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Comparing Lobectomy and Segmentectomy: Which Elements Affects an Optimal Oncological Outcome?

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Abstract

In this research work in recent years, Low Dose Computed Tomography (LDCT) is being used for lung cancer screening in high risk groups. According to USPSTF guidelines, people aged between 55 and 80 years old, who have a smoking history of 30 pack-years or have quit for less than 15 years, are recommended to take a LDCT scan. Other possible candidates for lung cancer screening can be patients with radon exposure, family history associated with lung cancer or history of pulmonary fibrosis or chronic obstructive lung disease. Detecting lung cancer at an early stage raises the question of optimal treatment and overall survival. This article aims to compare segmentectomy *vs*. lobectomy as surgical options, in case of stage I Non-Small-Cell Lung Carcinoma (NSCLC), ideally IA.

In order to compare the two previously referred strategies, data has been collected from articles (40 studies have been reviewed), reviews and systematic analyses in PubMed Central and also reviewing recent literature. Tumor size and location, patient age, comorbidities and nodal status have been examined as factors that affect the choice between segmental or lobar tumor resection. R_0 resection and distance between resection margin and tumor was taken into consideration.

Segmentectomy could be an equal alternative to lobectomy in early stage NSCLC (tumor<2 cm). It could mainly be preferred for >75 y.o. and/or multimorbid patients with low cardiopulmonary reserve and struggle to survive a lobectomy. However, the anatomical segmentectomy requires among other a peripheral tumor position. Some segments, such as posterior segments of left upper lobe, are not removed separately. In this case, for anatomic reasons a bi- or tri-segmentectomy could be performed.

As far as early stage NSCLC is concerned anatomic segmentectomy is an acceptable procedure in a selective group of patients. For a better tumor and stage classification a systematic lymph node dissection should be performed.

Keywords: NSCLC • Stage Ia • Segmentectomy *vs*. lobectomy •LN status • Disease free survival

Introduction

Ginsberg and Rubenstein in 1995 [1] published the results of randomized LCSG trial. They randomized 276 patients with T1N0 NSCLC, but 247 of them where eligible for analysis. In detail, 40 patients that underwent wedge resection were randomized to 40 patients that underwent lobectomy and 82 patients that underwent segmental resection were randomized to 85 patients that underwent lobectomy. The statistical analysis showed that in patients that underwent a sublobar resection the recurrence rate was by 75%, the overall death rate was 30% higher compared to lobectomy patients. The authors have advocated for lobectomy with systematic hilar and mediastinal lymphnode (LN) sampling or dissection, but despite higher risk of locoregional recurrence, they have suggested that sublobar resection should be performed in patients with insufficient preoperative pulmonary function and especially in patients that have underwent a contralateral pneumonectomy.

For several years after this study lobectomy was the procedure of choice, as most thoracic surgeons had been skeptical towards segmentectomy and wedge resection. However, the study has also received criticism. D' Andrilli et al. [2] criticised that the selected patients were more or less understaged because of non-proper preoperative staging. Additionally, recurrence and death rates for tumors smaller than 2 cm were not statistically analyzed separately,

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while one out of three patients in sublobar resection group underwent a wedge resection, which means that resection margins in those patients might be inadequately examined and that hilar LN dissection has not been performed. The authors of this paper suggested a segmentectomy for peripheral tumors smaller than 2 cm that do not affect the intersegmental fissure and highlighted that more than one segments could be respected, but with questionable benefit over lobectomy. Finally, they suggested that in order to avoid understaging and to reveal possible occult metastases a systematic hilar and mediastinal LN dissection shall be performed.

Literature Review

Patient selection for segmental resection

Selecting patients for a segmentectomy is currently under discussion. Possible indications, as far as NSCLC is concerned, include need for functional parenchyma sparing in multimorbid patients, elder age, poor preoperative cardiopulmonary status, small tumors without LN involvement and multiple synchronous or metachronous tumors.

Landreneau et al. [3] advocate for anatomical segmentectomy in multimorbid patients with a small, peripheral (Stage Ia) NSCLC aiming to spare lung function and reduce morbidity. The authors have also suggested that segmentectomy should be completed with interlobar, hilar and mediastinal LN sampling/dissection as to avoid understaging. In a similar direction, Zhang et al. [4] suggest segmentectomy in elderly patients with low cardiopulmonary reserve and comorbidities. The authors have highlighted the importance of the number of lymph nodes that are examined as a prognostic factor in node-negative NSCLC and have suggested that more than 7 LNs should be dissected. Additionally, they argumented that (elder) age itself is not an indication for segmentectomy.

Bilgi et al. [5] have underlined that segmentectomy in patients with small tumor size (<2 cm, St Ia), adequate resection margins and LN dissection lead to comparable outcomes with lobectomy, while Filosso et al. [6] have recommended non anatomic resections, such as wedge resections, for patients with low cardiopulmonary reserve or for patients with multiple synchronous or metachronous tumors.

Meacci et al. [7] have suggested that segmentectomy is indicated for small <1 cm GGO lesions, tumors less than 2 cm in diameter without thoracic lymph node involvement (T1N0) and benign disease, as a lung–sparing procedure. This allows a second or third future surgical resection for a newly diagnosed NSCLC and suggested interventional and non-interventional procedures for intraoperatively tumor localisation.

Technical issues

Sequence of surgical steps, selection between anatomical resection of a segment or resection of the adjacent segments as well, identification of difficult to resect segments, possible intraoperative pitfalls and subxiphoid versus intercostal access in thoracoscopic procedure have been examined.

Pham et al. [8] have examined indications and techniques of frequently used segmental resections. The authors have suggested segmentectomy for resection of primary NSCLC, pulmonary metastases and benign conditions, such as fungal disease and have underlined that the most commonly performed procedures include lingula sparing upper lobectomy, lingulectomy, superior segmentectomy and basilar segmentectomy. The author's advice against thoracoscopic segmentectomy if sufficient resection margins cannot be obtained, if a preoperative N2 or N3 situation is present or single lung ventilation cannot be achieved. They are, also, skeptical towards T2 tumors, N1 disease, and history of thoracic irradiation or induction therapy. After ligation/dissection of segmental pulmonary vein, visible hilar LNs adjacent to segmental bronchus and artery can be removed and afterwards segmental bronchus and artery can be stapled. The parenchymal excision should follow the intersegmental fissures followed by a systematic mediastinal LN dissection. If the tumor is located close to the intersegmental fissures, a bi–or trisegmentectomy should be performed.

In the same direction, Hernandez–Arenas et al. [9] have described the surgical technique in Uniportal VATS segmentectomies. The authors advocate for the inflation and deflation method, before the final stapling of the segmental bronchus. While the segmental bronchus is clamped, the anesthetist insufflates the remaining parenchyma. If the remaining segments can expand properly, the selected segment(s) can be removed.

Due to arterial and bronchial anatomy, not all segments can be anatomically resected, as Zhai et al. [10] have underlined. Apical right upper segment, posterior segment, dorsal right lower segment, posterior left upper segment plus anterior (inherent upper), the lingual and left posterior dorsal segments are classified as respectable, whereas anterior upper segment and basilar segment are classified as anatomically difficult to resect.

Operational access and incisions

Regarding (MG1) operational access and incisions Abdellateef et al. [11] have compared subxiphoid uniportal (SVATS) and intercostal uniportal VATS segmentectomy (UVATS). In SVATS group operative time was longer, more blood was lost intraoperatively, but postoperative pain score was lower and postoperative quality of life score along the first postoperative year was higher. UVATS segmentectomy was found to cost less than SVATS segmentectomy. Regarding postoperative drainage, duration of chest tube, postoperative hospital stay, operative conversion or postoperative complications did not differ significantly between the two groups. After SVATS and the UVATS completion, the surgical margins were evaluated and the specimen was sent for frozen section analysis. If the lesion could not be palpated or if margins were inadequate, a lobectomy should be performed. LN sampling from at least three N2 stations was also performed. More LN was sampled in UVATS group, but more LNs were dissected in SVATS group. Therefore, SVATS segmentectomy can be a safe surgical option for stage IA NSCLC, but as the authors have suggested, it should be avoided in case of history of cardiac disease or cardiac arrhythmia and in patients with left sided lesions.

Segmentectomy indications, as presented by Hirji et al. [12], include peripheral T1N0 lesions and at the same time low cardiopulmonary reserve, synchronous lung primary tumors, or possibility for metachronous primary tumors, for instance, following a small contralateral lesion. The authors have also suggested that an additional resection of adjacent segments can be performed depending of the spatial location of the tumor.

Effect on pulmonary function

As it has been previously stated segmental resection has been considered as a surgical option in patients with low cardiopulmonary reserve. Postoperative changes in pulmonary function values after segmentectomy and lobectomy have been assessed in studies that are presented subsequently.

Donington et al. [13] argumented for the lobectomy with systematic mediastinal LN evaluation as the treatment of choice for stage I NSCLC, but they have stated that 1out of 4 patients with stage I NSCLC are not eligible for lobectomy because they are multimorbid. In case lobectomy cannot be tolerated, sublobar resection followed by adjuvant intraoperative brachytherapy, in order to reduce involved lobe recurrence, can be an alternative.

Bedat et al. [14] compared postoperative complications between VATS lobectomy and VATS segmentectomy. Minor or major complications appeared in 33.3 % of segmentectomies and 38% of lobectomies. Rate of complications and their severity were analog to ASA score, presence of COPD, decreased FEV1 and decreased DLCO. Length of hospital stay and drainage duration was shorter after segmentectomy. Segmentectomy seems to preserve lung function better than lobectomy, because the function of the ipsilateral non-operated lobe is increased, but this type of operation is more technically demanding, as it requires more extensive and deeper dissection into the hilum and division of intersegmental planes. Using staplers to divide intersegmental planes can induce compression of the adjacent parenchyma, atelectasis and pneumonia of the non–operated lobe, possibly more often in patients with COPD. Dissection of hilar and mediastinal LN was performed in both procedures, but systematic LN dissection was more often performed in lobectomy patients.

Factors that predict recurrence

Rami-Porta et al. [15] suggested that complete resection is linked to free of tumor margins, proven microscopically, systematic or lobe-specific systematic LN removal, without extension of the tumor outside of the nodal capsule. If the highest mediastinal LN that is dissected is positive, if there is carcinoma *in situ* at the bronchial margin, even though there is no residual tumor macroscopically, of if pleural lavage cytology is positive, the resection is characterized as incomplete. In the same direction, Schuchert et al. [16] have stated that factors that influence recurrence in stage I NSCLC include increased size and grade, vessel and LN invasion and decreased tumor inflammation. The authors suggested that risk of overall complications is lower in segmentectomy. In this study risk of recurrence did not differ statistically between segmentectomy and lobectomy, as resection margins were examined intraoperatively and found to be adequate.

The suggested margin: tumor ratio should be higher than one. If this condition cannot be completed the operation must be converted to lobectomy. Sawabata et al. [17] evaluated presence of malignancy in resection margins. In negative for malignancy sample (61% of total) group maximum tumor diameter was lower, margin distance was higher, lesions were located in easily resected parenchyma regions and more often stapling was required only. This study presented maximum tumor diameter and margin distance as independent factors of recurrence. Margin distance higher than 2 cm and margin distance greater than maximum tumor diameter has led to negative for malignancy margins in 100% of cases in this study and was considered to prevent local recurrence.

Ensuring sufficient resection margins might be associated with the exact tumor location. Sato et al. [18] suggested virtual – assisted lung mapping as a technique that aids identifying location of lesions in the lung parenchyma. Indigo carmine was injected to the targeted bronchus under bronchoscopic guidance, in order to mark the exact location of the tumor. This technique was used to identify and resect 209 lesions, including mixed and pure ground glass nodules as well as solid nodules. Consequently, 178 of 209 lesions were successfully resected and 190 of 209 were identified. The authors concluded that their technique can target lung lesions, but successful resection rate did not reach their primary goal and underlined that insufficient depth of resection margin is the main reason that leads to unsuccessful removal of the lesion.

Okada et al. [19] studied 5 and 10 year survival rate in case of segmentectomy and lobectomy for tumors <2 cm and >2 cm. If tumor size was lower than 2 cm, 5-year survival rate was found to be 83%in segmentectomy and 81% in lobectomy and 10-year survival rate 83% and 64%, respectively. In case of tumors larger than 2 cm, 5-year survival rate was found to be 58% in segmentectomy and 78% in lobectomy and 10 year survival rate 58% and 60%, respectively. The authors suggested that histological type and tumor size could determine if an intentional segmentectomy or an intentional lobectomy is performed and that segmentectomy should be performed in NSCLC stage IA. In the same direction, Zheng et al. [10] compared patients treated with segmentectomy and patients treated with lobectomy. Age, sex, pulmonary function, tumor size, local recurrence, incidence of postoperative complications, 5 year OS and DFS did not differ significantly among the two groups. The authors suggest that tumor size is an independent prognostic factor of DFS in Stage IA NSCLC (≤2 cm) and advocate for segmentectomy with resection margins ≥2 cm in this group of patients.

Baig et al. [20] studied survival difference between segmentectomy and lobectomy. Lobectomy was associated with improved 5-year survival. Adenocarcinoma histology and number of LN sampled had a favorable effect towards survival, while age and male sex were linked to worse survival outcomes. Interestingly married status was associated with better survival. Neuroendocrine tumors were associated with worse survival after wedge resection or segmentectomy than after lobectomy. Small peripheral ≤ 2 cm, but high-grade tumors are linked with better survival after lobectomy than after segmentectomy. In addition, in this study it has been demonstrated that lobectomy is preferred over segmentectomy in

young patients, with aggressive tumor histology and clinical N1/N2 disease, as the risk of developing metachronous, recurrent or second primary lung cancer is estimated at 1%-2% per year. Therefore, the authors advocate for appropriate patient selection in both segmentectomy andlobectomy.

Discussion

LN status

Histologically positive nodal status is linked to higher possibility of recurrence, especially in case of inaccurate nodal staging. Detection of metastatic hilar or mediastinal LNs, that thought to be disease free, has been described as nodal upstaging after surgery for NSCLC during the final histopathologic evaluation. Nodal upstaging takes place in 28% of clinical stage I patients according to Cancer and Leukemia Group B prospective clinical trial (CALGB 9761). Positive hilar and mediastinal LN can be detected through chest CT scan, PET scan or mediastinoscopy, EBUS or VATS. Inaccurate nodal staging might take place in patients with history of tuberculosis, rheumatoid arthritis, and diabetes mellitus, as stated by Toker et al. [21]. In these cases, especially interlobar lymph nodes are closely attached to pulmonary artery and its branches and therefore, dissection is difficult.

van schil et al. [22] stated that patients with ipsilateral hilar or intrapulmonary lymph-node metastases (N1) should be treated with a combination of surgery and adjuvant chemotherapy and patients with ipsilateral mediastinal lymph-node metastases (N2) should mostly be treated with chemoradiation. If downstaging takes place after induction therapy, surgery becomes an option. Patients with contralateral mediastinal or supraclavicular lymph-node involvement (N3) are not treated surgically because of poor prognosis although individual cases of possible curative concepts after a successful neoadjuvant therapy have been described. In case of suspicious lymph nodes, 28% of patients with N2 disease were diagnosed by mediastinoscopy, although EBUS was negative.

NCCN guidelines refer to results of ACOSOG Z0030 randomized trial that compared mediastinal LN sampling versus total LN dissection in N0 (no demonstratable metastasis to regional LN) or N1 (ipsilateral peribronchial and/or hilar region metastasis) NSCLC patients. The trial did not show additional survival benefit of total mediastinal LN resection over systematic LN sampling in patients with early NSCLC and negative nodes in systematic sampling. For right- sided cancers NCCN guidelines propose sampling of stations 2R, 4R, 7, 8 and 9, whereas for left–sided cancers sampling of 4L, 5, 6, 7, 8 and 9 stations is suggested. At least 3 mediastinal LN stations should be sampled. In case of suspected nodal disease, NCCN suggests, additionally, EBUS for 2R/2L, 4R/4L, 7 and 10R/10L station biopsies, EUS for 5,7,8 and 9 station biopsies and mediastinoscopy, in case of positive mediastinum in PET and/or CT, but negative in EBUS. NCCN guidelines conclude that surgical strategy in early stage (Ia and Ib) patients should involve resection of the tumor, exploration of adjacent tissue and mediastinal LN dissection or sampling. If positive for disease LNs are found, radiation therapy or chemotherapy are options depending on the exact disease stage. ESTS recommends CT, PET scan and EUS/EBUS over surgical staging as the initial procedure, as far as mediastinal nodal staging is concerned. If EUS/EBUS does not reveal nodal involvement, surgical staging *via* mediastinoscopy is suggested as the next step. Surgeons are advised to assess mediastinal and hilar nodal stations and to sample at least three different nodal stations (4R, 4L, 7), if CT and/or PET show nodal involvement. ACCP guidelines underline that NSCLC resection should include at least lymph node sampling. In stages I and II mediastinal lymph node sampling or dissection at the time of anatomic resection is suggested over selective or no sampling for accurate pathologic staging. In case of anatomic resection for stage I disease in patients who have undergone hilar and mediastinal lymph node staging (intraoperative N0 status), the completion of the procedure with a mediastinal lymph node dissection does not provide a survival benefit. On the contrary, in patients with stage II NSCLC undergoing anatomic resection, mediastinal lymph node dissection may provide additional survival benefit over mediastinal LN sampling.

Darling et al. [23] explain in detail how mediastinal LND is performed and prove that at early stage NSCLC if mediastinal and hilar nodes at LN sampling are negative, mediastinal lymph node dissection does not improve survival. In case of right–sided tumors, LN stations 2R (upper paratracheal) and 4R (lower paratracheal), between right upper lobe bronchus, innominate artery, superior vena cava, and trachea should be removed. If the tumor is left–sided, LNs between the phrenic and vagus nerves up to the left main stem bronchus should be removed (stations 5 and 6). LNs of the aortopulmonary window should, also, be removed without damaging the recurrent nerve. Also, subcarinal nodes, adjacent to the carina, right and left main bronchi are removed (station 7). Lymph nodes from stations 8 (paraoesophageal) and 9 (inferior pulmonary ligament) are extracted. Finally, at the end of the procedure the main bronchi, posterior pericardium and esophagus should lack lymphatic tissue.

Preoperative mediastinal evaluation consists of identifying mediastinal LN ≥1 cm in short axis in CT scan or increased uptake in FDG-PET Scan. These LNs are intraoperatively biopsied. Lackey et al. [24] present cervical mediastinoscopy and anterior mediastinotomy (Chamberlain procedure) as procedures that are used to evaluate N2 disease, especially in patients with large tumors, central tumors, PET avidity in ipsilateral hilum or bilateral synchronous primary tumors. Authors advocate for systematic mediastinal LN sampling.

Lopez Guerra et al. [25] suggest that harvesting more than 6 LN during surgery, leads to observing more instances of nodal metastasis in examination at the pathology laboratory and significantly higher 3- year RFS than harvesting less than 6 LN during surgery, while Osarogiagbon et al. [26] found that lowest mortality risk occurs in dissecting and examining 18–21 LN. If LN status is inadequately examined, there is high risk of underestimating long-term mortality and ignoring candidates for post- operative adjuvant therapy. In that case, a corrective intervention is suggested.

Lobectomy was associated with better OS and DFS, as Wang et al. [27] have presented. As far as OS is concerned: BML is superior to SND and LSND that have advantage over SNS or SLNB. As far disease free survival is concerned: BML or SND are proven superior to LSND or SNS or SLNB.

After PSM, lobectomy with SND compared with lobectomy with SNS or SLNB, resulted in more favorable OS and DFS, but there was no survival benefit in different types of lymph node resection in sublobar resection. LN involvement in any tumor size, metastasis and micrometastasis could be missed in case of sublobar resection or inadequate LN resection. It was proven that SND stages NSCLC more accurately because all possible metastatic tissue is resected, BML aids examining nodal status the most. Fan et al. [28] are skeptical towards segmentectomy and advocate for lobectomy. In this study, lobectomy and segmentectomy present higher CSR than wedge resection. CSR in segmentectomy is lower, if tumor grade is higher. Additionally, CSR in segmentectomy is lower than CSR in lobectomy for the first two years but becomes higher after the third year. The authors have attributed this difference in CSR to inadequate hilar LN resection and therefore tumor understaging, recurrence and metastasis in case of segmentectomy. In this study, male patients younger than 65 years old and grade I NSCLC who underwent segmentectomy present comparable CSR to the lobectomy group, but patients in adenocarcinoma group and female patients in the early postoperational period presented lower CSR to the lobectomy group. Therefore, the authors have concluded that age, sex, tumor histological features and type of operation can affect OS.

Qu et al. [29] presented segmentectomy with proper lymph node resection or sampling as a good alternative option to lobectomy. In segmentectomy less LNs are typically dissected than lobectomy, which may lead to higher recurrence. In segmentectomy it is technically difficult to remove more than three regional LN stations. On the contrary, in lobectomy more than three regional stations of LNs are removed. A higher number of resected LNs are linked to more accurate staging and less cases of false negative Stage I NSCLC. In the same direction, Khullar et al. concluded that median OS for lobectomy, segmentectomy, and wedge resection were 100, 74, and 68 months, respectively, and explained that patients who were treated with sublobar resection were more likely to have inadequate LN resection (<3 LNs) and positive tumor resection margins.

Al-Shahrabani et al. [30] advocate for lobectomy with MLND or SLNS in operable patients. MLND or SLNS stage disease more accurately, but studies have shown that MLND reduces local and systemic recurrence significantly, because it stages disease more accurately than SLNS and aids thorough examination of LNs and detection of skip metastasis and micrometastasis. The authors of this paper state also that the improved outcome after MLND might be attributed to Will Rogers's phenomenon by some researchers. In detail, technological advances are responsible for high sensitivity in tumor spread, stage migration and survival improvement. In the same paper sublobar resection in early stage NSCLC is suggested in patients with low cardiopulmonary reserve, tumor <2 cm, N0 LN status and free resection margins in frozen section.

Oncologic outcome and efficacy of LN dissection in thoracoscopic segmentectomy is comparable to thoracoscopic lobectomy, as presented by Shapiro et al. [31]. Additionally, Zheng et al. [10] have concluded that in case of stage I NSCLC, VATS segmentectomy is safe and effective and can be used to remove one or two segments, while systematic LN dissection, including parabronchial, segmental and sub segmental (12,13,14 stations) can also be performed by VATS segmentectomy.

Okada et al. [19] present extended segmentectomy as an alternative for patients with cT1N0M0 non–small cell lung cancer of 2 cm or smaller. Extended resection includes removal of both the affected segment and adjacent sub segments plus exploration of mediastinal and hilar lymph nodes, which were examined pathologically as intraoperative frozen sections. If intraoperative frozen section proves LN involvement, the procedure should be converted to lobectomy with complete hilar LN resection, in order to resect possible satellite lesions and involved LN. According to the author, intrapulmonary metastases or involved intralobar nodes (1, 4% possibility) at the segment with the main tumor might be hidden in the remaining lung parenchyma.

Effect on survival

According to Villamizar et al. [32] preserving lung function in elderly patients, in patients with inadequate cardiopulmonary status and in case of synchronous and metachronous cancers, that may require multiple resections over the years, is crucial. A second primary cancer might occur at 3% per year. If a patient survives 5 or more years after the first operation there is 9% risk for second cancers. The authors have suggested that lobectomy is associated with lower recurrence rate and higher disease free interval and that LN metastasis in case of clinical Stage Ia NSCLC can occur in 10% of patients, attributing this to possible infiltration by cancer cells of station 13 LNs of segments adjacent to the resected segment.

Koike et al. [33] have presented that 5 year OS and DFS rates are not significantly different between lobectomy and limited resection, but median postoperative/ preoperative FEV1 and postoperative/ preoperative FVC ratios were significantly higher in limited resection group. Therefore, the authors have concluded that both procedures have similar oncologic outcome, but if limited resection is performed postoperative lung function is more preserved.

Survival advantage of lobectomy over segmentectomy for tumors greater than 3 cm was presented by Koike et al. [34]. The authors have presented that locoregional recurrence after segmentectomy was found in 22.7% of patients versus 4.9% after lobectomy and therefore follow-up of these patients is highly suggested.

Deng et al. [35] have found that segmentectomy and lobectomy present comparable hospital stays, mean OS and DFS time in T1a NSCLC, but lobectomy has a slight advantage over segmentectomy as far as OS and DFS in T1b NSCLC are concerned. Both procedures were completed by mediastinal lymphadenectomy. The authors have found that PET impact did not differ significantly after segmentectomy or lobectomy. It suggested that lobectomy with mediastinal lymphadenectomy should be performed in patients with stage IA NSCLC, especially in T1b cases.

Lobectomy is preferred for large or right- sided tumors, high maximum Standardized Uptake Value (SUV_{max}), tumors invading lymphatic, vascular, or pleural structures and lymph node metastasis according to Okada et al. [19]. Three-year RFS was higher after segmentectomy compared to lobectomy, but three-year OS did not significantly differ. In PSM analysis three-year OS and RFS after segmentectomy and lobectomy were comparable. Therefore the authors advocate for segmentectomy in clinical stage Ia NSCLC even in low-risk patients. On the other hand, Liu et al. [36] have performed a Meta–analysis and have concluded that sublobar resection (wedge resection and segmentectomy) is linked

to lower OS than lobectomy in Stage Ia NSCLC patients. Additionally, OS in case of segmentectomy is; also, lower than in lobectomy, according to the same meta- analysis. Liang et al. [37,38] compared ACS and CCS rates linked to lobectomy, sublobar resection, radiation and observation in a retrospective study of 27,116 patients with Stage I NSCLC. ACS ratein lobectomy decreased from 86.9% (3rd year) to 73.6 % (8th year), while CCS rate increased from 86.9 % (3rd year) to 91.7% (8th year). ACS rate in sublobar resection decreased from 80.8% (3rd year) to 62.2% (8th year) and CCS increased from 80.8% to 86.4%. The smallest increase in CCS3 among four groups has been noted in lobectomy group, because ACS in this group decreased in the slowest rate .

Conclusion

Segmentectomy is indicated for older and/or multimorbid patients, as a parenchyma sparing procedure, small (≤2 cm) peripheral tumors without LN involvement and multiple synchronous or metachronous tumors. Additionally, segmental resection can be performed for GGO lesions ≤1 cm, and histologically confirmed benign tumors.Segmental resection is considered as being a technically demanding procedure due to arterial and bronchial anatomy. If insufficient resection margins cannot be obtained, for instance, if the tumor invades the intersegmental plane or if anatomic variations complicate the operation, a bi- or trisegmentectomy can be performed.

Both thoracoscopic intercostal and subxiphoid access could be used depending of the exact tumor location and surgeons' experience. Segmental resection can be proceeded in order to preserve pulmonary function, but special attention is needed to avoid technical pitfalls. The accurate patients' selection for this procedure is of major importance. Factors associated with recurrence are macro-and microscopic malignant infiltration of resection margins, extracapsular extension, LN involvement, low grade of differentiation. Ensuring a Margin: tumor ratio higher than 1 and sufficient LN dissection/sampling are crucial. Otherwise, conversion of segmental to lobar resection is mandatory according to oncologic principles.

Careful assessment of nodal status is linked with lower possibility of recurrence, because understaging can be avoided. Hilar and mediastinal dissection/sampling is suggested. Mediastinal sampling should be completed by sampling at least 3 LN stations, but always subcarinal LNs. Systematic dissection aids a more thorough nodal examination than systematic sampling, because of detection of skip metastasis and micrometastasis, but NCCN, ESTS and ACCP guidelines have not excluded systematic sampling.

Finally, segmental resection shows similar OS and DFS rates to lobectomy in carefully selected patients. However, randomized trials JCOG0802 and CALBG 140503 are expected to give further insight into the role of segmentectomy in patients with early stage NSCLC.

Authors Contributions

Theoni Kontou and Michail Galanis contributed to the manuscript equally and should both therefore be accepted as first authors.

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