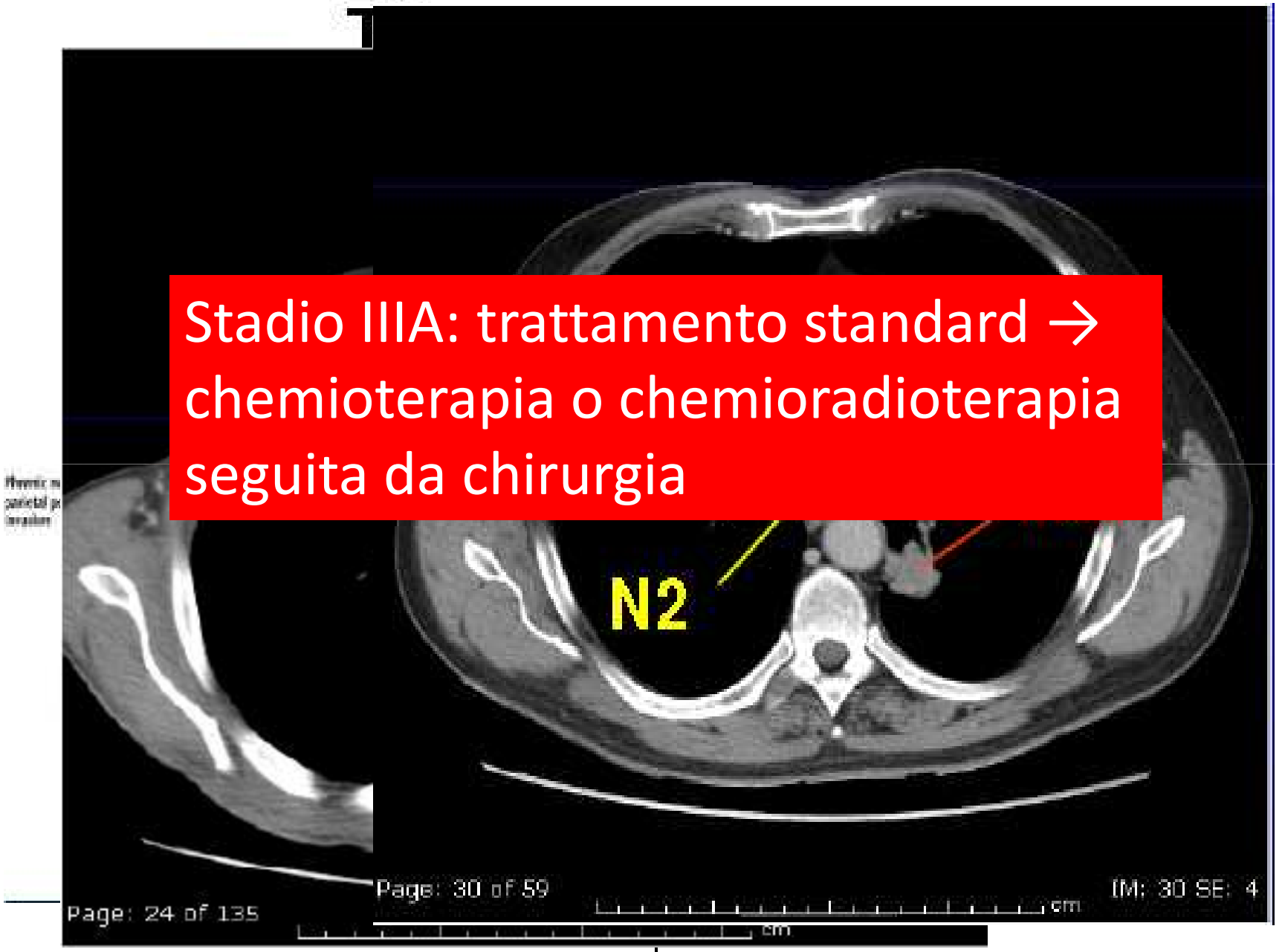
Morbidità e mortalità perioperatoria in pz sottoposti a RT preoperatoria per NSCLC


Stadio IIIA: trattamento standard → chemioterapia o chemioradioterapia seguita da chirurgia
N2
Page: 24 of 135
Page: 30 of 59
IM: 30 SE: 4
cm
cm

Carcinoma polmonare "Non a Piccole cellule" :
Le diverse opzioni chirurgiche

RESEZIONI MAGGIORI STANDARD →	PNEUMONECTOMIA BILOBECTOMIA LOBECTOMIA
RESEZIONI SUBLOBARI →	SEGMENTARIE WEDGE
RESEZIONI TRACHEOBRONCOPLASTICHE →	SLEEVE RESECTION CARINAL RESECTION

Thorax 2001; 56: 89-108 " BTS Guidelines on the selection of patients with lung cancer for surgery "

VALUTAZIONE FUNZIONALE PREOPERATORIA

EGA : $PaCO_2 < 45$ mm Hg.
$SaO_2 > 90\%$

SPIROMETRIA

(FEV1)

PNEUMONECTOMIA

>2 L. (>80%)

LOBECTOMIA

> 1.5 L.

DLCO (interstiziopatie) > 80%

SCINTIGRAFIA VASCOLARE POLMONARE

Calcolo di FEV1 + TLCO postoperatorio (> 40%)

Tests dinamici Cardiopolmonari

(es. VO_2 max > 15 mL / Kg. / min.)

Colice G.L. et al. Chest 2007 132: 161s – 177s

Variabili correlate alla radioterapia

- Dose: 45-50Gy
- Frazionamento: convenzionale vs non
- Volumi: “involved field”
- Tecnica: 2D vs 3D vs tecniche speciali (IMRT, V-MAT, Tomo ecc)
- Associazione chemioterapia

Variabili correlate al paziente

- Comorbidità:
  - Polmonari
  - Cardiache
  - Metaboliche
  - Vascolari
- età; KPS
- Stadio di malattia

Morbidità maggiori

Major morbidity was defined as:
-pneumonia,
-adult respiratory distress syndrome,
-sepsis
-empyema
-bronchopleural fistula
-pulmonary embolism
-ventilatory support beyond 48 hours
-reintubation
-tracheostomy
-atrial or ventricular arrhythmias requiring treatment
-myocardial infarct
-reoperation for bleeding
-central neurologic event

Eur J Cardiothorac Surg. 2002 Aug;22(2):292-7.

Postoperative morbidity and mortality after induction chemoradiotherapy for locally advanced lung cancer: an analysis of 350 operated patients.

Stamatis G, Djuric D, Eberhardt W, Pöttken C, Zaboura G, Fechner S, Fujimoto T.

METHODS: We reviewed the charts of 350 patients who underwent thoracotomy in the course of two phase II and one phase III studies with preoperative chemotherapy followed in all 350 patients by concurrent Chemoradiotherapy

RESULTS: Of 350 consecutive patients 278 (79%) had a non-small cell lung cancer (154 stage IIIA and 124 IIIB) and 72 (21%) a small cell lung cancer (12 stage IIA/B, 35 stage IIIA and 25 stage IIIB). Resections included 125 pneumonectomies (35%), 15 bilobectomies (4.3%), 37 sleeve lobectomies (11%), 157 lobectomies (45%), and two segmentectomies (0.6%); 14 patients (4%) had an exploration only. Additionally to pulmonary resection 32 patients underwent a partial chest wall resection. One hundred and fifty-four patients (44%) developed early or late complications; the hospital mortality rate was 4.9% (17 patients). The causes of death were sepsis (n=5), pneumonia and respiratory failure (n=4), adult respiratory distress syndrome (n=3), cardiac failure (n=3) and lung embolism (n=2). Multivariate analysis extracted increased age, lower Karnofsky status, abnormal echocardiographic findings and no bronchial stump covering technique to be risk factors for perioperative morbidity. Lower Karnofsky status and increased age were significant risk factors for postoperative mortality.
CONCLUSION: This retrospective analysis demonstrates that in patients with locally advanced lung cancer and induction chemoradiotherapy, surgery can be feasible with acceptable mortality but increased morbidity. Accurate cardiopulmonary evaluation before surgery and standard operative techniques with protection of bronchial stump or anastomosis can contribute to a reduced complication rate with this intensive approach.

Ann Thorac Surg. 2010

STS database risk models: predictors of mortality and major morbidity for lung cancer resection.

Kozower BD, Sheng S, O'Brien SM, Liptay MJ, Lau CL, Jones DR, Shahian DM, Wright CD.

BACKGROUND: The aim of this study is to create models for perioperative risk of lung cancer resection using the STS GTDB (Society of Thoracic Surgeons General Thoracic Database).

METHODS: The STS GTDB was queried for all patients treated with resection for primary lung cancer between January 1, 2002 and June 30, 2008. Three separate multivariable risk models were constructed (mortality, major morbidity, and composite mortality or major morbidity).

RESULTS: There were 18,800 lung cancer resections performed at 111 participating centers. Perioperative mortality was 413 of 18,800 (2.2%). Composite major morbidity or mortality occurred in 1,612 patients (8.6%). Predictors of mortality include the following: pneumonectomy ($p < 0.001$), bilobectomy ($p < 0.001$), American Society of Anesthesiology rating ($p < 0.018$), Zubrod performance status ($p < 0.001$), renal dysfunction ($p = 0.001$), induction chemoradiation therapy ($p = 0.01$), steroids ($p = 0.002$), age ($p < 0.001$), urgent procedures ($p = 0.015$), male gender ($p = 0.013$), forced expiratory volume in one second ($p < 0.001$), and body mass index ($p = 0.015$).

CONCLUSIONS: Thoracic surgeons participating in the STS GTDB perform lung cancer resections with a low mortality and morbidity. The risk-adjustment models created have excellent performance characteristics and identify important predictors of mortality and major morbidity for lung cancer resections. These models may be used to inform clinical decisions and to compare risk-adjusted outcomes for quality improvement purposes.

J Thorac Cardiovasc Surg. 2012

An analysis, systematic review, and meta-analysis of the perioperative mortality after neoadjuvant therapy and pneumonectomy for non-small cell lung cancer.

Kim AW, Boffa DJ, Wang Z, Detterbeck FC.

METHODS: A systematic PubMed search was performed for original articles from 1990 through 2010 describing pneumonectomy after neoadjuvant therapy. Specific data on 30-day and 90-day perioperative mortalities were abstracted from these articles.

RESULTS: The search strategy yielded 27 studies. Overall, 30-day and 90-day perioperative mortalities were 7% and 12%, respectively. Among 15 studies providing side-specific 30-day mortality, cumulative mortalities were 11% and 5% for right and left pneumonectomies, respectively. In the meta-analysis that included 10 studies, 30-day mortality for right pneumonectomy remained greater than for left pneumonectomy (odds ratio, 1.97; 95% confidence interval, 1.11-3.49; P = .02). Among 6 studies providing side-specific 90-day mortality, cumulative mortalities were 20% and 9% for right and left pneumonectomies, respectively. In the meta-analysis that included 4 studies, 90-day mortality for right pneumonectomy was greater than for left pneumonectomy (odds ratio, 2.01; 95% confidence interval, 1.09-3.72; P = .03). Among 11 studies providing both 30-day and 90-day mortalities, mortality difference was 5% (95% confidence interval, 4%-7%, P < .0001). Pulmonary complications were the most common cause of 30-day and 90-day deaths.

CONCLUSIONS: Right pneumonectomy is associated with significantly higher 30-day and 90-day mortalities after neoadjuvant therapy than left pneumonectomy. Also, 90-day mortality for all pneumonectomies appears to be greater than expected, suggesting that the 30-day mortality figure may inadequately assess the perioperative mortality.

J Thorac Cardiovasc Surg. 2010

Pneumonectomy is a valuable treatment option after neoadjuvant therapy for stage III non-small-cell lung cancer.

Weder W, Collaud S, Eberhardt WE, Hillinger S, Welter S, Stahel R, Stamatis G.

OBJECTIVE: The mortality of pneumonectomy after chemotherapy or chemoradiotherapy for locally advanced non-small-cell lung cancer is reported to be as high as 26%. We retrospectively reviewed the medical records of patients undergoing these procedures in 2 specialized thoracic centers to determine the outcome.

METHODS: Retrospective analyses were performed of all patients who underwent pneumonectomy after neoadjuvant chemotherapy or chemoradiotherapy for locally advanced non-small-cell lung cancer from 1998 to 2007. Presurgical treatment consisted of 3-4 platin-based doublets alone in 20% of patients or combined with radiotherapy (45Gy) to the tumor and mediastinum in 80% of patients.

RESULTS: Of 827 patients who underwent neoadjuvant therapy, 176 pneumonectomies were performed, including 138 (78%) extended resections. Post-induction pathologic stages were 0 in 36 patients (21%), I in 33 patients (19%), II in 38 patients (21%), III in 57 patients (32%), and IV in 12 patients (7%). Three patients died of pulmonary embolism, 2 patients of respiratory failure, and 1 patient of cardiac failure, resulting in a 90 postoperative day mortality rate of 3%; 23 major complications occurred in 22 patients (13%). For the overall population, 3-year survival was 43% and 5-year survival was 38%.

CONCLUSION: Pneumonectomy after neoadjuvant therapy for non-small-cell lung cancer can be performed with a perioperative mortality rate of 3%. Thus, the need of a pneumonectomy for complete resection alone should not be a reason to exclude patients from a potentially curative procedure if done in an experienced center.

Eur J Cardiothorac Surg. 2012

Pneumonectomy: calculable or non-tolerable risk factor in trimodal therapy for Stage III non-small-cell lung cancer?

Steger V, Spengler W, Hetzel J, Veit S, Walker T, Mustafi M, Friedel G, Walles T.

OBJECTIVES: Especially in the case of pneumonectomy as the completing procedure, mortality rate can exceed over 40%. Therefore, chest physicians often shy away from recommending pneumonectomy as final step in trimodal protocols. We analysed our experience with pneumonectomy after neoadjuvant chemoradiotherapy in advanced non-small-cell lung cancer (NSCLC) with a focus on feasibility, outcome and survival.

METHODS: Retrospective, single-centre study of 146 patients with trimodal neoadjuvant therapy for NSCLC Stage III over 17 years time span. Follow-up was taken from our own outpatient files and with survival check of central registry office in Baden-Württemberg, Germany.

RESULTS: A total of 118 men and 28 women received 62 lobectomies, 6 bi-lobectomies and 78 pneumonectomies after two different neoadjuvant protocols for Stage III NSCLC. Overall morbidity rate was 53 and 56% after pneumonectomy. Overall hospital mortality rate was 4.8 and 6.4% after pneumonectomy. Overall median survival rate was 31 months with a 5-year survival rate of 38% (Kaplan-Meier). Pneumonectomy, right-sited pneumonectomy and initial T- and N-stages were no risk factors for survival (log-rank test). Significant factors for survival were ypT-stage, ypN-stage, yUICC-stage in univariate testing (log-rank test) and ypUICC-stage in multivariate testing (Cox's regression).
CONCLUSIONS: Pneumonectomy in neoadjuvant trimodal approach for Stage III NSCLC can be done safe with acceptable mortality rate. Patients should not withhold from operation because of necessitating pneumonectomy. Not the procedure but the selection, response rate and R0-resection are crucial for survival after trimodal therapy in experienced centres.

Ann Surg Oncol. 2010 Feb;17(2):476-82.

Pneumonectomy after neoadjuvant chemotherapy and radiation for advanced-stage lung cancer.

Ng T, Birnbaum AE, Fontaine JP, Berz D, Safran HP, Dipetrillo TA.

BACKGROUND: Intergroup 0139 Trial suggests an increase in mortality after pneumonectomy in patients receiving preoperative chemotherapy and radiation. We evaluate our outcomes with pneumonectomy after neoadjuvant chemotherapy and radiation.

METHODS: From a prospective database, results after pneumonectomy were compared between patients receiving and not receiving neoadjuvant chemotherapy and radiation during the same time period.

RESULTS: Over 7 years, 50 pneumonectomies were performed for non-small-cell carcinoma; 18 received neoadjuvant chemotherapy and radiation (group A) and 32 did not (group B). Comparing group A with group B, there was no significant difference in patient demographics, blood loss, transfusion requirements or pneumonectomy side. Group A had more patients with stage III disease [17/ 18 (94%) versus 15/32 (47%), P = 0.001] and also more often had vascularized flap for bronchial stump coverage [17/18 (94%) versus 4/32 (13%), P < 0.001]. There was no significant difference in operative morbidity or mortality. Mortality for group A was 0/18 and for group B was 2/32 (6.3%) (P = 0.530). Group A patients with IIIA(N2) disease (n = 13) had median recurrence-free survival of 12.4 months, median overall survival of 25 months, and 3- year overall survival of 22.2%.

CONCLUSIONS: Using a multidisciplinary team approach at a tertiary care center, pneumonectomy can be performed successfully after neoadjuvant chemotherapy and radiation for advanced-stage lung cancer. Vascularized flap for bronchial stump coverage may be important in this regard.

Ann Thorac Surg. 2010

Predictors of major morbidity and mortality after pneumonectomy utilizing the Society for Thoracic Surgeons General Thoracic Surgery Database.

Shapiro M, Swanson SJ, Wright CD, Chin C, Sheng S, Wisnivesky J, Weiser TS.

METHODS: All patients who had undergone pneumonectomy between January 2002 and December 2007 were identified in the STS GTDB. Among 80 participating centers, 1,267 patients were selected. Logistic regression analysis was performed on preoperative variables for major adverse outcomes.

RESULTS: The rate of major adverse perioperative events was 30.4%, including 71 patients who died (5.6%). Major morbidity was defined as pneumonia, adult respiratory distress syndrome, empyema, sepsis, bronchopleural fistula, pulmonary embolism, ventilatory support beyond 48 hours, reintubation, tracheostomy, atrial or ventricular arrhythmias requiring treatment, myocardial infarct, reoperation for bleeding, and central neurologic event. Patients with major morbidity had a longer mean length of stay compared with patients without major morbidity (13.3 versus 6.1 days, $p < 0.001$). Independent predictors of major adverse outcomes were age 65 years or older ($p < 0.001$), male sex ($p = 0.026$), congestive heart failure ($p = 0.04$), forced expiratory volume in 1 second less than 60% of predicted ($p = 0.01$), benign lung disease ($p = 0.006$), and requiring extrapleural pneumonectomy ($p = 0.018$). Among patients with lung carcinoma, those receiving neoadjuvant chemoradiotherapy were more at risk for major morbidity than patients without induction therapy ($p = 0.049$).

CONCLUSIONS: The mortality rate after pneumonectomy by thoracic surgeons participating in the STS database compares favorably to that in previously published studies. We identified risk factors for major adverse outcomes in patients undergoing pneumonectomy.

J Thorac Cardiovasc Surg. 2009
POINT: Operative risk of pneumonectomy--influence of preoperative induction therapy.
Gaissert HA, Keum DY, Wright CD, Ancukiewicz M, Monroe E, Donahue DM, Wain JC, Lanuti M, Allan JS, Choi NC, Mathisen DJ.
BACKGROUND: Prior data indicate increased perioperative morbidity and mortality in patients receiving induction chemoradiotherapy before pneumonectomy for lung cancer.

RESULTS: Over a 15-year period, 183 patients underwent pneumonectomy for lung cancer. Forty-six received combined preoperative radiochemotherapy (25.2%), and 137 patients underwent resection only. Indications for induction therapy were stage IIB disease in 1, IIIA in 35, IIIB in 8, and IV in 2 patients. Patients receiving induction therapy were younger (mean age 58.4 vs 61.9 years; P = .033),had less heart disease (6.5 vs 26.3%; P = .0035), higher preoperative forced expiratory volume in 1 second (2.48 vs 2.13 L; P = .0018), a lower rate of endobronchial tumor (34.8 vs 67.2%; P = .0002), and underwent intrapericardial procedures more often (71.7 vs 43.1%; P = .0011). Hospital mortality was 4.3 % (2/46) after preoperative therapy and 6.6% (9/137) after resection only (P =.73); the difference in cardiopulmonary morbidity was not significant (51.1% vs 40.4%; P = .22). Induction did not predict hospital mortality after adjustment for a propensity score derived from non operative and operative variables correlated with neoadjuvant therapy.

CONCLUSIONS: A regimen of induction radiation and chemotherapy does not increase the operative mortality of pneumonectomy in carefully selected patients.

Ann Thorac Surg. 2009

The incidence of perioperative anastomotic complications after sleeve lobectomy is not increased after neoadjuvant chemoradiotherapy.

Milman S, Kim AW, Warren WH, Liptay MJ, Miller C, Basu S, Faber LP.

METHODS: Clinical records of patients with non-small cell lung cancer undergoing sleeve lobectomy between 1983 and 2008 were reviewed for age, sex, type of sleeve resection, clinicopathologic TNM stage, complications, and 90-day mortality. Chemotherapy and radiation therapy regimens were recorded for the patients undergoing neoadjuvant treatment. Kaplan-Meier survival curves were compared.

RESULTS: There were 64 patients identified as having undergone sleeve resection for non-small cell lung cancer. Of the 64 total patients, 43 did not receive concurrent neoadjuvant chemoradiotherapy [NCR] versus 21 patients who did [CRS]. All of the CRS patients underwent platinum-based chemotherapy and radiation (range, 2,000 to 6,100 cGy). Thirteen patients (62%) were downstaged, with 4 complete responders. The 90-day mortality was 2.7% (2 patients) in the NCR group and 0% in the CRS group. The incidence of major complications in the NCR group was 46.5% (20 of 43) with 4.7% (2 of 43) anastomosis-related complications (stenosis, 1; bronchovascular fistula, 1). The incidence of major complications in the CRS group was 42.9% (9 of 21) with no anastomosis-related problems. Five-year survival in the NCR group was 48% compared with 41% in the CRS group (p= 0.63). There were 9% (4 of 43) of patients with local recurrence in the NCR group versus 10% (2 of 21) of patients in the CRS group (p = 0.65).

CONCLUSIONS: Anastomosis-related complications were not increased among the patients receiving neoadjuvant therapy compared with those who did not. Sleeve lobectomy after chemoradiotherapy for advanced non-small cell lung cancer can be performed with acceptable morbidity and mortality.

Eur J Cardiothorac Surg. 2012
Sleeve lobectomy after induction chemoradiotherapy.
Gómez-Caro A, Boada M, Reguart N, Viñolas N, Casas F, Molins L.
General Thoracic Surgery Department, Hospital Clinic, University of Barcelona, Barcelona, Spain.
RESULTS: Of 79 patients, who underwent SL during this period, 53 (67%) patients were directly assigned to surgery and 26 (33%) patients had pre-induction treatment for N2 pathologically confirmed. Induction treatment (CRT) was based on platinum-based chemotherapy and radiation (range 45-60 Gy). Twenty-one (80%) patients of the CRT group achieved a complete mediastinal pathological response.
Mortality occurred in only three cases in the non-CRT [bronchovascular fistula, pulmonary artery thrombosis (reoperation and pneumonectomy and exitus due to pneumonia) and ADRS]. There were no differences with respect to complication rate between the non-CRT and CRT patients (33 versus 37%, P > 0.05), and overall 5-year survival was 69 and 33%, respectively (P = 0.017). Overall survival in the subgroup of CRT patients with mediastinal complete response after induction resulted significantly worse than the non-CRT group (43 versus 69%, P < 0.01).
The rate of distant metastases was similar in both groups and only one patient experienced local recurrence.
CONCLUSIONS: Neoadjuvant CRT does not increase surgical morbidity, anastomotic complications or mortality in SL. SL appears to be safe and reliable after neoadjuvant concurrent CRT and can be considered the primary surgical option to save the complications related to pneumonectomy in central tumours.

Eur J Cardiothorac Surg. 2012

Sleeve resections with unprotected bronchial anastomoses are safe even after neoadjuvant therapy.

Storelli E, Tutic M, Kestenholz P, Schneiter D, Opitz I, Hillinger S, Weder W.

OBJECTIVES: Sleeve resection is the operation of choice in patients with centrally located tumours, in order to avoid a pneumonectomy. Most surgeons protect the bronchial anastomoses with tissue to prevent insufficiencies. The purpose of this study is to report on outcome of unwrapped bronchial anastomoses,especially after neoadjuvant chemo- or chemoradiotherapy.

METHODS: We retrospectively reviewed the data for morbidity, mortality and survival,especially with regard to the type of resection, neoadjuvant therapy and stage.

RESULTS: Sleeve lobectomy was performed in 88, sleeve bilobectomy in 8, sleeve pneumonectomy in 4 and sleeve resection of the main bronchus in 3 patients. Twenty-seven patients had a combined vascular sleeve resection. Neoadjuvant chemotherapy was performed in 20 and radiochemotherapy in 5 patients. Non-small cell lung cancer (NSCLC) was present in 76 patients (squamous cell carcinoma in 44, adenocarcinoma in 24, large cell carcinoma in 6 and mixed cell in 2) and neuroendocrine tumour in 20 and other histological types in 7 patients. The pathologic tumour stage in NSCLC was stage I in 26, stage II in 26, stage IIIA in 16, stage IIIB in 7 and stage IV in 1 patient. There were no anastomotic complications, especially no fistulas. One patient developed narrowing of the intermediate bronchus without need for intervention. Twenty-four patients had early postoperative complications, including 11 surgery-related complications (air leakage, nerve injury, haemothorax or mediastinal emphysema). The 30-day mortality was 3% (one patient died due to heart failure and two with multiorgan failure). The 5-year survival rate was 63% in NSCLC patients and 86% in neuroendocrine tumour patients. CONCLUSIONS: Sleeve resection without wrapping the bronchial anastomoses with a tissue flap is safe even in patients who underwent neoadjuvant chemo- or chemoradiotherapy. Therefore, wrapping of the bronchial anastomoses is not routinely mandatory.

J Thorac Cardiovasc Surg. 2010

The impact of induction therapy on morbidity and operative mortality after resection of primary lung cancer.

OBJECTIVE: Use and operative results of neoadjuvant therapy before major elective resection for primary lung cancer were examined in the Society of Thoracic Surgeons General Thoracic Surgical Database.

RESULTS: In 525 of 5376 procedures (9.8%), chemotherapy (n = 153), radiotherapy (23), or chemoradiotherapy (349) preceded resection. Compared with resection only, patients receiving induction therapy were younger and had fewer comorbidities, more reoperative surgery, and higher rates of pneumonectomy. Clinical IIIA-N2 disease was treated with induction therapy in only 203 of 397 patients (51.1%). Propensity-adjusted rates detected no difference in discharge mortality, prolonged length of stay, or a composite of major morbidity for patients receiving induction therapy. Similar results were obtained in a logistic regression model (discharge mortality P = .9883; prolonged hospital stay P =.9710; major morbidity P = .9678).

CONCLUSION: Less than 10% of all major lung resections for primary carcinoma and just more than half of all resections for clinical stage IIIA-N2 disease are preceded by neoadjuvant chemotherapy or radiation. This study does not support concerns over excessive operative risk of induction therapy.

World J Surg. 2012

Risk Associated with Bilobectomy after Neoadjuvant Concurrent Chemoradiotherapy for Stage IIIA-N2 Non-small-cell Lung Cancer.

Cho JH, Kim J, Kim K, Shim YM, Kim HK, Choi YS.

BACKGROUND: The aim of the present study was to evaluate the outcomes of surgical resection, especially bilobectomy, after chemoradiation therapy to treat stage IIIA-N2 non-small-cell lung cancer.

METHODS: Data from all patients who underwent surgical resection after neoadjuvant chemoradiation therapy for stage IIIA-N2 non-small-cell lung cancer between 1998 and 2007 were analyzed retrospectively.

RESULTS: Of 186 patients who underwent neoadjuvant therapy, 23 bilobectomies, 28 pneumonectomies, and 135 lobectomies were performed. The early postoperative mortality rate (within 30 days after operation) was 7.1, 8.7, and 1.5% for the pneumonectomy, bilobectomy, and lobectomy groups, respectively. The late postoperative mortality rate (within 90 days) of the lobectomy, bilobectomy, and pneumonectomy groups was 5.9, 13, and 10.7%, respectively. Overall survival was significantly higher among patients treated by lobectomy than among those treated by bilobectomy ($p = 0.041$) or pneumonectomy ($p = 0.010$). Recurrence was significantly lower in patients treated by lobectomy than in those treated by pneumonectomy ($p = 0.034$).

CONCLUSIONS: Bilobectomy is associated with high operative mortality and poor long-term survival after neoadjuvant concurrent chemoradiotherapy for stage IIIA-N2 non-small-cell lung cancer. The outcomes of bilobectomy were similar to those of pneumonectomy in terms of overall survival, disease-free survival, and postoperative mortality.

Ann Thorac Surg. 2009

Changes in pulmonary function tests after neoadjuvant therapy predict postoperative complications.

Cerfolio RJ, Talati A, Bryant AS.

METHODS: A retrospective review of a prospective database of patients with non-small cell lung cancer who underwent neoadjuvant therapy, had pulmonary function tests performed both before and after therapy, and then underwent elective pulmonary resection was performed.

RESULTS: There were 132 patients. The mean duration between pretherapy and posttherapy pulmonary function tests was 4.1 months. The mean change in the percent forced expiratory volume in 1 second, in the percent diffusion capacity of the lung for carbon monoxide, and in the percent diffusion capacity of the lung for carbon monoxide corrected for the alveolar volume was +1.0, -6.4%, and -6.6%, respectively. Fifty-five patients (42%) experienced a postoperative complication, and 39 of those patients experienced a major or respiratory complication. There were 7 (5.3%) operative mortalities (5 were respiratory related). On multivariate analysis the change in the percent diffusion capacity of the lung for carbon monoxide corrected for the alveolar volume was the only factor associated with major or respiratory morbidity ($p = 0.028$). When the posttherapy percent diffusion capacity of the lung for carbon monoxide corrected for the alveolar volume fell by 8% or more, there was an increased likelihood of major morbidity ($p = 0.01$).

CONCLUSIONS: A decrease in the percent diffusion capacity of the lung for carbon monoxide corrected for the alveolar volume after neoadjuvant chemotherapy or chemoradiotherapy may predict increased risk for pulmonary resection, especially if the decrease is 8% or greater. These results should be considered in the preoperative risk assessment of patients who are to undergo pulmonary resection after induction therapy.

Ann Thorac Surg. 2006

Fall in diffusing capacity associated with induction therapy for lung cancer: a predictor of postoperative complication?

Takeda S, Funakoshi Y, Kadota Y, Koma M, Maeda H, Kawamura S, Matsubara Y.

BACKGROUND: Pulmonary resection after induction therapy is associated with high rates of pulmonary morbidity and mortality. However, the impact of induction therapy on the pulmonary toxicity and associated pulmonary complications has not been fully investigated in the setting of lung cancer surgery.

METHODS: We assessed the 66 consecutive patients who underwent a pulmonary resection after induction therapy, 48 of whom received chemoradiotherapy and 18, chemotherapy alone. Results of pulmonary function before and after induction therapy were compared, and logistic regression analyses utilized to explore the risk factors of pulmonary morbidity.

RESULTS: After induction therapy, forced expiratory volume in 1 second (FEV1) was increased significantly (from 2.28 +/- 0.61 L to 2.40 +/- 0.62 L; $p < 0.05$); however, percent vital capacity (%VC) and FEV1/FVC did not change significantly. The diffusing capacity of lung for carbon monoxide (D(LCO)) was decreased significantly by 21% (from 90.3% +/- 18.3% to 71.1% +/- 12.5%; $p < 0.0005$). Patients with respiratory complication showed lower predicted postoperative %FEV1 (49.5% +/- 11.1% versus 57.2% +/- 14.2%; $p = 0.031$) and predicted postoperative %Dlco (41.9% +/- 8.0% versus 55.4% +/- 10.1%; $p < 0.0001$) results than those without complications. Univariate and multivariate analyses revealed that predicted postoperative %D(LCO) alone was an independent factor to predict postoperative pulmonary morbidity.

CONCLUSIONS: For patients who undergo a pulmonary resection after induction therapy, predicted postoperative %D(LCO) is more important to predict pulmonary morbidity rather than static pulmonary function (predicted postoperative %VC or %FEV1). The decrease in D(LCO) is thought to reflect a limited gas exchange reserve, caused by the potential toxicity of chemotherapy or chemoradiotherapy.

J Thorac Oncol. 2011 Sep;6(9):1530-6.

Contemporary results of surgical resection of non-small cell lung cancer after induction therapy: a review of 549 consecutive cases.

Barnett SA, Rusch VW, Zheng J, Park BJ, Rizk NP, Plourde G, Bains MS, Downey RJ, Shen R, Kris MG.

METHODS: Eligible patients were identified from our prospective surgical database. Complications were graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events 3.0.

RESULTS: From January 2000 to December 2006, 549 patients underwent surgery after induction therapy. Median patient age was 64 years (range: 30-86), and 54% were women (298/549). All received chemotherapy, and 17% also had radiation. Lobectomy (388/549, 71%) and pneumonectomy (70/549, 13%) were the most common procedures.

Complications occurred in 250 patients (46%), with grade 3 or higher in 23% (126/549). In-hospital mortality was 1.8% (10/549), with only one death after right pneumonectomy (1/30, 3%). Multivariate analysis showed that predicted postoperative (PPO) pulmonary function was associated with postoperative morbidity. By receiver operating characteristic curves, PPO product (AUC = 0.75, $p < 0.001$), PPO diffusion capacity (AUC = 0.70, $p < 0.001$), and preoperative % predicted PPO diffusion capacity (AUC = 0.66, $p < 0.001$) predicted mortality.

CONCLUSION: Our current experience shows that resection of non-small cell lung cancer after induction therapy, including pneumonectomy, is associated with low mortality. PPO pulmonary function is the strongest predictor of operative risk and should be used to select patients for surgery.

Lancet 2009

Radiotherapy plus chemotherapy with or without surgical resection for stage III non-small-cell lung cancer: a phase III randomised controlled trial.

Albain KS, Swann RS, Rusch VW, Turrisi AT 3rd, Shepherd FA, Smith C, Chen Y, Livingston RB, Feins RH, Gandara DR, Fry WA, Darling G, Johnson DH, Green MR, Miller RC, Ley J, Sause WT, Cox JD.

FINDINGS: 202 patients (median age 59 years, range 31-77) were assigned to group 1 and 194 (61 years, 32-78) to group 2. Median OS was 23.6 months (IQR 9.0-not reached) in group 1 versus 22.2 months (9.4-52.7) in group 2 (hazard ratio [HR] 0.87 [0.70-1.10]; p=0.24). Number of patients alive at 5 years was 37 (point estimate 27%) in group 1 and 24 (point estimate 20%) in group 2 (odds ratio 0.63 [0.36-1.10]; p=0.10). With N0 status at thoracotomy, the median OS was 34.4 months (IQR 15.7-not reached; 19 [point estimate 41%] patients alive at 5 years). Progression-free survival (PFS) was better in group 1 than in group 2, median 12.8 months (5.3-42.2) vs 10.5 months (4.8-20.6), HR 0.77 [0.62-0.96]; p=0.017); the number of patients without disease progression at 5 years was 32 (point estimate 22%) versus 13 (point estimate 11%), respectively. Neutropenia and oesophagitis were the main grade 3 or 4 toxicities associated with chemotherapy plus radiotherapy in group 1 (77 [38%] and 20 [10%], respectively) and group 2 (80 [41%] and 44 [23%], respectively). In group 1, 16 (8%) deaths were treatment related versus four (2%) in group 2. In an exploratory analysis, OS was improved for patients who underwent lobectomy, but not pneumonectomy, versus chemotherapy plus radiotherapy.

INTERPRETATION: Chemotherapy plus radiotherapy with or without resection (preferably lobectomy) are options for patients with stage IIIA(N2) non-small-cell lung cancer.

We think that anesthesiologists
should consider the impact of IT and its association
with extended resection in perioperative care, including
recognition of the decrease in Hb and Dlco,
to prevent complications.

Groups	Minor Complication, No.	Major Complication, No.	Reoperation, No.	Morbidity, No. (%)	Mortality, No. (%)
1 (n = 560)*	73	11	9	77 (12.8)	2 (0.3)
2 (n = 106)†	30	15	7	35 (33.0)	4 (3.8)
3 (n = 35)‡	15	4	1	15 (42.9)	1 (2.9)
4 (n = 57)§	30	12	9	36 (63.2)	4 (7.0)

Histology‖	0.751	0.468–1.462	0.171	0.597	0.139–2.562	0.488
Pathologic stage¶	1.198	0.764–1.876	0.116	5.793	2.545–37.010	0.014‡
Induction therapy#	4.255	2.579–7.022	< 0.0001‡	5.698	1.865–20.877	0.092
Extended surgery**	2.378	1.507–3.751	0.0002‡	5.708	1.074–30.355	0.041†

mortality rates were 65.2% and 7.0%, respectively, for extended resection after IT, and 12.3% and 0.3%, respectively, for those who underwent a standard resection without IT.

Conclusions: The morbidity and mortality of lung resection are both significantly increased after IT, and the patients with the greatest risk are those who have undergone IT and extended resection. The impact of IT on risk stratification should be emphasized in perioperative care.

(CHEST 2005; 128:3519–3525)

Pneumonectomy After Chemoradiation

The Dana-Farber Cancer Institute/Brigham and Women's Hospital Experience

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BACKGROUND. The current study was conducted to examine the outcomes of pneumonectomy after induction chemoradiotherapy in patients with locally advanced nonsmall cell lung cancer (NSCLC).

METHODS. All patients undergoing pneumonectomy after induction therapy at the Brigham and Women's Hospital were retrospectively evaluated for 30-day and 100-day mortality and treatment-related complications with Institutional Review Board approval. Multivariate and univariate analyses for clinical factors correlating with toxicity and/or survival were calculated.

RESULTS. Between 1995 and 2005, 73 patients underwent pneumonectomy for NSCLC after induction therapy. All patients received radiation (median dose of 54 gray [Gy]) and 69 patients (95%) received concurrent chemotherapy. The median age was 62 years and 43 patients (59%) were male; Thirty-seven patients (51%) had American Joint Committee on Cancer stage IIIA NSCLC, 27 (37%) had stage IIIB, 6 had stage IIB, and 4 had stage IV NSCLC because of a resected solitary brain metastasis. A majority (44; 60%) of patients received the combination of carboplatin and paclitaxel, whereas 15 (21%) received the combination of cisplatin and etoposide. Forty-five patients (62%) underwent left pneumonectomy. With a median follow-up of 28 months, the 1-year and 2-year overall survival rates were 70% and 49%, respectively. The 30-day and 100-day mortality rates were 6% and 10%, respectively. Only 4 of 73 patients (6%) died of acute respiratory distress syndrome. The rate of nonfatal treatment-related morbidity was 11%. On univariate analysis, right-sided pneumonectomy was associated with a higher risk of treatment-related mortality (P = .099).

CONCLUSIONS. With an acceptable mortality rate, a single-institutional series demonstrated that trimodality therapy including pneumonectomy can be safely accomplished in patients with advanced NSCLC. ***Cancer* 2008;112:1106–13.**

Studies Evaluating Induction Chemoradiotherapy Followed by Pneumonectomy

Study (No. of patients)	Chemotherapy	Radiotherapy dose, Gy	Treatment mortality rate
Albain 1995[1] (41)	Cisplatin/etoposide	45 Gy	15% (6/41)
Albain 1995[1] (54)	Cisplatin/etoposide	45 Gy	26% (14/54)
Bedini 2003[2] (11)	Daily cisplatin	RT to 50–60 Gy	45% (5/11)
Bernard 2001[3] (24)	Details not given	Details not given	Overall 7% CT/RT rate not defined
Cyjon 2002[4] (8)	Cisplatin daily	45 Gy	38% (3/8)
Daly 2006[5] (30)	Cisplatin/etoposide	59.4 Gy	13% (4/30)
Pezzetta 2005[6] (19)	Cisplatin/docetaxel	1.6 Gy twice daily for 5 d every 2 wk	0% (0/19)
Sonett 2004[7] (29)	Varied platinum-based chemotherapies	Once daily >59 Gy	0% (0/29)
Takeda 2006[8] (19)	Cisplatin-based chemotherapy	RT, median 41.5 Gy	11% (2/19)
Vora 2000[9] (9)	Cisplatin/etoposide	59.4 Gy	0% (0/9)
Current study (73)	Cisplatin-based chemotherapy	RT once daily, median 54 Gy	10% (7/73)

Gy indicates grays; RT, radiotherapy; CT, chemotherapy.

Table 6—*Studies of Overall Operative Morbidity and Mortality**

Study/Year	Country	Study Type	Cases, No.	Morbidity Rate, %	30-Day Mortality Rate, %	In-Hospital Mortality Rate, %
Pulmonary resection for lung cancer						
Nagasaki et al[11]/1982	US	S	961	17	2.0	
Ginsberg et al[12]/1983	US	M	2,220		3.7	
Keagy et al[13]/1983	US	S	369	41	2.2	
Deslauriers[14]/1994	Canada	M	783	18.8	3.8	
Duque et al[15]/1997	Spain	M	605	32.4	6.6	
Bernard et al[16]/2000	France	M	500	40.3	6.6	
Wada et al[1]/1998	Japan	M	7,099		1.3	
Watanabe et al[17]/2004	Japan	S	3,220		0.6	
Present series	Japan	S	758	21.5	0.5	
Following IT						
Fowler et al[6]/1993	US	S	13	62		23.0
Sugarbaker et al[4]/1995	US	S	46	29		4.3
Albain et al[5]/1995	US	S	89			9.0
Roberts et al[7]/2001	US	S	34	47.1		5.9
Martin et al[18]/2001	US	S	412	48		4.8
Stamatis et al[20]/2002	Germany	S	350	48		4.9
Present series	Japan	S	92	55.4		5.4

*M = multicenter study, S = single-center study. US = United States.

Morbidità-mortalità perioperatoria

- Livello HB
- DLCO, PFR
- Comorbidità
- Chemioradioterapia preoperatoria
- Estensione chirurgia
- Pneumonectomia destra
- Protezione moncone bronchiale

Morbidità-mortalità perioperatoria

- Benefici potenziale terapia trimodale
- Importanza selezione paziente
- Mancanza di studi randomizzati