

Surgical management of bronchial carcinoid tumors: 11-year experience

Bronşiyal karsinoid tümörlerde cerrahi tedavi: 11 yıllık deneyim

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Background: This study aims to present surgical treatment, postoperative complications, and long-term outcomes in patients with a bronchial carcinoid tumor.

Methods: Between January 2000 and December 2010, 57 patients (34 females, 23 males; mean age 43 years; range 13 to 83 years) underwent pulmonary resection for pre- and postoperatively pathologically confirmed bronchial carcinoid tumors. Type of surgery, histopathological types of carcinoid tumor, postoperative complications, and long-term results were evaluated.

Results: Pathological examination revealed 44 (77%) typical and 13 (23%) atypical carcinoid tumors. Bronchial sleeve resection, pneumonectomy, lobectomy and sublobar resection were performed on 23 (40.3%), three (5.2%), 27 (47.3%) and four patients (7%), respectively. Eight patients (14%) had postoperative complications. There was no perioperative mortality. During the follow-up period, no mortality or local recurrence occurred.

Conclusion: During long-term follow-up period, parenchyma-sparing resections (sleeve lobectomy and bronchial sleeve resection) can achieve good prognosis in patients with typical carcinoid tumor if tumor free surgical margins can be obtained.

Keywords: Bronchial carcinoid tumor; long-term result; paranchyma sparing resection.

Amaç: Bu çalışmada, bronşiyal karsinoid tümürlü hastalarda cerrahi tedavi, ameliyat sonrası komplikasyonlar ve uzun dönem sonuçlar sunuldu.

Çalışma planı: Ocak 2000 - Aralık 2010 tarihleri arasında ameliyat öncesi ve sonrası patolojik olarak bronşiyal karsinoid tümör olduğu doğrulanmış 57 hastaya (34 kadın, 23 erkek; ort. yaş 43 yıl; dağılım 13-83 yıl) akciğer rezeksiyonu uygulandı. Cerrahi tipi, karsinoid tümörün histopatolojik tipi, ameliyat sonrası komplikasyonlar ve uzun dönem sonuçlar değerlendirildi.

Bulgular: Patolojik muayenede 44 (%77) tipik, 13 (%23) atipik karsinoid tümör saptandı. Hastaların 23'üne (%40.3) bronşiyal sleeve reseksiyon, üçüne (%5.2) pnömonektomi, 27'sine (%47.3) lobektomi, dördüne (%7) sublobar rezeksiyon uygulandı. Sekiz hastada (%14) ameliyat sonrası komplikasyon gözlemedi. Ameliyat sonrası mortalite gözlemedi. Takip döneminde hiçbir hastada ölüm ve lokal nüks olmadı.

Sonuç: Parenkim koruyucu rezeksiyonlar (sleeve lobektomi ve sleeve bronşiyal rezeksiyon), tipik karsinoid tümürlü hastalarda, negatif cerrahi sınır elde etmek koşulu ile uzun dönem takip sürecinde iyi prognoz sağlayabilir.

Anahtar sözcükler: Bronşiyal karsinoid tümör; uzun dönem sonuç; parenkim koruyucu rezeksiyon.



Bronchial carcinoid tumors are neoplasms originating in the neuroendocrine system that account for approximately 25-30% of these types of tumors.^[1] They are characterized by slow, primarily endobronchial growth, and most are centrally located in the main or lobar bronchus.^[2] Bronchial carcinoid tumors can be either typical or atypical depending on their histological and clinical features. Atypical carcinoids tend to have less predictable biological behavior and are associated with a poorer prognosis than those that are typical.^[3] In addition, atypical carcinoid tumors present with regional lymph node metastases in 10-15% of cases while 15% of these patients have distant metastases of the liver, bone, adrenal gland, or brain,^[4] with surgery being the gold standard for treatment.^[5] Bronchial carcinoids are rarely presented as multiple lesions, but there are a few examples of this in the literature.^[6] Furthermore, only a few case reports exist that describe both synchronous and metachronous multiple carcinoids.^[6] The aim of our study was to review our patients with bronchial carcinoid tumors who underwent surgery and evaluate the long-term results of paranchyme-sparing resections.

PATIENTS AND METHODS

Between January 2000 and December 2010, 57 patients (34 females and 23 males; mean age 43 years; range 13 to 83) who had a pre- or postoperative pathologically confirmed carcinoid tumor were retrospectively analyzed. All patients were evaluated based on their patient history, physical examinations, chest and upper abdomen (including the liver and adrenal glands) computed tomography (CT), and positron emission tomography (PET)/CT. In addition, we also examined the results of four patients who underwent octreotid scintigraphy, whole body bone scintigraphy which was carried out on one patient, and one patient who underwent pulmonary perfusion scintigraphy. Spirometry tests were routinely carried out on all of the patients, and preoperative fiberoptic bronchoscopy (FOB) was also performed. The presence of a carcinoid tumor was confirmed in 42 patients via either a bronchoscopic or CT-guided transthoracic needle biopsy while a definitive diagnosis was achieved via frozen section (FS) examination in 15 others (26%).

We performed various types of thoracotomies on these patients based on the localization of the tumor and we planned pulmonary resection under single-lung anesthesia. We also performed either an anatomic or non-anatomic complete resection while preserving most of the functioning lung tissue. During the operation, undiagnosed tumors were confirmed via FS examinations. For centrally located lesions, the FS

examination of the cut edges was performed routinely, with the hope of finding a tumor-free margin of at least 5 mm. In addition, systematic mediastinal and hilar lymph node sampling was done, and mediastinal lymph node dissection was carried out if lymph node metastases was confirmed via FS after sampling. The specimens were pathologically examined and then classified as either a typical or atypical carcinoid after the surgery.

The patients' data were retrospectively analyzed in terms of age, gender, histological type, surgical procedure, duration of hospital stay, postoperative complications, adjuvant therapy, and nodal status. During the follow-up period, this data was prospectively recorded in the database, and all of the patients were then contacted either in person or by telephone.

RESULTS

The type of resection that was performed on each patient is listed in Table 1. A histopathological diagnosis showed that 44 patients (77%) had a typical carcinoid tumor, whereas it was atypical in 13 others (23%). The postoperative pathological nodal status is detailed in Table 2.

No operative or postoperative mortality was noted. Eight patients (14%) had postoperative complications, with chylothoraces in two and wound infection in two others. Additionally, prolonged air leak (PAL), microbronchial fistula, pleural effusion, and total atelectasis were seen in one patient each. The median hospital stay was 10 days (range 1-20), and the median follow-up period was 50 months (range 1-120). Fifty-five of the patients were still alive at that time, but we could not reach two of them by telephone or mail to determine their status. One patient with an atypical carcinoid tumor and hilar nodal metastases had liver metastases one year after the operation, but

Table 1. Type of resections

| Type of resection | n |
|---------------------------------|----|
| Parenchyma-sparing resection | 23 |
| Sleeve lobectomy | 14 |
| Bronchial sleeve resection | 9 |
| Conventional anatomic resection | 32 |
| Lobectomy | 23 |
| Thoracoscopic lobectomy | 4 |
| Open surgery | 19 |
| Bilobectomy | 4 |
| Pneumonectomy | 2 |
| Completion pneumonectomy | 1 |
| Segmentectomy | 2 |
| Wedge resection | 2 |

Table 2. Distribution of nodal status and histopathological type

| Nodal status | Typical carcinoid | | Atypical carcinoid | | Overall | |
|----------------|-------------------|----|--------------------|----|---------|----|
| | n | % | n | % | n | % |
| N ₀ | 41 | 93 | 11 | 84 | 52 | 91 |
| N ₁ | 3 | 7 | 2 | 15 | 5 | 9 |
| N ₂ | 0 | 0 | 0 | 0 | 0 | 0 |

the remainder had no distant organ metastases or local recurrences. Furthermore, seven of the 13 patients with an atypical carcinoid tumor underwent oncological therapy, with four receiving chemotherapy and three chemoradiotherapy.

DISCUSSION

Even though carcinoid tumors have structural, morphological, and immunohistochemical features similar to large cell neuroendocrine tumors and small cell carcinomas, the biological characteristics of carcinoid tumors vary considerably.^[7] Studies also indicate a relatively good prognosis for these tumors following surgery compared with the prognosis for other non-small-cell lung carcinomas (NSCLCs), even when a tissue-sparing resection was performed.^[8]

While studies have determined that bronchial carcinoids affect both genders equally,^[4] there are large series that have demonstrated a female preponderance for typical carcinoids.^[9] On the other hand, Marty-Ané et al.^[10] noted that there is a male predominance for atypical carcinoids. In our study, the female-to-male ratio was about 1.5:1, and there was a female predominance. We had 26 female (59%) and 18 male (41%) patients with typical carcinoids, whereas there were eight females (61%) and five males (39%) with atypical carcinoids. These findings differed from other reports in the literature.^[5,10]

Various studies found that the median age ranged between 46 and 52 years old,^[8,9,11,12] and patients with bronchial carcinoids are on average 10 years younger than those with other malignant pulmonary tumors.^[13] In our study, the median age was 45 years old, which fell within the normal range. In addition, the mean ages of the typical and atypical carcinoid cases were approximately equal. Detterbeck^[14] noted that in younger patients, more than 90% of carcinoids are typical carcinoids, whereas for patients over 50 years of age, 20-25% are atypical.

In our study, 44 patients (77%) had typical carcinoid tumors, and three of these (7%) had a nodal

invasion. In addition, 13 (23%) had atypical carcinoid tumors, and only two (15%) had a nodal invasion. The patient with liver metastasis was included in the atypical carcinoid group. That same patient also had Cushing syndrome and was treated with somatostatin. This was not unexpected and was the result of a poor prognosis and the aggressive nature of atypical carcinoid tumors.^[3,4] Furthermore, two cases were misdiagnosed with NSCLC preoperatively, but they were subsequently diagnosed as having carcinoids postoperatively (one typical and one atypical).

Four patients underwent octreotide scintigraphy in our study. It was performed on two patients with Cushing's syndrome to detect whether there was an ectopic neuroendocrine focus, one to determine whether there was a local recurrence, and another patient suspected of having renal metastasis to check whether there was a metastatic focus. Octreotide imaging is relatively costly and should not be routinely used for bronchopulmonary carcinoids since approximately 33% of bronchial carcinoids test negative for somatostatin receptors and the rest typically exhibit weak intensity that is difficult to differentiate from inflammation. Furthermore, octreotide imaging is positive in nearly all patients with NSCLC, small cell lung cancer (SCLC), pneumonia, sarcoidosis, granuloma, or lymphoma.^[15]

We preferred parenchyma-sparing resections (14 sleeve resections and nine bronchial sleeve resections) for 23 patients (40%) because they had a typical carcinoid tumor and a proximal tumor, and no local or distant recurrence was seen in the patients who underwent this type of resection. However, one of these patients had to undergo a completion pneumonectomy due to total atelectasis. The latest publications have noted that it is suitable to perform parenchyma-sparing resections for proximal and typical carcinoid tumors.^[5,16] For example, Machuca et al.^[11] expressed that the modern management of bronchial carcinoids should consist of parenchyma-sparing procedures whenever feasible, and Ferguson et al.^[17] concluded that limited resections, such as wedge resections or segmentectomies for peripheral tumors and isolated bronchial sleeve resections or sleeve lobectomies for proximal tumors, should be considered whenever possible for early-stage typical carcinoid tumors because local recurrence is unlikely and the chance of survival is excellent. On the other hand, two of our patients who underwent wedge resections had a peripheral typical carcinoid tumor without lymph node invasion.

The median hospital stay for our patients was 10 days, which was longer than estimated. Prolonged hospital stays can result from postoperative complications. For example, one patient had microbronchial fistula and was in the hospital for 23 days while another with chylous leakage was there for 32 days. Eight of our patients (14%) had complications, five of which had typical carcinoid tumors and three atypical carcinoid tumors.

The long-term results vary in the literature. Todd et al.,^[18] reported a five-year survival rate of only 65% in a study conducted on 65 patients with carcinoid tumors, whereas Stamatis et al.,^[19] reported a survival rate of 98% over the same period of time for 210 patients with typical carcinoids. Furthermore, Aydın et al.^[20] noted that the five-year overall survival rate was 92% for typical carcinoid tumors and 73% for atypical carcinoid tumors. Some studies have also concluded that the patient's histology is the major prognostic factor in pulmonary carcinoid tumors.^[19,20] The median follow-up period was 50 months (range 1-120) in our study, but the absence of death in our series made it impossible to determine a survival rate. Hence, we could not compare the typical and atypical group with respect to survival rate and prognosis. In our study, we also detected no cases of recurrence in the typical and atypical groups.

No patients have undergone endobronchial therapy at our institution, but two patients with typical carcinoid tumors underwent this type of therapy from a pulmonologist at a different facility preoperatively, with one having a bronchoscopic resection and the other undergoing laser therapy. In prospective studies, complete resection is achieved in about 50% of selected patients. Recurrence occurs in 5% of these cases (median follow-up of eight years), and these are then subsequently resected. Brokx et al.^[21] even determined that the rate of recurrence might be higher with atypical carcinoid tumors. In comparison, Kurul et al.^[22] found that no recurrences occurred after patients underwent either a thoracotomy, bronchotomy, or resection of endobronchial polypoid tumors. Selecting patients for endobronchial removal is important because only 5-10% contain polyp-like endobronchial structures that don't extend through the cartilaginous wall.^[21] Therefore, advanced endobronchial skills are essential when performing this procedure, and prospectively planned, careful, frequent follow-up is necessary. Under these conditions, endobronchial removal may be a reasonable option.^[14]

Adjuvant therapy was administered in seven of our patients (12%) who had high-grade atypical carcinoid

tumors, with four receiving chemotherapy and three chemotherapy plus radiotherapy. Unfortunately, we had limited information regarding these therapies that were administered to these patients because they were managed by oncologists.

As previously reported by Davila et al.,^[23] regional nodal involvement in typical carcinoid tumors is low with a range of between 3 and 20%, and our findings (7%) were within this range. However, nodal metastasis in atypical carcinoids ranges from 48-75% in the literature,^[23,24] which differs significantly from our results (15%).

Conclusion

Although we could not provide survival rates for our patients since none died, our patients with typical and atypical carcinoids had a good prognosis. We also determined that an early diagnosis of carcinoid tumors is usually possible, and our results indicate that sleeve resection is a good choice for proximally located typical carcinoids since they do not lead to local recurrence.

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