Lung Retransplantation

All for One or One for All?

Long-term preservation of allograft function remains an elusive goal following lung transplantation. Despite current immunosuppressive strategies, bronchiolitis obliterans syndrome (BOS), a disorder characterized by irreversible airflow obstruction and presumed to be a consequence of chronic allograft rejection, develops in the majority of lung transplant recipients. Although its course may be interrupted by periods of relative stability, BOS is invariably a progressive disorder that ultimately robs the recipient of the functional gains that accompanied transplantation. A wide range of therapies, centering on augmentation of the magnitude of immunosuppression, have been employed, but there is no consensus on the optimal approach. At best, treatment appears to slow the rate of decline rather than to permanently arrest or reverse the process. Retransplantation represents the only definitive option, but lingering questions about optimal surgical approach, patient selection, outcomes, and ethics have tempered its widespread acceptance.

Answers to these questions are emerging from two principal sources: the Pulmonary Retransplantation Registry and published reports of single-center experiences. The Pulmonary Retransplantation Registry, spearheaded by Canadian transplant surgeon Dr. Richard Novick, had at the time of its most recent publication in 1999 accrued 230 patients from 47 centers across the United States, Canada, Europe, and Australia. Actuarial survival of this group following retransplantation was documented to be only 47% at 1 year, significantly below the 73% 1-year survival rate for primary transplantation. Factors associated with improved survival following retransplantation included retransplantation for BOS (vs causes of acute graft dysfunction such as primary graft failure, intractable airway complications, and severe acute rejection), ambulatory and ventilator-independent preoperative status, and an interval of > 2 years from the time of initial transplantation. By logistic regression analysis, a patient fulfilling these criteria had a calculated probability of 1-year survival of 69%, suggesting that with application of stringent selection criteria, survival following retransplantation can approximate that of the primary procedure. Analysis of pulmonary function revealed an ominous trend among the subgroup of patients undergoing retransplantation because of severe BOS. These patients demonstrated a more rapid decline in FEV₁ and a fourfold higher incidence of BOS by 3 years, compared to the group of patients who underwent retransplantation for acute graft dysfunction. Future iterations of the Pulmonary Retransplantation Registry, involving more patients and a longer period of follow-up, should provide further insight into whether BOS returns in an accelerated fashion in those undergoing retransplantation for this indication.

In this issue of CHEST (see page 1832), Brugiere and colleagues from Hopital Beaujon present their experience in retransplantation of 15 patients with BOS. In light of the much larger collective experience documented by the Pulmonary Retransplantation Registry, what role is served by the observations from a single center? First, while the Pulmonary Retransplantation Registry provides a measure of the average outcomes achieved by a collective group of centers of varying experience, single-center studies often provide a glimpse of the optimal outcomes achieved by a highly accomplished center. Indeed, Brugiere and colleagues achieved an impressive 1-year survival rate of 60% among a group of high-risk patients, 40% of whom were nonambulatory prior to surgery. Second, while the Pulmonary Retransplantation Registry relies on analysis of "second-hand" data collected from a questionnaire, a study emanating from a single center has the advantage of drawing from the direct observations made by the clinicians caring for the patients. This permits a more detailed description of events and complications than can be gleaned from a questionnaire. This is illustrated by the description that Brugiere and colleagues provide about the problems posed when an original allograft was left in place following retransplantation. Of 11 patients who had a retained graft, 6 patients acquired bacterial pneumonia in this graft; in four of these instances, the infection proved fatal. The susceptibility of the old graft to infection was ostensibly related to the progressive development of bronchiectasis within the graft and resultant colonization with virulent Gram-negative organisms. In addition to pneumonia, bronchorrhea requiring daily chest physiotherapy developed in three patients as a consequence of underlying bronchiectasis. Based on these observations, the authors recommend that the retransplantation procedure of choice should be one that does not leave an old graft behind (i.e., ipsilateral single-lung following initial single-lung transplantation, and bilateral lung following initial bilateral or heart-lung transplantation). Given the small number of patients in the series and the failure of the larger Pulmonary Retransplantation Registry to discern a statistically significant survival difference between patients with and without a retained graft following retransplantation, these recommendations must be viewed as preliminary. At the very least, the article by Brugiere and colleagues should prompt those who...
maintain the Pulmonary Retransplantation Registry
to collect more detailed data on this issue so that
more definitive conclusions can be reached in the
future.

The most vexing questions about retransplantation
are not addressed by either the Pulmonary Retrans-
plantation Registry or by the study by Brugiere and
colleagues. In an era marked by a scarce and static
donor organ supply that meets the needs of only one
fourth of listed candidates, can we justify a policy of
retransplantation that affords a patient a second
opportunity while depriving another of a first? If we
accept retransplantation as a legitimate therapeutic
option, should its use be restricted to only those
patients with a profile favoring survival (ie, ambula-
tory patients at least 2 years beyond initial transplan-
tation with BOS) and to only those centers judged by
volume and outcomes to possess the experience to
perform this technically challenging procedure?
Should there be, as some have advocated, an annual
cap on the number of organs allocated for the
purpose of retransplantation? The transplant com-
11
13
14
15
munity needs to confront these questions and to
establish guidelines to ensure that this procedure is
not applied in an arbitrary and uncontrolled fashion.
Ultimately, we must strike a balance between the
competing goals of maximizing the distribution of a
scarce resource to the greatest number of patients vs
optimizing the outcome of the individual patient.

Robert M. Kotloff, MD, FCCP
Philadelphia, PA

Dr. Kotloff is Associate Professor of Medicine, and Director,
Program for Advanced Lung Disease and Lung Transplantation,
Pulmonary, Allergy, and Critical Care Division, University of
Pennsylvania Medical Center.

Reproduction of this article is prohibited without written permis-
sion from the American College of Chest Physicians (e-mail:
permissions@chestnet.org).

Address correspondence to: Robert M. Kotloff, MD, FCCP, 838
West Gates, University of Pennsylvania Medical Center, 3400
Spruce St, Philadelphia, PA 19104; e-mail: kotloff@mail.med.
upenn.edu

REFERENCES
1999; 340:1051–1091
2 Novick RJ, Stitt LW, Al-Kattan K, et al. Pulmonary retrans-
plantation: predictors of graft function and survival in 230
patients; Pulmonary Retransplant Registry. Ann Thorac Surg
1998; 65:227–234
3 Hertz MI, Taylor DO, Trulock EP, et al. The Registry of the
International Society for Heart and Lung Transplantation:
2002; 21:950–970
4 Novick RJ, Stitt L, Schafers HJ, et al. Pulmonary retrans-
plantation: does the indication for operation influence postoper-
ative lung function? J Thorac Cardiovasc Surg 1996; 112:
1504–1513; discussion 1513–1504
5 Novick RJ. Heart and lung retransplantation: should it be

Cardiac Biomarkers in
Pulmonary Embolism

Pulmonary embolism (PE) encompasses a wide
spectrum of illnesses, with diverse prognoses and
management strategies. Some PEs, detected seren-
dipitously by chest CT scanning, cause no apparent
adverse symptoms or signs. They are anatomically
tiny and have minimal clinical impact, at least in
patients without concomitant proximal leg deep vein
thrombosis. The heparin treatment is required as a
“bridge” to warfarin treatment. In this situation, the
major debate is about whether to hospitalize the
patients for the traditional 5 to 7 days, to abbreviate
the hospital stay by using low-molecular-weight hepa-
arin in lieu of continuous IV infusion of unfrac-
tionated heparin, or even to consider complete outpa-
tient therapy1,2 with subsequent office follow-up. At
the other end of the spectrum are patients who are
critically ill in cardiogenic shock. Their survival
will depend on the rapid detection of the PE fol-
lowed by implementation of the following emerg-
cy treatment plan: successful debulking of the
clot, either with thrombolysis3,4 or embolectomy.5,6

These two divergent scenarios represent the ex-
tremes, not the every day “usual” PEs that confront
those of us who commonly treat patients with this
disease. Most patients with PE have mild symptoms
and signs of cardiopulmonary distress but do not, at
least initially, appear to have a life-threatening ill-
ness. They are often triaged to a stepdown unit
rather than to an ICU. They usually maintain a
normal systemic arterial pressure, although they
often present for initial evaluation with tachycardia
and anxiety. Most patients survive and improve
clinically within a day or two. However, recurrent PE
will unexpectedly strike some patients who appear to
be on the path to recovery. Those who relapse will
require an escalation of therapy, with emergently
administered thrombolysis, catecholamine agents,
cardiopulmonary resuscitation, or mechanical venti-
lation.

The group of patients presenting with PE of
intermediate severity poses a challenge. How can we
risk stratifying them appropriately at the time the PE
is initially diagnosed? What predictive tools are
available to assist us in our clinical assessment?
The medical history and physical examination are
excellent starting points. Transient syncope or cy-
nosis portend a major PE with a complicated hospital