

## Current aspects on the selection of patients who are candidates for lung transplantation

Aspectos atuais sobre a seleção de pacientes candidatos a transplante pulmonar

Aspectos actuales sobre la selección de pacientes candidatos a trasplante pulmonar

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### **Abstract**

Currently, the main indications for lung transplantation worldwide are chronic obstructive pulmonary disease (COPD), pulmonary fibrosis, cystic fibrosis, alpha-1-antitrypsin (alpha-1) deficiency, idiopathic pulmonary arterial hypertension, bronchiectasis, retransplantation, sarcoidosis and severe lung injury caused by COVID-19, and these candidates must demonstrate knowledge regarding the procedure, good adherence to the medical treatment performed, adequate psychosocial structure and family support. Furthermore, the proper assessment of contraindications contributes to a lower occurrence of unfavorable clinical outcomes unrelated to the graft, benefiting patients with a greater chance of success and, thus, improving overall survival with treatment. Among the absolute contraindications, lung cancer, cardiac dysfunction unrelated to lung disease, significant organic dysfunction of any other noble organ, hepatitis B and C virus infections, active pulmonary tuberculosis and severe rib cage deformity stand out. Furthermore, among the relative contraindications, there is age over 65 years, severe clinical instability, HIV infection, obesity, severe osteoporosis and decompensated systemic diseases.

**Keywords:** Lung transplantation; Selection; Contraindications.

### **Resumo**

Atualmente, as principais indicações de transplante pulmonar em todo o mundo são doença pulmonar obstrutiva crônica (DPOC), fibrose pulmonar, fibrose cística, deficiência de alfa-1-antitripsina (alfa-1), hipertensão arterial

pulmonar idiopática, bronquiectasias, retransplante, sarcoidose e lesão pulmonar grave causada pela COVID-19, devendo esses candidatos demonstrar conhecimento sobre o procedimento, boa adesão ao tratamento médico realizado, estrutura psicossocial adequada e apoio familiar. Além disso, a avaliação adequada das contraindicações contribui para a menor ocorrência de desfechos clínicos desfavoráveis não relacionados ao enxerto, beneficiando os pacientes com maior chance de sucesso e, assim, melhorando a sobrevida global com o tratamento. Dentre as contraindicações absolutas, destacam-se câncer de pulmão, disfunção cardíaca não relacionada à doença pulmonar, disfunção orgânica significativa de qualquer outro órgão nobre, infecções pelos vírus das hepatites B e C, tuberculose pulmonar ativa e deformidade grave da caixa torácica. Além disso, entre as contraindicações relativas, estão idade acima de 65 anos, instabilidade clínica grave, infecção pelo HIV, obesidade, osteoporose grave e doenças sistêmicas descompensadas.

**Palavras-chave:** Transplante de pulmão; Seleção; Contra-indicações.

### Resumen

Actualmente, las principales indicaciones para el trasplante de pulmón a nivel mundial son la enfermedad pulmonar obstructiva crónica (EPOC), la fibrosis pulmonar, la fibrosis quística, el déficit de alfa-1-antitripsina (alfa-1), la hipertensión arterial pulmonar idiopática, las bronquiectasias, el retransplante, la sarcoidosis y la lesión pulmonar grave causados por el COVID-19, y estos candidatos deberán demostrar conocimiento sobre el procedimiento, buena adherencia al tratamiento médico realizado, adecuada estructura psicossocial y apoyo familiar. Además, la evaluación adecuada de las contraindicaciones contribuye a una menor ocurrencia de resultados clínicos desfavorables no relacionados con el injerto, beneficiando a los pacientes con mayores posibilidades de éxito y, por lo tanto, mejorando la supervivencia global con el tratamiento. Entre las contraindicaciones absolutas destacan el cáncer de pulmón, la disfunción cardíaca no relacionada con enfermedad pulmonar, la disfunción orgánica significativa de cualquier otro órgano noble, las infecciones por virus de la hepatitis B y C, la tuberculosis pulmonar activa y la deformidad severa de la caja torácica. Además, las contraindicaciones relativas incluyen edad mayor de 65 años, inestabilidad clínica severa, infección por VIH, obesidad, osteoporosis severa y enfermedades sistémicas descompensadas.

**Palabras clave:** Trasplante de pulmón; Selección; Contra indicaciones.

## 1. Introduction

The first successful cardiopulmonary transplant performed in the world was in 1981, by the Stanford University team. Proportionally, in Brazil, lung transplantation is less frequent than other solid organ transplants, despite survival results being comparable to those reported in the literature. The high complexity of the surgical procedure and the resources needed to care for lung transplant patients, in addition to the need for training a highly specialized medical team, makes it difficult to create transplant centers. Another limiting factor for performing more procedures is the low utilization of the lungs of multiple organ donors (Bennett et al., 2020).

Lung transplantation is an established therapeutic option for the treatment of patients with advanced or terminal lung disease who are refractory to other conventional modalities. As is well known, there is a great disproportion between the availability of organs for donation and the number of patients waiting on the transplant waiting list. For all these reasons, the optimization of this process begins with a process of judicious selection of patients who present a good probability of a satisfactory perioperative course. Such selection depends on a careful balance between the risks and benefits related to carrying out such a procedure. The selection process for lung transplant candidates is not unique to each center (Camargo et al., 2014).

However, it is their responsibility to develop an assessment program that considers the severity of the disease and the timing of the transplant itself. In addition, the factors that interfere in the referral of the patient to the transplant center are specific to each disease and should be treated in their particularities. These considerations cannot be made without a careful evaluation of the results accepted as reference standards of the various transplant centers in the world (Império, 2016). The results obtained after transplantation are peculiar to each initial diagnosis (base disease) and these results must be considered when selecting the candidate, as well as the particularities regarding the possibilities of clinical deterioration. In selection, the patient must have a disease advanced enough to compromise his life, but healthy enough to undergo the transplant procedure. In this way, the thesis that indication criteria should be individualized according to specific diseases is reinforced (Shweish et al., 2019).

## 2. Methodology

This is a descriptive research of the integrative literature review type, which sought to show, through empirical and current analyses, which are the main indications for lung transplantation. The research was carried out through online access to the National Library of Medicine (PubMed MEDLINE), Scientific Electronic Library Online (SciELO), Google Scholar, Virtual Health Library (BVS) and EBSCO Information Services databases, in October 2022. To search for the works, the keywords present in the Health Sciences (DeCS) descriptors were used, in English: "*lung transplantation*", "*selection*", "*patients*", "*indications*" and in Portuguese: "*pulmonary transplantation*", "*selection*", "*patients*", "*indications*".

As inclusion criteria, original articles and books were considered, which addressed the researched topic and allowed full access to the study content, published between 2012 and 2022, in English and Portuguese. The exclusion criterion was imposed on those works that did not address inclusion criteria, as well as articles that did not undergo a peer review process. The article selection strategy followed the steps of searching the selected databases, reading the titles of all articles found and excluding those that did not address the subject, critically reading the abstracts of the articles and reading the articles selected in the previous steps in full. Thus, 16 materials were totaled for the review.

## 3. Results and Discussion

According to Jatene et al. (2019), Afonso et al. (2015), Camargo et al. (2015) and Ferreira et al. (2018), lung transplantation should be considered for adults with advanced lung disease who meet the following general criteria:

- High risk of death (>50%) from lung disease within 2 years if lung transplantation is not performed;
- High probability (>80%) of surviving at least 90 days after lung transplantation;
- High probability (>80%) of 5-year post-transplant survival from a general medical perspective, provided there is adequate graft function.

### 3.1 Contraindications

Lung transplantation is a complex therapy with a significant risk of perioperative morbidity and mortality. Therefore, it is prudent to consider all contraindications and comorbidities. The following lists are not intended to cover all possible clinical scenarios, but rather highlight common areas of concern (Camargo et al., 2015).

#### 3.1.1 Absolutes

- Lung transplantation should not be offered to adults with a recent history of malignancy. A disease-free interval of 2 years combined with a low predicted risk of recurrence after lung transplantation may be reasonable, for example, in skin cancers other than melanoma that have been adequately treated. However, a disease-free interval of 5 years should be demonstrated in most cases, particularly for those with a history of hematologic malignancy, sarcoma, melanoma, or breast, bladder, or kidney cancer. Unfortunately, for some patients with a history of cancer, the risk of recurrence may remain too high to proceed with lung transplantation, even after a 5-year disease-free interval (Camargo et al., 2015; Ferreira et al., 2018);
- Significant, poorly controlled dysfunction of another major organ system (e.g., heart, liver, kidney, or brain), unless a multiple organ transplant is being considered (Camargo et al., 2015; Ferreira et al., 2018);
- Uncorrected coronary artery disease with ischemia or end-organ dysfunction and/or coronary artery disease not amenable to revascularization (Camargo et al., 2015; Ferreira et al., 2018);

- An unstable medical condition, including, but not limited to, acute sepsis, myocardial infarction, and liver failure (Camargo et al., 2015; Ferreira et al., 2018);
- Uncorrectable bleeding disorder (Camargo et al., 2015; Ferreira et al., 2018);
- Poorly controlled infection by virulent and/or resistant microbes (Camargo et al., 2015; Ferreira et al., 2018);
- *Mycobacterium tuberculosis* infection (Camargo et al., 2015; Ferreira et al., 2018);
- A deformity of the chest wall or spine that can cause severe restriction after transplantation (Camargo et al., 2015; Ferreira et al., 2018);
- Class II or III obesity ( $BMI \geq 35.0 \text{ kg/m}^2$ ) (Camargo et al., 2015; Ferreira et al., 2018);
- Current non-adherence to drug therapy or a history of repeated or prolonged episodes of non-adherence to drug therapy that are perceived to increase the risk of non-adherence after transplantation (Camargo et al., 2015; Ferreira et al., 2018);
- Psychiatric or psychological problems that may render the patient unable to comply with a complicated medical regimen;
- Inadequate social support system (Camargo et al., 2015; Ferreira et al., 2018);
- Functionally limited with inability to participate in a rehabilitation program (Camargo et al., 2015; Ferreira et al., 2018);
- A history of abuse or dependence on illegal substances (eg, alcohol, tobacco, marijuana, or other illegal substances). Convincing evidence of risk-reducing behaviors (such as participation in substance abuse and/or dependence therapy) must be demonstrated before lung transplantation is considered. Periodic blood and urine tests can be used to check for abstinence (Camargo et al., 2015; Ferreira et al., 2018).

### 3.1.2 Relative

- Age over 65 years associated with low physiological reserve and/or other relative contraindications. Although there cannot be endorsement of an upper age limit as an absolute contraindication, adults over 75 years of age are less likely to be candidates for lung transplantation. While age alone should not exclude a patient from receiving a lung transplant, increasing age is often associated with comorbidities that are absolute or relative contraindications (Svartman et al., 2017; Jatene et al., 2018; Barr et al., 2018; Barr et al., 2018; Barr et al., 2017). al., 2015);
- Class I obesity ( $BMI 30.0$  to  $34.9 \text{ kg/m}^2$ ), mainly truncal (central) obesity (Svartman et al., 2017; Jatene et al., 2018; Barr et al., 2015);
- Significant malnutrition (Svartman et al., 2017; Jatene et al., 2018; Barr et al., 2015);
- Significant osteoporosis (Svartman et al., 2017; Jatene et al., 2018; Barr et al., 2015);
- Prior extensive chest surgery with lung resection (Svartman et al., 2017; Jatene et al., 2018; Barr et al., 2015);
- Mechanical ventilation and/or extracorporeal life support (ECLS). However, carefully selected candidates without other acute or chronic organ dysfunction can be successfully transplanted (Svartman et al., 2017; Jatene et al., 2018; Barr et al., 2015);
- Colonization with resistant or highly virulent pathogens (Svartman et al., 2017; Jatene et al., 2018; Barr et al., 2015);
- For candidates infected with hepatitis B and/or C, lung transplantation may be considered in patients without significant clinical, radiological, or biochemical signs of cirrhosis or portal hypertension and who are stable with appropriate therapy. Lung transplantation in hepatitis B and/or C candidates should be performed in centers with experienced hepatology units (Svartman et al., 2017; Jatene et al., 2018; Barr et al., 2015);

- For patients infected with the human immunodeficiency virus (HIV), lung transplantation may be considered in those with controlled disease with undetectable HIV-RNA and adherent to antiretroviral therapy (cART). Lung transplantation in HIV-positive candidates should be performed at centers with experience in caring for HIV-positive patients (Svartman et al., 2017; Jatene et al., 2018; Barr et al., 2015);
- *Burkholderia cenocepacia*, *Burkholderia gladioli* and multidrug resistant *Mycobacterium abscessus* infection if the infection is sufficiently treated preoperatively and there is a reasonable expectation of adequate postoperative control. In order for patients with these infections to be considered suitable transplant candidates, patients must be evaluated by centers with significant experience in managing these infections in the transplant setting, and patients must be aware of the increased risk of transplantation due to these infections (Svartman et al., 2017; Jatene et al., 2018; Barr et al., 2015);
- Sufficient coronary artery disease burden to place the candidate at risk for end-organ disease after lung transplantation. The preoperative evaluation, the type of coronary stent used and the extent of coronary artery disease considered acceptable vary between transplant centers (Svartman et al., 2017; Jatene et al., 2018; Barr et al., 2015);
- Extrapulmonary conditions that did not result in significant organ damage, such as diabetes mellitus, systemic hypertension, epilepsy, central venous obstruction, peptic ulcer, or gastroesophageal reflux should be well controlled before transplantation (Svartman et al., 2017; Jatene et al., 2018; Barr et al., 2015).

### 3.1.3 Special surgical considerations

- Prior surgery is not a contraindication to lung transplantation (Pierre et al., 2012; Orens et al., 2013);
- Prior pleurodesis may present operative challenges, but it is not a contraindication (Pierre et al., 2012; Orens et al., 2013);
- Pneumothorax in a patient who may become a future transplant recipient should receive the best immediate management. The choice of intervention is unlikely to affect future acceptance of the transplant (Pierre et al., 2012; Orens et al., 2013);
- Higher rates of bleeding, re-exploration and renal dysfunction are expected in patients with previous thoracic procedures. This can be exacerbated by longer times on cardiopulmonary bypass (Pierre et al., 2012; Orens et al., 2013);
- In well-selected patients, the mid- and long-term outcome is not affected by previous thoracic procedures (Pierre et al., 2012; Orens et al., 2013);
- On the other hand, older patients (> 65 years) with other comorbidities have worse outcomes, and the previous intrapleural procedure should be taken into account in the selection (Pierre et al., 2012; Orens et al., 2013).

In addition, some patients referred for lung transplantation will have undergone previous thoracic surgery. If previous chest tube insertion is included, the percentage of patients referred can be up to 40% or up to 90% in conditions such as lymphangioleiomyomatosis (LAM). Surgery may be coincidental, eg previous coronary artery bypass graft (CABG) surgery, but usually related as a diagnostic or therapeutic step in pre-transplantation management. Examples of the latter range from simple video-assisted thoracoscopic biopsy (VATS) in interstitial disease to previous lung volume reduction surgery (LVRS). Conditions associated with recurrent pneumothorax, such as cystic fibrosis (CF) or LAM, may require pleurodesis, prior lung resection, or pneumonectomy (Pierre et al., 2012; Orens et al., 2013);

Some general conclusions can be drawn from the published literature. Any prior surgery, but particularly pleurodesis (surgical or chemical), is associated with increased blood loss and early postoperative morbidity, such as renal dysfunction and primary graft dysfunction. There is also a higher incidence of phrenic nerve injury, chylothorax and re-exploration. Not

surprisingly, where multivariate analysis can be applied, the combinations of age >65 years, pulmonary hypertension, transfusion >20 units, and prolonged cardiopulmonary bypass are all predictors of early death. Prior cardiac surgery appears to have little specific effect, but the reported experience is very small (Pierre et al., 2012; Orens et al., 2013);

The specific issue of the previous LVRS is examined in several articles. Initial experience indicated that LVRS had no effect, but a more recent report in which 25 of 177 chronic obstructive pulmonary disease (COPD) transplant patients who underwent previous LVRS had worse outcomes. There were the highest expected rates of bleeding and early morbidity, but also significantly worse early graft function and worse outcomes in older, frail patients (Pierre et al., 2012; Orens et al., 2013);

### 3.2 Selection of patients

Several factors must be considered when evaluating the patient, considering that the ideal candidate for lung transplantation is one who has a prospect of being successfully submitted to surgery, with estimates of early and late survival after surgery both higher than 80%. The number of lungs offered for donation is not enough to effectively fill the waiting list, and mortality on the waiting list is around 22%. The entire process, from the initial assessment to the postoperative follow-up - from which the patient will never be discharged - is complex and costly; therefore, each patient must be carefully evaluated so that unnecessary expenses are not generated in cases with high chances of failure, in addition to the fact of not offering a lung to a patient who is known to have a higher probability of survival with the procedure (Orens et al. al., 2016).

#### 3.2.1 Indications

As previously mentioned, in general, lung transplantation is indicated in those patients who meet all the criteria below:

- High risk (>50%) of 2-year mortality secondary to lung disease if lung transplantation is not performed (Jatene et al., 2019; Afonso et al., 2015; Camargo et al., 2015; Ferreira et al., 2018; );
- High probability (> 90%) of survival after 90 days of transplantation (Jatene et al., 2019; Afonso et al., 2015; Camargo et al., 2015; Ferreira et al., 2018);
- High probability (> 80%) of survival after 5 years of transplantation, from a clinical point of view, if the graft is in good condition (Jatene et al., 2019; Afonso et al., 2015; Camargo et al., 2015; Ferreira et al., 2015; Ferreira et al., 2019; Afonso et al., 2015; Camargo et al., 2015; Ferreira et al. al., 2018);
- Obstructive diseases: This group includes diseases such as COPD and bronchiolitis obliterans. Patients should be referred for evaluation under the following conditions: progressive disease despite optimal treatment; COPD patients not candidates for lung volume reduction treatment (surgical or endoscopic); Body mass index, *airflow Obstruction, Dyspnea, and Exercise capacity* (BODE) <sup>4</sup> between 5 and 6; PaCO<sub>2</sub> > 50 mmHg and/or PaO<sub>2</sub> < 60 mmHg; and FEV<sub>1</sub> < 25% of predicted. Patients should be included in the list when there is at least one of the following criteria: BODE index ≥ 7; FEV<sub>1</sub> < 15-20% of predicted; three or more severe exacerbations in the last year; a severe exacerbation with acute hypercapnic respiratory failure; and moderate to severe pulmonary hypertension (Weil et al., 2015; Higemura et al., 2022; Reynaud-Gaubert et al., 2018);
- Suppurative diseases: This group includes diseases such as cystic fibrosis, ciliary dyskinesia and bronchiectasis. Patients should be referred for evaluation when there is FEV<sub>1</sub> < 30% of predicted, especially with rapid decline despite optimal therapy; distance covered in the six-minute walk test < 400 m; development of pulmonary hypertension in the absence of hypoxemia secondary to exacerbation; and clinical worsening characterized by an increase in exacerbations accompanied by one of the following criteria: episode of acute respiratory failure requiring non-invasive ventilation; increased antimicrobial resistance and poor recovery from exacerbation; worsening of



nutritional status despite supplementation; pneumothorax; and/or life-threatening hemoptysis not controlled with embolization. Patients should be included in the list when there is at least one of the following criteria: chronic respiratory failure ( $\text{PaCO}_2 > 50$  mmHg and/or  $\text{PaO}_2 < 60$  mmHg); need for non-invasive ventilation; pulmonary hypertension; frequent hospital admissions; rapid decline in lung function; and functional class IV according to the *World Health Organization*. In patients with bronchiectasis secondary to cystic fibrosis, two factors must be observed: pancreatopathy, both endocrine and exocrine, which also influences the choice of immunosuppressant (tacrolimus is more pancreatotoxic than cyclosporine) and chronic sinusopathy, since colonization upper airway is a frequent cause of pulmonary infection after transplantation (post-transplant sinusectomy is quite common) (Weil et al., 2015; Higemura et al., 2022; Reynaud-Gaubert et al., 2018);

- **Interstitial diseases:** This group includes restrictive fibrosing diseases, such as idiopathic pulmonary fibrosis, hypersensitivity pneumonitis, and nonspecific interstitial pneumonia. Patients should be referred for evaluation when there is: histological or radiological evidence of usual interstitial pneumonitis or nonspecific fibrosing interstitial pneumonitis, regardless of lung function;  $\text{FVC} < 80\%$  of predicted or  $\text{DLCO} < 40\%$  of predicted; dyspnea or functional limitation attributable to lung disease; need for oxygen supplementation, even if only on exertion; and, for inflammatory interstitial lung disease (non-usual interstitial pneumonitis and non-specific fibrosing interstitial pneumonitis), inability to improve symptoms and/or need for oxygen supplementation and/or functional improvement with appropriate therapy. Patients should be included in the list when there is:  $\geq 10\%$  decline in FVC at 6 months of follow-up;  $\geq 15\%$  decline in DLCO value at 6-month follow-up; desaturation  $< 88\%$  or distance covered  $< 250$  m in the six-minute walk test or fall  $> 50$  m in the distance covered in this test at 6-month follow-up; pulmonary hypertension; and/or hospitalization due to functional deterioration, pneumothorax or acute exacerbation (Weil et al., 2015; Higemura et al., 2022; Reynaud-Gaubert et al., 2018);
- **Vascular diseases:** This group includes diseases such as pulmonary arterial hypertension. Patients should be referred for evaluation when there is: *New York Heart Association* (NYHA) functional class III or IV with optimized therapy; rapidly progressive disease; use of parenteral therapy despite NYHA functional classification (not available in Brazil); and/or known or suspected pulmonary veno-occlusive disease or diagnosis of pulmonary capillary hemangiomas. Patients should be included in the list when there is: NYHA functional class III or IV with optimized therapy, including prostanoids (not yet widely available in Brazil); cardiac index  $< 2$  l/min/m<sup>2</sup>; mean right atrial pressure  $> 15$  mmHg; distance covered in the six-minute walk test  $< 350$  m; and/or development of hemoptysis, pericardial effusion, or signs of right heart failure (Weil, 2018; Yusen et al., 2016; Pavec et al., 2018);
- **Pediatric population:** The indication for evaluation of the pediatric population is the same as for the adult population. Some particularities must be considered, mainly due to the size of the receivers, which can lead to a longer waiting time in the list. Another important aspect is adherence to treatment, which tends to be worse in this population, increasing the risk of complications such as acute rejection or chronic graft dysfunction. However, success rates in the pediatric population are similar to those in the adult population (Weil, 2018; Yusen et al., 2016; Pavec et al., 2018);
- **Retransplantation:** There are growing worldwide cases of patients undergoing lung transplantation who evolve with chronic graft failure and, consequently, with a picture of chronic respiratory failure and indication for retransplantation (Weil, 2018; Yusen et al., 2016; Pavec et al., 2016; Pavec et al., 2016; Pavec et al., 2016; Pavec et al., 2018).

#### 4. Final Considerations

Knowing the best time to indicate and transplant considerably improves the results of lung transplantation, which is the only effective treatment option for several progressive and fatal lung diseases. Currently, the main indications for lung transplantation worldwide are chronic obstructive pulmonary disease (COPD), pulmonary fibrosis, cystic fibrosis, alpha-1-antitrypsin (alpha-1) deficiency, idiopathic pulmonary arterial hypertension, bronchiectasis, retransplantation, sarcoidosis and severe lung injury caused by COVID-19, and these candidates must demonstrate knowledge regarding the procedure, good adherence to the medical treatment performed, adequate psychosocial structure and family support. Furthermore, the proper assessment of contraindications contributes to a lower occurrence of unfavorable clinical outcomes unrelated to the graft, benefiting patients with a greater chance of success and, thus, improving overall survival with treatment. Among the absolute contraindications, lung cancer, cardiac dysfunction unrelated to lung disease, significant organic dysfunction of any other noble organ, hepatitis B and C virus infections, active pulmonary tuberculosis and severe rib cage deformity stand out. Furthermore, among the relative contraindications, there is age over 65 years, severe clinical instability, HIV infection, obesity, severe osteoporosis and decompensated systemic diseases.

#### References

- Afonso, J. E., et al. (2015). Lung transplantation. *Albert Einstein's Journal of Medicine*, 13 (2).
- Barr, M. L., et al. (2015). Living donor lobar lung transplantation: current status and future directions. *Transplant Proc.*, 37(9), 3983-3986.
- Bennett, D., et al. (2020). Lung transplantation in patients with familial pulmonary fibrosis. *Brazilian Journal of Pulmonology*, 46 (6).
- Camargo, J. J., et al. (2014). Lung transplantation: current indications. *Brazilian Journal of Pulmonology*, 23 (1), 36-44.
- Camargo, P. C. L. B., et al. (2015). Lung transplantation: a general approach on its main aspects. *Brazilian Journal of Pulmonology*, 41 (6).
- Ferreira, L. L., et al. (2018). Functional clinical profile of lung disease patients undergoing pre-lung transplantation physiotherapeutic evaluation. *Conscientiae Saúde*, 17 (1), 72-77.
- Higemura N., et al. (2022). Lung transplantation in patients with previous cardiothoracic surgical procedures. *Am J Transplant*, 12 (8), 1249-1255.
- Empire, F. (2016). Criteria for indication and selection of candidates for lung transplantation. *Brazilian Journal of Pulmonology*, 15 (3), 175-183.
- Jatene, F. B., et al. (2018). Lung transplantation challenges. *Brazilian Journal of Pulmonology*, 34 (5).
- Jatene, F. B., et al. (2019). Lung transplantation. *Journal of Medicine of USP*, 88 (3).
- Orens, J. B., et al. (2013). A review of lung transplant donor acceptability criteria. *J Heart Lung Transplant.*, 22(11), 1183-1200.
- Orens, J. B., et al. (2016). International guidelines for the selection of lung transplant candidates: 2006 update - a consensus report from the Lung Scientific Council of the International Society for Heart and Lung Transplantation. *J Heart Lung Transplant*, 25 (1), 745-55.
- Pavec, J. L., et al. (2018). Lung transplantation: current indications, prognosis and specific considerations. *Journal of Thoracic Disease*, 5 (9).
- Pierre, A. F., et al. (2012). Marginal donor lungs: A reassessment. *J Thorac Cardiovasc Surg.*, 123 (3), 421-427.
- Reynaud-Gaubert, M., et al. (2018). Lung transplantation for lymphangioleiomyomatosis: the French experience. *Transplant*, 86 (3), 15-20.
- Shweish, O., et al. (2019). Indications for lung transplant referral and listing. *Journal of Thoracic Disease*, 7(8).
- Svartman, F. B., et al. (2017). Lung transplantation in cystic fibrosis. *Clin Biomed Res.*, 31 (2).
- Weil, D. (2018). Lung transplantation: indications and contraindications : *Journal of Thotacic Disease*, 4 (8).
- Weill, D., et al. (2015). A consensus document for the selection of lung transplant candidates: 2014 – an update from the Lung Transplant Board of the International Heart and Lung Transplant Society. *J Heart Lung Transplant*, 34 (8), 1-15.
- Yusen, R. D., et al. (2016). The Registry of the International Society for Heart and Lung Transplantation: Thirty-third Adult Lung and Heart–Lung Transplant Report—2016; Focus Theme: Primary Diagnostic Indications for Transplant. *The Journal of Heart and Lung Transplantation*, 35 (10), 1170-1184.