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LUNG TRANSPLANTATION: AN INTEGRATIVE REVIEW ON SURVIVAL, INDICATIONS AND OUTCOMES IN PATIENTS

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Abstract: Lung transplantation is an advanced treatment for terminal lung diseases, offering improved survival and quality of life. However, challenges such as organ shortages and surgical risks remain. This integrative review analyzed 21 studies published in the last five years to understand the advances made in this period in relation to survival, indications and clinical outcomes of lung transplantation. Advances in surgical techniques and perioperative management have improved survival rates. Ex vivo lung perfusion (EVLP) has shown survival rates of 100% at 30 days, while extracorporeal membrane oxygenation (ECMO) has shown potential for stabilizing patients before transplantation. Physical rehabilitation showed benefits, with an 18% increase in functional capacity in adults and a 22% improvement in lung function in children. The main indications include idiopathic pulmonary fibrosis, cystic fibrosis and pulmonary sequelae of COVID-19. Antifibrotic therapies help with transplant eligibility by reducing disease progression. Patients in specialized centers have shown better prognoses, while geographical barriers negatively affect survival. Complications such as diaphragmatic paralysis (10% of cases) and atrial arrhythmias (4.1% per year) impact outcomes. Technologies such as Pocket PATH help with treatment adherence, improving long-term results. Thus, this review highlights important findings for improvements in organ allocation, post-operative management and equitable access to transplantation. Future research could optimize selection criteria and clinical protocols, contributing to better outcomes and greater accessibility to the procedure.

Keywords: Lung Transplant, Review, Thoracic Surgery

INTRODUCTION

Lung transplantation is an advanced therapeutic intervention for patients with terminal lung diseases for whom there are no other effective treatment options. Since the first successful procedure in the 1980s, the technique has evolved significantly, allowing greater survival and better quality of life for patients with terminal lung diseases transplant.

However, factors such as the limited availability of organs, the complexity of the procedure and the associated risks still represent major challenges. Given this scenario, it is essential to understand the main indications for lung transplantation, as well as the factors that influence the clinical outcomes patients undergoing this therapy.

The survival of transplant patients has increased over the years due to advances in surgical techniques, immunosuppressive management and careful selection of recipients. However, complication rates still have a significant impact on the longevity and quality of life of transplanted individuals. In addition, the scarcity of available organs limits access to the procedure, making it necessary to develop strategies to optimize the allocation and use of lung grafts.

The indications for lung transplantation are widely discussed in the scientific literature. The careful selection of candidates for transplantation is a determining factor in the success of the procedure, as aspects such as nutritional status, cardiac function and the presence of comorbidities can influence post-operative results. Therefore, clinical guidelines are constantly being updated to ensure that the procedure is carried out on patients with the highest probability of success.

In this context, the aim of this study is to carry out an integrative review of recent literature on survival, the main indications and the clinical results of lung transplantation. The analysis of the scientific findings together

could contribute expanding knowledge on the subject, providing subsidies for optimizing clinical practices and improving the protocols used in the selection and management of transplant patients. It is hoped that the results of this review will help to improve the care provided to individuals who need this complex therapeutic modality, which is essential for survival in advanced cases of lung disease.

METHODOLOGY

This study consists of an integrative literature review, structured in five main stages: a) formulation of the research objective; b) selection of the studies with based on inclusion and exclusion criteria; c) data collection and organization; d) analysis of the selected studies; and e) presentation of the results and discussion.

The research objective and guiding question were defined as: What are the main findings related to survival, indications and results in articles published in the last five years?

Based on this question, the selection criteria were established. The searches were carried out on the Scientific Electronic Library Online (SciELO), National Library Medicine (PubMed/Medline) and Latin American and Caribbean Health Sciences Literature (LILACS) platforms. The inclusion criteria included studies published from 2020 onwards, written in Portuguese or English and freely available. Articles that did not meet the guiding question were excluded, as were letters, monographs, documents and studies that addressed topics outside the scope of lung transplantation.

The search terms used were “Lung Transplant” combined with the Boolean operator AND and the term “Surgery”, as well as its full translation into English.

The initial search resulted in 193 articles. After a preliminary screening based on reading the titles and abstracts, 39 articles were selected for detailed analysis. The 39 articles were then read in their entirety, and during

the analysis process, data was collected on the journal (title, year of publication), the authors (full names) and the study (objective, academic affiliation, theoretical framework, type of study, methodological aspects, results and recommendations). 17 articles were eliminated because they did not fit in with the research topic and 2 articles because they were repeated. Thus, 21 articles were used to carry out this review.

The 21 articles selected were divided according to their findings in terms of survival, indication and results, which were critically assessed and compared with the current literature to prepare the research.

RESULTS

The results of the articles analyzed focused mainly on post-operative results, with around 42.3% of the articles studied presenting relevant results in this regard.

The articles analyzed presented results that included improvements in quality of life, lung function and a reduction in complications. One of the articles showed that inspiratory muscle training increased respiratory muscle strength by 15% and reduced dyspnea by 20% in the postoperative period (POLASTRI, 2024). In addition, the combination of echocardiography and tomography achieved a sensitivity of 72% and specificity of 79% for screening pulmonary hypertension in transplant candidates (HELENA, 2021).

Of the postoperative outcomes, diaphragmatic paralysis was observed in 10% of transplant patients, negatively impacting hospitalization and recovery times (ELTONSY, 2024). Studies on physical rehabilitation have reinforced the importance of perioperative interventions, with gains of 18% in functional capacity in adult patients who underwent early rehabilitation (POLASTRI, 2022).

Furthermore, the use of oxygen therapy in transplant candidates referred for pulmonary rehabilitation showed that all groups of

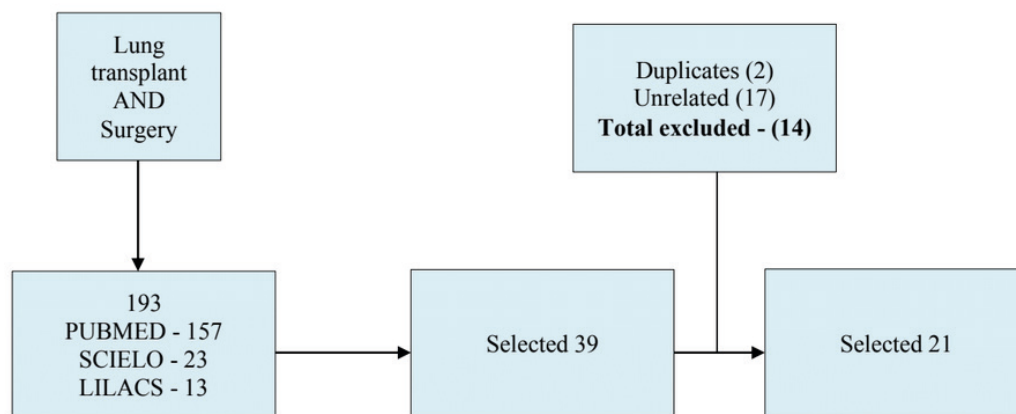


FIGURE 1: Article selection process. SOURCE: Research authors.

NO.	Article Title	Main Author
1	Outcomes of marginal donors for lung transplantation after ex vivo lung perfusion: A systematic review and meta-analysis	Dong Tian
2	Late atrial arrhythmias after lung transplantation: a meta-analysis	Andréa Saglietto
3	Inspiratory Muscle Training for Lung Transplant Candidates and Recipients	Massimiliano Polastri
4	Elderly patients with multiple comorbidities: insights from the bedside to the bench and programmatic directions for this new challenge in lung transplantation	Norihisa Shigemura
5	Pulmonary volume-feedback and ventilatory pattern after bilateral lung transplantation using neurally adjusted ventilatory assist ventilation	Giacomo Grasselli
6	Lung autotransplantation for the treatment of locally advanced tumors	João Marcelo Lopes Toscano de Brito
7	Lung transplantation in patients with familial pulmonary fibrosis	David Bennett
8	Access to Lung Transplantation in the United States: The Potential Impact of Access to a High-volume Center	Ernest G. Chan
9	Accuracy of echocardiography and chest tomography for screening pulmonary hypertension	Luiza Helena
10	Antifibrotic therapy in lung transplant candidates with idiopathic pulmonary fibrosis	Monica Pruss Pereira
11	Lung Transplantation for COVID-19 Pulmonary Sequelae	Hiromu Kehara
12	Diaphragmatic palsy following lung transplantation	Amr M. Eltonsy
13	Extracorporeal membrane oxygenation (ECMO) as a bridge to lung transplantation	Brittany Koons
14	Impact of a Mobile Health Intervention on Long-term Nonadherence After Lung Transplantation	E.M. Rosenberger
15	Impact of pulmonary rehabilitation pre- and post-lung transplantation in a child with cystic fibrosis	Gonzalo Hidalgo
16	Ambulatory oxygen therapy in lung transplant candidates with idiopathic pulmonary fibrosis	Aline Paula Miozzo
17	Exercise training for adult lung transplant recipients	Ruvistay Gutierrez-Arias
18	Does Preoperative Rehabilitation Influence the Quality of Life in Patients Who Are Candidates for Lung Transplant?	Massimiliano Polastri
19	Clinical outcomes associated with computed tomography-based body composition measures in lung transplantation	Dmitry Rozenberg
20	Risk Factors and Management of Osteoporosis Post-Transplant	Karthik Kovvuru
21	Antifibrotic therapy and quality of life in patients with pulmonary fibrosis	Monica Pruss Pereira

TABLE 1 : Articles analyzed and their main authors.

patients, regardless of the use or flow of oxygen during pulmonary rehabilitation, showed improvements in walking ability, while the groups that used oxygen showed additional improvements in aspects such as physical function, general health status, social interaction and mental health (MIOZZO,2023).

One of the articles showed that in the post-operative period, late atrial arrhythmias are not an uncommon event after lung transplantation, with incidence rate of 4.1%/year, while the incidence of late atrial fibrillations was rare, at 0.9%/year. Post-surgery with early rehabilitation has been shown to be the best way to recover from these arrhythmias; transcatheter ablation of the pulmonary veins is still indicated in patients who have undergone double transplantation, in order to prevent possible episodes of atrial fibrillation (SAGLIETTO, 2020).

Pediatric patients undergoing rehabilitation showed a 22% improvement in lung function and resumed school activities within 6 months (HIDALGO, 2023). In addition, bone density assessment revealed that bone loss tends to be more pronounced in the first six months after transplantation, with a higher risk in patients who develop diseases such as Graft versus Host Disease (KOVVURU, 2020). In the post-operative period, one of the studies presented a literature review, where there were doubts about the effects of physical training on improving any of the outcomes. Some studies reported improvements in the distance covered in 6 minutes (exercise versus no exercise, different exercise programs), muscle strength (exercise or multimodal exercise versus no exercise) and bone mineral density (exercise versus no exercise). However, most studies reported no differences in adverse events, quality of life, lung function or risk of death (GUTIERREZ-ARIAS, 2021). Another study sought to assess body composition, which is closely linked to exercise and post-operative outcome in transplant patients. In this article, computed tomography (CT)

was used to assess body composition and the relationship with survival in these transplant patients was subsequently analyzed. It was observed that transplant patients with a low muscle index and/or sarcopenia had a higher risk of mortality. However, other studies have not found a significant association between body composition and post-transplant survival (ROZENBERG, 2020).

In elderly patients with multiple comorbidities, minimally invasive approaches have been associated with lower perioperative mortality and better functional outcomes (SHIGEMURA, 2019). In patients with an indication for lung transplantation due to idiopathic pulmonary fibrosis, anti-fibrotic therapy was related to a 20% reduction in disease progression, allowing eligibility for transplantation in advanced stages (PEREIRA, 2023). A case report of a child with cystic fibrosis showed that rehabilitation programs increased functional capacity, significantly improving preparation for transplantation (HIDALGO, 2023).

Another study showed the survival of two transplant groups, patients with familial pulmonary fibrosis (FPF) and pulmonary fibrosis (PF). One-year overall survival was similar between the groups, 66.7% for FpF and 58.4% for . One-year survival free of CLAD (chronic lung rejection disease) was 87.5% for patients with FPF and 73.8% for those with PF. In addition, patients with PFF underwent more bilateral lung transplants than the other group, as well as receiving more intense immunotherapy (BENNETT, 2020). A retrospective observational study conducted at a lung transplant reference center in Brazil suggested that Advanced Functional Training is associated with improvements in the 6-minute walk distance (6MWD) test.

- 6-Minute Walk Distance) after 36 sessions of Pulmonary Rehabilitation (PR) in patients with idiopathic pulmonary fibrosis on the waiting list for lung transplantation. In addition, the group of patients who received

anti-fibrotic therapy (AFT) while undergoing PR reported a positive intra-group change in the physical component of Health-Related Quality of (HRQoL) at the end of 12 weeks of PR (PEREIRA, 2023).

Other studies have shown that advances in lung transplant management and techniques have been associated with promising survival rates. One study showed that ex vivo lung perfusion (EVLP), showed 30-day survival rates similar to transplants with standard donors. The 30-day survival rate in the EVLP group was 100% compared to 95.8% in the non-EVLP group (TIAN, 2020). In addition, another study demonstrated that Neurally Adjusted Ventilatory Assist (NAVA) ventilation in two patients, undergoing bilateral lung transplantation, in whom the NAVA catheter was left in place after extubation, the initially undetectable EAdi signal reappeared within 1 day, suggesting that the “stunning” of the nerve may be reversible (GRASSELLI, 2021). Some patients, after contracting covid, had to undergo unilateral or bilateral lung transplantation due to sequelae, research data showed that lung transplantation showed favorable initial results in a heterogeneous cohort of patients, including the elderly, obese and patients with coronary artery disease or pre-existing chronic lung disease (KEHARA, 2021).

One of the articles presented a series of clinical cases in which lung autotransplantation is a viable option for some patients with locally advanced tumors, providing an alternative to complete resection of the affected lung, a procedure that can preserve lung function and increase survival in cases where complete resection of the lung is not an option, focusing on patients with locally advanced tumors (LOPES, 2021).

In a clinical study carried out in the United States, 13,743 adult patients who underwent lung transplantation in the US between 2005 and 2014 were analyzed. It was observed that patients who lived in regions farther from

specialized lung centers had a higher risk of mortality, moving to larger centers did not significantly increase survival, although smaller volume centers are associated with lower 5-year survival (CHAN, 2020).

When it comes to technological advances, two studies have looked at devices capable of improving transplant success rates. The use of extracorporeal membrane (ECMO) allows patients to be stabilized until an organ becomes available, contributing to their maintenance and rehabilitation. Although the use of ECMO is associated with a higher risk of complications in the immediate postoperative period, long-term survival rates are comparable to those of patients who do not use this support, showing that its use is still questionable in some cases. (KOONS,2020)

In addition, the use of devices, such as Pocket PATH, has shown promise, since their adherence contributes to a better self-care routine and contributes to better clinical outcomes, including the maintenance of patients' health and survival after transplantation, through the use of their medications, such as immunosuppressants, for example (ROSEMBERGER, 2020).

DISCUSSION

SURVIVAL

Breaking down the findings, the advances in survival rates after lung transplantation reflect the evolution of surgical techniques and perioperative management. Ex vivo lung perfusion (EVLP) has stood out as a promising approach, with 30-day survival rates of 100% in the EVLP group, compared to 95.8% in transplants with standard donors (Tian, 2020). This technology makes it possible to optimize the quality of the organ before transplantation, increasing the possibility of success, especially in cases where the donated lungs have suboptimal initial conditions. Future studies in Bra-

zil could assess the feasibility of this technique in high-demand transplant centers, considering its logistical and financial implications. In addition, the use of extracorporeal membrane (ECMO) in conjunction with EVLP could increase the number of transplants performed, since ECMO can stabilize patients and keep them in ideal conditions for transplantation for longer until an organ becomes available.

The geographical location of patients also plays a crucial role in survival. Patients living in remote areas, far from specialized centers, have a higher risk of mortality, even when treated in high-volume centers, which, interestingly, have not shown a significant improvement in five-year survival (CHAN, 2020). Although this study was carried out in a North American context, it is likely that similar results will be observed in Brazil, where regional inequalities in access to healthcare are marked. For example, patients living in regions with poorer health infrastructure face additional challenges, such as delays in diagnosis, transportation difficulties and limited access to advanced therapies. In this sense, a national study could identify these disparities and guide the allocation of resources and the decentralization of lung transplant services.

In addition, the articles reviewed indicated that post-operative follow-up in lung transplant patients revealed a number of benefits, but also some complications.

Studies have shown that patients experienced significant improvements in quality of life and lung function after transplantation. Respiratory muscle training, for example, increased muscle strength by 15% and reduced shortness of breath by 20% (POLASTRI, 2024). Atrial arrhythmias were also detected, with an annual rate of 4.1%, with late atrial fibrillations being much less frequent (0.9% per year) (SAGLIETTO, 2020).

Early physical rehabilitation showed positive effects, such as an 18% increase in the functional capacity of adult patients (POLAS-

TRI, 2022). Patients who used oxygen during rehabilitation had additional improvements, not only in their ability to walk, but also in their general state of health and mental health (MIOZZO, 2023). These references indicate the importance of rehabilitation in the post-operative period, with multiple studies showing data that point to a better prognosis.

Recovery after lung transplantation benefits from interventions such as respiratory training, early rehabilitation and constant monitoring of complications. Although the impact on lung function and quality of life is clear, issues such as bone loss and body composition require ongoing attention to minimize complications and improve patient survival, and further research is essential to fill gaps in the literature and refine strategies.

INDICATION

Lung transplantation is indicated in cases of advanced lung disease, in which the progression of the pathology results in irreversible functional impairment and an imminent risk of death. Among the clinical conditions, it is important to highlight idiopathic pulmonary fibrosis (IPF), familial pulmonary fibrosis (FPF) and cystic fibrosis. The selection of candidates for the procedure requires a careful approach, based not only on clinical and functional assessments, but also on technological resources that allow a more precise analysis of the patient's condition and the viability of the transplant. Patients with IPF benefit from antifibrotic therapies in order to slow down the progression of the disease and favor the eligibility for transplantation. In PFF, there are reports of successful bilateral transplants, even under intensified immunotherapy regimens, with survival outcomes similar to those of patients with IPF. This data reinforces the importance of pre-transplant interventions that optimize candidates and increase the chances of success. Further studies could explore the application of this technique in Brazil, asses-

sing its clinical and logistical feasibility.

In addition, patients with severe pulmonary sequelae resulting from COVID-19 or conditions such as emphysema and bronchiectasis are also potential candidates. Several studies have highlighted the importance of rigorous criteria for selecting candidates, including clinical, functional and technological assessments, such as the combined use of echocardiography and tomography, which showed a sensitivity of 72% and specificity of 79% in screening for pulmonary hypertension (HELENA, 2021). This approach has been an important pillar in screening candidates, especially in populations with cardiac comorbidities. However, the widespread application of these tests can be limited by infrastructure and the cost of resources, which makes it crucial to improve diagnostic techniques and form networks of specialized centers, especially in regions with restricted access to healthcare.

Thus, deciding on lung transplantation goes beyond assessing the severity of the disease. It is necessary to consider aspects such as the patient's general health, access to advanced technologies such as EVLP and ECMO, and the ability to follow the prescribed treatment. While these innovations expand the possibilities, their large-scale application still requires careful planning to ensure that they are viable both financially and in practice.

SURGICAL RESULTS

Post-operative repercussions have been profuse, ranging from favorable outcomes to complex adversities. Among the main points highlighted, it is worth mentioning how the indications for lung transplantation have expanded to include severe sequelae of COVID-19. Patients who required bilateral or unilateral transplants due to complications of the disease showed favorable initial outcomes, even in high-risk populations such as the elderly and patients with pre-existing comorbidities (KEHARA, 2021). These findings

highlight the adaptability of lung transplantation in response to emerging conditions.

In addition, post-transplant outcomes show a wide range of benefits, but certain challenges remain in the current scenario. Patients who underwent pre- and post-transplant physical rehabilitation showed significant improvements in quality of life and lung function. In adults, gains of 18% in functional capacity have been reported, while in children lung function increased by 22%, with a return to school activities within six months (Polastri, 2022; Hidalgo, 2023). These findings reinforce the importance of rehabilitation programs as an integral part of transplant care.

In addition, advances in perioperative management and physical rehabilitation have shown promising results. Early rehabilitation, for example, increased functional capacity by 18% in adult patients (POLASTRI, 2022) and 22% in the pulmonary function of pediatric patients, enabling them to return to school activities within six months (HIDALGO, 2023).

However, undesirable outcomes are pointed out in the articles investigated. A significant number of patients suffered from diaphragmatic paralysis, a worrying and common complication after lung transplantation, with the potential to negatively affect patient recovery, ranging from chronic episodes to fatal cases (ELTONSY, 2024). Atrial arrhythmias and familial pulmonary fibrosis are also examples of setbacks that can compromise postoperative results. Thus, more innovative studies and new technologies are important in controlling complications during surgical recovery.

Finally, technologies such as Pocket PATH, an app that helps lung transplant recipients follow their post-operative routine, have also brought important benefits, such as improving adherence to the use of immunosuppressive drugs (Geramita, 2020). Adherence to treatment is one of the biggest post-operative challenges, and solutions like this help to maintain good results in the long term.

CONCLUSION

The articles and results analyzed in this study demonstrate significant advances in lung transplantation techniques, perioperative management and physical rehabilitation, with emphasis on the constant progress in patient survival, quality of life and lung function. Ex vivo pulmonary perfusion (EVLP) and the use of devices such as Pocket PATH have shown promising approaches to optimizing results, while early rehabilitation is proving to be a key element in post-transplant recovery and functionality.

However, the scenario still presents important challenges, such as the occurrence of complications, including diaphragmatic paralysis and atrial arrhythmias, which require further investigation and the improvement of therapeutic approaches. In addition, regional inequalities and the lack of access to advanced technologies highlight the need for approaches that promote equal conditions in patient care, especially in countries with limited resources.

This study also highlights the importance of personalized interventions, such as inspiratory muscle training, which help the recovery of specific groups, such as pediatric patients and the elderly with multiple comorbidities. On the other hand, the relationship between body composition, bone loss and survival outcome still needs more in-depth research,

reinforcing the need for studies that propose effective interventions.

In conclusion, although lung transplantation is constantly evolving as an exceptional alternative in cases of advanced lung disease, advances in rehabilitation, management of complications and equitable access to treatment are fundamental to guaranteeing its transformative relevance. Investments in research, technology and infrastructure are crucial to ensure greater success for this modality, which has evolved exponentially over the years, and to guarantee better long-term outcomes.

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