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Commentary: Extracorporeal membrane oxygenation as a bridge to heart transplantation: Will we revisit Heisenberg's uncertainty principle and the observer effect?

James K. Kirklin, MD

For many years, the decision to transplant patients supported by extracorporeal membrane oxygenation (ECMO) was often couched in gloom, with dire predictions of likely death with heart transplantation. Ivey-Miranda and colleagues¹ have generated an important analysis that provides clarity about the relative risk of ECMO under various circumstances. This report is particularly important in the current era of increased use of ECMO, given the revised allocation system. The fact that posttransplant survival was similar among patients transitioned off ECMO and those transplanted on ECMO with no risk factors helps inform the transplant team in their decision process.

It's noteworthy that this experience (2001-2017) predated the current donor allocation algorithm, which prioritizes ECMO in gaining access to donor hearts. In view of the marked reduction in priority of ventricular assist device (VAD)-supported patients, the substantial group of ECMO-supported patients who transitioned to VAD therapy will likely be importantly reduced in the current era. This exposes an important limitation of this analysis, specifically, if most of those who transitioned to VADs were

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The risk profile of ECMO as bridge-to-transplant therapy may inform its selected application, but the changing allocation environment may complicate the decision process.

instead left on ECMO until transplant, would the risk model have changed? Are the inferences still applicable today? In discussing with families and in planning by the transplant team, the calibration of the model (how well the predicted probability of posttransplant death for cohorts with a specific risk profile matches what is actually observed) may be affected by the changing decision environment.

In 1927, Werner Heisenberg articulated the uncertainty principle in quantum mechanics, which asserts that the more precisely the position of a subatomic particle is known, the less precisely its momentum can be predicted. This is often conflated with the "observer effect," perhaps first referred to also in quantum mechanics, which states that the method of measuring certain systems may alter a fundamental property of the system. This principle has since been applied to many scientific disciplines.² As we study (implement) a new allocation system, the method of studying (manipulating) the details of the allocation system may fundamentally alter an important component, in this case the risk profile associated with ECMO.

The dramatic change in the cardiac organ allocation algorithm in 2017 assigned support on ECMO as essentially the greatest priority for a donor heart. This decision was made in the context of ECMO being the major risk factor in most analyses for both waitlist and posttransplant mortality. The assumption was that ECMO would be employed sparingly, applied only to those sickest patients with a favorable risk

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profile. who could then receive rapid access to a donor. This assumption is likely flawed, since ECMO is now being offered to many patients who previously would have received a VAD, with physicians working within the revised algorithm in hopes of getting the patient transplanted. These “less-sick” patients may soon dominate the ECMO cohort, fundamentally changing the landscape that is under study.

So, to complement this excellent study, updated analyses are critically needed that focus on the period since implementation of the revised allocation system. We may

uncover a new risk profile that will further inform ways to guide the increasing number of patients receiving ECMO to successful transplantation.

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Commentary: A bridge to somewhere

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Modern outcomes of patients bridged to heart transplant (orthotopic heart transplantation [OHT]) with venoarterial extracorporeal membrane oxygenation (ECMO) continue to be poor.¹ The 2018 update to the heart allocation system places ECMO and temporary ventricular assist device (VAD) support in Status 1 priority. In this modern context, it is increasingly valuable to understand the outcomes of OHT in various subsets of patients bridged with ECMO to guide patient selection in this high-risk population.

In the current issue of the *Journal*, Ivey-Miranda and colleagues² present a novel analysis of the United Network for Organ Sharing registry seeking to further elucidate this important issue. Among patients who underwent OHT, subsets of patients who underwent transplantation on ECMO versus being decannulated before transplant were compared. The decannulated before transplant group,

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Patient selection and timing of interventions are key considerations in patients being considered for bridge to heart transplantation with VA ECMO.

90% of whom were transitioned to some form of more durable circulatory support, demonstrate survival comparable to that of patients who never required ECMO support. This trend was supported by a propensity score-matched analysis of patients transitioned from ECMO to VAD versus those on ECMO at the time of transplant, with similar outcomes between groups. Further subanalysis showed a sequential increase in hazard after OHT in patients on ECMO with added risk factors, such as mechanical ventilation and renal impairment.

The authors should be commended for performing a sound analysis of a powerful database. The conclusions from this analysis have important implications for the transplant surgeon: Patients bridged to transplant with ECMO are a heterogeneous cohort. As risk factors,

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