preoperative VAD support had similar early and long-term survival as those not requiring VAD support. In our series, we found that, as an individual risk factor, mechanical support (which included ECMO and VAD) did not incur an increased risk for death after transplant. On the other hand, patients who received VAD support and developed renal insufficiency and/or needed dialysis were at a significantly higher risk of death. Similarly, we found that SV patients who required VAD/ECMO support were also at an increased risk for death after heart transplant. There is evidence that mechanical support instituted appropriately and in a timely manner improves end-organ function and has optimized outcomes after heart transplant.[19]

The short-term shortage in donor organs for adult heart transplantation prompted the development of alternate lists for high-risk recipients, using donor organs that would conventionally be turned down.[20] Controversy surrounds the use of these alternate lists in heart transplantation. Intuitively, these alternate lists could result in higher mortality and resource use.[21] However, acceptable outcomes have been demonstrated.[20] Because complex

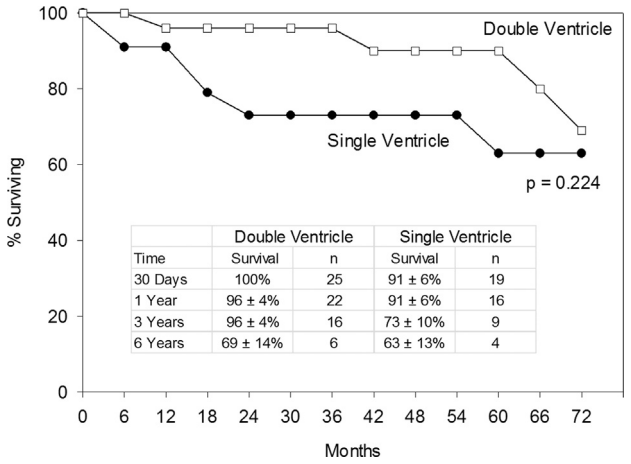



| | Ventricular Assist and Creat > 1.5 | | Others | |
|---|---|---|---|---|
| Time | Survival | n | Survival | n |
| 30 Days | 50 ± 35% | 1 | 98 ± 2% | 43 |
| 1 Year | 50 ± 35% | 1 | 95 ± 3% | 37 |
| 3 Years | 50 ± 20% | 1 | 87 ± 5% | 24 |
| 6 Years | 0% | 0 | 72 ± 10% | 10 |

| | Ventricular Assist and Dialysis | | Others | |
|---|---|---|---|---|
| Time | Survival | n | Survival | n |
| 30 Days | 68 ± 27% | 2 | 98 ±2% | 42 |
| 1 Year | 68 ± 27% | 2 | 95 ± 3% | 36 |
| 3 Years | 33 ± 27% | 1 | 90 ± 5% | 24 |
| 6 Years | 0% | 0 | 73 ± 10% | 10 |

**FIGURE 2.** A, Survival in patients with VAD and preoperative renal insufficiency. B, Survival in patients with VAD and dialysis. *Creat*, Creatinine.

congenital heart disease recipients constitute a high-risk group, alternate lists could potentially result in better allocation of donor hearts, matching borderline donors with high-risk recipients. This would expand the limited donor pool and theoretically match the good donor organs with standard-risk recipients. Although alternate lists have been suggested for high-risk patients with congenital heart disease, they have yet to be developed. To effectively use alternate lists, objective and accurate identification of groups at increased risk is essential. A previous study identified individual risk factors that were independantly associated with mortality.[5] The study concluded that avoiding matching high-risk donors with high-risk recipients, as recommended by alternate lists, could actually reduce morbidity and mortality after pediatric heart transplantation.




| | Double Ventricle | | Single Ventricle | |
|---|---|---|---|---|
| Time | Survival | n | Survival | n |
| 30 Days | 100% | 25 | 91 ± 6% | 19 |
| 1 Year | 96 ± 4% | 22 | 91 ± 6% | 16 |
| 3 Years | 96 ± 4% | 16 | 73 ± 10% | 9 |
| 6 Years | 69 ± 14% | 6 | 63 ± 13% | 4 |

**FIGURE 3.** Overall survival, single versus double ventricle.

Identification of specific composite high-risk groups would certainly help in developing criteria that could be used to either exclude high-risk recipients from receiving standard organs or match these recipients with borderline donors. Davies and colleagues[6] demonstrated that increasing numbers of high-risk criteria resulted in a cumulative increase in mortality. We found similar results with certain unique composite risk factor groups that were predictive of mortality. We found no significant differences between SV and BV groups, except for more previous sternotomies and longer bypass times. SV diagnosis, donor-recipient weight ratio, and other individual factors were not independantly associated with mortality. Preoperative renal failure, the need for dialysis, and 3 or more previous sternotomies were associated with mortality. In contrast, when composite risk group analyses were performed, we identified composite risk factor groups that were strong predictors of mortality. Preoperative renal insufficiency and SV with dialysis were strongly predictive of overall mortality and identified high-risk congenital heart transplant recipients.

Our study is limited by its retrospective nature and the small sample size. Longer follow-up would also be essential to evaluate the long-term impact of these composite risk factor groups. Another shortcoming of this study is our definition of *renal failure*. We defined this as a creatinine level higher than 1.5 mg/dL and/or need for dialysis to identify a clinically significant degree of renal insufficiency compared with both the Risk, Injury, Failure, Loss, End-stage renal disease and Acute Kidney Injury Network criteria,[22] which include mild degrees of renal insufficiency that are often not clinically significant. Furthermore, most patients did not have a urinary catheter placed preoperatively to allow for accurate urine output and creatinine clearance assessment, which are essential elements of these renal failure scores. We did not use oliguria as a criterion because it is not unusual for our patients to have borderline urine output for the first 16 to 24 hours posttransplant.

In conclusion, at medium-term follow-up, although individual risk factors were not strong predictors of outcome, a composite of risk factors may be more useful

in identifying the high-risk recipient. This, in turn, could help improve the allocation of donor organs and overall outcomes in heart transplantation for congenital heart disease.

## References


1. Castaneda A. Congenital heart disease: a surgical-historical perspective. *Ann Thorac Surg*. 2005;79:S2217-20.
2. Chen JM, Davies RR, Mital SR, Mercando ML, Addonizio LJ, Pinney SP, et al. Trends and outcomes in transplantation for complex congenital heart disease: 1984 to 2004. *Ann Thorac Surg*. 2004;78:1352-61; discussion 1352-61.
3. Kirk R, Edwards LB, Aurora P, Taylor DO, Christie J, Dobbels F, et al. Registry of the International Society for Heart and Lung Transplantation: eleventh official pediatric heart transplantation report–2008. *J Heart Lung Transplant*. 2008;27: 970-7.
4. Russo MJ, Davies RR, Sorabella RA, Martens TP, George I, Cheema FH, et al. Adult-age donors offer acceptable long-term survival to pediatric heart transplant recipients: an analysis of the United Network of Organ Sharing database. *J Thorac Cardiovasc Surg*. 2006;132:1208-12.
5. Huang J, Trinkaus K, Huddleston CB, Mendeloff EN, Spray TL, Canter CE. Risk factors for primary graft failure after pediatric cardiac transplantation: importance of recipient and donor characteristics. *J Heart Lung Transplant*. 2004;23:716-22.
6. Davies RR, Russo MJ, Mital S, Martens TM, Sorabella RS, Hong KN, et al. Predicting survival among high-risk pediatric cardiac transplant recipients: an analysis of the United Network for Organ Sharing database. *J Thorac Cardiovasc Surg*. 2008;135:147-55, e1-2.
7. Tang L, Du W, L'Ecuyer TJ. Perioperative renal failure in pediatric heart transplant recipients: outcome and risk factors. *Pediatr Transplant*. 2011;15:430-6.
8. Sahney S, Chinnock R. Management of infants and young children with combined heart and kidney failure. *Pediatr Transplant*. 2006;10:408-12.
9. Groetzner J, Kaczmarek I, Mueller M, Huber S, Deutsch A, Daebritz S, et al. Freedom from graft vessel disease in heart and combined heart- and kidney-transplanted patients treated with tacrolimus-based immunosuppression. *J Heart Lung Transplant*. 2005;24:1787-92.
10. Mahle WT, Tresler MA, Edens RE, Rusconi P, George JF, Naftel DC, et al. Allosensitization and outcomes in pediatric heart transplantation. *J Heart Lung Transplant*. 2011;30:1221-7.
11. Jacobs JP, Quintessenza JA, Boucek RJ, Morell VO, Botero LM, Badhwar V, et al. Pediatric cardiac transplantation in children with high panel reactive antibody. *AnnThorac Surg*. 2004;78:1703-9.
12. Everitt MD, Boyle GJ, Schechtman KB, Zheng J, Bullock EA, Kaza AK, et al. Early survival after heart transplant in young infants is lowest after failed single-ventricle palliation: a multi-institutional study. *J Heart Lung Transplant*. 2012; 31:509-16.
13. Lamour JM, Kanter KR, Naftel DC, Chrisant MR, Morrow WR, Clemson BS, et al. The effect of age, diagnosis, and previous surgery in children and adults undergoing heart transplantation for congenital heart disease. *J Am Coll Cardiol*. 2009;54:160-5.
14. Bernstein D, Naftel D, Chin C, Addonizio LJ, Gamberg P, Blume ED, et al. Outcome of listing for cardiac transplantation for failed Fontan: a multi-institutional study. *Circulation*. 2006;114:273-80.
15. Kanter KR, Mahle WT, Vincent RN, Berg AM, Kogon BE, Kirshbom PM. Heart transplantation in children with a Fontan procedure. *Ann Thorac Surg*. 2011;91: 823-9; discussion 829-30.
16. Jayakumar KA, Addonizio LJ, Kichuk-Chrisant MR, Galantowicz ME, Lamour JM, Quaegebeur JM, et al. Cardiac transplantation after the Fontan or Glenn procedure. *J Am Coll Cardiol*. 2004;44:2065-72.
17. Fiser WP, Yetman AT, Gunselman RJ, Fasules JW, Baker LL, Chipman CW, et al. Pediatric arteriovenous extracorporeal membrane oxygenation (ECMO) as a bridge to cardiac transplantation. *J Heart Lung Transplant*. 2003;22:770-7.
18. Gajarski RJ, Mosca RS, Ohye RG, Bove EL, Crowley DC, Custer JR, et al. Use of extracorporeal life support as a bridge to pediatric cardiac transplantation. *J Heart Lung Transplant*. 2003;22:28-34.
19. Davies RR, Russo MJ, Hong KN, O'Byrne ML, Cork DP, Moskowitz AJ, et al. The use of mechanical circulatory support as a bridge to transplantation in pediatric patients: an analysis of the United Network for Organ Sharing database. *J Thorac Cardiovasc Surg*. 2008;135:421-7.e1.
20. Chen JM, Russo MJ, Hammond KM, Mancini DM, Kherani AR, Fal JM, et al. Alternate waiting list strategies for heart transplantation maximize donor organ utilization. *Ann Thorac Surg*. 2005;80:224-8.
21. Laks H, Marelli D, Fonarow GC, Hamilton MA, Ardehali A, Moriguchi JD, et al. Use of two recipient lists for adults requiring heart transplantation. *J Thorac Cardiovasc Surg*. 2003;125:49-59.
22. Bagshaw SM, George C, Bellomo R. A comparison of the RIFLE and AKIN criteria for acute kidney injury in critically ill patients. *Nephrol Dial Transplant*. 2008;23:1569-74.