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ORIGINAL SCIENTIFIC REPORT

Does Induction Therapy Increase Anastomotic Complications in Bronchial Sleeve Resections?

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Abstract

Background Sleeve lobectomy represents a safe and effective treatment for central NSCLC to avoid the risks of pneumonectomy. Induction therapy (IT) may be indicated in advanced stages; however, the effect of IT on bronchial anastomoses remains uncertain. The purpose of the study was to evaluate the impact of IT on the complications of the anastomoses.

Methods Between 2000 and 2012, 159 consecutive patients were submitted to sleeve lobectomy for NSCLC at our Institution. We retrospectively compared the results of patients who underwent IT before operation with those who received upfront surgery.

Results In the study period, 49 (30.8%) patients received IT (37 chemotherapy, 1 radiotherapy and 11 chemo-radiotherapy) and 110 (69.2%) patients were directly submitted to surgery (S). The two groups were comparable for sex, age, comorbidities, ASA score, pulmonary function, side, type of procedure and histology. Pathological stage was statistically higher for IT group ($p = 0.001$). No differences between IT and S groups were observed in terms of post-operative mortality (2% vs 0%, p = NS), morbidity (45% vs 38%, p = NS), including early (6% vs 9%, p = NS) and long-term (16% vs 14%, p = NS) bronchial complication rates. Patients undergoing induction mediastinal radiotherapy, however, are at higher risk of bronchial complications.

Conclusion In our experience, the use of induction chemotherapy did not significantly increase mortality and morbidity rates, in particular, neither for early nor for late anastomotic complications. We, therefore, conclude that sleeve lobectomy after induction chemotherapy is safe and reliable procedure for the treatment of locally advanced NSCLC.

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Introduction

In recent years, bronchial sleeve procedures have been validated as a safe and proven alternative to pneumonectomy especially in non-small cell lung cancer (NSCLC) without nodal involvement [1–3]. Concurrently, surgery is part of the multimodal therapy for tumours with N2 disease that show response after neoadjuvant treatment (chemotherapy or chemo-radiotherapy) [4, 5].

Some concerns have been raised about a possible detrimental effect of induction therapies (IT) on bronchial anastomosis in cases of sleeve resection, in particular for patients treated with pre-operative radiotherapy [6]. Recent studies focusing on sleeve lobectomy did not show any significant difference regarding early outcomes of surgery among patients undergoing IT and those directly submitted to surgery, thus reducing the fear of bronchial complications and consequently expanding the indication for this type of reconstructive procedures [7–11].

The purpose of our study is to determine the influence of IT on bronchial anastomoses after sleeve lobectomy comparing this population to a group that did not received a pre-operative treatment.

Materials and methods

Patient selection

A retrospective study was performed reviewing the clinical and pathological data of 159 consecutive sleeve lobectomies performed at our institution between January 2000 and December 2012 for NSCLC. Among them, 49 patients were previously treated with induction treatment (IT group), while 110 subjects were directly submitted to surgery (S group).

Patients submitted to sleeve resection for diseases other than NSCLC were excluded from the study, together with patients submitted to main carinal resection.

All patients underwent careful medical screening and scoring of coexisting medical conditions and current medications. Pulmonary function was assessed using basal spirometry and arterial blood gas analysis. Patients with forced expiratory volume in one second and carbon monoxide lung diffusion <80% of the predicted capacity underwent exercise testing. Cardiac assessment was based on a physical examination and electrocardiography; patients older than 50 years and those with a history of coronary artery disease underwent transthoracic echocardiography.

Pre-operative staging included a chest X-ray, computed tomography (CT) scans of the chest and upper abdomen, and after 2004, positron emission tomography (PET–CT) scan was performed in all patients. Distant metastases detection techniques included brain CT and NMR. Every patient underwent bronchoscopy to carefully assess the extent of airway involvement and to aid in the planning of the surgical strategy.

Our surgical policy was to perform sleeve lobectomy in every technically feasible case, reserving pneumonectomy for tumours where a complete resection seemed not feasible through a parenchymal-sparing procedure. A systematic mediastinal lymph node dissection was carried out in all cases. All patients underwent surgery trough a thoracotomic approach.

The technique of sleeve lobectomy is well known and described in many articles [12]; in our centre, we usually perform the bronchial anastomosis with interrupted suture using 3-0 polyglactin (Vicryl, Ethicon, Inc., Somerville, NJ). In some cases of difficult sleeves (e.g. left lower sleeve lobectomy, right lower sleeve bilobectomy), we adopted a multiple running suture technique by using three continuous sutures of 4-0 polydioxanone (PDS, Ethicon, Inc., Somerville, NJ) [13].

Frozen section examinations of both bronchial margins were routinely performed.

In most patients, we covered the anastomosis with a viable tissue flap (pericardial, pleural or intercostal muscle) to separate the bronchial anastomosis from the vascular structures and to create a blood support to the suture line. Post-operatively, we routinely prescribed a low dose of systemic and inhaled steroid therapy in order to reduce the oedema of the bronchial mucosa [14].

The anastomosis was checked immediately after sleeve procedure with a bronchoscopy in the operative room and then on post-operative days 1 and 7. After that, it was checked again during follow-up at the end of the first, third and sixth post-operative months and then every year afterwards or when clinically indicated.

Bronchial complications included alterations at the level of the anastomosis and its proximity. Moreover, they were divided in two categories: early complication, as those presenting within 30 days after surgery, and late complication, those presenting after the first month.

Patients operated before 2009 were retrospectively restaged according to the seventh edition of the TNM staging classification [15].

Peri-operative mortality was defined as all deaths observed within 30 days from the operation or during the same hospitalisation. Follow-up data were obtained from the hospital database, from the patients, their families or the referring physicians, and no patient was lost in the long-term follow-up.

Our institutional review board approved the study.

Induction treatment

Most of the patients were evaluated, treated and followed up in our hospital by a multidisciplinary team.

Patients without suspicion of having positive mediastinal lymph nodes (CT scan short axis <1 cm or 18FDG-PET/CT uptake SUV_{max} <2.5 and negative pathological staging in case of centrally located tumour or tumours >3 cm) were treated with upfront surgery.

Induction therapy was planned for patients who were diagnosed with N2 disease after pathological confirmation of suspect mediastinal lymph nodes through mediastinoscopy or endobronchial ultrasound-guided biopsy.

Forty-eight patients underwent IT with three cycles of platinum-based chemotherapy, and in 11 cases, sequential radiotherapy of 44 Grays was delivered to the tumour and to the positive mediastinal target station(s) according to the European recommendations [16]. Additional radiotherapy was dictated by infiltration of mediastinal structures and pulmonary apex (Pancoast tumour). In one patient, radiotherapy was the only pre-operative treatment.

The clinical response after IT was assessed by CT scan and 18FDG-PET/CT, and surgery was performed in patients without tumour progression within 6 weeks after completion of IT.

Statistical analysis

The distribution for quantitative variables was assessed by means of Shapiro–Wilcox statistics. Grouped data was expressed as mean and standard deviation (SD), or as median and IQR when appropriate. The relationship between the binary short-time events and predictive factors was evaluated by means of Chi-square tests or Mann–Whitney *U* test for not normal distributed variables. For all statistical analyses, the significance level was set at 0.05. Statistical analysis was performed using SAS version 9.1 software (SAS Institute Inc, Cary, NC). The overall survival and the disease-free survival rates have been estimated through Kaplan–Meier approach. The differences across survival curves, between induction and surgical therapy, have been evaluated using a log-rank test estimation approach. Survival Analyses have been performed using R 3.3.3 with survival package.

Results

In the study period, 3175 patients underwent lung resection for NSCLC. Among them, 159 subjects were submitted to sleeve lobar resection. Forty-nine patients (30.8%) received pre-operative IT, while the other 110 subjects (69.2%) underwent upfront surgery. Table 1 reports patient characteristics in the two groups.

Among patients undergoing neoadjuvant treatment, there were 38 males and 11 females with a median age of 63 years (range 46–74 years).

Concerning surgical aspects (Table 2), 35 patients were operated on the right side and 14 on the left side. In 42 cases (86%), the bronchial anastomosis was wrapped with a pericardial flap. In 29 patients (59%) the extent of resection included resection and reconstruction of other structures (Table 2).

The surgery group showed comparable characteristics in terms of gender, ASA class and lung function, except for median age that was significantly higher in this group (68 vs 63 years, $p = 0.01$) (Table 1). Moreover, no differences were observed analysing the side and type of procedure, with a prevalence of right upper lobectomy, and need of resection of other structures (Table 2). Wrapping of bronchial anastomosis was performed in 81 patients (74%), in most cases with pericardial tissue (75 cases).

Pathological analysis showed a comparable distribution of histological subtypes between the two groups, with the squamous cell carcinoma being the most frequent histology. However, in the IT group the adenocarcinoma was more frequent (29% vs 14%, $p = 0.04$) and 5 cases presented a complete histological response on the surgical specimen. As expected, pathological stage in the IT group was significantly higher ($p = 0.001$) compared to the surgery group with 18% of patients presenting stages 3B or 4 disease.

In the surgery group, we reported one stage IV for adrenal gland metastasis without nodal disease, 8 cases of stage 3B mainly due to T4 because of the tumour local invasion and nodal involvement (4 N1, 3 N2 and 1 N3), and 48 patients with 3A stage, where 28 cases presented N1 disease and 20 presented N2 disease due to micrometastases.

Positive bronchial margin was higher in the surgery group without a statistically significant difference (8% vs 2% $p = 0.18$).

Median follow-up time was 32 months (IQR 18-81). In the post-operative period, 73 patients underwent adjuvant treatment, 26 in the IT group (8 chemotherapy, 12 radiotherapy and 6 chemo-radiotherapy) and 47 in the S group (18 chemotherapy, 12 radiotherapy and 17 chemo-radiotherapy). Microscopic positive bronchial margin was an indication to radiate the anastomosis in 10 cases: one in the IT group and 9 in the S group, without local progression in any of the cases. In the IT group, 12 (24.4%) patients had tumour relapse and 22 (20.0%) in the S group, with no statistical difference between the two populations ($p = 0.35$). Overall survival was not statistically different

Table 1 Demographic and tumour characteristics of study population

	Inductive therapy group (n = 49)	Surgery group (n = 110)	p
Sex			
Males (%)	38 (77.5)	87 (79)	0.84
Females (%)	11 (22.5)	23 (21)	
Median age (range)	63 (46–74)	68 (36–84)	0.01
ASA score (%)			
1	5 (10.2%)	13 (11.8%)	0.87
2	28 (57.1%)	60 (54.5%)	
3	15 (30.7%)	32 (29.1%)	
4	1 (2%)	5 (4.6%)	
Lung function			
FEV1 (% of predicted)	2.45 ± 0.59 (84)	18.2 ± 8.11 (68)	0.53
DLCO (% of predicted)	2.21 ± 0.55 (83)	18.4 ± 5.71 (77)	0.97
Histology (%)			
Squamous cell	24 (49%)	81 (73.7%)	0.12
Adenocarcinoma	14 (28.6%)	15 (13.7%)	
Adenosquamous	1 (2%)	3 (2.7%)	
Large cell carcinoma	2 (4,1%)	5 (4.5%)	
Other	3 (6,1%)	6 (5.4%)	
Tumour regression	5 (10.2%)	–	
Pathological stage (%)	2 (4.1%)	1 (0.9%)	0.001
Ia	3 (6.1%)	6 (5.3%)	
Ib	0	8 (7.7%)	
IIa	9 (18.6%)	38 (34.4%)	
IIb	21 (42.7%)	48 (43.5%)	
IIIa	7 (14.2%)	8 (7.3%)	
IIIb	2 (4.1%)	1 (0.9%)	
IV	5 (10.2%)	–	
Tumour regression			
Adjuvant treatment (%)	26 (53%)	47 (42.8%)	0.23
Chemotherapy	8 (16.3%)	18 (16.4%)	
Radiotherapy	12 (24.5%)	12 (10.9%)	
Chemo-radiotherapy	6 (12.2%)	17 (15.5%)	

among the two groups (p = 0.89) and neither was the disease-free survival rate (p = 0.25) (Figs. 1, 2).

Analysis of early post-operative results showed comparable mortality in the two groups (2% vs 0% in IT and S group, respectively, p = 0.31); mortality in the IT group was caused by a case of sepsis due to an early bronchopleural fistula (Table 3). In addition, the morbidity rate showed no significant difference between the two groups (34.7% vs 27.3%, p = 0.35), with atrial fibrillation being the most frequent event in both groups (16.3% and 9.1% in IT and S group, respectively).

No differences were found in terms of early and delayed anastomotic problems between groups even though in the IT group the early complications seemed to be perceptually less than those in the surgery group (6% vs 9% respectively, p = 0.76). However, focusing only on the IT group, there was a statistically significant difference in terms of anastomotic complication between patients undergoing induction chemotherapy and patient undergoing pre-operative chemo-radiotherapy or radiotherapy alone (10.8% vs 41.6%, respectively, p = 0.01).

Focusing on early anastomotic problems, the IT group showed one fatal bronchopleural fistula and 2 cases of anastomotic stenosis. One of the stenosis was successfully treated with bronchoscopic dilatation, while the other underwent a completion pneumonectomy after an unsuccessful attempt of endoscopic dilatation.

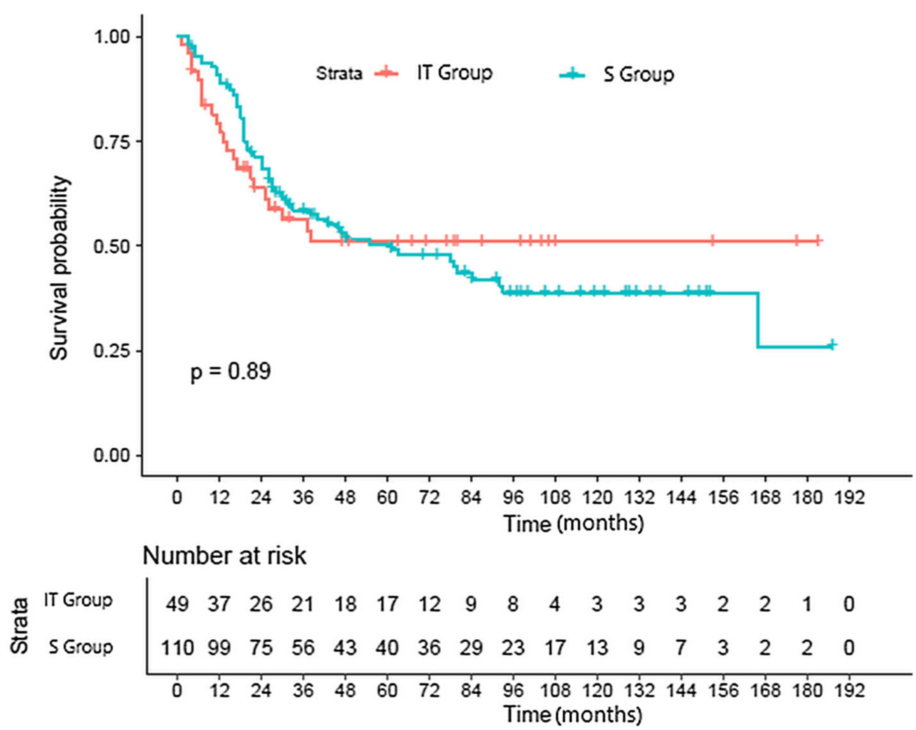
In the surgery group, we recorded three cases of bronchopleural fistula and seven cases of early anastomotic stenosis. Regarding the anastomotic dehiscences, one case

Table 2 Type of surgical procedure

	Induction therapy group (n = 49)	Surgery group (n = 110)	p
Lobectomy (%)			
Upper	42 (85.7%)	97 (88.2%)	0.37
Middle	2 (4.1%)	1 (0.9%)	
Lower	2 (4.1%)[a]	6 (5,5%)	
Bilobectomy (%)			
Upper	0	4 (3,6%)	0.17
Lower	3 (6.1%)	2 (1.8%)	
Additional procedures	29 (59.2%)	51 (46.4%)	0.17
Pulmonary artery reconstruction	23	41	
Circumferential sleeve	13	19	
Angioplasty	10	22	
Pulmonary vein reconstruction	2	5	
Superior vena cava reconstruction	3	4	
Pulmonary resection	5	6	
Chest wall resection	3	2	
Wrapping of bronchial anastomosis	42 (85.7%)	81 (73.6%)	0.10
Pericardial flap	42	75	
Other	0	6	
$R0$ resection (%)	48 (98%)	101 (91.8%)	0.18
$R1$ resection (%)	1 (2%)	9 (8.2%)	

[a]1 with segmental resection of upper lobe

Fig. 1 Overall survival in the two groups; *IT* induction therapy, *S* surgery



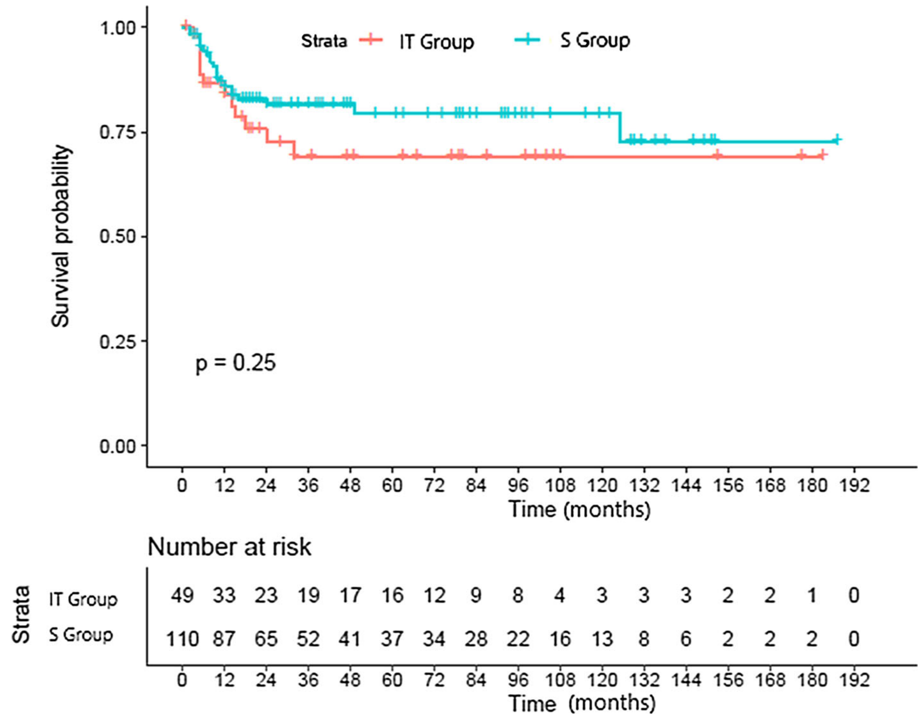


Fig. 2 Disease-free survival in the two groups; *IT* induction therapy, *S* surgery

Table 3 Post-operative mortality and morbidity

	Induction therapy group (*n* = 49)	Surgery group (*n* = 110)	*p*
Mortality (%)	1 (2%)	0 (0%)	0.31
Morbidity (% of patients)	17 (34.7%)	30 (27.3%)	0.35
Atrial fibrillation	6	11	
Anastomosis complications	3	10	
Haemotorax	1	0	
Respiratory failure	1	1	
Prolonged air leak	3	4	
Other	3	4	
Early anastomotic complications (%)	3 (6%)	10 (9%)	0.76
Bronchopleural fistula	1 (2%)	3 (2,7%)	
Stenosis	2 (4%)	7 (6,3%)	
Long-term bronchial complications (%)	6 (12%)	10 (9%)	0.57
Bronchopleural fistula	1 (2%)	0 (0%)	
Stenosis	5 (10%)	10 (9%)	

resolved spontaneously without surgery or endoscopic procedures and two cases received an endoscopic treatment with topical application of silver nitrate. Treatment led to a favourable evolution in one case and a delayed inflammatory reaction with stenosis in the other case, requiring the placement of an endobronchial prosthesis. Concerning the cases of bronchial stenosis, four patients showed a favourable spontaneous evolution with stabilization of the stenosis with a sufficient calibre, while three cases needed an endoscopic treatment with mechanical dilation and stent placement.

Late anastomotic complications occurred in six patients (12%) in IT group and in 10 patients (10%) in S group without any statistically significant difference ($p = 0.57$).

Particularly, in the first population, there were one bronchopleural fistula, requiring a completion pneumonectomy, and five cases of bronchial stenosis, successfully treated by means of endoscopic dilatation (two with associated stent insertion). In surgery group, no patients developed anastomotic dehiscence, 10 subjects presented severe stenosis that was favourably treated with bronchial stent in 9 cases and with dilatation in one.

Discussion

Multimodal therapy has been validated as the treatment of choice in patients with stage IIIA–IIIB lung cancer, due to its cytoreductive effect and to the reduction in the risk of recurrence [4, 5]. Despite these positive effects, there are issues related to the detrimental effect of IT on tissue healing, especially at the level of bronchial sutures. These aspects are particularly important when dealing with sleeve resection, which is now widely accepted as alternative to pneumonectomy even for advanced stages [2].

The end-to-end bronchial anastomosis is associated with a moderate peri-operative ischaemia, due to the interruption of the bronchial circulation, and the neoadjuvant therapies could worsen this situation by causing an abnormal healing processes that may favour anastomotic complications as fistulae, dehiscence and stenosis. Different authors suggest in these cases to cover the bronchial suture with a pedicle of viable tissue for prophylaxis against bronchial complications [17].

Several authors focused their attention on post-operative complications in sleeve resections after inductive therapy achieving satisfactory short-term results [7–11, 18]. In most cases, mortality ranged from 2 to 4%, comparable with the mortality rates of patients undergoing surgical procedures without pre-operative therapy. Similar findings were observed also for peri-operative morbidity, with particular attention to anastomotic complications. However, one of the major limitations of these studies is the small number of patients analysed that rarely reached 40 subjects for the group of chemo-radiotreated patients.

In our paper, we present a larger series of patients restricting the analysis to the last 12 years of our activity. The decision to start the study from this date was mainly based on the availability of PET-CT at our centre that led to a greater uniformity in the pre-operative treatment.

The two groups were comparable for most of the clinical, surgical and pathological characteristics, especially considering pulmonary function, comorbidities and type of resection, including vascular procedures that may affect the post-operative period.

Concerning short-term results, there were no significant differences in terms of 30-day mortality and morbidity for patients with and without IT, with the IT group presenting even a decreased rate of bronchial complications, although not statistically significant.

In this study, we did not find cases of bronchial-vascular fistulae related to pre-operative radiation therapy, as we faced at the beginning of our experience [6]. These findings may be due to the refinement of radiotherapy technique, in addition to an improvement of the surgical technique. However, we noticed a higher risk of anastomotic complications in patients undergoing radiotherapy as part of the induction treatment, as previously described by our group [6]. All cases were treated successfully without related mortality, but in two cases, a completion pneumonectomy was necessary. Based on our experience, we prefer to avoid mediastinal induction radiotherapy in patients potentially eligible for sleeve procedures.

We routinely cover the anastomosis even if the use of viable flap has not been highlighted as a clear protective factor for bronchial complications [19]. A meticulous surgical technique to avoid tension at the level of the anastomosis or bronchial de-vascularisation during dissection is mandatory to reduce the occurrence of other anastomotic alterations. The rates of occurrence of fistulas and stenosis in our experience are comparable to other main series (1–5% for fistulas, 1–4% for stenosis) [8–11].

In our experience, bronchoscopic surveillance has a fundamental importance for early diagnosis and management of these complications in order to prevent progression towards life-threatening situations. In addition, we believe that regular endoscopic follow-up should be extended for at least 1 year after the surgical procedure because of the risk of late events.

In fact, many studies often limited the analysis only to the peri-operative period, without reporting the bronchial complications in the long-term, which conversely are well described after sleeve procedures [20, 21]. Our rate of late anastomotic complication is slightly higher compared to other experiences [20, 21], even though some of these patients presented moderate asymptomatic stenosis and most of the cases resolved with endoscopic procedures.

In our opinion, the bronchoscopic treatment is effective most of the times, particularly for patients with stenosis, with the advantage that it may be repeated in relapsing cases. Regarding the use of endobronchial stent, in our experience, both silicon and covered self-expanding nitinol prosthesis were successfully employed. The self-expanding nitinol stent could have an important advantage in cases where pre-positioning dilatation appears difficult and not adequate [22].

Based on our findings, we strongly conclude that for locally advanced NCSLC treated with induction chemotherapy, sleeve lobectomy is a safe and valid procedure with post-operative results comparable to nonpretreated patients, whereas patient undergoing induction mediastinal radiotherapy are at higher risk of bronchial complications. These results are emphasised when the procedures are performed in a high-experience centre where anastomotic complications are infrequent, but when faced, the majority can be treated effectively with endoscopic procedures, reserving surgery for non-responsive and life-threatening cases.

Compliance with ethical standards

Conflict of interest The authors declare that there is no conflict of interest.

References

1. Ma Z, Dong A, Fan J et al (2007) Does sleeve lobectomy concomitant with or without pulmonary artery reconstruction (double sleeve) have favorable results for non-small cell lung cancer compared with pneumonectomy? A meta-analysis. Eur J Cardiothorac Surg 32:20–28
2. Ferguson MK, Lehman AG (2003) Sleeve lobectomy or pneumonectomy: optimal management strategy using decision analysis techniques. Ann Thorac Surg 76:1782–1788
3. Okada M, Yamagishi H, Satake S et al (2000) Survival related to lymph node involvement in lung cancer after sleeve lobectomy compared with pneumonectomy. J Thorac Cardiovasc Surg 119:814–819
4. Martins RG, D'Amico TA, Loo BW Jr et al (2012) The management of patients with stage IIIA non-small cell lung cancer with N2 mediastinal node involvement. J Natl Compr Cancer Netw 10:599–613
5. Ripley RT, Rusch VW (2013) Role of induction therapy: surgical resection of non-small cell lung cancer after induction therapy. Thorac Surg Clin 23:273–285
6. Rea F, Marulli G, Schiavon M et al (2008) A quarter of a century experience with sleeve lobectomy for non-small cell lung cancer. Eur J Cardiothorac Surg 34:488–492
7. Gonzalez M, Litzistorf Y, Krueger T et al (2013) Impact of induction therapy on airway complications after sleeve lobectomy for lung cancer. Ann Thorac Surg 96:247–252
8. Milman S, Kim AW, Warren WH et al (2009) The incidence of perioperative anastomotic complications after sleeve lobectomy is not increased after neoadjuvant chemoradiotherapy. Ann Thorac Surg 88:945–950
9. Gómez-Caro A, Boada M, Reguart N et al (2012) Sleeve lobectomy after induction chemoradiotherapy. Eur J Cardiothorac Surg 41:1052–1058
10. Bagan P, Berna P, Brian E et al (2009) Induction chemotherapy before sleeve lobectomy for lung cancer: immediate and long-term results. Ann Thorac Surg 88:1732–1735
11. Burfeind WR Jr, D'Amico TA, Toloza EM et al (2005) Low morbidity and mortality for bronchoplastic procedures with and without induction therapy. Ann Thorac Surg 80:418–421
12. Fadel E, Yildizeli B, Chapelier AR et al (2002) Sleeve lobectomy for bronchogenic cancers: factors affecting survival. Ann Thorac Surg 74:851–858
13. Hamad AM, Marulli G, Rizzardi G et al (2009) Multiple-running suture technique for bronchial anastomosis in difficult sleeve resection. Ann Thorac Surg 87:975–976
14. Rendina EA, Venuta F, Ricci C (1992) Effects of low-dose steroids on bronchial healing after sleeve resection. A clinical study. J Thorac Cardiovasc Surg 104:888–891
15. Vallières E, Shepherd FA, Crowley J (2009) The IASLC lung cancer staging project: proposals regarding the relevance of TNM in the pathologic staging of small cell lung cancer in the forthcoming (seventh) edition of the TNM classification for lung cancer. J Thorac Oncol 4:1049–1059
16. Senan S, De Ruysscher D, Giraud P et al (2004) Literature-based recommendations for treatment planning and execution in high-dose radiotherapy for lung cancer. Radiother Oncol 71:139–146
17. Yamamoto R, Tada H, Kishi A et al (2000) Effects of preoperative chemotherapy and radiation therapy on human bronchial blood flow. J Thorac Cardiovasc Surg 119:939–945
18. Rendina EA, Venuta F, De Giacomo T et al (1997) Safety and efficacy of bronchovascular reconstruction after induction chemotherapy for lung cancer. J Thorac Cardiovasc Surg 114:830–835
19. Storelli E, Tutic M, Kestenholz P et al (2012) Sleeve resections with unprotected bronchial anastomoses are safe even after neoadjuvant therapy. Eur J Cardiothorac Surg 42:77–81
20. Tedder M, Anstadt MP, Tedder SD et al (1992) Current morbidity, mortality, and survival after bronchoplastic procedures for malignancy. Ann Thorac Surg 54:387–391
21. Veronesi G, Solli PG, Leo F et al (2002) Low morbidity of bronchoplastic procedures after chemotherapy for lung cancer. Lung Cancer 36:91–97
22. Saji H, Furukawa K, Tsutsui H et al (2010) Outcomes of airway stenting for advanced lung cancer with central airway obstruction. Interact Cardiovasc Thorac Surg 11:425–428