

“Old people suffer the ravages of the years”: changes of treatments in elderly patients with early stage non-small cell lung cancer

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Abstract: The increase in life expectancy and the spreading of lung cancer screening led to a further rise of newly detected non-small cell lung cancer (NSCLC) cases. Age, per se, should not be considered a contraindication for treatments in fit patients. Early stage NSCLC is more and more treated with minimally invasive surgery. Stereotactic ablative radiation therapy (SABR) has been developed as an innovative therapy for stage I NSCLC and is now considered a standard treatment option for medically inoperable patients or for patient who refuse operation. Preoperative careful functional evaluations either respiratory or cardiovascular, as well as preoperative staging, are mandatory to pose indication for surgery in elderly. On the other hand, all elderly patients with lung cancer should have some form of assessment of physiologic age. As minimally invasive thoracic surgery has reduced the postoperative morbidity and has led to a decrease in the length of hospital stay, lobectomy remains the treatment of choice for early stage NSCLC in elderly patients. Discussion by experienced multidisciplinary team is the best approach to evaluate the advantages/disadvantages of each treatment modality in elderly patients with early-stage NSCLC.

Keywords: Lung cancer; video assisted thoracic surgery (VATS) lobectomy; segmentectomy; stereotactic ablative body radiotherapy (SABR); elderly patients

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The title in quotation marks is from “*the Old Man and the Child*”, a song written in 1972 by the amazing Italian songwriter Francesco Guccini about the elderly condition. In these apparently far years, the age itself was a contraindication not only to surgery but, also, to others therapies in elderly patients with lung cancers. Current imaging technology has become more sensitive with the identification of smaller and indolent lesions. As life expectancy is increasing and lung cancer screening by low-dose computed tomography is more and more used, a rise of newly detected non-small cell lung cancer (NSCLC) cases is expected. There are few treatment strategies for elderly patients with an early stage NSCLC (surgery, stereotactic radiation therapy, radiofrequency ablation, etc.); however, no recent randomized trials have compared these treatment strategies. Advances in surgical techniques for NSCLC allows to perform most lung resections for

early stage lung cancer by minimally invasive techniques to reduce postoperative pain and, in most cases, the length of hospital stay (1). Stereotactic ablative radiation therapy (SABR) has been developed as an innovative therapy for stage I NSCLC and is now considered a standard treatment option for medically inoperable patients or for patients who refuse operation (2).

Recently, Shirvani *et al.*, from the MD Anderson Cancer Center of Houston (TX, USA), published a paper about the clinical characteristics and the survival outcomes of patients who underwent surgery or SABR for early stage NSCLC in the elderly (3). According to their data, lobectomy is still the optimal treatment for elderly patients fit for surgery. At 3 years, patients who underwent lobectomies have an unadjusted overall mortality of 25%; on the other hands, the effectiveness of SABR in frail elderly patients is promising, because this technology appears to offer a lower

risk of periprocedural mortality compared with surgery and although it does not appear to offer long-term survival comparable to surgery (3).

Age, per se, should not be considered a contraindication for treatments in fit patients. All elderly patients with lung cancer should have some form of assessment of physiologic age, including an estimation of mortality risk. Preoperative careful functional evaluations, either respiratory or cardiovascular as well as preoperative staging, are essential to pose indication for surgery in elderly. Multivariable proportional hazards regression in previous trials demonstrated that male sex, higher burden of comorbid illness, use of medical assistance devices, and larger NSCLC were associated with worse outcomes (4). Since the median age of patients with lung cancer is over 70 years, evidence is needed to guide clinical decision to find a way to balance surgical risk and therapeutic treatment efficacy in the elderly population (5).

Video assisted thoracic surgery (VATS) lobectomy is more and more used in general thoracic surgery. Nowadays, VATS lobectomy is considered a reasonable and acceptable alternative to open surgery for NSCLC (6). A lot of studies suggest that VATS lobectomy is superior to thoracotomy with less intraoperative blood loss, reduced hospital length of stay, decreased postoperative pain, better treatment compliance, low postoperative complications, better postoperative pulmonary function, similar operative time, and equal long-term outcomes (7,8). This is also true for elderly patients who achieve acceptable long-term survival with a good quality of life. According to a recent paper, differently from younger patients, octogenarians with lung cancer died of non-cancer related disease and this point might explain the reduced impact of pathological stage on the overall survival (OS) (9). Postoperative careful observation and management after lung resection has been stressed in elderly patients as postoperative morbidity tended to be more severe than in younger patients, possibly due to physical weakness and preoperative comorbidity (10).

An answer to the question whether a lobectomy or a sublobar resection should be performed in elderly is given by Shirvani *et al.*, who underline that sublobar resections were associated with worse OS and worse lung cancer specific survival (LCSS) in proportional hazards regression when compared to lobectomy. Their findings were preserved even if the sublobar resection cohort was limited to those who underwent VATS or anatomic segmentectomy. Furthermore, survival analysis of the cohorts, demonstrated significantly worse LCSS and OS among patients

undergoing sublobar resection (3).

Anatomical segmentectomy performed by VATS is a safe and effective alternative to open techniques in the surgical management of NSCLC (11). Segmentectomies for early lung cancer is used frequently as an alternative to lobectomy to resect marginal candidates (elderly, patients with poor respiratory reserve, previous pulmonary resection) or patients with multifocal ground-glass opacities, synchronous tumors or history of other solid malignancies where diagnosis of metastasis is a possibility) (12,13). At present, sublobar resections are an alternative treatment for a very selected population of NSCLC patients with a peripheral stage IA disease or with a predominantly ground glass aspect and this is even more true in patients with advanced age and poor lung function. The best results of sublobar resection are obtained only if a segmentectomy and not a wedge resection is performed with complete lymph node dissection. However, it is also not yet clear whether or not sublobar resections offer reduced morbidity than lobectomy in patients who can tolerate a lobectomy (14,15).

A comparison between lobectomy and SABR in elderly patients shows that, in the first 6 months of follow-up, SABR was associated with a lower risk for death compared with lobectomy. Later, regarding the LCSS, SABR was associated with a higher risk of death (3). Although results of SABR are promising, follow-up of lobectomy series are longer and these solid data should not be ignored. A definitive conclusion regarding the comparative effectiveness of SABR and surgery must be derived from randomized clinical trials (16), keeping in mind that serious complications of SABR have been reported (2). Moreover the favorable local control rate of SABR is only referred to the primary tumor site; the residual parenchymal scar is difficult to differentiate from cancer; and, last but not least, there is no pathological confirmation of negativity of lymph nodes (mandatory to correctly stage the disease) (17).

In conclusion, thoracic surgery remains the treatment of choice for early stage NSCLC in elderly including octogenarian patients. VATS has reduced the postoperative morbidity and has led to a decrease in the length of hospital stay. Sublobar resections demonstrated the safety of their perioperative course; nevertheless, to date, segmentectomies are performed most often as an alternative to lobectomy, in patients with peripheral tumors and limited pulmonary reserve or other comorbidities. The discussion among members of an experienced multidisciplinary team is the best approach to evaluate the advantages/disadvantages of each treatment modality in elderly patients with early-stage NSCLC.

*The child stopped, his gaze was sad,
and his eyes looked at things never seen;
and, then, told the old man, with dreamy voice:
“I like fairy tales, tell me more”.
Francesco Guccini, the Old Man and the Child.*

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