The Peculiarities of Surgery for Advanced Stage IIIB Lung Cancer.

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ABSTRACT. 50 patients underwent surgery as initial treatment for advanced complicated non-small-cell lung cancer (NSCLC). 1 chest organ or structure was invaded in 29, more than one - in 21. Complete tumour excision was achieved in 47 (94%) patients. Bronchial stumps/anastomoses were routinely closed by interruptive manual suture plus pedicled pericardial, omental, or muscular flaps. 22 reconstructive procedures were performed simultaneously. Life quality was evaluated according to Karnofsky scale before and 2 months after surgery. **Results:** Postoperative mortality made up 16%, morbidity - 34%. There was no one bronchial stump/anastomotic dehiscence. Survival rate at 12 months postoperatively made up 100%, at 24 months - 32%. Median life quality made up 46 before surgery and 87 at 2 months postsurgically for chest wall invasion, 26 and 85 respectively for other kinds of invasion. **Conclusion:** Life quality improvement after surgery for advanced NSCLC vindicates mortality and morbidity rates. Manual interruptive suture plus pedicled pericardial/muscular flap prevents bronchial stump/anastomotic dehiscence and is mandatory in pneumonectomies for Stage IIIb NSCLC. Those may require great vessel reconstruction, automyoplasty, alloplasty, pericardioplasty, omentoplasty. The only strict contraindication for surgery in Stage IIIb NSCLC is functional inoperability.

1. The role of surgery in treatment of advanced lung cancer.

1.1. Historical aspects. The history of surgery for pulmonary neoplasms ascends to the first half of the XIXth century. On March 4, 1821, Anthony Milton (Augusta, the North-American United States) successfully removed *en bloc* a tumor of the lung and the chest wall. The same procedure was successfully repeated by Kronlein (Zurich, Germany) in 1884, and then by Ch.Cedillot (1887) and Muller (1887, 1888). After their publications, in 1895, Jule Emile Pean (Paris, France) reported his own successful pulmonary resection with partial pleurectomy which he performed for a malignant invasive tumour of the lung in 1861. Thus, surgery of lung neoplasms was started with combined procedures!

Then, in 1910, Kummell was the first to attempt a pneumonectomy for advanced lung cancer – unfortunately his patient died 3 days after surgery. All the following attempts

of surgery for lung cancer, such as those of Davies (1912), Maier (1915), Hinz (1922), Churchill (1930), Archibald (1932) were also unfortunate except 6 cases of successful limited atypical lung resections (Sauerbruch, 1920; C.I.Allen, F.J.Smith, 1932; Tudor Edwards, 1932; E.D.Churchill, 1933). In Russia (the USSR), a number of lobectomies for lung cancer was reported in 1938 by B.E.Linberg, in 1941 by A.V.Vishnevsky.

Then came 1933 when E.A.Graham and J.S.Singer performed their world-first pneumonectomy for lung cancer which occurred to be more than successful: not only did the patient survive surgery - he survived his surgeon as well. The same year 1933, reports of W.F.Rienhoff came out, which was the beginning of modern surgical oncological pulmonology. First successful pneumonectomy for lung cancer in Russia (the USSR) was reported by A.N.Bakulev in 1946.

The tendency towards extending of surgical aggression against invasive malignancies may be tracked throughout the historical progress of thoracic surgery. In 1943, A.Brock became the first to perform a pneumonectomy with intrapericardial division of pulmonary vessels and pericardial resection due to invasion, which may be regarded as the first combined pneumonectomy executed in modern technique. Later on, A. Abbot (1950), J. Mathey (1951), W. Cahan (1951) contributed much to formation of modern surgical approaches to locally-advanced lung cancer. In 1961, Abbruzini invented additional closure of main bronchial stump with a pedicled pericardial flap (published in 1963), which appeared to be of remarkable importance in surgery of advanced lung cancer.

1.2. Relevance of the problem. In our days, the problem of optimal therapy for advanced forms of malignant pulmonary neoplasms remains actual, first of all due to the leading place of lung cancer in morbidity and causes of death in most developed countries [1, 2, 3, 4]. This is almost similar in modern Russia where lung cancer became the first (28.9%) among all malignancies in male and the 7^{th} (5.6%) – in female patients by the last decade of the XX century. Incidence of lung cancer in Russia is now about 82.3 per 100,000 of population for men and 13.7 per 100,000 in women.

This high frequency of lung cancer is combined with modest and late clinical presentation, difficulties of wide screening, and lack of methods for early diagnosis [5]. As a result, 3 of every 4 cases of lung cancer appear to be either locally advanced or generalized at the moment of primary diagnosis [4] which makes their treatment a hard and controversial task. Thus, in St.Petersburg (Russia), 1-year mortality rate for lung cancer exceeded 55% in 1994, and in Great Britain it is known to be about 80%.

1.3. Controversies of surgery. In general, surgery remains the most effective method in therapy of lung cancer, and also presents the opportunity to apply chemotherapy more effectively in adjuvant regimen [6, 7, 8]. Yet, its application remains quite limited in treatment of advanced (Stage IIIB-IV) disease. Up to our days, Stage IIIB lung cancer is regarded as inoperable in the majority of surgical clinics of the world: in the cases of N2-3, surgery is prevented by poor long-term results due to generalized disease; as for T4, the chief obstacle appears to be local invasion. Surgery for T4 lung cancer demands multiple resections of invaded chest organs and structures, simultaneous complex reconstructive procedures, and is known for its high morbidity and mortality rates [9, 10]. 1/3 of mortality has been reported to be caused by bronchial stump dehiscence leading to bronchial fistula and pleural empyema [11, 12].

1.4. Potentials of alternative treatment methods. Standard alternatives for surgery in advanced malignancies are chemotherapy for systemic treatment and radiotherapy for local tumor control. Yet, the potential of these toxic methods is rather modest in lung cancer, due to its poor sensitivity to both. Chemotherapy has not yet been reported to produce high effect in advanced non-small-cell lung cancer [13]. This is the same with radiotherapy, and combination of both.

The potential of another, minor invasive alternative - modern interventional pulmonology - is limited to reopening and maintaining of major airway in bronchial cancer, though for a comparatively long time, but this does not prevent extraluminal tumor growth and invasion of neighboring organs and structures.

1.5. Complicated advanced process. The specific group of patients with complicated locally-advanced lung cancer deserves a special comment. These are patients with severe complications of inflammatory or purulent (destructive pneumonitis, secondary pulmonary abscesses or gangrenes, pleural empyema), ventilatory (pulmonary atelectasis, major airway obstruction, respiratory failure), and hemorrhagic type (haemoptysis), or intractable pain. Purulent infection prevents them from chemotherapy; haemoptysis is a contraindication for radiotherapy; due to complications, a lot of them are in poor general condition which does not allow to apply any kind of toxic methods of therapy. Thus, there seems to be no way for treatment of this large group of severely diseased except symptomatic therapy only – at least within the limits of contemporary standards of care. At the same time, median survival rate of patients with lung cancer without surgery and / or other kinds of specific anti-tumor treatment varies from 3 to 9 months only [14], to say nothing of the life quality levels in presence of the complications mentioned above.

1.6. Benefits and prospects of surgery. But it is well-known that Stage IIIB of lung cancer is heterogenous, and the immediate causes of death for these patients are different [15]. While the patients referred to Stage IIIB due to N criterion die mostly of generalization of the disease, those with T4 are known to die rather of complications caused by local invasion [15]. This fact might vindicate more aggressive surgical approach as alternative methods fail to provide local control comparable with that achieved by surgery [16]. Advocates of active surgery for this group underline its advantages, such as effective local control [17], prevention of local recurrence [16], and at least good palliation and prompt elimination of tumor-related complications [15].

As for long-term results, the possibility of prolonged life duration and good life quality level after successful surgery was shown for the patients with T4 NSCLC in a number of recent papers [15, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27]. In particular, there are reports of significant prolongation of life duration after pneumonectomies combined with pericardial, myocardial, and pulmonary trunk resections [28, 29], resections of superior vena cava and thoracic aorta [29, 30]. For cases of lung cancer with chest wall invasion, surgery by radical plan was also shown to be superior to conservative treatment in elimination of chronic pain, prolongation of life duration, and improvement of its quality [31, 32, 33, 34, 35, 36, 37]. Based upon these data, E.Bardet et al. [38] claim surgery to be indicated for treatment of locally-advanced non-small-cell lung cancer, including T4 and N2 cases. The advantages of surgery were demonstrated also for some N3 ones [39, 40].

Moreover, some authors consider that certain patients with advanced lung cancer not only in Stage III but even in Stage IV may still benefit from pulmonary resection – even not radical but tumor-reductive, - particularly when reduction of their somatic complaints can be achieved [41, 42, 43]. Benefits of surgery were recently demonstrated even for lung cancer with malignant pleuritis and pericarditis [44] previously considered absolutely inoperable.

Another highly important and disputable aspect of surgery for advanced lung cancer is mediastinal lymphatic dissection versus sampling. Routine systematic mediastinal lymphatic dissection aimed to reveal and remove any chance of micrometastases in N2 and N3 lymph node groups has been advocated since 70ies (Kolesnikov I.S. et al., 1975) till our days [28, 45, 46, 47]. A number of works published in the last decade of the past century demonstrate higher life duration after prompt and thorough mediastinal lymphadenectomy when compared with simple pneumonectomy [48, 49].

Thus, we may assume that despite development of modern chemo- and radiotherapy, there still are certain reasons and grounds for extension of operability limits in advanced lung cancer. Yet, extended combined surgical procedures in locally-advanced and often complicated lung cancer may bear a comparatively high morbidity and mortality rates. On the other hand, local invasion of lung cancer is a challenge to surgical technique demanding wide dissection of the mediastinum, multiple resections of chest organs and structures, and simultaneous complex reconstructive procedures.

2. Authors' experience

Our surgical team has been dealing with extended and combined surgery of a broad spectrum of advanced thoracic and abdominal solid malignant tumors since 1994 [8]. At the moment, our experience covers 50 cases of Stage IIIB (T4) non-small-cell lung cancer who underwent combined therapy including surgery by radical plan as initial treatment.

2.1. Materials and methods. 10 female and 40 male patients were aged from 32 to 77 (mean 59.9+-1.8 years). In 21, the tumor was localized in the left lung, in 29 – in the right one.

All the patients presented with local tumor invasion. In 29 cases, the primary tumor spread to one of the neighboring chest organs and structures; in 21, the tumor involved more than one organ or structure. Pericardium was invaded in 31 cases, superior vena cava – in 9 (in 4 of them, the tumor also invaded the trachea), chest wall – in 6, right atrium – in 4, muscular layer of the esophageal wall – in 4, thoracic aorta – in 3, subclavian vessels – in 1, brachial plexus – in 1, thoracic vertebra – in 1.

Besides that, 47 (94%) patients presented with severe, often life-threatening complications: haemoptysis; atelectasis with signs of respiratory failure or obstructive pneumonitis; mediastinal compression; superior vena cava syndrome; major airway obstruction; secondary pulmonary abscess or gangrene; pyopneumothorax; pleural empyema. These complications precluded chemo- and radiotherapy in the majority of cases. As for remaining 3 patients (6%), they had no life-threatening complications but did have chronic intractable pain caused by chest wall invasion.

47 (94%) patients underwent combined extended procedures with complete tumor removal: 42 total pneumonectomies (including 4 carinal ones), 3 lobectomies, 2 bilobectomies. Palliative pneumonectomies with incomplete tumor removal appeared only to be possible in 3 cases.

Technical peculiarities of surgery in Stage IIIB lung cancer were the following:

1. Intrapericardial division of pulmonary vessels in central localization of bronchial cancer. A pericardial flap is formed at this stage, preserving its blood vessels, for future covering of the bronchial stump or tracheal suture. If the tumor extends to the intrapericardial portion of right pulmonary artery, it may be transected behind the radix of aorta; in one case, the artery was transected to the left of the radix. If the tumor extends along the intrapericardial portions of pulmonary veins to right atrium, the latter may be resected using either a stapler (“AutoSuture”) or manual suture through the strips. The latter is preferable in case of dystrophy of the atrial wall.
2. We always close the bronchial stump using modified Overholt’s manual suture, provided its length is not less than 5 mm. Additional coverage of the stump with a pedicled pericardial flap is mandatory in our clinic. If the pericardial wall is totally infiltrated by the tumor, we cover the bronchial stump with a pedicled periosteo-muscular flap resecting one rib. In cases of chest wall invasion combined with metastatic pericardial

lesion, we cover the bronchial stump or tracheobronchial anastomosis with a pedicled omental flap.This method was always used in circular tracheal resections.

3. In one patient with total excision of invaded pericardial wall and hemidiaphragm, we reconstructed both with a pedicled flap of latissimus dorsi muscle, using it at the same time to cover the bronchial stump. It appeared necessary to fix the

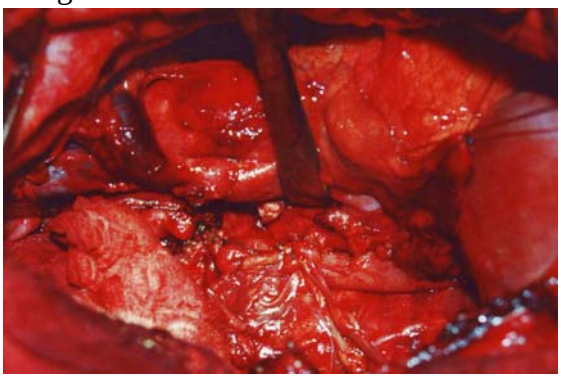

Fig. 1. Main bronchial stump covered with a pedicled pericardial flap.

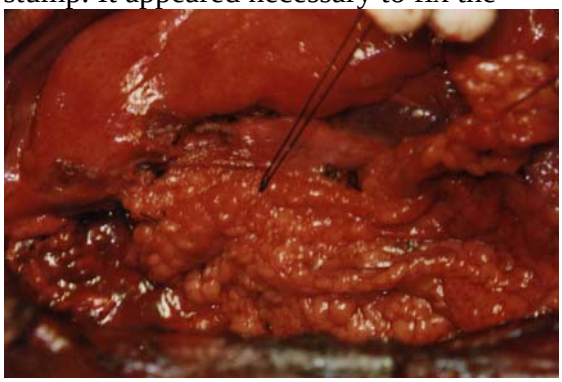

Fig.2. Main bronchial stump covered with a pedicled omental flap.

wedge of resected diaphragm to the ribs with a synthetic strip, in order to prevent enormous mediastinal shift.

4. Superior vena cava invasion required wedge resection in 5 patients and circular resection with polytetrafluorethylene (PTFE) graft reconstruction (Fig. 3) in 5.

5. When major pericardial resection results in a large defect which bears the risk of cardiac luxation, such a defect may be closed with a patch of PTFE mesh (Fig. 3).

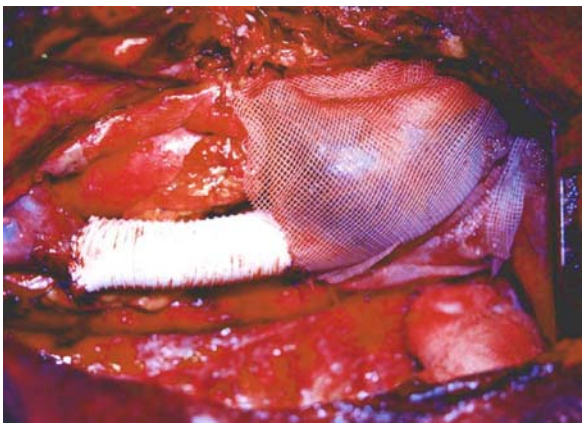

Fig. 3. Reconstruction of resected superior vena cava with an armed PTFE prosthesis; a large pericardial defect is closed with PTFE mesh.

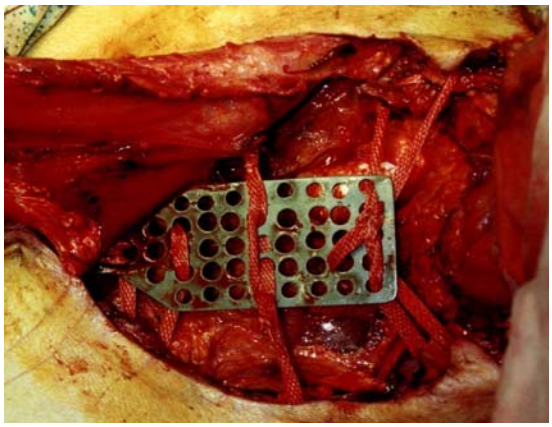

Fig. 4. Complex reconstruction of resected chest wall with a pedicled omental flap, a metal (nickelide-titanium) construction, and a pedicled musculocutaneous flap.

6. Wedge resection of thoracic aorta and brachiocephalic trunk was performed in 2 cases. In one case, after circular resection of invaded descending aorta we performed graft reconstruction using cardiopulmonary bypass.

7. Subclavian vessels were resected in 1 case, with graft reconstruction of the artery and ligation of the vein.

8. In the case of vertebral invasion, bodies of 2 vertebrae were resected and replaced with an autologous bone graft, with posterior corporodesis by a titanium construction.

9. Chest wall after major resection was reconstructed using a complex technique: a pedicled omental flap lining mediastinal organs, plus a metal (nickelide-titanium) construction covered by a pedicled musculocutaneous flap of latissimus dorsi muscle.

10. Mediastinal lymphatic dissection on the side of the tumor location with sampling frozen-section microscopy of contralateral tracheobronchial nodes was obligatory. Detection of metastases in the contralateral tracheobronchial lymph nodes was an indication for contralateral mediastinal lymphatic dissection.

2.2. Results. Postsurgical N criterion appeared to be N0 in 6 (12%) patients, N1 - in 10 (20%), N2 - in 29 (58%), N3 - in 5 (10%).

Postoperative non-lethal morbidity made up 32% (16 patients), mortality -16% (8 patients). 2 patients died of pneumonia in the single lung, 2 - of pulmonary embolism, 1 - of myocardial infarction, 3 - of cardiac failure. There was no one bronchial stump dehiscence.

1-year survival rate made up 100%, 2-year - 32%, maximal life duration – 5 years. 7 patients are alive at the moment. Among the patients with chest wall invasion, median life quality change (Karnofsky scale) was from 46 before surgery to 87 2 months postsurgically, among those with chest organs involved - 26 and 85 respectively.

2.3. Conclusions. Improvement of life quality after surgery for advanced NSCLC vindicates comparatively high mortality and morbidity rates.

Effective prevention of both bronchial stump and tracheobronchial anastomosis dehiscence is achieved by manual interruptive suture with additional closure by pericardial or muscular flaps with good blood supply. This technique is mandatory in pneumonectomies for Stage IIIB lung cancer.

Surgery for Stage IIIB (T4) lung cancer may require great vessel replacement; chest wall, pericardial, and diaphragmatic defect closure; automyoplasty, alloplasty, pericardio- and omentoplasty.

The only contraindication for surgery in locally advanced Stage IIIB non-small-cell lung cancer seems to be functional inability of a patient to tolerate surgery.

Relying upon the published data, as well as upon our own experience, we really can’t but agree with P.Dartevelle that "it is the duty of the community of thoracic surgeons to do everything possible for extension of surgery for T4 non-small-cell lung cancer because the alternative methods of treatment available at the moment cannot be compared with surgery by long-term results".

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