

Clinical Investigation

Adverse Effects of Delayed Transplant Listing Among Patients With Implantable Left Ventricular Assist Devices

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ABSTRACT

Background: The timing of transplant listing after implantation of a left ventricular assist device (LVAD) remains uncertain, given high device complication rates and apparent stability of some LVAD-supported patients. This investigation quantifies the effect of delayed transplant listing and transplantation rates on medium-term survival and LVAD complications.

Methods and Results: A Markov model was used to simulate the effects of delaying initial transplant listing after LVAD implantation. Modeled parameters were derived from the Standard Transplant Analysis and Research file. When transplant listing was delayed and 5-year results were examined, fewer persons underwent transplantation (53% in base model vs 51% in 180-day-delay model) and the fraction of deaths while waiting increased (17% in base model vs 21% in 180-day delay model). Life expectancy changed minimally from the base model (3.50 y) when initial listing was delayed by 180 days (3.51 y).

Conclusions: Delaying initial transplant listing increased the likelihood of death while waiting for a transplant and decreased the likelihood of transplantation. In aggregate, life expectancy was unchanged by delays in listing. This study suggests that delaying transplant listing with the expectation of providing additional life expectancy is not likely with current LVAD technology. (*J Cardiac Fail* 2018;24:243–248)

Key Words: Heart transplantation, mechanical circulatory support, outcomes research.

Left ventricular assist device (LVAD) therapy has proven to be successful as a bridge to transplant (BTT) by reducing the risk of death while waiting for a transplant.^{1,2} The decision to list an LVAD-supported candidate after initial implantation is highly variable, with some centers listing patients immediately after implantation and others allowing time

for recovery. In addition, myriad clinical scenarios are encountered that influence the timing of listing. The variable timing of listing is complicated by reports of both high complication rates and the apparent stability of some candidates.³ The current National Coverage Decision encourages early transplant listing via the mandate that BTT patients be actively listed at the time of LVAD implantation.⁴ Thus, the ideal timing of initial listing of LVAD-supported candidates is not clear, but is a balance among surgical recovery, impending complications, and regulatory pressures. The present study was designed to estimate the incidence of adverse events and rates of transplant and life expectancy resulting from either delaying or accelerating transplant listing after LVAD implantation.

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Methods

The aim of this study was to test the hypotheses that delaying transplant listing of an LVAD-supported registrant increases mortality. A simulation approach was chosen over a survival analysis approach to allow exact specification of

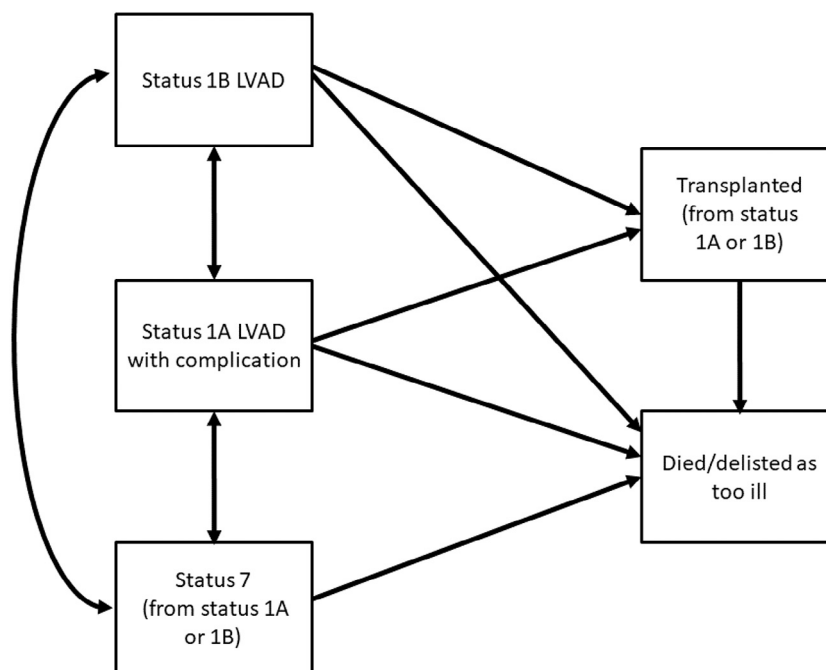


Fig. 1. Markov model state diagram. States modeled in the Markov simulation. Bidirectional arrows indicate the ability to return to a given state. LVAD, left ventricular assist device.

the experimental variable—delay in transplant listing—while retaining all other features of LVAD-supported candidates. Survival analysis is also complicated by unmeasured confounders of time to transplantation and survival while listed. A Markov model was created for this purpose and was designed to track a cohort of LVAD-implanted candidates from initial listing until delisting as too ill or death for candidates still waiting or until death for those after transplantation. The Markov model states are depicted in Fig. 1. Patients moved between states or experienced the composite outcome based on probabilities estimated from candidates registered in the United Network for Organ Sharing (UNOS) and supported at initial listing with the use of a continuous-flow LVAD from January 1, 2008, to September 1, 2014. Transition probabilities were based on time of transition from one state to another, occurrence of death or delisting as too ill while waiting, and graft failure after transplantation. Parametric survival models were used to estimate the time-dependent probabilities. The model estimated new probabilities for each additional day in the model. The model time limit was 5 years following initial listing, which included all waiting list and post-transplantation survivals.

A base model with fixed values for all transitions and a probabilistic model using the 95% confidence interval for each transition were created. These 2 models were used to evaluate the effects of delays in transplant listing, LVAD survival, LVAD complication rates, post-transplantation survival, and other factors (Appendix). The base model used 30 days of elective status 1A time, per UNOS regulations in effect at the time of this analysis, and active transplant listing at day 1.⁵ The timing of elective status 1A time varies among programs; for the purpose of this model, elec-

tive status 1A time was uniformly used 30 days after initial active listing (eg, from day 30 to day 60 in the base model).

Analysis

The outputs of the model were days alive (summarized as life-years [LY]) and fraction of candidates in each listing status (health state) at specific times. For each condition evaluated in the probabilistic sensitivity analysis, simulation of 100 cohorts was performed with random drawing from all parameter distributions for each simulated condition of delays in listing, transplantation rates, and LVAD mortality rates.

Stata 13.0 (College Station, Texas) was used to generate all parametric survival analysis and for analysis of covariance. The Markov model was created with the use of Microsoft Excel (Redmond, Washington).

The data reported here were supplied by UNOS as the contractor for the Organ Procurement and Transplantation Network (OPTN). The interpretation and reporting of these data are the responsibility of the authors and in no way should be seen as an official policy of or interpretation by the OPTN or the US Government.

Results

Base Model

At 1 year after initial listing, the base model estimated that 28% of the cohort remained on LVAD support and listed status 1B, 5% were listed status 1A with an LVAD complication, and 6% were status 7 (Fig. 2). At 1 year, 13% died while waiting for a transplant (Table 1). Of these deaths, 12% were

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