

Mahr and colleagues (1) compared neurological outcomes between patients with Heartmate 3 and Heartware left ventricular assist devices (LVADs). The authors discussed some of the limitations of their analysis, but we believe the limitations of this study merits further examination to help clinicians “make evidence-based and informed decisions”.

Firstly, the authors selectively included the ADVANCE CAP and the ENDURANCE SUPPLEMENTAL studies, and excluded other ADVANCE (2) and ENDURANCE (3) randomized trials. The rationale of this selective exclusion of datasets was not explained. The results will be biased by the exclusion of trials with less favourable outcomes.

Secondly, a study of neurological complications is certainly important in the field of LVAD therapy. However, it is not clear why other clinically significant events were not studied; most notably device exchange and mortality. The 6-month device exchange rates were 4.5% and 0% in the combined ADVANCE studies (4) and MOMENTUM 3 (5), respectively, despite 21.4% of patients undergoing transplantation (or recovered) in the former, which would have reduce the denominator, as highlighted by the authors. The 1-year survival in the combined ADVANCE studies was 84% (4), compared to 2-year survival of 82.8%, despite a similar proportion of patients undergoing heart transplantation (21.2%) in MOMENTUM 3 (6).

Thirdly, it is axiomatic that randomized controlled trials are considered the gold standard approach for estimating the effects of treatments on outcomes, as random allocation ensures that treatment status will not be confounded with either measured or unmeasured baseline characteristics. Propensity score matching is commonly used in the absence of randomization. Conditional on the propensity score, the distribution of observed baseline covariates is similar between treated and untreated subjects. Propensity score matching will, on average, result in *measured* baseline covariates being balanced between treatment groups. Propensity score matching or some other reasonable technique for making comparison outside randomised trials should be used to minimise bias when making comparison between studies.

Finally, we agree with the authors that careful consideration of statistical designs and analyses are essential, and arguably even more pertinent in such indirect cross-trial comparisons that are fraught with biases.

## References

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