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The Registry of the International Society for Heart and Lung Transplantation: Thirty-second Official Adult Heart Transplantation Report—2015; Focus Theme: Early Graft Failure

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Since the first heart transplant was performed in 1967, heart transplantation has grown worldwide. This 32nd adult heart transplant report is based on data submitted by the Registry of the International Society for Heart and Lung Transplantation (ISHLT) on 120,992 heart transplants in recipients of all ages (including 108,151 adult heart transplants) through June 30, 2014.

Data collection and statistical methods

Data are submitted to the ISHLT Registry by national and multinational organ/data exchange organizations and individual centers. Since the Registry's inception, 418 heart transplant centers, 242 lung transplant centers and 174 heart–lung transplant centers have reported data. The Registry website (www.ishlt.org/registries) provides spread sheets that show data elements collected in the Registry. The online slide set (http://www.ishlt.org/registries/slides.asp?slides=heartLungRegistry) provides POWERPOINT slides of figures and tables that support this study. The site contains additional slides for this report and slide sets from the previous annual reports.

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General methods

This series of reports used standard statistical methodology. Where appropriate, a more detailed explanation about the methodology accompanies the website slides (in the "Notes Page" view). Survival graphs (i.e., time-to-event graphs) underwent truncation when the number of analyzable individuals was <10. Within the era undergoing assessment, the analyses censored the follow-up of the surviving recipients: (1) at the time last reported to be alive (e.g., most recent annual follow-up); or (2) at the time of retransplantation. Median time to event estimated the time-point at which 50% of all recipients experienced the event (e.g., death). Conditional analyses only included those patients who met the required criterion (e.g., survival past 1 year post-transplant). The log-rank test was used to compare survival curves among groups. To prevent spuriously statistically significant findings, we adjusted all pairwise tests for multiple comparisons (Scheffé or Bonferroni).

For multivariable time-to-event analyses, we used Cox proportional hazards regression. The analyses used the censoring approaches just described. Cox models only included transplant recipients with data available for most of the risk markers in the final model. The non-conditional models used the latest data available at the time of the transplant. In contrast to non-conditional analyses, the conditional analyses also adjusted for post-transplant factors. We used restricted cubic splines to fit continuous

data variables. Model assumptions were tested and regression diagnostics were performed. The Cox models calculated hazard ratios (HRs) and corresponding *p*-values and 95% confidence intervals (CIs). Forest plots and tables show HRs and 95% CIs for categorical variables in final models. A more detailed explanation of the analytical methodology is available online (www.ishlt.org/registries) and in previous annual reports.[1–4] The data in this report were paralleled with additional and extended analyses presented in the online slide sets (3 separate slide sets, named "Introduction," "Heart Overall" and "Heart Adult"). The article refers to specific online eSlides when particular data are discussed but not shown in the article due to space limitations; eSlide numbers refer to the online heart adult slides, unless otherwise specified. The authors recommend interpretation of unadjusted analyses and predictive/com parative risk models in the context of limitations typical of registry data.

Focus theme methods

For this report, the Registry Steering Committee selected the focus theme of early graft failure (EGF). The granularity of data collected in the Registry influenced the definition of EGF. We defined EGF as a composite end-point of death or retransplant associated with graft failure within the first 30 days after transplant (Table 1). Death or retransplant events associated with causes we believed were not due to intrinsic graft failure were excluded from the EGF definition (Table 2). Because our EGF definition required an association between these outcome events and graft failure, rather than all-cause death or all-cause retransplant, a significant number of transplant recipients had death or retransplant events that did not meet the EGF criteria. In addition, if the center reported the cause for a transplant recipient's death or retransplant as "unknown," we counted the recipient as having EGF. If the center did not report a cause for a transplant recipient's death or retransplant (i.e., field left blank), we did not count the recipient as having EGF. Of note, the composite end-point excluded graft failure that did not lead to death or retransplant within 30 days, although such events were rarely reported.

The definition of EGF in this report may partly reflect but certainly differs from the definition of primary graft dysfunction (PGD)[5] in thoracic transplantation, and reflects the most severe subgroup of early graft injury resulting in graft loss.

For estimating the cumulative incidence of EGF at 30 days and percentage of transplant recipients who developed EGF within 30 days, we used a competing risks extension of the Kaplan-Meier method. Competing events consisted of death or retransplant within 30 days post-transplant and not meeting the EGF criteria, or graft failure not associated with death or retransplant.

We used consistent EGF definitions for the pediatric and adult age groups within each organ (heart and lung). However, causes of death or retransplant that were included in the definition of EGF differed between heart and lung transplant.

Heart transplant donor and recipient demographics and characteristics

Transplant volumes

A total of 4,477 heart transplants (including 3,817 adult transplants) from 252 centers were performed in 2013 and

Table 1 Adult Heart Transplants Performed January Between 2005 and December 2013, With Outcome Meeting the EGF Definition.

		Total	
Source of graft failure	Reason for graft failure	*N*	%
Death	Total	1,155	100.0
	Cardiovascular: aortic aneurysm	2	0.2
	Cardiovascular: arterial embolism	6	0.5
	Cardiovascular: atherosclerosis	3	0.3
	Cardiovascular: cardiac arrest	72	6.2
	Cardiovascular: cardiogenic shock	29	2.5
	Cardiovascular: coronary artery disease	0	0.0
	Cardiovascular: myocardial infarction	16	1.4
	Cardiovascular: other specify	118	10.2
	Cardiovascular: rhythm disorder	5	0.4
	Cardiovascular: ventricular failure	23	2.0
	Graft failure: graft infection	1	0.1
	Graft failure: non-specific	56	4.8
	Graft failure: primary failure	492	42.6
	Graft failure: technical	13	1.1
	Unknown	319	27.6
Retransplant	Total	44	100.0
	Graft failure/dysfunction	44	100.0
	Necrosis/ischemia	0	0.0

Graft failure reason stratified by source of graft failure. EGF, early graft failure.