Completion pneumonectomy and chemoradiotherapy as treatment options in local recurrence of non-small-cell lung cancer

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Abstract

Introduction: The selection of treatment for local recurrence in patients with non-small-cell lung cancer (NSCLC) depends on the possibility of performing a radical tumor resection, the patient’s performance status, and cardiopulmonary efficiency. Compared with chemoradiotherapy, surgical treatment offers a greater chance of long-term survival, but results in complete pneumonectomy and is associated with a relatively high rate of complications.

Aim of the study: was to evaluate early and long-term results of surgery and conservative treatment (chemoradiotherapy) in patients with local NSCLC recurrence.

Material and methods: Between 1998 and 2011, 1697 NSCLC patients underwent lobectomy or bilobectomy at the Department of Thoracic Surgery in Poznań. Among them, 137 patients (8.1%) were diagnosed with cancer recurrence; chemotherapy or chemoradiotherapy was provided to 116 patients; 21 patients (15.3%) were treated with completion pneumonectomy. The median time from primary surgery to recurrence was 13.4 months. No metastases to N2 lymph nodes were observed among the patients undergoing surgery; in 7 patients N1 lymph node metastases were confirmed.

Results: The rate of complications after surgery was significantly higher in comparison with conservative therapy (80.9% vs. 48.3%). Patients treated with surgery were most likely to suffer from complications associated with the circulatory system (80.9%), while hematologic complications were dominant in the group undergoing oncological treatment (41.4%). There were no perioperative deaths after completion pneumonectomy. The age of the patients was the only factor which significantly influenced the incidence of complications in both groups of patients. Analysis of the survival curves demonstrated statistically significant differences in survival between the groups treated with surgery, chemoradiotherapy, and chemotherapy (p = 0.00001). Five-year survival probability was significantly higher among patients treated surgically as compared to patients undergoing systemic therapy.

Streszczenie

Wstęp: Wybór metody leczenia wznowy miejscowej niedrobnokomórkowego raka płuca (NDRP) zależy od możliwości radykalnego wycięcia guza, stanu sprawności chorego oraz wydolności układu oddechowego i układu krążenia. W porównaniu z chemioradioterapią leczenie chirurgiczne daje potencjalnie większą szansę na wieloletnie przeżycie, ale wiąże się z koniecznością wycięcia całego płuca i stosunkowo dużym ryzykiem powikłań.

Cel pracy: była ocena wczesnych i odległych wyników leczenia chirurgicznego i zachowawczego (chemioradioterapia) chorych ze wznową miejscową NDRP.

Materiał i metody: Spośród 1697 chorych na NDRP, u których w latach 1998–2011 w Klinice Torakochirurgii w Poznaniu wykonano lobektomię lub bilobektomię, u 137 stwierdzono wznowę miejscową (8,1%). Stu szesnastu zostało poddanych chemio- lub chemioradioterapii, u 21 wykonano uzupełniającą pneumonektomię. Średni czas do wystąpienia wznowy wyniósł 13,4 miesiąca. W grupie chorych leczonych chirurgicznie w żadnym przypadku nie stwierdzono przerzutów w węzłach grupy N2, u 7 chorych potwierdzono przerzuty w węzłach N1.

 Wyniki: Odsetek powikłań po leczeniu chirurgicznym był istotnie wyższy w porównaniu z leczeniem zachowawczym (80,9% vs 48,3%). W grupie chorych leczonych operacyjnie dominowały powikłania systemowe (80,9%), a w grupie leczonej chemio- lub chemioradioterapią powikłania hematologiczne (41,4%). Nie stwierdzono zgonów w okresie okołooperacyjnym. Jedynym czynnikiem wpływającym istotnie na częstość powikłań w obu grupach był wiek chorych. Porównując krzywe przeżycia, stwierdzono istotne statystycznie różnice w czasie przeżycia pomiędzy grupą leczoną chirurgicznie, grupą poddaną chemoradioterapii i grupą leczoną chemioterapią (p = 0,00001). Czas przeżycia był najdłuższy u chorych leczonych operacyjnie, najkrótszy u chorych po leczeniu systemowym.

Wnioski: Mimo stosunkowo dużego odsetka powikłań pooperacyjnych wyniki odległe leczenia chirurgicznego wznowy miejscowej NDRP są korzystniejsze niż w przypadku chemio-
Conclusions: Despite the significant rate of postoperative complications (mostly circulatory), the long-term results of the surgical treatment of local NSCLC recurrence are more favorable than those achieved with chemoradiotherapy. The success of surgical treatment is conditioned on the exclusion of metastasis in N2 lymph nodes.

Key words: lung cancer, local recurrence, completion pneumonectomy, chemoradiotherapy.

Introduction

In patients with non-small-cell lung carcinoma (NSCLC) after radical surgical treatment, the recurrence of neoplasia most often takes the form of distant metastases, and the only method of prolonging the patient’s life that remains in such cases is palliative chemotherapy. However, in approx. one fourth of patients after NSCLC resection, hematogenous spread does not occur; instead the disease recurs locally, which does not preclude radical surgical management in some cases. Typically, pneumonectomy is the only available procedure in this context, offering a chance for complete recovery despite being associated with a substantial risk of serious postoperative complications and with mortality reaching 12% [1-3]. The alternative is chemoradiotherapy, which is associated with a much smaller percentage of complications, but is characterized by worse long-term results [4, 5]. Due to the previous partial lung resection, completion pneumonectomy is a technically demanding procedure, particularly because of massive adhesions and problems with dissecting the structures of the pulmonary hilum; hence, it constitutes a challenge for thoracic surgeons. As the number of such procedures is relatively small, there are few publications concerning the results of treating lung cancer recurrence with this method, and they involve small patient groups [6-8].

The aim of the present study was to assess the early- and long-term results of surgery (completion pneumonectomy) and conservative treatment (chemoradiotherapy or chemotherapy) in patients with local NSCLC recurrence.

Material and methods

Between 1998 and 2011, 1697 NSCLC patients underwent lobectomy or bilobectomy at the Clinic of Thoracic Surgery in Poznań. Among them, 137 patients (8.1%) were diagnosed with local cancer recurrence during the follow-up period. Chemo- and/or radiation therapy was provided to 116 patients (84.7%; 78 – chemotherapy, 38 – chemoradiotherapy); 21 patients (15.3%) were treated with completion pneumonectomy. The study group included 102 men and 35 women; their mean age was 63 years. The most frequently performed primary procedure was right upper lobectomy (Table I). Histopathological examination revealed squamous cell carcinoma in 49.6% of cases ($n = 68$), adenocarcinoma in 43.8% of cases ($n = 60$), and other

### Tab. 1. Clinical characteristics of the studied patient groups – part 1

| Variable                  | Method of treating local recurrence | Statistical significance ($p$) |
|---------------------------|-------------------------------------|-------------------------------|
| Age (median, years)       | Overall ($n = 137$)                 | Pneumonectomy ($n = 21$)     | Conservative treatment ($n = 116$) |
|                           | 63 (44-84)                          | 62                            | 63.5                          | ns             |
| Gender                    |                                     |                               |                               |                |
| Men                       | 102 (74.4%)                         | 17 (81%)                      | 85 (73.3%)                    | ns             |
| Women                     | 35 (25.6%)                          | 4 (19%)                       | 31 (26.7%)                    | ns             |
| Type of primary procedure |                                     |                               |                               |                |
| Lower lobectomy           | 30 (21.9%)                          | 5 (23.8%)                     | 25 (21.5%)                    | ns             |
| Middle lobectomy          | 6 (4.4%)                            | 1 (4.8%)                      | 5 (4.3%)                      | ns             |
| Upper lobectomy           | 86 (62.8%)                          | 11 (52.4%)                    | 75 (64.7%)                    | ns             |
| Lower bilobectomy         | 12 (8.8%)                           | 3 (14.2%)                     | 9 (7.8%)                      | ns             |
| Upper bilobectomy         | 3 (2.2%)                            | 1 (4.8%)                      | 2 (1.7%)                      | ns             |
| Side of the primary procedure |                                     |                               |                               |                |
| Right                     | 87 (63.5%)                          | 12 (57.1%)                    | 75 (64.7%)                    | ns             |
| Left                      | 50 (36.5%)                          | 9 (42.9%)                     | 41 (35.3%)                    | ns             |
| Median recurrence-free survival (months) | 13.4 | 9 | 13.5 | ns |
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Histological types in 6.6% of cases ($n = 9$). The most often diagnosed grade of cancer differentiation was G2 (62.4%, $n = 78$). After the primary resection, the following TNM stages were diagnosed: IA in 12 patients (9%), IB in 30 patients (22.5%), IIA in 23 patients (17.3%), IIB in 32 patients (24.1%), IIIA in 33 patients (24.8%), and IIIB in 3 patients (2.3%). The primary procedure was oncologically radical (R0) in 84.5% of cases ($n = 115$). In 19 cases (14%), R1 resection margins were noted, and in 2 (1.5%) – R2 margins were observed (Table II). Of the 21 patients with positive resection margins (R1 or R2) after the primary procedure, only one was qualified for completion pneumonectomy.

Local recurrence was defined as a renewed increase in tumor mass at the site of the excised lobe (infiltration in

| Variable                          | Method of treating local recurrence | Statistical significance ($p$) |
|-----------------------------------|-------------------------------------|-------------------------------|
| Overall ($n = 137$)               | Pneumonectomy ($n = 21$)            | Conservative treatment ($n = 116$) |
| Histological type                 |                                     |                               |
| squamous cell carcinoma           | 68 (49.6%)                          | 12 (57.1%)                    | 56 (48.3%)                     | ns                            |
| adenocarcinoma                    | 60 (43.8%)                          | 9 (42.9%)                     | 51 (44.0%)                     | ns                            |
| large cell carcinoma              | 5 (3.6%)                            | 0                             | 5 (4.3%)                       | ns                            |
| pleomorphic carcinoma             | 2 (1.5%)                            | 0                             | 2 (1.7%)                       | ns                            |
| undifferentiated carcinoma        | 2 (1.5%)                            | 0                             | 2 (1.7%)                       | ns                            |
| Grade of cancer differentiation   |                                     |                               |                               |
| G1                                | 17 (13.6%)                          | 2 (9.5%)                      | 15 (14.5%)                     | ns                            |
| G2                                | 78 (62.4%)                          | 14 (66.7%)                    | 64 (61.5%)                     | ns                            |
| G3                                | 30 (24.0%)                          | 5 (23.8%)                     | 25 (24.0%)                     | ns                            |
| T stage                           |                                     |                               |                               |
| Tis                               | 3 (2.2%)                            | 0                             | 3 (2.6%)                       | ns                            |
| T1                                | 24 (17.5%)                          | 1 (4.8%)                      | 23 (19.8%)                     | ns                            |
| T2                                | 88 (64.2%)                          | 20 (95.2%)                    | 68 (58.6%)                     | 0.0013                        |
| T3                                | 17 (12.4%)                          | 0                             | 17 (14.7%)                     | ns                            |
| T4                                | 5 (3.7%)                            | 0                             | 5 (4.3%)                       | ns                            |
| N stage                           |                                     |                               |                               |
| N0                                | 65 (47.4%)                          | 14 (66.7%)                    | 51 (44.0%)                     | ns                            |
| N1                                | 44 (32.1%)                          | 7 (33.3%)                     | 37 (31.9%)                     | ns                            |
| N2                                | 28 (20.4%)                          | 0                             | 28 (24.1%)                     | 0.0117                        |
| TNM stage                         |                                     |                               |                               |
| IA                                | 12 (9.0%)                           | 2 (9.5%)                      | 10 (8.9%)                      | ns                            |
| IB                                | 30 (22.5%)                          | 9 (42.9%)                     | 21 (18.7%)                     | 0.0144                        |
| IIA                               | 23 (17.3%)                          | 3 (14.3%)                     | 20 (17.9%)                     | ns                            |
| IIB                               | 32 (24.1%)                          | 7 (33.3%)                     | 25 (22.3%)                     | ns                            |
| IIIA                              | 33 (24.8%)                          | 0                             | 33 (29.5%)                     | 0.0041                        |
| IIIB                              | 3 (2.3%)                            | 0                             | 3 (2.7%)                       | ns                            |
| R parameter                       |                                     |                               |                               |
| R0                                | 115 (84.5%)                         | 19 (95.5%)                    | 96 (82.8%)                     | ns                            |
| R1                                | 19 (14.0%)                          | 1 (5.0%)                      | 18 (15.5%)                     | ns                            |
| R2                                | 2 (1.5%)                            | 0                             | 2 (1.7%)                       | ns                            |
the stump of the bronchus or the stumps of the pulmonary vessels, infiltration in the parenchymal stapler line, the neighboring lobe, or the lung’s hilum with or without regional lymph node involvement), as confirmed by cytological or histopathological examination. Local recurrence was diagnosed with the use of imaging examinations (chest computed tomography [CT] and positron emission tomography coupled with computed tomography [PET/CT]), endoscopy (bronchoscopy, autofluorescence bronchoscopy, endobronchial ultrasound-guided transbronchial needle aspiration – EBUS-TBNA) and other diagnostic procedures (blind transbronchial aspiration, transthoracic fine-needle biopsy). Each patient with local recurrence was treated as a potential candidate for repeat surgical treatment. Patients with locally operable tumors (as assessed by CT and bronchoscopy) and adequate results of examinations evaluating the functioning of their respiratory and circulatory systems qualified for completion pneumonectomy after the exclusion of distant metastases (PET/CT, abdominal and cerebral CT, cerebral NMR, bone scintigraphy) and metastasis to mediastinal lymph nodes (PET/CT, EBUS). To evaluate the functioning of the respiratory system, spirometry was performed routinely, as were examinations assessing the diffusing capacity of the lung for carbon monoxide (DLCO) and capillary blood gas; some patients performed a 6-minute walk test and a stair climbing test. In cases of doubt, the predicted values of postoperative forced expiratory volume in 1 second (ppoFEV1) and postoperative DLCO (ppoDLCO) were calculated. The evaluation of the circulatory system was based on electrocardiography (ECG) and echocardiography; additional examinations were performed in individual cases (exercise test, 24-hour Holter electrocardiogram, coronary angiography). Patients with locally inoperable recurrence, high operative risk (based on the number and type of concomitant diseases as well as results of respiratory function tests and cardiological examinations), and patients who did not provide their consent to surgery were qualified for conservative treatment. Completion pneumonectomy was performed using anterolateral or posterolateral thoracotomy. In 85.7% of cases, the vessels of the lung’s hilum were repaired intrapericardially. In 18 patients (85.7%), the bronchial stump was closed with hand suturing (double stapler). In the remaining 3 patients (14.3%), mechanical suturing was employed (linear stapler). In 14 patients (66.7%), the bronchial stump was strengthened by suturing the neighboring tissues onto it (intercostal muscle, pericardium, thymus, pleura, or mediastinal fat tissue).

In 78 patients, systemic treatment was applied in the form of 4-6 courses of chemotherapy according to the PN regimen (cisplatin + vinorelbine); 38 patients underwent combination therapy (induction chemotherapy according to the PN regimen with subsequent or concurrent radiotherapy) with a radiation dose not exceeding 60 Gy.

Statistical analysis was conducted using Statistica 10 software. In order to characterize the study groups, basic descriptive statistics were employed. Furthermore, the Mann-Whitney U test and Spearman’s rank correlations were used. Survival time was analyzed using the Kaplan-Meier method as well as log-rank and χ² tests. The influence of variables on survival time were determined based on Cox’s proportional hazard regression model.

**Results**

The mean duration between surgery and recurrence was 13.4 months; it did not differ significantly between the groups receiving surgery (9 months) and conservative treatment (13.5 months).

The age and sex distribution of the two groups did not differ in a statistically significant manner (Table I). Similarly, the groups were not significantly different in terms of the prevalence of individual histological types and degrees of cancer cell differentiation. Among the patients in whom recurrence was treated surgically, primary stage IB was diagnosed significantly more often, while stage IIIA was significantly more frequent in the conservative treatment group. In the group treated with completion pneumonectomy, postoperative histopathological examination after the primary procedure revealed no metastases to N2 lymph nodes; in 7 patients N1 lymph node metastases were confirmed. In turn, the N2 disease was significantly more frequent in the conservative treatment group: it was histologically confirmed in 28 patients – 24.1% (Table II). The procedure performed in the surgical treatment group lasted from 70 to 340 min. (mean: 177 min.) with intraoperative blood loss ranging from 200 to 1000 ml (mean: 560 ml). The mean in-hospital stay in this group was 15.2 days (7-42 days).

In 73 out of 137 patients (53.3%), at least one complication occurred. The complications differed in severity between the groups, and they were more frequent in the surgical treatment group. At least one complication occurred in 80.9% of surgically treated patients and in 48.3% of patients undergoing conservative therapy (p = 0.0019). Complications related to the circulatory system occurred significantly more often in the group undergoing completion pneumonectomy (p = 0.0001). Patients treated with surgery were most likely to suffer from complications associated with the circulatory system (80.9%), while hematologic complications were dominant in the group undergoing oncological treatment (41.4%). The most frequent complication after completion pneumonectomy was supraventricular cardiac arrhythmia (38.1%), whereas after conservative treatment: neutropenia (16.4%) and anemia requiring blood transfusion (12.9%). Most frequently (in 24.1% of cases), the patients suffered from one complication; two complications were noted in 13.9% of patients; in one patient, 9 complications were observed, which constituted the largest number of complications in a single patient. The types and incidence of complications in each group are presented in Table III. According to the conducted statistical analysis, the only factor influencing the number of complications was the age of the patient. The type and number of complications occurring in individual patients
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**Tab. III. Type and frequency of complications in the study groups**

| Complication type                  | Pneumonectomy (n = 21) | Conservative treatment (n = 116) | Statistical significance (p) |
|------------------------------------|------------------------|---------------------------------|------------------------------|
| Hematologic                        |                        |                                 | ns                           |
| Neutropenia                        | 0                      | 19 (16.4%)                      | ns                           |
| Neutropenic fever                  | 0                      | 5 (4.3%)                        | ns                           |
| Thrombocytopenia                   | 0                      | 8 (6.9%)                        | ns                           |
| Hemorrhagic diathesis              | 0                      | 1 (0.9%)                        | ns                           |
| Anemia                             | 5 (23.8%)              | 15 (12.9%)                      |                              |
| Circulatory                        |                        |                                 |                              |
| Hypotonia                          | 7 (33.3%)              | 1 (0.9%)                        | 0.0001                       |
| Lowered cardiac ejection fraction  | 0                      | 1 (0.9%)                        |                              |
| Hydropericardium                   | 0                      | 1 (0.9%)                        |                              |
| Cardiac arrhythmias                | 8 (38.1%)              | 0                               |                              |
| Circulatory failure                | 2 (9.5%)               | 2 (1.7%)                        |                              |
| Cardiac herniation                 | 2 (9.5%)               | 0                               |                              |
| Myocardial infarction              | 1 (4.5%)               | 0                               |                              |
| Respiratory                        |                        |                                 |                              |
| Pulmonary embolism                 | 0                      | 2 (1.7%)                        | ns                           |
| Pneumonia                          | 0                      | 2 (1.7%)                        |                              |
| Radiation-induced pneumonitis      | 0                      | 2 (1.7%)                        |                              |
| Bronchopleural fistula             | 1 (4.8%)               | 1 (0.9%)                        |                              |
| Atelectasis                        | 1 (4.8%)               | 0                               |                              |
| Respiratory failure                | 1 (4.8%)               | 0                               |                              |
| Nephrologic                        |                        |                                 |                              |
| Renal failure                      | 5 (23.8%)              | 12 (10.3%)                      | ns                           |
| Elevated serum levels of creatinine| 1 (4.8%)               | 11 (9.5%)                       |                              |
| Alimentary                         |                        |                                 |                              |
| Dysphagia                          | 0                      | 2 (1.7%)                        | ns                           |
| Diarrhea                           | 0                      | 1 (0.9%)                        |                              |
| Constipation                       | 0                      | 2 (1.7%)                        | ns                           |
| Abdominal pain                     | 1 (4.8%)               | 2 (1.7%)                        |                              |
| Bleeding from the gastrointestinal tract | 0                      | 1 (0.9%)                        |                              |
| Nausea                             | 0                      | 2 (1.7%)                        |                              |
| Vomiting                           | 0                      | 3 (2.6%)                        |                              |
| Infectious                         |                        |                                 |                              |
| Oral mycosis                       | 1 (4.8%)               | 1 (0.9%)                        | ns                           |
| Other infections                   | 0                      | 6 (5.2%)                        |                              |
| Neuropsychiatric                   |                        |                                 |                              |
| Epileptic seizures                 | 2 (9.5%)               | 4 (3.5%)                        | ns                           |
| Peripheral neuropathy              | 0                      | 1 (0.9%)                        |                              |
| Recurrent laryngeal nerve palsy    | 1 (4.8%)               | 0                               |                              |
| Mental disorders                   | 1 (4.8%)               | 0                               |                              |
| Other                              |                        |                                 |                              |
| Allergic reaction                  | 0                      | 1 (0.9%)                        | ns                           |
| Adynamia                           | 0                      | 9 (7.8%)                        |                              |
| Glucose level disorders            | 1 (4.8%)               | 1 (0.9%)                        |                              |
| Electrolyte disorders              | 0                      | 3 (2.6%)                        |                              |
| Repeat thoracotomy (bleeding)      | 1 (4.8%)               | 0                               |                              |
did not significantly influence the time of survival. No perioperative deaths occurred among the patients undergoing completion pneumonectomy.

Using the Kaplan-Meier method, survival curves were calculated for the whole study group (Fig. 1) and depending on the applied treatment (Fig. 2). The mean survival time for the whole group was 15.5 months. The median survival times for patients treated with chemotherapy, chemoradiotherapy, and surgical treatment amounted to 11.1 months, 14.4 months, and 27.1 months, respectively. Comparison of the survival curves revealed statistically significant differences both between the group treated with surgery vs. the group undergoing conservative therapy \((p = 0.00001)\) and between the groups treated with surgery, chemotherapy, and chemoradiotherapy \((p = 0.00001)\). The best long-term results were observed among the patients who underwent surgical treatment. In the conservative therapy group, the probability of achieving 5-year survival was significantly higher in the case of multimodality therapy (chemoradiotherapy).

Focusing the analysis solely on patients with N0 and N1 disease demonstrated significantly longer survival among surgery patients (there were no patients with N2 disease in the group undergoing completion pneumonectomy).

**Discussion**

According to various authors, local recurrence after the surgical treatment of NSCLC is observed in 5-50% of cases; its incidence depends primarily on the stage of cancer at the time of surgery \([4, 9]\). Factors predisposing to recurrence include, among others, metastasis to N1 lymph nodes (primarily station 10), infiltration of lymphatic vessels, and infiltration of visceral pleura. The mean time from surgery to the diagnosis of recurrence amounts to 12 months, and the mean survival time is 8-18 months \([4, 9]\). The guidelines of the National Comprehensive Cancer Network published in 2014 recommend treating patients with surgery whenever possible if local recurrence is confirmed. If radical resection is not possible, the treatment of choice should be radiochemotherapy. Our study is among the few to analyze three different methods of treating local lung cancer recurrence both in terms of the number and type of complications and the length of patient survival. Although it is not a randomized prospective study, but only a retrospective analysis, it may still shed light on the efficacy and safety of each of the analyzed treatment methods. The number of surgically treated patients in the study group is low \((n = 21)\), but similar rates of completion pneumonectomy are reported by authors from other centers, where the number of analyzed cases rarely exceeds 50 \([7, 10, 11]\). They point to the fact that in most patients with recurrent lung cancer, there are contraindications for repeat surgery (recurrence location precluding radical procedures, mediastinal lymph node involvement, high operative risk associated with concomitant disorders, results of functional tests disqualifying the patient from pneumonectomy).

In view of this, can completion pneumonectomy still occupy a prominent role in the treatment of local lung cancer recurrence, considering that it is characterized by higher rates of mortality and serious complications in comparison with standard lung excision procedures? Some authors question its role, pointing firstly to its high rates of perioperative mortality reaching 21% \([1, 11, 12]\). Even leading centers such as the Mayo Clinic report the rates of complications after these procedures to exceed 62% \([12]\). The technical challenge and the extent of the operative trauma can be attested by the relatively large intraoperative blood loss ranging from 700 to 2400 ml in various publications and the mean hospitalization time reported by most studies to exceed 16 days \([11, 13]\). Terzi underscores that most perioperative deaths are caused by intra- or postoperative bleeding \([14]\). In our material, the mean intraoperative loss of blood amounted to 560 ml, and the hospitalization lasted...
15.2 days on average. On the other hand, according to the results of the largest multicenter examination concerning completion pneumonectomy (165 patients) published in 2012, the study’s rate of perioperative mortality amounted to 10.5%, while the rate of complications – 55.1% [13]. Some researchers point out that the cardiovascular and respiratory systems adapt better in the case of two-stage procedures (lobectomy followed by completion pneumonectomy) in comparison with single-stage pneumonectomy [8]. No perioperative deaths were observed in our material, which may be associated with the fact that qualification for the procedure was very cautious, especially with regard to the risk of serious respiratory and circulatory complications. Although the rate of complications in the completion pneumonectomy group was high (80.9%), it did not influence postoperative mortality. The difference between the complication rate observed in this study and that reported by other authors (30-62%) may stem from the fact that the analysis of the cited authors included only selected, mostly severe complications [11-15]. The present study considered all observed complications, including postoperative anemia requiring the transfusion of blood (23.8%) or arterial pressure drops requiring catecholamine therapy (33.3%). As in other publications, the most frequently observed postoperative complication was supraventricular cardiac arrhythmias (38.1%) [13, 16]. The reported rate of bronchopleural fistulas after completion pneumonectomy is similar to that after standard pneumonectomy and amounts to 4-13.3%. In our material, a fistula was found in one patient (4.8%). In an analysis by Cardillo, the rate of fistulas was 7.9%, and the occurrence of this complication was not influenced by factors such as the method of closing the bronchial stump (stapler vs. hand sutures), the operated side, surgical access (thoracotomy vs. sternotomy), or the use of induction therapy [13].

In the group of patients undergoing conservative therapy, the incidence of complications was significantly lower (48.3%), and they consisted primarily in neutropenia (16.4%) and anemia requiring blood transfusion (12.9%). Similar results were reported by Canadian researchers assessing the efficacy of chemoradiotherapy in the treatment of local lung cancer recurrence: they noted that neutropenic fever and body weight loss were the most frequent adverse effects [17]. In turn, Kim points to radiation pneumonitis and esophagitis as the most frequent complications after chemoradiotherapy; they occurred in 52% and 62% of patients, respectively, even though the study group included only 21 patients [18].

The prognosis for patients with lung cancer recurrence is usually unfavorable. According to various studies included in the analysis conducted by Fedor et al., the mean survival time from the diagnosis of recurrence does not exceed one year [9]. Although the available literature lacks randomized studies comparing surgical treatment and chemoradiotherapy in patients with local NSCLC recurrence, analysis of long-term results published in retrospective studies indicates that better results are achieved with surgical treatment. The mean survival time after completion pneumonectomy ranges from 25 to 27 months, whereas the rate of 5-year survival from 31% to 44% [10, 15, 19, 20]. In the aforementioned multicenter study by Cardillo, the rate of 5-year survival after completion pneumonectomy amounted to 37.6% and was significantly higher among squamous carcinoma patients as compared with adenocarcinoma patients (5-year survival: 48.9% vs. 23.9%) [13]. In turn, the mean survival time of patients treated with chemoradiotherapy ranges from 11 to 17 months with the rate of 2-year survival reaching 34% [4, 5, 18]. Only Bar’s study reported a higher median of survival after conservative therapy (26.9 months), but the study group included only 30 patients, and only 10% of the tumors were initially classified as stage III cancer [17]. In the present study, the median survival time for the whole study group (independent of the applied treatment method) amounted to 15.5 months and was higher than in the aforementioned study by Fedor. The mean survival time was significantly longer in the surgical treatment group (27.1 months) than in the groups receiving chemoradiotherapy (14.4 months) or chemotherapy (11.1 months). It should, however, be noted that no cases of the N2 disease were initially noted in the surgical treatment group, while, in the conservative therapy group, metastases to N2 lymph nodes were confirmed in 24.1% of cases. Hence the clear focus of other authors as well on the exclusion of metastases in the mediastinal lymph nodes using all available methods (PET/CT, EBUS, EUS) during the process of qualifying patients for completion pneumonectomy.

Conclusions

Despite the significant rate of postoperative complications (mostly circulatory), the long-term results of surgical treatment for local NSCLC recurrence are relatively good. The success of surgical treatment is conditioned on the exclusion of metastasis in N2 lymph nodes. In patients who are precluded from undergoing completion pneumonectomy, combination therapy (chemoradiotherapy) should be considered as it offers a greater chance for long-term survival than chemotherapy, while being burdened with a similar rate of complications.

Disclosure

Authors report no conflict of interest.

References

1. Jungrahmay W, Hasse J, Olischewski M, Stoeben E. Indications and results of completion pneumonectomy. Eur J Cardiothorac Surg 2004; 26: 189-196.
2. Fujimoto T, Zaboura G, Fechner S, Hillejan L, Schröder T, Marra A, Krbek T, Hinterthaner M, Greschuchna D, Stamatis G. Completion pneumonectomy: current indications, complications and results. J Thorac Cardiovasc Surg 2001; 3: 484-490.
3. McGovern E, Trastec V, Pairolero P, Payne WS. Completion pneumonectomy: indications, complications and results. Ann Thorac Surg 1988; 46: 141-146.
4. Sugimura H, Nichols F, Yang P, Allen MS, Cassivi SD, Deschamps C, Williams BA, Pairolero PC. Survival after recurrent non-small cell lung cancer after complete pulmonary resection. Ann Thorac Surg 2007; 83: 405-417.
5. Kelsey C, Clough R, Marks L. Local recurrence following initial resection of NSCLC: salvage is possible with radiation therapy. Cancer J 2006; 12: 283-288.

6. Van Schill PE, Brutel de la Rivière A, Knaepen PJ, van Swieten HA, De-fauw JJ, van den Bosch JM. Completion pneumonectomy after bronchial sleeve resection: incidence, indications and results. Ann Thorac Surg 1992; 53: 1042-1045.

7. Massard G, Lyons G, Wihlm J, Fernoux P, Dumont P, Kessler R, Roeslin N, Morand G. Early and long term results after completion pneumonectomy. Ann Thorac Surg 1995; 59: 196-200.

8. Chataigner O, Fadel E, Yildizeli B, Achir A, Mussot S, Fabre D, Mercier O, Dart-evelle PG. Factors affecting early and long-term outcomes after completion pneumonectomy. Eur J Cardiothorac Surg 2008; 33: 837-843.

9. Fedor D, Johnson W, Singhal S. Local recurrence following lung cancer surgery: incidence, risk factors and outcomes. Surg Oncol 2013; 22: 156-161.

10. Guggino G, Doddoli C, Barlesi F, Acri P, Chetaillie B, Thomas P, Giudicelli R, Fuentes P. Completion pneumonectomy in cancer patients: experience with 55 cases. Eur J Cardiothorac Surg 2004; 25: 449-455.

11. Haraguchi S, Koizumi K, Hirata T, Hirai K, Mikami I, Kubokura H, Shimizu K. Surgical results of completion pneumonectomy. Ann Thorac Cardiovasc Surg 2011; 17: 24-28.

12. Miller D, Deschamps C, Jenkins G, Bernard A, Allen MS, Pairolero PC. Completion pneumonectomy: factors affecting operative mortality and cardio-pulmonary morbidity. Ann Thorac Surg 2002; 74: 876-883.

13. Cardillo G, Galetta D, van Schil P, Zuin A, Filosso P, Cerfolio RJ, Forcione AR, Carleo F. Completion pneumonectomy: a multicentre international study on 165 patients. Eur J Cardiothorac Surg 2012; 42: 405-409.

14. Terzi A, Leonardoni A, Falezza G, Scanagatta P, Santo A, Furlan G, Calabrò F. Completion pneumonectomy for non-small cell lung cancer: experience with 59 cases. Eur J Cardiothorac Surg 2002; 22: 30-34.

15. Volotolini L, Paladini P, Luzzi I, Ghiribelli C, Di Biscaglie M, Gotti G. Iterative surgical resections for local recurrent and second primary bronchogenic carcinoma. Eur J Cardiothorac Surg 2000; 18: 529-534.

16. Seok Y, Lee E, Cho S. Respiratory complications during mid- and long-term follow-up periods in patients who underwent pneumonectomy for non-small cell lung cancer. Ann Thorac Cardiovasc Surg 2010; 16: 335-340.

17. Bar J, Ng D, Moretto P, Goss GD, Sun A, Maccar A, Laurie SA, Leighl N, Nicholas G. Chemoradiotherapy for locoregional recurrence of non-small cell lung cancer after surgical resection: a retrospective analysis. Clin Lung Cancer 2013; 14: 200-204.

18. Kim M, Kim J, Lee J. Radiotherapy for locoregional recurrent non-small cell lung cancer. J Lung Cancer 2011; 10: 37-43.

19. Campione A, Ligabue T, Luzzi L, Ghiribelli C, Paladini P, Volotolini L, Di Biscaglie M, D’Agata A, Gotti G. Late outcome and perioperative complications for surgery of locally recurrent bronchogenic carcinoma. J Cardiovasc Surg 2005; 46: 515-518.

20. Hotta K, Sekine I, Suzuki K, Kondo H, Asamura H, Sumi M, Yamamoto N, Kunitoh H, Ohe Y, Tamura T, Kodama T, Saijo N, Tsuchiya R. Distant failure after treatment of postoperative locoregional recurrence of non-small cell lung cancer. Thorac Cardiovasc Surg 2003; 51: 283-287.