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Post-transplant medication and follow up strategy

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Lung transplantation has become an increasingly important mode of therapy for patients with a variety of end-stage lung diseases. Despite many advances in the field of lung transplantation, however, lung transplant recipients have the lowest median survival of any solid organ transplant population. Improvements in immunosuppression and therapeutic management of infections have resulted in improved long-term survival and a decline in allograft rejection. However, allograft rejection continues to be a serious complication following lung transplantation, thereby leading to acute graft failure and, subsequently, chronic lung allograft dysfunction (CLAD). Bronchiolitis obliterans syndrome (BOS), the most common phenotype of CLAD, is the leading cause of late mortality and morbidity in lung recipients, with 50% having developed BOS within 5 years of lung transplantation. Infections in lung transplant recipients are also a significant complication and represent the most common cause of death within the first year. Therefore, the success of lung transplantation depends on careful monitoring of transplant lung function to detect graft dysfunction early, while monitoring recipients for infections and complications to help identify problems early. Routine monitoring after lung transplantation is intended to prevent complications or to detect them as soon as possible. While monitoring is most intensive during the first year after transplantation, it must continue for the lifetime of the recipient. The method includes check-ups by a clinician, spirometry, chest radiographs, and selected blood tests to regulate the immunosuppressive medications. Maintenance immunosuppressive therapy is administered to all lung transplant recipients to help prevent acute and chronic rejection and the loss of the lung allograft. ubstantial progress has been made in developing immunosuppressive regimens to prevent acute and chronic rejection, while trying to reduce the side effects of immunosuppression. However, despite improvements in immunosuppressive therapy, acute and chronic transplant rejection remain important obstacles to successful lung transplantation. Maintenance regimens typically consist of three drugs, including a glucocorticoid, a calcineurin inhibitor (cyclosporine, tacrolimus), and a nucleotide blocking agent (azathioprine, mycophenolate mofetil). The mTOR inhibitors (sirolimus and everolimus) are alternative agents used in lung transplantation maintenance immunosuppression and have been used as replacements for the nucleotide blocking agents or, less commonly, for calcineurin inhibitors, but not

approved in lung transplantation in Korea. The maintenance immunosuppressive regimen used in a given individual is based upon side effect profile and tolerability of medication, because there is no consensus regarding the optimal maintenance regimen for immunosuppression following lung transplantation. In the 2019 registry report from the International Society for Heart and Lung Transplantation (ISHLT), however, 62% of all lung transplant recipients were on a combination of tacrolimus, mycophenolate, and prednisone a year after lung transplantation. Important anatomic and physiologic changes occur over the months to years following lung transplantation. Postoperative respiratory function of the recipient will reflect these changes in addition to any lung injury that occurs related to the transplantation. The use of early, sensitive testing in monitoring the status of the graft is essential for detecting changes in functional progress. Forced spirometry is carried out periodically and routinely in the monitoring of lung transplant patients. Over the first few months after transplantation, forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV_1) usually improve, generally reaching a plateau by one year although the best post-transplant values might be achieved at different time points for FEV_1 and for FVC. Declines in the FEV_1/FVC ratio following lung transplantation, representing increased airflow obstruction, may be a manifestation of acute or chronic rejection, infection, or airway stenosis. When all other causes have been ruled out, an otherwise unexplained decline in FEV and/or forced expiratory flow (FEF) 25-75 represents an obstructive type of CLAD, also known as BOS. In addition to BOS, other phenotypes of CLAD have been suggested. Rigorous spirometry follow-up for dynamic lung volumes other than FEV_1 and its comparison to the best post-transplant values may help to identify these physiologic subtypes. The loss of FVC (FVC/FVC best <0.8) with a more restrictive pattern is associated with restrictive allograft syndrome (RAS) and correlates with worse survival than other types of CLAD. Chest X-ray is routinely performed in the early post-transplant phase, every 3–6 months in the late phase and any time that it is clinically indicated. Computed tomography during the first month after surgery detects changes in vascular anastomoses and/or in the pulmonary parenchyma. Subsequently, it no longer appears to offer an advantage in the early diagnosis of bronchiolitis obliterans, so it should be indicated only if the clinical symptoms or pulmonary function tests suggest some change not visible on chest X-ray Periodic, surveillance transbronchial lung biopsy in asymptomatic, clinically and physiologically stable recipients is controversial, and the practice varies among centers. In the absence of symptoms, routine graft surveillance with bronchoscopy is currently under discussion, while it allows for the diagnosis of asymptomatic rejection episodes, it does not appear to modify patient survival. For patients with a clinical syndrome suggestive of acute rejection or infection, bronchoscopy with bronchoalveolar lavage and lung biopsy is the most sensitive diagnostic study to identify the etiology of pulmonary infection and rule out atypical etiologies (eg, hemorrhage, malignancy). Patients with end-stage lung disease waiting for a transplant have varying significant comorbidities, which are typically chronic in nature. These comorbidities require ongoing management and may be exacerbated following transplantation, potentially resulting in poor quality of life and shortened post-transplant survival. Immunosuppressive medications contribute to cardiovascular comorbidities such as hyperlipidemia, diabetes, hypertension, and renal disease. Renal dysfunction from calcineurin inhibitors is the most common long-term complication encountered in lung

recipients. In summary, the lung transplant patient's prognosis will depend largely on the degree of efficacy in the prevention, early diagnosis and appropriate treatment of possible complications. Accordingly, regardless of how long it is since the transplantation, graft recipients undergo close functional and clinical monitoring.