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EDITORIAL

Ten tips for the intensive care management of transplanted lung patients

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Introduction

Complications following lung transplantation (LTx) are diverse and range from immunologic reactions to cancerous malignancies. The correct identification of the causative pathology requires a purposive diagnostic strategy that considers all these possibilities (Fig. 1). Here, we present ten general tips for the intensive care management of post-LTx patients. However, case-by-case decisions on volume therapy and ventilator strategies should be obtained in a specialized center.

1. Consider multiple causes of acute respiratory failure (ARF)

Infections are the main cause of ICU admission beyond the postoperative period. These patients may also develop severe ARF as a consequence of graft dysfunction, requiring bronchoscopy with transbronchial lung biopsy (TBB) and determination of antibodies. Pulmonary edema, tracheal stenosis, and drug toxicity are other causes to be considered.

2. Protective ventilation of LTx donors can improve LTx outcome

Lung donors are scarce and the criteria for potential donor lungs are stringent. To reduce stress on the donor organs it is recommended to use protective ventilation settings not only after LTx but also for potential donor lungs [1]. In addition, overall survival rate after LTx is comparable between donors that received short-term or long-term mechanical ventilation. Criteria for lung donation have been updated recently [2].

3. Apply ventilatory lung-protective strategies and early extubation

Lung-protective ventilator strategies are based on practices from other diseases (e.g., acute respiratory distress syndrome, ARDS). Positive end-expiratory pressure (PEEP) of 5 cmH_2O is generally preferred and should not exceed 12.5 cmH_2O. However, PEEP is contraindicated for LTx patients suffering from emphysema. Tidal volumes should be based on the donor's predicted body weight, with an average tidal volume of 5 mL/kg [3]. Extubation reduces complications such as pulmonary infections and should thus be attempted early after LTx [4]. Third-degree primary lung graft dysfunction and prolonged mechanical ventilation should be anticipated in case of preoperative pulmonary hypertension, intraoperative extracorporeal membrane oxygenation (ECMO), bleeding, and ex vivo reconditioning donors anticipate delayed weaning.

4. Short-term pulses of steroids are indicated for acute graft rejection

Symptoms of acute graft rejection are non-specific (e.g., low-grade fever, shortness of breath, opacities on chest X-ray, hypoxemia) and may be mistaken for infection or drug toxicity. Acute graft rejection is characterized by lymphocytic infiltrates in arterioles and bronchioles. Diagnosis should, therefore, be histologically confirmed by TBB, ideally by reference laboratories with long-standing expertise in the assessment of acute graft rejection. Donor-specific antibodies need to be assessed. Along with the adjustment of the immunosuppressive maintenance therapy, short-term pulse treatment with corticosteroids is indicated [5].

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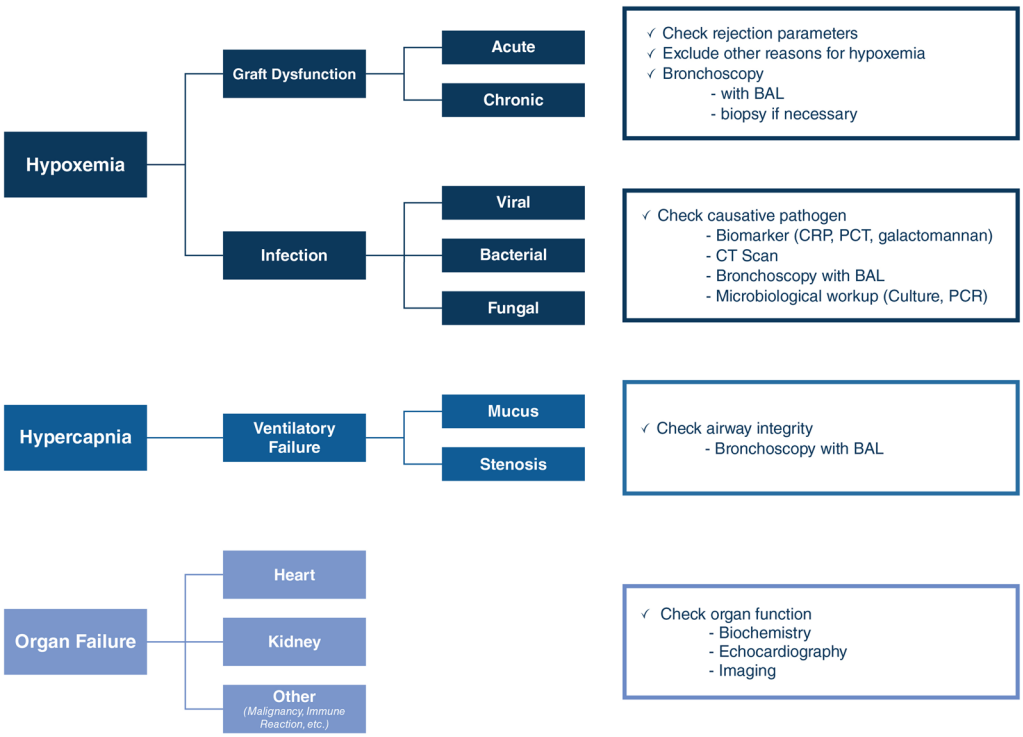

Fig. 1 Common causes of post-LTx ICU admission and diagnostic suggestions. Common complications encountered following LTx include hypoxemia, hypercapnia, and organ failure. To properly address these complications the correct diagnosis of the underlying pathology is paramount

5. Acute kidney injury is usually reversible by reducing calcineurin inhibitors

Acute kidney injury (AKI) following LTx is associated with both increased morbidity and mortality. Kidney dysfunction after LTx is often the result of the application of calcineurin inhibitors (CNIs) as immunosuppressive agents. AKI is usually reversible by reduction of CNIs. To accurately diagnose AKI, decreases of creatinine clearance levels should be analyzed proportionally to the preoperative renal function [6]. Using aprotinin increases the risk of AKI [6]. Alternative therapies are limited, but basiliximab provides a "CNI-free window" allowing recovery from an episode of AKI [7].

6. *Pseudomonas aeruginosa* is the most common cause of pneumonia

Nosocomial infections (NI) significantly increase perioperative LTx mortality [5]. Healthcare-acquired pneumonia is the most common infectious complication after LTx [8]. Compared to non-transplant surgical patients, gram-negative bacteria, especially *P. aeruginosa*, are the predominantly observed pathogens, followed by *Staphylococcus aureus*. Double-lung LTx patients are more likely to develop NI than single-lung recipients (1). Unclear deterioration of pulmonary function needs to be immediately examined bronchoscopically, ideally using the highly sensitive bronchoalveolar lavage (BAL) with galactomannan test and semiquantitative cultures [9]. In particular, invasive fungal infections are a major burden in severely immunocompromised patients.

7. Community-acquired respiratory viruses (CARV) should be considered using molecular diagnostic testing

Viral infections are known to support the development of a chronic graft rejection and may, in addition, lead to respiratory failure. Rhinovirus, influenza, parainfluenza, RSV, and other CARV are often the cause of ARF in LTx recipients, after the implementation of viral molecular diagnostic tests, which should be standard of practice after 2014 [9, 10]. The introduction of more specific and effective prophylaxis has represented a shift in the causes of lung infection in LTx recipients.

8. Consecutive bronchoscopy is paramount to diagnosis of airway complications

Airway complications (AC) are relatively common. The reported incidence varies greatly, mostly because of the absence of a uniform diagnostic classification. Six forms

of AC have been identified (necrosis-dehiscence, infection, stenosis, malaise, fistula, and granulation tissues). They mostly result from infection, rejection, persistent ischemia, or (inadequate) surgical technique. Improvement of surgical techniques, immunosuppression, and antibiotic therapy reduces AC. Therapeutic approaches comprise medical treatment (infection, immunosuppression), stenting, and flap wrapping (omentum, peribronchial fat, and pericardium) [11].

9. Primary graft dysfunction (PGD) can be anticipated by plasma procalcitonin

PGD occurs in 10–25% of LTx making it the most frequent cause of mortality within 72 h of LTx. It can be characterized as a severe form of ischemia-reperfusion syndrome with reduced oxygenation and pulmonary opacities. Just as for ARF, treatment of PGD is supportive. In severe cases, inhaled nitric oxide may be applied and ECMO might be indicated [12]. Procalcitonin may be used for identification of patients with low-risk of 3rd degree PGD [13]. PGD patients show impaired long-term graft function and are at higher risk of developing bronchiolitis obliterans syndrome (BOS) and chronic lung allograft dysfunction (CLAD).

10. CLAD is not an exclusion criterion for ICU admission

CLAD is progressive and irreversible. It continues to be the main obstacle to long-term survival of LTx patients. CLAD responds only poorly to therapy; however, CLAD is not a homogenous entity. It is a common misunderstanding that CLAD patients always present with near-terminal disease and that therapeutic limitation dictates ICU admission restriction. This, however, should be reconsidered and CLAD should not represent a limitation for ICU admission [5].

Electronic supplementary material
The online version of this article (https://doi.org/10.1007/s00134-019-05578-1) contains supplementary material, which is available to authorized users.

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