



The lymphadenectomy in non-small cell lung cancer

Marco Chiappetta^{1,2}

¹Thoracic Surgery, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy; ²Università Cattolica del Sacro Cuore, Rome, Italy

Correspondence to: Dr. Marco Chiappetta. Thoracic Surgery, Università Cattolica del Sacro Cuore, IRCCS Fondazione Policlinico Universitario A. Gemelli, LARGO A. Gemelli 8, 00100 Rome, Italy. Email: marcokiaps@hotmail.it; marco.chiappetta@policlinicogemelli.it.

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Lung cancer leads the cause of death for cancer worldwide, presenting an increase incidence even if a small decline is ongoing in the western countries (1). However, despite diffuse information regarding the risk of lung cancer development in former and ex-smokers, about the 25% of cases seems not to be related to smoking (2).

One of the most important prognostic factors remains the presence of lymph node involvement, and in particular the presence of mediastinal nodal involvement, as demonstrated in the VIIIth TNM staging system edition (3) with a clear prognosis stratification considering the presence of nodal metastases.

The mediastinal status assessment results a focal point in non-small cell lung cancer (NSCLC) cancer patients management, starting in the preoperative workout and continuing during surgery. In particular, in the recent years, the presence of radiologic-metabolic improvement (18 fluorodeoxyglucose PET-CT) and new minimally invasive techniques (EBUS and EUS) permitted an increased rate of pre-operative N2 detection (1,4). The cN2 diagnosis is fundamental for the treatment planning, that might include up-front surgery, multimodality treatment or definitive radio-chemotherapy. In this setting, a multidisciplinary discussion is needed to plan a tailored and appropriate treatment (5).

On the other hand, despite these improvements in preoperative mediastinal staging, the 5–15% of patients present unexpected N2 involvement at the pathological exam (6,7), and the N2 identification permits the adjuvant therapy administration with consequent survival benefit (7,8). For these reasons, intraoperative lymph node assessment needs a careful evaluation, and different indications and guidelines are present.

In detail, the UICC suggests the removal of six lymph

nodes from hilar and mediastinal stations (9), while the NCCN guidelines (10) suggests the prognostic equivalence of systematic nodal sampling and radical mediastinal dissection based on the ACOSOG Z0030 trial (11), that did not report any survival difference considering the two techniques. In detail, their actual guidelines suggest systematic lymph node sampling for station 2, 4, 7, 8, 9 on the right side and station 5, 6, 7, 8, 9 on the left side.

The European Society of Thoracic Surgeons proposed a more detailed indication for intraoperative nodal assessment, based on the preoperative workout, 18-FDG PET and minimally-invasive nodal evaluation results and tumour dimension and location (12). In particular, a systematic nodal dissection is recommended in any case to obtain a complete resection, even if in some cases (peripheral small squamous cancers), a systematic lobe specific lymphadenectomy is possible. However, it is recommended to harvest almost 3 mediastinal stations always including station 7.

Finally, the America College of Chest Physician (13) suggests the mediastinal radical node dissection in case of cN1/cN2 disease, while systematic node sampling seems to be equivalent in case of small N0 cancers.

This attention on mediastinal assessment is due its influence on two crucial points in NSCLC: staging and prognosis.

Indeed, as previously mentioned, an appropriate lymph node evaluation permits a more precise staging, with a better prognosis stratification but also the possibility to individuate appropriate post-operative treatments. Also for this reason, the TNM staging committee proposed a specific sub-classification regarding the kind of nodal involvement (14), showing a clear survival difference comparing patients with single or multiple N2 station involvement or in presence of skip metastases. This survival stratification should represent the base to plan tailored post-

operative surveillance schedules or therapies, considering that the prognostic role of the number of positive lymph nodes is still debate, and might be argument of further prospective research. Indeed, despite some encouraging results are present in literature, it is not clear if the number of N2 metastatic lymph nodes may have a prognostic value or it is necessary the addition of the number of N1 metastatic lymph nodes (15,16).

On the other hand, the prognostic role of the number of resected lymph nodes was evaluated and confirmed in different studies (17-19), especially in early stages lung cancer. Conversely, the number of resected nodes in patients with lymph node spreading do not seems to have a predictive value, while the ratio between the number of positive and resected nodes (node ratio), seems to be more effective in these cases (8,18). In particular, an elevate number of resected nodes (more than 10) seems to permit an appropriate stage discrimination among the TNM nodal sub-classification proposal (14,19), explaining its limits in terms of curves overlap and confirming the effectiveness of this sub-classification in NSCLC with nodal involvement.

It is clear that the goal during lung cancer resection is to obtain a complete resection with the most appropriate lymph node assessment, and in recent past, minimally invasive techniques permitted to obtain the same results of open surgery. Moreover, considering the less surgical stress, these approaches present the advantage of length of stay reduction, less painkillers administration and less complications and are now recommended as the approaches of choice in lung cancer surgery (1,10,13).

However, these techniques are the new instruments in cancer treatment, but the same oncological principles must be respected to guarantee the best approach in terms of survival possibility.

In particular, the extent of lymphadenectomy might be reproducible during video assisted thoracic surgery (VATS) or robotic assisted thoracic surgery (RATS), and since 2010 several authors reported excellent and comparable results in terms of resected lymph node and node stations, mediastinal upstaging and survival outcome compared to open surgery (20-22).

It is important to note that minimally invasive techniques might require technical skills and time to reach the same confidence present with open surgery, but this learning curve should not influence the oncological principles, ensuring the same treatment quality.

To obtain these results, many possibilities are present, consisting in active training in certified courses, presence in certified expert centres, watching videos but also considering pertinent literature showing the different techniques and the tip and trick for the correct intervention execution.

The aim of this special series is to offer a panoramic view on the state of the art of the nodal assessment in minimally invasive surgery and in particular during VATS and RATS, offering the possibility to expand the knowledge on this argument and give useful tools for surgeons approaching these techniques.

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