Sixth International Joint Meeting on THORACIC SURGERY

Barcelona - 20th, 21st and 22nd November 2024
Auditorio Foment del Treball Nacional. Barcelona (Spain)

11th International Meeting on General Thoracic Surgery
Clínic Barcelona | Universitat de Barcelona | Hospital Universitari Sagrat Cor

5th Meeting of the Thoracic Oncology, Thoracic Surgery, Techniques & Transplant, Respiratory Nursing and Respiratory Physiotherapy Areas of the Spanish Society of Pneumology and Thoracic Surgery (SEPAR)
Sociedad Española de Neumología y Cirugía Torácica (SEPAR)

10th International Workshop on Surgical Exploration of the Mediastinum and Systematic Nodal Dissection
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SECT Sociedad Española de Cirugía Torácica

30th Congress of the "Asociación Iberoamericana de Cirugía Torácica" AIACT

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MEDIASTINAL DOWNSTAGING AFTER INDUCTION TREATMENT IS A SIGNIFICANT PROGNOSTIC FACTOR TO SELECT PATIENTS WHO WOULD BENEFIT FROM SURGERY

Paul E. Van Schil, MD, PhD
Antwerp University Hospital, Belgium

Treatment of patients (pts) with stage IIIA-N2 non-small cell lung cancer (NSCLC) remains controversial and many different treatment options exist ranging from primary surgery, neoadjuvant or perioperative therapy consisting of chemotherapy or chemoimmunotherapy, to chemoradiation followed by immunotherapy (1). In case of specific mutations as EGFR or ALK, targeted therapies may also be considered.

Although large randomized trials included patients with “resectable” or “unresectable” disease, there is no precise definition of resectable stage IIIA NSCLC. To obtain more uniform definitions, the IASLC created a specific task force and distinction is made between resectable, unresectable and potentially resectable disease depending on the associated T-descriptor and whether N2 involvement is bulky, invasive, limited to a single station, or whether multiple stations are invaded (2).

In the 9th edition of the TNM classification N2 involvement is subdivided into N2a and N2b disease when respectively, single or multiple ipsilateral mediastinal lymph node stations are involved (3).

Equally controversial is the further management of persistent N2 after neoadjuvant therapy. An important aspect to consider is the volume and extension of remaining N2 nodal involvement. Currently, no randomized evidence is available to provide general recommendations.

Prognostic factors affecting long-term outcomes in patients with resected stage IIIA-N2 NSCLC were studied in a series of 75 patients (4). Neoadjuvant therapy consisted of cisplatin and docetaxel. Median overall survival (OS) was 35 months and event-free survival (EFS) 15 months. After 3 years 36% were alive and tumor-free. After 5 years 60% had a local relapse and 65% distant metastases, mostly lung and brain. Factors associated with OS, EFS, risk of local recurrence or distant metastases were complete tumor resection and chemotherapy activity consisting of clinical and pathological response and mediastinal downstaging.

The prognosis of patients with persisting N2 disease after neoadjuvant chemotherapy was examined in a retrospective, single-center study including 145 patients (5). Lobectomy was performed in 56.5% and pneumonectomy in 33.1% of patients. R0 resection was obtained in 88.3%. Operative mortality was 2.6% and morbidity 35.2%. Five-year OS rates for single N2

with skip metastasis (N2a1), single N2 with N1 involvement (N2a2), and N2b were 47.3%, 30.2% and < 5%, respectively. Five-year disease-free survival (DFS) rates for ypN2a1, ypN2a2, and ypN2b were 30.6%, 23.4% and < 5%, respectively.

So, volume of persisting N2 disease plays a critical role in determining prognosis after neoadjuvant therapy with in general, mediastinal downstaging as an important prognostic factor. This was also demonstrated in a combined series of 104 patients who were thoroughly restaged after neoadjuvant chemotherapy (79 pts) or chemoradiation (25 pts)(6). Remediastinoscopy was positive in 40 pts and negative in 64 pts. The latter group underwent thoracotomy and remediastinoscopy was found to be false-negative in 17 pts. Sensitivity, specificity, and accuracy of remediastinoscopy were 71, 100, and 84%, respectively. Median survival times after positive, negative, and false-negative remediastinoscopy were 14, 28, and 24 months, respectively. On multivariate analysis only nodal status was a significant independent prognostic factor (p=.008).

Recently, immunotherapy has been added to neoadjuvant and perioperative protocols (7). Pathologically complete response and major pathologic response (<10% viable tumor cells in primary tumor and lymph nodes) were significantly higher in those patients undergoing combined chemoimmunotherapy compared to chemotherapy alone, resulting in better EFS and OS rates. In all phase III trials restaging was only performed by chest CT scan and there are no data on invasive, pathological restaging. The topic of microscopically remaining or persisting N2 disease and resulting prognosis was not yet specifically addressed, although, in general, downstaging of N2 disease was more pronounced in the experimental arm treated with chemoimmunotherapy compared to chemotherapy alone, as nicely demonstrated in the Checkmate-77T study (8).

In conclusion, pts with downstaging of N2 disease to N0 or N1 disease after neoadjuvant therapy have a better prognosis than those with persisting N2 disease. Patients with microscopically remaining N2 involvement have an intermediate prognosis and may be considered for surgery after multidisciplinary discussion. Any surgical treatment should aim at a complete R0 resection which ultimately determines prognosis.

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