References

1. Gaudino M, Zamparelli R, Andreotti F, Burzotta F, Iacoviello L, Glieca F, et al. Normothermia does not improve postoperative hemostasis nor does it reduce inflammatory activation in patients undergoing primary isolated coronary artery bypass. *J Thorac Cardiovasac Surg.* 2002;123:1092-100.
2. Misawa Y, Konishi H, Kawahito K, Fuse K. Platelet activation and aggregation during normothermic cardiopulmonary bypass. *Jpn J Thorac Cardiovasc Surg.* 2002;49:21-8.
3. Misawa Y, Kawahito K, Konishi H, Fuse K. Cytokine mediate endothelial activation during and after normothermic cardiopulmonary bypass: heparin-bonded versus non heparin-bonded circuits. *ASAIO J.* 2000;46:740-3.

doi:10.1067/mtc.2003.266

Reply to the Editor:

In contrast to the studies quoted by Misawa and Fuse, our investigation was aimed at comparing the effect of normothermic versus hypothermic cardiopulmonary bypass (CPB) on postoperative hemostasis and inflammatory activation. For this purpose, patients were randomly assigned to one of the two CPB temperatures (37°C vs 28°C), and several inflammatory and coagulative markers were evaluated at different time intervals in the postoperative period. We found no difference between the two groups and concluded that, at least for our CPB times, CPB temperature has no effect on postoperative hemostasis and inflammatory activation.

However, we congratulate Misawa and Fuse for their interesting studies on the effects of normothermic CPB on platelet function and cytokine production and we applaud their efforts to clarify the systemic effects of normothermia.

Mario Gaudino, MD
Gianfederico Possati, MD
Department of Cardiac Surgery
Catholic University
Rome, Italy
doi:10.1067/mtc.2003.267

An economic evaluation of lung transplantation

To the Editor:

In the March 2002 issue of this *Journal*, Anyanwu and associates[1] reported a prospective multicenter study about cost-effectiveness and cost-utility for the different types of lung transplantation. Although the study is an important addition to the existing literature, the method by which survival gain was calculated and the impact on their sensitivity analyses should be discussed further.

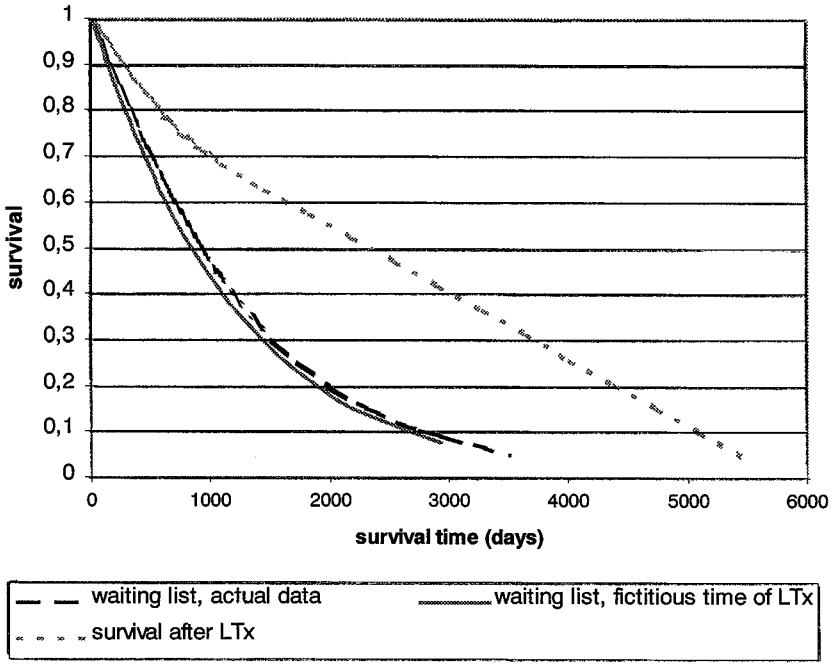

Figure 1. Actual waiting list survival, fictitious waiting list survival, and survival after lung transplantation *(LTx)* in Groningen lung transplant program, 1990 through 1995.

First, in the presented study Anyanwu and associates[1] calculated survival for the first 4 years from actual data and from years 4 to 15 by using a parametric Weibull model, in accordance with a previous analysis by our group.[2] At 15 years, the survival curve after transplantation was cut off despite a survival of at least 25%, depending on the type of transplantation. Survival on the waiting list declined to 0% after 11 years. For a valid comparison of costs and effects of both conditions from a lifetime perspective, a survival curve after transplantation should be constructed with further extrapolation until a survival of 0%.[3,4] Therefore the survival after lung transplantation in the presented study was underestimated, because prolonged survival beyond 15 years was neglected. A rough calculation indicates that extrapolation to 0% survival would amount to an estimated additional survival gain after transplantation of 2 years. This is why, in contrast to others,[5] Anyanwu and colleagues[1] did not find survival as a principal determinant of cost-effectiveness in their sensitivity analyses.

Second, the survival curve for the waiting list, to which the survival after lung transplantation was compared, was not constructed in accordance with previously reported methods.[3,4] In previous studies the transplantation date was chosen as the starting point for this comparison, because it would be unrealistic to assume that differences in survival occur before transplantation. For the situation on the waiting list, no real transplantation date exists, and a fictitious transplantation moment should be created (Figure 1). This moment should be based on the average stay of patients on the waiting list before transplantation (about 12 months in the study by Anyanwu and associates[1]). However, day 0 was used as the starting point for the waiting list. Applied to our own data, these two methods result in a difference in the cumulative number of life years on the waiting list of 0.5 years (17%).

Obviously, changing the method for the calculation of survival gain will also influence the number of quality-adjusted life years gained. It is possible that this would affect the results of the sensitivity analyses with respect

to the effects of varying utility values and posttransplantation maintenance costs as well, thereby changing the conclusions formulated by Anyanwu and associates.[1]

J. P. Ouwens, MD, PhD[a]
H. Groen, MD, PhD[a]
W. van der Bij, MD, PhD[b]
E. M. TenVergert, PhD[a]
Office for Medical Technology Assessment[a]
Department of Pulmonology[b]
University Hospital Groningen
PO Box 30.001
9700 RB Groningen, The Netherlands

References

1. Anyanwu AC, McGuire A, Rogers CA, Murday AJ. An economic evaluation of lung transplantation. *J Thorac Cardiovasc Surg.* 2002;123:411-20.
2. van Enckevort PJ, TenVergert EM, Bonsel GJ, Geertsma A, van der Bij W, de Boer WJ, et al. Technology assessment of the Dutch Lung Transplantation Program. *Int J Technol Assess Health Care.* 1998;14:344-56.
3. Bonsel GJ, Klompmaker IJ, Essink-Bot ML, Habbema JD, Slooff MJ. Cost-effectiveness analysis of the Dutch liver transplantation programme. *Transplant Proc* 1990;22:1481-4.
4. van Hout BA, Bonsel G, Habbema D, van der Maas P, de Charro F. Heart transplantation in the Netherlands; costs, effects and scenarios. *J Health Econ.* 1993;12:73-93.
5. Ramsey SD, Patrick DL, Albert RK, Larson EB, Wood DE, Raghu G. The cost effectiveness of lung transplantation: a pilot study. University of Washington Medical Center Lung Transplant Study Group. *Chest.* 1995;108:1594-601.

doi:10.1067/mtc.2003.286

Reply to the Editor:

We appreciate the comments of Ouwens and colleagues regarding our article on economic evaluation of lung transplantation. These comments highlight a major limitation of any economic study, which is the reliance on assumptions. Economic studies of therapies that have long-term benefits necessarily make predictions of future events. Because the future is always unknown, assumptions have to be imposed to allow modeling of data into the future. Methods used for modeling data vary from study to study. For this reason most economic studies include sensitivity analyses that examine the impact of alternative assumptions on the study conclusions.

Ouwens and colleagues propose two alternative approaches to examining the benefits of lung transplantation—assessing lifetime benefits and imposing a fictitious "transplant date" for the waiting list survival. Although it is true that the benefits of transplantation will continue beyond the 15-year time frame of our study, we elected to restrict benefits to those occurring in the first 15 years. We chose to restrict our analysis to 15 years because the robustness of the conclusions diminish as predictions go further over the horison. The Weibull method used to predict long-term survival is based on the observed short- to medium-term survival of a cohort of patients. In our study we predicted long-term survival on the basis of observed 4-year survival. We believe that this method overestimates survival after transplantation, however, because it does not allow for late deaths resulting from long-term complications of immunosuppression and chronic graft rejection or failure. For example, extrapolation of our data to 20 years suggests that 25% of patients will still be alive 20 years after lung transplantation, a figure that we consider overly optimistic. Indeed, if we were to continue our survival curve until there were no survivors, as suggested by Ouwens and colleagues, we would end up with several patients surviving to 100 years of age after having received a lung transplant.

Although such scenarios are statistically correct, we do not think that they are clinically plausible. Furthermore, any benefits after 15 years would be modest, because discounting means that future benefits carry less weight than do immediate benefits. For example, if we had examined benefits through 20 rather than 15 years, the benefit of single-lung transplantation would only improve from 2.1 to 2.2 quality-adjusted life years.

Assumptions also have to be imposed on defining the start of the waiting list episode, because there is no objective point to define as the start of medical treatment on the waiting list. Unlike transplantation, there is no medical intervention or event that can be ascribed to a particular day. There is at present no clear definition of the time of onset of end-stage lung disease, nor is there an objective method of deciding the point at which a patient should be listed for transplantation. Patients are listed at different stages of the disease process, depending on all sorts of patient-related, logistic, and local factors. We argue that the date a patient is registered on the waiting list is itself a robust measure neither of onset of end-stage lung disease nor of the need for lung transplantation. Methods of ascribing day 0 for waiting list survival (as a proxy for survival without transplantation) are therefore arbitrary and are bound to vary from study to study. As demonstrated by Ouwens and colleagues, different methods of ascribing day 0 for waiting list cohorts simply result in a small shift of the whole survival curve; they do not change its profile.

Although the approaches suggested by Ouwens and colleagues are valid alternatives to the methods that we used, they would not affect our study conclusions. We believe that the explanation for the modest benefit we found with lung transplantation lies not in our mathematical assumptions or techniques but in the relatively high early mortality after lung transplantation, which is observed on a global scale.[1] Our findings are indeed not unique; analyses of large North American databases have also questioned the notion that lung transplantation results in large survival improvements.[2,3]

A. C. Anyanwu
A. J. Murday
Glasgow Royal Infirmary
Glasgow, United Kingdom

References

1. Hertz M, Taylor D, Trulock E, Boucek M, Mohacsi P, Edwards L, et al. The registry of the International Society for Heart and Lung Transplantation: nineteenth official report—2002. *J Heart Lung Transplant.* 2002;21:950-70.
2. Liou TG, Adler FR, Cahill BC, FitzSimmons SC, Huang D, Hibbs JR, Marshall BC. Survival effect of lung transplantation among patients with cystic fibrosis. *JAMA.* 2001;286:2683-9.
3. Hosenpud JD, Bennett LE, Keck BM, Edwards EB, Novick RJ. Effect of diagnosis on survival benefit of lung transplantation for end-stage lung disease. *Lancet* 1998;351:24-7.

doi:10.1067/mtc.2003.287

To close or not to close?

To the Editor:

In their article "Intrapericardial Left Pneumonectomy after Induction Chemotherapy: The Risk of Cardiac Herniation," Baisi and associates[1] reported the use of a polytetrafluoroethylene patch for closure of the pericardium after herniation of the heart and recommended routine use of a patch for closure of pericardium without tension. I agree wholeheartedly that pericardial closure, if done at all, must always be without tension. However, pericardium does not always have to be closed. When lung resection for cancer requires excision of part of