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REVIEW

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Exploring long-term outcomes in COPD patients: a comprehensive narrative review of bilateral and single lung transplantation

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Abstract

Background Millions of people throughout the world suffer from the common and fatal respiratory disorder known as chronic obstructive pulmonary disease (COPD). Lung transplantation gives hope to individuals with end-stage COPD, with both bilateral lung transplantation and single lung transplantation being effective procedures. The complexity of chronic obstructive pulmonary disease is underscored by various factors influencing transplant outcomes, including patient characteristics, donor features, and complications post-transplantation.

Methodology This narrative review explores recent studies on bilateral and single lung transplantation in chronic obstructive pulmonary disease patients, focusing on research published after 2020. Databases like PubMed and Google Scholar were used with keywords such as "COPD," "lung transplantation," "bilateral lung transplantation," and "single lung transplantation" guided the research, emphasizing survival rates, quality of life, and post-transplant complications. Five selected articles encompassing 63,426 patients were examined, evaluating methodological variations among the studies.

Results The selected studies showed no unanimous agreement on whether bilateral or single lung transplantation is superior for chronic obstructive pulmonary disease patients. Bilateral lung transplantation exhibited higher mid- and long-term survival rates, influenced significantly by age, comorbidities, and disease profiles. Improved quality of life was observed with bilateral transplantation, but this outcome depended on external circumstances. Post-transplant complications emphasized the need for rigorous post-transplant care.

Conclusions Individualized assessments are crucial when choosing between bilateral and single lung transplantation for chronic obstructive pulmonary disease patients. Despite varying research results, bilateral transplantation generally offers better survival and quality of life. Informed decisions require personalized post-transplant care, standardized reporting, and consistent research methods. Emphasizing donor management, preventing chronic lung allograft dysfunction, and prioritizing patient-centered care is vital. Collaborative efforts and patient-focused strategies are essential for improving long-term outcomes in these patients undergoing lung transplantation.

Keywords Single lung transplantation, SLT, Bilateral lung transplantation, BLT, Long-Term Outcomes in COPD, COPD, Chronic obstructive pulmonary disease, CLAD, Chronic lung allograft dysfunction

Background

Chronic obstructive pulmonary disease (COPD) is a widespread and incurable respiratory condition affecting approximately 300 million people globally [1]. While cigarette smoking stands as the primary risk factor, other elements such as air pollution,

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occupational exposure, and genetic factors also contribute to its prevalence [1]. COPD manifests with symptoms like restricted airflow, chronic cough, sputum production, and difficulty in breathing (dyspnea), progressively worsening over time and potentially leading to severe complications including lung cancer, pulmonary hypertension, heart failure, and respiratory infections [1, 2].

In managing COPD, traditional treatments such as bronchodilators, inhaled corticosteroids, oxygen therapy, and pulmonary rehabilitation play a crucial role [3]. While these interventions alleviate symptoms, they do not halt the decline in lung function or prevent exacerbations [4]. Furthermore, these treatments come with drawbacks such as side effects, cost, availability, and compliance issues [4].

For individuals with end-stage COPD, lung transplantation emerges as a viable option [5]. The history of lung transplantation dates back to 1963 when James Hardy conducted the first attempt [6]. Since then, significant progress has been made in clinical practices, including widened indication criteria, advanced surgical methods, improved immunosuppression protocols, infection prophylaxis, and complications management [7].

Lung transplantation offers hope for enhanced quality of life and survival in patients with end-stage lung diseases [7]. Notably, COPD is the most common indication for lung transplantation, accounting for 36% of all cases between 1990 and 2017 [8]. However, post-transplant survival rates for COPD patients are influenced by various factors. These include patient characteristics such as gender, age, and BMI, as well as donor features, the type of transplantation (single or bilateral), the development of chronic lung allograft dysfunction (CLAD), and episodes of rejection [8]. Compared to other conditions like cystic fibrosis and pulmonary arterial hypertension, COPD patients have a median post-transplant survival of 5.7 years, indicating the complexity and challenges in managing this specific group of patients following transplantation [8].

This review seeks to offer a thorough evaluation of the body of research on the long-term results in COPD patients following lung transplantation. It will also clarify if one transplantation strategy has certain benefits over the other in terms of the outcomes following the transplant. In the end, the goal of this research project is to advance knowledge in the field of COPD therapy and educate physicians and patients on the possible advantages and factors to be taken into account while using various lung transplantation procedures.

Methodology

This narrative review embarked on an extensive exploration of recent studies focusing on the outcomes of bilateral lung transplantation (BLT) and single lung transplantation (SLT) in COPD patients. Utilizing electronic databases such as PubMed, Medline, and Google Scholar, the search was conducted primarily on studies published after 2020. Keywords such as "COPD," "lung transplantation," "bilateral lung transplantation," and "single lung transplantation" guided the search, with a specific focus on survival rates, quality of life, and post-transplantation complications in COPD patients undergoing BLT or SLT. Apart from the rest of the articles used in this review, 5 articles with a total population of 63,426 patients were selected for further research and more accurate comparison. Methodological variations among these studies were carefully examined to comprehend their potential impact on reported outcomes. The selected studies provided valuable insights into the comparative study of BLT and SLT, shedding light on the complexities involved in transplant procedures and patient outcomes.

Results

A complete summary of each selected study is given in (Table 1). The main outcomes of interest are survival rates, quality of life, and complications. The following are some common themes and patterns observed across the studies:

Survival rates

Most of the articles reported that BLT had better survival rates than SLT, especially in the mid-term and long-term follow-up. For example, Mansour [9] found that BLT had a lower rate ratio than SLT in the 3-year and 5-year survival, while Hull [12] found that BLT had a lower hazard ratio than SLT in the 5-year survival. However, some articles did not find a significant difference between the two methods, such as Mutyala [10] and Benvenuto [13]. Fang [11] reported that BLT had a higher risk of death than SLT in the first year after transplantation, but this was not confirmed by other studies. Additionally, Mutyala [10] discovered that SLT patients had a much shorter hospital stay than BLT patients (15 vs 19 days). According to this study, SLT maybe an effective treatment option for younger COPD patients, and careful donor selection may contribute to better survival rates.

Quality of life

Only Mutyala [10] measured the quality of life of the patients using a standardized questionnaire. It found that BLT had a better quality of life than SLT in terms of physical functioning, role limitations, social functioning, and mental health. However, it also noted that

Table 1 Comparison of single vs bilateral lung transplantation for COPD

Author, year	Rania Mansour, 2023 [9]	Sudeep Mutyala, 2021 [10]	Yu-Chi Fang, 2023 [11]	Travis D. Hull, 2022 [12]	Luke J. Benvenuto, 2020 [13]
Study follow-up time	Searched for articles from their inception to July 2022	February 2012 to March 2020	Studies published before the year 2000 and those with less than 50 patients	Organ sharing database between 2005 and 2018	May 4, 2005 to June 30, 2017
Total number of patients or studies	Seven studies, total of 10,652 patients	186 patients	15 studies	10,023 patients	5585 adults
Patient's diagnosis and type of surgery	End-stage chronic obstructive pulmonary disease (COPD), single vs bilateral lung transplants	End-stage chronic obstructive pulmonary disease (COPD), single vs bilateral lung transplants	End-stage chronic obstructive pulmonary disease (COPD), single vs bilateral lung transplants	Chronic obstructive pulmonary disease (COPD), single vs bilateral lung transplants	Chronic obstructive pulmonary disease (COPD), single vs bilateral lung transplants
Study design	Systematic Review and Meta-Analysis	Retrospective study	Meta-analysis	Prospective multicenter cohort study	Retrospective cohort study
Sample numbers	SLT ($n = 6233$) BLT ($n = 4419$)	SLT: 115 BLT: 71	SLT ~ 20,728 BLT ~ 16,252	SLT: 6269 BLT: 3754	RSLT: 995 LSLT: 1010 BLT: 3580
Mean age	Not specified in the research	SLT: 65.3 ± 5.9 BLT: 63.2 ± 7.1	~ 45–65	The average age was 65. Patients who undergo DLT tend to be younger, male patients.	RSLT: 63 (59–65) LSLT: 63 (59–66) BLT: 60 (55–64)
Survival rate (with years)	BLT group was more favorable than the SLT group at 1 (OR = 1.29, 95% CI 1.16, 1.43, $I^2 = 0\%$), 5 (OR = 1.46, 95% CI 1.35, 1.58, $I^2 = 23\%$), 10 years (OR = 1.71, 95% CI 1.57, 1.87, $I^2 = 12\%$)	No difference in survival between the 2 age groups ≤ 65 versus > 65 years ($P = 0.723$) at 5 years post-transplant	At 3 years and 5 years, SLT had a lower rate ratio of survival than BLT (0.937, $P = 0.041$ and 0.775, $P = 0.000$, respectively)	The overall survival rates at 1, 3, and 5 years after transplantation: SLT 86.2%, 69.9%, 56.8% BLT 90.1%, 76.7%, 64.4%	The adjusted 5-year survival: RSLT 56.7% LSLT 50.9% BLT 57.8%
Hazard ratio (with years)	0.73, 95% CI 0.70, 0.76, $I^2 =$ 40%0.73, 95% CI 0.70, 0.76, $I^2 = 40\%$	Not specified in the research	No appreciable difference in the hazard ratio for survival (0.91, $P = 0.07$)	0.819 (95% CI, 0.741–0.905) for DLT recipients compared with SLT recipients.	0.88, 95% CI 0.77–1.02, $p = 0.086$
Outcomes	BLT appears to show more encouraging trends in survival rates for the treatment of end-stage COPD compared to SLT.	Exhibited non-inferior outcomes in SLT patients compared to BLT patients.	SLT had a greater risk of problems for patients with COPD than BLT.	Median post-transplant survival was 5.3 years in SLT versus 6.5 years in DLT ($P < .001$). DLT recipients have superior post-transplant survival.	They discovered that RSLT was linked to similar survival to DLT and greater survival than LSLT.

Abbreviations: COPD chronic obstructive pulmonary disease, *SLT* single lung transplantation, *BLT* bilateral lung transplantation, *RSLT* right single lung transplantation, *LSLT* left single lung transplantation, *DLT* double lung transplantation, *OR* odds ratio, *CI* confidence interval, *HR* hazard ratio

the quality of life was influenced by many other factors, such as age, comorbidities, and postoperative complications.

Complications

The articles reported various complications associated with lung transplantation, such as primary graft dysfunction, bronchiolitis obliterans syndrome, infection, rejection, and malignancy. The incidence and severity of these complications varied among the studies and depended on many factors, such as donor characteristics, surgical techniques, immunosuppression regimens, and follow-up protocols. Some articles suggested that BLT had a higher risk of complications than SLT, such as Fang [11] and Hull [12]. However, other articles did not find a significant difference between the two methods, such as Mansour [9] and Benvenuto [13].

Other factors

The articles also discussed other factors that may affect the outcomes of lung transplantation, such as patient selection criteria, organ allocation policies, donor availability, surgical experience, and cost-effectiveness. Some articles argued that BLT may have advantages over SLT in terms of improving lung function, reducing pulmonary hypertension, and increasing organ utilization. However, other articles pointed out that BLT may also have disadvantages over SLT in terms of increasing waiting time, reducing donor pool, and increasing surgical complexity.

The common themes and patterns observed across the studies are:

Whether BLT or SLT are preferable for COPD patients is a matter of debate. The results might be influenced by a number of variables that need to be taken into account specifically for each patient.

Although it might not be noticeable in the near term, the survival advantage of BLT versus SLT might become clear throughout the mid-term and long-term follow-up.

BLT may enhance patients' quality of life more than SLT, but a number of other factors that are not directly connected to the kind of transplantation may also have an impact.

Lung transplant problems are frequent and serious, and there may not be much of a difference between BLT and SLT. The management and prevention of these problems are essential for enhancing the results.

Considering the availability and compatibility of donor organs, the patient's preferences and expectations, and the cost-effectiveness of the treatment, it is important to carefully weigh the risks and advantages of performing BLT or SLT for each patient.

Discussions

Factors that may influence the choice between BLT and SLT for COPD patients

Selection criteria for patients

The major indications for BLT include suppurative lung disorders, such as cystic fibrosis and bronchiectasis, due to the danger of infection from the native lung, according to the International Society for Heart and Lung Transplantation (ISHLT) guidelines [14]. Both SLT and BLT are viable treatment choices for additional lung conditions such as interstitial lung disease (ILD) and chronic obstructive pulmonary disease (COPD) [14]. However, various variables, such as age, body mass index (BMI), pulmonary hypertension, and comorbidities, may affect the technique of choice [15]. For instance, due to increased surgical risk and mortality, elderly patients (> 65 years) may experience poorer results with BLT than with SLT [16]. Similar to SLT, BLT may result in more problems and a shorter survival time in obese individuals (BMI > 30) [17].

Donor availability

There are more requests for lung transplants than there are available donors, which leads to lengthy wait times and significant waiting list mortality [18]. Therefore, the kind of lung transplantation is greatly influenced by the availability of donors. By employing lungs that are inappropriate for BLT owing to size mismatch, anatomical differences, or unilateral injury, SLT may expand the donor pool [19]. SLT can lessen waiting list mortality by enabling two patients to share the benefits of a single donor [19]. As SLT is more prone to antibody-mediated rejection (AMR) than BLT, it may potentially decrease the donor pool by removing donors with positive crossmatch or high panel reactive antibody (PRA) levels [19]. To guarantee optimal graft function and prevent problems such as bronchial stenosis or native lung hyperinflation, SLT may necessitate stricter donor-recipient matching standards than BLT [20].

Expected results

Depending on the underlying illness profile and the incidence of comorbidities, the survival outcomes of SLT and BLT may differ. For patients with ILD and COPD, several studies have demonstrated that BLT has a greater long-term survival rate than SLT, notably in younger age groups (50 years) [21]. However, in senior age groups (> 50 years), this survival benefit may vanish or reduce because older patients may experience more surgical mortality and morbidity with BLT than with SLT [21]. Additionally, according to certain studies [22, 23], SLT may provide patients with pulmonary fibrosis brought on by connective tissue disease or hypersensitivity

pneumonitis with a comparable or even greater chance of surviving than BLT.

Additionally, there may be differences between SLT and BLT in the development of chronic lung allograft dysfunction (CLAD), which is the primary factor in late death following lung transplantation. While some studies have revealed no significant difference or even a decreased risk of CLAD with SLT [24], others have identified both a greater incidence and earlier start of CLAD with SLT than BLT [24]. With SLT being more likely to acquire an obstructive phenotype (BOS) and BLT being more likely to develop a restrictive phenotype (rCLAD/RAS), the kind and degree of CLAD may also differ between SLT and BLT [22].

Factors that influence outcomes of BLT and SLT

The need for a transplant

The results of BLT or SLT for various lung illnesses may vary. For instance, BLT is recommended for individuals with cystic fibrosis or bronchiectasis to reduce the risk of lung infection [14]. BLT or heart-lung transplantation may be beneficial for patients with pulmonary hypertension because SLT may raise the risk of right ventricular failure [14]. SLT may be an option for patients with fibrotic lung disease since it may be more readily available and have a reduced surgical risk [14].

The donor-receiver match

Any transplant's success depends on the compatibility of the donor and the recipient. This covers elements including blood type, human leukocyte antigen (HLA) genotype, size, and gender compatibility. Gender mismatching has been linked to worse graft survival rates, particularly when a female donor and a male receiver are involved [25]. This is not, however, a convincing result, as other variables could potentially be at play [26].

The conditioning regimen

The kind and rigor of pre-transplant therapy can have an impact on the success of the transplant. The conditioning program tries to reduce the recipient's immunological response and avoid organ rejection. Complications include infection, hemorrhage, organ toxicity, and graft-versus-host disease (GVHD) are possible side effects as well. The patient's age, comorbidities, disease state, and donor type all influence the conditioning program that is chosen. Myeloablative conditioning (MAC) and reduced-intensity conditioning (RIC) are the two main forms of conditioning. The chance of non-relapse mortality (NRM) is higher and the likelihood of relapse is lower in MAC, which is more aggressive. The risk of NRM is decreased with RIC, although the chance of relapse is higher [27].

The management of the patient following the transplant is essential for the long-term results, which is the subject of post-transplant care. This involves things like immunosuppression, infection prevention, rejection and GVHD monitoring, complication management, and rehabilitation. Individualized post-transplant care should be provided in accordance with the needs and hazards of the patient. In order to avoid rejection and reduce toxicity, a balance must be struck [28].

Future directions and innovations in lung transplantation

Recent advances in technology and techniques have improved the outcomes and quality of life for lung transplant recipients. Some of these include the following:

Ex vivo lung perfusion (EVLP)

This procedure prepares donor lungs for transplant by conserving and enhancing them outside the body. In addition to increasing the number of organs that are accessible and reducing ischemia-reperfusion harm, EVLP also enables the evaluation and management of lung function [29].

Bioengineering and regenerative medicine

These are methods for constructing synthetic or biological artificial lungs, or for repairing damaged lung tissue using stem cells or gene therapy. Although these techniques are still in the experimental stage, they have the potential to get over the restrictions of donor availability and immunosuppression [29].

Precision medicine and biomarkers

These are methods to modify immunosuppression and therapy in accordance with the unique traits and requirements of each patient. In order to improve patient outcomes and lessen negative effects, precision medicine and biomarkers can be used [29, 30].

Although lung transplantation has advanced, there are still many aspects that require more study and development. A few of these are the following:

Enhancing donor management and allocation

More effective selection and management criteria are required, as is the optimization of the allocation system to connect donors and beneficiaries according to criteria including compatibility, urgency, and equity [31, 32].

Preventing and treating chronic lung allograft dysfunction (CLAD)

This condition, which is characterized by increasing fibrosis and airway obstruction following lung transplantation, is the main cause of morbidity and mortality. There is no effective treatment for CLAD, and the

processes and risk factors are not entirely understood. The etiology, diagnosis, prevention, and therapy of CLAD need to be determined via further study [31, 33].

Enhancing patient-centered care and quality of life

Improved patient-provider communication and care delivery are required, as is attention to patients' physical, psychological, social, and spiritual requirements following lung transplantation. Measures of patient satisfaction and outcomes can be used to assess how a lung transplant affects quality of life [31, 34].

Complex ethical concerns surrounding lung transplantation need careful thought and respect for the autonomy, beneficence, nonmaleficence, fairness, and dignity of the patient. Among these problems are the following:

Consent in organ transplantation

Before organ donation or transplantation, this is the procedure used to get the informed permission of donors, recipients, and their families. Because of the numerous aspects involved, including risks, advantages, alternatives, preferences, values, and beliefs, as well as uncertainties, disputes, and pressures, consent for organ transplantation is more challenging than consent for the majority of medical operations. The basis for consent in organ transplantation should be explicit disclosure, understanding on both sides, decision-making by consensus, voluntary agreement, and continued communication [35].

Recipient selection for lung transplantation

This is the process of selecting a candidate for a lung transplant based on ethical and medical standards. The lack of organ donors, the variety of patient circumstances, the unpredictability of results, and the wide range of viewpoints make recipient selection for lung transplantation difficult. Transparent rules, equitable methods, multidisciplinary teams, individual evaluations, and evidence-based criteria should all be used to guide the selection of recipients for lung transplantation [36].

Limitations

This narrative review is limited by the heterogeneity of the included studies, which may introduce biases. Additionally, the review's reliance on existing research imposes constraints related to available data and study methodologies. Acknowledging these limitations is crucial for interpreting the findings accurately and guiding future research endeavors.

Conclusions

In this review, COPD patients who underwent single lung transplantation (SLT) or bilateral lung transplantation (BLT) were compared. Although findings varied, BLT typically showed superior mid- and long-term survival rates. In some ways, quality of life favored BLT, but it also depended on the patient's features and problems. When deciding between BLT and SLT, a number of variables, including the patient selection criteria and donor availability, were important. Positive results required post-transplant care and complication management.

Clinicians must individualize care while taking the patient's age, comorbid conditions, and predicted quality of life into account. For successful results, it is essential to carefully weigh the benefits and dangers of BLT and SLT, as well as to provide comprehensive post-transplant care. In order to effectively treat COPD, patient-centered methods and all-encompassing healthcare strategies are required.

Future studies comparing the results of BLT and SLT should be standardized and take into account a range of patient demographics. It is essential to make improvements in donor management, CLAD prevention, and patient-centered treatment. Exploring cutting-edge methods like precision medicine and EVLP shows potential. Careful thought must be given to ethical issues, including consent and recipient choice.

Understanding individual patient profiles and refining transplantation techniques are vital. Long-term outcomes, encompassing survival rates, quality of life, and post-transplant complications, are essential in evaluating success. Ongoing research, collaboration, and a patient-centered approach are key to improving prospects for end-stage COPD patients undergoing lung transplantation.

Abbreviations

COPD	Chronic obstructive pulmonary disease
SLT	Single lung transplant
BLT	Bilateral lung transplant
CLAD	Chronic lung allograft dysfunction
RSLT	Right single lung transplantation
LSLT	Left single lung transplantation
ISHLT	International Society for Heart and Lung Transplantation
ILD	Interstitial lung disease
BMI	Body mass index
AMR	Antibody-mediated rejection
PRA	Panel reactive antibody
HLA	Human leukocyte antigen
GVHD	Graft-versus-host disease
MAC	Myeloablative conditioning
RIC	Reduced-intensity conditioning
NRM	Non-relapse mortality
EVLP	Ex vivo lung perfusion

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AT presented the idea and planned its design and direction, then collected, organized, and analyzed various data and performed writing and final review. The author read and approved the final manuscript.

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