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Review Article

Recent advances in surgical management of early lung cancer

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The broad application of low-dose computed tomography screening has resulted in the detection of many more cases of early lung cancer than ever before in modern history. Recent advances in the management of early-stage non-small cell lung cancer have focused on making therapy less traumatic, enhancing recovery, and preserving lung function. In this review, we discuss several new modalities associated with minimally invasive surgery for lung cancer. Firstly, less lung parenchyma resection via sublobar resection has become an acceptable alternative to lobectomy in patients with tumors less than 2 cm in size or with poor cardiopulmonary reserve. Secondly, thoracoscopic surgery using a single-portal or needlescopic approach to decrease chest wall trauma is becoming common practice. Thirdly, less invasive anesthesia, using nonintubated techniques, is feasible and safe and is associated with fewer intubation- and ventilator-associated complications. Fourthly, preoperative or intraoperative image-guided localization is an effective modality for identifying small and deep nodules during thoracoscopic surgery.

Introduction

Lung cancer is the leading cause of cancer-related deaths worldwide, and non-small cell lung cancer (NSCLC) is the most common type. In Taiwan, lung cancer accounted for 12.09% of total newly reported cancers and ranked the highest in cancer-related mortality in 2012.[1,2] Despite advances in multimodality treatments including target

Abbreviations: LDCT, low-dose computed tomography; NSCLC, non-small cell lung cancer; VATS, video-assisted thoracoscopic surgery; VDT, volume doubling time.

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therapy and immunotherapy, the long-term survival of patients with advanced-staged lung cancer remains dismal[3]; furthermore, lung cancer ranked the highest in cost per quality-adjusted life year in a national cost-effectiveness analysis.[4] Although advance-staged lung cancer still garners the majority of newly diagnosed lung cancer cases, the incidence of early-stage lung cancer, defined as clinical T1-2N0M0 disease,[5] greatly increased in recent years because of low-dose CT (LDCT) screening, enabling detection, treatment, and cure of many of early stage lung cancers. The aim of this review is to summarize the new advances and ongoing research topics on the surgical management of early-stage lung cancer focusing on making therapy less traumatic, enhancing recovery, and preserving lung function.

Management of screened lung nodules

Following the publication of the National Lung Screening Trial,[6] lung cancer screening using LDCT has been performed in many countries and is effective in detecting smaller lung cancers at earlier stages than in the past.[2] However, only about 5% of detected lung nodules are found to be cancerous,[7] and it is important to have evidence-based guidelines for timely and efficient management of screening-detected or incidentally found lung nodules. Several professional societies such as the Fleischner Society,[8] the National Comprehensive Cancer Network,[9] the British Thoracic Society,[10] the American College of Radiology,[11] and the American College of Chest Physicians[12] have issued similar formal guidelines for the management of screened lung nodules. Among these guidelines, screened nodules are classified as solid, partly solid, and non-solid types, each managed with a different algorithm based on the size and interval growth of the nodules. Rather than going through the details of the treatment algorithms, a simplified rule for clinical practice according to the guidelines was made: 1) Solid nodules with clear morphologically benign appearance are not recommended for any further intervention. 2) Solid nodules larger than 8 mm with a high suspicion of malignancy are considered for intervention, including biopsy or surgical resection. 3) Partly solid nodules should be managed like solid nodules with the same or a lower size threshold of its solid part, and the surveillance of interval growth should focus on the solid component. 4) Persist non-solid nodules larger than 10 mm with interval growth or development of a solid component are considered for intervention. During the surveillance for interval growth of lung nodules, volume doubling time (VDT) was shown to be a reliable marker of nodule growth,[13,14] and both the updated British Thoracic Society guidelines and the NELSON study, which was the largest trial after the National Lung Screening Trial, adopted VDTs as a standard risk predictor. Automated volumetric analysis detects nodule growth earlier compared to manual 2-dimensional caliper measurements, and it facilitates a confident assessment of nodule stability. Nonetheless, where automated volume measurement is not available or possible, two-year manual surveillance is recommended.[15,16]

Most of these clinical practice guidelines come from Western Europe and the United States, and implementation of the guidelines in Asian countries requires modification. Firstly, the high incidence of tuberculosis in Asia reduces the confidence in predicting malignancy on serial imaging studies alone,[17] and it favors less reliance on positron emission tomography scanning and greater use of nonsurgical biopsy over surgical diagnosis.[18] Second, a greater proportion of lung cancer arises in Asian women that have never smoked cigarettes, which may be attributed to both genetic differences and other factors.[19,20] Third, air pollution is common and severe in many Asian countries. Practitioners should be as aware of the risk of air pollution as they are of the risk of cigarette use, although none of the lung cancer risk models published so far includes the risk of exposure to air pollution.[21,22]

Sublobar resection including segmentectomy and wedge resection

Based on the negative results of the randomized trial conducted by Lung Cancer Study Group,[23] most clinical societies recommended standardized lobectomy as the treatment of choice for stage IA NSCLC, and this treatment has guided the surgical management of stage IA NSCLC for the past 20 years. However, the application of sublobar resection in early lung cancer has regained attention due to a better understanding of CT imaging and improved resolution allowing precise identification of tumor textures,[24] which correlated with different histopathologic types and prognosis.[25,26]

According to the current evidence, there are several tumor characteristics and resection specifications associated with improved survival following sublobar resection. Tumor size greater than 2 cm is an independent risk factor for recurrence in patients undergoing sublobar resection,[27,28] and the current ongoing trials have limited patients' tumors to 2 cm or less.[29] Sublobar resections are also recommended for pure ground-glass nodules and part-solid nodules with a consolidation to tumor size (C/T) ratio less than 0.25, which are associated with adenocarcinoma in situ and minimally invasive adenocarcinoma consisting of purely lepidic growth without invasion or less than 0.5-cm invasion. These indolent lesions usually present with absence of nodal involvement and 100% disease-specific survival following resection.[30] In elderly patients, the importance of tolerability and pulmonary function preservation appear to outweigh local control. Retrospective series[31,32] and a recent database analysis[33] showed equivalent overall survival in patients 75 years of age and older who underwent sublobar resection compared with lobectomy. Several studies showed that adequate surgical resection margin is an important determinant of local recurrence after sublobar resection. A section margin less than 1 cm is considered to be inadequate and is associated with a high recurrence rate,[34,35] and the National Comprehensive Cancer Network currently suggests a resection margin of 2 cm or greater or a margin/tumor ratio 1 or greater.[36] Although segmentectomy and wedge resection are grouped as sublobar resections and analyzed with lobectomy in many previous studies, recent reports emphasize the distinct oncological differences between them. Wedge resections are frequently performed in video-

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