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En bloc resection of non-small-cell lung cancer invading the spine☆

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Abstract

Objective: To describe our surgical *en bloc* approach and to assess the outcome and survival of non-small-cell lung cancer (NSCLC) invading the spine. **Methods:** We retrospectively reviewed our prospective database of all patients, who underwent lung resection with *en bloc* hemivertebrectomy or total vertebrectomy for NSCLC between January 2003 and December 2008 in an individualized multimodality treatment concept. Survival was estimated by the Kaplan—Meier method. Log-rank analyses were used to compare groups. **Results:** Twenty-eight patients (age 58.9 ± 12.9 years) were diagnosed with NSCLC invading the spine at a single center. Eight of those patients were inoperable. Twenty patients proceeded to surgery with *en bloc* hemivertebrectomy ($n = 16$) or total vertebrectomy ($n = 4$). Six patients had induction chemotherapy (30%). Complete resection could be achieved in 16 patients (80%). Morbidity was observed in eight patients (40%); no mortality occurred. Adjuvant radiation ($n = 14$) or chemoradiation ($n = 6$) was administered with 66 Gy. The mean survival and 5-year survival for patients, who underwent surgery ($n = 20$), were 46.0 months and 47%, respectively. Inoperable patients had poorer survival (14.0 months; $p = 0.004$). Sublobar resections ($p = 0.002$) and incomplete resections ($p = 0.02$) were associated with inferior survival. Adjuvant chemoradiation ($p = 0.088$), hemivertebrectomy ($p = 0.062$), and age < 70 years ($p = 0.076$) trended toward prolonged survival. **Conclusions:** Multimodality treatment including *en bloc* lung resections with hemivertebrectomy or total vertebrectomy offer promising long-term survival in highly selected patients with NSCLC invading the spine. These extended resections can be performed with acceptable morbidity and mortality in specialized centers. Patients aged ≥ 70 years should be selected very carefully for radical resection. Sublobar resections should be avoided.

Keywords: Spine; NSCLC; Surgery; Multimodality Treatment; Vertebrectomy

1. Introduction

Resections of advanced non-small-cell lung cancer (NSCLC) in stage IIIB-T4 have been associated with high morbidity and mortality combined with disappointing long-term results. Thus, the risk of surgical resection was not justified by the outcome for many years. Therefore, patients with NSCLC invading the spine historically have been considered to have unresectable disease [1]. As combined neurosurgical—thoracic surgical management demonstrated promising long-term results, various interdisciplinary and multimodality treatment strategies were reported [2]. Aggressive surgical approaches within a multimodality therapy concept resulted in improved long-term survival with acceptable morbidity and mortality [3,4].

Incomplete and discontinuous resections are associated with poor survival. The goal remains complete resection, even in these most challenging thoracic malignancies [5,6]. The number of patients treated with curative intent is low. There is a lack of information on short-term and long-term outcomes in the management of NSCLC invading the spine. Thus, the aim of this study was to describe our surgical *en bloc* approach within a multimodality setting, and to assess the short-term outcome and survival of patients with NSCLC invading the spine.

2. Materials and methods

We retrospectively reviewed our prospective database of all patients, who underwent lung resection with *en bloc* hemivertebrectomy or total vertebrectomy for NSCLC between January 2003 and December 2008. Follow-up data

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were obtained from records of the patients' most recent clinic visits, correspondence from primary care providers, and telephone interviews. Institutional review board approval was obtained for this study. Written consent was obtained from each study patient prior to study initiation. The patients were aware that these data would be used for research purposes. The study was conducted according to the revised Declaration of Helsinki and the requirements of good clinical practice.

2.1. Preconditions for the resection of NSCLC invading the spine

Preconditions for the resection of NSCLC invading the spine are as follows: (1) histologically proven diagnosis of NSCLC; (2) no N2-disease; (3) no distant metastases; (4) radiological criteria of spine infiltration; (5) no infiltration of the plexus above C8; and (6) neo-adjuvant treatment, as appropriate, depending on tumor board decision.

2.2. Diagnostic work-up

All patients underwent preoperative pulmonary and cardiac evaluation: pulmonary function test, quantitative perfusion scans, stress tests and echocardiography. All patients had to meet standard cardiopulmonary criteria for the proposed resections, according to the algorithm of Miller [7]. Clinical staging included a computed tomography (CT) scan of the chest and abdomen, bone scintigraphy, bronchoscopy as well as magnetic resonance imaging (MRI) of the brain, chest and spine in all patients. Furthermore, patients suspected of having disseminated disease underwent additional imaging studies. Mediastinal staging was done routinely with endobronchial ultrasound (EBUS) and transbronchial needle aspirations in case of suspected N2-disease. Positron emission tomography (PET) scans and mediastinoscopies were not performed routinely, but only in selected cases.

2.3. Interdisciplinary surgical approach

The goal of the surgical approach was to obtain *en bloc* resection of the involved lung, chest wall and vertebra with wide safety margins. The steps of our surgical approach are as follows:

1. *Posterior midline incision with dorsal release for hemivertebrectomy or total vertebrectomy*
   The surgery started with a posterior midline incision in the prone position by the spine surgeon. Depending on extent of vertebra involvement evaluated on pre-surgical MRI (Fig. 1(A)), dorsal release for hemilaminectomy or total vertebrectomy was carried out. After ipsilateral hemilaminectomy, the nerve roots and accompanying segmental vessels were exposed and ligated inside the spinal canal to avoid cerebrospinal fluid leakage. An incomplete osteotomy of the vertebral body was performed from the spinal canal toward the thoracic cavity in terms of semifinished intravertrebral groove in the event of hemilaminectomy. In case of total vertebrectomy, pediculotomy and *en bloc* laminectomy were done. The intervertebral disks of the superior and inferior to the involved vertebral body are resected. Finally, the specimen was left in place and the midline incision was closed. Posterior stabilization was required only in event of total vertebrectomy. No stabilization was necessary for hemilaminectomy at that time of surgery.

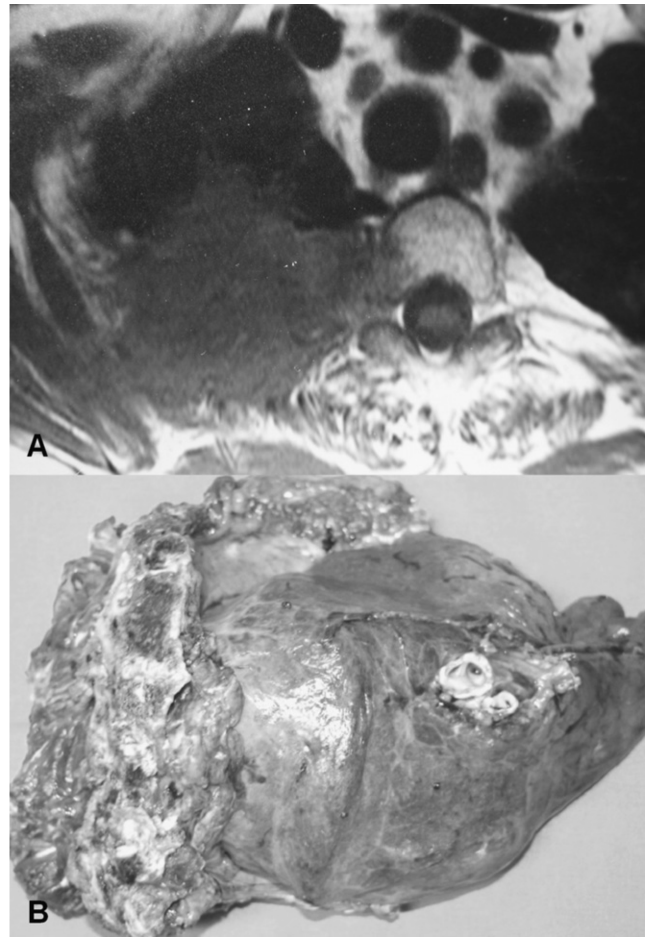

Fig. 1. (A) MRI of the spine and (B) *en bloc* specimen. (A) NSCLC fixed to the vertebral column with radiological criteria of invasion of the periosteum and bony cortex of the vertebra; (B) *en bloc* specimen sent for frozen section to ensure negative margins at the bronchus and vessels.

2. *Posterolateral thoracotomy with en bloc resection of the chest wall, spine and lung including systematic lymph node dissection*
   Posterolateral thoracotomy was performed in the lateral decubitus position. The thoracotomy incision was extended to the midline incision facilitating exposure to the spine. The chest wall was transected anteriorly in tumor-free margins. A tumor-free partial rib was preserved for bone grafting.
   Hemivertebrectomy: In the next step, the *en bloc* specimen was transected from the vertebrae via the spinal canal and the pre-existing and semifinished intravertrebral groove with hammer and chisel under direct visualization of the spinal cord and protection of the underlying intrathoracic organs and great vessels.
   Total vertebrectomy: After dissection anteriorly on both sides, the vertebral bodies are totally freed. At this point, the *en bloc* specimen can be completely mobilized from the spine. Lung resection can be performed in the

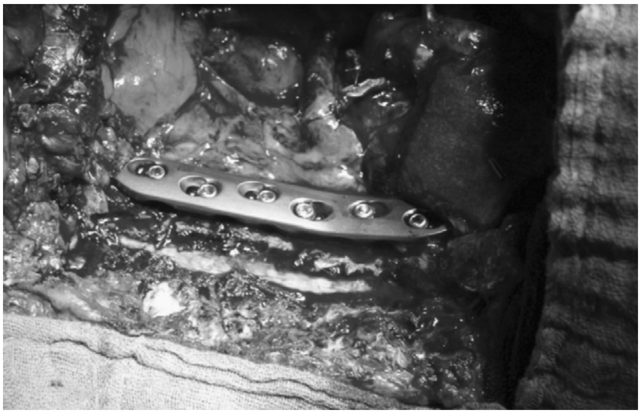

Fig. 2. Anterior spine stabilization after hemivertebrectomy. Intra-operative view after 4-level-hemivertebrectomy showing the spinal cord and anterior stabilization.

standard manner. Systematic, complete mediastinal, hilar and interlobar lymph node dissection was carried out after removal of the *en bloc* specimen (Fig. 1(B)). Frozen section confirmed tumor-free margins at the bronchus and vessels.

3. *Stabilization of the spine*

   The stabilization of the spine was achieved by bone grafting of a tumor-free rib and ventral osteosynthesis in the event of hemivertebrectomy in neutral lateral position (Fig. 2). A titanium mesh cage in conjunction with bone grafting and ventral osteosynthesis was done after total vertebrectomy. The posterior instrumentation was adjusted to compress the inserted spacer slightly (Fig. 3). These procedures were the responsibility of the spine surgeon.

4. *Reconstruction of the chest wall*

   The chest wall was always reconstructed using a double layer of polypropylene mesh (Bard® Mesh, C.R. Bard Inc., Karlsruhe, Germany) also in neutral lateral position after placement of two chest tubes. The mesh is sutured to the ribs and transverse processes. Finally, the thoracotomy was closed subsequent to confirmation of homeostasis.

2.4. Multimodality treatment

In general, patients having either colliquation of the tumor with imminent septic complications or tumors invading the intervertebral foramina with existing or imminent neurological complications proceeded to surgery without induction therapy. Induction chemotherapy included three cycles of platinum-based protocols. Patients proceeded to surgery in case of stable disease or partial response after induction chemotherapy. In the adjuvant setting, four cycles of platinum-based chemotherapy were given. Radiation therapy was administered 4—6 weeks after surgery as a single adjuvant modality after induction chemotherapy or concurrently with chemotherapy. Radiation field included the pre-surgical tumor region at the spine and chest wall.

2.5. Statistical analysis

Means and standard deviations are used for description of continuous measures. Descriptive statistics for discrete variables are presented as frequencies and percentages. Operative mortality included all patients, who died within 30 days of surgery or during the same hospitalization. Survival was estimated by the Kaplan—Meier method, and the log-rank analyses were used to compare the survivals. Survival was calculated from the date of resection to the date of death or the date of last follow-up. Treatment-related deaths were included in the survival analyses. The two groups were compared with respect to the demographics and clinical outcomes using Student's *t*-tests or Fisher's exact tests, as appropriate. A probability value of less than 0.05 was considered statistically significant. Confidence intervals (95%, CIs) were used to quantify extent of the observed differences. Data were stored using Excel (Microsoft, Seattle, WA, USA). Statistical Package for Social Sciences (SPSS) 15.0 software (SPSS Inc, Chicago, IL, USA) was used to analyze the data.

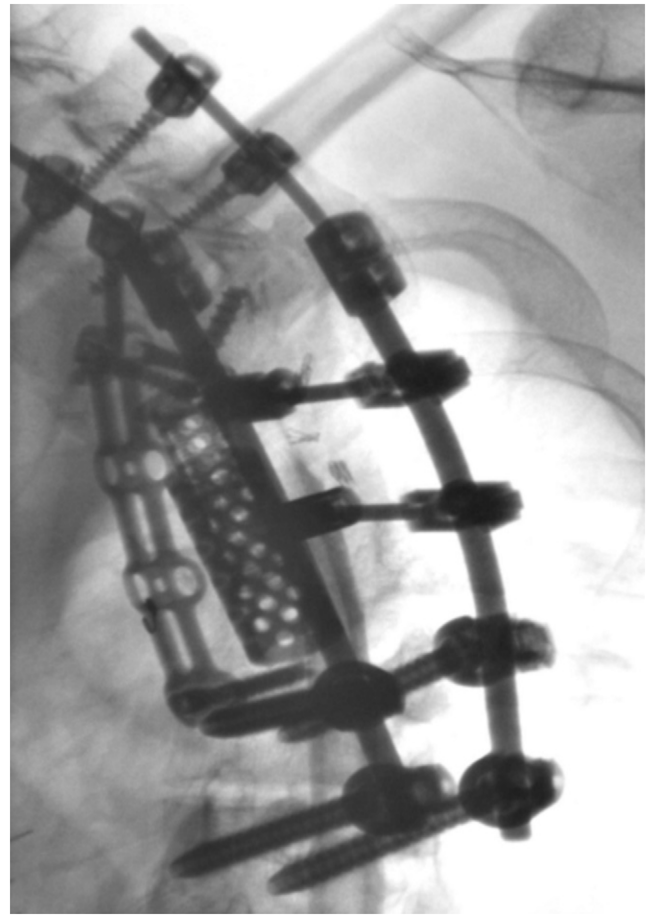

Fig. 3. Post-surgical roentgenogram. Spine stabilization with cage implant, as well as anterior and posterior spine stabilization after multilevel vertebrectomy.

3. Results

During the study period, 28 patients (age 58.9 ± 12.9 years) were diagnosed with NSCLC invading the spine and referred to our Department of Thoracic Surgery. Eight of those patients were inoperable at the time of diagnosis. The contraindication for surgery included tumor invasion into the

Table 1. Patients' demographics.

#	Neo-adjuvant treatment	Type of pulmonary resection	Type of neurosurgical resection	Number of resected levels	Histology	Pathological tumor stage	Completeness of resection	Adjuvant treatment	Status	Follow-up (months)
1	Chemotherapy	Lobectomy	Hemivertebrectomy	3 (Th1-3)	Adenocarcinoma	ypT4 ypN0	R0	Radiation	Dead	61
2	None	Pneumonectomy	Hemivertebrectomy	4 (Th5-8)	Squamous cell carcinoma	pT4 pN1	R1	Chemotherapy and radiation	Alive	36
3	None	Lobectomy	Hemivertebrectomy	2 (Th2-3)	Adenocarcinoma	pT4 pN1	R0	Chemotherapy and radiation	Alive	23
4	None	Sublobar resection	Vertebrectomy	1 (Th6)	Adenocarcinoma	pT4 pN1	R0	Radiation	Dead	24
5	Chemotherapy	Sublobar resection	Hemivertebrectomy	3 (Th1-3)	Adenocarcinoma	ypT4 ypN2	R2	Radiation	Dead	6
6	None	Lobectomy	Hemivertebrectomy	5 (Th4-8)	Adenocarcinoma	pT4 pN0	R0	Radiation	Dead	79
7	Chemotherapy	Lobectomy	Hemivertebrectomy	3 (Th3-5)	Adenocarcinoma	ypT3 ypN3	R0	Chemotherapy and radiation	Alive	70
8	None	Sublobar resection	Vertebrectomy	3 (Th2-4)	Adenocarcinoma	pT3 pN1	R0	Radiation	Dead	27
9	None	Lobectomy	Hemivertebrectomy	2 (Th2-3)	Adenocarcinoma	pT4 pN1	R0	Radiation	Alive	21
10	None	Sublobar resection	Hemivertebrectomy	2 (Th4-5)	Adenocarcinoma	pT3 pN0	R0	Radiation	Dead	2
11	Chemotherapy	Sublobar resection	Hemivertebrectomy	3 (Th3-5)	Adenocarcinoma	ypT4 ypN0	R0	Radiation	Alive	73
12	None	Lobectomy	Hemivertebrectomy	5 (Th2-6)	Adenocarcinoma	pT4 pN0	R0	Radiation	Alive	75
13	None	Sublobar resection	Vertebrectomy	1 (Th3)	Adenocarcinoma	pT4 pN0	R0	Radiation	Dead	27
14	Chemotherapy	Lobectomy	Hemivertebrectomy	3 (Th4-6)	Squamous cell carcinoma	ypT3 ypN0	R0	Chemotherapy and radiation	Alive	74
15	None	Sublobar resection	Vertebrectomy	3 (Th2-4)	Adenocarcinoma	pT3 pN0	R0	Radiation	Dead	29
16	None	Lobectomy	Hemivertebrectomy	4 (Th3-6)	Adenocarcinoma	pT4 pN1	R1	Chemotherapy and radiation	Dead	38
17	None	Lobectomy	Hemivertebrectomy	2 (Th4-5)	Adenocarcinoma	pT4 pN0	R0	Radiation	Alive	26
18	Chemotherapy	Sublobar resection	Hemivertebrectomy	3 (Th2-4)	Adenocarcinoma	ypT4 ypN1	R2	Radiation	Dead	8
19	None	Sublobar resection	Hemivertebrectomy	2 (Th1-2)	Squamous cell carcinoma	pT3 pN0	R0	Radiation	Dead	5
20	None	Lobectomy	Hemilaminectomy	2 (Th3-4)	Adenocarcinoma	pT4 pN0	R0	Chemotherapy and radiation	Alive	12

spinal canal at multiple levels ($n = 3$), unfitness for anesthesia and surgery at the time of diagnosis ($n = 2$), multilevel N2-disease ($n = 2$), and pre-existing paraplegia ($n = 1$).

Twenty patients were eligible for a multimodality treatment approach with curative intent (Table 1). Six patients had three cycles of platinum-based induction chemotherapy (30%). After surgery, four of these patients underwent adjuvant radiation and two patients continued to concurrent adjuvant chemoradiation. Fourteen patients proceeded to surgery without induction therapy (70%). Ten of these 14 patients had only adjuvant radiation, whereas four patients went on with concurrent adjuvant chemoradiation. Adjuvant radiation ($n = 14$) or chemoradiation ($n = 6$) were always administered with 66 Gy.

The types of pulmonary resections (Table 1) were as follows: sublobar resection ($n = 9$), lobectomy ($n = 10$), and pneumonectomy ($n = 1$), respectively. Surgery included hemivertebrectomy in 16 patients (80%) and total vertebrectomy in four patients (20%), respectively. The ribs were resected partially with tumor-free margins at the area of the involved spine and chest wall segments in all cases. In three cases with superior sulcus tumors (patient #1, #5, and #19), resection of the nerve root Th1 was necessary. One patient (#5) underwent resection of the subclavian vein without reconstruction. Phrenic nerve resection had to be performed in one patient (#12) because of tumor involvement.

Complete resection (R0) could be achieved in 16 patients (80%). Adenocarcinoma (85%) was the primary histology. T4-tumors were diagnosed in 14 patients (70%). No tumor invasion of the vertebral body or intervertebral foramina could be found in six patients (30%) in the final pathological examination. Two patients had mediastinal lymph node micrometastases after induction chemotherapy.

All patients were extubated immediately after a mean surgery time of 395.7 ± 75.2 min (range 269—509 min) in the operating room (OR). The patients had a median intensive care unit (ICU) stay of 3 days (range 1—22 days). Morbidity was observed in eight patients (40%). Postoperative complications included pneumonia ($n = 3$), postoperative bleeding requiring re-thoracotomy ($n = 2$), failure of ventral vertebral stabilization requiring secondary dorsal stabilization ($n = 2$), and cerebrospinal fluid leakage ($n = 1$), respectively. No mortality occurred within 30 days or during the in-hospital stay. All patients could be discharged after a median hospital stay of 13.5 days (range 9—38 days).

The mean and 5-year survival (Table 2 and Fig. 4) for patients, who underwent surgery, were 46.0 ± 7.6 months (CI 95% 31.2—60.8) and 47%, respectively. Inoperable patients had poorer survival (14.2 ± 5.0 months; CI 95% 4.4—23.9; $p = 0.003$). Incomplete resections (Fig. 5; $p = 0.02$) and sublobar resections (Fig. 6; $p = 0.002$) were associated with inferior survival. There was a trend toward prolonged survival

Table 2. Survival analyses.

	Mean survival (CI 95%)	*p*-value
Operability		0.003
Multimodality treatment (*n* = 20)	46.0 ± 7.6 (31.2—60.8)	
Inoperability (*n* = 8)	14.2 ± 5.0 (4.4—23.9)	
Completeness of resection		0.02
R0 (*n* = 16)	50.0 ± 8.6 (33.1—66.8)	
R1 (*n* = 2)	38.0	
R2 (*n* = 2)	7.0 ± 1.0 (5.0—8.9)	
Pulmonary resection		0.002
Sublobar resection (*n* = 9)	26.2 ± 7.2 (12.1—40.3)	
Lobectomy/ pneumonectomy (*n* = 11)	70.8 ± 10.4 (50.5—91.1)	
Spine surgery		0.062
Hemilaminectomy (*n* = 16)	54.2 ± 8.9 (36.9—71.6)	
Vertebrectomy (*n* = 4)	26.8 ± 1.0 (24.7—28.8)	
Age		0.076
<70 (*n* = 16)	49.8 ± 7.8 (35.5—65.1)	
≥70 (*n* = 4)	14.8 ± 5.7 (3.7—25.8)	
Adjuvant treatment		0.088
Radiation (*n* = 14)	38.0 ± 8.7 (20.8—55.1)	
Chemoradiation (*n* = 6)	62.0 ± 9.8 (42.8—81.2)	
Pathological T-factor		0.49
pT4/ypT4 (*n* = 14)	35.2 ± 12.0 (11.8—58.6)	
pT3/ypT3 (*n* = 6)	50.1 ± 9.2 (32.1—68.1)	

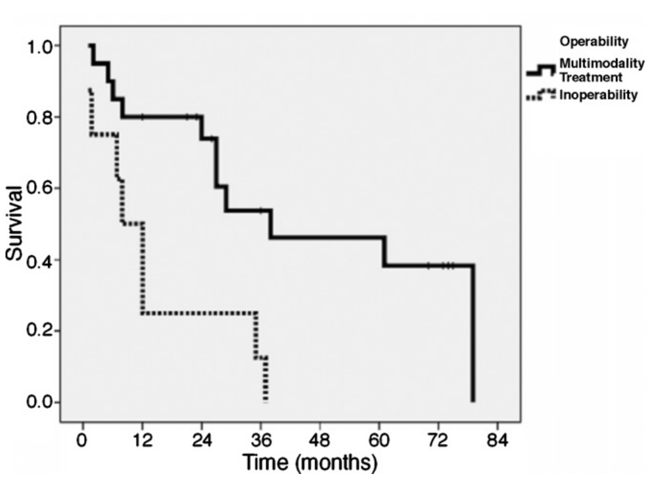

Fig. 4. Survival depending on operability.

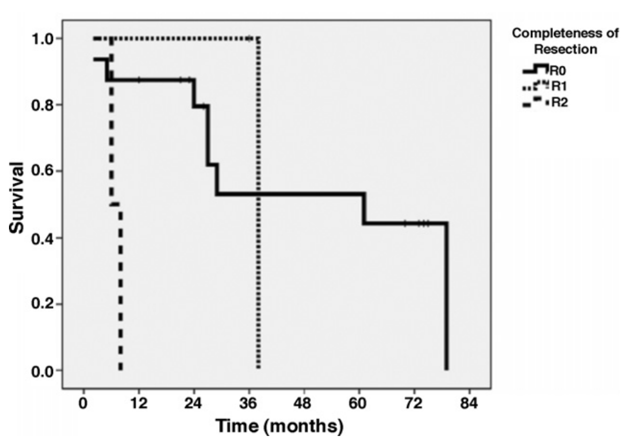

Fig. 5. Survival depending on completeness of resection.

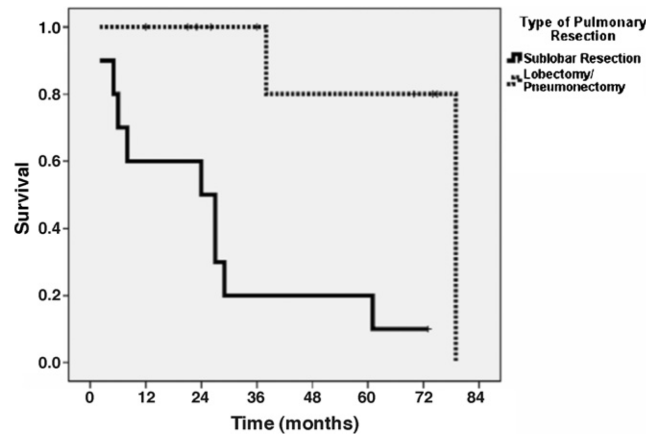

Fig. 6. Survival depending on pulmonary resection.

in patients aged < 70 years ($p = 0.076$), patients who underwent hemivertebrectomy ($p = 0.063$), and patients who proceeded to adjuvant chemoradiation ($p = 0.088$). There was no survival difference between pT3/ypT3 and pT4/ypT4 ($p = 0.49$) in this study. Finally, no trend or significance could be observed with regard to lymph node involvement. Nodal factor pN0/ypN0 was not related to superior survival compared with pN1/ypN1 ($p = 0.27$) or pN1/ypN1/ypN2/ ypN3 ($p = 0.42$), respectively. Further survival analyses were not done because there was only one patient each with N2- or N3-disease.

The mean follow-up period was 35.8 months. No patient was lost to follow-up. Nine patients were alive on the day of last follow-up. These patients are currently disease free. Three out of the 11 dead patients had local and distant recurrence (15%). Seven patients died because of metastatic disease (35%). The primary sites for distant metastases were localized in the brain (*n* = 5), in the contralateral lung (*n* = 3), and at multiple sites (*n* = 2). One patient (Table 1, #6) died 79 months after surgery at the age of 73 years because of myocardial infarction without evidence of recurrence.

4. Discussion

The results of surgical series have to be compared with baseline survival data with definitive chemoradiation to address the rationale of surgery in locally advanced NSCLC. Definitive chemoradiation with two cycles of cisplatin/etoposide concurrent with radiation of the chest (45 Gy) followed by a boost to 61 Gy and with additional two cycles of chemotherapy in the absence of progressive disease resulted in a 3-year survival of 17% and median survival of 15 months, respectively [8]. Inoperable patients undergoing definitive chemoradiation with four cycles of platinum-based chemotherapy and radiation with 64 Gy had a disappointing mean survival of 14.2 months in our series. Only one patient survived 38 months. The mean and 5-year survival for patients who underwent surgery were 46.0 months and 47%, respectively. The 3- and 5-year survivals range between 39% and 67.7% as well as 14% and 67.7% in the previously published series, respectively [3,9—13]. Thus, surgery offers long-term survival and is a rational option for highly selected patients.

Correspondingly, morbidity and mortality rates vary between 0% and 8.7% and between 28% and 53% [3,9,11—13]. These rates reflect the complexity of the complicated interdisciplinary surgical approaches. We observed morbidity in eight patients (40%). Even if homeostasis was secured at the end of surgery, postoperative re-thoracotomy was required due to bleeding in two patients. The most probable reasons were dilutional coagulopathy after transfusions, diffuse bleeding out of the vertebral body, and hypothermia. We had two failures of ventral vertebral stabilization after hemivertebrectomy of four and five levels, respectively. Partial ipsilateral resection of the erector spinae muscles was indicated in these patients with osteoporosis. Postoperative functional physiotherapy failed and secondary dorsal stabilizations were carried out after 3 and 5 months. Based on our experience and depending on intra-operative findings, we recommend additional dorsal stabilization under the following circumstances:

- hemivertebrectomy of $\geq$4 levels;
- necessity of partial resection of the erector spinae muscle $\geq$2 vertebral body levels because of oncological reasons; and
- patients with severe osteoporosis.

No mortality occurred. One patient died two months after surgery after starting chemotherapy. The cause of death remained unanswered. Thus, these complex interdisciplinary surgeries can be performed with acceptable morbidity and mortality at specialized centers.

Multimodality treatment is recommended in locally advanced NSCLC [14]. The timing (neo-adjuvant vs adjuvant) of chemotherapy and radiotherapy remains unclear. Higher rates of complete resections are reported after induction therapy [4,12,13,15,16]. However, these patients underwent complex surgery at specialized centers. The possible roles of induction therapy and the surgical expertise remain indistinguishable with regard to complete resections. Complete response rates vary between 16.7% and 43% after induction chemoradiation [12,13]. However, the surgical strategy to resect the tumor completely with safety margins remains the same even after induction therapy. On the contrary, residual disease remains untreated locally and systematically, if chemotherapy and or radiation therapy is administered only in the neo-adjuvant setting. We observed a trend toward improved survival in patients, who underwent adjuvant chemoradiation ($p = 0.088$). Consequently, we favor chemoradiotherapy in the adjuvant setting to address the possible local and systemic residual disease in patients without mediastinal nodal disease. There is a lack of prospective randomized trials providing answers to this debatable issue about the timing of the non-surgical treatment options within a multimodality treatment.

Complete resection is precondition for the local control of the disease. There are two possible definitions for complete resection: (1) *en bloc* resection of the tumor with surrounding normal tissue in all direction and (2) intra-lesional resection without leaving any of the tumor tissue behind. In intra-lesional resections, the vertebral dissection is carried out separately from the involved lung and chest wall [9,10]. The resection was complete in 56% of the patients in the updated study of the MD Anderson group [9]. The Memorial Sloan Kettering Cancer Center had a complete R0/R1-resection rate of 64% with this intra-lesional approach [17]. However, the confirmation of complete resection at the vertebral margin remains difficult in intra-lesional resections. Only the surrounding tissue of the vertebrae can be checked for positive margins [9]. Nevertheless, only 28% of the completely resected patients developed local recurrence [9]. The 5-year survival ranged between 26% and 27% [9,17]. On the contrary, the oncological principles are respected in *en bloc* resections. Complete resection rates vary between 79% and 83% [3,12]. Yokomise et al. achieved complete resection in all of the treated six patients [13]. Correspondingly, 5-year-survival rates range between 14% and 67.7% [3,12,13]. Our results are comparable in terms of complete resection (80%) and 5-year survival (47%). Excellent local control with 4% local recurrence rate was monitored after *en bloc* resection by Anraku et al. [12]. No local recurrence was observed by Yokomise et al. as well as in this study after R0-resection [13]. No patient survived 1 year after macroscopic incomplete resection (R2) in our study, which is in line with previously published reports [12]. Considered as a whole, it appears that *en bloc* resections might have advantages over intra-lesional resections with regard to complete resection, local control, and long-term survival. This hypothesis must be verified by prospective randomized studies.

The surgical strategy was based on radiological criteria of spine infiltration (T4 tumor). Nonetheless, six patients had no tumor invasion of the vertebral body in the final section (T3 tumor). Even if there was no survival difference between pT3/ypT3 and pT4/ypT4 ($p = 0.49$), the question arises whether such kind of complex surgical approaches including hemivertebrectomy are justified in T3 tumors. Non-invasive functional imaging in terms of motion MRI of the chest and spine could give more information about the presence or absence of spine invasion [18]. Another important invasive option might be the thoracoscopic evaluation of the involved chest before spine surgery. Nevertheless, both approaches have gray zones in distinguishing between tumor invasion and inflammatory attachments. These tumors were fixed to the vertebral column without invasion of the periosteum or the bony cortex. But these microscopic findings can only be detected after bone decalcification of the resected specimen after approximately 1 week. In cT4 tumors, all dissections have to be made in tumor-free tissue to achieve complete resection and to minimize the local recurrence even in pT3 tumors. Incomplete resections do result in inferior survival [6]. Thus, aggressive surgical approaches are justified, if radiological criteria of spine infiltration are met.

The philosophy of sublobar resection is based on the hypothesis that peripheral located tumors invading the spine or the thoracic inlet might have predominantly a centrifugal invasive growth. Deriving from this idea, sublobar resections were performed without survival differences to lobectomy previously [10,19]. Parenchyma-sparing sublobar resections were associated with significant inferior survival ($p = 0.002$) in our series. Five-year survivals for sublobar and lobar resections were 20% and 82%, respectively. Surveillance Epidemiology and End Results (SEER)—Medicare database analysis of 1177 T4 NSCLC showed a hazard ratio of 1.55 for sublobar resections compared with lobectomy [20]. Although we did not observe local recurrence at the pulmonary resection margin, our own results suggest lobectomy as the surgical treatment of choice in lung cancer invading the spine. Parenchyma-sparing sublobar resections should be reserved only for exceptional cases, even if there is no prospective randomized study proving the superiority of lobectomy over sublobar resections for NSCLC invading the spine.

In general, pulmonary resections for NSCLC are justified in patients over 70 years of age [21,22]. Selected elderly patients with locally advanced NSCLC (stage IIIA and IIIB) are candidates for multimodality treatment including induction chemoradiation and surgery [23]. Nonetheless, we observed a trend toward shortened survival in patients aged ≥ 70 years. Highly selected elderly patients had only a median survival of 14.8 months compared with 49.8 months for patients < 70 years of age ($p = 0.076$). The outcome in this patient cohort was inferior to the above-mentioned definitive chemoradiation [8]. As a result, patients aged ≥ 70 years should be selected very carefully for radical resection for NSCLC invading the spine.

This study represents a retrospective analysis of a prospective database from a single center. The relative small number of patients in this study limits the results of the presented study. Because of the small number of patients, the differences in the analyses could be due to chance. Contributions of the different treatment modalities to the overall survival remain unanswered in this study. Furthermore, these survival rates could be attributed to the patient selection in conjunction with only few 'resectable' superior sulcus tumors and the fact that only two patients had N2/N3-disease. These facts should be taken into consideration when the results of the present study are interpreted.

5. Conclusions

In conclusion, multimodality treatment including *en bloc* lung resection with hemivertebrectomy or total vertebrectomy offers promising long-term survival in highly selected patients with NSCLC invading the spine. These extended resections can be performed with acceptable morbidity and mortality in specialized centers with interdisciplinary teams of thoracic and spine surgeons. Patients aged ≥ 70 years should be selected very carefully for radical resection. Sublobar resections should be avoided. Larger prospective randomized trials are needed to answer the question of the timing of chemoradiation within a multimodality treatment concept.

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Appendix A. Conference discussion

Dr G. Walsh (*Houston, TX*): A question from a technical perspective. When do you decide to do a hemivertebrectomy or a total vertebrectomy? Do you use your MRI imaging to help in the assessment, because you are obviously planning differently depending on whether you are going to do a total vertebrectomy or hemivertebrectomy.

Dr Schirren: The preoperative staging with MRI is important for us. Intra-operatively we see we have to do a resection for a T3 tumor or for a T4 tumor. This intra-operative staging by the surgeon is essential here. In my opinion, we need the moving pictures of the MRI to detect how the tumor invades the structures.

Dr W. Weder (*Zurich, Switzerland*): From these cases you cannot make any conclusions on the value of chemotherapy as induction or chemoradiotherapy as induction or on the value of adjuvant treatment. You presented your expert opinion based on your data, but this is not a study answering these questions. Most likely there will never be such a study, unfortunately, because these are rare, and highly selected cases.

Dr Schirren: I agree with you. If you do preoperative radiochemotherapy, then you compromise the tumor area. The dose of radiation is between 45 and 50 Gy. This radiation is not effective to the tumor. And the boost after surgery does not have the effect as in radiation with 60 Gy postoperatively. Therefore, we prefer chemotherapy first, then surgery, and after that, radiation. The role of chemotherapy is most probably to avoid micrometastases in the body. You have seen here that we reached R0 resection in 80% without preoperative radiation.

Dr Weder: I understand, but this is expert opinion not proven by data.

Dr Schirren: I know, but it is okay.

Dr A. Turna (*Istanbul, Turkey*): You obviously had patients with pT3 tumors. Did you perform pneumonectomy or radical lobectomy in the patients with tumor without vertebral invasion; did you make the decision before their chemoradiotherapy, because some of the patients had tumors without any vertebral invasion.

Dr Schirren: I have some problems understanding the question.

Dr Turna: Why did you have patients with pT3 tumors? By definition it must be T4.

Dr Schirren: Yes.

Dr Turna: If you have a patient with vertebral body invasion, the patients have T4 tumors, not T3. Did make the decision before neo-adjuvant therapy?

Dr Schirren: Preoperatively we classified all these tumors as T4. Therefore the strategy of resection was planned for a T4 tumor. The pathologist told us after the final examinations if we had resected a T3 or T4 tumor. In this strategy the surgeon guarantees a real en bloc resection and the risk of intra-operative tumor dissemination is very low. We have to do this because we have no frozen section for this situation during the operation.

Dr Turna: But did you do a mediastinoscopy to exclude N2 patients?

Dr Schirren: Please repeat.

Dr Turna: Did you perform a mediastinoscopy?

Dr Schirren: No. We used PET-CT scan and examination of suspicious lymph nodes by EBUS. I don't like mediastinoscopy in this case.

Dr S. Cassivi (*Rochester, MN*): I applaud you for your interdisciplinary collaboration on a very tough problem. In the light of what Dr Weder spoke about in terms of this being expert opinion, this is understandable since these are small numbers and a highly selected group. But I would also encourage everyone in this room, as surgeons, not to take the comment of someone saying you have a highly selected group as being a criticism. We are surgeons. Our job is to select our patients appropriately. So I think that it is a good thing that you have shown that we can select our patients appropriately.

My question, or rather my suggestion, to you is this: Because it is such a potentially morbid operation, I would encourage you to include in your results in the survival graph of R0, R1, and R2 resections, the eight patients that you evaluated and did not bring to surgery, in order to show what their survival is. My further question to you is, if you have that data right now, what is their median survival? I would encourage you, for the publication, to include that data in that graph.

Dr Schirren: Yes. Thank you.

Dr K. Athanassiadi (*Athens, Greece*): All of us have faced the problem many times after a simple stabilization of the spine that we are getting empyemas operated without having patients immunocompromised due to cancer or due to chemotherapy. Did you have a special strategy with your spine surgeon? Because I have seen your morbidity, there were no empyemas. Can you tell us about that?

Dr Schirren: Yes, we had no empyema. Intra-operatively on an interdisciplinary basis, we check that the dura is closed. In these cases, fluid from the myelon cannot leave the dura. Fluids from the thorax have to be drained well by chest tube and then the risk of infection is very low. If there is a leakage, then, together with the spine surgeon, we put a catheter into the peridural space. By this procedure, the leakage will close.

My last comment is to the audience. If we had 100 patients with this kind of surgery, then we could do an evidence-based analysis. Therefore, I will offer to do this surgery. It is an honor that Professor Dartevelle from Paris is here, one of the pioneers of this surgery. I think we have to thank him for his innovation.

Editorial comment

En bloc vertebrectomy for lung cancer invading the spine: surgical serenity and optimism warrant innovation

Keywords: Lung cancer; Vertebrectomy; Thoracic surgery; Spine; T4 NSCLC; Pancoast tumor

Innovation in medicine increasingly becomes challenging. Ethical considerations and regulations discourage progressively skilled surgeons to develop new techniques, particularly as it pertains to extended aggressive resections. The case of *en bloc* vertebrectomy for lung cancer attached to the spine is a pure demonstration of surgical developments that were possible in a recent past but that would probably not be allowed today.

In the current issue of this journal, Dr Schirren and his colleagues emphasize the benefits of such surgical aggressiveness, as they report a 5-year survival rate of 47% in patients, who underwent radical *en bloc* surgery including spinal resection [1]. Nearly one out of two patients can thus hope to survive 5 years following surgical resection of a lung cancer invading the vertebral column! These fascinating results confirm previously published data [2,3]. Such survival rates, associated with a very low postoperative mortality, support the suggestion by the Association for the Study of Lung Cancer (IASLC) Staging Committee to downstage these T4 tumors from stage IIIB to stage IIIA, provided the nodal status be limited to N0 or N1 [4]. Accordingly, in centers of excellence, a surgical resection can be offered to selected patients with such disease. Appropriately, in the study by Dr Schirren and colleagues, patients with N2 disease were precluded from resection [1].