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Letters

RESEARCH LETTER

Systematic Review of Advanced Heart Failure Therapy Outcomes in People With Human Immunodeficiency Virus

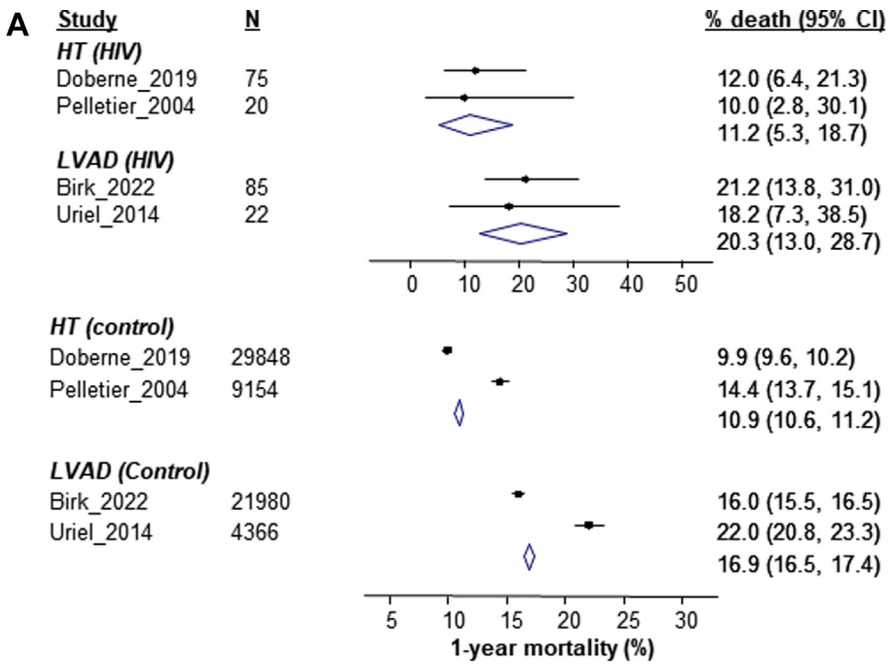
With the improving life expectancy of people living with human immunodeficiency virus (PLWH) and increasing prevalence of heart failure (HF) in this population, more patients with comorbid HIV and HF will need to be considered for advanced HF therapies such as heart transplantation (HT) and left ventricular assist devices (LVAD).[1] Although the United Network for Organ Sharing recommended that HIV status should not preclude a patient's candidacy for transplantation since the early 2000s, HT and LVAD were not routinely offered to PLWH due to concerns for survivorship, complex medical regimen, and risk of complications.[2] The amendment of the HIV Organ Policy Equity Act in 2013 paved the way for more research and inclusion of PLWH for solid organ transplantation.[2] Since the HIV Organ Policy Equity Act, the overall number of PLWH with HF who have received HT and LVAD implantations has increased; however, data on the survivorship and complications of advanced HF treatment remain limited for this population.[1,2] We aimed to synthesize the limited data on HT and LVAD outcomes among PLWH compared to people without HIV.

We searched OVID Medline, EMBASE, and Web of Science for all available articles from inception until August 2022 using terms related to HIV, advanced HF, HT, LVAD, and mechanical support. We also reviewed the references of relevant articles. Articles were selected if they included: 1) PLWH and a comparator group without HIV; 2) recipients of HT or LVAD; and 3) follow-up data on clinical outcomes after hospitalization. Search and data extraction were done in duplicate (M.H. and H.A.) and further adjudicated by 2 authors (C.S. and S.E.). Mortality rates were pooled across studies by type of advanced HF treatment using fixed-effect model meta-analysis. Stratified analyses were not performed because there were too few studies to perform meaningful subgroup comparisons. We report this study according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.

An initial search yielded 3,786 studies, which were screened using titles, abstracts, and full texts. From this, 9 studies were identified that met the inclusion criteria for this review. After rigorous full-text review and data extraction, it was determined that there were potential overlaps in the patient populations of multiple articles with respect to study dates and databases. We further restricted the review to 4 studies (2 HT and 2 LVAD) to avoid potential inclusion of duplicate patients in the analysis dataset. The final analysis comprised 95 PLWH who received HT (mean age 49 years) and 107 PLWH who received LVAD (mean age 53 years), as well as 39,002 patients without HIV who received HT (mean age 54 years) and 26,346 patients without HIV who received LVAD (mean age 59 years).[1-4] The HIV patients were about 5 years younger than HIV-negative patients among those who had HT or LVAD. Racial composition differed between the PLWH (53% White, 38% Black) and HIV-negative patients (70% White, 20% Black) who received HT. The proportion of males was broadly comparable between PLWH (82%) and HIV-negative patients (74%). Similar percentages of patients were bridged with LVAD to HT for both PLWH (39%) and HIV-negative patients (37%). The pooled average 1-year mortality for PLWH after HT (11.2% [95% CI: 5.3%-18.7%]) was similar to that of the HIV-negative population (10.9% [95% CI: 10.6%-11.2%]). The 1-year mortality for PLWH after LVAD (20.3% [95% CI: 13.0%-28.7%]) was comparable to non-HIV population (16.9% [95% CI: 16.5%-17.4%]) with overlapping CIs. (**Figure 1A**). Three-year survivorship data were reported for the heart transplant studies,[1,4] and 2-year survivorships were reported for LVAD studies.[2,3] These longer-term data were also comparable between PLWH and HIV-negative patients (**Figure 1B**).

Overall, our findings suggest comparable mortality in advanced HF therapy between those with and without HIV, while the PLWH were generally younger. In parallel with the data on HT, a recent 2022 cohort study of liver and kidney transplants in

FIGURE 1 Mortality and Survivorship for PLWH and HIV-Negative Patients on Advanced Therapies



B

Therapy	Outcome	Study	PLWH	Controls
HT	3-year survival	Doberne, 2019	80%	84%
		Pelletier, 2014	90%	79%
LVAD	2-year survival	Birk, 2022	74%	78%
		Uriel, 2014	72%	69%

(A) One-year mortality after HT or LVAD and (B) longer-term survivorship after HT (3 years) or LVAD (2 years) among PLWH and HIV-negative controls. Box and whisker chart showing that there is no statistically significant difference in 1-year mortality for PLWH for HT or LVAD patients. HF = heart failure; HIV = human immunodeficiency virus; HT = heart transplantation; LVAD = left ventricular assist device; N = number of subjects; PLWH = people living with human immunodeficiency virus.

PLWH showed comparable 15-year mortality outcomes compared to non-HIV cohorts.[5] As more data is gathered, mortality outcomes within transplant populations in PLWH and patients without HIV appear to be comparable. On the other hand, although data on PLWH receiving LVAD therapy are more limited, prior studies have reported that PLWH with few HIV-related comorbidities have comparable outcomes with non-HIV groups. Overall, mortality rates tended to be higher for those receiving LVAD vs HT, possibly because: 1) patients may have been excluded from HT due to older age, psychosocial barriers, or comorbidities; 2) those receiving LVAD may have had a more fulminant course of disease that did not allow for eventual HT; and 3) a significant proportion of HT recipients had received a bridging LVAD and represent the group who survived to HT, which may lead to survivor bias favoring HT recipients. Limitations of this systematic review include the small sample sizes for PLWH, likely due to the concerns for transplant programs to include this population in advanced therapies, as well as the overlapping nature of multiple studies, requiring the exclusion of multiple articles to avoid double-counting individuals, and the lack of long-term follow-up data beyond 2 years.

This systematic review aggregated the limited extant data of contemporary studies for 2 advanced HF interventions and suggests that the HIV status of a patient may not be a significant predictor of post-

treatment outcomes. Future studies can delineate the optimal characteristics of PLWH for best outcomes, provide more information on trends of referral for advanced HF intervention, and identify post-intervention outcomes besides mortality.

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

REFERENCES

1. Doberne JW, Jawitz OK, Raman V, et al. Heart transplantation survival outcomes of HIV positive and negative recipients. *Ann Thorac Surg*. 2021;111:1465–1471. https://doi.org/10.1016/j.athoracsur.2020.06.120

2. Uriel N, Nahumi N, Colombo PC, et al. Advanced heart failure in patients infected with human immunodeficiency virus: is there equal access to care? *J Heart Lung Transplant*. 2014;33:924–930. https://doi.org/10.1016/j.healun.2014.04.015

3. Birk SE, Campbell R, Herre J, Baran DA, Yehya A. Clinical outcomes and survival of HIV positive and negative patients on LVAD Support. *J Heart Lung Transplant*. 2022;41:S121. https://doi.org/10.1016/j.healun.2022.01.283

4. Pelletier SJ, Norman SP, Christensen LL, Stock PG, Port FK, Merion RM. Review of transplantation in HIV patients during the HAART era. *Clin Transpl*. 2004:63–82.

5. Zarinsefat A, Gulati A, Shui A, et al. Long-term outcomes following kidney and liver transplant in recipients with HIV. *JAMA Surg*. 2022;157:240–247. https://doi.org/10.1001/jamasurg.2021.6798