ISHLT JOURNAL WATCH
January 2024 | Heart Transplant and MCS

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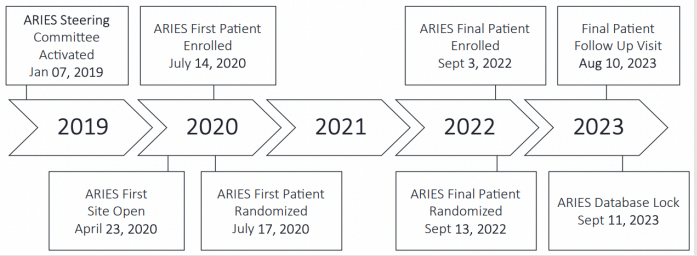
Aspirin and Hemocompatibility Events With a Left Ventricular Assist Device in Advanced Heart Failure: ARIES-HM3 Trial

Mehra, et al. *JAMA* Nov 2023 | DOI: https://doi.org/10.1001/jama.2023.23204

Study Highlights

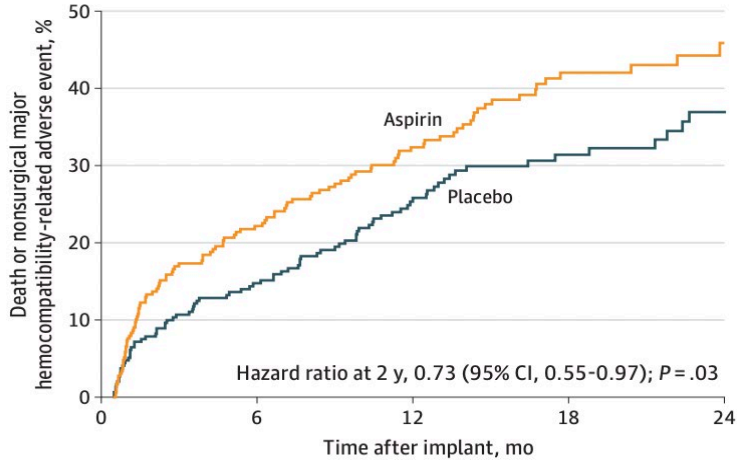
Objective: To evaluate whether aspirin can be safely avoided from an antithrombotic regimen of vitamin K antagonist (VKA) in patients with a HeartMate 3 (HM3) left ventricular assist device (LVAD).

Methods: A multi-centre double-blinded non-inferiority trial of 628 patients with HM3 LVAD randomized to aspirin 100 mg daily or matching placebo in addition to a VKA (INR goal 2.0-3.0).



Results: The primary outcome, survival-free from non-surgical major hemocompatibility-related adverse events for placebo vs. aspirin at 1 year was: 74.2 vs. 68.1 events per 100 patient-years (p for noninferiority < 0.0001). Avoiding aspiring reduced 14.5 bleeding events per 100 patient-years of follow-up and decreased days spent in hospital by 47%.

Figure 1. Death or nonsurgical major hemocompatibility-related events*

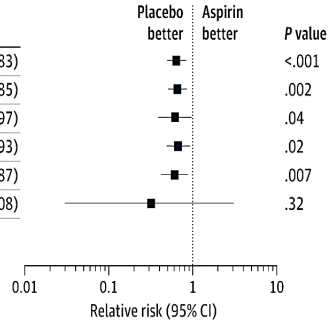


***Nonsurgical hemocompatibility-related adverse events include: stroke, pump thrombosis, major bleeding, or arterial thromboembolism**

Strengths	Limitations
Time in therapeutic INR range was similar between study groups	Females were under-represented (23% only). Females are known to have higher amount of hemocompatibility-related adverse events. *(Ramu et al. JACC Heart Fail. Published online Oct 2, 2023)*
Blinded assessment of compliance using thromboxane B_2 testing confirm benefits were solely driven by aspirin avoidance	
Results were consistent in multiple sensitivity analyses that both excluded patients with events within 14 days of implant (considered to be procedural-related) as well as including all the randomized patients.	Exclusion of patients with mandated need for aspirin and modest sample size of groups with established vascular disease limits generalizability in those with traditional indications for aspirin
Included patients with history of PCI	Outcomes past 2 years are unknown

Figure 2. Principal secondary endpoints

Source	Events per 100 patient-years (No. of events) Placebo (n = 296; 366.41 patient-years)	Aspirin (n = 293; 351.64 patient-years)	Relative risk (95% CI)
Bleeding components of the primary end point	26.2 (96)	40.7 (143)	0.64 (0.50-0.83)
Nonsurgical bleeding	25.9 (95)	39.5 (139)	0.66 (0.51-0.85)
Moderate bleeding	8.5 (31)	13.7 (48)	0.62 (0.39-0.97)
Severe bleeding	17.5 (64)	25.9 (91)	0.67 (0.49-0.93)
Gastrointestinal bleeding (moderate or severe)	13.1 (48)	21.6 (76)	0.61 (0.42-0.87)
Hemorrhagic stroke	0.3 (1)	0.9 (3)	0.32 (0.03-3.08)
Ischemic stroke with hemorrhagic conversion[a]	0	0.3 (1)	



Take home points

- Exclusion of aspirin in patients with HM3 LVAD is associated with reduction in major bleeding without increasing the risk of thromboembolic complications.
- Avoiding aspirin is cost-saving, leading to 41% reduction in cost of bleeding events in the trial.
- Addition of aspirin in patients with a prior LVAD-related device or systemic thrombotic events, or withdrawal of aspirin in patients already tolerating it remain uncertain.

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Transplantation Outcomes with Donor Hearts after Circulatory Death

Schroder, et al. *NEJM* Jun 2023 | DOI: https://doi.org/10.1056/NEJMoa2212438

Study Highlights

Objective: To determine clinical outcomes after heart transplantation from a donor after circulatory death (DCD) compared to a donor after brain death (DBD)

Methods: A multicenter, unblinded, non-inferiority trial of 180 patients randomized to receive a heart from a DCD preserved with a portable extracorporeal perfusion system (Organ Care System Heart, TransMedics) or a DBD preserved with traditional cold static storage. Important exclusion criteria were: re-transplantation, recipient renal dysfunction, DCD hearts with known CAD, valvular heart disease, or sustained LVEF < 50%.

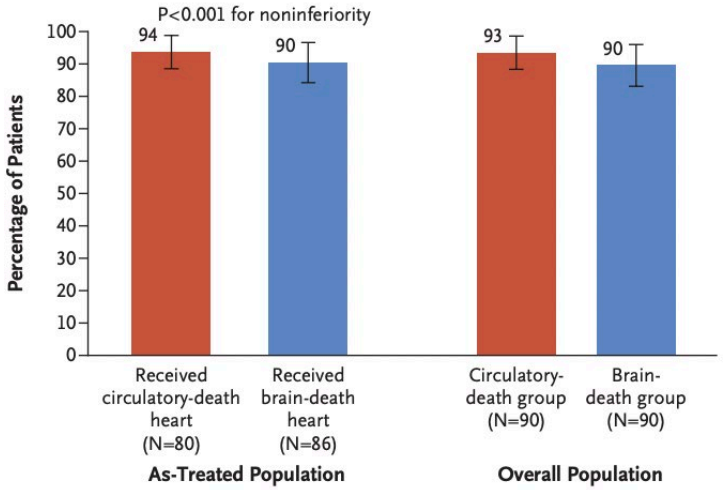
Results: The primary end-point of risk-adjusted 6-month post-transplant survival was similar in DCD and DBD group. Comparable results were seen at 1-year post-transplant. Primary graft dysfunction (PGD) was more common in DCD group but this did not affect patient or graft survival at 30 days or 1 year.

Table 1. Baseline characteristics of donors and recipients

DONOR	DCD n=90	DBD n=90
Age, yrs (SD)	29.3 ±7.5	33.2 ±11.4
Male	93%	77%

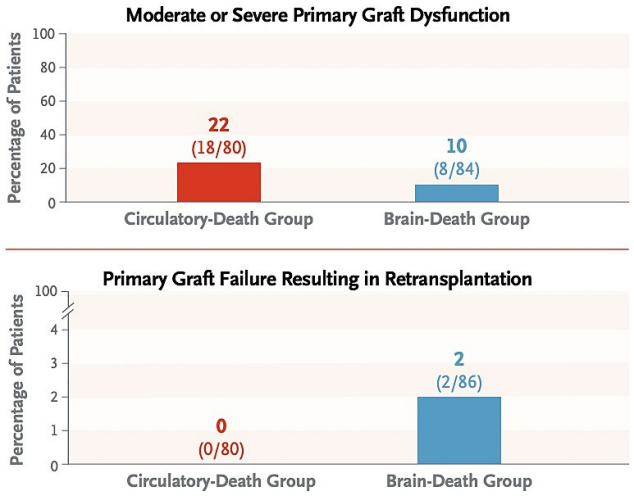
RECEPIENT	DCD, n=90	DBD, n=90
Age, yrs (SD)	51.3±12.6	55±11.4
Male	73%	73%
UNOS status 1 or 2	21%	58%
LVAD pre-txp	49%	30%

Figure 1. Risk-adjusted 6 months survival



** 14 patients were excluded in "as-treated population" due to protocol violations (i.e. age < 18, warm ischemic time > 30 min, transplant despite rising donor lactate)*

Figure 2. Serious adverse events related to the heart graft at 30 days after transplant



Strengthes	Limitations
3:1 randomization, where patients assigned to DCD group were able to receive a DBD organ, ensured patients will receive a suitable heart at earliest availability.	The unblinded design with high crossover rate from circulatory-death to brain-death cohort potentially resulted in significant donor and recipient selection bias.
	DCD recipients were younger and less sick with lower priority UNOS status likely inflating survival outcomes despite adjusted analysis.
	Long-term results and late complications of DCD heart transplantation is uncertain.

Take home points

- Heart transplant with DCD using a portable extracorporeal perfusion preservation system is safe and non-inferior to standard care transplant with DBD.
- DCD transplant with ex-vivo perfusion can expand donor pool and shorten wait times. Mean waiting time from consent to transplant was shorter in DCD group and 89% of DCD hearts were successfully utilized in this trial.
- The increased rates of PGD in DCD group can be related to warm ischemic time. The use of normothermic regional perfusion (NRP) during procurement can reduce this injury. A large single-centre retrospective study DCD vs. DBD using NRP in majority of patients, found no difference in incidence of PGD. (Siddiqi et al. *JACC* 2023;82(15):12-20)

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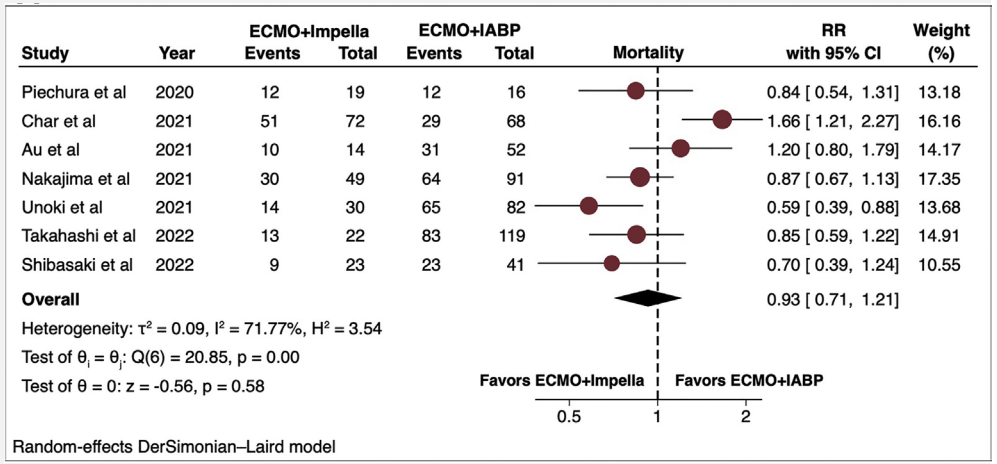
Left Ventricular Unloading With Impella Versus IABP in Patients With VA-ECMO: A Systematic Review and Meta-Analysis

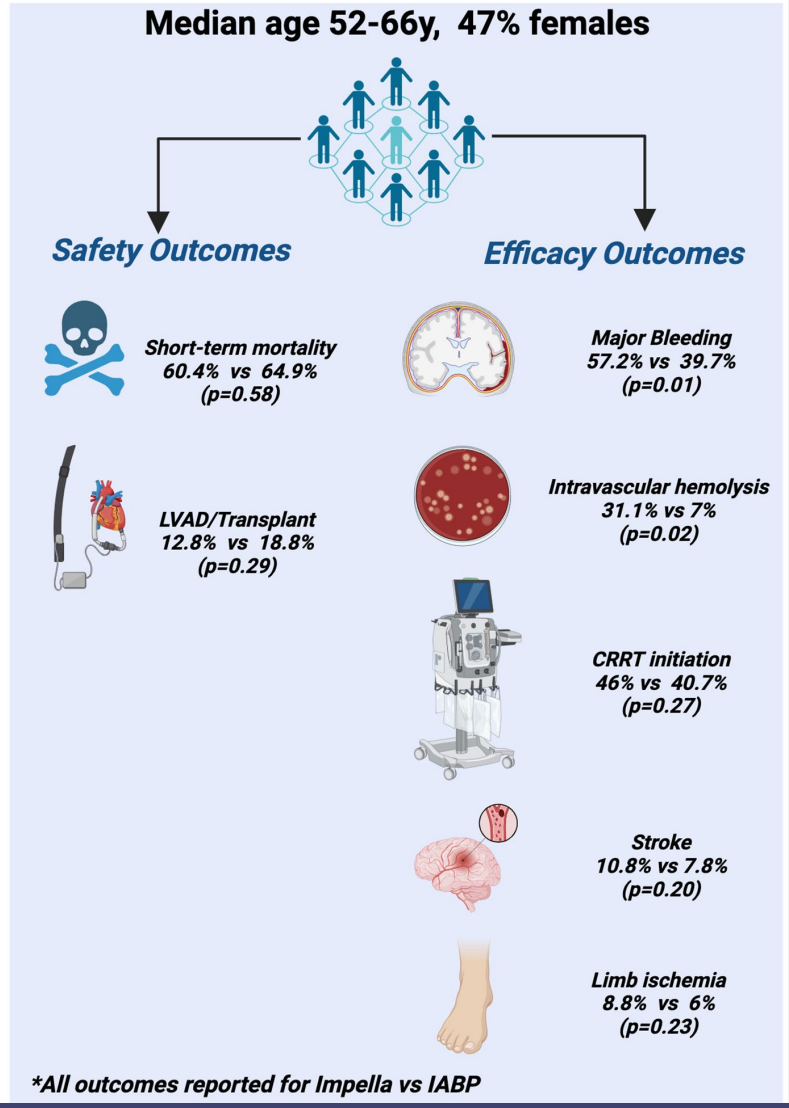
Kruti D Ghandi et al. *JACC* October 2023 | DOI: https://doi.org/10.1016/j.amjcard.2023.09.023

Study Highlights

- Study inclusion criteria: Adults, compared IABP vs Impella used for LV unloading in VA-ECMO supported patients.
- Primary outcome: 30 days or in the hospital all-cause mortality.
- A total of retrospective 7 studies (698 patients) were included. All were and published between 2021-2022.
- The in-hospital survival was similar between groups (Impella 60.8% vs IABP 64.9%).



- The majority (> 93%) used impella CP or 2.5, the remainder used 5.0 (not reported Takahashi et al 22).
- Concurrent or pre-ECMO unloading was used in 71% (not reported by Shibasaki et al 22).
- Reactive unloading was used in 29% (not reported by Shibasaki et al 22).



Take home points

- The use of Impella alongside VA-ECMO showed similar short-term mortality rates as IABP with VA-ECMO. However, Impella was associated with more bleeding and hemolysis compared to IABP, which is consistent with the current stream of science
- This report builds on prior analyses that showed benefit from LV unloading while on VA-ECMO using IABP (1.6 higher survival odds, Zeng et al, Front Cardiovasc Med, 2022) or impella (1.8 higher survival odds, Iannaccone et al, Cardiovasc Revasc Med 2022).
- Until now, no randomized controlled trial has directly compared the outcomes of using IABP versus Impella in conjunction with VA-ECMO.
- The studies by Unoki et al, Takahashi et al, and Shibasaki et al showed signal toward superiority of impella, however, they notbly studied predominently extracorporeal cardiopulmonary resuscitation (ECPR) population (60-100%).
- Limitations: The retrospective nature of the included studies introduces biases in device selection, heterogeneity in patient characteristics, and outcome reporting. Perhaps more importantly, patient hemodynamics and unloading efficacy were not included.

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Waitlist and transplant outcomes in heart transplant candidates bridged with temporary endovascular RVAD

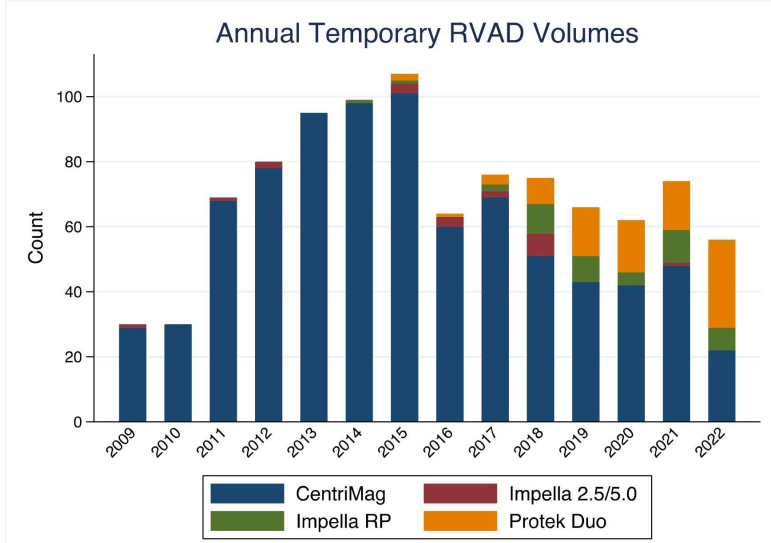
Kwon et al. *JHLT* November 2023 | DOI: https://doi.org/10.1016/j.healun.2023.11.001

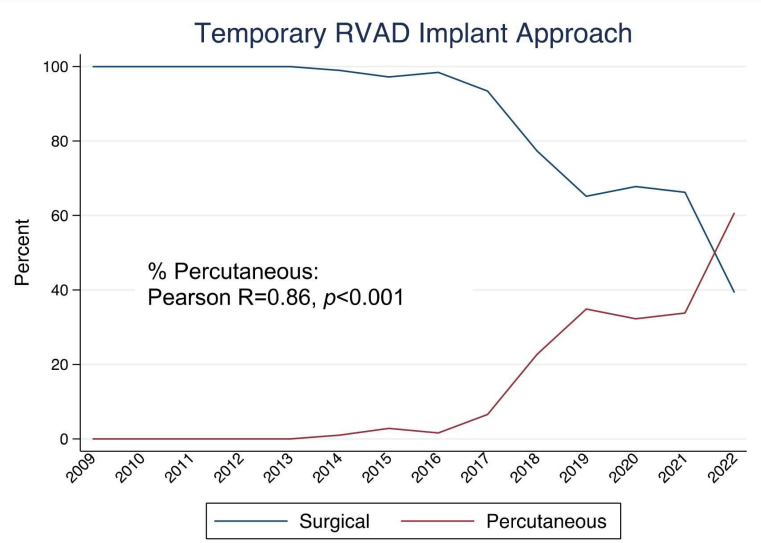
Study Highlights

- Retrospective analysis of United Network of Organ Sharing (UNOS), of patients listed between Jan 2009 and June 2022 and who required temporary endovascular RVAD at ***any*** point during their listing.
- Exclusion criteria: durable RVAD, centrally cannulated Centrimag, total artificial heart, and ECMO.
- tRVAD group was propensity-matched 1:4 to non-tRVAD patients.
- Of the 41,507 patients included, 133 (0.3%) utilized tRAVD.

		Unmatched				Matched			
	Waitlist Time	No tRVAD	tRVAD	HR	p-value	No tRVAD	tRVAD	HR	p-value
Death	1 month	4.5%	7.5%	1.46	0.067	4.5%	7.5%	1.68	0.208
	12 months	13.5%	18.8%	1.46	0.067	10.0%	18.8%	**2.15**	**<0.001**
HTx	1 month	24.6%	42.1%	1.19	0.176	36.9%	42.1%	1.21	0.166
	12 months	60.4%	62.4%	1.19	0.176	60.2%	62.4%	0.93	0.582

- Concomitant durable LVAD was used in 47 patients without difference in waitlist deterioration or transplantation risk.
- Concomitant temporary LVAD was used in 25 patients with a HR for deterioration or death of 3.04 (p = 0.001).
- Transplantation occurred in 48 patients (55.8%) with tRVAD in place at a median of 14 days after device implantation, while 21 patients (24.4%) died or were delisted at a median of 8 days.
- In 24 patients, tRVAD was removed (median 6 days) due to: recovery (n= 6), conversion to another device (n=5), or device failure (n=5).





Annual volumes of heart transplant candidates receiving temporary endovascular right ventricular assist devices (RVADs) while waitlisted, grouped by device type (left). Proportion of temporary RVADs implanted using surgical (CentriMag) vs percutaneous approaches (Impella RP and Protek Duo; right). Note, off-label use of Impella 2.5/5.0 as RVAD was excluded from the analysis of implant approach.
The year of introduction of Impella 2.5 and CP: 2009, Impella RP: 2012, and Protek Duo: 2014.

Limitations: The UNOS registry has a significant data missingness rate. Details of device indications and management are not included. The sample is small, necessitating combining several tRVAD platforms. A matching imbalance (1:4) may artificially increase the treatment effect. Black HT candidates were under-represented in this cohort.

Take home message

The use of endovascular tRVAD is increasing. While UNOS database trends reflect a mixture of therapeutics advancements, allocation system-driven patterns, and clinical practice evolution, this study signals that tRVAD patients are a particularly vulnerable group for deterioration while on the waitlist.