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Danial Ahmad
Thomas Jefferson University

Thomas J O'Malley
Thomas Jefferson University

Andrew M Jordan
Thomas Jefferson University

Elizabeth J Maynes
Thomas Jefferson University

Abhiraj Saxena
Thomas Jefferson University

Original Article

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Danial Ahmad[1], Thomas J. O'Malley[1], Andrew M. Jordan[1], Elizabeth J. Maynes[1], Abhiraj Saxena[1], Kyle W. Prochno[1], Taufiek K. Rajab[2], Howard T. Massey[1], Richard C. Daly[3], Vakhtang Tchantchaleishvili[1]

[1]Division of Cardiac Surgery, Thomas Jefferson University, Philadelphia, PA, USA; [2]Division of Cardiothoracic Surgery, Medical University of South Carolina, Charleston, SC, USA; [3]Department of Cardiovascular Surgery, Mayo Clinic, Rochester, MN, USA

Contributions: (I) Conception and design: V Tchantchaleishvili, TJ O'Malley, EJ Maynes, D Ahmad; (II) Administrative support: V Tchantchaleishvili, TJ O'Malley; (III) Provision of study materials or patients: AM Jordan, A Saxena, KW Prochno, TJ O'Malley; (IV) Collection and assembly of data: AM Jordan, A Saxena, KW Prochno, TJ O'Malley; (V) Data analysis and interpretation: D Ahmad, TJ O'Malley, V Tchantchaleishvili, EJ Maynes, RC Daly, TK Rajab, HT Massey; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Vakhtang Tchantchaleishvili, MD. Assistant Professor of Surgery, Division of Cardiac Surgery, Thomas Jefferson University, 1025 Walnut St, Suite 607, Philadelphia, PA 19107, USA. Email: Vakhtang.Tchantchaleishvili@jefferson.edu.

Background: Bronchial artery revascularization (BAR) during lung transplantation has been hypothesized to improve early tracheal healing and delay the onset of bronchiolitis obliterans syndrome (BOS). We aimed to assess the outcomes of BAR after lung transplantation.

Methods: Electronic search in Ovid Medline, Cumulative Index of Nursing and Allied Health Literature (CINAHL), Scopus, and Cochrane Controlled Trials Register (CCTR) databases was performed to identify all relevant studies published about lung transplantation with BAR. Studies discussing lung transplantation utilizing BAR were included while those without outcome data such as BOS and survival were excluded. Cohort-level data were extracted and pooled for analysis. A binary outcome meta-analysis of proportions with logit transformation was conducted. Newcastle-Ottawa scale was used for risk of bias assessment.

Results: Seven studies were selected for the analysis comprising 143 patients. Mean patient age was 47 (95% CI: 40–55) years. Sixty-one percent (48–72%) were male. Seventy-three percent (65–79%) of patients underwent double lung transplant while 27% (21–25%) underwent single lung transplant. In patients with postoperative angiography, successful BAR was demonstrated in 93% (82–97%) of all assessed conduits. The 30-day/in-hospital mortality was 6% (3–11%). Seventy-nine percent (63–89%) of patients were free from rejection at three months. Eighty-three percent (29–98%) of patients were free from signs of airway ischemia at three and six months. Pooled survival at one year and five years was 87% (78–92%) and 71% (46–87%), respectively, with a mean follow-up time of 21 (3–38) months. Pooled freedom from bronchiolitis obliterans was 86% (77–91%) at two years.

Conclusions: While this systematic review and meta-analysis is limited by the available surgeons, institutions, and papers discussing a highly specialized technique, it does show that BAR is a viable technique to minimize BOS and early anastomotic intervention following lung transplantation.

Keywords: Lung transplant; bronchial artery revascularization (BAR); bronchiolitis obliterans syndrome (BOS)

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Introduction

Lung transplantation has been the standard of care for the treatment of end-stage chronic respiratory failure with the registry of the International Society for Heart and Lung transplantation following over 55,000 cases from 250 lung transplant centers since the 1990s (1). The United States performed 2,562 lung transplantations in 2018 alone contributing to a 31% increase in the number of operations

performed over the preceding five years (2). Survival after lung transplant has also been improving over the years (1). Despite this, when compared to other solid-organ transplants, lung transplant survival is substantially lower (1). The survival curve following lung transplant, shows a steady drop after the first-year of transplant (3,4). This has been attributed to the development of chronic lung allograft dysfunction (CLAD), which develops in 50% of grafts at five years and has remained relatively stable over time (1,4). CLAD encompasses multiple distinct phenotypes with one of the main problematic types being bronchiolitis obliterans syndrome (BOS) (5). This CLAD phenotype has been specifically noted to be present in over 40% of lung transplant recipients within five years, has a median onset of 2.3 years, and has accounted for 27.5% of deaths in lung transplant recipients from 1990 to 2017 (6-12).

The development of BOS has been hypothesized to occur due to many factors, such as acute rejection, cytomegalovirus infection, and ischemia-reperfusion injury (13). Airway ischemia, inflammation, and subsequent necrosis due to reduced oxygenated blood supply have also been implicated in the development of progressive inflammation and fibrosis-potentially leading to BOS. This could be because following a typical lung transplantation; the lower airways are perfused via minimal retrograde flow from the pulmonary veins as the arterial flow from the bronchial arteries is sacrificed in the transplantation process. A permanent reduction in adequately oxygenated blood to the pulmonary airways could thus increase the risk of chronic ischemia and hypoxic damage (7,14-16).

Given this hypothesis, reducing lung ischemia in the early post-transplant period could be of importance in order to reduce the chances for development of late BOS; however, a clear link between ischemia related airway anastomotic problems and late BOS has not been found so far (17,18). One proposed strategy, bronchial artery revascularization (BAR), has been utilized as a surgical technique to supply the airway with oxygenated blood (19,20). After early implementation in specialized centers, BAR has demonstrated promise in delaying the onset of BOS (20-23), but has since not been implemented as standard of care given its technically demanding nature and lack of extensive experience with it. By revascularizing the bronchial arteries through anastomosis of the donor bronchial artery to the internal mammary artery or utilizing a saphenous vein graft to form a new vascular conduit from the descending aorta, direct ischemia to the airways is reduced. Early results from uncontrolled single center studies in reduction of post-operative BOS development are encouraging (20-23). In order to systematically analyze this technique, we performed a systematic search and meta-analysis of bronchial artery revascularization to assess its outcomes and success following lung transplantation. We present the following article in accordance with the PRISMA reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-22-213/rc).

Methods

Literature search strategy

An electronic search was performed in September 2019 using Ovid Medline, Cumulative Index of Nursing and Allied Health Literature (CINAHL), Scopus and Cochrane Controlled Trials Register (CCTR). To achieve maximum sensitivity of the search strategy, combined terms such as “lung”, “transplantation”, “transplant”, “bronchial”, “artery”, “revascularization”, “BAR”, “lung transplantation”, “bronchial artery revascularization”, “lung transplant”, “en bloc double lung transplant”, “single lung transplant”, “sequential lung transplant”, “lung transplant recipient”, “right intercostobrachial artery”, “bronchial artery”, “bronchial arteries”, “graft rejection”, “bronchiolitis obliterans syndrome”, “internal thoracic artery”, “mammary arteries”, “bronchial artery anastomosis” were used as either keywords or MeSH terms. The reference lists of all eligible studies were reviewed for further identification of potentially relevant studies and assessed using the inclusion and exclusion criteria.

Selection criteria

Eligible studies for the systematic review included all articles discussing lung transplantation utilizing bronchial artery revascularization. Articles were excluded if they did not contain information regarding post-transplant outcomes including development of BOS or survival. When institutions published duplicate studies with overlapping data, only the most complete reports with the longest follow-up period were included for quantitative assessment. Articles published from 1987 onwards were included. Patients under the age of 16 were excluded. Studies not published in the English language and those not involving human subjects were excluded. Abstracts, case reports, conference presentations, editorials, reviews, expert opinions, and studies without adequate extractable data were

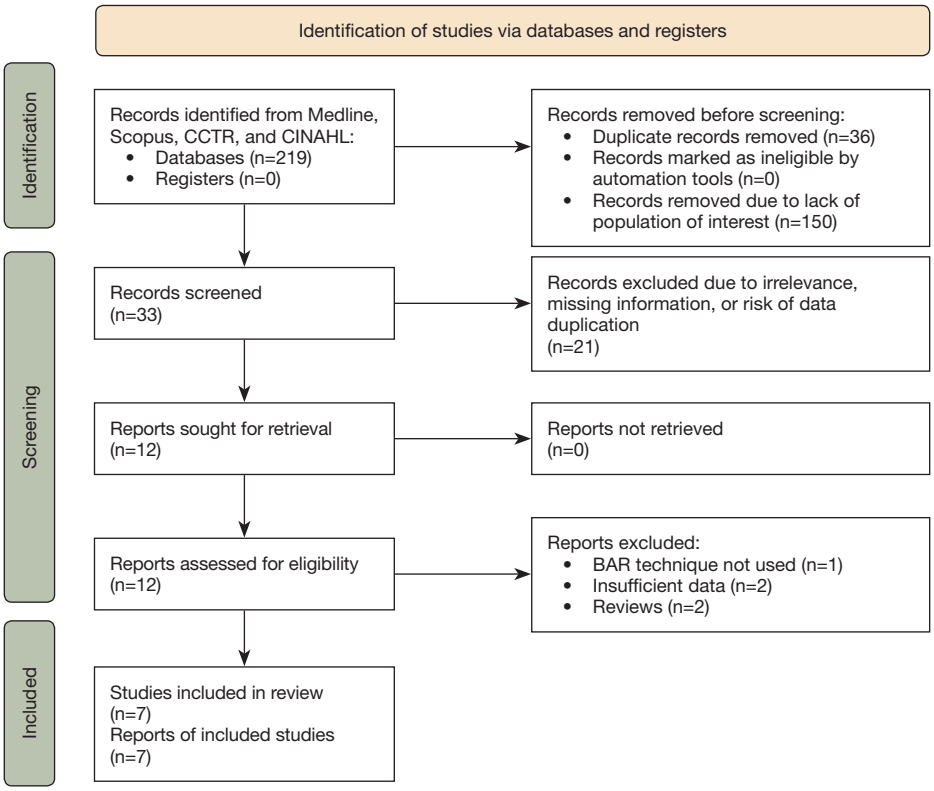

Figure 1 PRISMA flow diagram illustrating the search strategy. CCTR, Cochrane Controlled Trials Register; CINAHL, Cumulative Index of Nursing and Allied Health Literature.

also excluded. A PRISMA diagram reflecting the search strategy is demonstrated in *Figure 1*. Risk of bias assessment was carried out using the Newcastle-Ottawa scale (NOS) score (Tables S1,S2). A PRISMA 2020 checklist is provided as supplementary material.

Data extraction and critical appraisal

Data were extracted from article texts, tables, and figures. Discrepancies and disagreements were resolved by discussion, consensus, and adjudication by a senior coauthor.

Statistical analysis

A binary outcome meta-analysis of proportions was conducted for the available main perioperative and postoperative variables with logit transformation. Heterogeneity was evaluated using Cochran Q and the I^2 test. Survival data from each study were collected and pooled to retrieve a weighted mean and 95% confidence interval at specific time points. Such data were then graphically displayed to visualize survival over time. Meta-regression analysis was also done to assess the impact of time on mortality. R software, version 3.6.0 (R Foundation for Statistical Computing, Vienna, Austria) was used for all data analysis and visualization. The meta-analysis was performed using metafor package for R. P values less than 0.05 were considered statistically significant. This review did not have a previously published protocol nor was it registered. IRB approval was not required since publicly available deidentified data was used for the study.

Results

Baseline study and patient characteristics

Seven studies comprising 143 patients were included in this meta-analysis (20-26). Five of the studies comprising 105 patients were conducted from the year 1990 to 2000 (20-23,26). Of the remaining two, one was conducted from 1993 to 2003 (25) while the other was from 2007 to 2010 (24). Additional details are presented in the supplementary tables. The mean patient age was 47 (95% CI: 40–55)

Table 1 Baseline characteristics and indications

Variable	Pooled value [95% CI]	Number of studies	Events/total (n/N)	Heterogeneity, (%)
Age, years	47 [40–55]	3	67	32
Male (%)	61 [48–72]	4	47/77	0
Single lung transplant (%)	27 [21–25]	7	39/143	0
Double lung transplant (%)	73 [65–79]	7	104/143	0
Indications				
Emphysema (%)	71 [38–91]	3	57/79	36
Alpha-1 AT deficiency (%)	40 [2–96]	3	38/75	85*
Pulmonary fibrosis (%)	26 [4–75]	4	22/77	69*
Cystic fibrosis (%)	24 [0–100]	3	14/76	87*
Pulmonary HTN (%)	6 [2–17]	3	5/84	0

*, indicates significant heterogeneity, P<0.05. CI, confidence interval; AT, antitrypsin; HTN, hypertension.

years. 61% (95% CI: 48–72%) of patients were male. Of all transplants, 73% (95% CI: 65–79%) were double lung transplants while 27% (95% CI: 21–25%) were single lung transplants. Indications for transplant included emphysema [71% (95% CI: 38–91%)], alpha-1 antitrypsin deficiency [40% (95% CI: 2–96%)], pulmonary fibrosis [26% (95% CI: 4–75%), cystic fibrosis [24% (95% CI: 0–100%)], and pulmonary hypertension [6% (95% CI: 2–17%)]. These baseline characteristics are listed in *Table 1*.

Perioperative characteristics

A total of 91% (95% CI: 46–99%) of bronchial artery revascularizations were performed using an internal mammary artery conduit. Seven percent (95% CI: 1–51%) of the remaining transplants were performed with a saphenous vein graft as the conduit for bronchial artery revascularization. Of the total patients, 89% (95% CI: 79–95%) underwent angiography to evaluate bronchial artery revascularization. Ninety-three percent (95% CI: 82–97%) of patients who underwent angiography demonstrated successful bronchial artery revascularization with contrast passing through the conduit. Of these, 96% (95% CI: 94–97%) of patients utilizing an internal mammary artery conduit had patent revascularization of the bronchial artery. Eighty-seven percent (95% CI: 65–96%) ultimately healed their tracheal anastomosis (*Table 2*).

Postoperative outcomes and complications

Re-operation for any reason was required by 20% (95% CI: 9–38%) of patients while 14% (95% CI: 4–41%) of patients required re-exploration due to bleeding complications. 18% (95% CI: 9–31%) of patients experienced bleeding complications of any kind. Development of BOS or its precursor, pre-BOS, was demonstrated in 19% (95% CI: 8–37%) of patients. Cause of death was related to respiratory failure in 8% (95% CI: 0–99%) of patients and multi-organ failure in 6% (95% CI: 3–11%) of patients.

The mean follow-up time was 21 months (95% CI: 3–38 months) with a 30-day/in-hospital mortality of 6% (95% CI: 3–11%). 79% (95% CI: 63–89%) of patients were free from rejection at three months. Eighty-four percent (95% CI: 49–97%) of patients were free from anastomotic intervention at both three and six months. Eeighty-three percent (95% CI: 29–98%) of patients were free from signs of airway ischemia (assessed via bronchoscopy) at three and six months (*Table 3*). Pooled survival analysis, seen in *Figure 2*, demonstrates 87% (95% CI: 78–92%) and 71% (95% CI: 46–87%) survival at one year and five years respectively. Pooled freedom from bronchiolitis obliterans is demonstrated in *Figure 3* with 86% (95% CI: 77–91%) of patients free from BOS at two years. A meta-regression analysis to assess the relationship between Log 30-day/in-hospital mortality and time (publication year), shown in *Figure 4*, showed no significant effect of time on the mortality outcome (P=0.58).

Discussion

With the increasing number of lung transplants being

Table 2 Peri-operative characteristics, outcomes, and complications

Variable	Pooled value [95% CI]	Number of studies	Events/total (n/N)	Heterogeneity (%)
Conduit type				
Internal mammary artery (%)	91 [46–99]	7	123/143	72*
Saphenous vein (%)	7 [1–51]	7	18/143	73*
Patent angiography, any conduit (%)	93 [82–97]	6	116/133	7
Patent angiography, IMA conduit (%)	96 [94–97]	5	103/106	0
Fully healed tracheal anastomosis (%)	87 [65–96]	3	57/65	0
Complications				
Re-exploration (any) (%)	20 [9–38]	5	24/125	50
Re-exploration due to bleeding (%)	14 [4–41]	3	11/80	0
Bleeding, all (%)	18 [9–31]	5	19/115	11
BOS/pre-BOS (%)	19 [8–37]	6	14/93	31
Cause of death				
Respiratory failure (%)	8 [0–99]	2	3/45	0
Multi-organ failure (%)	6 [3–11]	4	4/77	0

*, indicates significant heterogeneity, P<0.05. CI, confidence interval; IMA, internal mammary artery; BOS, bronchiolitis obliterans syndrome.

Table 3 Long-term outcomes

Variable	Pooled value [95% CI]	Number of studies	Events/total (n/N)	Heterogeneity, (%)
Follow up, months	21 [3–38]	4	70	94*
30-day/in-hospital mortality (%)	6 [3–11]	6	8/135	0
Freedom from airway ischemia (%)				
3 months	83 [29–98]	3	48/55	48
6 months	83 [29–98]	3	48/55	48
Freedom from anastomotic intervention (%)				
3 months	84 [49–97]	4	57/63	37
6 months	84 [49–97]	4	57/63	37
Freedom from rejection (%)				
3 months	79 [63–89]	4	51/63	0

*, indicates significant heterogeneity, P<0.05. CI, confidence interval.

performed and a continual lagging median survival rate when compared to other solid-organ transplants, the field of lung transplantation has been hampered by the long-term development of CLAD. In order to strive to reach the survival rates attained by other solid-organ transplants, strategies to mitigate development of BOS must be developed. Whether through surgical technique or medications, reducing BOS is of paramount importance to lengthening the survival time of lung transplant recipients. Given the hypothesis of ischemia in the early peri-operative period potentially leading to late development of BOS, it stands to reason that improvements in surgical technique

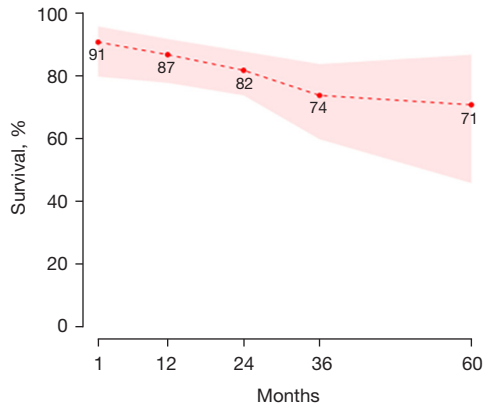

Figure 2 Pooled survival of patients undergoing lung transplant with bronchial artery revascularization. BOS, bronchiolitis obliterans syndrome.

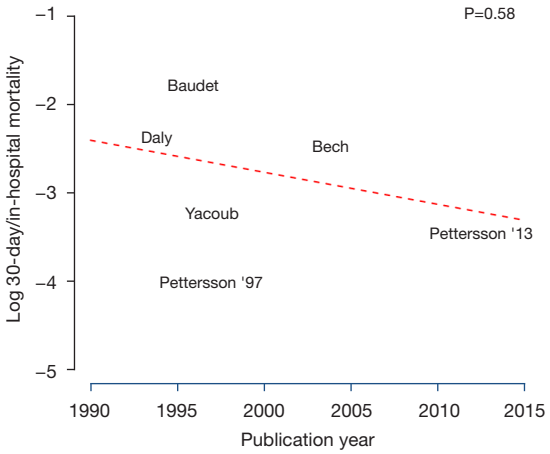

Figure 4 Meta-regression analysis between Log 30-day/in-hospital mortality and time (publication year).

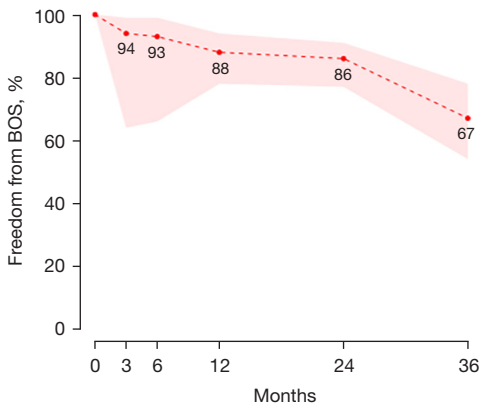

Figure 3 Demonstration of freedom from bronchiolitis obliterans following bronchial artery revascularization.

may limit its development and therefore improve patient survival. Following conventional lung transplantation without bronchial artery revascularization, the recipient's lungs are dependent on collateral flow from the pulmonary vein in the submucosal plexus with bronchial arterioles and retrograde flow through these vessels (23,27,28). Revascularization of the donor organ by recipient bronchial arteries may take up to two to four weeks to restore flow which represents a critical period for healing. Restoring bronchial artery flow at the time of transplant could potentially result in reduced early ischemia to the bronchial anastomosis, improved overall survival, and reduced rates of BOS development.

As a contributing factor to the development of BOS, understanding airway ischemia and its effects on the lung may be helpful in outlining the evolution of BOS (6,7,13,15,16). In our study, 83% (95% CI: 29–98%) of patients did not have any signs of airway ischemia following bronchial artery revascularization at both three and six months post-transplantation. This percentage is largely consistent with the rate of airway complications following conventional lung transplantation, reported as 15.7% in a large scale study (29). The reported incidence of airway complications with conventional lung transplantation ranges from 2% to 33% and these complications vary in their requirement for intervention, ranging from simple conservative management to angioplasty, stenting, and surgical intervention (30). In the BAR cohort, 84% (95% CI: 49–97%) of patients were free from anastomotic intervention at both three and six months. When comparing this intervention rate with conventional lung transplantation, 14.6% of patients required stent insertion at an average of 76 days for anastomotic complications in a cohort of 123 conventional lung transplant patients (31). However, based on these data, BAR has yielded similar airway ischemia and airway intervention rates among lung transplant recipients compared to conventional lung transplants.

While airway ischemia rates may be similar between BAR and conventional lung transplant recipients, in order to truly evaluate the results of the BAR cohort, long-term survival needs to be examined. The United Network for Organ Sharing (UNOS) reports overall survival percentages for lung transplantation at 1-, 3-, and 5-year as 89.4%, 74.8%, and 61.2%, respectively (32). While these numbers

include all types of lung transplant techniques, and given that BAR is rarely performed, these percentages are then more likely to represent conventional transplantation without BAR. When comparing these survival rates with those in our study, survival percentages at one year, three years, and five years are 87%, 74%, and 71% respectively. These numbers are similar at the one year and three year mark, yet the survival at 5 years is almost 10% better in the BAR cohort. One of the many possible reasons for this difference could be CLAD (33) which has a median onset of 2.3 years (12). It thus stands to reason that reduction in CLAD may contribute to improved long term survival. This is further supported by our data demonstrating 19% (95% CI: 8–37%) of patients who underwent BAR developed BOS or showed signs of pre-BOS over the mean follow up period of 21 months (95% CI: 3–38 months). When demonstrated as freedom from development of BOS, 67% of patients had no signs of BOS at 36 months. In comparison, approximately 43% of patients develop CLAD (without subtype distinction) at a median time of 2.3 years (12). This difference may suggest a correlation between BAR, reduction of BOS development, and improved survival outcomes. Further long-term data is needed to determine if this difference is statistically significant.

While there may be benefits to patients following BAR for lung transplantation, it is a demanding technique requiring additional focus on conduit preservation and monitoring of post-operative complications. Procuring the donor organ requires additional meticulous preservation of the bronchial artery and understanding of variant bronchial artery anatomy. This additional understanding requires further specialized training and has only been accomplished in limited number of centers with expert surgeons. Further, the additional preservation and formation of an additional arterial anastomosis increases the risk of bleeding complications and has been historically suggested as a reason for increased operative and cardiopulmonary bypass times (34). However, a propensity matched trial by Pettersson *et al.* indicated similar cardiopulmonary bypass time [BAR (n=20) *vs.* Non-BAR/Double lung (n=37): 164±32 *vs.* 178±78; P=0.3] and skin-to-skin times [BAR *vs.* Non-BAR/Double lung: 350±71 *vs.* 318±86; P=0.07] (24). Despite this smaller scale study, concerns persist regarding the feasibility of BAR and its effect on short-term outcomes.

When evaluating the short-term success of BAR, the two important factors to note are peri-operative mortality and bleeding complications. In evaluation of peri-operative mortality, when examining all transplants from 1989 to 2014, the UNOS lung transplantation 30-day mortality was 5.5% (35). In this cohort of BAR patients, the 30-day/in-hospital mortality was 6% (95% CI: 3–11%). These mortality rates are similar given the UNOS-reported overall rate is within the 95% confidence interval from our pooled cohort. With respect to bleeding complications in our study, 18% (95% CI: 9–31%) of patients suffered a hemorrhage of any kind with 14% (95% CI: 4–41%) requiring re-operation due to bleeding. Re-exploration for any cause was seen in 20% (95% CI: 9–38%) of patients. In comparison, a study of 224 patients undergoing conventional lung transplantation revealed a hemorrhage rate of 25.3% while re-operation for bleeding was required in 5.8% of patients. In this series, reoperation was needed in 7.2% of patients. Therefore, re-operation for bleeding and re-operation for any reason were higher in our cohort of patients with BAR, while overall hemorrhage rates were similar in both groups (36). Previous studies have thus listed risk of bleeding from revascularization sites as a potential complication from the BAR procedure and this is reflected in our systematic review too (23,24).

In evaluating BAR, surgeons should compare the increased technical requirements and peri-operative bleeding complications with the potential reduction or delay of BOS onset, which may outweigh the complications (20,24,26). It is possible that advancement in lung transplantation techniques and policies may have resulted in the improved overall survival after lung transplantation. By extension, it can be argued that BOS rates may also have improved (8,37). However, our results showed no effect of time on the 30-day/in-hospital mortality. It is also possible that offsetting the period of early ischemia following transplantation can reduce BOS and improve survival times. Despite this theoretical difference, freedom from airway ischemia and airway intervention was similar between BAR and non-BAR patients. Further long-term, large-scale analysis is needed to determine if the reduction in BOS development and improvement in long-term survival remain true for BAR.

Limitations and future directions

This systematic review and meta-analysis is limited by the available surgeons, institutions, and papers discussing a highly specialized technique. Given these limited numbers, direct evaluation via double-armed studies comparing BAR to similarly matched non-BAR patients was not possible, and therefore the technique was compared to overall

numbers as cited by UNOS. Further, as the surgeons and centers who performing BAR are likely invested in its positive portrayal, they may be subject to some selection and publication bias. This systematic review indicated many positive aspects of utilizing BAR in lung transplantation and provided early signs of high survival, low development of BOS, and low interventions for airway ischemia. However, long-term studies directly comparing similar patients undergoing BAR and non-BAR lung transplantation are needed to further evaluate BAR's effect on outcomes relative to conventional transplantation. While it is possible for double lung transplant patients to undergo a tracheal anastomosis with a left bronchial artery revascularization, analysis of included papers shows lack of sufficient granularity to differentiate that. Additionally, for the sake of this review the single-lung transplant patients were assumed to have undergone unilateral BAR with no subsequent contralateral single-lung transplant with contralateral BAR. The promising nature of this intervention will require a more granular study of sequential bilateral single-lung transplant with bilateral BAR versus double-lung transplant with bilateral BAR as well as double-lung transplant with unilateral BAR. However, it should be noted that the literature on survival differences between single *vs.* double lung transplantation is still conflicting (38,39). Donation after circulatory death (DCD) is another aspect that would be worth investigating. Lung transplant outcomes are generally comparable between DCD and Donation after Brainstem Death (DBD) (40); however, a higher rate of BOS following DCD lung transplantation has been reported (41). These conflicting results warrant further investigation into the relationship, if any, between airway ischemia and development of BOS. Given that, DCD has been gaining gradual acceptance, and that the studies included in this analysis span the last three decades, not much information was available to analyze this. Future comparative studies on BAR with results stratified by donor type (DCD *vs.* DBD) would help in answering such questions. Further, due to the technical requirements, all surgeons participating in a comparative study should be adequately trained at centers with extensive experience in BAR, otherwise, true results may be masked by imperfect technique.

Conclusions

Bronchial artery revascularization is a viable lung transplantation technique that results in high long-term survival, low long-term development of bronchiolitis obliterans, and low early anastomotic intervention due to ischemia at the cost of increased short-term bleeding complications. Further comparative analysis should be performed to evaluate this surgical technique versus conventional lung transplant.

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Footnote

Reporting Checklist: The authors have completed the PRISMA reporting checklist. Available at https://jtd.amegroups.com/article/view/10.21037/jtd-22-213/rc

Peer Review File: Available at https://jtd.amegroups.com/article/view/10.21037/jtd-22-213/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jtd.amegroups.com/article/view/10.21037/jtd-22-213/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Supplementary

Table S1 Characteristics of studies included in the meta-analysis

Title	Authors	Year published	Institution	Journal	Study type	Study date(s)	Total patients	New-Castle Ottawa Scale Score
Comparative study of bronchial artery revascularization in lung transplantation	Pettersson *et al.*	2013	Dept of Thoracic and Cardiovascular Surgery, Cleveland Clinic	Cardiothoracic Transplantation	Retrospective	2007–2010	27	7
Long-term outcome of lung transplantation for cystic fibrosis-Danish results	Bech *et al.*	2004	Dept of Cardiothoracic Surgery, Rigshospitalet, Copenhagen University Hospital, Copenhagen	European Journal of Cardio-thoracic Surgery	Retrospective	1993–2003	11	6
Bronchial artery revascularization improves tracheal anastomotic healing after lung transplantation	Hyytinen *et al.*	2000	Depts of Thoracic and Cardiovascular Surgery, Pulmonary Medicine and Radiology, Helsinki University Central Hospital, Helsinki, Finland	Scandinavian Cardiovascular Journal	Retrospective	1992–1997	8	7
Direct bronchial artery revascularization and en bloc double lung transplantation—surgical techniques and early outcome	Pettersson *et al.*	1997	Dept of Thoracic Surgery RT, Diagnostic Radiology and Medicine, The national University Hospital Copenhagen Denmark	The Journal of Heart and Lung Transplantation	Retrospective	1992–1995	47	6
Medium term results of direct bronchial arterial revascularisation using IMA for single lung transplantation (SLT with direct revascularisation)	Yacoub *et al.*	1997	Harefield Hospital, Harefield, Middlesex United Kingdom	European Journal of Cardio-thoracic Surgery	Retrospective	1991–1993	22	6
Intermediate-term results after en bloc double-lung transplantation with bronchial arterial revascularization. Bordeaux Lung and Heart-Lung Transplant Group	Baudet *et al.*	1996	Dept of Cardiovascular and Pediatric Cardiac Surgery, Bordeaux Heart Hospital, a Dept of Surgery, Haut-Leveque Hospital, Dept of Cardiac and Vascular Surgery, Bordeaux Heart Hospital, Bordeaux-Pessac, France	The Journal of Thoracic and Cardiovascular Surgery	Retrospective	1990–1994	18	6
Routine immediate direct bronchial artery revascularization for single-lung transplantation	Daly *et al.*	1994	Section of Cardiac Surgery, Mayo Clinic	Annals of Thoracic Surgery	Retrospective	–	10	6

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Table S2 Newcastle-Ottawa Scale (NOS) scoring system to assess risk of bias for the studies included

Study name	Representatives of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Outcome of interest Was not present at start of study	Comparability of cohorts on the bases of the design or analysis	Assessment of outcome	Was follow-up long enough for outcome to occur	Adequacy of follow-up	Total quality score (out of 9)
Comparative study of bronchial artery revascularization in lung transplantation	1	1	1	1	0	1	1	1	7
Long-term outcome of lung transplantation for cystic fibrosis - Danish results	1	0	1	1	0	1	1	1	6
Bronchial artery revascularization improves tracheal anastomotic healing after lung transplantation	1	1	1	1	0	1	1	1	7
Direct bronchial artery revascularization and en bloc double lung transplantation—surgical techniques and early outcome	1	0	1	1	0	1	1	1	6
Medium term results of direct bronchial arterial revascularisation using IMA for single lung transplantation (SLT with direct revascularisation)	1	0	1	1	0	1	1	1	6
Intermediate-term results after en bloc double-lung transplantation with bronchial arterial revascularization. Bordeaux Lung and Heart-Lung Transplant Group	1	0	1	1	0	1	1	1	6
Routine immediate direct bronchial artery revascularization for single-lung transplantation	1	0	1	1	0	1	1	1	6

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