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Clinical impact of the use of the revised International Association for the Study of Lung Cancer staging system to operable non-small-cell lung cancers

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ARSTRACT

Introduction: The purpose of this study, therefore, was to evaluate the impact of the use of the present classification IASLC staging system (TNM7) on the categorization of patients and survival after resection. *Methods:* Between August 1985 and January 2007, 414 consecutive patients underwent pulmonary resection with a curative intention for NSCLC at the British Hospital in Buenos Aires were included in this study only if they were pathologically staged as N0-M0. Preoperative staging was performed according to the TNM classification system of the International Union Against Cancer (173 men, 58 women).

Results: 231 tumours were identified as pathological No. Mean age was 61.4 years. 173 patients (74.9%) were men. When the TNM7 was applied, 28 patients (12.1%) changed their T factor staging (14 were moved towards a higher T and 14 were moved to a lower T) and 41 patients (17.7%) changed their pathological staging by applying the TNM7: 14 patients were downstaged (6.1%) and 27 (11.7%) were upstaged. With the present T definition among 103 patients in stage IB 27 were upstaged (18 to IIA and 9 to IIB) and in the group of stage IIIB (n = 14) all of them were downstaged (5 to IIB and 9 to IIA). The current T definition showed a statistically significant difference between the two T1 subgroups (93% versus 70% 5 year survival between T1a and T1b, p = 0.027).

Conclusion: This study shows that the clinical impact of the using the IASLC proposed staging system would be modest but relevant, identifying a subgroup with a better prognosis (T1a).

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1. Introduction

Several investigators have reported that tumour size may have an independent predictive value on survival; particularly in patients with stage I resected (T1NOMO NSCLC) [1,2]. After analysis of the T component of the TNM classification in the IASLC international database, the working group for the IASLC International Staging Committee recently concluded that there was sufficient validated information to recommend changes in the seventh edition of the TNM (TNM7) classification of lung cancer. The purpose of this study, therefore, was to evaluate the impact of the present IASLC staging system on the categorization of patients and survival after resection.

2. Methods

Between August 1985 and January 2007, 414 consecutive patients underwent pulmonary resection with a curative intention

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for NSCLC at the British Hospital in Buenos Aires. Patients were included in this study only if they were pathologically staged as N0-M0. Patients were excluded if they had exhibited small cell lung cancer or a rare histological result or if they had been included in a neoadjuvant chemotherapy protocol. Most of these patients had been included in a previous report about the impact on survival of the size of the tumour [3]. Patients were included only after institutional review board approval.

Preoperative staging was performed according to the TNM classification system of the International Union Against Cancer using chest computed tomography (CT) and abdominal CT or ultrasonography in all patients. Brain computed tomography or magnetic resonance imaging was done only in case of clinical suspicion of brain metastases. In cases of uncertain clinical or radiologic findings, further examinations were performed to exclude extrapulmonary metastases. Mediastinal and hilar lymph node status was assessed as positive if the chest CT showed that the shorter axis of any node was larger than 1.0 cm. Mediastinoscopy has not been performed routinely in this series unless the CT scan demonstrated mediastinal lymph node enlargement. Bronchopulmonary, hilar and mediastinal lymph nodes were systematically sampled. After surgery a final pathologic stage was stated based on the operative findings.

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Table 1 Clinical characteristics of tumours p N0 M0 (*n* = 231).

	n	%
Symptoms from primary tumour	83	35.9
Asymptomatic	144	62.3
Paraneoplasic symptoms	4	1.7
Side (%)		
Right side	138	59.7
Left side	93	40.3
Upper lobes (%)	153	66.2
Central location (%)	46	19.9
Clinical stage		
IA	103	44.6
IB	98	42.4
IIA	1	0.4
IIB	20	8.7
IIIA	7	3.0
IIIB	2	0.9
Histology (%)		
Adenocarcinoma	146	63.2
Bronchioloalveolar carcinoma	14	6.1
Epidermoid Carcinoma	55	23.8
Large cell carcinoma	16	6.9
Pathological stage		
IA	93	40.3
IB	103	44.6
IIB	21	9.1
IIIB	14	6

Tumours were staged using the previous T factor definition (TNM6) and also by using the present T factor definition (TNM7) coined by the International Association for the Study of Lung Cancer (IASLC). The recommendations for that TNM7 classification include: (1) to subclassify T1 as T1a (≤2 cm) or T1b (>2–3 cm); (2) to subclassify T2 as T2a (>3–5 cm) or T2b (>5–7 cm); (3) to reclassify T2 tumours >7 cm as T3; (4) to reclassify T4 tumours by additional nodule(s) in the lung (primary lobe) as T3; (5) to reclassify M1 by additional nodule(s) in the ipsilateral lung (different lobe) as T4; and (6) to reclassify pleural dissemination (malignant pleural or pericardial effusions, pleural nodules) as M1a [4]. In addition, it is suggested that T2b N0 M0 cases be moved from stage IB to stage IIA, T2a N1 M0 cases from stage IIB to stage IIA, and T4 N0–1 M0 cases from stage IIIB to stage IIIA [5].

2.1. Statistical analysis

Statistical analysis was performed using SPSS 13.0 statistical software. The analysis of differences in categorical outcomes was determined using the Chi-squared test or Fisher's exact test. Probabilities of disease free survival rates were estimated using the Kaplan–Meier method. Cox proportional hazards regression models were used to ascertain the association between individual factors and survival. Statistical significance was assumed at p < 0.05 [6].

3. Results

Two hundred and thirty one tumours were identified as pathological No. Mean age was 61.4 (median 62, range, 38–88 years). One hundred and seventy three patients (74.9%) were men and 58 women (25.1%). Treatment included standard lobectomy (n= 204), pneumonectomy (n= 20) or bilobectomy (n= 7) with systematic lymphadenectomy of the hilum and mediastinum. Adenocarcinoma was the most common histological type (n= 146, 63.2%) (Table 1). Complications occurred in 66 patients (28.6%). Operative mortality was 3.5% (n=8). Resection was considered complete in 225 cases (97.4%).

When the TNM7 T definition was applied, 28 patients (12.1%) changed their T factor staging (14 were moved towards a higher

Table 2 Classification of T factors according TNM6 and TNM7.

TNM6			TNM7		
T	n	%	T	n	%
T1	93	40.3	1a	57	24.7
			1b	36	15.6
Total 1	93	40.3		93	40.3
T2	103	44.6	2a	76	32.9
			2b	18	7.8
Total 2	103	44.6		94	40.7
T3	21	9.1	3	35	15.2
T4	14	6.1	4	9	3.9
Total	231	100	Total	231	100

Table 3 Change of Stage according TNM7.

TNM6			TNM7		
Stage	n	%	Stage	n	%
IA	93	40.3	IA	93	40.3
IB	103	44.6	IB	76	32.9
IIA			IIA	18	7.8
IIB	21	9.1	IIB	35	15.2
IIIA			IIIA	9	3.9
IIIB	14	6.1	IIB		
Total	231	100	Total	231	100

Table 4Survival according the previous and present T definition.

TNM6	2 years	3 years	5 years	10 years
T1	97%	93%	85%	62%
T2	80%	76%	63%	54%
T3	69%	61%	49%	-
T4	57%	57%	42%	28%
TNM7	2 years	3 years	5 years	10 years
T1a	100%	100%	93%	70%
T1b	92%	84%	70%	61%
T2a	82%	77%	65%	55%
T2b	72%	72%	64%	_
T3	71%	66%	49%	_
T4	50%	50%	25%	0%

Long rank test 16.11 *p*: 0.0011. Long rank test 21. 16 *p*: 0.0008.

T and 14 were moved to a lower T) (Table 2). Forty one patients (17.7%) changed their pathological staging by applying the TNM7 (Table 3), 14 patients were downstaged (6.1%) and 27 (11.7%) were upstaged. With the TNM7 among 103 patients in Stage IB 27 were upstaged (18 to IIA and 9 to IIB) and in the group of Stage IIIB (n = 14) all of them were downstaged (5 to IIB and 9 to IIIA). While both the TNM6 and TNM7 were efficient to differentiate survival between different stages (Table 4 and Fig. 1) but the present T definition showed a statistically significant difference between the two T1 subgroups (93% versus 70% 5 years survival between T1a and T1b, p = 0.027) (Table 4) identifying a subgroup with a better prognosis (T1a).

The number of patients that change their surgical expectancy is quite modest: 7.8% of patients in Stage IB changed their 5-year survival only from 63% to 64% (because of being upstaged to IIA) and 3.9% from 63% to 49% (because of being upstaged to IIB). In the same way 2.2% improved their survival from 42% to 49% (because of changing IIIB to Stage IIB). It seems that in this group of patients only 3.9% had a difference of 5-year life survival higher than 10% and 6.1% higher than 5%.

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