



## Review

Long-Term Follow-Up of the Lung Transplant Patient<sup>☆</sup>

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## ABSTRACT

Since the outcomes of lung transplants are still poorer than those obtained with others, such as heart, kidney or liver transplants, the challenge for medicine remains focused on prolonging functional graft survival. The procedure triggers significant post-surgical physiopathological changes in the lung parenchyma, the rib cage, the airways and pulmonary circulation. The patient is exposed to risks that must be identified and controlled, such as complications fully or partially attributable to immunosuppressive treatment, including cardiovascular disease, tumours and infections and, of course, chronic graft dysfunction.

The 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. In this article, we will review the functional changes that characterise a lung transplant recipient and the usefulness of the various diagnostic techniques for patient follow-up.

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## Seguimiento a largo plazo del paciente trasplantado pulmonar

## RESUMEN

Debido a que los resultados del trasplante pulmonar son todavía inferiores a los obtenidos en otros trasplantes como el cardiaco, el renal o el hepático, los retos de la medicina se deben centrar en aumentar la supervivencia funcional de los injertos. La intervención provoca marcados cambios fisiopatológicos posquirúrgicos a nivel del parénquima pulmonar, la caja torácica, las vías aéreas y la circulación pulmonar. No obstante, el paciente está sometido a riesgos que es importante conocer y controlar, como las complicaciones atribuibles total o parcialmente al tratamiento inmunosupresor, entre ellas la patología cardiovascular, la aparición de tumores, infecciones y, por supuesto, la disfunción crónica del injerto.

El pronóstico del paciente va a depender, en gran medida, de la mayor o menor eficacia en prevenir, diagnosticar precozmente y en su caso tratar de forma adecuada las posibles complicaciones. Por ello, independientemente del tiempo postrasplante, los receptores son sometidos a una estrecha monitorización funcional y clínica. En este artículo revisaremos las alteraciones funcionales características del receptor de un trasplante pulmonar y la utilidad en el seguimiento del paciente de las diferentes técnicas diagnósticas.

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## Palabras clave:

Trasplante pulmonar

Calidad de vida

Supervivencia

## Introduction

The advances of recent years mean that lung transplantation has become an essential treatment option for some irreversible lung diseases. The patient must confront the risks derived from immunosuppressive treatment and complications with the transplanted

lung. Close patient monitoring allows the detection and diagnosis of foreseeable complications at an early stage when they are still easily reversible, before the clinical manifestations become fulminant and irreversible. The monitoring protocol must be tailored to each individual patient and to each specific stage, in accordance with the time since the transplant and the patient's progress.

Post-transplantation monitoring aims to maintain optimal immunosuppression for each specific patient, maximising pharmacological efficacy while minimising toxicity, and to detect and control any systemic side effects<sup>1–4</sup> (Table 1) and graft complications, such as early dysfunction, infections, tumours and acute or chronic rejection.

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**Table 1**  
Principal Side Effects of Immunosuppressive Drugs.

Drug	Side effect
Steroids	Hypertension, hyperlipidaemia, hypocalcaemia-osteoporosis, weight gain, cataracts, psychological changes
Antimetabolites (mycophenolate, azathioprine)	Myelosuppression, liver toxicity, alopecia, gastrointestinal intolerance, acute pancreatitis, infections, malignant disease
Calcineurin inhibitors (cyclosporin, tacrolimus)	Nephrotoxicity, hypertension, hyperuricemia, hyperkalaemia, diabetes, hyperlipidaemia, neurotoxicity, gingival hyperplasia, infection, lymphoproliferative disease
m-TOR inhibitors (everolimus, rapamycin)	Hyperlipidaemia, diabetes, oedemas, proteinuria, pneumonitis

Awareness of the functional progress of the transplanted organ is indispensable for patient management. Post-surgical physiopathological changes are largely influenced by factors such as irreversible denervation of the graft and muscle involvement. The afferent and efferent nerves are severed during surgery without any evidence of subsequent re-innervation. Accordingly, even if the patient recovers practically complete lung function, tolerance to exercise is often reduced and there are changes in the response to hypercapnia, the cough reflex and mucociliary clearance. The functional progress of the transplant can be evaluated by maximum post-surgical pulmonary function, exercise tolerance, quality of life and survival.

#### Maximum Post-Surgical Pulmonary Function

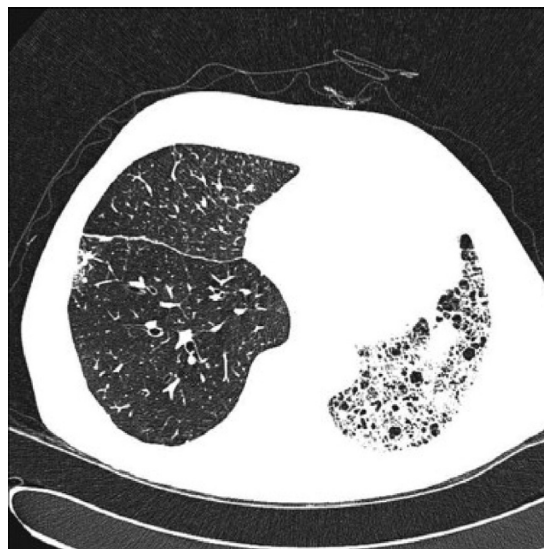
Scarring from the trauma of surgery and the adaptation of the graft to the recipient's chest cavity affect progressive functional improvement.

Post-operative pulmonary function depends on the type of transplant, whether unilateral or bilateral, the underlying disease and post-operative complications.<sup>5</sup>

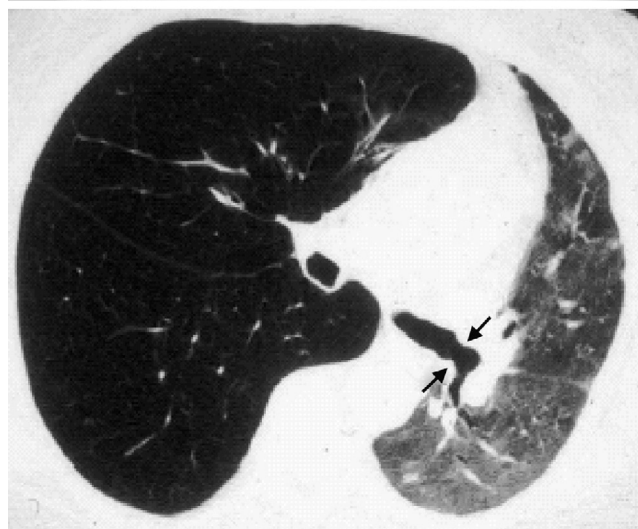
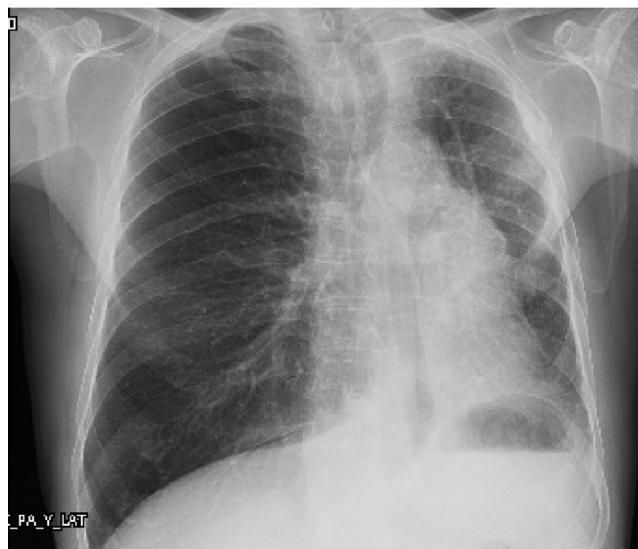
In bilateral transplant recipients, maximum post-operative pulmonary function is not affected by the underlying disease, but it is influenced by the characteristics of the graft, the recipient's chest cavity and post-operative complications. Between 6 and 9 months after surgery, FEV<sub>1</sub> figures of between 75% and 85% and FVC from 66% to 92% may be achieved. In the first months after surgery, mild restriction is observed which normalises after the sixth month. This is due to two different mechanisms: changes in chest wall mechanics caused by the thoracotomy, and the disparity in volume between the graft and the thoracic capacity of the recipient. DLCO and gas exchange usually normalise after the third month, and exercise tolerance increases progressively as time goes by.<sup>6,7</sup>

In unilateral transplant recipients, pulmonary function stabilises earlier, around the third month, because there is less trauma from the surgery. In these patients, maximum pulmonary function is lower than in bilateral transplant recipients and is also affected by the characteristics of the residual native lung. In recipients with interstitial disease, there is a tendency for the native lung to collapse, so the graft lung expands freely into the corresponding hemithorax (Fig. 1). There may be mild or moderate residual restriction and altered diffusion due to the presence of the native lung.<sup>8</sup>

When the underlying disease is emphysema, the residual native lung tends to distend and herniate into the contralateral hemithorax, causing partial collapse of the graft (Fig. 2). Progressive air trapping produces hyperinflation in the native lung, but this does not usually present problems when the lung is functioning adequately. On occasions, the progressive distention of an emphysematous lung may compromise graft function, so



**Fig. 1.** Chest CT of a patient with right unilateral lung transplant due to pulmonary fibrosis.



**Fig. 2.** Chest X-ray and chest CT of a patient with left unilateral lung transplant due to COPD.

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