PULMONARY PERFUSION SCINTIGRAPHY IN LUNG CARCINOMA AND LOBECTOMY

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ABSTRACT

PURPOSE: Most successful treatment of the lung cancer patients is the surgical resection. Lung perfusion scintigraphy is established method in the complex pre-operative diagnostics of lung carcinoma. It is used for selection of candidates for surgical treatment and in determination of operability and in decision on the operation volume.

MATERIALS AND METHODS: We analyzed retrospectively the value of lung perfusion scintigraphy in 27 cases with primary lung carcinoma who had a lobectomy. Survival probability was calculated by Kaplan-Meier method. The log rank test was used to compare survival rates between groups.

RESULTS: All patients with lobectomy were staged pre-operatively by noninvasive procedures at stages I-IIIA. The lung perfusion scintigraphy demonstrated an enlarged mediastinum at 1 of the patients. Impaired perfusion in homolateral hilum and in the contralateral hilum was found in some of the patients. Changes in affected lung perfusion varied from impaired in different rate to perfusion defect. Perfusion indices at affected lung have mean=48,59%. The survival of patients with Perfusion index less than 49% was mean = 56,333 months, and median = 35 months (3 years). The survival of patients with Perfusion index more than 49% was mean = 99,214 months, and median = 64 months (5.3 years). For I and II stage mean survival time was 120,727 months, and median survival time was 112 months (9.3 years). For IIIA and IIIB stage mean survival time was 48,667 months, and median survival time was 29 months (2,4 years).

CONCLUSION: Lung perfusion scintigraphy is a valuable method in pre-operative diagnosis of lung carcinoma in determination of the extent of perfusion impairment in the affected lung and for determination of functional operability. Lobectomy is possible when perfusion in affected lung is over 41%, but the lower perfusion is not surely a contraindication for lobectomy. The extent of perfusion impairment is proportional to survival rate. Patients with lower perfusion impairments have more than 5 years median survival. In post-operative period perfusion scintigraphy shows re-distribution of perfusion in the healthy lung and in the rest of the operated lung. The survival of patients with lobectomy is corresponding to the clinical stage statistically significant.

Key words: *lung carcinoma, lung perfusion scintigraphy, lobectomy*

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INTRODUCTION

The carcinoma of the lung is the first cause for death worldwide. The most successful treatment of the patients is the surgical resection. The right selection of candidates for surgical treatment is of significant importance for the result and survival of the patients. Lung perfusion scintigraphy is established

method in complex pre-operative diagnostics of lung carcinoma. It has importance in determination of the extent of impairment of lung perfusion from the tumor process and in determination of operability and planning of the operative intervention volume. It is a valuable method together with inhalation scintigraphy for determination of pulmonary function in patients with high risk for lung resection (6).

MATERIALS AND METHODS

We analyzed retrospectively 27 consecutive cases with primary lung carcinoma treated in our departments. Every patient was subject to a standard postero-anterior and lateral chest X-ray, fiberoptic bronchoscopy and to some of them chest CT and video-assisted thoracoscopy (VATS). There were 25 men and 2 women. The age range was from 48 to 69 years. The tumor was located in the right lung in 12 patients and in the left lung in the remaining 14 cases.

Lung perfusion scintigraphy was performed in all patients with ^{99m}Tc- human albumin microspheres with a particle size of 23-45μm (kit Sferotec – Sorin Biomedica-Italy).The injection was applied in supine position, intravenously in bolus, 1ml at an activity of 55-74MBq.The period of examination was between the 15th min and the 2nd hour after injection, at anterior, posterior, lateral and 45° detection, perfusion indices from 6 fields in front and posterior projection were calculated (Picker Dyna Camera 4 Scintillation Camera System – Picker Corporation Nuclear and Ultrasound, USA).

We considered 4 pathological criteria for interpretation of lung perfusion scintigraphy:

1. Absent or minimal perfusion of the affected lung or a perfusion defect less than 1/3 of the affected lung.
2. Perfusion defect and enlargement of the hilum of the affected lung.
3. Enlargement and displacement of the mediastinum in anterior and/or posterior detection.
4. Perfusion defect in the contralateral hilum.

Lobectomy was performed at 27 patients. An invasive staging with mediastinoscopy before lobectomy was not performed. The patients were staged in accordance with TNM classification (13).

Survival probability was calculated by Kaplan-Meier method with the date of resection as a starting point and included deaths from all cases with the presence of censored cases (for which the event has not occurred yet). The log rank test was used to compare survival rates between groups and Wilcoxon rank sum test was used to compare groups by stage and perfusion index (less 49% and higher than 49%). A P value of 0.05 was considered statistically significant.

RESULTS

All patients with lobectomy were staged pre-operatively by noninvasive procedures at stages I-IIIA. The presence of NSCLC histology and performance status (Karnofsky index = 70-80). Four patients were with SCLC, which was diagnosed during the operation and on permanent histological preparation. The lung perfusion scintigraphy demonstrated an enlarged mediastinum in front and posterior at 1 of the patients. Impaired perfusion in a zone with polycyclic outlines in homolateral hilum was present in 12 of the patients, and in 2 – presented with only slightly impaired perfusion. Impaired perfusion in the contralateral hilum was found in 2 of the patients, and in 2 – slightly impaired. Changes in affected lung perfusion varied from impaired in different rate to perfusion defect. Impaired perfusion in only one segment and partially in second one was present in 7 of the patients. Impaired perfusion from slight to severe extent in not more than 3 segments was found in 11 of the patients. Impaired perfusion in more than 3 segments was present in 7 of the patients. Only one patient presented with perfusion defect in the whole lobe. No patient with perfusion defect involving less than 1/3 of the affected lung, a sign indicating unresectability was found (16,17). Perfusion indices at localization in the right upper lobe (7 of the patients) were mean=50,15%, SD=4,7%, SE=2,4%. Perfusion indices at localization in the right lower lobe (4 of the patients) were mean=53,5%, SD=4,3%, SE=2,2%. Perfusion indices at localization in the right lung (11 of the patients) were mean=51,8%, SD=4,5%, SE=1,6%. Perfusion indices at localization in the left upper lobe (8 of the patients) were mean=43%, SD=5,8%, SE=2,6%. Perfusion indices at localization in the left lower lobe (6 of the patients) were mean=49,15%, SD=11,2%, SE=5,6%. Perfusion indices at localization in the left lung (14 of the patients)

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were mean=24,72%, SD=8,7%, SE=2,9%. Perfusion indices at affected lung, independently of right or left lung, were mean=48,59%, SD=7,5%, SE=1,8%.

On Fig. 1 is presented front and posterior projection of lung perfusion scintigraphy before operation of a man, 54 years of age with definitive diagnosis: Left lung carcinoma. Status after left upper lobectomy with circular resection of left main bronchus and anastomosis with left lower lobe bronchus T2N1M0. After bronchoscopy is established full obliteration of left upper-lobe bronchus from blastoma tissue with uneven surface and rose color. From perfusion scintigraphy severely impaired to lacking perfusion in the region of 1, 2 and 3 segments of left lung is found. Perfusion indices: right lung 68%, left lung 32%. Intra-operatively in the lumen of upper-lobar bronchus a tumor is found, originating from short peduncle of 0,5 cm from the bifurcation of its lateral wall, with coral-like shape, occupying the lumen of upper-lobar bronchus as well as the lumens of segment bronchi, without sprouting in regional structures and without macroscopic data for metastases in hilar lymph nodes. Left upper lobectomy is performed with circular resection and anastomosis between left main bronchus and lower-lobe bronchus. Permanent preparation histology: small-cell undifferentiated carcinoma with metastasis from para-aortal lymph nodes.

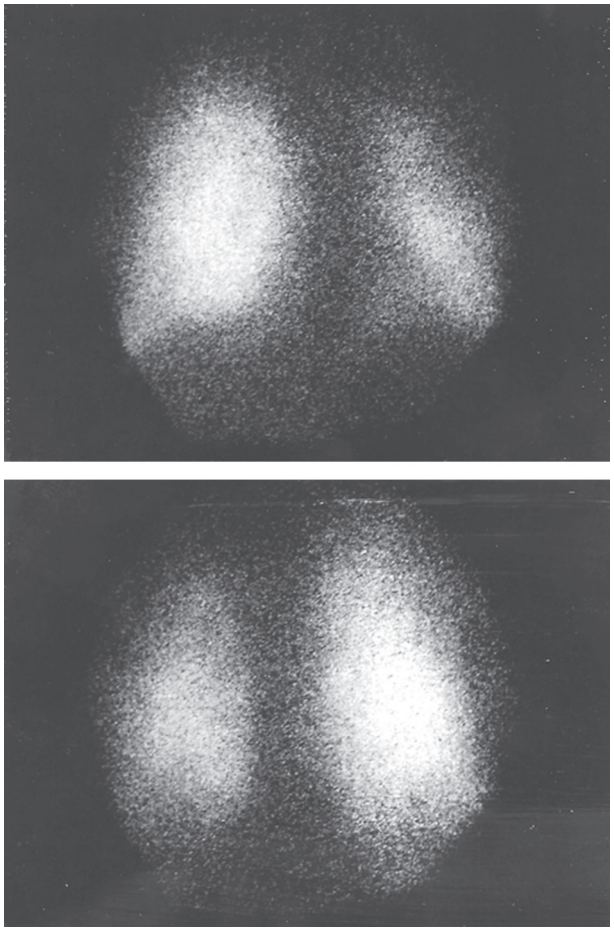

Fig. 1. Perfusion scintigraphy in front and posterior projection before operation of male 54 years of age patient with definitive diagnosis: Left pulmonary carcinoma. Status after left upper lobectomy with circular resection of left main bronchus and anastomosis with left lower lobar bronchus. T2N1M0

Perfusion scintigraphy in 4 of the patients was performed in different term after the operation (from 9 days to 2 years). In post-operative period it is of importance to follow the perfusion of the preserved lung part, especially in case of anastomosis.

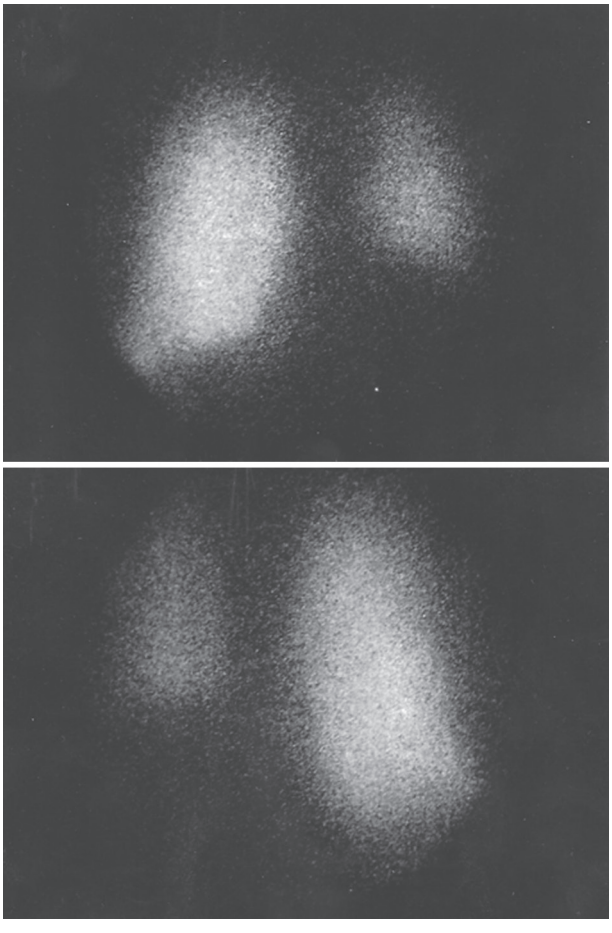

Fig. 2. Perfusion scintigraphy of the patient from Fig 1 on day 9 after operation

On Fig. 2. is shown the lung perfusion in front and posterior projection of the same patient from Fig.1, 9 days after the operation. The functioning lobe after the anastomosis is seen. Perfusion indices: right lung - 81,8%, left lung – 18,2%.

In peripheral carcinoma the smallest size tumor which has influenced perfusion is 4 cm. On Fig. 3 – perfusion scintigraphy before operation in front and posterior projection of a man on 55 years of age with definitive diagnosis: Right lung carcinoma T2N0M0 I clinical stage. Status after upper right lobectomia. Histological result: undifferentiated spinocellular carcinoma. From perfusion scintigraphy is visualized a small round zone with slight to moderate impairment of perfusion in the region of the border of segment 1 and predominantly in segment 2 laterally of right lung in posterior projection. Intra-operatively a solid peripheral tumor is found in the right upper lobe – 4 cm in diameter.

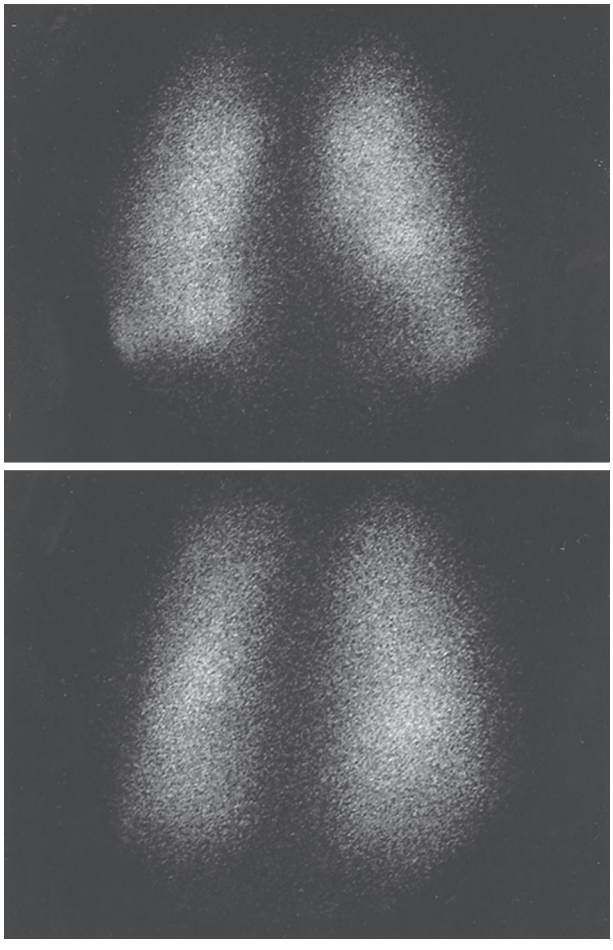

Fig. 3. Perfusion scintigraphy before operation in front and posterior projection of male 55 years of age with definitive diagnosis: Right lung carcinoma. T2N0M0, I clinical stage. Status after right upper lobectomy

Upper left lobectomy was performed on 9 of the patients (33,3%), and in 1 case a circular resection of main bronchus and anastomosis of the lower lobe was performed. Lower left lobectomy was performed on 6 of the patients (22,3%), and in 1of the cases a wedge resection of S3 was performed and on another segmentectomy of S6. Right upper lobectomy was performed on 7 of the patients (25,9%), including 2 cases with additional wedge resection of S6. Right lower lobectomy was performed on 4 of the patients (14,8%). Right lower bilobectomy was performed on one of the patients (3,7%). All patients had systemic lymph dissection of hilar and mediastinal lymph nodes.

Follow up of survival was performed on 23 of the patients, for the rest 4 there were no data available. We established that 3 of the patients have survived until now more than 15 years (187 months), over 18 years (220 months) and over 19 years (236 months). They were staged respectively as stage I (broncho-alveolar carcinoma), stage II (small cell carcinoma) and stage IIIA (squamous cell carcinoma). There is one patient with longest survival – 253 months (21 years and 3 months).

Survival probability was calculated by Kaplan-Meier method with the date of resection as a starting point. Overall mean survival time was 83,879 months, with 95% CI (48,648; 119,091), SE= 17,970. Overall median survival time was 41 months (3,4 years), with 95% CI (22,218; 58,782), SE= 9,583. This means that for a particular patient, the chances of living beyond 3,4 years are 50%. On Fig. 4 is the graph for the process of development of the event in dynamics where censored are survivors. For I and II stage mean survival time was 120,727 months, with 95% CI (65,565; 175,890) SE=28,144 and median survival time was 112 months, with 95% CI (40,79; 183,21), SE=36,332. For IIIA and IIIB stage mean survival time was 48,667 months, with 95% CI (15,267; 82,066), SE=17,041 and median survival time was 29 months, with 95% CI (18,816; 39,184) SE=9,583. The median survival of patients with stage I or II is 112 months (9,3 years). This means that for a particular patient, the chances of living beyond 9,3 years are 50%. The median survival of patients with stage IIIA

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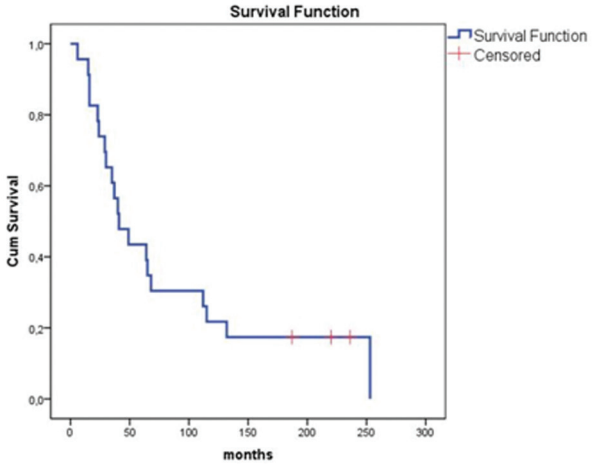

Fig. 4. Survival of the patients after lobectomy independently from the stage where censored are the survivors

or IIIB is 29 months (2,4 years). This means that for a particular patient, the chances of living beyond 2,4 years are 50%. Data for survival according to stages are statistically significant (P=0,019). On Fig. 5 is a graph for survival according to the stage where censored are the survivors.

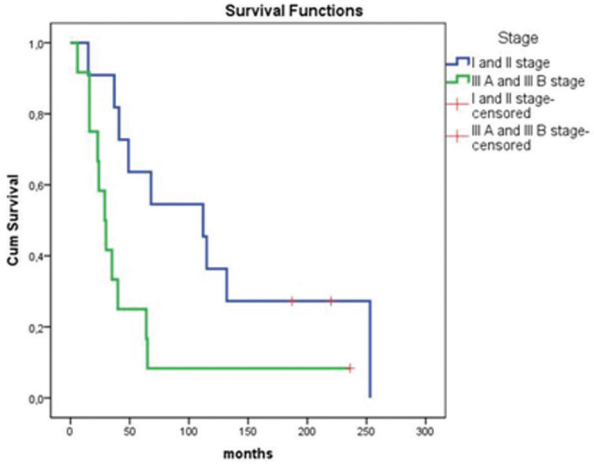

Fig. 5. Survival of the patients after lobectomy grouped by stages (I and II stage) (IIIA and IIIB stage), where censored are the survivors

The survival of patients with Perfusion index less than 49% is mean = 56,333 months, 95% CI (17,386; 95,281), SE=19,871 and median = 35 months, 95% CI (20,391; 49,609), SE=7,454. The survival of patients with Perfusion index more than 49% is mean = 99,214 months, 95% CI (50,693; 147,735), SE=24,756 and median = 64 months, 95% CI (19,998; 108,002), SE=22,450. The median survival of patients with Perfusion index less than 49% is 35 months (3 years). This means that for a particular patient, the chances of living beyond 3 years are 50%. The median survival of patients with Perfusion index more than 49% is 64 monts (5.3 years). This means that for a particular patient, the chances of living beyond 5.3 years are 50%. Data for survival in relation to Perfusion index are not statistically significant (P=0,263).

On Fig. 6 is presented the graph of survival and relation to Perfusion index, where censored are the survivors.

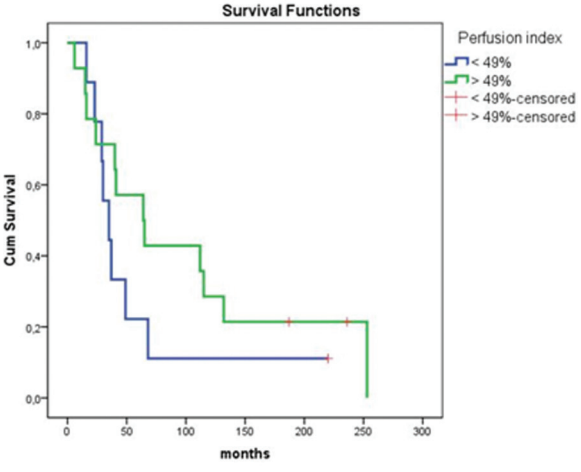

Fig. 6. Survival of the patients after lobectomy with Perfusion index less and more than 49%, where censored are the survivors

DISCUSSION

Levcheva V. et al. (11) in examination of patients with central bronchial carcinoma found defects in perfusion adequate to hypo-ventilated zones, which gives the opportunity to predict the size of the planned pulmonary resection. They consider that diagnostic potential of perfusion lung scintigraphy exclude or indicate additional invasive methods to diagnose pulmonary diseases.

Reduction of perfusion is expressed more than this of ventilation and to high extent in lobar and bilobar cases, where in segment infiltration the values of both are in the normal range. For reduction of pulmonary perfusion and ventilation, more important role has the parenchymal infiltration than bronchial obstruction (21).

The smallest peripheral tumor, which leads to perfusion changes in planar scan is with diameter 4 cm (12), while with SPET a tumor over 3 cm is detected (15). We have found that peripheral tumor of 4 cm induces impaired perfusion.

If the perfusion in the affected lung is over 40%, lobectomy is always possible (17). Lobectomy is impossible in patients with perfusion less than 33% of the whole (14), but decreased perfusion of the involved lung should not be considered a contraindication for resection (14,19). In our series of patients lobectomy has been possible in perfusion of 32% and bilobectomy in perfusion of 25%.

Ali M.K. et al. (1) describes the phenomenon of early disproportional loss of pulmonary function after lobectomy, which is a serious consequence for the patients with borderline pulmonary reserves. Predicting of this transient decline of pulmonary function is important for increase of survival and reduction of incidents of respiratory impairment of these patients. Chenuel B. et al. (2) study the effect of loading with lung perfusion scintigraphy of lung carcinoma patients to predict the post-operative pulmonary function and establish that scintigraphy in rest gives clear picture of lung functional capacity before resection.

Conventional functional tests of the lungs have low importance for predicting the output from the operation in individual cases (8). The accuracy of the quantitative perfusion scintigraphy for predicting the pulmonary function after operation is better than the simple calculation (7). Perfusion scintigraphy is simple and probably the best method for predicting the pulmonary function (19). Each lobectomy has specific magnitude of ventilation loss and perfusion or forced vital capacity in the operated lung. Left upper lobectomy is related with higher functional losses than right upper lobectomy or left lower lobectomy (9). Predicting by scintigraphy of residual functional after lobectomy has greater extent of inaccuracy than in pulmonectomy (5). When lobectomy is combined with inductive chemo- or radiotherapy it is connected to additional pulmonary functional loss in the late post-operative phase (3). Ventilation-perfusion scans can predict postoperative pulmonary function and help evaluate the risk of surgery for lung cancer patients with borderline pulmonary functions (20).

The assessment of regional perfusion is better prognostic indicator than regional ventilation. There is better co-relation between perfusion and survival than between ventilation and survival. Patients with small circulatory changes have 5 year survival of 31,7% (18). In our series of examination median survival time of the patients with small perfusion defects of the affected lung (>49%) is 64 months (5,3 years).

When comparing the median survival according to the stage in our series versus data from Goldstraw P. et al. (4) the data for stage I and II are corresponding – 112 months, but in stage III A and stage IIIB median survival length of our patients is higher. There is a probability that assessment of pulmonary function in the late stages by perfusion indices to have prognostic value for indicating better survival which is observed in our series of operated patients. The emerging from the comparison of data question would be investigated in further analysis.

Carcinomatous lung almost always has decreased perfusion. Only about 6% of the patients with bronchogenic carcinoma has perfusion of more than 50% from the whole lung perfusion with carcinoma. In this small number of patients pulmonectomy would represent high risk and they should be identified before resection (10). In our patients 8 presented with perfusion over 50% in the affected lung from carcinoma, 7 with localization in the right lung and 1 localized in the left lung.

CONCLUSION

Lung perfusion scintigraphy is a valuable method for pre-operative diagnostics of lung carcinoma to determine the size of perfusion impairments in the affected lung and functional operability. Lobectomy is possible when perfusion of the affected lung is over 41%, but lower perfusion is not a clear contraindication for lobectomy. The extent of perfusion changes is proportional to survival. Patients with small perfusion changes have over 5 years median survival. In postoperative period perfusion scintigraphy shows the re-distribution of perfusion in the non-affected lung and in the residual part of the operated lung. The survival of the patients with lobectomy corresponds with clinical stage statistically significant.

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