Transplantation

Restoring blood supply to the heart while replacing the lungs; is it worth the risk?

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Lung transplantation (LTx) is a potentially life-saving treatment for well selected patients with end-stage lung disease [1]. Coronary artery disease (CAD) is a frequent co-morbidity in LTx candidates with previous smoking history [2] which can accelerate post-transplant in patients on life-long immunosuppressive therapy [3].

According to the 2014 updated consensus document for the referral and listing of LTx candidates from the International Society for Heart and Lung Transplantation, untreatable cardiac dysfunction is considered an absolute contraindication for LTx unless combined heart-lung transplantation can be performed [4]. CAD with preserved cardiac function is to be considered a relative contraindication. Patients with end-stage lung disease with mild to moderate CAD can benefit from medical therapy while transplant candidates with more severe CAD will need revascularization with percutaneous coronary interventions (PCI) or coronary artery bypass grafting (CABG). The degree of coronary artery disease deemed acceptable as well as the timing of these coronary interventions may vary among transplant centers [4].

In a retrospective study published in this issue of *Transplantation*, Halloran et al. from the University of Alberta in Edmonton, Canada, examined the possible impact of CAD on survival in a cohort of 333 LTx recipients between 2004-2013 [5]. Outcome was compared between CAD patients undergoing concomitant CABG and LTx (7%) with those not requiring CABG (25%) and with a group without CAD (68%). Using a Cox multivariable proportion hazards regression model adjusted for age, gender, and LTx indication, CAD status itself was not

identified as a risk factor associated with overall survival. However, incidence of grade 3 primary graft dysfunction was higher and duration of mechanical ventilation, ICU and hospital stay were longer in both CAD groups. Interestingly, unadjusted survival analysis by Kaplan Meier and log rank testing did reveal a significant difference between the three groups in median and three-year survival, but not in hospital and one-year survival [5]. It is fair to state that the older recipient age (about 10 years) and the higher proportion of male gender in both CAD groups were largely responsible for the inferior overall three-year survival compared to the non-CAD group. Likely, transplant indication negatively influenced survival since a higher proportion of patients with interstitial lung disease were transplanted in both CAD groups. These three recipient characteristics, adjusted for in the multivariable analysis, are well known risk factors for survival [6,7]. The authors correctly concluded that CABG at the time of LTx can be safely performed in highly selected candidates.

PCI with or without stenting can be a valuable option in lung transplant candidates with proven CAD and a critical stenosis. Of note, patients with coronary stents will temporarily need dual antiplatelet therapy for a minimum of 3-6 months depending on the type of stent used. Continued stent patency should preferably be reassessed with coronary angiography prior to acceptance on the waiting list, particularly in case of bare metal stent which has a higher prevalence of in-stent restenosis compared to drug eluting stents. It was interesting to notice that ±11% of their patients with CAD had PCI previously while 2% had CABG before LTx [5].

Another interesting discussion is the timing of intervention in patients needing both LTx and revascularization with CABG. When CABG is performed prior to listing, patients with end-stage lung disease carry a higher risk for developing pulmonary complications after sternotomy. This may result in respiratory insufficiency and death. Most centers, therefore, prefer to revascularize the heart at the time of LTx. The order of both concomitant procedures is debatable and will largely depend on the experience of the surgeons involved. Most teams prefer CABG immediately prior to LTx although this may result in lengthening of cold ischemic time for both pulmonary grafts. Good coordination between the lung retrieval team and the transplant team is critical to shorten this period. Alternatively, the first lung can be implanted followed by CABG [8]. Also the best strategy for extracorporeal life support (ECLS) to execute both procedures is debatable. For single-vessel disease of anteriorly located coronary arteries, revascularization can be performed off-pump using a saphenous vein graft or preferably an internal mammary artery graft harvested at the time of anterior thoracotomy or clam-shell incision. In patients with multi-vessel disease, some centers still favor off-pump CABG while others will use cardiopulmonary bypass (CPB) with or without cardioplegic arrest. Weaning the patient from CPB and continuing the implantation of both lungs off-pump will shorten the total time on ECLS. However, more manipulation and compression of the freshly revascularized heart is to be expected. An alternative way for ECLS would be to switch from CPB to veno-arterial extracorporeal membrane oxygenation (V-A ECMO) and continue LTx with beating heart.

Indeed, several recent case series and meta-analyses have demonstrated the superiority of V-A ECMO versus CPB for intraoperative support during LTx because of less bleeding complications (less heparin) and lower degree of systemic inflammatory reaction.

Irrespective the timing and technique of revascularization, the importance of adequate post-transplant cardiovascular prevention cannot be overestimated. Life-long antiplatelet therapy, statins, blood pressure control, and healthy lifestyle measures are key in order to reduce the risk of new cardiac events [9].

The authors are to be congratulated with their in-depth analysis and interesting results. Restoring blood supply to the heart while replacing the lungs does not seem to increase perioperative risk in well selected patients. These findings may encourage other lung transplant teams with less experience to accept more patients with CAD on their waiting list who may benefit from concomitant CABG and LTx. The presence of CAD discovered during pre-transplant work-up is too often used as an excuse not to accept an otherwise good candidate on the waiting list in countries with low donor rates. All possible options to revascularize the heart should be explored in lung transplant candidates with severe CAD and a well preserved cardiac ejection fraction.

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