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Sublobar resection for lung cancer

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ABSTRACT: **Sublobar resection for small lung cancers has been debated frequently and is still a controversial issue. The only randomised trial comparing lobectomy with sublobar resections found a significantly higher recurrence rate for the latter, but failed to show significant differences in survival, although survival was better for the lobectomy group. One meta-analysis and several nonrandomised comparisons have confirmed these results. In general, lobectomy and sublobar resections have similar 5-yr survival rates. Local recurrence after wedge resection is higher than after segmentectomy. However, for patients aged >71 yrs, lobectomy and wedge resection are associated with similar survival. For tumours of ⩽2 cm, segmentectomy is equivalent to lobectomy, but survival after segmentectomy is worse if performed for larger tumours. For both segmentectomy and wedge resection, tumour margins should be ⩾1 cm wide to avoid recurrence. For pure bronchioloalveolar carcinoma of ⩽2 cm, diagnosed intraoperatively with certainty, sublobar resection seems equivalent to lobectomy, and because there is no nodal involvement, systematic nodal dissection may not be necessary. In case of doubt, however, lobectomy with systematic nodal dissection will ensure complete resection and adequate staging. More randomised trials are needed to confirm all these issues.**

KEYWORDS: **Bronchioloalveolar carcinoma, lobectomy, nonsmall cell lung cancer, segmentectomy, sublobar resection, wedge resection**

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GRAHAM and SINGER [1] are credited with having performed the first pneumonectomy for lung cancer in 1933 and, for some years, it was thought that the removal of the whole lung was the standard operation for lung cancer. In the 1950s and 1960s, CAHAN and co-workers [2, 3] standardised pneumonectomy and lobectomy with mediastinal lymph node dissection very much as they are still performed today. However, ever since patients with lung cancer have undergone surgical treatment, thoracic surgeons have been faced with the impossibility of performing the intended lung resection in patients whose lung function would not allow such a parenchymal loss. Sublobar resections, both segmentectomies and wedge resections, were common in the treatment of tuberculosis [4], and it was just a matter of time before such an operation found its way into oncological surgery. In 1973, JENSIK *et al.* [5] reported their first experience with 69 patients, which was expanded in 1979 with the addition of 99 patients, for a total of 168 [6]. Their decision to perform segmentectomy was not functional, but anatomical: peripheral tumours with no lobar or mediastinal nodal involvement. The 5-yr survival rate of their series of patients with tumour (T)1 and T2 tumours was 53%, with a 2% post-operative mortality rate. Of their patients, 45 (27%) died with recurrence: 29 (17%) distant and 16 (10%) local. WEISBERG *et al.* [7] reproduced the same results 14 yrs later, with a series of 170 patients with stage I lung cancer who underwent sublobar resections (segmentectomy 58, wedge resection 97 and unspecified 15). Their 5-yr disease-free survival was 54.7%, and their post-operative mortality 3.5%. Local recurrence with or without metastases was observed in 22 (14.1%) patients. Between these two series, PASTORINO *et al.* [8] published a retrospective comparison of lobectomy and sublobar resection, with similar results and with no significant differences in 5-yr survival and recurrences between the two groups. Global 5-yr survival for sublobar resections and lobectomies was 55% and 49%, respectively. For pathological (p)T1 and pT2 tumours, 5-yr survival was 73% and 35%, respectively, for sublobar resections; and 55% and 46%, respectively, for lobectomies. The recurrence rate was 36% for sublobar resections and 38% for lobectomies.

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Despite these relatively good results, sublobar resection for lung cancer has been, and still is, a controversial issue. The only randomised clinical trial conducted to date [9] not only failed to clarify the controversy, it raised new ones because of the mixture of wedge resections and segmentectomies, and the loss to follow-up of some patients [10]. Sublobar resections were associated with a significant increase in locoregional recurrence compared with lobectomies, but cancer-related death rates and overall death rates did not show significant differences, although they were higher in the sublobar resection group [11]. Because of the increased risk of recurrence in sublobar resections, lobectomy was established as the minimal acceptable resection for lung cancer, while sublobar resections were considered a compromise solution for those patients who could not undergo lobectomy. A recent meta-analysis on survival following lobectomy and limited resection for stage I lung cancer confirmed the results of the randomised trial: there were no statistically significant differences between the two groups, but there was a small benefit in the lobectomy group. However, there was some interstudy heterogeneity that suggests that the results should be interpreted with caution [12]. At the same time, the routine use of computed tomography (CT) in clinical practice and in some screening programmes increased the number of small peripheral lung cancers, both in the form of solid or partly solid lesions, and pure bronchioloalveolar carcinomas as ground-glass opacities (GGOs), for which a lobectomy seems excessive. WATANABE *et al.* [13] reported that the rate of lung cancer $\leqslant$2 cm in diameter rose from 4.3% when CT was not used to 11% after introducing CT in their clinical practice, and to 17% after the introduction of high-resolution CT (HRCT); the equivalent figures for cancers $\leqslant$1 cm were 0.4%, 1% and 1.5%, respectively. This represents a four-fold increase in the number of tumours of both sizes. Additionally, 78–100% of lung cancers identified in screening programmes using low-dose spiral CT are in stage I [14].

In this scenario of increasing numbers of patients with small tumours and the possibility of second-lung primaries in long-term survivors, for whom the preservation of lung function is important, there has been an increasing interest in sublobar resections for small lung cancers. This has been shown in several revisions that have extensively addressed the issue in the past few years [15–18]. The purpose of the present review is to summarise the available evidence on sublobar resections for nonsmall cell lung cancer, making a distinction between solid and partly solid lesions, and bronchioloalveolar carcinoma, because their degree of invasiveness differs.

TYPES OF SUBLOBAR RESECTION

Lung resections that comprise less than a lobe are called sublobar, sublobular, conservative, lesser, substandard or limited resections. The term sublobar will be used throughout the present review. It includes wedge resections and segmentectomies. A wedge resection is the removal of part of the lung regardless of its anatomical boundaries. It can be part of one segment or a portion of lung parenchyma comprising two or more neighbouring segments. It is also called atypical resection (fig. 1). A segmentectomy implies the removal of an anatomical unit (fig. 2). It requires the identification and dissection of the segmental bronchus and artery, which are sutured and ligated, respectively, and the identification of the common vein of the two adjacent segments, which must be respected. The tributary veins from the resected segment are ligated only as they appear in the intersegmental plane. A segmentectomy is an anatomical lung resection together with lobectomy, bilobectomy and pneumonectomy. An extended segmentectomy, as defined by OKADA *et al.* [20], is a resection of both the affected

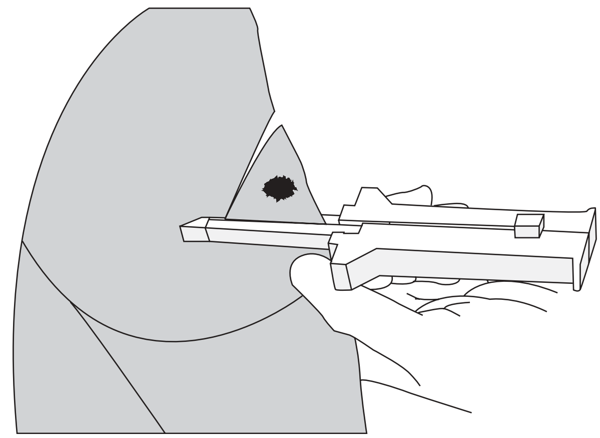

FIGURE 1. Wedge resection. Reproduced from [19], with permission from the publisher.

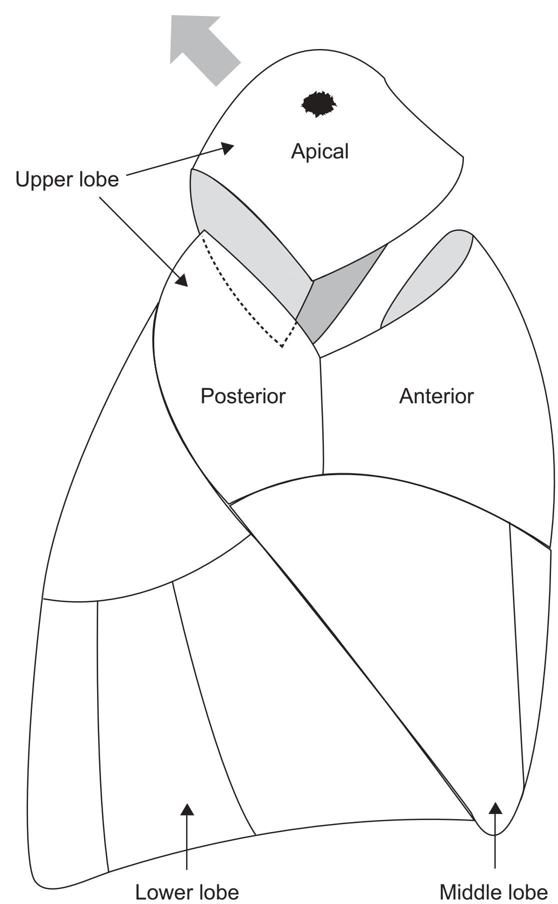

FIGURE 2. Segmentectomy. Reproduced from [19], with permission from the publisher.

segment and adjacent subsegments plus exploration of mediastinal and hilar lymph nodes, which are examined pathologically as intra-operative frozen sections to confirm pathological node (N)0 status. In sleeve segmentectomies, the segmental bronchus is not incised at its origin, but it is removed with part of the lobar bronchus, which is then reconstructed with an end-to-end anastomosis. This is indicated when the tumour is too close to the origin of the segmental bronchus, in order to avoid a lobectomy [21]. Sublobar resections can be performed as open or videothoracoscopic procedures [22, 23]; the latter has been found to reduce hospital stay when compared with open segmentectomy [24].

SUBLOBAR RESECTIONS FOR SMALL SOLID AND PARTLY SOLID PERIPHERAL TUMOURS

Indications

Table 1 shows the most relevant data from 20 studies comparing lobectomy with sublobar resection [8, 20, 25–42]. All but three were retrospective: one was a prospective but nonrandomised study [28] and two were prospective observational studies [20, 34]. In most studies, sublobar resections were indicated in patients with poor lung function, cardiac comorbidity, old age or previous lung surgery. However, in six studies from five different institutions, sublobar resections were intentional in patients who could otherwise tolerate a lobectomy [20, 25, 28, 32, 37, 41]. Most studies were limited to patients with stage I tumours, but three also included higher-stage tumours [30, 34, 40].

Survival and recurrence

The 5-yr survival rates of lobectomy and sublobar resection were equivalent, except in six studies [25, 27, 35, 36, 40, 42]. WARREN *et al.* [25] compared the survival of 103 patients who had undergone lobectomy with the survival of 66 patients who had undergone segmentectomy: 5-yr survival was significantly better for those who had undergone lobectomy (65% *versus* 45%). However, for those patients with tumours $\leqslant$2 cm or less, the two resections were associated with similar survival. Local/regional recurrence was significantly higher after segmentectomy (22.7% *versus* 4.9%).

MILLER *et al.* [27] reported on 100 patients with nonsmall cell lung cancer of $\leqslant$1 cm in diameter who had undergone lung resection; in 94 of them, mediastinal lymph node dissection had been performed. A total of 75 patients had undergone lobectomy or bilobectomy, 12 had undergone segmentectomy and 13 had undergone wedge resection. Their overall 5-yr survival rates were 71%, 57% and 27% ($p=0.03$), respectively. Seven patients in the series had lymph node metastasis, and the overall (43%) and lung cancer-related (64%) 5-yr survival rates of these patients were significantly lower than those for patients without nodal involvement: 66% and 87%, respectively. In the study of MILLER *et al.* [27], the overall recurrence rate was not statistically different in patients who had undergone lobectomy and sublobar resection, but when overall recurrence was analysed according to type of resection, wedge resection was associated with a significantly higher recurrence rate (38.5%) compared with lobectomy (14.7%) and segmentectomy (16.7%). Although significant differences could not be found in local recurrence rates among the three groups, that for wedge resection (30.8%) was much higher than those for lobectomy (13.3%) and segmentectomy (8.3%). Based on their results, MILLER *et al.* [27] recommended lobectomy with mediastinal lymph node dissection even for these small tumours.

In the series of EL-SHERIF *et al.* [35], both stage IA and IB tumours were included. Lobectomy was performed in 577 patients, and sublobar resection in 207 (122 wedge resections and 85 segmentectomies). The overall 5-yr survival rate was significantly better for lobectomy (54%) than for sublobar resection (40%), but when survival was analysed according to stage, the differences were maintained in patients with stage IB tumours only. Survival rates for patients with stage IA tumours were similar for both types of resection. However, when adjusted for age and number of lymph nodes removed at lymphadenectomy, sublobar resection had no adverse effect in patients with stage IB tumours. Overall recurrence was similar in both groups, but the local recurrence rate was significantly higher for sublobar resections (7.2% *versus* 4.2%).

The series of GARZON *et al.* [36] included 25 patients with poor lung function who underwent either video-assisted thoracic surgery (VATS) lobectomy (13 patients) or VATS wedge resection (12 patients). Follow-up was very short (median 15.1 months), but within 2 yrs after the operation, five patients had died, four of them from cancer. All were in the wedge resection group, which was the only factor significantly associated with poorer survival. However, there were no differences in post-operative complications between both groups.

OKUMURA *et al.* [40] compared a series of 1,241 patients who had undergone lobectomy with 144 patients who had undergone segmentectomy. Six patients who had undergone segmentectomy had large cell carcinoma, of whom five died within 5 yrs after the operation. Consequently, this histological type was considered especially unsuited for this type of resection. Among patients with pT1N0-metastasis(M)0 tumours of $\leqslant$2 cm diameter who had undergone lobectomy, 5- and 10-yr survival rates, excluding large cell carcinomas, were 81% and 64%, respectively; these rates were not statistically different from those for patients who underwent segmentectomy (83% and 83%, respectively). However, 5- and 10-yr survival rates for those patients with pT1N0M0 tumours >2 cm in diameter were significantly better after lobectomy (78% and 60%, respectively) than after segmentectomy (58% and 58%, respectively; $p=0.057$). Additionally, among patients undergoing segmentectomy, there was a significant progressive degradation of survival as tumour size increased. The 10-yr survival rates of patients with tumours <1 cm, 1.1–2.0 cm, 2.1–3.0 cm and 3.1–4.0 cm in diameter were 92%, 71%, 47%, and 34%, respectively ($p=0.0015$), with no 10-yr survivors among those with tumours >4 cm. Other than tumour size, nodal involvement, pleural invasion and histological type were found to have prognostic value in multivariate analysis.

Finally, in the series of SIENEL *et al.* [42], the cancer-related 5-yr survival rate for 150 patients who had undergone lobectomy was 83%, which was significantly higher than the 67% found in 47 patients who had undergone segmentectomy. However, again, when patients with tumours of $\leqslant$2 cm in diameter were considered, survival differences were not statistically significant. Local recurrence was significantly higher in patients who

TABLE 1 Retrospective (RC) and prospective nonrandomised comparison (PC) between lobectomy and sublobar resection

First author [ref.]	Type of study	Study period	Type of resection and number of patients	5-yr survival or other survival information as specified	Significance or other information as specified
Pastorino [8]	RC	1971–1988	L & Bl: 411	49%	NS
			W & S: 61	55%	
Warren [25]	RC	1980–1988	L	65%#	S
					But NS for tumours ⩽3 cm
			S	45%#	
Kodama [26]	RC	NA	L: 77	88%	L *versus* iS: NS
			iS: 46	93%	L & iS *versus* cS: S
			cS & W: 17	48%	
Okada [20]	PC	1984–1998	L: 139	pT1N0M0	NS
				⩽2 cm: 87.7%	
			eS: 70	pT1N0M0	
				⩽2 cm: 87.1%	
Miller [27]	RC	1980–1999	L & Bl: 75	71%	L *versus* S & W: S
			S: 12	S: 57%	L *versus* W: S
			W: 13	W: 27%	L *versus* S: NS
Koike [28]	PC	1992–2000	L: 159	90.1%	NS
			S: 60	89.1%	
			W: 14		
Campione [29]	RC	1987–1997	L & Bl & Pn: 99	Median: 98 months	NS
			S: 21	Median: 104 months	
Mery [30]	RC	1992–1997	<65 yr	Median: 71 months	L better than W
			W: 380		L better than W
			L: 3784		L & W have similar survival
			65–74 yr	Median: 47 months	
			W: 626		
			L:4223		
			⩾75 yr	Median: 28 months	
			W: 397		
			L: 1868		
Martin-Ucar [31]	RC	1997–2004	S: 17	70%	NS
			L: 17	64%	
Watanabe [32]	RC	NA	L: 57	84%	NS
			eS: 20¶	93%	
			W: 14+	100%	
Okada [33]	RC	1985–2002	L: 919	p-stage I:	⩽2 cm: NS
				⩽2 cm: 92.4%	2–3 cm:
				2–3 cm: 87.4%	L & S *versus* W: S
				>3 cm: 81.3%	L *versus* S: NS
			S: 258	p-stage I:	>3 cm: S
				⩽2 cm:96.7%	
				>2–3 cm: 84.6%	
				>3 cm: 62.9%	
			W: 64	p-stage I:	
				⩽2 cm:85.7%	
				>2–3 cm: 39.4%	
				>3 cm: 0%	
Griffin [34]	PC	1988–1992	L & Pn: 96	30%	NS
			W: 31	32%	
El-Sherif [35]	RC	1990–2003	L: 577	54%	S
			W: 122	40%	
			S: 85		
Garzon [36]	RC	2000–2005	VATS L: 13	2-yr mortality: 0%	S
			VATS W: 12	2-yr mortality: 55.5%	

TABLE 1 continued

First author [ref.]	Type of study	Study period	Type of resection and number of patients	5-yr survival or other survival information as specified	Significance or other information as specified
OKADA [37]	RC	1992–2001	L: 262	89.1%	NS
			S & W: 305	89.6%	
KRAEV [38]	RC	1993–1998	L: 215	Mean: 5.8 yr	L better than W in tumours <3 cm,
			W: 74	Mean: 4.1 yr	but equal to W in tumours >3 cm
SCHUCHERT [39]	RC	2002–2006	L: 246	~80%#	NS
			S: 182	~85%#	
OKUMURA [40]	RC	1980–2002	L: 1241	pT1N0M0:	⩽2 cm: NS
				⩽2 cm: 81%	
				>2 cm: 78%	>2 cm: (p=0.057)
			S: 144	pT1N0M0:	
				⩽2 cm: 83%	
				>2 cm: 58%	
MONDELLO [41]	RC	2000–2003	L: 25	88%	NS
			S & W: 11	82%	
SIENEL [42]	RC	1987–2002	L: 150	83%	S
			S: 49	67%	But NS for tumours ⩽2 cm

L: lobectomy; Bl: bilobectomy; W: wedge resection; S: segmentectomy; NS: nonsignificant; NA: not available; iS: intentional segmentectomy; cS: compromised segmentectomy; S: significant; p: pathological; T: tumour; N: node; M: metastasis; eS: extended segmentectomy; Pn: pneumonectomy; VATS: video-assisted thoracic surgery. #: calculated from published survival graphs; ¶: non-Noguchi type A and B; +: bronchioloalveolar carcinoma, Noguchi type A and B.

had undergone segmentectomy, both in the group of patients as a whole and among those with smaller tumours.

Tumour size

The 2-cm landmark is consistently found in other studies. OKADA *et al.* [20] reported that extended segmentectomy was an alternative to lobectomy in patients with clinical (c)T1N0M0 tumours of ⩽2 cm in diameter. Their 5-yr survival rates after extended segmentectomy and after lobectomy were 87.3% and 77.7%, respectively (p=0.1644). The 5-yr survival rates of their pT1N0M0 counterparts were 87.1% for extended segmentectomy and 87.8% for lobectomy (p=0.8008). WARREN *et al.* [25], KOIKE *et al.* [28], WATANABE *et al.* [32] and SIENEL *et al.* [42] reported similar results in this selective group of patients with small T1 tumours.

Age

Patient age also seems to play a role in the outcome of sublobar resections. MERY *et al.* [30] studied this issue in the population of patients registered in the Surveillance, Epidemiology, and End Results database of the National Institutes of Health (Bethesda, MD, USA), and compared the results of lobectomy, pneumonectomy and wedge resection in patients aged <65 yrs, patients aged 65–74 yrs of age and patients aged ⩾75 yrs. Lobectomy conferred significantly better survival in patients of the first two age groups, but in those aged ⩾75 yrs, both lobectomy and wedge resection had similar survival. Further analysis of the data showed that the benefit of lobectomy was lost in patients aged >71 yrs.

Segmentectomy versus *wedge resection*

Two reports present retrospective comparisons of segmentectomy and wedge resection [43, 44]. The report by EL-SHERIF *et al.* [43] focuses on the relationship between resection margin and local recurrence in patients with stage I nonsmall cell lung cancer who underwent either segmentectomy or wedge resection. In the group of patients who underwent segmentectomy, there were more resections with resection margins >1 cm. Local recurrence was significantly higher when resection margin was <1 cm (14.6%) than when it was ⩾1 cm (7.5%). Wedge resections had, therefore, narrower resection margins and were associated with higher local recurrence. In the series of EL-SHERIF *et al.* [43], resection margins had no impact on regional or distant recurrence. In the study of SIENEL *et al.* [44], 56 patients underwent segmentectomy with systematic nodal dissection and 31 underwent wedge resection with selective nodal sampling at the surgeon's discretion for stage I nonsmall cell lung cancer. Sublobar resections were indicated because of cardiopulmonary impairment. Both groups were similar in terms of sex, age, performance status, forced expiratory volume in one second (FEV1), tumour size, histology, grading, complication rate and follow-up duration. Segmentectomy was associated with a significantly better cancer-related 5-yr survival compared with wedge resection (71% and 48%, respectively). Local recurrence was significantly lower in segmentectomy (16%) than in wedge resection (55%). The same results were found when the population of patients with tumours ⩽2 cm in diameter was analysed independently: 5-yr survival rates were 80% for segmentectomy and 48% for wedge resection. Local recurrence rates were 11% for segmentectomy and 40% for wedge resection. Although the mean number of resected lymph nodes differed (six in wedge resections and 12 in segmentectomies), in the multivariate analysis type of resection, age and tumour size were the only significant prognostic factors. Another study from the same institution [42] focusing on segmentectomy and on the location of the resected segments showed that local recurrence tended to be more frequent when segmentectomy was performed in segments 1–3, compared with other segmental locations, and when resection margins are ⩽1 cm in width. Additionally, the 5-yr survival rate of patients who underwent segmentectomy (63%) was significantly lower than that of patients undergoing lobectomy (83%). Local recurrence rates were also significantly different: 16% for segmentectomy and 5% for lobectomy. When the selected group of patients with tumours ⩽2 cm in diameter was analysed, differences in 5-yr survival rates for lobectomy (85%) and segmentectomy (68%) were not statistically significant. However, differences in local recurrence rate were significant: 2% for lobectomy and 12% for segmentectomy.

Post-operative pulmonary function

Although the most common indication of sublobar resection is impaired pulmonary function, its role in preserving pulmonary function post-operatively has seldom been studied. TAKIZAWA *et al.* [45] studied post-operative lung function in 40 patients who had undergone segmentectomy but who could otherwise have undergone lobectomy, and in 40 matched patients who had undergone lobectomy. Pre-operative forced vital capacity (FVC) and preoperative FEV_1 were similar. Overall, 2 weeks post-operatively, FVC, as % of pre-operative value, was significantly higher in the segmentectomy group (72.7% *versus* 67.2%), but this advantage was not maintained at 12 months after the operation (94.9% *versus* 91.0%). However, the significant benefit observed 2 weeks post-operatively in FEV_1, as % of pre-operative value, in the group of patients who had undergone segmentectomy (73.0% *versus* 66.6%) was maintained at 12 months (93.3% *versus* 87.3%). Although segmentectomy was associated with better post-operative lung function, the authors did not recommend it for good-risk patients because of the difficulties in identifying involved lymph nodes during the operation. The study of HARADA *et al.* [46] was also conducted in patients who could tolerate a lobectomy, but who were assigned to radical segmentectomy (38 patients) or lobectomy (45 patients) in a nonrandomised way after the patients had given their consent. In this study, FVC, FEV_1 and anaerobic threshold were measured pre-operatively and at 2 and 6 months after the operation. In the segmentectomy group, the post-operative reduction of FVC and FEV_1 was significantly smaller than in the lobectomy group, but there were no differences in the anaerobic threshold.

These two studies [45, 46] were performed in patients with good pre-operative pulmonary function. In patients with lung disease, careful evaluation of the type, degree and location of the lung abnormalities is important in order to select the best lung resection. This is particularly relevant in patients with emphysema of the upper lobes in whom a lobectomy will have a lung volume reduction effect, with improvement of post-operative lung function, whereas a segmentectomy would not achieve the same results [47]. Conversely, the preservation of lung function in patients with small lung cancers and anticipated long survival is important, considering the possibility of further lung resections to treat second primary lung tumours.

Combined therapies

Wedge resection of stage I tumours followed by external radiotherapy has already been tested, with heterogeneous results. In a study including 58 eligible patients, a mixture of benign and malignant lesions were wedge resected and the nonsmall cell lung cancers were post-operatively irradiated with 56 Gy if completely resected, or 66 Gy if incompletely resected [48]. It was found that clinical staging was inaccurate in 45% of cases, and that resection margins were positive in 6% of T1 and 23% of T2 tumours [48]. However, in a shorter series of six patients with T1N0M0 tumours who could not undergo lobectomy, wedge resection was followed by 40–50 Gy post-operative radiotherapy to the remnant lung besides the tumour and the hilum, and all patients survived ⩾5 yrs with no recurrence [49].

The combination of wedge resection and intraoperative brachytherapy is feasible with no added complications. VOYNOV *et al.* [50] treated 65 patients with stage IA and 45 with stage IB nonsmall cell lung cancer, who could not undergo lobectomy, with wedge resection and intra-operative application of ^{125}I Vicryl mesh over the stapler line and 2-cm margin. There were four recurrences only in the treated field, 13 regional recurrences and nine distant recurrences. The 5-yr local control, locoregional control, and overall survival rates were 90%, 61%, and 18%, respectively. Another study from the same institution [51] comparing sublobar resection and brachytherapy (41 patients) with lobectomy (126 patients) for stage IB nonsmall cell lung cancer found no differences in local recurrence (4.8% for sublobar resections and 3.2% for lobectomies), disease-free survival (43.0% for sublobar resection and 42.8% for lobectomies), and overall survival (54.1% for sublobar resections and 51.8% for lobectomies). In the light of these results, the authors concluded that both treatments were equivalent and recommended the administration of brachytherapy whenever wedge resection had to be performed instead of lobectomy for stage IB tumours.

Intra-operative radiofrequency ablation immediately followed by wedge resection has also been applied to treat a small recurrent tumour in a patient who could not undergo anatomical resection [52]. Provided that the proper prospective studies are conducted, radiofrequency ablation could also be an adjuvant to sublobar resection for small lung cancers.

THE SPECIAL CASE OF BRONCHIOLOALVEOLAR CARCINOMA

Bronchioloalveolar carcinoma (BAC) is a subtype of adenocarcinoma that grows along alveolar structures without stromal, vascular or pleural invasion [53]. Pure BAC is at one end of the spectrum of adenocarcinoma (Noguchi types A, B, and C) and has an excellent prognosis because there are no invasive features and no lymph node involvement, while papillary adenocarcinoma with compressive and destructive growth is at the other end [54]. The World Health Organization recently tried to clarify the classification of adenocarcinomas [53]. The present review will focus on small BAC, pending a consensus between clinicians and pathologists, because there is still some confusion about noninvasive BAC and invasive adenocarcinoma with BAC features (an International Association for the Study of Lung Cancer/European Respiratory Society/American Thoracic Society Task Force on lung adenocarcinoma: international multidisciplinary consensus subclassification, chaired by E. Brambilla and W. Travis, began work in October 2008).

Small localised BACs may be detected by HRCT as pure GGO. Table 2 summarises the data from nine Japanese reports focused on the surgical treatment of small BACs, currently ≤2 cm in diameter or less, although two series include larger tumours [13, 55–62]. In most reports, these small BACs represent <2% of the lung cancer series, and were treated by either lobectomy or sublobar resection. No nodal involvement was found. The 5-yr survival rates were 100% in all but one of the series (in the other, a patient died from an unrelated cause) and there was no recurrence at follow-up.

When a GGO is found on HRCT, it is important to assess whether it is pure GGO or partly-solid GGO. While pure GGOs will be BACs or benign lesions, such as atypical adenomatous hyperplasia, partly-solid GGOs will have a component of invasive adenocarcinoma. The tumour disappearance rate on HRCT may also help in assessing the nature of the lesion. Most BACs have a tumour disappearance rate of ≥50% [63]. A recent report established the maximum standardised uptake value of positron emission tomography as an important tool in assessing the aggressive nature of adenocarcinomas ≤3 cm in diameter, in combination with the GGO ratio and tumour disappearance rate [64].

If a sublobar resection has been performed, the tumour must be studied intra-operatively by a frozen section to make sure that it is BAC and has no invasive adenocarcinoma component. In the trial reported by YOSHIDA *et al.* [61], this intra-operative assessment took ~1 h. There was agreement with the definitive post-operative pathological study in all specimens but one, which was changed from Noguchi's type B to C. However, other authors have reported difficulties in assessing the difference between BAC, atypical adenomatous hyperplasia, peripheral carcinoid tumours and other lesions [65]. If the intra-operative diagnosis of BAC is certain to the best of the pathologist's knowledge, then, according to the results of the series shown in table 2, a sublobar resection with no nodal dissection may be enough to ensure complete resection. Ongoing prospective trials in Japan and the USA [66] will have to confirm this strategy, and see whether systematic nodal dissection can be removed from the definition of complete resection in the case of this particular tumour. However, in case of doubt, lobectomy with systematic nodal dissection should be performed to ensure complete resection and adequate intra-operative staging [67].

SUMMARY OF EVIDENCE AND RECOMMENDATIONS

1) The results from the only randomised clinical trial comparing lobectomy with sublobar resections for T1N0 nonsmall cell lung cancer show that the latter are associated with higher local recurrence rates, but this study failed to show significant differences in overall and cancer-related survival (Level of evidence: Ib). Therefore, in patients who can tolerate lobectomy, sublobar resections should be avoided (Grade of recommendation: A).

2) One meta-analysis, most retrospective studies, and a few prospective nonrandomised studies comparing lobectomy with sublobar resections for stage I nonsmall cell lung cancer, performed mainly in patients unfit for lobectomy but also in patients with adequate pulmonary function, show that the 5-yr survival rates are similar (Level of evidence: III). Therefore, in

TABLE 2 Surgical treatment for small bronchioloalveolar carcinomas (BAC)

First author [ref.]	Study period	Patients n	BAC n (%)	Tumour size	Noguchi type or other	N status	Type of resection	Recurrence	5-yr survival or other information
HIGASHIYAMA [55]	1973–1997	1590	17 (1.1)	<2 cm	A, B	N0	Various	0	100%
WATANABE [13]	1973–1998	1713	24 (1.4)	≤2 cm	A, B	N0	Lobectomy	0	100%
ASAMURA [56]	1991–2000	1769	28 (1.6)	≤1 cm	Pure GGO: 19 Partly-solid GGO: 9	N0	Lobectomy or sublobar resection	0	100%
NAKATA [57]	1997–2000	NA	28	≤2 cm	Pure GGO	N0	Wedge by VATS	0	No deaths at a mean follow-up of 18 months
NAKAMURA [58]	1981–2002	2051	27 (1.3)	Mean: 9.3±3.5 mm	A, B, C	N0	Wedge or segmentectomy	0	95% (one death from ruptured aortic aneurism)
YAMADA [59]	2000–2002	NA	31	≤2 cm	A, B, C	NA	Wedge by VATS	0	No deaths at a median follow-up of 29.3 months (range 12–41 months)
SAKURAI [60]	1985–2002	334	25 (7.5)	≤3 cm	NA	N0	Lobectomy, segmentectomy or wedge	0	100%
YOSHIDA [61]	1998–2002	NA	40	Mean: 11 mm (range 2–21 mm)	A, B, C	N0	Lobectomy, segmentectomy or wedge, open or VATS	0	No deaths at a median follow-up of 50 months (range 19–68 months)
OHTSUKA [62]	1997–2005	NA	10	Mean: 6±3 mm (range 2–10 mm)	NA	N0	Lobectomy or wedge	0	No recurrence at a mean follow-up of 44 months (range 4–84 months)

N: node; GGO: ground-glass opacity; NA: not available; VATS: video-assisted thoracic surgery.

patients unable to undergo lobectomy, sublobar resection is an alternative that will confer similar prognosis (Degree of recommendation: B).

3) When segmentectomy and wedge resections have been compared in retrospective studies, wedge resection is associated with worse survival and increased local recurrence (Level of evidence: III). Therefore, when a sublobar resection is the only resection a patient can tolerate, segmentectomy is a better choice than wedge resection (Degree of recommendation: B).

4) When tumour size has been analysed, it has been found that lobectomy and segmentectomy are equivalent for tumours ⩽2 cm in diameter, but not for larger ones (Level of evidence: III). Therefore, segmentectomy should be reserved for tumours ⩽2 cm in diameter; and lobectomy, for larger tumours, if possible (Degree of recommendation: B).

5) When patients' age has been considered, it has been found that, in terms of survival, lobectomy and wedge resection are equivalent in patients aged >71 yrs, but lobectomy is associated with improved survival in younger patients (Level of evidence: III). Therefore, wedge resection should be reserved for patients aged >71 yrs (Degree of recommendation: B).

6) Wedge resections tend to have more resection margins <1 cm in width than segmentectomies, and this has been associated with increased local recurrence (Level of evidence: III). Therefore, for both segmentectomies and wedge resections, resection margins should be ⩾1 cm wide (Degree of recommendation: B).

7) Post-operative radiotherapy or intraoperative brachytherapy may improve local control after wedge resection for nonsmall cell lung cancer (Level of evidence: III). Therefore, if wedge resection is the only resection the patient can tolerate, adjuvant radiotherapy seems advisable (Degree of recommendation: B).

8) Both lobectomy and sublobar resections for bronchioloalveolar carcinomas of ⩽2 cm in diameter are associated with a 5-yr survival rate of 100% and lack of recurrence (Level of evidence III). Therefore, if the intra-operative diagnosis of bronchioloalveolar carcinoma is certain, because of its non-invasive nature and lack of nodal involvement, sublobar resection with no systematic nodal dissection may be sufficient treatment for this particular type of tumour (Degree of recommendation: B).

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