

Interactive CardioVascular and Thoracic Surgery

Typical and atypical pulmonary carcinoids: our institutional experience

Alessandro Bini, Jury Brandolini, Nicola Cassanelli, Fabio Davoli, Giampiero Dolci,
Francesco Sellitri and Franco Stella

Interact CardioVasc Thorac Surg 2008;7:415-418; originally published online Mar 18,
2008;

DOI: 10.1510/icvts.2007.173328

The online version of this article, along with updated information and services, is
located on the World Wide Web at:

<http://icvts.ctsnetjournals.org/cgi/content/full/7/3/415>

Interactive Cardiovascular and Thoracic Surgery is the official journal of the European Association for Cardio-thoracic Surgery (EACTS) and the European Society for Cardiovascular Surgery (ESCVS). Copyright © 2008 by European Association for Cardio-thoracic Surgery. Print ISSN: 1569-9293.

Institutional report - Thoracic general

Typical and atypical pulmonary carcinoids: our institutional experience

Alessandro Bini, Jury Brandolini, Nicola Cassanelli, Fabio Davoli*, Giampiero Dolci, Francesco Sellitri, Franco Stella

Department of Thoracic Surgery, University of Bologna, 'S. Orsola – Malpighi' Hospital, Via Massarenti, 9, 40138 Bologna (BO), Italy

Received 4 January 2008; received in revised form 10 February 2008; accepted 11 February 2008

Abstract

Pulmonary carcinoids are rare malignant neoplasms, accounting for 2–5% of all lung tumors, with an approximate annual incidence of 2.3–2.8 cases per million of the population. We relate our experience of 54 patients (21 male, 33 female, mean age 53 ± 15 years) treated between July 1986 and April 2006. All the patients underwent preoperative fibrobronchoscopy: preoperative diagnosis was made in 28 patients (52%). Surgical treatment consisted of: 31 standard lobectomies, 6 pneumonectomies, 5 bilobectomies, 2 sleeve lobectomies, 2 anatomic segmentectomies, 6 wedge resections; two patients were managed with sleeve bronchial procedure of the left main bronchus without lung resection. Fifty-four patients were followed with a mean time of observation of 67 months: 6 (11%) deaths occurred, at a mean period of 49 months after surgery; there were no postoperative deaths. Overall, 5-year survival was 91%, 10 years 83%: 5-year survival was 91% for typical carcinoids (TC) vs. 88% for atypical (AC), 10 years 91% for TC and 44% for AC (significant value, $P=0.0487$). Carcinoid tumors are a distinct group of neuroendocrine tumors with a good prognosis in most cases. Surgery currently represents the best treatment with good results at mid- and long-term survival, according to an acceptable risk.

© 2008 Published by European Association for Cardio-Thoracic Surgery. All rights reserved.

Keywords: Pulmonary carcinoid; Neuroendocrine; Diagnosis; Treatment

1. Introduction

Bronchial carcinoids are rare malignant neoplasms, accounting for 2–5% of all lung tumors, with an approximate annual incidence of 2.3–2.8 cases per million of the population [1]. The classification in use (WHO 1999) makes a distinction between typical (TC) and atypical carcinoids (AC): although this separation was noted first by Engelbreth-Holm in 1944, the distinguishing criteria for separating these tumors were proposed only after thirteen years [2].

In 1998, Travis et al. modified this diagnostic criteria, dictating the bases for the Travis–WHO classification (1999): a typical carcinoid is based upon four elements: a morphological base, a number of mitoses <2 per 10 high power fields (HPFs), absence of necrosis, dimension ≤ 0.5 cm [3]; an atypical carcinoid has the following morphological characteristics: carcinoid morphology with a number of mitoses ≥ 2 and <10 per 10 HPFs, and areas of coagulative necrosis [2, 4].

In 10–15% of cases the tumor can present with regional lymphonal metastases, and that is why they may be classified as malignant neoplasms, even if with a low degree [4].

Distant metastases occur in 15% of cases, and are typically located in the liver, bone, adrenal gland and brain [5]. At

present, surgery is the gold standard for treatment of this tumor, with a different approach between typical carcinoids, in which a parenchyma-sparing resection is preferred, and atypical carcinoids, in which a limited resection should be obviated [2].

2. Materials and methods

We relate our experience of 54 patients affected by bronchial carcinoids, who came to our observation and underwent surgery at the Operative Unit of Thoracic Surgery of S. Orsola – Malpighi Hospital in Bologna between July 1986 and April 2006.

Survival rates are defined as the interval between the date of surgery and the date of death or the date of the last follow-up examination for the 'censored' cases.

Survival was estimated according to the Kaplan–Meier method and compared by the log-rank test. A two-sided $P < 0.05$ was considered statistically significant.

2.1. Epidemiology

The 54 patients consisted of 21 males (39%) and 33 females (61%), with a M/F ratio = 1:1.6, and aged 53 ± 15 years.

Females were aged 52 ± 15 years, whereas males presented an age of 54 ± 14 years.

One patient had a brother who died of a pulmonary tumor.

*Corresponding author. Tel.: +39 051 6363580; fax: +39 051 307022.

E-mail address: fab_78_16l@hotmail.com (F. Davoli).

2.2. Smoking

Twenty-one patients were smokers or ex-smokers (39%), 17 out of 45 (38%) with typical carcinoids, 5 out of 9 (44%) with atypical carcinoids; 33 (61%) were non-smokers.

2.3. Presenting symptoms

Twenty-one patients (39%) were asymptomatic at presentation. In the remaining cases, the symptoms of the presentation most frequently found were respiratory or thoracic: cough (43%) (productive or not), fever (26%), chest pain (19%), hemoptoe and/or hemoptysis (17%), dyspnea (15%) and pneumonitis (15%).

No patients showed a carcinoid syndrome.

2.4. Diagnostic path

Most of the carcinoid tumors appeared at the chest X-ray and chest CT as hilar or perihilar masses in 26 patients (48%), central pulmonary nodules in 14 (26%), peripheral nodules in 13 (24%), other radiological finding were: atelectasis in 17 (31%), air trapping in 3 (6%) and in three patients the chest X-rays were negative.

All the 54 patients in our case study were submitted to preoperative fibrobronchoscopy (FBS): with a preoperative diagnosis of carcinoid tumor in 28 patients (52%).

The neoplasm was detected intrabronchially in 19 patients and the histological examination was positive in 18 patients (94.7%); since in the remaining 35 cases the fibrobronchoscopy revealed no macroscopic obstruction, diagnosis was obtained by transbronchial biopsy in eight patients and by fine needle aspiration or biopsy in two.

We experienced no massive hemorrhage or other major complications following endoscopic biopsy.

A scintigraphy with Octreo-Scan was performed in all patients: there were no cases found to be positive for metastases.

3. Results

3.1. Size

The tumoral mass had a mean size of 2.4 ± 1.5 cm. The lesions ranged in size from 0.6 to 6 cm.

The carcinoid tumors were ≤ 3 cm in 38 cases (70%) and 3 cm in 16 cases (30%).

The mean dimension of the typical carcinoids was 2.1 ± 1.2 cm, that of atypical carcinoids 3.6 ± 2.1 cm.

The size of the pT1 carcinoid was 1.6 ± 0.6 cm (minimum value 0.6 cm), while in the pT2 cases it was 3.5 ± 1.6 cm (minimum value 1.3 cm).

In the 3 pN1 cases, the tumor size was 1, 2 and 2.8 cm, and in the pN2 case the tumor size was 6 cm. In this last case, the greater mass and the distant lymphonodal involvement can be explained with a long period of growth of the neoplasm.

3.2. Histological features

Of the 54 patients treated, 45 had a typical carcinoid (83%) and 9 (17%) an atypical carcinoid.

Typical carcinoids were present in 19 males (42%) and 26 females (58%) with a M/F ratio 1:1.4, at an age of 52 ± 14 years (median 56, range 23–81); atypical carcinoids were found in 2 males (22%) and 7 females (78%), at an age of 57 ± 16 years, with a M/F ratio 1:3.5.

In six cases (11%) we found tumorlets in the parenchyma near the neoplastic mass, and in four cases (7%) calcifications or foci featured by osteo-cartilage metaplasia.

3.3. Location

The tumor was central in 37 cases (69%) and peripheral in the remaining 17 (31%).

The location in relation with the histological features showed that 31 of the central tumors (37) were typical (84%) and six atypical (16%), 14 of the peripheral tumors were typical (82%) and three atypical (18%). Inversely, the typical carcinoid (45) was central in 69% of patients (31), peripheral in 31% (14); if atypical (9), the percentages were respectively 67% (6) and 33% (3). The neoplasm was more often located in the right lung (67%), and the most frequent site was the inferior lobe (30%). The carcinoids were located in the main bronchus (5 cases), in the lobar bronchus (16 cases) and in the segmental bronchus (5 cases).

3.4. Surgical treatment

Surgery was performed in all 54 patients consisting of: 31 standard lobectomies, 6 pneumonectomies, 5 bilobectomies, 2 sleeve lobectomies, 2 anatomic segmentectomies, 6 wedge resections; two patients were managed with sleeve bronchial procedure of the left main bronchus without lung resection.

So, the most frequently performed surgery was lobectomy (33 cases, 61%), which was combined with a bronchoplastic procedure in two patients (2 sleeve lobectomies). Eight patients (15%) underwent conservative resections: two anatomic segmentectomies, six wedge resections (Table 1).

There were no postoperative deaths or significant complications.

The postoperative duration of hospital stay was 8 ± 6 days.

3.5. pTNM staging

In 51 patients the tumor involved only the pulmonary tissue, in two cases we also found an extension to the

Table 1
Type of surgery in relation of location of the tumor

Surgery	No. (%)	Typ	Atyp	Centr	Periph
Pneumonectomies	6 (11)	4	2	6	
Lobectomies	30 (56)	25	5	21	9
Bilobectomies	5 (9)	5		5	
Conservative lung resections					
Segmentectomies	2 (4)	2			2
Wedge resections	6 (11)	6		1	5
Sleeve resection	2 (4)	1	1	2	
Sleeve lobectomy	2 (4)	2		2	
Lobectomy + wedge	1 (2)		1		1

Typ, typical carcinoids; Atyp, atypical carcinoids; Centr, central lesions; Periph, peripheral lesions.

visceral pleura, and in another case an additional involvement of the pericardium.

pTNM staging was: 32 pT1 (59%), 19 pT2 (35%), 2 pT3 (4%) and only one pT4 (2%).

The typical carcinoids were divided as follows: 29 pT1 (64%), 14 pT2 (31%), 1 pT3 (2%), 1 pT4 (2%); the atypical: 3 pT1 (33%), 5 pT2 (56%), 1 pT3 (11%).

Involvement of the lymph nodes was present in four cases (7%): 2 typical central, 2 atypical: 3 pN1 cases (5%) and 1 pN2 case (2%) (typical central). No patients had N3 disease.

The postoperative TNM stage was [T1N0] (29 cases, 54%, 28 typical), [T2N0] (19 cases, 35%, 14 typical), [T1N1] (3 cases, 6%, 1 typical), [T2N1] (2 cases, 4%, 1 typical), [T4N2Mx] (1 case, 2%, typical).

3.6. Survivals

Our follow-up ended on 30 August 2006.

Fifty-four patients were followed for a total of 3549 months with a mean observation time of 67 months. Only for 21 patients was it possible to analyze a complete 10-year follow-up; 6 (11%) deaths occurred, at a mean period of 49 months after surgery: they all showed evidence of recurrence of disease.

There were no deaths in the immediate postoperative period or during hospital stay.

The overall (TC+AC) 5-year survival was 91%, while the 10-year survival was 83% (Fig. 1): for typical carcinoids at 5 years it was 91% vs. 88% for atypical ones; at 10 years 91% for TC and 44% for AC (significant value, $P=0.0487$) (Fig. 2). The five-year survival of central and peripheral tumors was respectively 92% vs. 86%, 10-year survival was 86% vs. 73% (not significant value, $P=0.2616$).

The survival at five years of the subjects with T1 and T2 carcinoids was respectively 92% and 100%, at 10 years 92% and 83%. We would point out here the worse behavior of T3 with respect to T2 and T1.

The 5-year survival rate for stages 1A and 1B was respectively 92% and 100%, at 10 years it decreased to 92% and 83%. As before, we point out the worse behavior of stage 2B with respect to 1A, 1B and 2A. The information about T3 and T4 carcinoids and about stages 2A and 2B is difficult to interpret because the representative sample is too small.

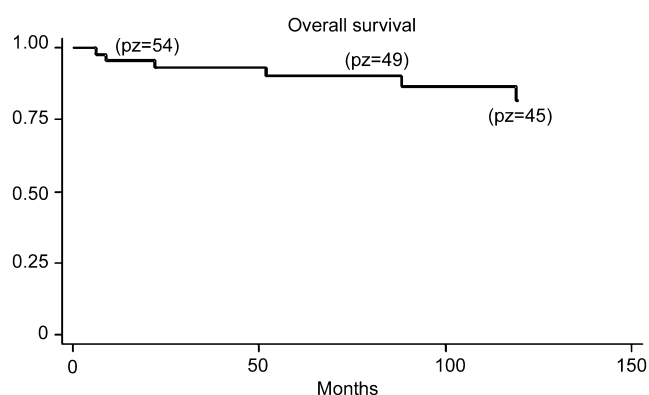


Fig. 1. Overall survival curves.

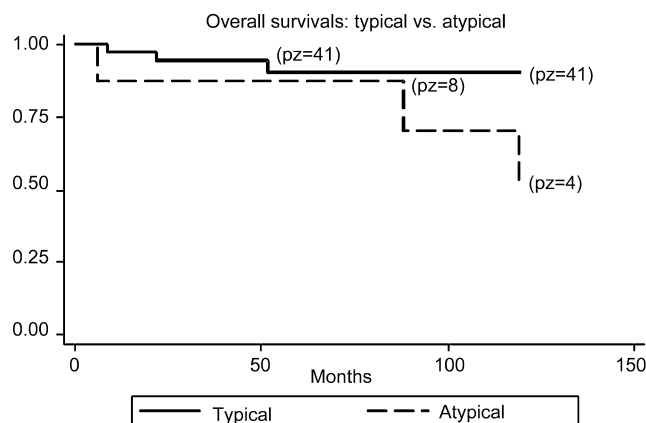


Fig. 2. Survival curve according to typical vs. atypical carcinoids.

There were no deaths among the 4 N+ patients: they are currently in the 63rd, 51st, 5th and 4th month of follow-up.

With respect to the type of surgery, wedge resection had a five-year survival of 100%, lobectomy 96%, other parenchyma-sparing surgery 80%, pneumonectomy 54%. At 10 years, these procedures presented the following values respectively: 100%, 89%, 80%, 27% (Fig. 3).

4. Discussion

In our case study of 54 patients, bronchial carcinoids presented essentially between the age of 40 and 60 years (on average 53 years), proving to be distributed throughout the lifetime, affecting the female sex more frequently (ratio M/F=1:1.57), it has no correlation with heritage or with smoking habits.

Before the operation, an accurate diagnosis is not always possible (our preoperative diagnosis was possible in 52% of cases), since carcinoid tumors have no clinical specificity. In fact, in almost half of the patients we found no symptoms (39%), and diagnosis was therefore accidental.

The presentation symptoms most frequently seen are cough (with or without expectorate), thoracic pain, hemoptoe or hemoptysis, dyspnea and pneumonitis. The carcinoid syndrome was not present in our case study.

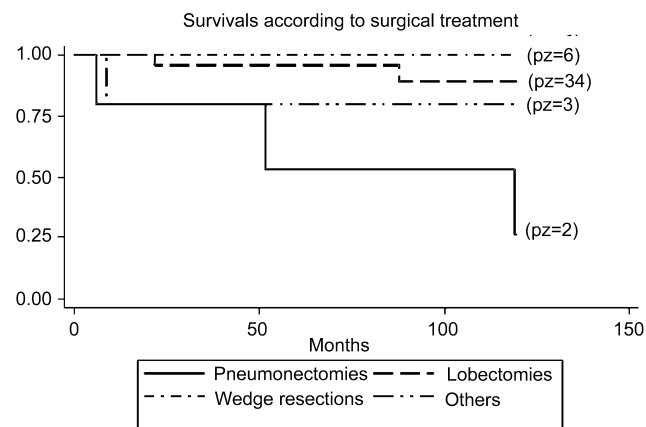


Fig. 3. Survival curve according to the surgical treatment.

We found typical carcinoids to be more frequent than atypical (83% vs. 17%), its onset to be five years earlier (average age 52 years vs. 57 years) and it seemed less connected with smoking (38% of the patients with typical carcinoids were smokers, 44% of those with atypical carcinoids were smokers); we found also that carcinoids are more likely to have a central (69%) than a peripheral location (31%), and in these last cases they occur on average nine years later than the first (59 years vs. 50 years).

In 11% of patients we found tumorlets in the pulmonary parenchyma attached to the main tumor.

In 7% of cases, the histological examination revealed multiple foci of calcification.

Hematogenous metastases, most likely osseous (deepening in progress), were present in only one case.

Lobectomy with or without sleeve resection of the bronchus is still the standard procedure, as in our patient group, especially for atypical carcinoids and for central typical ones. According to that, the surgical treatment performed most frequently is lobectomy (56%), followed by pneumonectomy (11%), wedge resection (11%) and bilobectomy (9%). Segmentectomy or wedge parenchymal resections were all made in relation to poor planned resection volume tolerable by the patients, that did not allow even the lobectomy.

From the analysis of the Kaplan–Meier survival curve, it appears that the 5-year survival is 91% and the 10-year

survival 83%. At five years, typical carcinoids present a better survival percentage than atypical ones, 91% vs. 88%; in the same way, at 10 years survival is 91% vs. 44% (significant value, with $P < 0.05$).

Carcinoid tumors are a distinct group of neuroendocrine tumors with a good prognosis in most cases. Octreotide is an interesting tool for diagnosis and management but surgery, however, remains the best treatment. The role of radiotherapy and chemotherapy is still debated.

Both typical and atypical carcinoids, in our opinion, require an aggressive therapeutic approach like a primary lung cancer; prognosis is good for typical, although it is worse for atypical ones.

References

- [1] Cardillo G, Sera F, Di Martino M, Graziano P, Giunti R, Carbone L, Facciolo F, Martelli M. Bronchial carcinoid tumors: nodal status and long-term survival after resection. *Ann Thorac Surg* 2004;77:1781–1785.
- [2] Mezzetti M, Raveglia F, Panigalli T, Giuliani L, Lo Giudice F, Meda S, Conforti S. Assessment of outcomes in typical and atypical carcinoids according to latest WHO classification. *Ann Thorac Surg* 2003;76:1838–1842.
- [3] Thomas CF Jr, Tazelaar HD, Jett JR. Typical and atypical pulmonary carcinoids: outcome in patients presenting with regional lymph node involvement. *Chest* 2001;119:1143–1150.
- [4] Hage R, Brutel de la Rivière A, Seldenrijk CA, van der Bosch JMM. Update in pulmonary carcinoid tumors: a review article. *Ann Surg Oncol* 2003;10:697–704.
- [5] Jeung MY, Gasser B, Gangi A, Charneau D, Ducroq X, Kessler R, Quoix E, Roy C. Bronchial carcinoid tumors of the thorax: spectrum of radiologic findings. *RadioGraphics* 2002;22:351–365.

Typical and atypical pulmonary carcinoids: our institutional experience
Alessandro Bini, Jury Brandolini, Nicola Cassanelli, Fabio Davoli, Giampiero Dolci,
Francesco Sellitri and Franco Stella
Interact CardioVasc Thorac Surg 2008;7:415-418; originally published online Mar 18,
2008;
DOI: 10.1510/icvts.2007.173328

This information is current as of December 27, 2011

Updated Information & Services	including high-resolution figures, can be found at: http://icvts.ctsnetjournals.org/cgi/content/full/7/3/415
References	This article cites 5 articles, 3 of which you can access for free at: http://icvts.ctsnetjournals.org/cgi/content/full/7/3/415#BIBL
Citations	This article has been cited by 3 HighWire-hosted articles: http://icvts.ctsnetjournals.org/cgi/content/full/7/3/415#otherarticles
Permissions & Licensing	Requests to reproducing this article in parts (figures, tables) or in its entirety should be submitted to: icvts@ejcts.ch
Reprints	For information about ordering reprints, please email: icvts@ejcts.ch

Interactive CardioVascular and Thoracic Surgery