Comparative study evaluating outcomes of lobectomy and extended segmentectomy used in the treatment of primary non-small cell bronchial carcinoma*

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Background: The use of partial lobectomy for primary tumors remains controversial.

Method: During the period from 1995 to 2000, we treated 733 cases of non-small cell bronchial carcinoma. After clinical evaluation and surgical staging, 191 patients were submitted to surgical resection. Of those 191 surgeries, 63 were for locally advanced tumors and 128 (69 segmentectomies and 59 lobectomies) for primary tumors. Post-operative FEV_1 of at least 800 ml was used as a measure of surgical success. Extended segmentectomies, in which the resection passes the intersegmental line, including the parenchyma of the adjoining segment, were used.

Results: Among the 128 patients with primary tumors, there were 3 deaths and 10 patients fell out of contact. Therefore, 62 segmentectomies and 53 lobectomies were evaluated. There were 72 adenocarcinomas and 43 epidermoid carcinomas. The 5-year survival of lobectomy patients was 80% (T1N0), 72.7% (T2N0), 50% (T1N1) and 31.8% (T2N1), whereas that of segmentectomy patients was 80% (T1N0), 66.6% (T2N0), 41.1% (T1N1) and 30% (T2N1) ($p > 0.05$). Tumor size and enlarged interlobar lymph nodes were prognostically significant ($p < 0.001$), although method of resection influenced neither survival nor local or remote recurrence ($p > 0.05$).

Conclusion: Extended segmentectomy represents an alternative treatment for primary tumors in patients with limited lung reserve.

Key words: Lung Neoplasms, surgery. Pulmonary Surgical Procedures. Carcinoma, Non-Small-Cell Lung.

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INTRODUCTION

The incidence of non-small cell bronchogenic carcinoma (NSCBC) in the United States is approximately 140,000 new cases per year. Approximately 14% of those new cases may be cured, principally those in which the carcinoma is localized (stages 1 and 2)[1]. It is known that lobectomy is the only curative treatment for early-stage NSCBC. However, a recommendation for lobectomy is made based not only on the extent of the disease but also on the potential resultant postoperative lung capacity[2]. Since most NSCBC patients present pulmonary comorbidities that restrict their functional reserve, lobectomy becomes limited as a therapeutic option.

Compared to lobectomy, limited resection may offer less loss of function for NSCBC patients, reducing postoperative morbidity and enhancing the chances for a second resection to treat a new primary carcinoma or pulmonary metastasis[3]. The objective of the present study was to present the results obtained from reviewing our experience in the clinic, comparing limited resection to lobectomy for the treatment of early-stage NSCBC.

METHOD

During the period from 1995 to 2000, 733 cases of NSCBC were diagnosed. Patients were submitted to detailed physical examination, laboratory and cardiologic evaluation, pulmonary function tests, computed tomography scans of the chest, mediastinum, and upper abdomen, and fiber-optic bronchoscopy. All metastatic lesions, identified through clinical evaluation or imaging, were confirmed by anatomopathological examination. All patients eligible for resection were submitted to cervical mediastinoscopy and left parasternal mediastinostomy for tumors in the upper left lobe. Only 199 patients could be treated surgically. Of those, 69 were submitted to segmentectomy, 59 to lobectomy, 52 to lobectomy involving resection of the chest wall, artery or bronchus, and 19 to pneumonectomy. In 128 patients, tumors in the initial stages (T1-2N01M0) were treatable (69 segmentectomies and 59 lobectomies). The criterion for deciding between lobectomy and segmentectomy was based on predictive postoperative FEV_1 values of at least 800 mL. The differential in the present study was the type of segmentectomy performed. We used the extended segmentectomy technique described by Tsubota et al.[4] In this type of resection, the bronchus and the segmental artery were isolated. After inflating the lung, segmental bronchi were stapled, and the remaining non-affected segments were collapsed. At this moment, the inflated portion was identified, corresponding to the intersegmental line. The resection line was taken beyond the affected segment (i.e. resection included part of the adjacent segment) by means of surgical staple or electrocauterization. Samples of hilar and mediastinal lymph nodes were also obtained during the surgical procedure. Whenever possible, frozen biopsy of the lymph node into which the segment drained was performed. That lymph node was defined as the segmental sentinel lymph node. In order for the segmentectomy to be considered complete during the intraoperative period, biopsy results for this sentinel lymph node should be negative, as should those for the resection margins. When the sentinel lymph node was positive and the reserve prevented lobectomy, the resection line also included the local lymph node draining zone. The resected material was studied and classified in accordance with the World Health Organization classification[5]. Surgical staging was performed in accordance with the international system for staging lung cancer[6]. Surgery mortality was defined as death within 30 days following surgery. Local recurrence was defined as any cancer recurrence adjacent to the resected area that presented the same histological results. Patients submitted to chemotherapy or radiotherapy were excluded from the study. After hospital discharge, patients had periodical visits with their attending physicians every 3 months during the first year, every 4 months during the second year and every 6 months from the third year on. Patients were submitted to physical examination and chest X-ray in every visit.

Survival was estimated and calculated using Kaplan-Meier survival curves[7], in which the starting point was the date of the surgical procedure and the endpoint was either mortality or the last day of the year 2000. The influence of each variable on survival was calculated using the chi-square test and Cox multivariate analysis[8]. Statistical significance was set at $p < 0.05$. Continuous variables were studied and tested using

Abbreviations used in this paper:

NSCBC	– Non-small cell bronchogenic carcinoma
FEV_1	– Forced expiratory volume in one second
CNS	– Central nervous system
DNA	– Deoxyribonucleic acid

Wilcoxon test[9] and paired variables were studied using Fisher's exact test. In these cases, statistical significance was also set at $p < 0.05$.

RESULTS

There were 3 deaths (2 cases of ventilatory insufficiency caused by infection and 1 case of myocardial infarction) and 10 patients fell out of contact. Sixty-two patients were submitted to segmentectomy and 53 patients were submitted to lobectomy. Seventy-two patients (62.6%) were diagnosed with adenocarcinoma, whereas 43 patients (37.4%) were diagnosed with epidermoid carcinoma. The proportion of both types of tumors was the same between the two groups (lobectomy and segmentectomy) ($p < 0.05$). Follow-up examinations were performed from the surgical procedure either to mortality or until the end of the year 2000. In the segmentectomy group, the 5-year survival among the 10 T1N0 patients was 80%. There were 2 deaths in this group: 1 caused by local recurrence and 1 due to metastasis in the central nervous system (CNS). The 5-year survival among the 15 T2N0 patients was 66.6%. Of the 5 deaths occurring in this group, 3 were due to causes unrelated to the cancer, 1 was due to local recurrence, and 1 was attributed to metastasis to the CNS. The 5-year survival among the 17 T1N1 patients submitted to staging was 41.1%. Of the 10 deaths occurring in this group, 2 were from local recurrence, 3 from metastasis, and 5 from other causes. The 5-year survival among the 20 T2N1 patients was 30%. Of the 14 deaths occurring in this group, 5 were from local recurrence, 5 from dissemination of the disease, and 4 from other causes. When compared within the sample, tumor size and the presence of positive lymph nodes were predictive of worse prognosis ($p < 0.05$). In the lobectomy group (n = 53), the 5-year survival among the 10 T1N0 patients was 80%; 1 of the deaths was caused by metastasis to the CNS and the other by lung cancer. The 5-year survival among the 11 T2N0 patients was 72.8%; 2 of the deaths were unrelated to the disease and 1 was due to generalized remote recurrence. The 5-year survival among the 10 T1N1 patients was 50%. Of the 5 patients in this group who died, 2 had other tumors, 1 died of myocardial infarction, 1 died due to metastasis to the CNS, and 1 died due to multiple metastases. The survival of the 22 T2N1 patients was 31.8% (n = 7). The 5-year survival of the 22 T2N1 patients was 31.8%. Of the 15 deaths occurring in this group, 3 were from other types of tumors, 3 from local recurrence, 3 from metastasis to the CNS, 1 from generalized metastasis, and 5 from other causes. Tumor size and the presence of positive lymph nodes were again prognostically significant for survival ($p < 0.05$). Figure 1 summarizes 5-year-survival results from the groups of patients submitted to either lobectomy or segmentectomy.

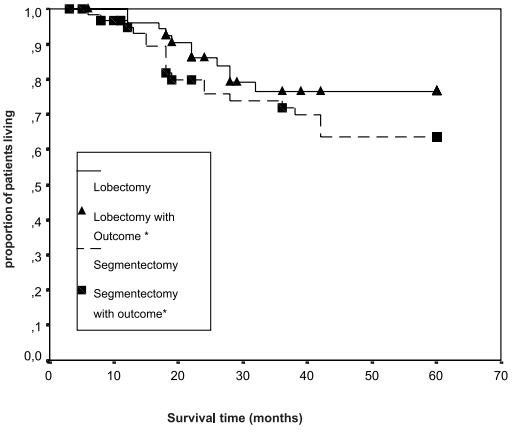

Figure 1 – Five-year (60-month) survival curves for all patients included in the study. *Negative outcome was designated as either death or loss of contact.

When we compared the results, we observed that survival, stage by stage, showed no statistically significant differences ($p > 0.05$; Fig. 2). Type of recurrence, cause of death and time intervals during which patients were disease-free showed no statistically significant differences ($p > 0.05$). Table 1 compares local recurrence in segmentectomy patients to that seen in lobectomy patients. Incidence of metastases is shown in Table 2.

DISCUSSION

The extent of pulmonary resection in patients diagnosed with early-stage bronchial carcinoma has been under discussion in the past few years. Historically, lobectomy followed by mediastinal lymphadenectomy has been recommended as the ideal procedure since it allows tumor resection and drainage of regional and mediastinal lymph nodes,

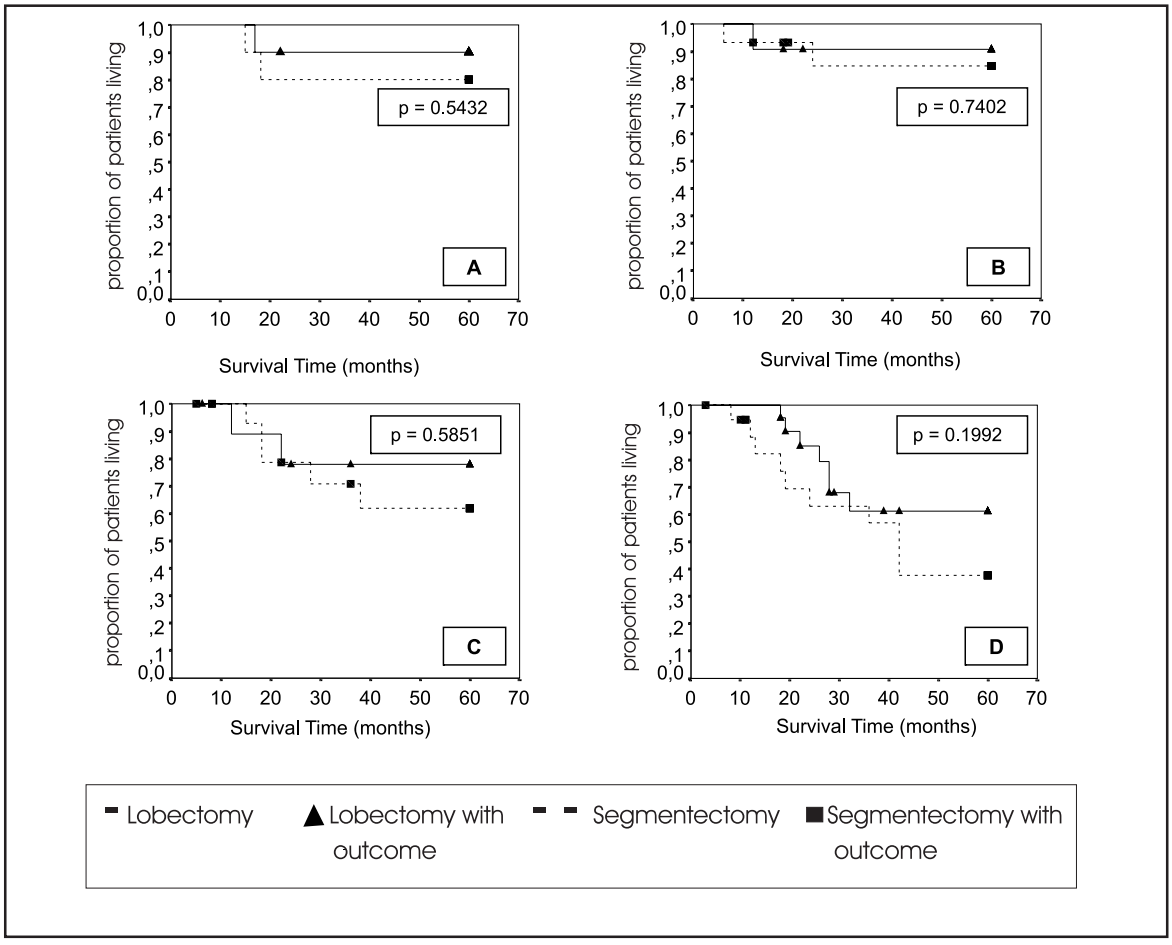

Figure 2 – Five-year (60-month) survival curves for patients in the various stages. A - T1N0 patients. B - T1N1 patients. C - T2N0 patients. D - T2N1 patients. *Negative outcome was designated as either death or loss of contact.

which are potential recurrence sites[10]. Some of justifications for limited resection are the preservation of parenchymal function, reduced morbidity and mortality, and shorter hospital stays[10]. Since the time that Jensik et al.[3] reported promising segmentectomy results for the treatment of early-stage bronchial carcinoma, it has been established that segmentectomy should be used in patients with impaired ventilatory reserve. These authors reported the 5-year survival among 69 patients to be 56.4%. Various other studies have reported that segmentectomy was not the only culprit responsible for the poor results obtained from surgical treatment of bronchial carcinoma. Macchiarini et al. reported no correlation between tumor size and survival[11]. The authors found vascular invasion and mitotic index to be more important. In a similar study, Ichinose et al. reported that the differentiation degree and DNA ploidy were more important as prognostic factors than was tumor size[12]. In a study coordinated by the Lung Cancer Study Group, the authors recommended that resection more limited than lobectomy should not be an option for the surgical treatment of early-stage NSCBC because local recurrence was more frequent and survival was lower when compared to lobectomy[10]. However, the authors performed wedge resection, which is rather different from segmentectomy, in 32.8% of the cases. Landreneau et al. reported that local recurrence after limited resection was higher,

TABLE 1
Incidence of postoperative recurrence in relation to resection technique used

		Recurrence	
		Yes	No
		n (%)	n (%)
Treatment	Segmentectomy	9 (14,5)	53 (85,5)
	Lobectomy	3 (5,7)	50 (94,3)
Total		12 (10,4)	103 (89,6)

TABLE 2
Incidence of postoperative remote metastasis in relation to resection technique used

		Remote metastasis	
		Yes	No
		n (%)	n (%)
Treatment	Segmentectomy	10 (16,1)	52 (83,9)
	Lobectomy	8 (15,1)	45 (84,9)
Total		18 (15,7)	97 (84,3)

although the definitive prognostic factor in their study was tumor biology. The same authors suggested that tumors smaller than 2 cm could be treated with limited resection procedures[13]. Warren & Faber concluded that lobectomy did not improve survival for patients diagnosed with tumors of less than 3 cm in diameter[14]. These authors highlighted the fact that local recurrence in patients submitted to segmentectomy was 4.6 times higher, but, since most patients that presented recurrence died of remote metastases, local recurrence did not actually affect survival in their study.

The first cause of local recurrence must be attributed to incomplete resection in the margins or in interlobular lymph nodes. Affected interlobular lymph nodes are present in approximately 10% to 20% of peripheral lung tumors. Yamanaka et al. reported that 11.7% of patients with tumors smaller than 3 cm presented affected intrapulmonary or intersegmental lymph nodes[15]. These findings explain the high recurrence rates after wedge resection. Wedge resection would have resulted in incomplete resection in approximately 6.4% of these patients, whereas conservative segmentectomy would have resulted in incomplete resection in approximately 11.7%.

There is no doubt that, if resection is anything less than lobectomy, local recurrence is greater. In the present study, 14.5% of the patients submitted to segmentectomy presented local recurrence. At the time of diagnosis, many of these patients (38%) were also diagnosed with remote recurrence. Although less local recurrence (only 5.7%) was seen in lobectomy patients, survival and the incidence of hematogenous metastasis were the same when compared to segmentectomy patients ($p > 0.05$).

In order to evaluate limited resection in patients with limited functional reserve, Kodama et al. compared intentional segmentectomy (in patients with sufficient reserve for lobectomy) to obligatory segmentectomy (in patients without sufficient reserve)[16]. The results revealed that, when segmentectomy was performed in patients that could have been submitted to lobectomy, survival was better, although there was no statistically significant difference when compared to those submitted to lobectomy (93% vs. 88%; $p > 0.05$). However, there was a statistically significant difference in comparison to the group of segmentectomy patients presenting insufficient reserve (in which lobectomy was not an option). The 5-year survival of these patients was 48%. Local recurrence was comparable between the intentional segmentectomy and lobectomy groups (2.2% and 1.3%, respectively), but differed in the obligatory segmentectomy group (11.8%)[16]. These findings suggest that intentional segmentectomy is an acceptable form of treatment for early-stage

tumors, even if there is sufficient reserve for lobectomy.

Various protocols have been used in attempts to reduce local recurrence after limited resection procedures. Miller & Hatcher reported lower incidence of recurrence (6.25% vs. 35%) when compared to other cases of limited resection when combined with radiotherapy in patients that presented FEV_1 < 1 liter[17]. Mc Grath et al. reported that recurrence was 5 times less when limited resection was combined with iodine-125 seed implantation[18]. In a recent study, Lee et al. reported a 47% 5-year survival among patients submitted to limited resection combined with brachytherapy[19].

Expanded or extended segmentectomy differs from conservative segmentectomy because the resection line surpasses the intersegmental line, including the parenchyma of the adjoining segment. This technique, described by Tsubota et al. in 1998, essentially uses the same steps as conservative segmentectomy. After isolating the bronchi of the segment to be resected, the anesthesiologist is asked to inflate the lung, the bronchi are clamped and the lung is allowed to collapse. This delimits the intersegmental line, which is included in the resection, usually closed with surgical staples. Intersegmental and intrapulmonary lymph nodes can thus also be resected.

In conclusion, the findings reported in this study suggested that extended segmentectomy can be an efficacious tool in the surgical treatment of patients with early-stage tumors when their functional reserve is insufficient for lobectomy. Survival was not statistically different among stages, although local recurrence was higher in patients submitted to segmentectomy. A multicenter, randomized prospective study should be carried out so that extended segmentectomy can be offered to patients whose reserve is sufficient for lobectomy.

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