ISHLT JOURNAL WATCH June 2026 | Cardiology

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Aortic insufficiency progression in patients with left ventricular assist devices and prior Impella support

Mihalj M, Nguyen DT, Sales de Armas IA, Tosun S, et al. *JHLT* 2025 Feb;44(2):161-170 | DOI: 10.1016/j.healun.2026.02.1665

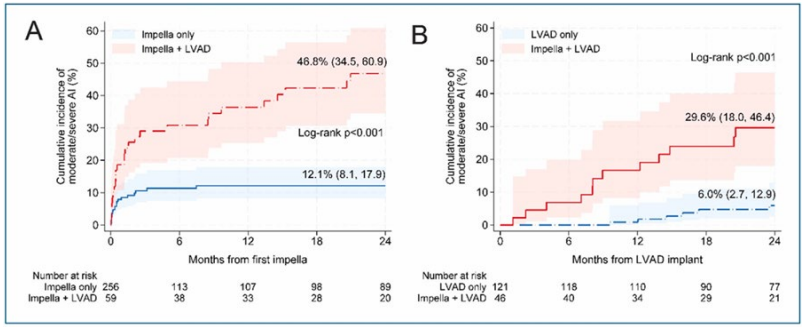
Study Highlights

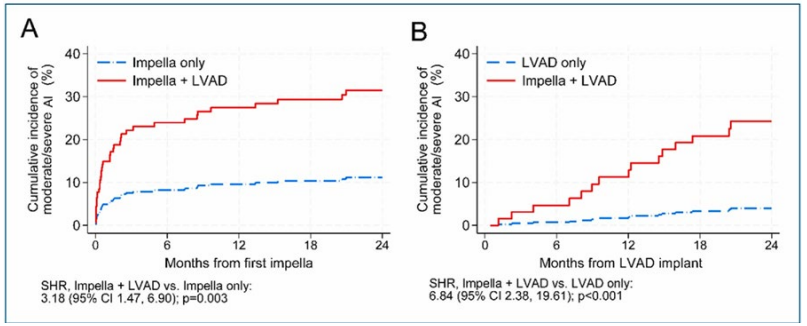
Objective: This study used two analytical frameworks to investigate the risk for aortic insufficiency (AI) in patients who received Impella only v.s. Impella+LVAD v.s. LVAD only.

Methods: A retrospective single center cohort study was performed in three defined patient groups within two frameworks: an Impella framework comparing Impella only vs. Impella+LVAD, and an LVAD framework comparing Impella+LVAD vs. LVAD only. Primary endpoint was new-onset moderate/severe AI or need for AVR; risk factors for progressive AI were also evaluated.

Results: 315 patients received Impella support, 167 underwent LVAD implantation. Follow-up was 24 months. In the Impella framework, Impella+LVAD was associated with higher AI progression compared with Impella only (aHR 3.27, 95% CI 1.57–6.82; p=0.002). In the LVAD framework, prior Impella support was associated with higher AI progression after LVAD compared with durable LVAD only (aHR 7.87, 95% CI 2.66–23.25; p<0.001). Additional independent risk factors included longer Impella support and prior cardiac surgery in the Impella framework, and prior cerebrovascular accident in the LVAD framework.

Conclusions: Prior Impella support was associated with an increased risk for moderate to severe AI after subsequent LVAD implantation.





Top 1 A/B: Unadjusted Kaplan–Meier models.

Bottom A/B: Competing risk model (Fine and Gray; adjusted). Progressive AI incidence was higher In Impella+LVAD group in both frameworks (46.8%) with higher cumulative incidence for 24 months in LVAD frameworks (CI 2.66-23.25 p<0.01 v.s. CI 1.57 -6.82 p<0.002).

Reviewer's Comments

- This retrospective study demonstrated an association between prior Impella support and AI progression after LVAD implantation.
- Impella runs were longer in patients bridged to LVAD. Longer Impella support was independently associated with AI progression, with each additional day increasing the risk by approximately 1%.
- With increasing Impella use before durable LVAD, progressive AI may become more relevant during follow-up, requiring standardized surveillance, treatment protocols, and prospective research.

Limitations

- A single centre retrospective study carries a risk for unmeasured confounding.
- Echo protocols were driven by clinical care rather than standardized protocols.
- The high-volume center's standardized Impella/LVAD practice may limit generalizability to lower-volume hospitals.
- The modest Impella+LVAD sample size limited subgroup and interaction analyses; larger multicenter studies are warranted.

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Donor-Derived Cell-Free DNA in Antibody-Mediated Rejection

Kim PJ, Alam AH, Teuteberg J, Khush K, et al. *JACC HF* 2026 Jan, 14 (1) | DOI: 10.1016/j.jchf.2025.102716

Study Highlights

Background: Antibody-mediated rejection (AMR) remains a major cause of graft dysfunction and long-term mortality after heart transplantation. Endomyocardial biopsy is the current gold standard for diagnosis but is invasive and resource-intensive. Donor-derived cell-free DNA (dd-cfDNA) has emerged as a promising non-invasive biomarker of allograft injury.

Objective: To evaluate the performance of dd-cfDNA for biopsy-proven AMR and its relationship with donor-specific antibodies (DSA), graft dysfunction, and clinical context in heart transplant recipients enrolled in the SHORE registry.

Methods: Multicenter observational registry analysis (2017–2022) including 2,240 heart transplant recipients with verified biopsy, dd-cfDNA, echocardiography, and DSA status.

Results: Higher dd-cfDNA levels were associated with higher AMR risk. In patients with no known DSA, AMR rates increased from 0.7% at dd-cfDNA <0.20% to 6.7% at ≥0.50%. In DSA-positive patients with normal graft function, AMR risk reached 15.5% with dd-cfDNA ≥0.50%. The highest AMR risk (20.4%) was seen in patients with DSA positivity and graft dysfunction.

Conclusions: dd-cfDNA may serve as a useful non-invasive adjunct for AMR surveillance, biopsy-yield prediction and risk stratification after heart transplantation.

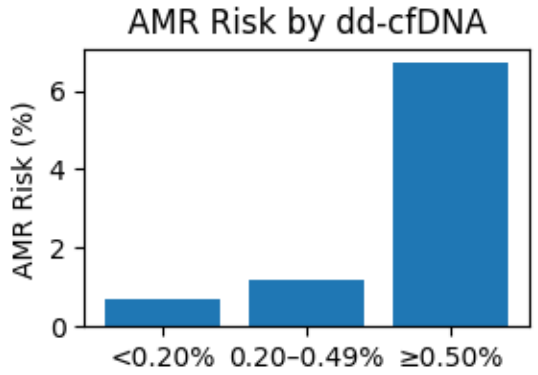

Figure 1. AMR risk by dd-cfDNA level. AMR = antibody-mediated rejection; dd-cfDNA = donor-derived cell-free DANN.

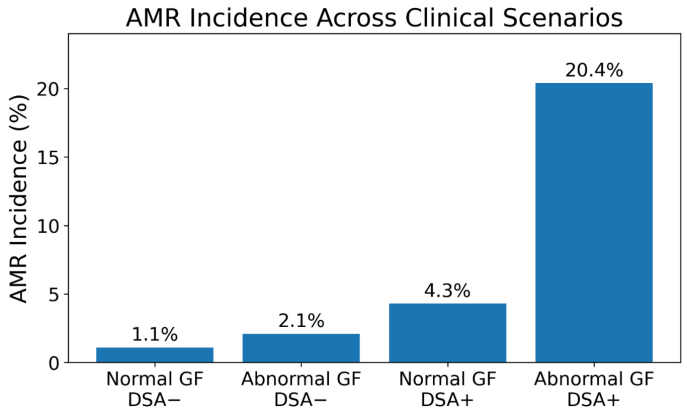

Figure 2. AMR incidence by graft function and DSA status. GF = graft function; DSA = donor-specific antibodies; AMR = antibody-mediated rejection.

Reviewer's Comments

- The study represents a large multicenter real-world registry supporting dd-cfDNA as a non-invasive adjunct after heart transplantation.
- Low dd-cfDNA levels may help reduce unnecessary surveillance biopsies, particularly in low-risk clinical settings.
- Combining dd-cfDNA with DSA status and graft function improves context-specific AMR risk stratification.
- The findings support more individualized and less invasive follow-up strategies integrating biomarkers, imaging, and immunologic assessment.

Limitations

- The observational design limits causal conclusions.
- Context-dependent AMR prevalence limits the use of a universal dd-cfDNA threshold.
- Potential variability in biopsy interpretation, DAS assessment, and center-specific surveillance patterns.
- dd-cfDNA and EMBs were not consistently obtained together.
- Timing of biomarkers sampling relative to biopsy may influence diagnostic accuracy.
- Prospective validation is needed.

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Low-dose apixaban in HeartMate 3 LVAD patients, interim analysis of the ApixiVAD trial, a randomized controlled study

Schnegg B, Deveza R, Barua S, Chavali S, et al. *JHLT* 2025 Aug;44(8):1331-1338. | DOI: 10.1016/j.healun.2025.04.012

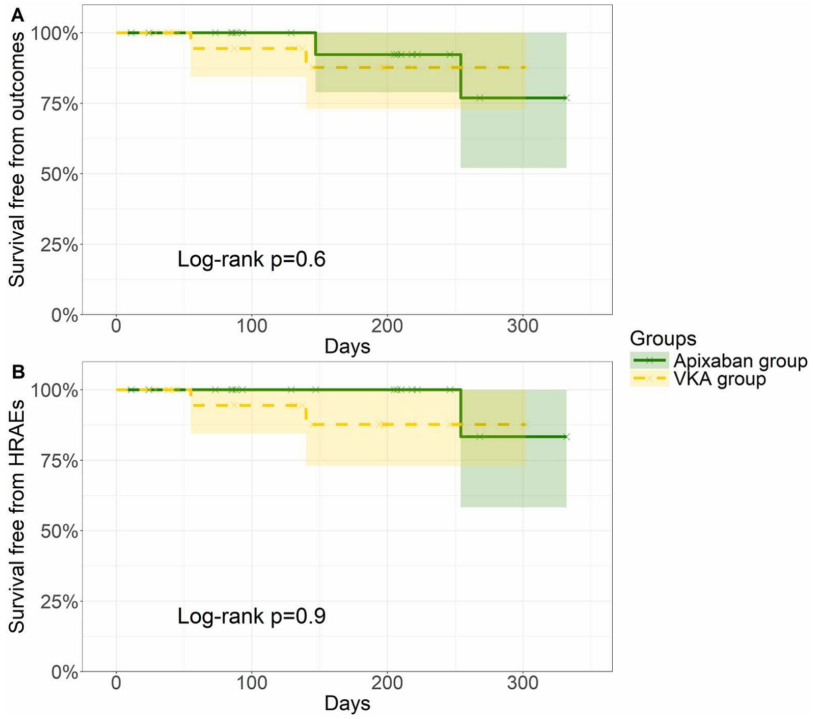
Study Highlights

Objective: To assess non-inferiority of low-dose apixaban (2.5 mg twice daily) vs. vitamin k antagonist (VKA) in stable HeartMate 3 (HM3) recipients.

Methods: The ApixiVAD study is an Investigator-initiated, randomized, controlled, open-label, international pilot trial. HM3 patients implanted for ≥2 months with a therapeutic range INR >60% were included. Patients were randomized 1:1 to VKA or low-dose apixaban with a maximum follow up of 24 months or until heart transplant (HT). The primary outcome was a composite of death, suspected/confirmed pump thrombosis, ischemic or hemorrhagic stroke, other thrombotic events, and major bleeding.

Results: Forty-four patients were randomized, 21 to apixaban and 23 to VKA. Median age 55 years (IQR 50-64); 14% were women. Twenty-five patients (57%) underwent HT during the study period. Median time from LVAD to randomization was 6 months (IQR 5-8) and median follow up was 6 months (IQR 2-8). Five patients (11%) experienced a primary outcome: 2 hemorrhagic events and 1 death from sepsis/palliation in the apixaban group; 1 hemorrhagic event and 1 stroke in the VKA group. The proportion of hemocompatibility-related events was 14% and 8.7% in the apixaban and VKA group, respectively (absolute difference 5.3%; 95% CI -0.39 to 0.79; p=0.7).

Conclusions: Interim analysis suggests that low-dose apixaban may provide adequate anticoagulation in the short-medium term in selected HM3 patients without excess bleeding or thrombosis. Given the limited sample size and short follow-up, the results should be interpreted as preliminary, serving to be hypothesis-generating.



(A) One-year survival follow up for patients **without any primary outcome event**

(B) One-year survival follow up for patients **without hemocompatibility-related adverse events**

Reviewer's Comments

- Low-dose apixaban may be a feasible alternative anticoagulation strategy in carefully selected HM3 patients.
- Bleeding events occurred in patients on concomitant aspirin therapy, and these prescribing patterns changed after publication of the ARIES trial.
- Many patients underwent HT during the study period, with cessation of anticoagulation upon organ allocation and use of a cytokine filter during CPB. No excess perioperative bleeding was observed in the apixaban cohort, although this strategy may not be universally available.

Limitations

- Small sample size limits statistical power for rare events and a low-risk population limit generalizability.
- An open-label design may introduce bias in reporting and management of adverse events.
- There was a low incidence of atrial fibrillation, which may limit the ability to use apixaban safely at low doses.
- The short follow-up period limits conclusions on long-term safety, particularly in destination therapy patients.

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Heart Replacement Therapy in Young Patients: A Comparative Analysis of HeartMate 3 LVAD and Heart Transplant Using MOMENTUM 3 and UNOS Registry

Uriel N, Sayer GT, Elad B, Fried JA, et al. *JACC HF* 2026 Apr, 14(4). | DOI: 10.1016/j.jchf.2026.102948

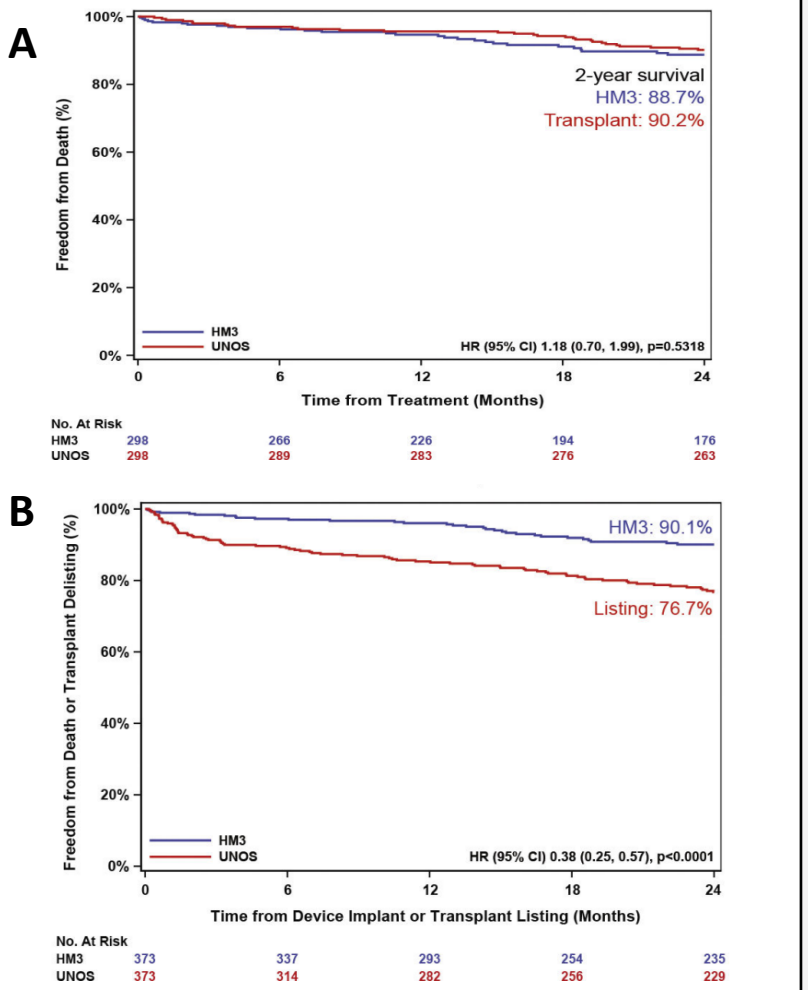
Study Highlights

Objective: To compare 2-year survival and 1-year major adverse events (AEs) between HeartMate 3 (HM3) LVAD support and heart transplantation (HT) in patients aged 18–49.

Methods: Post-hoc comparative analysis using propensity score matching to create comparable cohorts from the MOMENTUM 3 portfolio trial (HM3 cohort, n=420) and the UNOS registry (n=1,955 listed; n=1,176 transplanted) from 2014 to 2018. After matching, major baseline characteristics were generally well-balanced.

Results: In the propensity-matched treatment cohort, 2-year survival was similar between HM3 and HT recipients (88.7% vs. 90.2%, HR 1.18; p=0.53). When analyzed from LVAD implantation versus transplant listing, HM3 was associated with higher 2-year freedom from death compared with UNOS freedom from death or delisting due to clinical deterioration on wait-list (90.1% vs 76.7%, p <0.0001). HM3 recipients had lower 1-year rates of renal dysfunction requiring dialysis (5.0% vs 10.4%; p=0.016) and infection-related hospitalizations (24.8% vs 34.2%; p=0.012), but a higher incidence of debilitating stroke (3.4% vs 0.3%; p=0.027).

Conclusions: Contemporary HM3 LVAD therapy offers survival outcomes comparable to heart transplantation in selected patients under 50 years of age, while highlighting the relevance of immortal time bias in wait-list vs. HM3 first comparisons.



Comparison of 2-year survival from the time of HT vs. HM3 implantation (A) and freedom from death or delisting (B).

Reviewer's Comments

- This study highlights immortal time bias in treatment-based comparisons HM3 vs. HT listing, as HT patients must survive wait-list time before entering the HT cohort.
- Early HM3 may reduce wait-list exposure and organ uncertainty while preserving scarce grafts.
- HM3 may support a staged strategy in younger patients: durable support now, transplantation later.
- This requires allocation rules recognizing stable long-term VAD support as a bridge to future HT, without requiring life-threatening VAD complications.

Limitations

- HM3 data came from a clinical trials with defined trial criteria, whereas UNOS reflects a real-world registry, which may introduce selection bias and limit generalizability.
- The data (2014–2018) largely predates the 2018 allocation policy change, which has significantly altered transplant wait-list dynamics.
- The study is limited to a 2-year follow-up; long-term survival, device durability and post-HM3 TH outcomes remain unclear.
- Different AE definitions in MOMENTUM3 and UNOS limit safety comparisions.