

## **Pneumonitis after bronchoplastic surgery in stage I lung cancer**

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*From the year 1965 to 1990 1959 patients underwent complete resection for primary lung cancer. In 910 cases stage I was histologically proved. 827 (90.9%) patients were observed 5 years after treatment, 551 (60.3%) – 10 years. Following bronchoplastic lobectomy without irradiation in 4.5% cases local recurrence was observed, following this operation combined with irradiation – 1.5%. After lobectomy and radiation therapy (350 cases) remote lesions of the lung were observed in 20% without any impact of bronchoplasty. Following conservative resection (less than lobectomy) the rate was 12.8% ( $p < 0.09$ ). Remote lung lesions correlated with the incidence of bronchial obstruction. Survival of patients in complete remission depended on lung parenchyma volume sacrificed. Pneumonitis had not directly influenced survival in remission.*

**Key words:** lung neoplasms – surgery; lung diseases, interstitial

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### **Introduction**

Approximately 70% of stage I lung cancer patients survive at least 5 years. The problem of quality of their life is growing more and more insistent. So the fundamental principles in modern management (early diagnosis, organ-preserving treatment with multidisciplinary approach and second primary cancer screening) have not been yet thoroughly estimated in pulmonary oncology.<sup>1</sup>

Irradiation of the lung produces two histologic phases of damage. Radiation pneumonitis appears within 6 months after treatment. It is

characterized by edema, deposition of fibrin-like material in the alveolar spaces forming hyaline membranes and degeneration of epithelial cells lining the alveolar walls specifically type II pneumocytes. Consequently, the predominant lesions is a progressive diffuse fibrosis, multiple microatelectases, multifocal obliteration of the air spaces and replacement of the lung parenchyma with scar tissue. Secondary viral and bacterial infections produce refractory chronic pneumonia. These variety of atypical inflammation can hardly be distinguished from irradiation pneumonitis, the first phase of the complication, especially in combination with surgery. Terminology of late chronic lung lesions and atypical pneumonia (pneumonitis) has not been clearly set up.<sup>1</sup>

For many years we were greatly interested in optimal strategy in the treatment of early lung cancer. In order to prevent the local

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recurrences after bronchoplastic and conservative resections we used preoperative (PreRT) and postoperative external irradiation (PostRT). The remote iatrogenic complications and concomitant diseases were studied for more than twenty years.

Thoracic surgeons, radiologists and cancer practitioners should be made aware of, and familiar with setbacks of organ preserving treatment. We will try to share some experience that seems to be important not only for radiologists, but also for broad specter of medical specialists.

### Patients and methods

From 1966 to 1990 complete resection was carried out in 1959 cases of lung cancer. In 910 patients stage I was pathologically proved. Carcinoma in situ – 3 (0.3 %), T1 – 375 (41.2 %), T2 – 532 (58.5 %) cases.

The primary lesion localization, histology and sex ratio had no peculiarities. The analysis was based on the patients status at the end of April 1993. Survival was counted according Kaplan-Meier and Fisher methods with the use of computerized data base (FoxPro). 415 patients were alive including 336 in complete remission and 29 with recurrences.

From the year 1983 we used prospective randomization for three regimens of management: surgery, PreRT, PostRT. Methods of treatment are provided in Table 1.

**Table 1.** Stage I lung cancer: number of case and treatment regimens; in brackets – PreRT+PostRT.

Surgery	Irradiation			Sum
	None	PreRT	PostRT	
Conservative	41	19 (15)	64 (15)	139
Lob-Bilobectomy	277	147 (17)	224 (17)	665
Pneumonectomy	42	30 (6)	28 (6)	106
Total	360	196 (38)	316 (38)	910

Central cancer was observed in 335 patients. Lobectomy mainly with bronchial resection underwent 223 (66.3 %), segmentectomy with bronchoplasty 6 patients. Bronchoplastic seg-

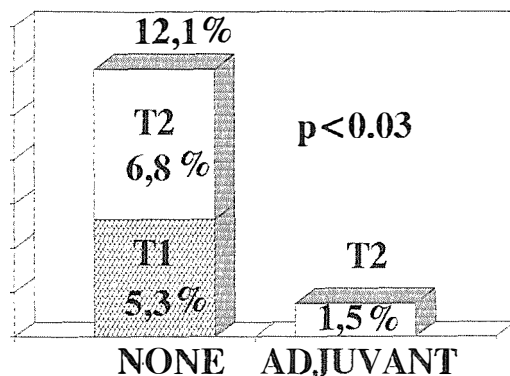
mentectomy technique with original automatic suture was presented elsewhere.<sup>1,2</sup>

Lobectomy with bronchial resection in central lung cancer was performed in 271 cases. Approximately 80 % of wedge and sleeve resections were connected with right upper lobe bronchus and the least of bronchoplastic operations – with left lower lobe bronchus.

PreRT with betatrone 25 MeV or telecobalt therapy was completed in 550 cases according to 3 protocols: total dose – 40–45 Gy (2–2.5 Gy daily fractions); total dose – 36 Gy (3 Gy in 12 fractions); single dose 7.5 Gy with thoracotomy on the next day. The irradiated volume included hilus, bifurcation and paratracheal zone on the side of the lesion. Lung resection was practiced 3–4 weeks following completion of radiation therapy. PostRT was accomplished in 512 cases. In 38 cases of PreRT (7.5 Gy) added PostRT (30 Gy).

### Result

Definite local effect of adjuvant irradiation was observed in patients subjected to bronchoplastic and conservative procedures. Following bronchoplastic lobectomy without irradiation in 99 cases of central stage I lung cancer 5 (4.5 %) local recurrences were observed, after this operation combined with radiation therapy (124 cases) – in 1 (1.5 %). The difference in the rate of local recurrences is evident in T1 and T2 tumors (Figure 1).



**Figure 1.** Rate of local recurrences following bronchoplastic lobectomy with and without adjuvant therapy in stage I lung cancer.

But this gain was paid by radiation pneumonitis. The rate of remote lesions of the operated lung was studied after lobectomy as typical resection in stage I peripheral and central lung cancer. Combined treatment completed in 350 patients, including 140 with wedge or sleeve resection of the bronchus. Following bronchoplastic procedures lesions of the preserved lung lobe was found in every tenth patient. Bronchoplasty generally had no impact on the rate of pneumonitis (Table 2).

**Table 2.** Incidence of pneumonitis following lobectomy and bronchoplasty ( $p>0.05$ ).

Remote lesion of the lung	L o b e c t o m y	
	No bronchoplasty	With bronchoplasty
Fibrosis & mild clinical symptoms	2.4%	2.1%
Fibrosis & marked clinical symptoms	11 %	7.8%
Abscesses	1.4%	2.8%
Bronchitis	3.8%	4.3%
Bronchiectases	0.9%	2.1%

Early postoperative atelectases and pneumonia had no definitive connection with remote lung lesion on the diseased side. In 53 patients with these postoperative complications remote lung lesions were observed in 9 (15.2%) cases. Of the 613 patients that had no complications after lobectomy, pneumonitis was detected in 76 (12.4%) cases ( $p>0.05$ ).

There was no significant difference in the incidence and character of pneumonitis after PreRT and PostRT. The rate of lung lesions was somewhat higher following 36 Gy total dose regimen (3 Gy fractions) or application of betratrone (the difference is not significant). After irradiation of central and peripheral cancer the results were nearly the same. We failed to demonstrate any difference in late unfavorable effects of irradiation in central and peripheral lung cancer.

The most important factor affecting the risk of pneumonitis after partial resections were complications in the anastomotic or bronchial

stump area (granulations, deformations, scars). In 363 cases of lobectomy without bronchial resection in 11 (3%) emerged distortions and stenoses of the lumen. After 250 bronchoplastic lobectomy these complications were detected in 12% cases ( $p<0.001$ ).

Late lesions of the preserved lung lobe after bronchoplastic procedures were observed without any irradiation as well, but their character and severity differed (Table 3).

**Table 3.** Incidence of pneumonitis following lobectomy with PreRT or PostRT.

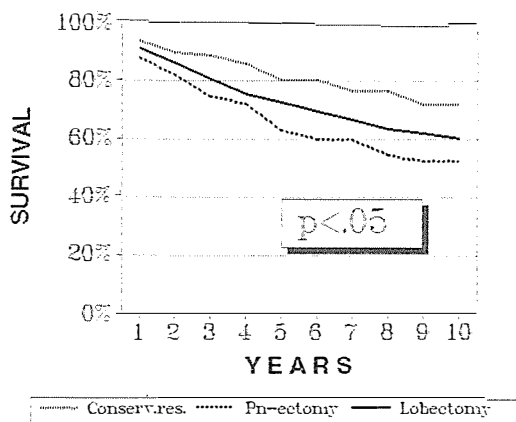
Remote lesion of the lung	B r o n c h o p l a s t y		p
	No irradiation 110 pts	With irradiation 140 pts	
Fibrosis & mild clinical symptoms	2.7%	2.1 %	<0.12
Fibrosis & marked clinical symptoms	0.9%	7.8%	<0.01
Abscesses	0	4%	<0.07
Bronchitis	1.8%	4.3%	>0.05
Bronchiectases	0	2.1 %	>0.05

The rate of remote pneumonitis in patients with bronchial passage disturbances was 72.7%, without any dependence on the type of surgery. In patients that had no complications this rate was 10.5% ( $p<0.001$ ).

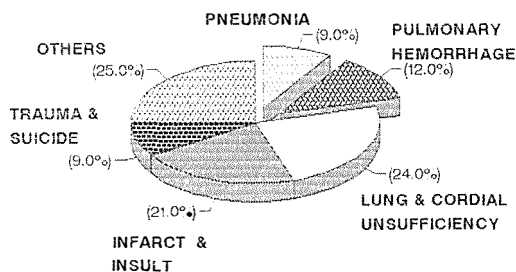
We failed to demonstrate any statistically significant difference in the rate of remote lung damage in connection with method of bronchial resection, but after wedge lobectomy the patients had some more complications than after sleeve resection. It was influenced by frequency of bronchial curve at the anastomotic area.

Survival of patients in complete remission depended on the volume of sacrificed lung parenchyma (Figure 2).

In order to find out the influence of pneumonitis on fatal concurrent diseases we considered the causes of noncancerous deaths of stage I lung cancer patients. The results are presented in Figure 3. There were no obvious differences from natural mortality of the general population. Rate of infectious lung complications are not of primary importance. Four patients had



**Figure 2.** Survival of stage I lung cancer patients in complete remission after conservative surgery, pneumonectomy and lobectomy.



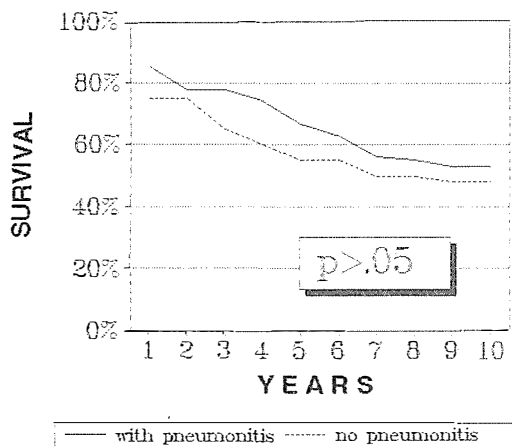
**Figure 3.** Noncancer causes of death after curative treatment of stage I lung cancer.

remote fatal pulmonary hemorrhage following sleeve lobectomy. In three of them there were no signs of pneumonitis or definite endoscopic disturbances of the anastomotic area before initial hemoptysis began.

Among patients that had died of heart and lung insufficiency there were some cases of pneumonitis. But in our series survival of the patients with remote pneumonitis was somewhat better than in group without this complication (Figure 4).

### Discussion

Most of investigators are in consensus that curativity of bronchoplastic lobectomy is com-



**Figure 4.** Survival of stage I lung cancer patients with and without pneumonitis in complete remission.

parable with that of pneumonectomy, but the quality of life is significantly better. Meanwhile the rate of local recurrences after organ-preserving surgery is rather high. The average incidence of noncancerous stenoses – 10%.<sup>3-4</sup>

We have used PreRT and PostRT from the early 1960th.<sup>5</sup> Few authors investigated the adverse effects of irradiation in combination with bronchoplastic resections.<sup>6,7</sup> But their experience in stage I lung cancer management was not enough to make any definite conclusions.

Both radiation reactions and common pneumonitis manifest in productive cough and fever. Radiological investigation reveals the diffuse densities of operated lung, multiple subsegmental atelectases and shadows of inflammation, local fibrosis of pleura. Then follows the productive alveolitis, fibrosis of septae and exudate organization. In cases of marked infection the atypical chronic pneumonia, bronchiectases, abscesses develop. In these circumstances one can hardly differentiate the adverse effect of irradiation and impact of surgical trauma. In most severe cases these patients need repeated hospitalizations for unspecified treatment.

The important role in prevention of postoperative pneumonitis plays the improving of surgical technique and the use of absorbable sutures in constructing the bronchial anastomosis. Complications in the anastomotic area were reported

in 12 % of cases.<sup>3-4</sup> In contemporary series the rate is to be lower.

The explanation of relatively good survival of patients with pneumonitis is difficult to find out. One could presume that in group with this complication were gathered the cases with augmented reaction to autoimmune and infectious irritation.

It is worth to remind that by chance the OECI conference on cancer and quality of life was held quite near the place where four and a half centuries ago Theophrast von Hugenheim named Paracelsus began his medical practice. He was the pioneer of prevention and chemotherapy of lung cancer. Who knows, maybe his methods of improving performance status were more effective than ours. He lived quite near Bled – in Villah, former Corinthia. It is high time to suggest to our hospitable Slovenians and dear guests to inspire his positive medieval principles for the management of lung cancer patients even in complete remission.

### Conclusions

1. Adjuvant radiation therapy decreases the probability of local recurrences after bronchoplastic resections in stage I lung cancer.

2. Pneumonitis is the major handicap of organ-preserving treatment. Remote lesions of the preserved lobes after combined treatment occur in 10–20 % cases of bronchoplastic resections.

3. Stenoses and deformation in the bronchial anastomotic area happen in 7–15 % of patients. This remote complication do not significantly

correlate with the type of bronchoplasty and essentially impact on the rate of pneumonitis.

4. The quality of life of stage I lung cancer patients decreases with the intensity of lung resection.

5. The least morbidity and maximal survival in complete remission of stage I lung cancer patients prove the conservative resections and remote mortality has no direct relation to pneumonitis.

6. Sudden pulmonary hemorrhage, the typical complication of sleeve resection of the bronchus, usually bursts out without pneumonitis or obvious endoscopic disorder of the anastomotic area.

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