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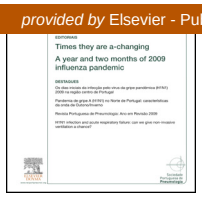

RESEARCH LETTERS

Adjuvant chemotherapy in stage IB non-small cell lung carcinoma: A survival analysis

Dear Editor,

Surgery is the primary treatment modality for non-small cell lung cancer (NSCLC), but only approximately 20% of tumors are suitable for potentially curative resection and even after surgery, with a high percentage of recurrence probability.[1,2] Therefore, 5-year survival rates after surgery are disappointingly low[2] and new strategies are needed to reduce mortality and recurrence rate in these patients. Stage IB NSCLC therapeutic approach remains a controversial issue. Adjuvant chemotherapy among this particular group of patients has never been demonstrated unequivocally as improving survival.[1,2]

Based on recent evidence,[3] the National Comprehensive Cancer Network (NCCN) guidelines[1] included an indication for adjuvant chemotherapy for high-risk stage IB NSCLC patients. These high-risk factors include tumor >4 cm, poorly differentiated tumor, vascular invasion, visceral pleura involvement, wedge resection, and incomplete lymph node sampling (Nx). In order to evaluate the impact of adjuvant chemotherapy on stage IB NSCLC patients undergoing surgery, we reviewed our center experience with these patients.

All completely resected stage IB NSCLC patients observed during the period between January 2006 and December 2013 were included. Only patients with proven pT2N0 samples were consecutively enrolled. To ensure maximum homogeneity, patients who had received induction chemotherapy were excluded, even if their definitive staging was pT2N0.

We then analyzed the effect of adjuvant chemotherapy, irrespective of the indication, on survival data of all patients included and of a high-risk patients' subgroup, as defined by the NCCN guidelines. The adjuvant chemotherapy regimen consisted of four courses of a platinum derivative and vinorelbine.

We analyzed 27 patients with a mean age of 65.3 ± 8.87 years and predominantly male ($n = 18$; 66.7%). Over 90% of patients had performance status ≤ 1 at diagnosis. There was no perioperative mortality (death within 30 days of surgery). General and high-risk subgroup population characteristics are presented in Table 1. Median follow-up time was 52.1 months.

Recurrence was detected in 9 (33.3%) patients (5 in the adjuvant chemotherapy group and 4 in the non-adjuvant chemotherapy group). Mean disease-free time was 45.3 months for the adjuvant chemotherapy group and 33.6 months for the non-adjuvant chemotherapy group and there was no statistically significant difference between the two groups. Eight (29.6%) deaths occurred in the study group (3 in the adjuvant chemotherapy group and 5 in the non-adjuvant chemotherapy group). Mean survival time was 50.0 months for the adjuvant chemotherapy group and 36.4 months for the non-adjuvant chemotherapy group and again there was no statistically significant difference between the two groups.

As for the high-risk subgroup, 19 patients had at least one NCCN high-risk factor. Mean disease-free time was 43.3 months for the adjuvant group and 32.8 months for the non-adjuvant group, with no statistically significant difference between the two groups. Mean survival time was 48.9 months for the adjuvant chemotherapy group and 34.0 months for the non-adjuvant chemotherapy group. No statistically significant difference was found between the two groups.

Our study did not find any clear benefit for the NCCN's high-risk patients in terms of overall survival and disease-free survival, and the same holds for all NSCLC stage IB patients who underwent surgical treatment. Despite this evidence, we did find a non-significant difference in terms of overall survival and disease free survival between non-adjuvant chemotherapy and adjuvant chemotherapy group, with an improvement of both in the latter group. Although obviously limited by our sample size and by the fact that the non-adjuvant chemotherapy group had a higher ratio of pneumectomies, which is associated with poorer survival,[5] this might indicate that adjuvant chemotherapy can play an important role in the treatment of these patients.

Unfortunately, adjuvant chemotherapy role in stage IB disease is not established yet. As in our study, subgroup stage IB analyses of larger trials have found a small but non significant overall survival benefit.[1,2] Recent evidence has demonstrated a significant benefit of adjuvant chemotherapy in stage IB patients with larger primary tumors (4.0 cm)[3] and the same seems to hold for stage IB patients with vascular invasion.[6] In spite of these results, at this point in time

Table 1 General population and high-risk subgroup population characteristics.

General population		
	Adjuvant chemotherapy ($n = 13$)	Non-adjuvant chemotherapy ($n = 14$)
Age (mean ± SD)	62.2 ± 7.80	68.1 ± 9.15
Gender (male/female)	9/4	9/5
PS > 1 (yes/no)	0/13	2/12
Histological type		
Adenocarcinoma	8	11
Squamous cell carcinoma	4	3
Large cell carcinoma	1	0
Heart disease (yes/no)	2/11	2/12
Smoking history (yes/no)	3/10	4/10
Resection type		
Pneumonectomy	1	3
Lobectomy	11	6
Bilobectomy	1	3
Wedge resection	0	2
High-risk subgroup population		
	Adjuvant chemotherapy ($n = 11$)	Non-adjuvant chemotherapy ($n = 8$)
Age (mean ± SD)	62.1 ± 7.94	71.9 ± 8.46
Gender (male/female)	7/4	6/2
PS > 1 (yes/no)	0/11	2/6
Histological type		
Adenocarcinoma	7	7
Squamous cell carcinoma	3	1
Large cell carcinoma	1	0
Heart disease (yes/no)	1/10	2/6
Smoking history (yes/no)	8/3	6/2
Resection type		
Pneumonectomy	1	2
Lobectomy	10	3
Bilobectomy	0	1
Wedge resection	0	2
Num of NCCN risk factors		
1	5	5
2	6	3

there is no available evidence to formally support routine use of adjuvant chemotherapy in stage IB.[1,2,4]

Conflicts of interest

The authors certify that there were no potential conflicts of interest at the time of redaction of this article.

Authors' contribution

Daniel Coutinho, Ana Antunes and Ana Barroso conceived the project idea. Daniel Coutinho and Ana Gonçalves collected the data. Daniel Coutinho and Ana Antunes conducted the analyses. All authors interpreted and discussed the results. All authors wrote the manuscript. All authors have read and approved the final version.

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Non-small cell lung cancer in young patients – A retrospective analysis of 10 years in a tertiary university hospital

Dear Editor,

Non-small cell lung cancer (NSCLC) in young adults is uncommon. Although there is limited data about clinical presentation and outcomes, it does seem that this population has some distinct clinicopathological characteristics and given the significant socio-economic implications NSCLC in young adults is increasingly important.[1–3]

The authors report the incidence, clinical characteristics, treatment and prognosis of NSCLC in young patients (≤45 years), in a tertiary academic hospital in Oporto. We retrospectively evaluated 2430 patients newly diagnosed with lung cancer, from January 2005 to December 2014. Our study identified 78 (3.2%) young adults. For analysis purpose, it only included patients with NSCLC who were followed up in our center.

Fifty-nine (75.6%) young adults were included: 37 (62.7%) were male with a mean age of 40.8 years (SD ± 3.8). 40 (67.8%) patients of the patients had a history of smoking. The median time from symptom onset to diagnosis was 1.0 months (0–12.0). Adenocarcinoma was the most common histopathological type, recorded in 44 (74.6%) patients, followed by squamous cell carcinoma in 7 (11.9%). EGFR mutations and ALK translocation were recorded in only 11 (18.7%) patients, and EGFR activating mutations were found in 2 (18.2%). The clinical staging revealed 5 (8.5%) patients with NSCLC in stages I and II, 6 (10.2%) III-A and 48 (81.4%) III-B and IV. The initial *Performance Status* (PS) was 0 and 1 in 41 (69.5%) patients, 2 in 6 (10.2%), and 3 and 4 in 8 (13.6%).

Surgical resection was performed in 9 (15.3%) patients, of whom 7 received chemotherapy and 2 received chemo-radiotherapy. In patients undergoing to surgery, lobectomy and mediastinal lymph node dissection was performed in 7 and pneumonectomy in 2. Chemotherapy alone was given to 32 (54.2%) patients and combination chemo-radiotherapy to 11 (18.6%). *Platinum-based doublet regimens* were used as first-line chemotherapy in more than two thirds of patients ($n = 41$). After progression, half of the patients ($n = 29$) were treated with second-line chemotherapy and 18.6% ($n = 11$) patients to third-line. A minority (11.9%) of patients received best supportive care (BSC) as initial treatment. Regarding response to first-line treatment, 5 (8.5%) patients obtained a complete response, 8 (13.6%) obtained a partial response, 3 (5.1%) stabilized, and the majority (72.9%) progressed. The median progression-free survival was 4.0 months (0–39.0).

During the follow-up period only 12 (20.3%) patients were still alive. In Kaplan–Meier analyses, the median survival rate was about 1.5 months in BSC group and 9.0 months in those submitted to other non-surgical treatments. Six (66.7%) operated patients are still alive (Fig. 1).

Lung cancer is considered a disease of the elderly. The incidence among young adults has been found to be

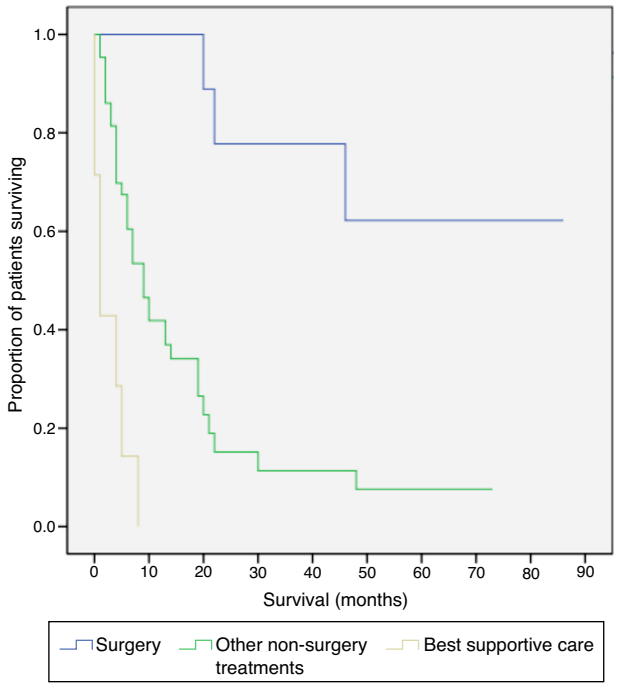

Fig. 1 Kaplan–Meier survival curves according to treatment performed (surgery, other non-surgical treatments and best supportive care).