Postprint: Analysis of Clinical Characteristics and Prognostic Factors of Bronchopulmonary Carcinoid

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Date: 2018-06-14T00:00:00+00:00

Abstract

Objective To investigate the clinical characteristics and surgical treatment experience of bronchopulmonary carcinoid tumors, including typical carcinoid (TC) and atypical carcinoid (ATC), and to analyze possible prognostic factors. Methods The clinical data of 57 patients who underwent surgical treatment at Peking Union Medical College Hospital between January 2000 and January 2014 and were pathologically confirmed as TC or ATC were retrospectively reviewed, and survival and prognostic analyses were simultaneously performed. Results Among the 57 patients, there were 35 males and 22 females, with a median age of 49 years (range 12-85 years) and a median disease course of 3 months (range 1-156 months). Clinical symptoms lacked specificity, and 12 cases were accompanied by ectopic adrenocorticotropic hormone syndrome. Postoperative pathology confirmed TC in 39 cases and ATC in 18 cases; the majority were stage I (41 cases), with 7 cases each of stage II and stage III, and 2 cases of stage IV. The 5-year and 10-year survival rates were 92.4% and 89.0%, respectively. Kaplan-Meier analysis showed that the P values for pathological type, T stage, and N stage were 0.001, 0.000, and 0.004, respectively. Conclusion Bronchopulmonary TC and ATC lack specific clinical manifestations, and surgical treatment yields favorable outcomes. Pathological classification, tumor T stage, and N stage may be prognostic influencing factors.

Full Text

Clinical Features and Prognostic Factors of Bronchopulmonary Carcinoid Tumors

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Abstract

Objective: This study aimed to evaluate the clinical features and surgical outcomes of bronchopulmonary carcinoid tumors, including typical carcinoid (TC) and atypical carcinoid (ATC), and to analyze potential prognostic factors.

Methods: The clinical data of 57 consecutive patients who underwent surgical resection and were pathologically confirmed as TC or ATC at Peking Union Medical College Hospital between January 2000 and January 2014 were retrospectively analyzed. Survival and prognostic analyses were also performed.

Results: The cohort included 35 males and 22 females with a median age of 49 years (range: 12–85) and median disease duration of 3 months (range: 1–156). Clinical symptoms lacked specificity, with 12 patients presenting with ectopic adrenocorticotropic hormone syndrome. Postoperative pathology confirmed 39 cases of TC and 12 cases of ATC. Disease staging consisted of 41 stage I, 7 stage II, 7 stage III, and 2 stage IV cases. The 5-year and 10-year survival rates were 92.4% and 89.0%, respectively. Kaplan-Meier analysis showed that pathological type, T stage, and N stage had P values of 0.001, 0.000, and 0.004, respectively.

Conclusions: Bronchopulmonary TC and ATC exhibit atypical clinical features, but patients have favorable prognoses following surgery. Pathological type, T stage, and N stage may represent prognostic factors.

Keywords: carcinoma, neuroendocrine; lung; surgery; prognosis

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Introduction

Bronchopulmonary neuroendocrine tumors (BP-NETs) are a heterogeneous group of neoplasms arising from the diffuse neuroendocrine system of the bronchopulmonary tract, accounting for 1%–3% of primary lung malignancies [1-2]. The World Health Organization (WHO) classifies BP-NETs into four major pathological types based on biological characteristics: typical carcinoid (TC), atypical carcinoid (ATC), large-cell neuroendocrine carcinoma (LCNEC), and small-cell lung cancer (SCLC) [3]. LCNEC and SCLC are highly malignant neuroendocrine tumors whose primary treatment modalities are chemotherapy and radiotherapy. TC and ATC are well-differentiated neuroendocrine tumors for which surgical resection is the mainstay of treatment. Due to their rarity, most clinical experience derives from small-sample, single-center retrospective analyses, and controversies remain regarding optimal treatment strategies and prognostic factors. This study retrospectively analyzed cases of

bronchopulmonary carcinoid treated at Peking Union Medical College Hospital to summarize clinical characteristics and evaluate prognostic factors.

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1. Subjects and Methods

1.1 Subjects and Grouping

All patients who underwent surgical treatment at Peking Union Medical College Hospital between January 2000 and January 2014 and were postoperatively pathologically confirmed with bronchopulmonary carcinoid were included. Cases undergoing biopsy only were excluded. The 57 patients represented 1.23% (57/4,631) of all lung cancer surgical resection cases performed by the Department of Thoracic Surgery at Peking Union Medical College Hospital during this period.

1.2 Observation Indicators and Follow-up

All patients underwent preoperative chest computed tomography (CT) scans. Postoperative survival period was calculated from the date of surgery to the date of death or last follow-up. Follow-up was completed by January 2014. Variables analyzed included pathological type (TC vs. ATC), TNM stage, presence of ectopic ACTH syndrome, central vs. peripheral tumor location, and adjuvant therapy.

1.3 Surgical Treatment

All patients received comprehensive treatment centered on surgical resection. Based on tumor location, size, and intraoperative frozen pathology results, patients underwent either thoracotomy or video-assisted thoracoscopic surgery (VATS) for lobectomy, pneumonectomy, or sublobar resection. Central lesions underwent fiberoptic bronchoscopy. Tumor staging followed the American Joint Committee on Cancer (AJCC) lung cancer staging manual. Postoperative adjuvant therapy was administered based on pathological stage.

1.4 Statistical Analysis

Data were analyzed using SPSS 19.0 software. Normally distributed measurement data were expressed as mean ± standard deviation and compared between groups using t-tests. Non-normally distributed data were expressed as median (range) and compared using non-parametric tests (Mann-Whitney U test). Count data were analyzed using chi-square tests. Survival curves were generated using the Kaplan-Meier method, and univariate analysis was performed to evaluate survival time and prognostic factors. A P-value <0.05 was considered statistically significant.

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2. Results

2.1 General Patient Data

The cohort comprised 35 males and 22 females (ratio 1.6:1) with a median age

of 49 years (range: 12–85). The median disease duration was 3 months (range: 1–156). There were no statistically significant differences between groups in age, gender, or smoking status.

2.2 Clinical Symptoms

Approximately 47.4% (27/57) of patients were asymptomatic, with lesions discovered incidentally on routine physical examination. Among symptomatic patients, 26.3% (15/57) presented with irritative dry cough, 8.8% (5/57) with hemoptysis, and 21.0% (12/57) with chest tightness. Ectopic adrenocorticotropic hormone syndrome was observed in 21.0% (12/57) of cases.

2.3 Imaging Findings

All patients underwent CT imaging. Peripheral lesions typically appeared as round or oval nodules with smooth margins, rarely showing spiculation or pleural retraction. Central lesions exhibited imaging features similar to other central lung cancers, often with obstructive atelectasis. Enhanced CT scans showed most lesions could be enhanced.

2.4 Fiberoptic Bronchoscopy

Thirty-eight central lesions underwent fiberoptic bronchoscopy, which revealed hypervascular neoplastic surfaces. Biopsy diagnosis was considered in 20 cases, with 15 cases confirmed as carcinoid and 5 cases suspected as small-cell lung cancer. Postoperative pathology confirmed 12 TC and 2 ATC cases; 2 cases were considered poorly differentiated squamous or adenocarcinoma, while 2 cases could not exclude ATC.

2.5 Perioperative Status

All 57 patients underwent surgical resection, including 38 (66.7%) who received lobectomy, with 12 cases converted from VATS to thoracotomy. Additional procedures included combined lobectomy, sleeve resection, bronchoplasty, and sublobar resection. Systematic lymph node dissection or sampling was performed in most cases, though 2 cases did not undergo lymph node evaluation. There were no perioperative deaths. Postoperative complications occurred in 2 patients: one with pulmonary infection resolved with antibiotics, and another requiring bronchoscopic suctioning.

2.6 Intraoperative Frozen and Final Pathological Diagnosis

Intraoperative frozen section examination was performed in 26 cases, with 20 (77.0%) diagnosed as neuroendocrine tumor (15 TC, 5 ATC) and 6 (23.1%) with non-specific results. Final pathology revealed a median tumor diameter of 2.3 cm (range: 0.5–7.5 cm). Thirty-nine cases (68.4%) were diagnosed as TC and 18 (31.6%) as ATC. Fifteen patients (26.3%) had lymph node metastasis (N1 in 5 cases, N2 in 8 cases). Two patients had pleural cavity dissemination (M1a), both pathologically confirmed as ATC.

2.7 Postoperative Adjuvant Therapy and Follow-up

The median follow-up duration was 57 months (range: 16–144). Adjuvant therapy included chemotherapy alone in 7 cases, radiotherapy alone in 1 case, and

sequential chemoradiotherapy in 7 cases. Two patients died from tumor progression due to hematogenous metastasis to brain and adrenal glands.

2.8 Survival Analysis

Kaplan-Meier survival analysis demonstrated 5-year and 10-year survival rates of 92.4% and 89.0%, respectively. Univariate analysis identified pathological type (P=0.001), T stage (P<0.001), and N stage (P=0.004) as risk factors affecting carcinoid prognosis. No significant differences were observed in postoperative adjuvant therapy between groups (P>0.05).

shows general patient data and clinical symptoms comparing typical and atypical carcinoids. presents surgical and pathological data. [Figure 1: see original paper] illustrates CT imaging features of peripheral typical and atypical carcinoids, showing round solid nodules with smooth margins.

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3. Discussion

Bronchopulmonary carcinoids are rare, well-differentiated neuroendocrine tumors with non-specific clinical and imaging manifestations. Preoperative biopsy of small specimens has limited accuracy, and definitive diagnosis relies on postoperative paraffin pathology and immunohistochemical examination. Surgical resection is the preferred treatment modality, with TNM stage being a key factor influencing prognosis and survival.

The median age of our cohort was 49 years, with no significant differences in age, gender, smoking status, or tumor location between TC and ATC groups—findings that differ substantially from our previously reported LCNEC cohort (median age 61.4 years, 82.8% male, 88.9% smokers) [8]. Approximately 25% of patients were asymptomatic at diagnosis, while 20% presented with ectopic ACTH syndrome. Respiratory symptoms predominated in central lesions (cough, hemoptysis), whereas peripheral lesions were more frequently asymptomatic [10]. Imaging studies, particularly chest CT, are crucial for diagnosis. Central lesions resemble other central lung cancers with obstructive atelectasis, while peripheral lesions appear as uniform, round nodules with smooth margins, rarely showing spiculation or pleural retraction—features that contrast with the irregular, heterogeneous appearance of LCNEC [8,11,13]. ATC may show variable morphology but infrequently demonstrates prominent spiculation.

Preoperative diagnosis is challenging due to the low accuracy of small specimen biopsies [3,7,14-15]. Among our central lesions undergoing bronchoscopic biopsy, only 15 of 38 cases yielded definitive diagnoses, with others misdiagnosed as SCLC or non-small-cell lung cancer. Intraoperative frozen section analysis also had limitations, with 6 of 26 cases yielding non-specific results, including one case ultimately confirmed as SCLC on final pathology. This highlights why most BP-NET studies are retrospective.

Although multidisciplinary treatment is advocated for BP-NET, radiotherapy

and chemotherapy have limited efficacy, and targeted therapies are lacking [7,16-17]. Surgical resection remains the first-line and only proven effective treatment for localized, resectable disease [7,16-17]. Our treatment strategy referenced non-small-cell lung cancer guidelines, with selective adjuvant chemoradiotherapy for stage II–III disease. Notably, two patients with preoperatively resectable disease were found to have pleural dissemination (M1a) intraoperatively, both confirmed as ATC on pathology. The overall 5-year and 10-year survival rates of 92.4% and 89.0% demonstrate favorable outcomes, though ATC showed more aggressive behavior with higher rates of lymph node metastasis (40–50%) and distant metastasis compared to TC (3–5% lymph node metastasis, 10–15% distant metastasis) [2,7,21].

Pathological type, T stage, and N stage significantly impacted prognosis, while adjuvant therapy showed no significant benefit in radically resected cases [20]. The RADIANT-4 trial evaluated everolimus, a mammalian target of rapamycin inhibitor, in advanced non-functional neuroendocrine tumors, showing prolonged progression-free survival, but its role in adjuvant settings remains unestablished [22].

This retrospective study has limitations, including small sample size, extended time span, and non-uniform diagnostic and treatment protocols, potentially introducing bias. Therefore, these results should be considered preliminary, and further multicenter studies are needed to validate our findings.

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Note: Figure translations are in progress. See original paper for figures.