Pulmonary Resection of Metastatic Renal Cell Carcinoma*

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Over a ten-year period, 44 patients with known primary renal cell cancer underwent thoracotomy for pulmonary metastases. The median postthoracotomy survival for all patients was 33 months. The five-year survival was 27 percent. Postthoracotomy survival was significantly better in those patients with a disease free interval of >24 months and patients with metastatic lesions ≥ 3 cm. No difference in survival was detected in patients with one versus more than one lesion or in patients undergoing complete resection versus incomplete resection or biopsy only. Age, sex, grade of tumor, or location of the pulmonary metastasis had no influence on survival.

Renal cancers account for 2 to 3 percent of all malignancies and 85 percent of these are due to renal cell carcinoma (RCC) (hypernephroma). The RCC is spread by direct extension and through lymphatics and hematogenous routes. Approximately one-third of all patients with RCC have distant metastasis at the time of diagnosis. Solitary metastasis has been reported to occur in 2 to 4 percent of patients at the time of initial diagnosis or relapse. Barney and Churchill* reported the first long-term survival (greater than 20 years) of metastatic disease treated with surgery in a patient who underwent pulmonary resection for a metastatic RCC. This observation, along with the absence of a satisfactory chemotherapeutic alternative, has induced physicians to treat patients with pulmonary metastasis from RCC with thoracotomy and resection in an effort to improve survival. Herein is reported a ten-year experience of patients with metastatic RCC to the lung(s) who underwent thoracotomy after the diagnosis of their primary cancer.

Patients and Methods

The records of all patients with pulmonary metastases from RCC who underwent a thoracotomy from January 1970 through December 1979 were reviewed. In all cases, the metastatic disease was believed to be confined to the chest before thoracotomy. To be eligible for study, all patients underwent a thoracotomy on the same day or subsequent to the diagnosis of primary RCC. Each patient had a potentially curable nephrectomy. In all cases, histologic documentation of metastatic RCC was obtained at the time of thoracotomy. Three patients had two thoracotomies and one patient had three thoracotomies for metastatic RCC. Patients were evaluated for age, sex, grade of cancer, interval between diagnosis of primary RCC and thoracotomy (disease free interval), number of pulmonary metastases at thoracotomy, location of pulmonary metastases (right, left, or both lungs), size of the largest pulmonary metastasis resected, and postthoracotomy survival. Patients undergoing thoracotomy were classified as having (1) total resection of metastatic lesion(s), (2) incomplete resection of metastatic lesion(s) (tumor reduction), or (3) biopsy only.

Many patients were asymptomatic (27) prior to their thoracotomy and the nodule(s) was detected by routine chest x-ray examination. Seven patients presented to their physician with cough and six others had hemoptysis. The diagnostic evaluation prior to thoracotomy varied, but in most cases, the nodule(s) was further evaluated with either standard tomograms (14), whole lung tomograms (10), or computerized axial tomograms (11). Prior to thoracotomy, many patients had other diagnostic tests to rule out metastasis such as excretory urograms, metastatic bone survey, and bone scan.

Sixteen patients had a solitary pulmonary metastasis. Sixteen additional patients had two to five pulmonary metastases, and 12 patients had more than five metastatic pulmonary lesions. Thirty-two patients had a wedge excision, nine underwent lobectomies, two had bilobectomies, and one had a pneumonectomy. Thirty-one patients were believed to have had total resection of metastatic disease at the time of thoracotomy. The reason for the unresectability varied, but in seven cases was due to diffuse pleural metastases that were not detected by the preoperative evaluation. In the other cases, the number of lesions or the location of the lesion prevented total resection. There was one operative death. This patient died 30 days postthoracotomy and had diffuse pleural metastases at thoracotomy that were unresectable.

Due to the referral nature of our practice, many of the patients were followed-up at home by their personal physicians after their nephrectomy until the discovery of the pulmonary metastasis. Those followed-up at Mayo had yearly examinations and chest roentgenograms. After the thoracotomy, ten patients were followed-up by their personal physician. The other patients had followup chest x-ray films and examinations at three to six months (19 patients) or yearly intervals (13) as necessary. The median postthoracotomy follow-up for all patients was 28 months.

Kaplan-Meier estimated survival curves were computed using the Statistical Analysis System (SAS) procedure SUBVFT. The statistical significance of the association of various patient characteristics with survival was assessed via the Cox regression approach using the COXREG procedure in SAS.

Results

Forty-four patients met the criteria for inclusion in the study: 27 males and 17 females. The patients' ages
The median postthoracotomy survival for all 44 patients was 33 months with a maximum of 133 months. The five-year survival was 27 percent (Fig 1).

A Cox covariate analysis of survival indicated that the disease-free interval and the size of the largest nodule resected, together and singly, were significantly associated with postthoracotomy survival (p < .05). The median disease-free interval was 3.6 years. Five patients had a disease-free interval of greater than ten years with 20.5 years being the maximum interval. Figure 2 compares the survival curves for those patients with disease-free intervals of greater than 24 months with those having intervals ≤24 months. The median survival for those 14 patients with a disease-free interval of ≤24 months was 18 months with only four surviving longer than two years. Thirty patients with a disease-free interval of greater than 24 months had a median survival of 41 months. Twenty-two of these 30 survived longer than two years.

Postthoracotomy survival was greater in those patients having larger metastatic lesions resected. Figure 3 shows survival for those patients with nodules ≥3 cm (median size was 4.0 cm) compared to those with nodules <3 cm (median size was 1.5 cm). Significant differences in survival were not detected between subgroups of patients with lesions less than 3 cm. In five of the 44 patients, the size of the largest resected pulmonary lesion could not be accurately determined. In three of these five patients, there was unresectable disease due to diffuse pleural metastasis at the time of thoracotomy and only a biopsy was performed to document the metastatic disease. The association of survival with the size of the resected metastatic lesion may be overly influenced by those 11 patients with lesions ≥3 cm.

Survival was not significantly associated with age, sex, grade of tumor, or location of pulmonary metastases. Figure 4 shows survival for those patients...
undergoing thoracotomy with a solitary metastasis versus those with more than one metastasis. There was no significant difference detected in the survival for these two groups. Likewise, there was no difference in survival observed in those patients undergoing total resection of metastatic disease versus those undergoing debulking or biopsy procedures only (Fig 5).

DISCUSSION

In the absence of effective chemotherapy, surgery is an acceptable therapeutic alternative for limited metastatic disease. Five-year survivals for resection of isolated pulmonary metastases average 30 percent. Many of the previously reported series have included patients with a variety of primary malignancies including carcinomas and sarcomas metastatic to the lung. In this report, all patients had primary RCC with histologically-documented pulmonary metastases at thoracotomy. The five-year postthoracotomy survival of 27 percent was similar to other reports. The disease-free interval was positively correlated with post-thoracotomy survival as previously reported by others (Fig 2).

Previous reports have suggested that smaller metastases are associated with better survival in patients treated with pulmonary resection. Katzenstein et al reported a better survival with extensive tumor necrosis in the metastases but noted that gross size of the lung metastasis did not correlate with survival. Our findings differ from previous reports. In 11 patients with metastasis ≥3 cm, the postthoracotomy survival was substantially better than survival for lesions <3 cm (Fig 3). While it is possible that our results essentially reflect the influence of patients with metastases ≥3 cm (n = 11), it is also possible that cellular diversity of some RCC are responsible for their forming large lesions before further metastasizing. Future reports, with larger numbers of patients, on the association of postthoracotomy survival with the size of the pulmonary metastases in RCC are needed to clarify this point.

Sixteen patients had a solitary pulmonary metastasis that was totally resected at thoracotomy. These 16 patients did not have a significantly better survival than those patients with two or more metastatic lesions (Fig 4). Similarly, there was no difference in survival detected for patients undergoing total resection of all metastatic disease versus incomplete resection or biopsy only (Fig 5). There are conflicting reports in the literature with regard to survival and the number of lung lesions resected. Takita et al reported no difference in survival with solitary versus multiple metastases in their 25-year experience from Roswell Park Memorial Institute. Their report, however, includes a variety of sarcomas and carcinomas metastatic to the lungs. Similarly, of 112 patients with nonosteogenic sarcomas who underwent resection of pulmonary metastases, there was no difference in survival of patients with solitary versus multiple lesions. We are unaware of any previous reports with a large number of RCC patients where this type of analysis has been performed.

The fact that patients who underwent a thoracotomy with total resection of metastatic disease did not have a significantly better survival than those patients with incomplete resection or biopsy only, questions the validity of the role of “curative resection” for pulmonary...
nary metastases from RCC. The data in this study suggest that a curative resection of isolated pulmonary metastasis is unusual and may not improve survival versus that of observation only. The number of patients followed, however, may not have been sufficient to detect differences in survival which are of medical significance, or the differences may have been confounded with factors which the current study did not control for.

This study, like previous reports, suffers from being a retrospective study. The current accepted medical practice of resecting isolated pulmonary metastasis has evolved based on retrospective studies. Other reports have not provided survival data on a comparison group such as our patients who underwent a thoracotomy with incomplete resection. To definitively answer the question of the role of resecting isolated pulmonary metastasis, a prospective randomized study is needed with half of the patients undergoing “curative resection” and half having observation only. Due to strong prejudices in the medical community, it will be very difficult to carry out such a study in the near future.

Our current approach is to resect any solitary pulmonary lesion because of inability to differentiate metastasis from a new primary malignancy. The approach to patients with more than one pulmonary metastatic lesion from RCC varies depending on the attending physician’s previous experience and his/her interpretation of the medical literature.

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REFERENCES