



Video-assisted thoracic surgery versus stereotactic radiotherapy

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Abstract: Lung cancer is the major cause of cancer death worldwide. The improvements of radiological techniques and the employment of screening programs often allow an early diagnosis of this disease. Surgical resection is considered the gold standard in early stages. However, the employment of less invasive techniques, both surgical and non-surgical, increased in the last decades. Video-assisted thoracoscopic surgery (VATS) demonstrated to obtain similar survival outcomes with less post-operative complications compared to open thoracotomy. Stereotactic body radiotherapy (SBRT) improves overall survival over conventional radiotherapy and offers a better safety profile compared to surgery.

Keywords: Non-small cell lung cancer (NSCLC); stereotactic body radiotherapy (SBRT); video-assisted thoracoscopic surgery (VATS)

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Introduction

Lung cancer is the major cause of cancer death worldwide. Despite this, the improvements of radiological exams and the use of screening programs often allow diagnosis of early stage disease.

In these cases, histopathological diagnosis should be obtained whenever safely feasible. Proper radiological staging with chest computed tomography (CT) scan and ¹⁸F-fluorodeoxyglucose (¹⁸F-FDG) positron emission tomography (PET) is mandatory. Guidelines recommend pathological staging of mediastinal lymph nodes with mediastinoscopy or endobronchial ultrasonography (EBUS) in case of CT-enlarged or PET-positive lymph nodes, or tumors sized more than 3 cm (1).

Despite surgical resection remains the gold standard with the aim of cure in early stage disease, in the last few decades the employment of less invasive techniques increased, both surgical and non-surgical ones.

Radiotherapy use raised not only in palliative settings, but also with curative purposes.

Unfortunately, phase III randomized studies comparing stereotactic body radiotherapy (SBRT) and surgery were closed early due to poor accrual [the STARS trial (NCT00840749), the ROSEL trial (NCT00687986), and the ACOSOG Z4099 trial (NCT01336894)]. Furthermore, in most trials surgery was thoracotomy, not minimally invasive surgical technique.

A pooled analysis of two trials (STARS trial and ROSEL trial) showed similar recurrence-free survival at 3 years [86% in the SBRT group versus 80% in the surgery group; hazard ratio (HR) 0.69, 95% CI: 0.21–2.29, log-rank P=0.54] as well as local, regional or distant failure, with an estimated overall survival at 3 years slightly favoring SBRT (95% versus 79%, HR 0.14, 95% CI: 0.017–1.90, log-rank P=0.037). In the SBRT group, 3 (10%) patients developed grade 3 adverse events, none of them grade 4. In the surgery group, one patient died of surgical complications and twelve patients (44%) developed grade 3–4 treatment-related adverse events including dyspnoea, lung infections and chest pain (2).

The aim of this paper is to review published data dealing

with video-assisted thoracoscopic surgery (VATS) and SBRT, with a particular mention of elderly patients who are often unsuitable for standard surgery.

VATS and SBRT

VATS can be defined as the same open procedure without chest wall muscle division or rib spreading, using a video screen for guidance (3). The principles of oncology surgery are completely respected: anatomical division of lobar structures, standard nodal dissection and radical resections, with the advantage of being minimally invasive compared with open thoracotomy. It should include N1 and N2 (at minimum three N2 stations) sampling or resection and free resection margins. Since the first description by Roviato in 1993 (4), over the past 24 years no randomized clinical trials have been planned to compare the two different techniques. However, some wide databases (5,6) or large institutional series (7) have been published and are useful to analyze several results, including short- and long-survival, length of hospital stay (LOS), rate of complications and oncologic efficacy.

Depending on the personal surgeon preference, a VATS lobectomy can be performed via a single to four small incisions, including a 3 to 6 cm utility incision. The distribution of the incisions and the position of the patient on the operative bed are a result of the lobe/segment to be removed and the type of approach to the hilar structures, being possible a posterior or an anterior manner. The dissection of the structures is obtained using different kinds of devices: blunt, sharp and/or electric tools; the ligation of the single structures and the completion of the fissures are obtained by using endoscopic staplers (8). At every moment, the rapid conversion from a VATS lobectomy to a standard procedure has to be possible, enlarging the utility incision, as a consequence of a major bleeding or any other reason.

The eligible patients for a VATS procedure should have a clinical early-stage non-small cell lung cancer (NSCLC), proven by CT and PET.

A propensity matched analysis using database from 17 cancer registries throughout the United States showed similar results in terms of overall survival, cancer-specific, and disease-free survival between patients undergoing thoracoscopic lobectomy and patients undergoing thoracotomy lobectomy (6). The significant improvement of outcomes in the VATS group is observed when LOS, post-operative pain and morbidity (including cardio-pulmonary complications, wound infections and sepsis) are compared,

with consequent costs decrease (5).

The amount of performed VATS lobectomies in the United States increased through decade, and is between 15% and 30% of all lobectomies (5). At least 30 consecutive operations are necessary for an experienced surgeon to achieve an adequate level of competence with VATS (9).

Despite many studies continue to debate to establish the value of this surgical technique, in terms of safety and oncologic efficiency, experienced surgical teams advocate the adoption of minimally invasive lung resections (10).

SBRT is a technique of radiotherapy that carries high radiation doses against a limited volume in a few fractions, thus reducing toxicities to the nearby normal tissues.

A dose 45–60 Gy over 1–14 days is delivered according to the position of the tumor (central versus peripherally located lesion), the size (> or <2 cm) and the presence of lung comorbidities (e.g., severe COPD, emphysema). The use of SBRT increased in the last decades and demonstrated an improvement of overall survival over conventional radiotherapy (11,12). SBRT showed better local control and lower toxicities advantages over conventional radiotherapy (11). It also evidenced a better safety profile compared to surgery and it can be delivered in outpatient setting.

Its disadvantage over surgery is due to higher distant recurrence (13). Furthermore, it needs pathologic confirmation of disease.

Prospective trials comparing VATS and SBRT are lacking. However, data from a retrospective analysis showed similar overall survival between VATS and SBRT, but better locoregional control with SBRT (14).

Elderly population

Elderly patients deserve a proper mention. Incidence of early NSCLC in elderly is increasing due to ageing of population. SBRT is especially appealing in this subset due both to the good safety profile of this technique and frailty of these patients. The increased use of SBRT in early NSCLC caused a reduction of untreated elderly patients and improved OS (11).

Histopathological diagnosis should be obtained whenever safely feasible. However, if the risks of invasive biopsy outweigh benefits, and radiological exams (CT scan and ¹⁸F-FDG- PET) are highly suggestive of malignant tumor, biopsy can be omitted. Indeed, the risk of benign disease is rare in these cases.

One retrospective cohort study evaluated survival in elderly

patients after SBRT or thoracoscopic for lung cancer (15). Authors evidenced improved cancer specific survival after thoracoscopic resections over SBRT in patients with tumors sized ≤ 5 cm (SABR *vs.* resection mortality: HR 2.10, 95%.CI: 1.52–2.89; $P < 0.001$), whereas no difference was observed in patients with tumors sized ≤ 2 cm. Thus, SBRT is a valid option for elderly patients unsuitable for VATS because of age, reduced cardiopulmonary reserve or comorbidities.

Conclusions

Surgery remains the standard of care for operable clinical stage I NSCLC. However, SBRT is a reliable alternative option with comparable efficacy but better safety for patients who cannot undergo or refuse surgery or patients with short life expectancy. A multidisciplinary team should evaluate each patient with early NSCLC. Phase III randomized controlled clinical trials with adequate follow-up are warranted evaluating also biomolecular alterations. Nowadays, the choice of the local approach is not influenced by genomic profiling and international guidelines do not recommend to test genetic alterations in early lung disease patients suitable for local treatment. However, added to clinical characteristics, genetic alterations deserve to be considered in clinical trials to support the choice of the proper approach thus personalizing the local treatment beyond medical therapies. Indeed, clinical trials in early-stage disease should evaluate if oncogene-addicted NSCLC patients should receive a proper local therapy or a particular follow-up compared to non-oncogene-addicted tumors.

New non-invasive techniques as SBRT are particularly intriguing for selected frail populations as elderly patients to avoid both intraoperative risks and post-operative complications, especially considering the increasing rate of elderly patients.

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