POST-OPERATIVE STAGING AND SURVIVAL BASED ON THE REVISED TNM STAGING SYSTEM FOR NON-SMALL CELL LUNG CANCER

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ABSTRACT

Objective: To study the factors affecting post-operative staging and survival in non-small cell lung cancer (NSCLC) patients based on the revised TNM staging system adopted by the UICC in 1977. Methods: Data were collected from 1757 consecutively operated NSCLC patients, including those receiving complete tumor excision, tumor debulking and exploratory thoractomy from April 1969 through Dec. 1993. the end point of follow-up was Nov. 30, 1998. Cumulative survival and its influencing factors were analyzed by Kaplan-Meier and Cox model of SPSS software. Results: In this series, 30 patients (1.7%) were lost from follow-up. The 5-year cumulative survival was 88.0% for patients in stage I A, and 53.9% in stage IB, 33.5% in stage II, 14.7% in stage IIIA, 5.5% in stage IIIB and 7.0% in stage IV. The overall 5-year survival rate was 28.2%. The 5-year survivals were 39.8%, 14.4% and 4.2% in patients treated with completely tumor resection, tumor debulking and explorative thoractomy, respectively. The 10-year survival rate was 31.4%, 9.5% and 0, respectively. Factors affecting long-term cumulative survival, in the order of decreasing significance, were the type of operation, lymph node status, staging, size and pathological type of the primary tumor. Conclusion: the revised staging system for NSCLC is superior to that used since 1986 as far as the end results of treatment in patients in different stage and the staging specificity are concerned. The T3N1M0 classification and the definition of M1 need to be further studied.

Key words: Surgery, Tumor staging, Survival analysis, Non-small cell lung cancer

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The revision in the international system for staging lung cancer have been adopted by the Union Internationale Contre le Cancer (UICC) and the American Joint Committee on Cancer (AJCC) in 1996 and published in 1997.[1,2] In this revisions, satellite tumor nodule(s) in the primary tumor lobe of the lung are designated T4. Separate metastatic tumor nodule(s) in the ipsilateral nonprimary-tumor lobe(s) of the lung are designated M1. The revised stage grouping rules divide stage I and stage II into A and b substage. The T3N0M0 category is placed in stabge II B. Based on the new revision of TNM staging system we researched the post-operative staging and influencing factors on survival of the records of 1757 cases with non small cell lung cancer. Our purpose was to determine if the revisions were appropriate in estimating prognoses and evaluating end results of treatment.

PATIENTS AND METHODS

From April 1969 through December 1993, a total of 1757 consecutive operable patients with non small cell lung cancer (NSCLC), including complete resection, debulking resection and thoractomy were in the Tumor Hospital of Sun Yat-sen University of Medical Sciences in China.

The male/female ratio in the 1757 patient was 1424/333. The age distribution ranged between 18 and 77 year old. Middle age was 55.00 years.

The post-surgical TNM staging was respectively determined according to the New International Staging system in 1986[3] and the Revision of Staging System for Lung Cancer in 1997 of the International Union against Cancer. The end point of follow-up was December 30, 1998. There were 30 cases that lost folow up. They were designated as uncencord case according statistic. The lost follow-up rate was 1.7%. Death from cancer, non-cancer or unknown cause was the cencord event for survival calculations. Survival analysis of kaplan-Maier and Cox Regression were carried out using the Statistical Program for the Social Sciences (SPSS inc.).

RESULTS

The post-operative cumulative survival rates of 1757 patients based on pTNM, 1986 staging and 1997 staging respectively are shown in Table 1 - 3. There are different survival results in different conditions (Table 4). The influencing survival factors were analyzed by Cox regression. The results are shown in Table 5 and Table 6.

Table.1. The post-operative cumulative survival rate of 1757 patients

PTNM	No.	5-year	10-year	15-year	20-year
T1N0M0	25	88.0	72.3	72.3	72.3
T2N0M0	403	53.9	46.3	32.4	27.4
T1N1M0	2	50.0	50.0	50.0	--
T2N1M0	138	24.5	20.1	18.5	--
T3N0M0	279	37.4	24.6	17.5	17.5
T3N1M0	128	24.7	17.6	14.7	14.7
T1N2M0	5	20.0	0		
T2N2M0	189	14.7	11.2	5.6	0
T3N2M0	291	10.1	5.6	--	
T4	128	6.4	0		
N3	19	0			
M1	167	7.0	0		
Total	1757	28.2	21.6	16.0	13.5

Table 2. the survival rate of 1757 patients based on 1986 staging

Staging	No.	5-year	10-year	15-year	20-year
I	428	55.9	47.6	33.8	29.0
II	140	25.6	20.3	18.7	--
IIIA	892	21.9	14.4	10.5	10.5
IIIB	130	5.5	0		
IV	167	7.0	0		

Table 3. the survival rate of 1757 patients based on 1997 staging

Staging	No.	50year	10-year	15-year	20-year
IA	25	88.0	72.3	72.3	72.3
IB	403	53.9	46.2	32.4	27.4
Stage I	428	55.9	47.6	33.8	29.0
IIA	2	50.0	--		
IIB	417	34.2	19.0	17.6	17.6
Stage II	419	33.5	23.1	17.6	17.6
IIIA	613	14.7	9.8	7.5	7.5
IIIB	130	5.5	0		
IV	167	7.0	0		

Table 4. The cumulative survival rate of 1757 patients by different conditions

	Completely resection(%)			Debulking resection(%)			Thoractomy (%)		
	No.	5-yr	10-yr	No.	5-yr	10-yr	No.	5-yr	10-yr
Op. nature	1072	39.8	31.4	329	14.4	9.5	356	4.2	0
Pathology									
Squamous	420	44.3	35.2	123	17.4	13.1	149	5.6	0
Adeno.	404	37.1	29.9	118	13.8	7.0	102	2.3	0
Large cell	31	34.2	34.2	10	30.0	30.0	12	0	0
Ade-squamou	133	34.9	26.0	61	8.4	6.7	10	10.0	0
Other	84	40.0	27.6	17	11.8	0	83	4.5	
Operation type									
Lobectomy	789	41.9	33.4	206	13.6	10.4			
Pneumnectomy	159	30.6	22.2	40	12.6	0			
Limitedresection	124	38.4	31.0	83	16.9	11.9			
TNM									
T1	27	88.9	69.4	6	16.7	0	1		
T2	635	42.3	35.9	116	16.8	13.7	47	2	--
T3	394	34.0	22.8	186	13.9	8.0	217	5.6	0
T4	16	13.8	--	21	10.0	--	91	2.6	0
N0	625	51.4	41.1	96	26.5	18.0	48	4.2	--
N1	214	29.6	22.6	58	12.1	10.1	55	5.8	0
N2	233	17.3	12.6	162	9.2	4.8	247	3.9	0
N3				13	0		6	0	
M0	1065	40.0	31.5	255	15.1	9.2	270	4.5	
M1	7	14.3	0	74	12.6	0	86	1.5	0

Table 5. Univariate analysis influencing survival by Cox regression

Variables	Score	Significant
Sex	2.3188	0.1278
Tumor location	0.2136	0.6139
Pathology	14.4076	0.0001
Resection type	203.4848	0.0000
Operative type	375.0225	0.0000
LN dissection	96.2506	0.0000
Adjuvant therapy	37.3577	0.0000
1997 stging	316.1652	0.0000
T factor	145.2120	0.0000
N factor	277.1617	0.0000
M factor	57.3537	0.0000

Table 6. Multivariable analysis influencing Survival by Cox regression

Variables	B	S.E	Sig.	Exp.(β)
Pathology	0.0457	0.0201	0.0234	1.0467
Operative type	0.3626	0.0423	0.0000	1.4371
1997 staging	0.2046	0.0523	0.0001	1.2270
T factor	0.1490	0.0489	0.0023	1.1607
N factor	0.2212	0.0442	0.0000	1.2476

DISCUSSION

The International Staging System for Lung Cancer has been recognized as an international language for community about this disease. It has played an important role in planning treatment, estimating prognoses, and evaluating end results of different therapies for lung cancer. It is two principles for lung cancer staging that there are the oneness of end results within same stage group and great specificity among different stage group. Table 1 showed that there is good specificity for pTNM subset. The survival cures were independent and different. But some exception exists between pT2N1M0 and pT3N1M0. The 5-years survival rates were 24.5% in pT2N1M0 subset and 24.7% in pT3N1M0. These two survival rates were too close and there was no difference in statistic. From this material some views may be considered: (1) there may be a oneness between pT2N1M0 and pT3N1M0. T3N1M0 category may be placed in stage IIB. Ginsberg, et al.[4] propounded same viewpoint. (2) In same N1 and M0, there may be some confusing problems of the definition for T2 factor and T3 factor. Accoridng to the definition of TNM descriptors, T3 means the tumor of any size directly invade chest wall, or diaphragm or mediastinal pleura or parietal pericardium.[5] The content of T3 descriptor may be too large. Do some conditions such as tumor invade other lobe(s) or partial pleura belong to T2 or T3? All of these should be continuous researched.

We agree that the revision placed T3N0M0 subset into stage IIB. In our material patients with T3N0M0 had a better survival than that with T2N1M0 and other subset of IIIA. The 5-year survival rate of II and IIIA were 33.5% and 14.7% in the revision and 25.6%, 21.9% in the 1986 staging respectively. Apparently the staging specificity of the 1997 staging is better than that of the 1986 staging.

Cox Regression was used to analyze influencing prognostic factors. The results showed in Table 4,5,6. In univariate analysis model ther were 9 significant variables that affected prognosis. But only 5 variables could enter multivariate analysis model. The important influencing factors were operative type, N factor, 1997 staging, T factor and pathologic type in order, especially operative type and N status variables. According to the rationale of Cox regression, when operative type changed from complete resection to debulking resection or from debulking resection to thoractomy, the death relative risk increased 43.71% [Exp(β)=1.4371]. Also, when lymph node status changed from N0 to N1 or N1 to N2, the death relative risk increased 24.76%. Staging of 1997 was close relative to N status, the stage increased one step and the relative risk increased 22.70%.

M factor had a poor influencing variable in univariate analysis model but not influencing in multivariable analysis. The cause may be relate to the definition of M. In the revision separate metastatic tumort nodule(s) in the ipsilateral non primary-tumor lobe(s) of the lung are designated M1. when only one nodule exist in non primary-tumor lobe, radical operation can be made. This condition is entirely different from other M1 in which other organ has matastatic focus. Urschel, et al.[6] collected 11 English-language medical articles about pulmonary satellite nodules and concluded that survival for resected lung cancer with satellite nodules in non-primary lobes consistent with M1 stage disease. But Motta[7] in a commentary pointed that many clinical reports[8-10] showed the evidence that the prognosis after resection of the ipsilateral non tumor lobe has a better survival than that of stage disease due to a formal distant metastases. Our experience showed that there is different prognosis in different M1 with satellite nodules. So, the definition of M1 in the revision must be further discussion. From Table 4 the 5-year survival was seen in patients with M1 in different perative type but not in N3. N3 was the worst factor which affecting prognosis.

From this series the 20-year survival was 29.0%

for stage I NSCLC based on 97'staging and the overall 20-year survival was 13.5% also. In the future we believe that the long-term survival rate can be further raised by rational multidiciplinary synthetic therapy.

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