CONSENSUS PERSPECTIVE

Authors' Perspective—Summary of the International Society for Heart and Lung Transplantation (ISHLT) Consensus Conference on Graft Dysfunction within the First 72 hours after Heart Transplantation: A 10-year Update

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BACKGROUND

The 2024 International Society for Heart and Lung Transplantation (ISHLT) Consensus Conference on primary graft dysfunction (PGD)[1] took place on April 9, 2024, and included 19 U.S. and 37 international experts in heart transplantation (HTx), including cardiologists, cardiac surgeons, anesthesiologists, and intensive care specialists as part of a 10-year update to the 2013-2014 ISHLT Consensus Conference on PGD.[2] Over the past decade, there has been a growing understanding of PGD incidence, presentation, risk factors, biomarkers, potential underlying

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pathophysiology, and prevention, including the use of advanced organ procurement and preservation technologies, management strategies, and outcomes.[3–13] However, current practices remain variable, attributable to a lack of objective data and largely influenced by center-specific practices. Therefore, the conference was designed to provide a forum for in-depth discussions among leading experts in the field to include the following:

- Reassess the ISHLT PGD definition and grading scale based on current practices and outcomes.
- Describe current and recently identified risk factors for the development of PGD and its impact on outcomes in HTx.
- Assess the novel procurement and preservation approaches and their association with the risk of PGD.
- Assess the utility of treatments for PGD based on risk stratification.
- Review the working definitions of secondary graft dysfunction (SGD).
- Discuss the interaction of graft dysfunction and vasoplegia syndromes.

TOP TAKEAWAYS

#1. Graft dysfunction within the first 72 hours after transplant is to be further categorized into cases with a discernible cause (SGD) and those with an unknown cause (Figure 1).
#2. Graft dysfunction with unknown cause should be further classified into early graft dysfunction occurring < 24 hours post-HTx (EGD), which replaces the previous term of PGD; or subsequent early graft Dysfunction at 24-72 hours post-HTx (sEGD). EGD and sEGD to be further classified into LV (left ventricular or biventricular dysfunction) or RV (isolated right ventricular dysfunction) (Figure 1).
#3. EGD-LV and EGD-RV are to be classified into 2 grades: non-severe or severe, based on the need to initiate MCS for cardiac dysfunction after transplantation. The inotrope score will no longer be used for grading the severity of EGD.
#4. Severe EGD-LV should be further categorized based on the timing of presentation into immediate presentation (EGD-LVip, failure to wean from cardiopulmonary bypass) or delayed presentation (EGD-LVdp, occurring after successful weaning from cardiopulmonary bypass), as this timing appears to hold significant prognostic value (Figure 1).
#5. Evaluation of donor, procedural, and recipient EGD risk factors is essential to guide EGD prevention and management strategies. Avoiding high-risk combinations and addressing modifiable risk factors, when possible, are likely to improve outcomes.
#6. The use of novel organ preservation and transportation technologies may mitigate the risk of EGD development.
#7. Discontinuation of amiodarone in patients listed for HTx and holding RAAS inhibitors prior to surgery may reduce the risk of EGD.
#8. Therapeutic plasma exchange, in combination with immunomodulatory therapies, may offer a potential strategy to attenuate the inflammatory milieu in patients with severe EGD; however, further evidence is needed to support this approach.
#9. SGD is defined as left ventricular (SGD-LV) and/or right ventricular (SGD-RV) dysfunction with a known cause (e.g., surgical, pulmonary hypertension, immunological, respiratory, or other) occurring within 72 hours after HTx, with further delineation to be established.
#10. In the context of graft dysfunction and vasoplegia, two clinical scenarios can be identified:
1) EGD may be complicated by vasoplegia, which can worsen clinical outcomes and pose significant management challenges.

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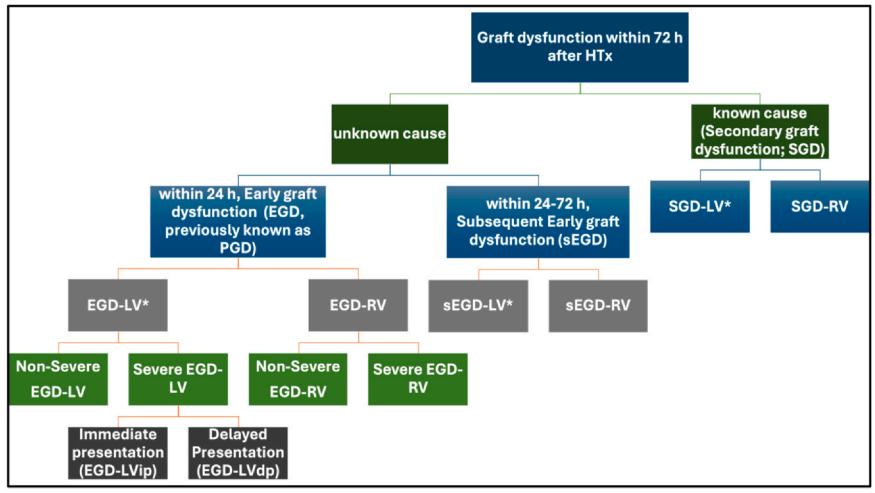
Figure 1 *Revised classification of graft dysfunction after heart transplantation based on the underlying cause and timing of presentation.* Abbreviations: CPB, cardiopulmonary bypass; EGD, early graft dysfunction; EGD-LVip, early graft dysfunction with the immediate presentation; EGD-LVdp, early graft dysfunction with the delayed presentation; LV, left ventricle; RV, right ventricle; PGD, primary graft dysfunction; sEGD, subsequent early graft dysfunction; SGD, secondary graft dysfunction. *Including left ventricular or biventricular dysfunction.



2) In patients with vasoplegia and an initially well-functioning graft, the onset of graft dysfunction should be assessed with consideration of vasoplegia as a potential contributor to secondary graft dysfunction.

CONCLUSION

The 2024 ISHLT conference on PGD represented a collaborative multidisciplinary effort by experts in cardiac transplantation worldwide to update current definitions and classifications of graft dysfunction, enrich the heart transplant community understanding of its risk factors and biomarkers, delve into potential prevention and management strategies, and unwind PGD overlap with vasoplegia. We hope the results of this consensus conference will provide a more standardized pathway for the prevention, diagnosis, and management of graft dysfunction after HTx and pave the way for future studies.

CONFLICTS OF INTEREST STATEMENT

Jon Kobashigawa: received research grants from CareDx Inc., Sanofi-Genzyme, and CSL-Behringer. Andreas Zuckermann reports speaker honoraria and advisory roles with Paragonix Technologies, Therakos (Mallinckrodt), Takeda, and Sanofi; serves as Local Principal Investigator for the XVIVO NHIP2019 study and the Cytotect NIS021 study (Biotest); is the European Principal Investigator for the GUARDIAN Registry (Paragonix); has received institutional (non-personal) study support from Biotest (NIS021); participates in advisory boards for Sanofi and Therakos; and serves as an independent adjudicator for primary graft dysfunction (PGD) for XVIVO study. Luciano Potena: received consulting fees from Biotest, Roche diagnostics, received honorarium from Takeda, Abbott,

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Biotest, and holds a leadership position at ESOT. Abbas Ardehali was an investigator in the Transmedics ESLP trials. Fardad Esmailian received a research grant from TransMedics. Maryjane Farr serves on TransMedics Inc., Natera, and the data safety monitoring board and also serves as Co-Chair, the Transthoracic and Critical Care Community of Practice, American Society of Transplantation. Shelley Hall received consulting fees from CVRx, Abbott, CareDx, and Honoria from Natera and serves as a board member for the American Society of Transplant. Eileen Hsich received NIH, NHLBI grant support R01HL164405. Yasbanoo Moayedi received funding from the AMO–UHN–Sinai Innovation Fund and ACT—Accelerating Clinical Trials. Peter MacDonald received consulting fees from AstraZeneca, Boehringer, and Novartis, and honoraria from Astellas, Abbott, Boehringer, as well as support to attend the Indian Society for Heart and Lung Transplantation and the Congress of the Asian Society of Transplantation meeting, and received equipment support from Transmedics and XVIVO, has stock in Infensa Bioscience, and serves on the data safety Monitoring Board for Eli Lilly. All other authors have no conflicts of interest to disclose.

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