GENERAL THORACIC SURGERY

BRONCHIOLOALVEOLAR CARCINOMA OF THE LUNG: RECURRENCES AND SURVIVAL IN PATIENTS WITH STAGE I DISEASE

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Objectives: The aim of our study was to retrospectively compare the patient characteristics, the frequency and pattern of recurrent disease, and survival in patients with stage I bronchioloalveolar carcinoma and adenocarcinoma of the lung.

Methods: Patients with stage I bronchioloalveolar carcinoma or adenocarcinoma other than bronchioloalveolar carcinoma resected between 1984 and 1992 with adequate clinical follow-up were studied. The clinical characteristics of the patients, extent of initial surgical resection, sites of recurrent disease, and overall survival were examined and compared between the 2 groups. The median follow-up for patients with bronchioloalveolar carcinoma and adenocarcinoma was 6.2 years and 5.9 years, respectively.

Results: A total of 138 patients were identified. Thirty-three patients had bronchioloalveolar carcinoma and 105 patients had adenocarcinoma. Eleven (33%) of the patients with bronchioloalveolar carcinoma had never smoked cigarettes versus 9 (9%) of the patients with adenocarcinoma ($P = .0036$). There were no significant differences between patients with bronchioloalveolar carcinoma and adenocarcinoma in sex distribution and overall recurrence rate. Of the 12 patients with recurrent bronchioloalveolar carcinoma, 1 patient (8%) had extrathoracic disease develop at the site of first recurrence compared with 49% of patients with recurrent adenocarcinoma ($P < .001$). The 5-year survival in patients with bronchioloalveolar carcinoma and in those with adenocarcinoma was 83% and 63%, respectively ($P = .04$).

Conclusions: Stage I bronchioloalveolar carcinoma is more likely to occur in nonsmokers. Survival is longer in patients with bronchioloalveolar carcinoma. Further research is warranted to define the etiology, clinical course, and molecular abnormalities in patients with bronchioloalveolar carcinoma to generate more effective therapeutic approaches. (J Thorac Cardiovasc Surg 2001;121:42-7)

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Bronchioloalveolar carcinoma of the lung (BAC) appears to be increasing in incidence, with up to a 3-fold increase reported between 1955 and 1992.¹⁻³ The cause of this increase is undefined. Proportionately more patients are women and nonsmokers than with other forms of lung cancer.⁴⁻⁶ Patients with BAC are often regarded as having a better prognosis than patients with similar stage non-small cell lung cancer (NSCLC), particularly adenocarcinoma.^{4,7-9} We have previously evaluated patients with advanced stage disease, contrasting clinical findings and outcomes in those patients with BAC to those with other forms of NSCLC. Patients with advanced stage BAC were more likely to have bilateral and multilobar lung parenchymal involvement,

Table I. Patient characteristics

	BAC		Adenocarcinoma	
	No.	%	No.	%
Patients	33	100	105	100
Age (y)				
Median	66	—	66	—
Range	42-84	—	39-83	—
Sex				
Male	13	39	56	53
Female	20	61	49	47
Smoking history				
Nonsmokers	11	33	9	9
Active smokers	15	46	58	55
Ex-smokers	6	18	26	25
Unknown	1	3	12	11

Adenocarcinoma, Adenocarcinoma other than BAC.

with subsequent progression predominantly within the lung parenchyma, and increased survival compared with patients with other forms of NSCLC.⁴

Previous reports of patients with resected stage I lung cancer have shown that such patients with BAC live longer than patients with other types of NSCLC.^{8,9} However, there are limited data in the literature regarding the role of limited versus more extensive resections in patients with stage I BAC. There is even less information on the pattern of recurrent disease and how this is influenced by the surgical approach. We aim to add information on patient characteristics, the pattern of disease at presentation and recurrence, and survival outcomes in patients with stage I BAC and contrast these findings against those in patients with a similar stage of adenocarcinoma.

Methods

Background and patient population. The patients reported in this study were identified in a prior study that developed a molecular pathologic substaging system in patients with stage I NSCLC.⁷ Three hundred seventeen patients underwent resection for stage I NSCLC at the Brigham and Women's Hospital from January 1, 1984, through December 31, 1992. The patients had preoperative stage I disease and were without evidence of systemic metastasis before surgery or in the immediate postoperative interval. All patients underwent mediastinoscopy and/or surgical sampling of hilar and mediastinal nodes. Seventy-three patients were excluded from the analysis; 39 patients had 2 or more primary cancers, 5 had surgery at another hospital and the nodal status could not be verified, 2 patients died within 30 days of the operation, and no follow-up information could be obtained for 27 patients. The Karnofsky performance status was 90% or greater in all patients. All patients included lived a minimum of 60 days after resection. The median periods of follow-up

Table II. Sites of initial progressive disease

	BAC (n = 12)		Adenocarcinoma (n = 39)	
	No.	%	No.	%
Intrathoracic recurrences				
Intrathoracic only	11	92	24	62
Lung	9	75	25	64
Pleural effusion	1	8	4	10
Pericardial effusion	1	8	0	0
Extrathoracic recurrences				
Extrathoracic only	1	8	12	31
Bone	0	0	7	18
Brain	0	0	5	13
Adenopathy (C; S/C)	0	0	4	10
Liver	0	0	2	5
Adrenal	0	0	1	3
Adenopathy (axilla)	1	8	0	0

Adenocarcinoma, Adenocarcinoma other than BAC; C, cervical; S/C, supraclavicular.

for patients with BAC and those with adenocarcinoma were 6.2 years and 5.9 years, respectively.

Of the remaining 244 eligible patients, 33 had a diagnosis of BAC, and 105 had a diagnosis of adenocarcinoma other than BAC. These patients were selected for this study, which aimed to further characterize the nature of BAC and to contrast the clinical features against those of patients with adenocarcinoma other than BAC. The medical records of all patients were reviewed for clinical characteristics including age, sex, cigarette smoking history, site of tumor, type of resection (limited resection, lobectomy, combination [lobectomy with limited resection], or pneumonectomy). Patient follow-up was acquired by retrospective chart review and with the assistance of the Brigham and Women's Hospital Tumor Registry. A median follow-up of 6 years was obtained in both groups, which included the time and location of any recurrent disease. The study was approved by the Dana Farber/Partners Cancer Care Investigational Review Board.

Pathology. The pathologic material was reviewed by 2 pathologists. The diagnosis of BAC was made according to the former description of a peripheral tumor manifesting the growth of well-differentiated cuboidal or columnar tumor cells along intact alveolar walls and no evidence of a primary adenocarcinoma at some extrapulmonary site.^{10,11} The specimens were consistent with the new classification by the World Health Organization (WHO), which describes BAC as a form of adenocarcinoma with a pure bronchioloalveolar growth pattern and no evidence of stromal, vascular, or pleural invasion.¹² Stage I NSCLC was pathologically confirmed in all patients; all resected hilar and mediastinal nodes were proved uninvolved with cancer. Patients were divided into 2 groups: those with BAC and those with adenocarcinoma other than BAC for the purpose of comparison.

Statistical methods. Comparisons of the groups defined by histology on the basis of clinical and demographic variables that are categoric are made by use of a Fisher exact test.

Table III. Comparison of sites of pulmonary recurrences in patients with BAC and those with adenocarcinoma after either limited resection or lobectomy

Site of recurrence	BAC		Adenocarcinoma	
	Limited resection (n = 13)	Lobectomy (n = 19)	Limited resection (n = 22)	Lobectomy (n = 72)
Ipsilateral lung	4* (31%)	2 (11%)	2* (9%), 5 [†] (23%)	4 [†] (6%)
Contralateral lung	0 (0%)	3 (16%)	2 (9%)	9 (12%)
Bilateral lung	1 (8%)	0 (0%)	1 (5%)	0 (0%)
Effusions				
Pleural	0 (0%)	1* (5%)	2* (9%)	1* (1%)
Pericardial	1 (8%)	0 (0%)	0 (0%)	0 (0%)

Adenocarcinoma, Adenocarcinoma other than BAC.

*Recurrence in ipsilateral primary lobe.

[†]Recurrence in ipsilateral nonprimary lobe.

For disease-free survival (DFS), time was measured from the operation until recurrence or death. Patients who were alive and disease free at the most recent follow-up were censored for this analysis. Survival comparisons reported are from a log rank test, and estimates of survival were made by the method of Kaplan and Meier, with the time measured from the date of the initial operation until death or most recent follow-up (censored).¹³

Results

Patient characteristics. A total of 138 patients with stage I NSCLC were eligible for this analysis. Thirty-three patients had a diagnosis of BAC, and 105 patients had adenocarcinoma (acinar, n = 54; papillary, n = 14; solid tumor with mucin, n = 25; mixed, n = 9; poorly differentiated, n = 3).¹² The patient characteristics are outlined in Table I. The median age at initial presentation was similar both in patients with BAC and in those with adenocarcinoma. There were more women (61%) than men (39%) within the BAC cohort as compared with near equal numbers within the patients with adenocarcinoma ($P = .23$). Eleven of the 33 patients (33%) with BAC had never smoked as compared with 9 patients (9%) in the adenocarcinoma group ($P = .0036$). Nine (45%) of the 20 women with BAC were never smokers compared with 2 (15%) of the 13 men. The median cigarette smoking exposure, expressed in pack years, in patients with BAC and adenocarcinoma was 30 (range 7-100 years) and 45 (range 10-160 years), respectively. The upper lobes were the most common site of the primary tumor in both patients with BAC (n = 21; 64%) and those with adenocarcinoma (n = 70; 67%), with a slight preference for the right side. Sixty-three percent of patients with BAC had T1 N0 lesions compared with 52% of patients with adenocarcinoma.

Surgical interventions. Nineteen patients (58%) with BAC had lobectomies compared with 72 patients

(69%) with adenocarcinoma. Of the 13 (39%) patients with BAC who had limited resections, all but 1 had wedge resections. One patient (3%) with BAC had a combined lobectomy and wedge resection. Eighteen patients (17%) with adenocarcinoma had wedge resections, and 4 (4%) had segmentectomies. Six patients (6%) with adenocarcinoma had combined lobectomy and limited resection, and an additional 5 patients (4%) had pneumonectomies.

Recurrence patterns. Twelve of the 33 patients (36%) with BAC had recurrent disease compared with 39 of the 105 patients (37%) with adenocarcinoma. These results are summarized in Table II. The 5-year DFS in patients with BAC and those with adenocarcinoma was 74% and 65%, respectively ($P = .6$). There was no significant difference in DFS in patients with BAC resected by lobectomy versus limited resection (5-year DFS: 83% vs 66%, respectively; $P = .38$). However, patients with adenocarcinoma resected by lobectomy had a statistically significantly longer DFS than those patients treated by limited resection (5-year DFS: 76% vs 31%; $P = .004$).

The recurrences within the patients with resected BAC (92%) occurred predominantly within the thorax compared with patients with adenocarcinoma (74%) ($P = .14$). Nine of the 12 recurrences in those patients with BAC were within the lung parenchyma. Malignant pleural effusion (n = 1) and pericardial effusions (n = 1) accounted for the sites of recurrence in 2 patients with BAC. One patient with BAC developed a metastasis in an axillary node. In contrast, extrathoracic metastases were common in the patients (19 of 39 patients, 49%) with adenocarcinoma. Of these patients with recurrent adenocarcinoma, 18% had metastases to bone (n = 7), 13% to brain (n = 5), 10% to cervical lymph nodes (n = 4), 5% to liver (n = 2), and 3% to the adrenal glands (n = 1). These findings are summarized in Tables II and III.

Fig 1. Postoperative survival in patients with pathologic stage I BAC compared with patients with stage I adenocarcinoma other than BAC (5-year survival: 83% vs 63%, respectively; $P = .04$). Circular marks represent censored data (●, BAC; ○, adenocarcinoma).

Table IV. Comparison of patients with stage I BAC reported in the surgical literature

Author	Stage I BAC (n)	Recurrent disease	Median survival (y)	Five-year survival (%)
Dumont et al ²⁵	71	Not specified	—	65
Fujimoto et al ²¹	25	Not specified	6.1	—
Greco et al ²⁶	65	Not specified	—	75
Harpole et al ¹⁶	80	34%,* 24%†	—	55
Heikkila ²⁷	28	Not specified	—	57
Regnard et al ³²	33	Not specified	—	56
Williams et al ⁸	67	Not specified	—	81
Present study	33	35%,* 38%†	7.0	83

*Recurrent disease after lobectomy.

†Recurrent disease after limited pulmonary resection.

Survival. The median survivals for patients with BAC and those with adenocarcinoma were 7 and 6.7 years, respectively. Patients with BAC lived longer (5-year survival 83%) than patients with adenocarcinoma (5-year survival 63%) after resection of their stage I disease ($P = .04$) (Fig 1). Men with BAC had a greater median survival than women (7.5 years vs 6.3 years; $P = .04$) as did patients with BAC who never smoked compared with cigarette smokers (7.8 years vs 6.3 years; $P = .04$). There was no statistical difference in survival between patients with BAC treated with either wedge resection ($n = 12$) or lobectomy ($n = 18$) ($P = .24$) or between patients with T1 or T2 lesions ($P = .9$). Patients with adenocarcinoma had a statistically significant difference in survival in favor of lobectomies ($n = 70$; 74% 5-year survival) over limited resections ($n = 22$; 43% 5-year survival) ($P = .02$).

Discussion

The original descriptions of BAC report on patients with advanced bilateral pulmonary tumors.^{10,14} Retrospective series of patients report that 35% to 39% of patients with BAC present with stage I disease^{15,16} compared with 20% of patients with NSCLC.¹⁷ Currently, BAC is pathologically classified as a form of adenocarcinoma,¹² although BAC has numerous distinguishing clinical features. Patients with advanced stage BAC show a specific tendency for intrapulmonary spread, with limited regional nodal involvement, and a reduced tendency for extrathoracic metastases, particularly to brain and liver.^{4,18,19} Patients with advanced stage (IIIB and IV) BAC are moderately responsive to chemotherapy, with response rates of 20% to 32%^{4,18,20,21} and have a 1-year survival that is significantly better than that

for patients with similar stage adenocarcinoma and other forms of NSCLC.⁴

Nineteen studies have reported on 1383 patients with various stages of BAC who have received surgical resections for curative or palliative intent.^{*} Of these, 13 studies reported data on 709 patients with stage I BAC.[†] The majority of these retrospective studies did not include a comparison group, and the pathology specimens were not reviewed again to confirm the diagnosis as was performed in our study. They focus predominantly on symptoms, pathologic features of BAC, and radiologic features as prognostic factors. However, there are limited data on the recurrence rates and sites of recurrent disease in patients with early stage BAC. This study adds information about the sites of disease at initial presentation, the patterns of surgical resection and subsequent recurrent disease, and survival of patients with stage I BAC and adenocarcinoma.

The majority of the 13 studies that include data on stage I BAC do not break down the patient characteristics per stage of disease. Three studies, including greater than 70% of patients with stage I BAC, report that 58%,⁹ 61%,³⁴ and 86%²⁵ of patients were male. This finding is in contrast to our results, which revealed a predominance of female patients. Significantly more patients with stage I BAC in our series were nonsmokers (33%) compared with patients with adenocarcinoma (9%). Between 10% and 32% of patients with BAC in the surgical literature are nonsmokers.^{3,19,29} The smoking status was unknown in 25% of the patients in the study that reported the rate of cigarette smoking of 10%.²⁹

The sites of disease at presentation in patients with BAC have been reported in 2 previous studies.^{24,29} Neither study specifies the number of patients with stage I disease, although they state that 56%²⁴ and 73%²⁹ had solitary nodules. Both studies report that these solitary nodules were most commonly found in the upper lobes (46% and 63%, respectively). Our data similarly show involvement of the upper lobes being the most common site of disease at presentation, both in patients with BAC (63%) and in those with adenocarcinoma (66%).

Lobectomy is the most commonly performed surgical procedure in patients undergoing resection for BAC, with between 56%²⁸ to 87%²⁵ of patients treated in this manner. Retrospective series including greater than 70% of patients with stage I BAC report that limited resections are performed on 3%²⁵ to 18% of the patients.¹⁹ Fifty-eight percent of our patients with BAC had a lobectomy, and the majority of the remainder (39%) had a limited

resection. Lobectomy was also more commonly performed in our patients with adenocarcinoma than limited resection (69% vs 21%, respectively).

Two studies compare recurrence rates after resection in patients with BAC and those with adenocarcinoma.^{9,27} Grover and Piantadosi⁹ reported a recurrence rate of 0.0723 and 0.12 per patient-year of exposure in patients with stage T1 N0 M0 BAC (n = 150) and adenocarcinoma (n = 504), respectively ($P = .007$). The second study included 33 patients with stage I to stage III BAC, of whom 28 patients (85%) had stage I disease.²⁷ However, only 59% of their patients with adenocarcinoma had stage I disease, making comparisons between the clinical characteristics of the patients with BAC and those with adenocarcinoma more difficult. The authors reported that 39% of patients with BAC had either ipsilateral or contralateral intrapulmonary metastases compared with 13% of patients with adenocarcinoma ($P < .025$). Twenty-nine percent of patients with BAC and 69% of the patients with adenocarcinoma had distant metastases, respectively ($P = .001$). Our data compare patients of similar stage BAC and adenocarcinoma and demonstrate the greater tendency for intrapulmonary metastases to develop, with limited extrathoracic recurrences in patients with BAC.

One other study, from Harpole and associates,¹⁶ reports on recurrences after surgical resection in patients with stage I BAC. No comparison group was included. They compared recurrences in patients with stage I BAC after lobectomy (n = 63) and wedge resection (n = 17) and reported a greater recurrence after lobectomy than after wedge resection (34% vs 24% at 3 years). Their data conflict with the results of our study, which show a greater DFS in patients with BAC resected by lobectomy.

Eight studies report on median and 5-year overall survival in patients with stage I BAC.^{*} The reported 5-year survivals range from 54% to 81%. One of these studies compared their patients with BAC to those with stage I adenocarcinoma (81% vs 65%, respectively). These findings are nearly identical to those reported in our series. These data support the belief that patients with BAC have a better prognosis than patients with adenocarcinoma. The survival of our patients with adenocarcinoma is comparable to that recently reported by Fry and coworkers.¹⁷ Grover and Piantadosi⁹ add additional support of a greater survival in patients with BAC in a study reporting mortality rates in patients with T1 N0 M0 NSCLC. Patients with T1 N0 M0 BAC and similar stage adenocarcinoma had mortality rates of 0.0737 and 0.10 per

^{*}References 3,8,9,14,16,19,21-33.

[†]References 8,9,16,19,21,22,25-29,32,33.

^{*}References 8,9,16,21,25,26,28,32.

patient-year of exposure, respectively ($P = .0542$). The results are summarized in Table IV.

In conclusion, this study confirms that patients with BAC exhibit a different clinical pattern to patients with adenocarcinoma. Although the DFS of patients with resected stage I BAC or adenocarcinoma is similar, patients with stage I BAC are nearly 4-fold less prone to the development of extrathoracic disease. Patients with stage I BAC had a longer overall survival than patients with similar stage adenocarcinoma and represent a more favorable prognostic group. Further research is required to define the etiology, clinical course, and molecular abnormalities in patients with BAC to generate more appropriate therapeutic interventions.

REFERENCES

- Auerbach O, Garfinkel L. The changing pattern of lung carcinoma. *Cancer* 1991;68:1973-7.
- Barsky SH, Cameron R, Osann KE, Tomita D, Holmes EC. Rising incidence of bronchioloalveolar lung carcinoma and its unique clinicopathologic features. *Cancer* 1994;73:1163-70.
- de Perrot M, Licker M, Robert J, Spiliopoulos A. Time trend in the surgical management of patients with lung carcinoma. *Eur J Cardiothorac Surg* 1999;15:433-7.
- Breathnach OS, Ishibe N, Williams J, Linnoila RI, Caporaso N, Johnson BE. Clinical features of patients with stage IIIB and IV bronchioloalveolar carcinoma of the lung. *Cancer* 1999;86:1165-73.
- Barkley JE, Green MR. Bronchioloalveolar carcinoma. *J Clin Oncol* 1996;14:2377-86.
- Morabia A, Wynder EL. Relation of bronchioloalveolar carcinoma to tobacco. *BMJ* 1992;304:541-3.
- Kwiatkowski DJ, Harpole DH Jr, Godleski J, Herndon JE 2nd, Shieh DB, Richards W, et al. Molecular pathologic substaging in 244 stage I non-small-cell lung cancer patients: clinical implications. *J Clin Oncol* 1998;16:2468-77.
- Williams D, Pairolero P, Davis C, Bernatz P, Payne W, Taylor W, et al. Survival of patients surgically treated for stage I lung cancer. *J Thorac Cardiovasc Surg* 1981;82:70-6.
- Grover FL, Piantadosi S. Recurrence and survival following resection of bronchioloalveolar carcinoma of the lung—The Lung Cancer Study Group experience. *Ann Surg* 1989;209:779-90.
- Liebow A. Bronchiolo-alveolar carcinoma. *Adv Intern Med* 1960;10:329-58.
- Clayton F. The spectrum and significance of bronchioloalveolar carcinomas. *Pathol Annu* 1988;23:361-94.
- Travis W, Colby T, Corrin B, Shimosato Y, Brambilla E. Histological typing of lung and pleural tumors. 3rd ed. Berlin: Springer-Verlag; 1999.
- Kaplan E, Meier P. Nonparametric estimation from incomplete observations. *J Am Stat Assoc* 1958;53:457-81.
- Ludington L, Verska J, Howard T, Kypridakis G, Brewer L. Bronchiolar carcinoma (alveolar cell), another great imitator: a review of 41 cases. *Chest* 1972;61:622-8.
- Donker R, Stewart DJ, Dahrouge S, Evans WK, Shamji F, Maziak DE, et al. Clinical characteristics of bronchioloalveolar carcinoma [abstract]. *Proc Am Soc Clin Oncol* 1999;18:1839a.
- Harpole D, Bigelow C, Young GW Jr, Wolfe W, Sabiston D Jr. Alveolar cell carcinoma of the lung: a retrospective analysis of 205 patients. *Ann Thorac Surg* 1988;46:502-7.
- Fry WA, Phillips JL, Menck HR. Ten-year survey of lung cancer treatment and survival in hospitals in the United States: a National Cancer Data Base Report. *Cancer* 1999;86:1867-76.
- Feldman ER, Eagan RT, Schaid DJ. Metastatic bronchioloalveolar carcinoma and metastatic adenocarcinoma of the lung: comparison of clinical manifestations, chemotherapeutic responses, and prognosis. *Mayo Clin Proc* 1992;67:27-32.
- Okubo K, Mark EJ, Flieder D, Wain JC, Wright CD, Moncure AC, et al. Bronchoalveolar carcinoma: clinical, radiologic, and pathologic factors and survival. *J Thorac Cardiovasc Surg* 1999;118:702-9.
- Sorensen JB, Hirsch FR, Olsen J. The prognostic implication of histopathologic subtyping of pulmonary adenocarcinoma according to the classification of the World Health Organization: an analysis of 259 consecutive patients with advanced disease. *Cancer* 1988;62:361-7.
- Fujimoto N, Segawa Y, Takigawa N, Hotta K, Kishino D, Shimono M, et al. Clinical investigation of bronchioloalveolar carcinoma: a retrospective analysis of 53 patients in a single institution. *Anticancer Res* 1999;19:1369-73.
- De Leyn P, Vansteenkiste F, Sciot R, Moerman P, Verougstraete L, Demedts M, et al. Bronchioloalveolar carcinoma: long-term survival of 23 resected patients. *Acta Chir Belg* 1995;95:220-2.
- Delarue N, Anderson W, Sanders D, Starr J. Bronchioloalveolar carcinoma of the lung: a reappraisal after 24 years. *Cancer* 1972;29:90-7.
- Dunn D, Hertel B, Norwood W, Nicoloff DM. Bronchioloalveolar cell carcinoma of the lung: a clinicopathological study. *Ann Thorac Surg* 1978;26:241-9.
- Dumont P, Gasser B, Rouge C, Massard G, Wihlm J. Bronchoalveolar carcinoma: histopathologic study of evolution in a series of 105 surgically treated patients. *Chest* 1998;113:391-5.
- Greco R, Steiner R, Goldman S, Cotler H, Patchefsky A, Cohn H. Bronchioloalveolar cell carcinoma of the lung. *Ann Thorac Surg* 1986;41:652-6.
- Heikkila L. Results of surgical treatment in bronchioloalveolar carcinoma. *Ann Chir Gynaecol* 1986;75:183-91.
- Hsu CP, Chen CY, Hsu NY. Bronchioloalveolar carcinoma. *J Thorac Cardiovasc Surg* 1995;110:374-81.
- James E, Schuchmann G, Hall R, Patterson J, Gillespie J, Gomez A. Preferred surgical treatment for alveolar cell carcinoma. *Ann Thorac Surg* 1976;22:157-62.
- Kemeny M, Block L, Braun D, Martini N. Results of surgical treatment of carcinoma of the lung by stage and cell type. *Surg Gynecol Obstet* 1978;147:865-71.
- Munnell E, Diling E, Grantham R, Harkey M, Mohr J. Reappraisal of solitary bronchiolar (alveolar cell) carcinoma of the lung. *Ann Thorac Surg* 1978;25:289-97.
- Regnard JF, Santelmo N, Romdhani N, Gharbi N, Bourcureau J, Dulmet E, et al. Bronchioloalveolar lung carcinoma: results of surgical treatment and prognostic factors. *Chest* 1998;114:45-50.
- Sorensen JB, Olsen JE. Prognostic implications of histopathologic subtyping in patients with surgically treated stage I or II adenocarcinoma of the lung. *J Thorac Cardiovasc Surg* 1989;97:245-51.
- Heikkila L, Harjula A, Suomalainen RJ, Mattila S. Results of surgical treatment of synchronous multiple primary lung carcinomas. *Ann Chir Gynaecol* 1985;74:155-8.