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Editorial

Extended Surgery for Non-Small Cell Lung Cancer (NSCLC)

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Extended surgery for Non-Small Cell Lung Cancer (NSCLC)

Lung cancer is the leading cause of death from cancer in the world [1]. Surgical resection still remains the best treatment option for NSCLC in the earlier stages of the disease, when the disease is confined within the lung parenchyma and does not extend beyond the lung hilum. The definition of extended resection is that of the resection of the necessary lung parenchyma for the clearance of the tumor (lobectomy, bilobectomy, pneumonectomy) en bloc with the invaded through tissue contiguity surrounded/neighboring organs and tissues. Extended resection may include the en blocresection of lung parenchyma withchest wall, diaphragm, spine, main carina or major mediastinal vessels (i.e. superior vena cava, azygos vein, descending aorta) [2]. One further distinct type of extended resection is the intrapericardial pneumonectomy with en bloc resection of pericardium and part of the left atrium of the heart [3].

The reported rate of the annually performed extended resections was 3.3% among all pulmonary parenchyma resections performed for NSCLC in Japan during the year 2010 (1,080 out of the 32,081 resections), most of them performed for T3 tumors (794 cases or 73.5% of all extended resections) [4]. Extended resections for T4 tumors comprise the 4.4% of the total of 6,091 operations performed for NSCLC in the Department of Thoracic and Vascular Surgery of Hôpital Marie-L annelongue (Paris-Sud University, Le Plessis Robinson) from 1981 to 2006 [5]. We can consequently conclude that extended resections represent only a small percentage (probably less than 5%) of curative lung cancer surgery in most Institutions.

Extended resections are performed for the eradication of locally advanced T3 and T4 lung tumors. T3 lung tumors are locally advanced lung carcinomas which are however considered to be resectable (tumors more than 7cm in their maximal diameter, tumors with a separate cancer nodule in the same lobe with the primary tumor or tumors with direct invasion of the chest wall, diaphragm, parietal pericardium, phrenic nerve, mediastinal pleura or tumors extending in the main bronchus in distance less than 2cm from the main carina). In the other hand, T4 tumors are locally advanced lung tumors which are generally considered unresectable at first glance. T4 tumors can be distinguished in two major subcategories: a) tumors with a separate tumor nodule in a different ipsilateral lobe and b) tumors which directly invade the heart or the great mediastinal vessels or the trachea orthe recurrent laryngeal nerve or the esophagus or the vertebral body or the main carina. T4 tumors can be resectable in some instances, in case of limited invasion of mediastinal structures and especially after effective down-staging by induction treatment. Indeed, resection of T4 tumors is accomplished by complex surgical procedures and it has to be made in specialized centers where multidisciplinary oncological and surgical teams are available. One's could further distinct two major categories of locally advanced T3 and T4 tumors which have different characteristics and different prognosis. The first category is that of peripheral lung tumors extending into the neighboring organs (i.e. chest wall, diaphragm, and spine) and the second one is that of centrally located tumors which extent to the mediastinal organs such as the main carina, thetracheobronchial angle, theleft atrium through the pulmonary veins or the mediastinal vessels. The tumors of the second category are more likely to be technically unresectable and/or to spread in the mediastinal nodes.

The most important requirement before any attempt to proceed with extended resection for NSCLC is the exclusion of the cancerous involvement of the mediastinal nodes (N2 or N3 disease) by strictly adhering to the currently existing guidelines [6], because locally advanced tumors with involvement of the mediastinal nodes have no chance for cure. In addition, the candidates for extended resections have increased risk of complications and mortality and therefore they need exhaustive preoperative workup and accurate estimation of their overall performance status [7]. The risk assessment before extended resection for NSCLC should

always include the postoperative cardiac event risk stratification (especially the exclusion of the clinically silent coronary artery disease), the estimation of the risk for postoperative death by using the "THORACOSCORE" and the estimation of the postoperative respiratory status by using all the available examinations and imaging techniques. [8] Any modifiable risk factors should be addressed carefully and the patient should be informed with details for the morbidity/mortality rates associated with the proposed procedure and for any possible influence of the extended resection on his lifestyle [8].

The benefits of extended surgery performed for the eradication of locally advanced T3 or T4 lung tumors can be seriously flawed by: a) the relatively high possibility of existence of occult distant micrometastases or microscopic mediastinal lymph node metastases at the time of surgery which cannot be detected by any imaging or invasive technique before surgery and b) by the relatively high possibility of incomplete resection or open-close thoracotomy. In addition, the accurate preoperative staging (T stage) by using all the available imaging techniques (PET/CT scan, MRI, CT scans with 3-D reconstructions is impossible in many instances [9]. Despite all the above mentioned limitations which put the extended resections in the "grey zone" of surgery for NSCLC, the expected benefits of surgery are the better local control of the disease, the prolongation of survival and the possible cure in 15-35% of the well selected patients for extended resection [2,3,5,10]. The responsible for the patient multidisciplinary team should make any effort to avoid either, overstaging of the tumor which can exclude some patients from surgery or under-staging of the tumor which will be responsible for incomplete (R1 or even R2 resections) or even for open-close thoracotomies [10]. Restaging of locally advanced tumors after induction treatment is a very difficult process and the PET criteria should be used for restaging [11].

According to the recently published guidelines byscientific societies (British Thoracic Society and Society of Cardiothoracic Surgeons of the Great Britain and Ireland, American College of Chest Physicians), government organizations (National Institute for Health and Care Excellence) or non-profit cancer networks (National Comprehensive Cancer Network) there is a general agreement that surgery should be offered in patients with T3N0-1M0 NSCLC [8,12-14]. Surgery should also be offered in "selected patients with T4N0-1M0 NSCLC as part of their radical multimodality treatment protocol". Complete resection with negative margins has to be the main goal of surgery [8,12-14].NCCN (2017 revised clinical guidelines) clearly states concerning resection of locally advanced T3 and T4 tumors that "If a surgeon or center is uncertain about potential resection, consider obtaining an additional surgical opinion from a high volume specialized center" [12].

Tumors with direct invasion of the chest wall and diaphragm should undergo en bloc lung parenchyma and chest wall/diaphragm resection with wide tumor free margins (more than 2cm if possible) in the absence of distant metastases and nodal mediastinal disease [12-14]. Superior sulcus (Pancoast) tumors are by definition T3 or T4 tumors and according to NICE (2011) should be treated as any other T3 or T4 lung tumor and not as a separate category of lung tumor [13]. The standard of care is the administration of neoadjuvant chemo-radiotherapy followed by en bloc resection of the upper lung lobe together with all the invaded strictures by tissue contiguity. [13,14]. There is a variety of surgical approaches described for the radical resection of superior sulcus tumors according to the location of the tumor within the thoracic inlet [15]. Invasion of the spine through tissue contiguity is more commonly observed in superior sulcus tumors located in the posterior compartment of the thoracic inlet. Invasion of less than 50% of one or two vertebral bodies allows radical tumor resection in selected cases, however combined thoracic and neurosurgical procedures are accompanied by serious increase of the complications rate and by high mortality [15]. Incomplete resection has similar survival with that of no resection [16]. Carinal resection is a technically demanding procedure which has to be performed in selected patients and in few centers with concentrating experience in the technique. There are some historical series reporting good long term results after extended resections of lung tumors invading the mediastinal vessels (i.e. resection and reconstruction of the superior vena cava or of the descending aorta) [5]. According to Bakhus and Wood (2014), "central vascular involvement that requires the use of cardiopulmonary bypass should be considered a contraindication for resection"[10]. Certainly, limited invasion of the superior vena cava which can be managed by the simple application of a site clamp or of the azygos vein do not preclude resection. In general, initially unresectable T4 locally advanced tumors should receive neoadjuvant treatment and resection should be offered only in selected patients with good response to induction treatment [12]. Indeed, we should remember that extended resections after induction treatment are associated with higher morbidity and mortality rates [17].

Pneumonectomies with en bloc resection of the pericardium and especially those with resection of part of the left atrium without the support of cardiopulmonary bypass are a separate type of extended resection. There are some published series including only few cases each [5,18,19]. This type of extended pneumonectomy has never been included in the published clinical guidelines probably due to the limited evidence. The procedure is associated with increased morbidity and mortality. In my personal experience the procedure can offer prolonged survival in selected patients with extension of the tumor within the inferior pulmonary vein. I have however to note that we experienced once a cerebral embolic event with fatal outcome, probably due to the separation during the surgical manoeuvers of an small neoplastic embolifrom the located within the lumen of the inferior pulmonary vein main embolus.

Overall, the completeness of resection and the absence of N2 disease are the main determinants of prolonged survival in locally advanced tumors undergoing extended resection. R1 and R2 resections are associated with survival rates similar to that of no resection. Induction treatment is the gold standard in superior sulcus lung carcinomas. Induction treatment can be applied in some T3 and in most of T4 tumors in order to succeed effective down-staging and R0 resection. Extended resections after induction treatment are associated with increased morbidity and mortality rates. The risk of incomplete resection and the risk of distal relapse of the diseases because of the existence of occult distant micrometastases at the time of surgery are also high.

References

1. Dela Cruz CS, Tanoue LT, Matthay RA (2011) Lung Cancer: Epidemiology, Etiology, and Prevention. Clin Chest Med 32: 605-644.
2. Kodama K, Higashiyama M, Yokouchi H, Takami K, Yasuda T, et al (1999) Survival and postoperative complications after extended surgery for non-small-cell lung cancer. Jpn J ThoracCaridovascSurg 47: 546-551.
3. Tsuchiya R, Asamura H, Kondo H, Goya T, Naruke T (1994) Extended resection of the left atrium, great vessels, or both for lung cancer. Ann Thorac Surg 57: 960-965.
4. Ikeda N (2013) [The role of extended surgery for lung cancer]. Nihon Geka Gakkai Zasshi 114: 173-175.
5. Yildizeli B, Dartevelle PG, Fadel E, Mussot S, Chapelier A (2008) Results of primary surgery with T4 non-small cell lung cancer during a 25-year period in a single center: the benefit is worth the risk. Ann ThoracSurg 86: 1065-1075.
6. De Leyn P, Dooms C, Kuzdzal J, Lardinois D, Passlick B, et al (2014) Revised ESTS guidelines for preoperative mediastinal lymph node staging for non-small-cell lung cancer. Eur J CardiothoracSurg 45: 787-798.
7. Brunelli A, Charloux A, Bolliger CT, Rocco G, Sculier JP, et al (2009) European Respiratory Society.; European Society of Thoracic Surgeons Joint Task Force on Fitness For Radical Therapy.The European Respiratory Society and European Society of Thoracic Surgeons clinical guidelines for evaluating fitness for radical treatment (surgery and chemoradiotherapy) in patients with lung cancer. Eur J CardiothoracSurg 36: 181-184.
8. Lim E, Baldwin D, Beckles M, Duffy J, Entwisle J, et al (2010) British Thoracic Society and the Society for Cardiothoracic Surgery in Great Britain and Ireland Guidelines on the Radical Management of Patients with Lung Cancer. Thorax 65: 1-27.
9. Wain JC (2004) Invasive Staging and Aggressive Surgical Resection: Essential to Management of Central NSCLC. Oncology (Williston Park) 28: 228-230.
10. Backhus LM and Wood DE (2014) Management of centrally located non-small-cell carcinoma. Oncology (Williston Park) 28: 215-221.
11. Wahl RL, Jacene H, Kasamon Y, Lodge MA (2009) From RECIST to PERCIST: evolving considerations for PETresponse criteria in solid tumors. J Nucl Med 50: S122 - S150.
12. NCCN Clinical practice guidelines in oncology. Non-small cell lung cancer. Version 4.2017. https://www.nccn.org/professionals/physician_gls/pdf/nscl_blocks.pdf
13. Baldwin DR, White B, Schmidt-Hansen M, Champion AR, Melder AM, Guideline Development Group(2011) Diagnosis and treatment of lung cancer: summary of updated NICE guidance. BMJ 342:d2110.
14. Kozower BD, Larner JM, Detterbeck FC, Jones DR (2013) Special treatment issues in non-small cell lung cancer: Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. Chest 143: e369S-99S.
15. Foroulis CN, Zarogoulidis P, Darwiche K, Katsikogiannis N, Machairiotis N, et al (2013) Superior sulcus (Pancoast) tumors: current evidence on diagnosis andradical treatment. J Thorac Dis 5: S342-S358.
16. Gandhi S, Walsh GL, Komaki R, Gokaslan ZL, Nesbitt JC, et al (1999) A multidisciplinary surgical approach to superior sulcus tumors with vertebral invasion. Ann Thorac Surg 68: 1778-1784.
17. Matsubara Y, Takeda S, Mashimo T (2005) Risk stratification for lung cancer surgery. Impact of induction therapy and extended resection. Chest 128: 3519-3525.
18. Kuehnl A, Lindner M, Hornung HM, Winter H, Jauch KW, et al (2010) Atrial resection for lung cancer: morbidity, mortality, and long-term follow-up.World J Surg 34: 2233-2239.
19. Borri A, Leo F, Veronesi G, Solli P, Galetta D, et al (2007) Extended pneumonectomy for non-small cell lung cancer: morbidity, mortality, and long-term results. J ThoracCardiovascSurg 134: 1266-1272.