References


Discussion

Dr Soon J. Park (Rochester, Minn). Dr Kirklin and his colleagues are to be congratulated for this timely and important presentation. They report that a significant fraction of DT patients are achieving a survival that is comparable with that of those who undergo heart transplantation. Such finding is especially astonishing in that these patients, by definition, were those deemed inappropriate to allocate donor hearts for the concern of poor posttransplant outcome.

Perhaps it is helpful to revisit the medical ethics governing heart transplantation, which was established well before the current development in LVAD therapy. Heart transplantation has been the only therapeutic option capable of prolonging life in these patients with end-stage heart failure. Although it is highly effective on an individual level, its epidemiologic impact has been trivial for there exists a significant mismatch between donors and recipients. The donor heart remains a precious and scarce resource for society. Therefore, the practice of heart transplantation has been guided by principles of justice, utility, and transplant benefit to maximize the number of years gained by the transplantation.

With the recent development in LVAD therapy, heart transplant no longer seems to be the only viable option. Now, LVAD therapy can be rendered immediately and abundantly, and it is going to change the natural history of patients with end-stage heart failure dramatically, whether transplant eligible or not.

As we have just been informed by Dr Kirklin, a significant fraction of patients who were destined to die because heart transplant was not an option, a typical scenario of despair that affects the vast majority of patients, are now able to enjoy life on LVAD support.

In regard to the transplant-eligible patients, many medical centers seem to witness a significantly enhanced rate of survival in these bridge-to-transplant patients compared with DT patients. What is the INTERMACS bridge-to-transplant experience? How does it compare with the attrition rate of 4% due to various causes such as rejection, infection, allograft vasculopathy, and malignancy after transplantation? What would be the appropriate LVAD strategy in terms of patient selection, duration of support, and timing of triggering transplantation in accordance with the principles of transplantation? Finally, would it ever make sense to consider LVAD as the primary therapy and reserve heart transplantation as a secondary therapy?

I would welcome Dr Kirklin’s insight into some of these questions, and, once again, congratulations for ushering in a truly exciting period of LVAD therapy.

Dr Kirklin. Thank you, Dr. Those are interesting questions.
You asked about the mortality or attrition rate with cardiac transplantation versus ventricular support. In the INTERMACS database, recall that the continuous flow technology is really now only exceeding 2 years, and during that time in the low-risk group, the mortality rate is about 10% per year, which compares with about 6% per year in the constant phase after cardiac transplantation. Thus it is not quite there yet, even though there are specific risk factor groups that are competitive out to 2 years. Of course, the mechanical support group includes older patients; the median age in the INTERMACS DT group was 67 years versus 55 years in the transplant group.

Regarding the issue of using LVAD therapy as primary therapy and transplantation secondary, of course, the goal in the future will be to have an array of therapies that maximizes long-term survival for patients. Whether that means initial VAD therapy followed by transplant or initial transplant followed by a total artificial heart for patients. Whether that means initial VAD therapy followed by transplantation versus ventricular support. In the INTERMACS pump group, the mortality rate is about 10% per year, which compares with about 6% per year in the constant phase after cardiac transplantation. Thus it is not quite there yet, even though there are specific risk factor groups that are competitive out to 2 years. Of course, the mechanical support group includes older patients; the median age in the INTERMACS DT group was 67 years versus 55 years in the transplant group.

The financial implications are complicated and will have to be determined by societal as well as medical priorities. Clearly, we are going to be looking at the financial implications over decades of patient care if we are going to be using a combination of mechanical support, transplantation, and potentially other therapies.

Dr Conte. To answer the question directly, are you ready as you stand today to refer that subgroup of patients for DT as opposed to transplantation? I am going to hang you on your words.

Dr Kirklin. Yes.

Dr R. Duane Davis (Durham, NC). Congratulations. I just want to be a little bit cautious when you use that 20% 2-year survival in heart transplant as your benchmark and then compare a 40-year-old who has never had surgery getting a VAD and saying it is equivalent. If you did a 40-year-old who never had previous cardiac surgery, the 2-year mortality would not be 20% after a heart transplant. It is clear that continuous VAD is getting into the ballpark, but I am not sure I am ready to agree that it is equivalent.

Finally, when are we going to be ready to randomize between those 2 therapies?

Dr Kirklin. The challenge in transplantation is to begin to set some benchmark about which we could begin to have this discussion, and I think a benchmark of 20% mortality at 2 years is certainly reasonable. Remember that the low-risk, 40-year-old patient undergoing cardiac transplantation without important other comorbidities is not the patient one would want to triage to mechanical support. The reason this benchmark is important is to begin the discussion of those kinds of patients who could potentially be triaged if they are a low enough risk with device therapy. However, it will only be those patients who are on the transplant list with multiple adverse comorbidities that we are going to initially select for triage. It will not be the otherwise healthy 40-year-old man with a good long-term expectation from cardiac transplantation.

Dr Joseph Amato (Chicago, Ill). Dr Kirklin, Dr Pagani, I congratulate you on your work. Last week, I was at the FDA meeting in regard to the INTERMACS pump. I witnessed the pump in action, and all the other committee members there approved this dynamic pump. I disagree with the comments made in regard to the continued improvement in searching for a bridge to transplant and that the impact as mentioned is trivial. The experience in Europe has been highly successful and we await a smaller version. It is a compact and beautiful little pump.