# Single running suture technique is associated with low rate of bronchial complications after lung transplantation



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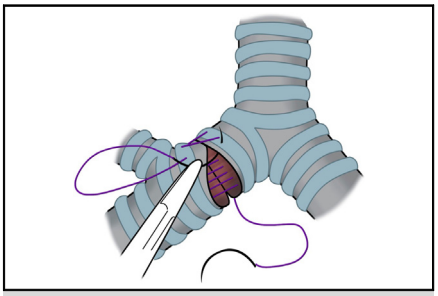
## ABSTRACT

**Background:** Lung transplantation has evolved to a routinely performed surgical procedure in patients with end-stage pulmonary disease. Bronchial healing problems are rare but represent a potential life-threatening complication. Herein, we aimed to define the incidence, classification, and treatment of bronchial complications after lung transplantation.

**Material and Methods:** All patients receiving lung transplantation between January 1999 and December 2017 were included in this retrospective study. All bronchial anastomoses were performed in a standardized technique using a single, polydioxanone running suture. The rate of anastomotic complications requiring an intervention, type of complication according the 2018 International Society for Heart and Lung Transplantation classification, and the clinical management were retrospectively analyzed.

**Results:** A total of 2941 anastomoses were performed in 1555 patients. The overall incidence of relevant anastomotic complications was 1.56%, 0.68% for left anastomoses, and 2.44% for right anastomoses. In 6 patients, a surgical revision or retransplantation was performed, whereas endoscopic treatment alone was sufficient in 39 patients. One patient underwent right-sided retransplantation 6 months after the first lung transplantation after failed endoscopic treatment attempts. International Society for Heart and Lung Transplantation grade ``S Lc Ec″ was the most common type of anastomotic complication. The overall incidence decreased within the study period from 2.4% in the era 1999 to 2003 to 0.8% in the era 2014 to 2017. We found no significant difference in overall survival of patients with and without anastomotic complications ($P = .995$; hazard ratio, 0.99; 95% confidence interval, 0.63-1.58).

**Conclusions:** The single running suture technique is associated with a very low rate of true anastomotic complications. Close follow-up and early endoscopic treatment of patients with anastomotic complications result in excellent long-term outcomes. (J Thorac Cardiovasc Surg 2020;160:1099-108)



**The single running suture technique for bronchial anastomosis in lung transplantation is easy, fast, and results in a very low rate of anastomotic complications.**

THOR

### CENTRAL MESSAGE

The use of a single-running suture technique results in a low incidence of airway complications after lung transplantation.

### PERSPECTIVE

Airway complications at the level of the anastomosis are extremely rare by using a single running suture technique, with an incidence of only 1.56%. In case of a clinically relevant airway stenosis, repeated endoscopic treatment is sufficient in the vast majority of patients.

See Commentaries on pages 1109 and 1110.

Anastomotic complications confer a relevant morbidity and mortality after lung transplantation. Lacking a standardized reporting system, the reported incidence of anastomotic complications varies between 2% and 41%.[1-8] To standardize the reporting of anastomotic complications, recent effort has been made by the International Society of Heart and Lung Transplantation (ISHLT) to implement a novel classification system. Post-transplant anastomotic problems (ischemia/necrosis, dehiscence, stenosis, and malacia) are classified according to their location in relation to the anastomosis and to severity.[3] During the past decades, the implementation of various technical refinements, eg, the use of absorbable suture

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**Abbreviations and Acronyms**

ATG = anti-thymocyte globulin
CF = cystic fibrosis
CI = confidence interval
COPD = chronic obstructive pulmonary disease
ISHLT = International Society for Heart and Lung Transplantation
OR = odds ratio
PDS = polydioxanone
POD = postoperative day

Scanning this QR code will take you to the article title page to access supplementary information.

materials and shortening of the donor bronchus, has decreased the incidence of bronchial complications.[5,9] Moreover, several anastomotic techniques have been described in the literature, including a running suture on the membranous portion and single stitches on the cartilaginous portion,[10] telescoping (running or interrupted) sutures,[6,9] interrupted figure-of-eight sutures,[11] and a single running suture.[4,5,7,12] However, none of these techniques is generally accepted as the gold standard. In 2003, we reported our initial experience with the single running suture technique in 141 patients.[4]

Since we have been using the single running suture technique in our institution for more than 15 years, we sought to analyze the results obtained with this technique and to compare them with results of the other techniques described in the literature. Moreover, we aimed to categorize the anastomotic complications based on the 2018 ISHLT consensus classification[3] and describe the management and long-term outcome of patients with anastomotic complications in a high-volume center.

## MATERIAL AND METHODS

### Study Population

All pediatric and adult patients undergoing primary lung transplantation between January 1999 and December 2017 at the Medical University of Vienna, Austria were included (Figure E1). Size-reduction, single-lung transplantation, and lobar transplantation were not considered exclusion criteria. Our institutional database was retrospectively reviewed to identify patients requiring endoscopic or surgical intervention(s) for anastomotic complications. Moreover, patients' records were reviewed for demographic variables, surgical procedure, early graft function, and long-term outcome. This study was approved by the institutional ethics committee (#1739/2019) and conducted according the Declaration of Helsinki.

### Surgical Procedure

Organ procurement was performed according to a standard protocol. After antegrade perfusion with Perfadex (Vitrolife, Gothenburg, Sweden) plus 500 mg of prostacyclin, retrograde perfusion with Perfadex was performed on the back table and the donor lungs were stored on ice. Ex vivo lung perfusion was performed in selected cases. For bilateral lung transplantation, a clamshell incision or bilateral anterior thoracotomies in the fourth or fifth intercostal space were used. Single-lung transplantation was performed via anterolateral thoracotomy. In case of significant size-mismatch between the donor and the recipient, lobar or trilobar (ie, upper and lower lobe on the right side and either upper or lower lobe on the left side) transplantation was performed.

The single running suture technique applied for the bronchial anastomosis was performed as described previously.[4] The main steps of this technique are as follows: (1) short bronchial stumps, leaving one bronchial ring on the donor side; (2) preservation of the surrounding tissue, especially medial to the right main bronchus; (3) use of resorbable 4-0 polydioxanone (PDS) sutures; use of 5-0 PDS for pediatric and lobar transplantation; (4) avoiding additional trauma of the bronchial wall by grasping with instruments ("no-touch" technique); and (5) no additional coverage of the anastomosis. A step-by-step illustration of the single running suture is provided in Figure 1 and in Video 1.

Induction therapy consisted of anti-thymocyte globulin (ATG) or alemtuzumab dependent on transplant era. Induction therapy became part of the standard regimen in 2013 at our institution, except patients colonized with *Burkholderia cepacia* or *Mycobacterium abscessus* or patients with graft-versus-host disease as underlying diagnosis. Standard maintenance immunosuppression consisted of a triple regimen (mycophenolate-mofetil, corticosteroids, and tacrolimus). Cortisone dosage was 0.2 to 0.3 mg/kg body weight during the first 3 months and was reduced to 0.1 to 0.15 mg/kg body weight during the first year after transplantation. After 12 months, 5 mg of prednisolone per day was used as standard dosage for all patients. Patients without induction and patients with ATG induction had greater initial cortisone dosages than patients with alemtuzumab as induction therapy.[13] In case of kidney insufficiency, tacrolimus was switched to everolimus. In addition, all patients received systemic broad-spectrum antibiotics perioperatively. Inhaled antibiotic therapy consisted of gentamicin perioperatively and amphotericin B during the first 3 months. Specific antibiotic therapy was added according the antibiogram of bronchoalveolar lavages. Pneumocystis prophylaxis consisted of trimethoprim–sulfamethoxazole.

### Bronchial Complications

Follow-up bronchoscopies were performed usually within the first week before extubation and 1, 3, 6, and 12 months after transplantation. Reports on the surveillance bronchoscopies were retrospectively reviewed for anastomotic complications requiring endoscopic or surgical interventions. Bronchial anastomoses were retrospectively graded according the 2018 ISHLT consensus, whenever photographs or video documentation of the anastomosis was available.[3] The first bronchoscopy with evidence for the pathology was used for the grading. In brief, ischemia and necrosis (I), dehiscence (D), stenosis (S), and malacia (M) were classified regarding the location (L descriptor) and extent (E descriptor). Moreover, the time from transplantation to occurrence of the airway complication was determined. Endoscopic interventions were the treatment of choice in stenosis and malacia (Figure 2). In case of stenosis, dilatations were performed with inflatable balloons with diameters ranging from 8 to 12 mm. The balloon was inflated and kept in position for 1 to 2 minutes. The dilatation was usually carried out stepwise with increasing diameters during the procedure. The success of the treatment was re-evaluated 10 to 14 days after the procedure and repeated if necessary. Stent placement was considered if the stent could safely be placed without occluding or narrowing of any distal airway branches. Normally, stents were left in place for 2 to 3 months.

### Statistical Analysis

Categorical variables were expressed as counts and percentage and continuous variables as mean and standard deviation, unless otherwise

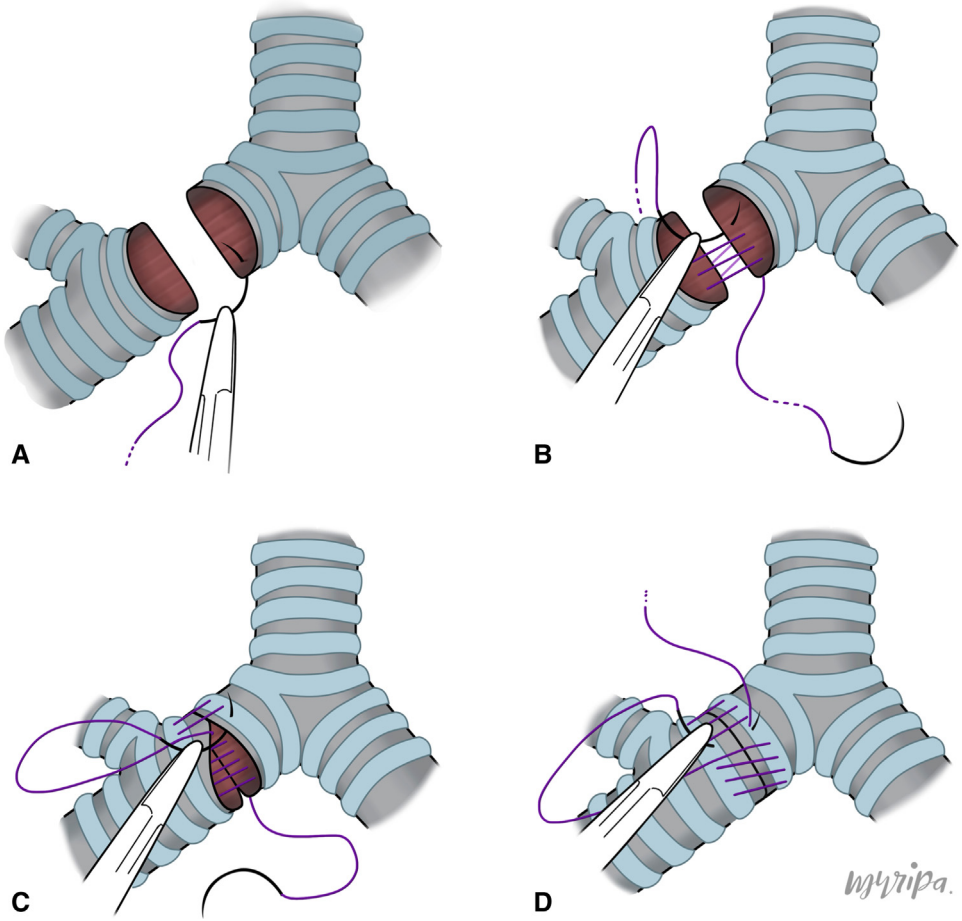



**FIGURE 1.** Schematic drawing of the single running suture technique for the bronchial anastomosis using a double-armed PDS suture. A, The first stitch is placed in the right dorsolateral corner from the outside to the inside at the recipient bronchial stump. B, The dorsal portion of the anastomosis is completed. C, After reaching the lateral portion on the *left side*, the direction of the stitches can be maintained by performing one stitch from the inside to the outside and vice versa on the same side of the anastomosis. Afterwards, the left and left-anterior portion of the anastomosis completed with backhand stitches. D, The free end of the thread is used to complete the remaining circumference of the anastomosis. Both ends are tied at the anterior aspect of the bronchus.

stated. $\chi^2$ test and Fisher exact tests were used to compare categorical variables. For multivariate analysis, binary logistic regression was used including all variables at a threshold of $P < .2$ in univariate analysis. Odds ratio (OR) and 95% confidence intervals (CIs) were calculated for each variable. Overall survival was defined as the time between the lung transplantation to death from any cause. The Kaplan–Meier method was used to plot survival curves and compared using the log-rank test. All statistical analyses were performed in SPSS, version 24 (IBM-SPSS Inc, Armonk, NY) and GraphPad Prism 6 (GraphPad Software, La Jolla, Calif).

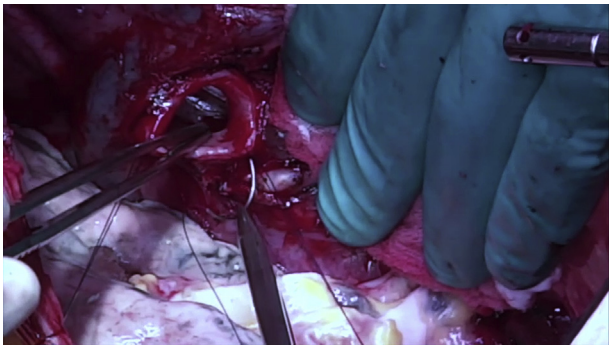
## RESULTS

### Study Cohort

A total of 1555 patients were included in this study. In total, 1386 received a double-lung transplantation, 88 a right-sided single-lung transplantation, and 81 a left-sided single-lung transplantation. This resulted in 2941 anastomoses at risk for bronchial problems (1474 right-sided and 1467 left-sided anastomoses). In total, 45 patients were identified who required endoscopic or surgical intervention due to anastomotic complications (Table E1). Only 1 patient had a bilateral anastomotic complication. A total of 34 (76%) of the patients with bronchial complications were male and 11 (24%) female. End-stage chronic obstructive pulmonary disease (COPD) was the most common indication for transplantation (42%), followed by cystic fibrosis (CF) (24%), pulmonary fibrosis (18%), pulmonary arterial hypertension (11%), and alpha 1-antitrypsin deficiency (4%). Detailed demographic and surgical data are provided in Table 1.

### Incidence of Anastomotic Complications

The overall incidence for a patient to develop an anastomotic complication was 2.89% (45/1555 patients); this corresponds to an incidence of 1.56% per anastomosis (46/2941 anastomoses). The incidence of right-sided anastomotic complications was 2.44% (per right-sided anastomosis), whereas problems on the left side occurred only in 0.68% (per left-sided anastomosis) ($P < .001$; relative risk, 1.58; 95% CI, 1.35-1.84). The median time to occurrence of any bronchial complication was 17 weeks (range 1-64) after transplantation. Median time to occurrence of



**VIDEO 1.** The single running suture technique is demonstrated and explained in this video file. The video shows a right-sided bronchial anastomosis through a clamshell incision. Video available at: https://www.jtcvs.org/article/S0022-5223(20)30439-6/fulltext.



stenotic complications was 18 weeks (range 4-64) (Figure E2), compared with markedly shorter times to occurrence of necrosis (2 weeks) and dehiscence (2 weeks [range 1-5]). The incidence per anastomosis for developing relevant stenosis, dehiscence, necrosis, or malacia was 1.4%, 0.1%, 0.03%, and 0.0%, respectively. Noteworthy, 7 of 45 patients with anastomotic complications received lobar or trilobar transplantation (Table 1). Overall, the risk for anastomotic complications was slightly greater in patients receiving a lobar transplantation (3.30% per patient; 7 of 212 patients). All anastomotic complications in this subgroup of patients were right-sided. However, after we excluded contralateral anastomotic complications, the rate of complications in lobar transplantation was 1.72% per lobar anastomosis (5 of 290). The overall incidence of anastomotic complications per anastomosis markedly decreased within the study period from 2.4% in the era 1999 to 2003 to 0.8% in the era 2014 to 2017 (Figure 3, *A*).

### Classification According 2018 ISHLT Consensus

In 37 of 45 patients (82%), a classification according the 2018 ISHLT consensus on bronchial complications was possible.[3] Detailed information on the distribution of bronchial complications according the ISHLT classification is provided in Table 2 and Figure 4. The most common type of bronchial complication were right-sided stenoses distal to the anastomosis involving the intermediate bronchus toward the orifice of the middle and lower lobe (S Lc Eb and S Lc Ec; 65%). Stenoses at the level of the anastomosis were present in 10 cases (S La Eb and S La Ec 30%). The remaining 2 cases (6%) were extended stenoses of anastomosis reaching distally (formula S Lb Eb). There was no malacia (M) requiring an intervention in our study cohort.

### Therapeutic Management of Anastomotic Complications

All patients with evidence for clinically relevant necrosis (n = 1) or dehiscence (n = 3) received early revision

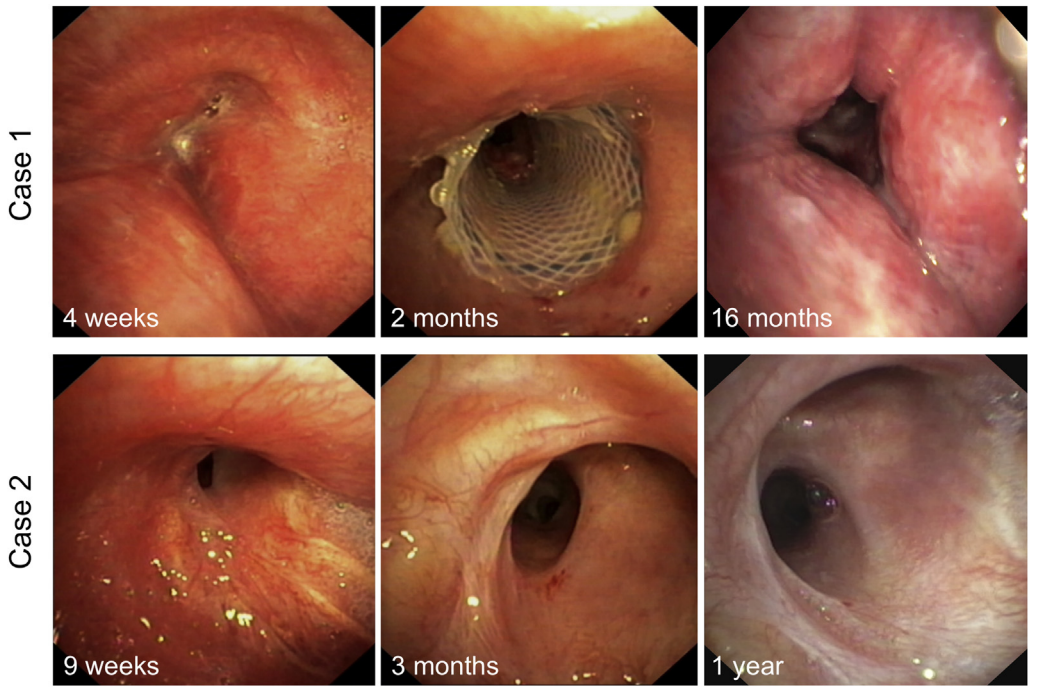



**FIGURE 2.** Representative bronchoscopic pictures of 2 patients: Case 1 with stenosis at the level of the left bronchial anastomosis (*upper row*; ISHLT grade S La Ec) and case 2 with a stenosis of the bronchus intermedius (*lower row*; ISHLT grade S Lc Ec). The first patient was treated using a Polyflex stent (Boston Scientific, Natick, Mass); the second patient received repeated balloon dilatations. In both patients, endoscopic interventions led to a sufficient lumen and stabilization of the stenosis.

**TABLE 1. Demographic data of 45 patients with anastomotic complications after lung transplantation**

| Demographics | Without anastomotic complication (n = 1510) | With anastomotic complication (n = 45) | Dehiscence (n = 3 patients) | Ischemia/necrosis (n = 1 patients) | Stenosis (n = 41 patients) |
|---|---|---|---|---|---|
| Age, y, median (range) | 45.6 (1-74) | 49.5 (15-66) | 62.5 (15-65) | 52 (52-52) | 47 (19-66) |
| Pediatric LuTx (<18 y) | 84 (6%) | 1 (2%) | 1 (33%) | 0 (0%) | 0 (0%) |
| Sex | | | | | |
| Male | 785 (52%) | 34 (76%) | 3 (100%) | 1 (100%) | 30 (73%) |
| Female | 725 (48%) | 11 (24%) | 0 (0%) | 0 (0%) | 11 (27%) |
| Indication | | | | | |
| COPD | 516 (34%) | 19 (42%) | 2 (67%) | 1 (100%) | 16 (39%) |
| Fibrosis | 345 (23%) | 8 (18%) | 0 (0%) | 0 (0%) | 8 (20%) |
| PAH | 112 (7%) | 5 (11%) | 0 (0%) | 0 (0%) | 5 (12%) |
| CF | 312 (21%) | 11 (24%) | 1 (33%) | 0 (0%) | 11 (24%) |
| Other | 225 (15%) | 2 (4%) | 0 (0%) | 0 (0%) | 2 (5%) |
| ECMO bridge-to-transplant | 91 (6%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| Type of LuTx | | | | | |
| Double-lung | 1343 (89%) | 43 (96%) | 2 (67%) | 1 (100%) | 40 (98%) |
| Standard | 1138 (83%) | 36 (84%) | 1 (50%) | 1 (100%) | 34 (85%) |
| Trilobar/bilobar | 205 (17%) | 7 (16%) | 1 (50%) | 0 (0%) | 6 (15%) |
| Single-lung right | 87 (6%) | 1 (2%) | 1 (33%) | 0 (0%) | 0 (0%) |
| Single-lung left | 80 (5%) | 1 (2%) | 0 (0%) | 0 (0%) | 1 (2%) |
| Intraoperative ECLS | | | | | |
| Bone | 505 (33%) | 20 (44%) | 2 (67%) | 1 (100%) | 17 (42%) |
| ECMO | 972 (64%) | 23 (51%) | 1 (33%) | 0 (0%) | 22 (54%) |
| CPB | 33 (2%) | 2 (4%) | 0 (0%) | 0 (0%) | 2 (5%) |
| EVLP | 68 (5%) | 1 (2%) | 0 (0%) | 0 (0%) | 1 (100%) |
| Induction therapy | | | | | |
| None | 674 (45%) | 26 (58%) | 2 (67%) | 1 (100%) | 23 (56%) |
| ATG | 210 (14%) | 9 (20%) | 1 (33%) | 0 (0%) | 8 (20%) |
| Alemtuzumab | 626 (42%) | 10 (22%) | 0 (0%) | 0 (0%) | 10 (24%) |
| Transplant era | | | | | |
| 1999-2003 | 245 (16%) | 14 (31%) | 1 (33%) | 0 (0%) | 13 (32%) |
| 2004-2008 | 369 (24%) | 17 (38%) | 2 (66%) | 1 (100%) | 14 (34%) |
| 2009-2013 | 488 (32%) | 7 (16%) | 0 (0%) | 0 (0%) | 7 (17%) |
| 2014-2017 | 408 (27%) | 7 (16%) | 0 (0%) | 0 (0%) | 7 (17%) |
| 90-d mortality | 139 (9%) | 4 (9%) | 3 (100%) | 0 (0%) | 1 (2%) |
| Anastomotic complications | – | n = 46 | n = 3 | n = 1 | n = 42 |
| Median time to occurrence, wk after transplantation (range) | – | 16 (1-64) | 2 (1-5) | 2 (2-2) | 18 (4-64) |
| Laterality | | | | | |
| Left-sided | – | 9 (20%) | 1 (33%) | 0 (0%) | 8 (20%) |
| Right-sided | – | 35 (78%) | 2 (67%) | 1 (100%) | 32 (78%) |
| Both | – | 1 (2%) | 0 (0%) | 0 (0%) | 1 (2%) |
| Type of intervention | | | | | |
| Dilatation | – | 42 | 0 (0%) | 0 (0%) | 42 (100%) |
| Stenting | – | 15 | 0 (0%) | 0 (0%) | 15 (36%) |
| Drainage | – | 3 | 3 (100%) | 0 (0%) | 0 (0%) |
| Surgery | – | 6 | 3 (100%) | 1 (100%) | 2 (5%) |

*LuTx*, Lung transplantation; *COPD*, chronic obstructive pulmonary disease; *PAH*, pulmonary arterial hypertension; *CF*, cystic fibrosis; *ECMO*, extracorporeal membrane oxygenation; *ECLS*, extracorporal lung support; *CPB*, cardiopulmonary bypass; *EVLP*, ex-vivo lung perfusion; *ATG*, anti-thymocyte globulin.

surgery. One patient (male, 51a, COPD) with extensive necrosis and dehiscence of the right anastomosis and the intermediate bronchus underwent lower bilobectomy with retrograde re-implantation of the right upper lobe on postoperative day (POD) 14. The further course was uneventful. Of the 3 patients with dehiscence, 1 patient (male, 62a, COPD) received reanastomosis of the right bronchial anastomosis and coverage with pericardial fat

pad on POD 18. Unfortunately, the patient died 2 days later due to subarachnoidal bleeding. The second patient (male, 14a, CF) with a dehiscence of the right anastomosis received revision on POD 32. The patient received venoarterial extracorporeal membrane oxygenation, evacuation of empyema, and an attempt to revise the right anastomosis, which was technically not possible as the necrosis involved the right main bronchus of the recipient. Given the overall situation, invasive treatment was stopped and the patient died on the same day. The third patient (male, 65a, COPD) received direct suturing and a pericardial patch on the POD 9 and was discharged to rehabilitation on the POD 22. The patient unfortunately was readmitted on the POD 31 and passed away due to fulminant sepsis.

Post-transplantation anastomotic stenoses (n = 42) occurred in 41 patients and were in general treated with endoscopic interventions (Figure 5). A total of 27 of 42 stenoses (64%) could be managed by repeated balloon dilatation without stenting. Dilatation and additional bronchial stenting were necessary in 15 stenoses (36%). Endoscopic treatment of stenosis was sufficient in 40 of 42 (95%) cases. Two stenoses (5%) required revision surgery. In the first patient (male, 52a, fibrosis) with a left-sided stenosis a resection of the stenotic bronchus and direct reanastomosis was possible. The further course was uneventful. The second patient (male, 59a, COPD) was listed for retransplantation after multiple attempts of dilatation and stenting due to a vanishing right main bronchus. A right-sided single-lung retransplantation 6 months after the primary transplantation was performed with an uneventful further course.

In univariate analysis, male sex ($P$ = .002; OR, 2.86; 95% CI, 1.44-5.68), diagnosis other than COPD/emphysema, CF, fibrosis, or pulmonary arterial hypertension ($P$ = .040; OR, 0.24; 95% CI, 0.06-1.05), induction therapy with ATG ($P$ = .034; OR, 2.68; 95% CI, 1.08-6.70) or no induction therapy ($P$ = .019; OR, 2.42; 95% CI, 1.16-5.04), and transplantation in the eras 1999-2003 ($P$ = .007; OR, 3.33; 95% CI, 1.33-8.37) and 2004-2008 ($P$ = .024; OR, 2.67; 95% CI, 1.10-6.55) were significantly associated with the occurrence of airway complications. Detailed variables on donor characteristics were available from 2010 onwards (patients n = 795). Donor–recipient size-mismatch, time of mechanical ventilation before organ procurement, donor age, type of organ donation, and ischemic time were not associated with anastomotic complications (Table E2).

## Outcome Analysis

Overall in-hospital mortality of patients with airway complications was 7% (3 of 45 patients). For patients with anastomotic dehiscence, the in-hospital mortality was 66% (2 of 3 patients). One patient with anastomotic stenosis died during the hospital stay (2% [1 of 41]). This patient, a 27 year-old man with primary pulmonary hypertension, developed a right-sided stenosis and passed away on the POD 89 due to uncontrollable endobronchial bleeding after dilatation. The overall survival in the cohort of 45 patients with bronchial complications was 82%, 73%, and 68% at 1 year, 3 years, and 5 years (Figure 3, *B*). Ninety-day mortality was 8.9% for patients with airway complications, compared with 9.2% without airway complications ($P$ = 1.000). Anastomotic

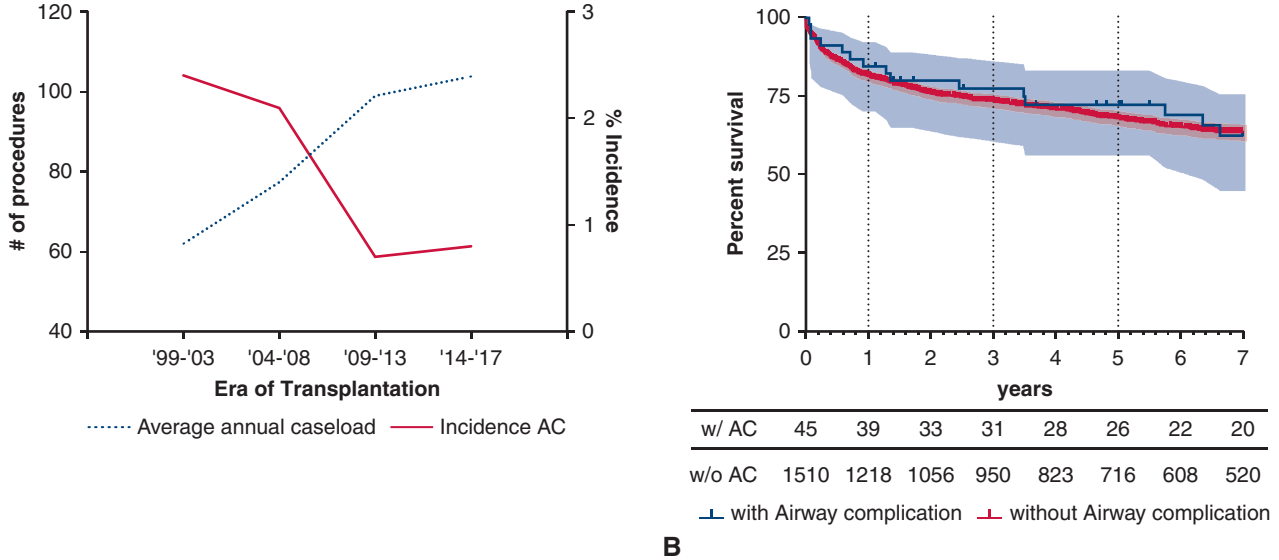



**FIGURE 3.** A, Incidence of airway complications by era and annually performed transplantations. The incidence was greatest in the early transplant eras (1999-2003 and 2004-2008) compared with the eras 2009-2013 and 2014-2017. B, Long-term survival after lung transplantation of patient with and without airway complications. Occurrence of anastomotic complications did not affect the long-term outcome after lung transplantation. *AC*, Airway complication.

**TABLE 2. Classification of anastomotic complications (n = 38) in 37 patients according the 2018 ISHLT consensus: the first bronchoscopy with evidence for the pathology was used for the grading**

| Location | | | | |
|---|---|---|---|---|
| Dehiscence (D) n = 2 | a. 0%-25% of circumference | b. >25%-50% of circumference | c. >50%-75% of circumference | d. >75 of circumference |
| a. Cartilaginous | – | – | – | – |
| b. Membranous | – | 1 (50%) | – | – |
| c. Both | – | – | – | 1 (50%) |
| Stenosis (S) n = 35 | a. 0%-25% reduction in cross-sectional area | b. >25%-50% reduction in cross-sectional area | c. >50%-<100% reduction in cross-sectional area | d. 100% obstruction |
| a. Anastomotic | – | 3 (9%) | 7 (20%) | – |
| b. Anastomotic plus lobar/segmental | – | 2 (6%) | – | – |
| c. Lobar/segmental only | – | 7 (20%) | 16 (46%) | – |
| Ischemia and necrosis (I) n = 1 | a. <50% circumferential ischemia | b. >50%-100% circumferential ischemia | c. <50% circumferential necrosis | d. >50%-100% circumferential necrosis |
| a. Perianastomotic | – | – | – | – |
| b. Extending >1 cm from anastomosis to major airways | – | – | – | 1 (100%) |
| c. Extending >1 cm from anastomosis into lobar or segmental airways | – | – | – | – |
| Malacia (M) n = 0 | | | | |
| a. Perianastomotic | – | | | |
| b. Diffuse | – | | | |

dehiscence with the need for surgical revision was associated with a 90-day mortality of 100% (3/3 patients) and therefore significantly worse than the other types of airway complications ($P < .001$). The long-term survival of patients was comparable with patients without airway complication (median survival 155 vs 154 months; $P = .995$; hazard ratio, 0.99; 95% CI, 0.63-1.58). In general, the clinical outcome of patients with bronchial complications was strongly dependent on the type of problem. Survival of patients with stenosis (the most common type of anastomotic problem) was not significantly different compared to patients without airway complications.

## DISCUSSION

This work aimed to summarize our institutional experience of airway complications after lung transplantation using a single, running suture for bronchial anastomoses (Figure 2). To the best of our knowledge, this study represents the largest published series focusing on airway complications in general and in particular the use of a uniform anastomotic technique. Moreover, this is the first clinical cohort, in which the recently published ISHLT consensus classification of bronchial complications was applied.

During the evolution from a surgical endeavor to a worldwide routinely performed procedure, several crucial lessons on bronchial anastomoses in lung transplantation had to be learned. By using resorbable monofilaments like PDS instead of nonresorbable materials, the number of anastomotic complications could significantly be lowered in patients receiving airway surgery.[5,14] Furthermore, a shortening of the donor bronchus to a level close to the lobar carina is mandatory. The 2 main bronchi are considered a transition zone, receiving their blood supply mainly from

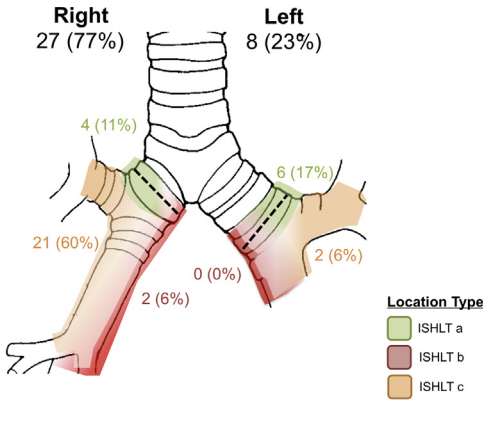



**FIGURE 4.** Spatial distribution of stenoses according the ISHLT classification (n = 35). Stenoses distant to the right anastomosis are the most common type of stenotic complications after lung transplantation. *ISHLT*, International Society for Heart and Lung Transplantation.

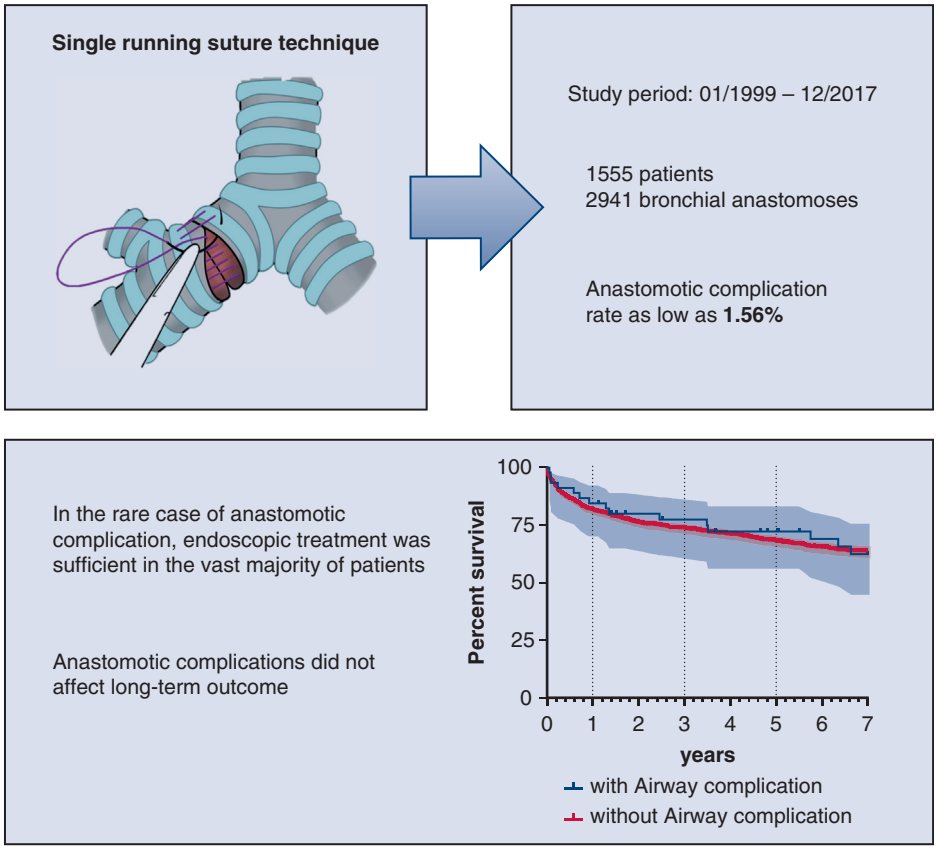



**FIGURE 5.** Central findings of this study. A total of 2941 anastomoses were assessed. Clinically relevant anastomotic complications at the level of the anastomosis are extremely rare, with an incidence of only 1.56%. Repeated endoscopic treatment is sufficient in the vast majority of patients.

the bronchial arteries and distally from the pulmonary artery vascular bed. By transection of the bronchial arteries during the lung retrieval, the blood supply of the main bronchi is significantly impaired. This might contribute to a relatively long healing period of bronchial anastomoses after lung transplantation. The time to establish a complete revascularization of the bronchial anastomosis by far exceeds the normal healing period of other central airway anastomoses. We have previously demonstrated that anastomotic revascularization after tracheal resection occurs early within the first days after the surgical procedure, whereas anastomotic revascularization in lung transplantation is thought to take up to 4 weeks.[15,16]

Several groups published their airway complication rates with and without shortening the donor bronchus. Using a single running suture, Van Berkel and colleagues[7] described a complication rate of 8.2%, which dropped to 2.1% when the donor bronchus was cut at the level of the lobar carina. Furthermore, a propensity score matching of 48 patients receiving the modified technique compared with the standard technique proved the superiority of the first. In a series of 232 consecutive lung transplantations, Van De Wauwer and colleagues[9] identified also the length of the recipient bronchus as a significant factor associated with anastomotic complications in univariate and multivariate analysis (relative risk, 1.065; 95% CI, 1.022-1.110; $P = .0029$).

In our study, the incidence of airway complications was 1.56% (per anastomosis). Yserbyt and colleagues[8] described an overall complication rate of 10.9% per anastomoses, which mainly resolved with conservative treatment. However, relevant complications needing endoscopic or surgical intervention occurred in 2.7% (per anastomosis), which is comparable with our rate of anastomotic complications. Interestingly, the Leuven group found a predominance of anastomotic complications on the right side (67%).[8] Our results confirm the susceptibility of the right-sided anastomosis for anastomotic complications (78%). In a retrospective analysis of the United Network for Organ Sharing database including 16,156 patients, male sex was associated with an increased risk for anastomotic complications (OR, 1.61, $P = .001$).[17] Although there is no clear explanation for the increased risk of male patients for anastomotic complications, significant, sex-specific differences in the of bronchial artery have been found.[18] In the current study, use of ATG as induction therapy or no induction therapy were significantly associated with anastomotic complications in

**TABLE 3. Univariate analysis of variables associated with airway complications (N = 1555 patients)**

| Recipient | Univariate analysis | |
|---|---|---|
| | OR (95% CI) | *P* value |
| Age >60 y | 0.97 (0.42-2.20) | .937 |
| Male | 2.86 (1.44-5.68) | **.002** |
| Diagnosis | | |
| COPD/emphysema | 1 | |
| CF | 0.96 (0.45-2.04) | .910 |
| Fibrosis | 0.63 (0.27-1.46) | .275 |
| PAH | 1.21 (0.44-3.32) | .707 |
| Other | 0.24 (0.06-1.05) | **.040** |
| Intraoperative ECLS | | |
| None | 1 | |
| ECMO | 0.60 (0.33-1.10) | .097 |
| CPB | 1.53 (0.34-6.83) | .577 |
| Induction therapy | | |
| Campath | 1 | |
| ATG | 2.68 (1.08-6.70) | **.034** |
| None | 2.42 (1.16-5.04) | **.019** |
| Type of LuTx | | |
| Standard LuTX | 1 | |
| Lobar Tx (bilateral) | 2.31 (0.89-6.05) | .087 |
| Lobar Tx (unilateral) | 0.44 (0.11-1.84) | .263 |
| Transplant era | | |
| 2014-2017 | 1 | |
| 2013-2009 | 0.84 (0.29-2.40) | .739 |
| 2004-2008 | 2.67 (1.10-6.55) | **.024** |
| 1999-2003 | 3.33 (1.33-8.37) | **.007** |

"Other" includes bronchiectasis, sarcoidosis, alpha 1-antitrypsin deficiency, lymphangioleiomyomatosis, chronic thromboembolic pulmonary hypertension, histiocytosis X, and pulmonary alveolar proteinosis. Values in bold are statistically significant. *OR*, Odds ratio; *CI*, confidence interval; *COPD*, chronic obstructive pulmonary disease; *CF*, cystic fibrosis; *PAH*, pulmonary arterial hypertension; *ECLS*, extracorporal lung support; *ECMO*, extracorporeal membrane oxygenation; *CPB*, cardiopulmonary bypass; *ATG*, anti-thymocyte globulin; *LuTx*, lung transplantation.

univariate analysis (Table 3). However, ATG or no induction therapy regimens were used predominantly in the early transplant eras. Beyond this, the dosage of corticosteroids was dependent on the induction therapy. Patients without induction or ATG induction had greater dosages of cortisone (0.3 mg/kg) during the first year than patients with alemtuzumab as induction therapy (0.2 mg/kg). Thus, the association of immunosuppressive regimens with anastomotic complications has to be interpreted with caution. Similarly, Olland and colleagues[2] described differences in anastomotic complications dependent on the type of immunosuppression; however, this difference was not significant in multivariate analysis.

In our opinion, a single running suture has several advantages over single-stitch techniques. By using the entire circumference, a size mismatch between the bronchi can be easily adjusted. This makes this technique also appealing, eg, in lobar transplantation. Although this can also be achieved by an interrupted suture technique, the running suture technique is simple, fast and convenient to the surgeon, especially when thoracotomy is used to perform the transplant. In contrast, it was recently argued that the running suture might result in purse stringing.[3] However, we did not observe this in our cohort. One reason for this might be the rigidity of the lobar carinal cartilage. The stability provided by the lobar carina might even prevent a malacic recipient bronchus from collapsing. As recently summarized in a review by Anile and colleagues,[1] similarly low rates of anastomotic complications (2.1%) were observed in a partial or complete running suture technique. Noteworthy, absorbable suture material, shortened bronchial cuffs, and the avoidance of telescoping were important factors of low anastomotic complication rates.[1] Out of the different anastomosis techniques, the single running suture technique is the most time-efficient one. Especially in organ transplantation time should be considered an important argument. A fast surgical technique contributes to short ischemic times.

Dependent on the clinical presentation and severity, the possible treatment options range from repeated balloon dilatation or stenting to a complete loss of the allograft with subsequent pneumonectomy or retransplantation.[19-21] In our study, the long-term outcome of patients with anastomotic complications was comparable with the patients without (median survival 155 vs 154 months; $P = .928$). Similar to our observation, Yserbit and colleagues did not observe a difference in survival in a cohort of 490 patients after transplantation (hazard ratio, 1.2; 95% CI, 0.8-1.9; $P = .2$).[8] Noteworthy, in a subgroup analysis stratified by the degree of anastomotic complication, this favorable overall survival could not be achieved in patients with high-grade complications (M3a, D2x, Sxe, or greater according the MDS [M: macroscopic aspect, D: diameter, S: sutures] classification).[8,22] In addition, Choong and colleagues[23] did not find a difference in overall survival ($P = .940$) or freedom of bronchiolitis obliterans syndrome ($P = .171$) in a cohort of 214 pediatric patients with 470 airway anastomoses at risk and 42 complications. In contrast, an analysis of the United Network for Organ Sharing registry revealed significantly reduced early and long-term survival rates (5-year survival 33.2% vs 54.2%, $P = .001$). However, this was mainly due to an excessively increased 1-year mortality. The conditional survival after one year was not different between patients with or without airway complications (conditional 5-year survival 60.8% vs 64.20, $P = .15$).[17] Our study underlines the importance of an aggressive and immediate treatment of patients with airway complications. A dedicated, interdisciplinary team should manage these patients since the spectrum of treatment modalities ranges from close follow-up to extended surgical procedures and should be adapted to the individual situation. As a result, excellent long-term survival can be achieved despite bronchial complications.

Several limitations are inherent to this work. First of all, this is a retrospective study. However, all bronchoscopies were performed and documented by a dedicated team of transplant pulmonologists and surgeons, which guarantees a high level of expertise in the diagnosis and treatment of anastomotic complications. Limited ischemia/necrosis without clinical consequence is usually diagnosed within the early postoperative course on the intensive care unit and was not documented in a standardized way in the early period. We minimized this reporting bias by focusing on anastomotic complication requiring treatment. Beyond this, the study period covers an era of nearly 2 decades. Changes during this time included a more liberal use of intraoperative extracorporeal membrane oxygenation support and induction therapy (Table E3).[24] Last, for a long time no generally accepted and standardized grading system on airway complications after lung transplantation was available. Recently, an ISHLT working group on airway complications published a proposed grading system, which was retrospectively applied in this study.[3] To the best of our knowledge, this work represents the largest series of uniformly performed anastomoses and identified stenoses of the intermediate bronchus distant to the anastomosis as the most relevant type of anastomotic complication.

In summary, we demonstrated herein that a single running suture for bronchial anastomoses is associated with an extremely low incidence of anastomotic complications. Therefore, it can be considered a fast and safe standard technique in lung transplantation. The majority of symptomatic bronchial complications can be managed by endoscopic treatment and results in excellent long-term outcome after lung transplantation.

## Conflict of Interest Statement

Authors have nothing to disclose with regard to commercial support.

Members of Vienna Lung Transplant Program include Costas Ieromonachos, MD, MBA,[b] Axel Scheed, MD,[a] Jose Ramon Matilla, MD,[a] Bernhard Moser, MD, FEBTS,[a] Shahrokh Taghavi, MD,[a] György Lang, MD, PhD,[a] Christopher Lambers, MD,[a] and Gabriela Muraközy, MD, PhD.[a]

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**Key Words:** anastomotic complication, airway complication, stenosis, dehiscence, lung transplantation

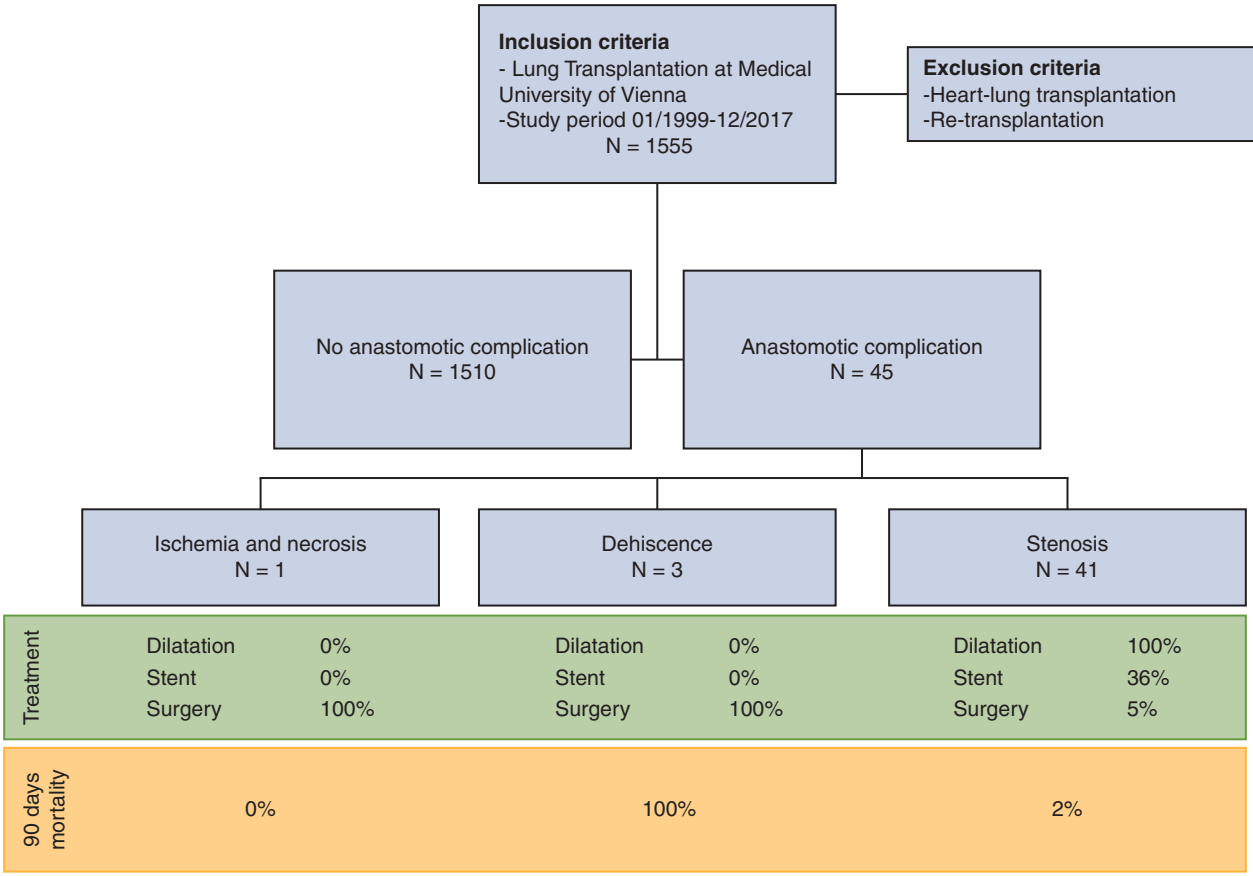


**FIGURE E1.** Flow chart of the study cohort (N = 1555).

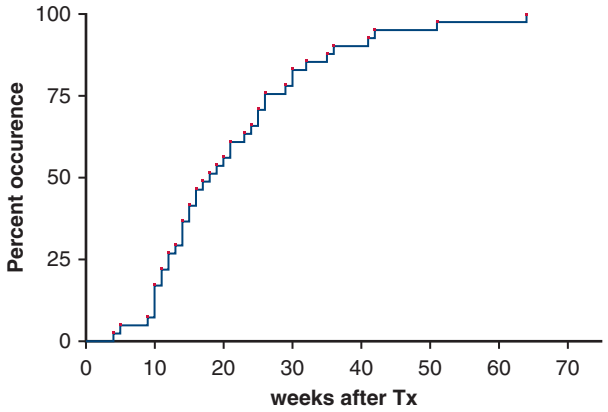


**FIGURE E2.** Time to occurrence of stenotic complications after lung transplantation in weeks. Median time to development and diagnosis of stenosis was 18 weeks. *Tx*, Transplantation.

**TABLE E1. ISHLT classification of airway complications after lung transplantation (N = 45)**

| Patient | Left/right | Type | Weeks after Tx | Location | Extent | Dilatation | Stent | Surgery |
|---|---|---|---|---|---|---|---|---|
| 1 | Right | Stenosis | 20 | c | c | Yes | Yes | No |
| 2 | Right | Stenosis | 12 | n/a | n/a | Yes | Yes | No |
| 3 | Right | Stenosis | 24 | c | c | Yes | Yes | No |
| 4 | Right | Stenosis | 13 | a | c | Yes | Yes | No |
| 5 | Left | Stenosis | 17 | a | c | Yes | Yes | No |
| 6 | Left | Stenosis | 10 | a | c | Yes | Yes | Yes |
| 7 | Right | Dehiscence | 1 | n/a | n/a | No | No | Yes |
| 8 | Right | Stenosis | 10 | n/a | n/a | Yes | Yes | No |
| 9 | Right | Stenosis | 21 | c | c | Yes | No | No |
| 10 | Right | Stenosis | 18 | c | b | Yes | No | No |
| 11 | Right | Stenosis | 5 | c | c | Yes | Yes | No |
| 12 | Right | Stenosis | 23 | c | b | Yes | No | No |
| 13 | Right | Stenosis | 12 | c | b | Yes | No | No |
| 14 | Left | Stenosis | 42 | c | c | Yes | Yes | No |
| 15 | Left | Stenosis | 35 | c | c | Yes | No | No |
| 16 | Right | Stenosis | 10 | c | c | Yes | No | No |
| 17 | Right | Stenosis | 14 | c | c | Yes | No | No |
| 18 | Right | Dehiscence | 5 | c | d | No | No | Yes |
| 19 | Right | Stenosis | 30 | c | c | Yes | No | No |
| 20 | Right | Stenosis | 19 | a | c | Yes | No | No |
| 21 | Right | Stenosis | 26 | c | b | Yes | No | No |
| 22 | Left | Stenosis | 25 | n/a | n/a | Yes | No | No |
| 23 | Right | Stenosis | 26 | n/a | n/a | Yes | Yes | No |
| 24 | Right | Stenosis | 16 | n/a | n/a | Yes | No | No |
| 25 | Left | Dehiscence | 2 | b | b | No | No | Yes |
| 26 | Right | Ischemia/necrosis | 2 | b | d | No | No | Yes |
| 27 | Right | Stenosis | 15 | n/a | n/a | Yes | No | No |
| 28 | Right | Stenosis | 32 | n/a | n/a | Yes | Yes | No |
| 29 | Right | Stenosis | 36 | c | c | Yes | No | No |
| 30 | Right | Stenosis | 10 | c | c | Yes | Yes | Yes |
| 31 | Right | Stenosis | 51 | c | b | Yes | No | No |
| 32 | Left | Stenosis | 21 | a | b | Yes | No | No |
| 33 | Right | Stenosis | 29 | c | b | Yes | No | No |
| 34 | Right | Stenosis | 25 | b | b | Yes | No | No |
| 35 | Right | Stenosis | 11 | c | c | Yes | No | No |
| 36 | Left | Stenosis | 11 | a | b | Yes | Yes | No |
|  | Right | Stenosis | 11 | c | c | Yes | No | No |
| 37 | Right | Stenosis | 41 | a | b | Yes | No | No |
| 38 | Right | Stenosis | 64 | c | c | Yes | No | No |
| 39 | Right | Stenosis | 30 | c | c | Yes | No | No |
| 40 | Right | Stenosis | 15 | c | c | Yes | No | No |
| 41 | Right | Stenosis | 9 | c | c | Yes | No | No |
| 42 | Left | Stenosis | 16 | a | c | Yes | Yes | No |
| 43 | Left | Stenosis | 4 | a | c | Yes | Yes | No |
| 44 | Right | Stenosis | 14 | a | c | Yes | No | No |
| 45 | Right | Stenosis | 14 | b | b | Yes | No | No |

*Tx*, Transplantation; *n/a*, not available.

**TABLE E2. Univariate analysis of donor characteristics and surgical procedures in a subgroup of 795 paired donors and recipients**

| | Univariate analysis | |
|---|---|---|
| | **Odds ratio (95% confidence interval)** | ***P* value** |
| Donor | | |
| Donor–recipient size-mismatch* | 0.89 (0.87-0.92) | .607† |
| Days mechanical ventilation >72 h | 0.92 (0.54-1.59) | .783 |
| Age >65 y | 1.03 (1.02-1.04) | 1.000† |
| Non-heartbeating donation | 2.26 (0.04-1.82) | .243 |
| Surgical procedure | | |
| Mean ischemic time ≥345 min | 0.84 (0.51-1.41) | .752† |
| Mechanical ventilation >48 h | 0.96 (0.50-1.84) | .000† |
| ECMO post-operative | 0.89 (0.75-1.06) | .705† |
| PGD 2 or PGD 3 at 72 h | 1.77 (0.29-11.62) | .000† |

*ECMO*, Extracorporeal membrane oxygenation; *PGD*, primary graft dysfunction. *Defined as donor/recipient-ratio of predicted total lung capacity <0.75 or >1.25. †Fisher exact test.

**TABLE E3. Patient characteristics and transplant procedures dependent on transplant era**

| **Demographics** | **1999-2003, n = 259** | **2004-2008, n = 386** | **2009-2013, n = 495** | **2014-2017, n = 415** | ***P* value** |
|---|---|---|---|---|---|
| Age, y median (range) | 49.5 (6-71) | 51.3.5 (1-69) | 49.6 (7-72) | 51.1 (3-74) | .747 |
| Pediatric LuTx (<18 y) | 15 (6%) | 23 (6%) | 28 (6%) | 19 (5%) | .825 |
| Sex | | | | | |
| Male | 146 (56%) | 203 (53%) | 252 (51%) | 218 (53%) | .564 |
| Female | 113 (44%) | 183 (47%) | 243 (49%) | 197 (47%) | |
| Indication | | | | | |
| COPD | 104 (40%) | 158 (41%) | 154 (31%) | 119 (29%) | |
| Fibrosis | 46 (18%) | 79 (21%) | 116 (23%) | 112 (27%) | **.001** |
| PAH | 29 (11%) | 18 (5%) | 33 (7%) | 37 (9%) | |
| CF | 37 (14%) | 78 (20%) | 108 (22%) | 100 (24%) | |
| Other | 43 (17%) | 53 (14%) | 84 (17%) | 47 (11%) | |
| ECMO bridge-to-transplant | 2 (1%) | 9 (3%) | 41 (8%) | 39 (9%) | **.001** |
| Type of LuTx | | | | | |
| Double-lung | 189 (73%) | 310 (80%) | 478 (97%) | 409 (99%) | |
| Standard | 154 (81%) | 256 (83%) | 389 (81%) | 375 (92%) | |
| Trilobar/bilobar | 35 (19%) | 54 (17%) | 89 (19%) | 34 (8%) | **.001** |
| Single-lung right | 43 (17%) | 33 (9%) | 9 (2%) | 3 (1%) | |
| Single-lung left | 27 (10%) | 43 (11%) | 8 (2%) | 3 (1%) | |
| Intraoperative ECLS | | | | | |
| None | 144 (56%) | 217 (56%) | 146 (30%) | 18 (4%) | |
| ECMO | 106 (41%) | 155 (40%) | 341 (69%) | 393 (95%) | **.001** |
| CPB | 9 (4%) | 14 (4%) | 8 (2%) | 4 (1%) | |
| EVLP | 0 (0%) | 0 (0%) | 28 (6%) | 41 (10%) | **.001** |
| Induction therapy | | | | | |
| None | 219 (85%) | 266 (69%) | 207 (42%) | 8 (2%) | |
| ATG | 40 (15%) | 108 (28%) | 66 (13%) | 5 (1%) | **.001** |
| Alemtuzumab | 0 (0%) | 12 (3%) | 222 (45%) | 402 (97%) | |
| 90-d mortality | 32 (12%) | 40 (10%) | 44 (9%) | 27 (7%) | .061 |

Values in bold are statistically significant. *LuTx*, Lung transplantation; *COPD*, chronic obstructive pulmonary disease; *PAH*, pulmonary arterial hypertension; *CF*, cystic fibrosis; *ECMO*, extracorporeal membrane oxygenation; *ECLS*, extracorporal lung support; *CPB*, cardiopulmonary bypass; *EVLP*, ex-vivo lung perfusion; *ATG*, anti-thymocyte globulin.