OUR EXPERIENCE IN THE DIAGNOSTICS AND THERAPY OF PATIENTS WITH SOLITARY PERIPHERAL LUNG TUMOURS

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ABSTRACT
Patients presenting with a solitary pulmonary nodule are often a serious diagnostic-therapeutic problem.
The aim of the present report is to share our experience with VATS in the diagnostics and therapy of patients with solitary pulmonary nodules.

Patients and Methods: Between 2005 and 2009 we performed primary videothoracoscopic tumor resection in 125 patients with peripheral lung tumours.

Results: In 93 (74.4%) of the cases complete successful thoracoscopic resection of the tumor and subsequent intraoperative frozen section histology was accomplished. In the remaining 32 cases (25.6%) various reasons demanded conversion to thoracotomie with wedge resection of the nodule. 54.2% of the removed tumours were malignant and 45.8% benign. In 18 of the patients the intraoperative frozen section histology diagnosis was primary bronchial carcinoma which required to do oncologic resection of the tumor. In 10 patients the intraoperative frozen section histology was unable to differentiate between pulmonary metastasis and primary bronchial carcinoma, and the oncologic resection was performed in another surgical session after the definitive pathomorphologic diagnosis had been available. In 28 of the cases pulmonary metastases of a primary extrapulmonary tumour were removed.

Conclusions: Despite improvement in the diagnostic techniques, only the video-thoracoscopic removal of the lung nodule and its subsequent histological examination enables the definitive diagnosis, solving definitively the problem with benign lesions and indicating appropriate treatment of the malignant pulmonary lesions.

Key words: peripheral solitary lung tumours, VATS

INTRODUCTION
Pulmonary nodules are alterations of unknown origin that are diagnosed on X-ray as a distinct shadow up to 3 cm in diameter surrounded by normal lung parenchyma, and are not associated with atelectasis or lymphadenopathy. More than 80 morphological entities represented as solitary pulmonary nodules varying from benign lesions to primary lung carcinoma or lung metastases are known.

In the recent years, the frequency of newly found solitary pulmonary lesions significantly increased, 30 to 55% of them being malignant according to the literature data. At the top of the list is bronchial carcinoma and its early surgical resection is the only therapy that is currently able to heal patients. This makes early and exact histological diagnosis indispensable.

Only the surgical removal of the nodule gives reliable histological diagnosis. A number of objections against thoracotomy are present, underlying its invasiveness, especially in the presence of benign lesions in young patients who are most commonly asymptomatic.

Perfecting video-assisted thoracoscopic surgery (VATS) in the early 90's made possible performing such interventions by minimally invasive approach and avoiding the disadvantages of thoracotomy.

The aim of the present report was to share our experience with VATS in the diagnostics and therapy of patients with solitary pulmonary nodules.

PATIENTS AND METHODS
One hundred and twenty-five patients who underwent VATS because of uncertain solitary peripheral lung lesions were included in the study. Fifty-six patients underwent surgery in the Clinics of Visceral, Vascular and Thoracic Surgery, University Hospital Aschersleben, Germany between 01.06.2005 and 31.08.2009, and 69 patients - in the Clinics of Thoracic Surgery at the University Hospital Bremen...
men - East between 01.01.2008 and 31.07.2009. In 5 of the patients the alterations were bilateral and bilateral VATS with interval between the contralateral interventions was done. The total number of accomplished interventions was 130.

The mean age of the patients is 62.60 ± 0.95 years. The youngest patient was 17, and the oldest - 82 years old. The investigated group consisted of 53 women and 72 men, the relative share of males (57.6%) being statistically significantly higher than that of females (42.4%) (P < 0.01). Age and sex distribution of the investigated group is presented on Fig. 1.

History of tumor was present in 60 (48%) of the studied patients, while in the rest 65 (52%) it was absent.

All patients underwent standard presurgical preparation, i.e. conventional X-ray, lung CT, fibrobronchoscopy with cytology, lung function testing. In patients with abnormal pulmonary function, cardio-pulmonary exercise testing or perfusion pulmonary scintigraphy was performed. Local recurrence or metastases in other organs were excluded in patients with history of tumours.

The following diagnostic-therapeutic algorithm was followed in the treatment of the described patients:

In all functionally operable patients with newly found solitary lung tumours, situated in the lateral 1/3 of the lung or in the interlobar sulci area, we indicate VATS with tumor resection and intraoperative frozen section histology. Preliminary transthoracic needle aspiration biopsy (TNAB) or positron-emission tomography (PET) in functionally operable patients is considered by us unnecessary and unjustified.

In cases of intraoperative diagnosis of lung carcinoma (LC) a standard method of treatment we adopted was lobectomy with systematic mediastinal, hilar and interlobar lymphadenectomy.

If the solitary lesion turned out to be metastasis, according to the intraoperative frozen section histology, the surgical intervention was completed thoracoscopically, in cases of radically removed tumor. In the presence of multiple metastases we proceeded to thoracotomy, aiming on palpation of the lung and radical resection.

When intraoperative frozen section histology was not sufficient to clearly differentiate between pulmonary metastasis and primary lung carcinoma, we waited for the final pathohistological results. In cases of LC, radical oncologic resection after an interval was done.

Intraoperative frozen section histology diagnosis of benign tumor led to atypical thoracoscopic resection.

In functionally inoperable patients CT-guided TNAB with subsequent histological verification of the tumor was performed. If the latter was inaccessible or TNAB was contraindicated, we verify the dignity of the lesion with PET. If primary LC is proven and metastases of other primary tumor origin are excluded, we apply stereotactic and conventional radiotherapy.

RESULTS

In 84 patients (67.2%) single solitary nodules were removed, in 22 (17.6%) - two tumours were removed, and in 19 patients (15.2%) multiple nodules were resected. The tumor diameter varied in the range between 0.30 cm and 3.00 cm, with mean diameter of 1.41 ± 0.06 cm. The tumours distribution according to their size is presented in Fig. 2.

Out of a total of 177 investigated and removed tumours, 96 (54.2%) were malignant, and 81 (45.8%) - benign, with no statistically significant difference between the relative shares (P > 0.05).

In 93 (74.4%) cases, the lung tumours were thoracoscopically localized and radically resected with intraoperative frozen section histology diagnostics. In the rest 32 (25.6%) cases we proceeded to conventional thoracotomy with atypical resection of the tumor. The most common reasons for that were as follows: massive adhesions in 9 (7.2%) cases, impossible localization in 8 (6.4%) cases,
poor pulmonary function and impossibility to tolerate unilateral ventilation in 4 (3.2%) patients, technical incapability for collapsing the lung in 2 (1.6%) patients.

In 34 (27.2%) of the patients primary lung carcinoma was diagnosed, in 18 of the cases the diagnosis was made by intraoperative frozen section histology. In 13 of these cases, radical conventional oncologic resection in the same surgery session (10 lobectomies, 2 segment resections and 1 bilobectomy) was performed. The remaining 5 patients underwent VATS lobectomy.

In 10 patients, because of uncertain intraoperative frozen section histology diagnosis, we performed oncologic resection in another surgical session (9 conventional and 1 VATS lobectomy).

In the rest 6 patients with LC, due to poor pulmonary function, severe concomitant diseases or pulmonary metastases, the intervention ended as atypical resection without radical oncologic resection.

The distribution of the patients with primary lung tumours, depending on their histology, is presented in Table 1.

Metastases were proved histologically only in 28 (46.6%) of the patients with history of malignancy, and 22 of the metastases were resected thoracoscopically. Primary LC as second primary carcinoma was found in 14 (23.3%) of the patients, and in 18 (30.1%) patients the tumours were benign.

The average duration of the drainages was 2.7 days, and the average hospital stay - 6.4 days.

No intra- or postoperative mortality or intraoperative complications leading to conversion were present. The most common, specific for VATS complications were: pneumothorax in 4 (3.07%) patients, with subsequent performance of re-drainage, 1 case of postoperative bleeding, which caused second VATS and 1 case of postoperative empyema, also with subsequent repeated VATS.

**DISCUSSION**

The presence of solitary pulmonary nodule is always associated with diagnostic and therapeutic problems. According to literature data, these lesions are malignant in 30 to 55% of the cases (54.55% in our series), which demands certain histological diagnosis as soon as possible. Despite this, there is no consensus in the literature concerning a single diagnostic-therapeutic approach in cases of newly found solitary lung tumours, with several possibilities indicated: observation of growth, TNAB, PET or resection of the tumor.

In the early 1980s the introduction of TNAB changed the diagnostic approach in cases of pulmonary lesions. It is moderately invasive and presents material for cytological examination. In the study of Lie et al., the diagnostic accuracy for large nodules (> 1.5 cm in diameter) is 96%, while for small nodules (< 1.5 cm in diameter) is 74%. Therefore, TNAB has good diagnostic accuracy for malignant lesions, but is limited in the assessment of benign lesions. The diagnosis “Absence of malignant tumor cells” in the sample is always indeterminate and gives no guarantees for the representativity of the sample. Comparatively often, up to 30% of the results are false negative and the frequency of complications is relatively high. The most common are: pneumothorax, mediastinal emphysema, as well as A-V fistulas of the intercostal blood vessels. The risk of pneumothorax increases with the increase of the tumor depth, the number of punctures and the presence of pulmonary emphysema or airways obstruction. It is present in 9 to 41% of the cases, 5-12% needing special treatment.

Development of modern technology in the field...
of nuclear medicine and especially the introduction of PET presented new opportunities in the diagnostic approach towards pulmonary lesions. This is a non-invasive method with good diagnostic accuracy, but similarly to TNAB, it is incapable of determining with absolute certainty the disease etiology.\textsuperscript{10} PET sensitivity, specificity and positive predictive values are respectively 93\%, 88\% and 92\% to find malignancy in cases of uncertain solitary lung nodules. The probability for malignancy in positive PET scan is 83\%, and in negative PET scan - 5\%. Inflammatory processes may give false positive, and carcinoid and bronchoalveolar carcinoma - false negative results.\textsuperscript{10}

Despite the diagnostic progress, the only way to acquire certain diagnosis is by histological examination of the resected tumor.\textsuperscript{11}

The problem of the clinician and the patient, confronting surgical intervention is due to the trauma related to the thoracotomy, accomplished in cases of often benign and asymptomatic lesion. The introduction of VATS significantly reduced the surgical trauma, hospital stay, postoperative pain and the time needed for complete recovery of patients’ normal activity, which is a good answer to the above-mentioned problems.\textsuperscript{12}

Our investigation shows that the surgical risk in atypical VATS resection is small with no intraoperative mortality and rare complications. Our opinion on the problem is supported by a study of Baldwin et al, published in 2002\textsuperscript{13} and confirmed by a large series of studies, published in the literature.\textsuperscript{14}

Removal of pulmonary nodules by VATS possesses fundamental advantages compared to various non-invasive or minimally-invasive diagnostic methods, such as bronchoscopy, TNAB, PET, namely the possibility of acquiring fast, certain and definitive diagnosis by intraoperative frozen section histology. In this way, lobectomy following atypical resection during one surgical session is made possible, allowing the performance of oncologically correct surgical therapy in the presence of primary pulmonary carcinoma.\textsuperscript{3} The early surgical resection is the only possible therapy, currently presenting possibility for healing the patients.\textsuperscript{15}

Despite lobectomy being a method of choice in the treatment of lung carcinoma, extended atypical resection is applicable in strictly selected cases. Such examples are older patients with severe cardio-pulmonary diseases, in whom large pulmonary resections are absolutely contraindicated, as well as patients, who had already undergone a contralateral resection, because of a tumor.\textsuperscript{11}

In our study, in 4 of the patients lobectomy was absolutely contraindicated and the surgery ended as atypical resection.

In cases of pulmonary metastasis of an extrapulmonary primary tumor that had been resected radically the surgical removal of the pulmonary lesion is also considered a method of choice.\textsuperscript{15} Most often, in the presence of uncertain lung nodule in patients with malignancy, pulmonary metastasis is supposed, but this is not always the case. In practice, our experience shows that only 28 (46.6\%) of the patients with history of tumours had pulmonary metastases. In 14 (23.3\%) of the patients, a primary LC was found as a second tumor and radical oncologic resection was performed, and in the rest 18 (30.1\%) patients the lesions were benign. In this respect, our data are similar to data reported by Laisaar et al.\textsuperscript{16}

However, whether resection of pulmonary metastases may be done by thoracoscopy is still debated in the literature. The origin of the primary tumor and the number of metastases is indisputably of great significance. The main argument against the application of this method is the impossibility for manual palpation of the lung, excluding the possibility for detection and removal of additional metastases that had not been seen on the preliminary imaging diagnostics.\textsuperscript{17}

On the other hand, in the recent years, the introduction of high definition CTs significantly increased the capabilities of imaging diagnostics allowing detection of tumours up to 4 mm in diameter. Nakas et al.\textsuperscript{18} concluded that “the eyes of the radiologist are not worse than the fingers of the surgeon”.

A number of reports comparing the survival and the recurrence-free interval in patients with pulmonary metastases operated thoracoscopically and conventionally, are present in the literature, finding no significant difference between the two groups.\textsuperscript{16,19-21}

We also think that solitary metastases may be radically resected thoracoscopically. We compensate the impossibility for palpation of the lung parenchyma with control CT of the lungs after 3 months. In the presence of “recurrence” or “forgotten metastases” we perform thoracotomy. In thoracoscopically operated 22 patients we observed no early recurrences.

Literature data suggest that increase of experience in the area of thoracoscopic surgery lead to significant decrease in the indications for TNAB of pulmonary nodules and increase in the indica-
tions for surgical VATS excision. The share of TNAB declined from 90% several years ago to 3% nowadays. TNAB has preserved its value in selected cases, like in patients with extremely high surgical risk, who may be assigned to a corresponding treatment, only based on proven presence of a malignant tumor. We also completely agree with the above-mentioned statement.

CONCLUSIONS

In conclusion, only the surgical resection of the tumor definitively eliminates all diagnostic uncertainties. That is why VATS resection takes a basic place in the diagnostic-therapeutic approach towards uncertain pulmonary solitary nodules and represents the golden standard for patients with that pathology. Its fundamental advantage is the fast, precise and certain diagnosis, with minimal concurrent functional damage and neglectable surgical risk.

REFERENCES

НАШ ОПЫТ В ДИАГНОСТИКЕ И ЛЕЧЕНИИ ПАЦИЕНТОВ С СОЛИТАРНЫМИ ПЕРИФЕРИЧЕСКИМИ ЛЕГОЧНЫМИ ОПУХОЛЯМИ
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РЕЗЮМЕ
Пациенты с периферической круглой тенью в легких часто представляют серьезную диагностическое-терапевтическую проблему.

Цель: Поделиться опытом в диагностике и лечении пациентов с солитарными легочными узлами.

Пациенты и методы: В течение пятилетнего периода (2005 - 2009 г.) 125 пациентов с периферическими легочными узлами подвергнуты первичной видеоторакоскопии с целью резекции опухоли.

Результаты: В 93 (74,4%) случаях достигнута полноценная торакоскопическая резекция опухоли интраоперативной гефрир-диагностикой. В остальных 32 (25,6%) случаях из-за разных причин проведена конверсия (атипичная резекция узла). Злокачественными оказались 54,2% удаленных опухолей; доброкачественными - 45,8%. В 18 случаях проведенная гефрир-диагностика показывает первичную бронхиальную карциному, из-за чего проведена резекция опухоли. У 10 пациентов гефрир-диагностика не оказалась категорической в дифференциональном диагнозе между легочным метастазом и первичной бронхиальной карциномой. После постановки окончательного патоморфологического диагноза проведена онкологическая резекция в интervalе. В 28 случаях удалены легочные метастазы с экстрапульмональной первичной опухоли.

Выводы: Несмотря на усовершенствование диагностических техник единственно видеоторакоскопическое устранение легочного узла и его последующее гистологическое исследование обеспечивает окончательный диагноз, при чем таким образом дефинитивно решаются проблемы доброкачественных лезий и корректного лечения малигенных легочных поражений.