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Research Article

Is It Necessary to Subdivide the pN2 Group of Non Small Cell Lung Cancer?

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Abstract

Background: The pathological TNM staging system has been revised in 2009 but the modifications made concerned only the Tumour and the Metastasis components. This fact made many authors wonder about the necessity of improving the lymph node component in order to reach a better reliability. One of the interrogations made in the literature was the possible necessity of dividing the pN2 group into multiple-station one and single-station one because of the better prognosis of the latter.

Material and methods: In this work, we tried to compare the survival curves between 28 single-station N2 patients and 26 multiple-station N2 patients. All the patients received a neo-adjuvant chemotherapy and were classified into IIIA category.

Results: Our study showed no significant statistical difference between both groups in term of survival ($p<0.5$).

Conclusion: Our results are in contradiction with many other results published in the literature. This fact puts emphasis on the necessity of paying more attention to other factors such as the number of the resected lymph nodes or their location that may be more relevant and reliable.

Key words:

TNM classification; Lung carcinoma; Prognosis; Metastatic lymph nodes; Non small cell lung carcinoma

Introduction

The TNM staging system for lung cancer, especially for non small cell lung carcinoma (NSCLC), has been revised since the first edition of the tumour, node, metastasis classification published in 1997 [1]. The revised classification was published in 2009 and contained new recommendations concerning the tumor and metastasis components [2,3]. Recently, many authors pointed out the necessity of improving also the node component. In fact, Yang and coworkers reported that the number of resected lymph nodes combined with tumor size represents a prognostic factor in patients with pathologic N0 and Nx non small cell lung cancer [4]. Recent studies on skip metastasis and sentinel lymph nodes have assessed that patients with skip metastasis, defined as mediastinal lymph nodes without N1 metastasis show a better prognosis than patients with non-skip N2 disease [5-8]. Other authors searched to investigate the impact of the number of the resected lymph nodes or the ratio of the metastatic lymph nodes. Besides, Fukui et al and Lee et al, have reported the usefulness of determining the number of metastatic lymph nodes [9,10].

In addition to all these interrogations, many authors reported that patients with multiple-station metastases have a poorer prognosis in comparison with those with single-station metastases in both N1 and N2 patients [11,12]. In order to assess this last finding, we tried to compare the survival of 54 patients with pN2 metastases divided into 28 patients with single-station metastases and 26 patients with multiple-station metastases.

Material and Methods

Patients

Between 2005 and 2011, 54 patients with pN2 NSCLC underwent surgical resection after a neo-adjuvant chemotherapy at our hospital.

Patients with mediastinal lymph node metastases weren't considered as a contraindication for surgery unless the swollen lymph nodes appeared unresectable. Systemic nodal dissection involves the complete resection of ipsilateral mediastino-hilar lymph nodes, hilar, interlobar and lobar lymph nodes were resected with affected lung lobes in the hilar lymph node dissection and remote mediastinal lymph node station such as subcarinal lymph nodes in the upper lobe tumor were note resected in the selective mediastinal dissection.

Microscopic examination

The microscopic examination was performed using a light microscope (Olympus, CX41, USA). The lymph node stations varying from 1 to 10 were individually removed by the surgeons and they were immediately either examined extemporaneously or fixed immediately in formalin and cut at either equator, stained with hematoxylin and eosin and examined by means of light microscopy. Interlobar lymph nodes were resected in combination with the lung and then these nodes were classified into each nodal station. The pathological stage was classified according to the seventh edition of the TNM classification. Hilar lymph node metastasis was classified as N2 stage.

Statistical analysis

The survival period was calculated from the date of surgery to the time of death or the point data (21 March 2013). Survival curves were calculated using the Kaplan-Meier method and differences in survival were determined by the log-rank test. We used the SPSS system (New York 13.0)

Results

Our study contained 30 men and 24 women with a mean age of 54 years (average 40 years to 70 years). 28 patients presented single station N2 metastases and 26 patients presented multiple-station N2 metastases.

The mean survival of the patients with single-station N2 metastases was 8 months (average 0, 24 months).

The mean survival of the patients with multiple-station N2 metastases was 10 months (average 0 to 72 months). All the patients received the same neo-adjuvant therapy and presented the same clinical stage.

The survival curves are represented in the figure 1. The comparison of the survival curves using the X2 Logrank showed no statistical difference between both groups of patients (p<0.5).

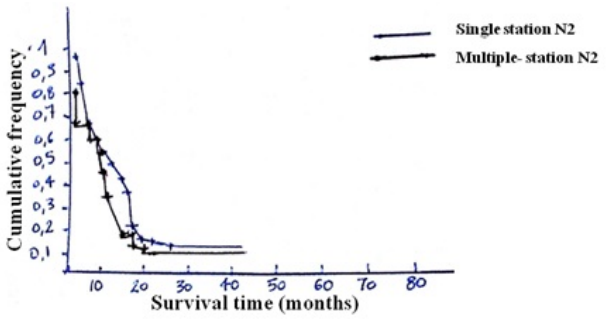

Figure 1: Survival curves of multi-station and single-station N2 patients. No significant statistical difference was shown. X2 logrank: 0.04 (p<0.5).

Discussion

Our results showed no statistical difference in the survival between the patients with multiple -station metastases and single-station metastases. This result is in contradiction with other published results. In fact, Ichinose and coworkers reported that the survival of patients with a primary tumor in each lobe except for the left lower lobe, a single N2 station resulted in a significantly better survival than did multiple N2 stations. Furthermore, the overall survivals classified according to each primary site showed a significant difference among the four primary sites (P =.04). In this study, like our study, only patients with IIIA N2 pathologic stage were included [11]. Besides, Andre F and colleagues reported in a study about 702 consecutive patients who underwent surgical resection of N2 NSCLC that two groups of patients were defined [12]. Those with clinical N2 (cN2) and those with minimal N2 (mN2) disease who were patients in whom N2 disease was and was not detected preoperatively at computed tomographic scan, respectively. The median duration of follow-up was 52 months (range, 18 to 120 months). A multivariate analysis using Cox regression identified four negative prognostic factors, namely, cN2 status (P <.0001), involvement of multiple lymph node levels (L2+; P <.0001), pT3 to T4 stage (P <.0001), and no preoperative chemotherapy (P <.01). For patients treated with primary surgery, 5-year survival rates were as follows: mN2, one level involved (mN2L1, n = 244): 34%; mN2, multiple level involvement (mN2L2+, n = 78): 11%; cN2L1 (n = 118): 8%; and cN2L2+ (n = 122): 3%. When only patients with mN2L1 disease were considered, the site of lymph node involvement according to the American Thoracic Society numbering system had no prognostic significance (P =.14). Preoperative chemotherapy was associated with a better prognosis for those with cN2 (P <.0001). Five-year survival rates were 18% and 5% for cN2 patients treated with and without preoperative chemotherapy, respectively. Inspite of the impossibility of comparison between this study and ours, it puts emphasis on the heterogeneity of the pathological N2 group and this result is in contradiction with our results.

Conclusion

Despite of the multiple reports showing the heterogeneity of the pN2 group of NSCLC, our results showed no statistical significant difference in survival between single-station and multiple-station N2 patients with the same stage. These results are effectively in contradiction with many other papers but cannot be taken into account. In fact, the studied population is too small and all patients underwent induction therapy which is a major source of bias. We can only conclude that induction therapy may ameliorate the prognosis of multiple-station N2 but a larger series is necessary to demonstrate it.

References

1. Sobin LH, Wittekind C (1997) International Union Against Cancer (UICC), TNM classification of Malignant Tumors. (5th edtn), New York: Wiley-Liss, USA.
2. Sobin LH, Wittekind C (1997) International Union Against Cancer (UICC), TNM classification of Malignant Tumors. (6th edtn), New York: Wiley-Liss, USA.
3. Sobin LH, Gospodarowicz MK, Wittekind C (2009) TNM Classification of Malignant Tumours. (7th edtn), New York, NY: Wiley, USA.
4. Yang M, Cao H, Guo X, Zhang T, Hu P, et al. (2013) The number of resected lymph nodes (nLNs) combined with tumor size as a prognostic factor in patients with pathologic N0 and Nx non-small cell lung cancer. See comment in PubMed Commons below PLoS One 8: e73220.
5. Riquet M, Assouad J, Bagan P, Foucault C, Le Pimpec Barthes F, et al. (2005) Skip mediastinal lymph node metastasis and lung cancer: a particular N2 subgroup with a better prognosis. See comment in PubMed Commons below Ann Thorac Surg 79: 225-233.
6. Prenzel KL, Mönig SP, Sinning JM, Baldus SE, Gutschow CA, et al. (2003) Role of skip metastasis to mediastinal lymph nodes in non-small cell lung cancer. See comment in PubMed Commons below J Surg Oncol 82: 256-260.
7. Nomori H, Horio H, Naruke T, Orikasa H, Yamazaki K, et al. (2002) Use of technetium-99m tin colloid for sentinel lymph node identification in non-small cell lung cancer. See comment in PubMed Commons below J Thorac Cardiovasc Surg 124: 486-492.
8. Liptay MJ, Grondin SC, Fry WA, Pozdol C, Carson D, et al. (2002) Intraoperative sentinel lymph node mapping in non-small-cell lung cancer improves detection of micrometastases. See comment in PubMed Commons below J Clin Oncol 20: 1984-1988.
9. Fukui T, Mori S, Yokoi K, Mitsudomi T (2006) Significance of the number of positive lymph nodes in resected non-small cell lung cancer. See comment in PubMed Commons below J Thorac Oncol 1: 120-125.
10. Lee JG, Lee CY, Park IK, Kim DJ, Park SY, et al. (2008) Number of metastatic lymph nodes in resected non-small cell lung cancer predicts patient survival. See comment in PubMed Commons below Ann Thorac Surg 85: 211-215.

11. Ichinose Y, Kato H, Koike T, Tsuchiya R, Fujisawa T, et al. (2001) Completely resected stage IIIA non-small cell lung cancer: the significance of primary tumor location and N2 station. See comment in PubMed Commons below J Thorac Cardiovasc Surg 122: 803-808.

12. Andre F, Grunenwald D, Pignon JP, Dujon A, Pujol JL, et al. (2000) Survival of patients with resected N2 non-small-cell lung cancer: evidence for a subclassification and implications. See comment in PubMed Commons below J Clin Oncol 18: 2981-2989.