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CLINICAL STAGING OF CENTRAL NON-SMALL CELL BRONCHIAL CARCINOMA

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SUMMARY – The aim of the study was to establish the value of clinical preoperative staging of central bronchial carcinoma according to TNM classification (cTNM). Postoperative histopathologic staging of bronchial carcinoma according to TNM classification (pTNM) was used as a reference value. The study included patients with central non-small cell bronchial carcinoma. Preoperative staging was correctly assessed in 50%, underestimated in 32%, and overestimated in 18% of patients. The difference between preoperative and postoperative staging was not statistically significant. In order to be as precise as possible on preoperative bronchial carcinoma staging, all diagnostic methods available should be used to distinguish resectable from nonresectable tumors. The extent of diagnostic work-up should be coordinated with therapeutic consequences.

Key words: *Lung neoplasms – diagnosis; Carcinoma non-small-cell, lung – diagnosis; Carcinoma, bronchogenic – diagnosis; Neoplasm staging – methods*

Introduction

Bronchial carcinoma is a malignant epithelial lung tumor. According to World Health Organization nomenclature, the term lung cancer can also be used[1]. According to localization in the bronchial tree, bronchial carcinomas can be divided into central and peripheral. Central bronchial carcinomas are situated in the main, lobar, segmental, subsegmental bronchi, but rarely more distally. Peripheral carcinomas are situated more distally from subsegmental bronchi. Seventy percent of bronchial carcinomas are central bronchial carcinomas[1]. They are always visible on bronchoscopy, while peripheral ones are not[2].

Histologically, 95% of all malignant epithelial tumors fall into one of the four main types: small-cell lung cancer, squamous cell carcinoma, adenocarcinoma, and macrocellular carcinoma[1]. Because of their similarity in therapy and prognosis, squamous cell carcinoma, adenocarcinoma and large cell carcinoma are classified in the group called non-microcellular lung cancers. Note that in this division of cancers cytologic verification is also sufficient[3].

The international system for staging lung cancer according to TNM markers is of greatest value on assessing the anatomical spread of bronchial carcinoma. "T" stands for primary tumor, "N" for metastases in regional lymph nodes, and "M" for distant metastases. Cancer stage is determined by combinations of these factors, all in favor of grouping patients with similar therapy and prognosis[1,4,5]. In this article, disease staging is shown according to combination of descriptors, and descriptors are not shown separately (Table 1). Clinical staging (cTNM) based on all diagnostic methods used before therapy should be distinguished from postoperative staging (pTNM) based on histopathologic tissue analysis. Analyzed tissue included resected lung fragments and intrathoracic lymph nodes resected and divided accord-

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Table 1. Stages of bronchial carcinoma according to TNM classification

Stage 0	Carcinoma in situ	N0	M0
Stage IA	T1	N0	M0
Stage IB	T2	N0	M0
Stage IIA	T1	N1	M0
Stage IIB	T2	N1	M0
	T3	N0	M0
Stage IIIA	T1	N2	M0
	T2	N2	M0
	T3	N1, N2	M0
Stage IIIB	T4	every N	M0
	every T	N3	M0
Stage IV	every T	every N	M1

ing to lymphonodal status. Division of intrathoracic lymph nodes according to lymphonodal status ties intrathoracic lymph nodes to stable anatomic structures[1,6,7]. This allows for a more reliable assessment of N metastases, lymphadenectomy, and postoperative pathologic assessment of metastases in these lymph nodes. Diagnostic methods should be oriented towards the best clinical staging possible. All noninvasive and invasive methods available should be used[8]. Only methods that can contribute to the choice of therapy should be employed.

Patients and Methods

Staging assessment was performed in 50 patients undergoing surgery for non-small cell carcinoma. Standard preoperative assessment included history, clinical examination, laboratory tests, classic x-ray and thorax CT scan, functional assessment, bronchofibroscopy in local anesthesia, and microscopy-cytology and/or histology verification of carcinoma. TNM classification was used to assess primary tumors and their spread to thoracic N1 and N2 lymph nodes. Patients diagnosed with stage IIIB and IV on clinical staging were not operated on.

Histopathology results confirmed bronchial carcinoma in all patients. Assessment of postoperative staging was done according to this analysis. Results of preoperative and postoperative assessment are shown in Table 2. The level of difference significance was determined by sign test.

Results

Fifty patients were operated on for non-small cell carcinoma. There were 38 male and 12 female patients, age range 41-73, mean age 59.9 (median 58) years. Histopathologic analysis indicated squamous cell carcinoma in 33, adenocarcinoma in 13, and large-cell carcinoma in four patients. Lobectomy was performed in 23, right lower bilobectomy in three, and pulmectomy in 24 patients. Primary tumor was correctly assessed in 44, overestimated in three, and underestimated in three patients. Tumor spread to intrathoracic lymph nodes (N1 and N2) was correctly assessed in 24, overestimated in 13, and underestimated in 13 patients.

Relations of preoperative and postoperative stages of disease are illustrated in Fig. 1. In relation to postoperative stage (pTNM), a number of patients with stages IB, IIA, and IIB were preoperatively overestimated, whereas stage IIIA was underestimated. There were no patients with stage IA, IIIB and IV.

Difference between the preoperative and postoperative staging is shown in Table 2. There were no patients in postoperative stages IA, IIA, and IIIB. Postoperatively, 19 patients were diagnosed with stage IB, whereas preoperatively 12 patients were diagnosed with stage IB, two patients with IIA, three patients with IIB, and two patients with IIIA. Postoperatively, 10 patients were diagnosed with stage IIB; preoperatively, four patients were diagnosed with stage IIB, four patients with IB, and two patients with IIIA.

Postoperatively, 21 patients were diagnosed with stage IIIA; preoperative, nine patients were diagnosed with stage IIIA, six patients with IB, and six patients with IIB.

Twenty-five of fifty patients (50%) had correct preoperative staging. Preoperatively, stage underestimate was recorded in 16 of 50 (32%) and stage overestimate in nine of 50 (18%) patients. The difference between preoperative and postoperative assessment was not statistically significant ($Z=1.2$, $p=0.23$, sign test).

Discussion

Assessment of the spread of bronchial carcinoma according to TNM classification is very important in defining the prognosis and choice of therapy for these patients[9]. The most reliable prognostic factor is tumor stage following radical resection[10]. Postoperative surgical-pathologic staging (pTNM) is more reliable than clinical staging (cTNM), and can be used as a reference value on cTNM assessment. Comparison of the two methods leads to validation of diagnostic methods.

In our study, primary tumors were correctly assessed in 88% (44/50), and tumor spread to intrathoracic N1

and N2 lymph nodes in 48% (24/50) of cases. Metastases to intrathoracic lymph nodes are more difficult to diagnose preoperatively than primary tumors, thus necessitating upgrading of their diagnosis. Intraoperative diagnosis of lymph node metastases is inadequate[11]. All this justifies mediastinal lymphadenectomy in all patients. It should also be done in stage I because micrometastases are possible[12]. Mediastinal lymphadenectomy is essential for correct assessment of pTNM stage[13]. For this reason mediastinal lymphadenectomy is performed in all our patients with lung resection.

Thorax CT scan should be done in all patients scheduled for surgery[14]. The high sensitivity and specificity from earlier CT reports has now been shown to be lower than previously believed[15]. Metastasis assessment is done in relation to the size of nodus, however, nodus size is not reliable for detecting metastases[16]. Recently, the importance of positron emission tomography (PET) as a supplementary procedure to CT in staging of non-small cell bronchial carcinoma has been emphasized because metastasis assessment is based on metabolic processes and not on nodus size[17].

When a metastatic lesion, important for the choice of therapy, is diagnosed by a radiologic method, it is important to get a microscopy-cytology and/or histology verification whenever possible[18]. Mediastinoscopy is important to obtain samples for this analysis, and it has to confirm radiology and even PET results[19]. It should be noted that transtracheal/transbronchial needle aspiration has been underutilized and should be more widely used in morphologic analysis of samples obtained from tumors or lymph nodes located paratracheally or parabronchially[20,21]. Nowadays it is done under the control of a CT or endobronchial untrasound[22,23]. Needles that allow for collection of samples for histologic analysis are also in use[24].

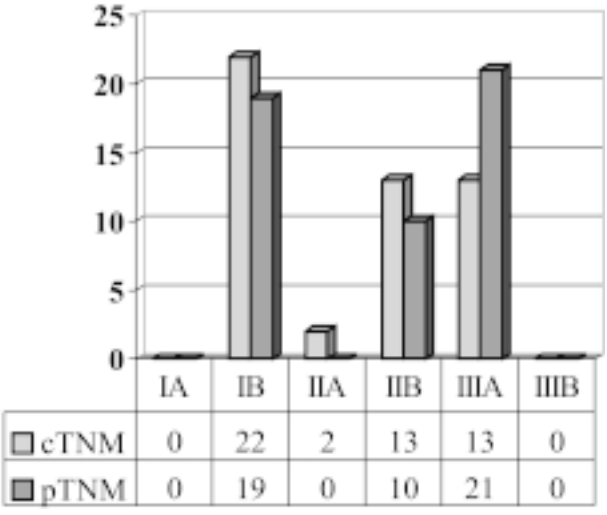

Fig. 1. Ratio of preoperative (cTNM) and postoperative (pTNM) stage of disease in patients with central bronchial carcinoma (N = 50)

Table 2. Ratio of preoperative (cTNM) and postoperative (pTNM) stage assessment in patients with central bronchial carcinoma (N=50)

cTNM	pTNM						Total
	IA	IB	IIA	IIB	IIIA	IIIB	
IA	**0**	0	0	0	0	0	0
IB	0	**12**	0	4	6	0	*22*
IIA	0	*2*	**0**	0	0	0	*2*
IIB	0	3	0	**4**	6	0	13
IIIA	0	*2*	0	*2*	**9**	0	13
IIIB	0	0	0	0	0	**0**	0
Total	0	19	0	10	21	0	**50**

$Z=1.2$, $p=0.23$, sign test

According to our results, in patients with central non-small cell bronchial carcinoma, lower stages of the disease, IB, IIA and IIB, were preoperatively overestimated. Stage IIIA was preoperatively underestimated compared to postoperative staging (Fig. 1). In all four stages mentioned above, the real spread of the disease was preoperatively underestimated.

In 50% of study patients, there was no difference between preoperative and postoperative staging. Patients with preoperatively underestimated stage of the disease had worse prognosis than expected according to clinical stage assessment. In our study, there were 32% of such cases (Table 2). In 18% of study patients the stage of the disease was preoperatively overestimated. Their real stage of disease was lower than preoperatively assessed, and their prognosis was better than expected according to clinical stage assessment, posing a risk that these patients may not have been operated on although their tumors were resectable.

Even though the difference between preoperative and postoperative staging of bronchial carcinoma in these patients was not statistically significant, accurate staging of carcinoma was recorded in only 50% of patients. That is why it is important to improve the diagnosis of primary processes, and of metastases in intrathoracic

lymph nodes in particular. Preoperative staging should be as accurate as possible. All diagnostic possibilities to upgrade clinical staging of bronchial carcinoma should be used. On considering a variety of diagnostic methods we should always keep in mind therapeutic consequences[25].

Conclusion

Clinical staging of central non-small cell bronchial carcinoma according to TNM classification (cTNM) in comparison to postoperative surgical-pathologic staging (pTNM) proved accurate in one half of patients. In 32% of patients the clinically diagnosed stage of disease underestimated the real stage of disease (cTNM stage was lower than pTNM stage). In 18% of patients the clinically diagnosed stage of disease overestimated the real stage of disease (cTNM stage was higher than pTNM stage). All diagnostic tools available should be used to assess the preoperative stage of disease as accurately as possible in order to distinguish resectable and nonresectable tumors. The diagnostic methods used should be coordinated with therapeutic consequences, which means that only methods that offer reliable assessment of prognosis and choice of therapy should be used.

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Sažetak

KLINIČKA PROCJENA STADIJA CENTRALNOG NEMIKROCELULARNOG KARCINOMA BRONHA

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U radu se vrednuje klinička prijeoperacijska procjena stadija centralnog karcinoma bronha prema klasifikaciji TNM (cTNM). Kao referentna vrijednost rabila se je poslijeoperacijska patohistološka procjena stadija karcinoma bronha prema klasifikaciji TNM (pTNM). Analizirani su operirani bolesnici s centralnim nemikrocelularnim karcinomom bronha. Prijeoperacijski je stadij bolesti bio točno procijenjen u 50,00%, potcijenjen u 32,00%, a precijenjen u 18,00% bolesnika. Razlika između prijeoperacijske i poslijeoperacijske procjene nije bila statistički značajna. Treba rabiti sve raspoložive dijagnostičke metode radi što točnijeg prijeoperacijskog određivanja stadija karcinoma bronha u cilju razdvajanja resektabilnih i neresektabilnih tumora. Opseg dijagnostike mora se uskladiti s terapijskim posljedicama.

Ključne riječi: *Plućne neoplazme – dijagnostika; Nemikrocelularni karcinom, plućni – dijagnostika; Karcinom, bronhogeni – dijagnostika; Određivanje stadija neoplazme - metode*