



Factors related to improved clinical outcomes associated with adrenalectomy for metachronous adrenal metastases from solid primary carcinomas



Jae Won Cho, Yu-mi Lee, Tae-Yon Sung*, Jong Ho Yoon, Ki-Wook Chung, Suck Joon Hong

Department of Surgery, Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea

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ABSTRACT

Background: Surgery for metachronous adrenal metastases from solid primary carcinoma has increased with the development of technical skills. Here we analyzed the postoperative clinical outcomes of patients who underwent adrenalectomy for metachronous adrenal metastases from solid primary carcinomas.

Methods: Patients who underwent adrenalectomy for metachronous adrenal metastases after initial treatment of primary carcinoma at Asan Medical Center from 2000 to 2010 were included. Clinicopathological parameters were analyzed to evaluate prognostic outcomes.

Results: A total of 30 patients with 19 hepatocellular carcinomas and 11 lung carcinomas were included. The mean age was 54.3 years. The mean time until adrenalectomy was 23 months. The size of the metastatic adrenal tumor and the disease status of the primary carcinoma at the time of adrenalectomy were associated with second recurrence after adrenalectomy ($P < 0.05$). There was no significant difference in disease-specific recurrence-free survival between patients who underwent open adrenalectomy and laparoscopic adrenalectomy ($P = 0.646$).

Conclusions: Surgical treatment should be recommended for metachronous adrenal metastases in patients with no evidence of primary carcinoma and/or in those having metastatic adrenal tumors ≤ 4.4 cm. This approach may increase the recurrence-free interval related to second recurrence. Further, laparoscopic adrenalectomy appears sufficient for the treatment of such patients.

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1. Introduction

Adrenal metastases from solid primary carcinoma is relatively common with a prevalence of 10%–25% in all carcinoma patients [1]. With the development of imaging modalities, the incidental detection of adrenal gland lesions, either at the time of initial diagnosis or during follow-up, has increased [2,3]. Adrenal metastases commonly occurs in patients with lung or gastrointestinal carcinomas [4].

Distant metastasis from a carcinoma can be divided into synchronous and metachronous metastasis. Synchronous metastasis is typically associated with a poor prognosis because of the advanced

stage at the time of diagnosis and requires multiple further treatments. However, metachronous adrenal metastasis has been shown to have favorable outcomes in certain studies, with some supporting the resection of metastatic adrenal tumors with curative intent in selected patients when there is no evidence of other metastatic lesions [5–7].

In addition, the type of surgical approach used to manage adrenal metastasis may affect surgical outcomes. In the early days, open adrenalectomy (OA) was the only choice of surgical method. However, laparoscopic adrenalectomy (LA) has been performed in cases of malignant adrenal lesions with tolerable surgical outcomes since its development [4,8–10].

The aims of the present study were to analyze clinical outcomes after adrenalectomy for metachronous adrenal metastases, identify factors related to improved clinical outcomes, and support patients expected to benefit from adrenalectomy. In addition, we compared patient outcomes between OA and LA.

* Corresponding author. Department of Surgery, Asan Medical Center, University of Ulsan College of Medicine, 88 Olympic-ro 43-gil, Songpa-gu, Seoul 05505, South Korea.

E-mail address: tysung@amc.seoul.kr (T.-Y. Sung).

2. Material and methods

2.1. Study population

Patients with metachronous adrenal metastases from solid primary carcinomas treated with adrenalectomy in Asan Medical Center, Seoul, Korea from January 2000 to December 2010 were selected. The study protocol was approved by our institutional review board, and the requirement for informed consent from each patient was waived.

We included patients who presented metachronous adrenal metastases on imaging studies after initial treatment of primary carcinoma that was pathologically proven after adrenalectomy. During this period, 77 patients underwent adrenalectomy for metastases. After a review of medical records, patients with synchronous metastasis, multiple metastases, or missing medical records were excluded. Eight cases having either only 1 or 3 patients for each cancer type were excluded in this study because these patients' data was not sufficient enough to draw any meaningful results; 3 colorectal cancer, 2 sarcoma, 1 bladder cancer, 1 breast cancer and 1 renal cancer. Finally, 30 patients were included in the present study. At the last follow up, five patients are still alive. For further analysis, we divided all patients into two groups according to the presence of second recurrence after adrenalectomy: no second recurrence group and second recurrence group.

2.2. Follow-up protocols

All patients underwent postoperative imaging, including abdominopelvic computed tomography (CT), chest CT, magnetic resonance imaging (MRI), and/or positron emission tomography (PET) for evaluation. Adrenal metastasis was diagnosed by CT, MRI, and/or PET during the follow-up period and confirmed by histopathological reports after adrenalectomy. Routine follow-up examinations were conducted every 6–12 months according to the patient's clinical condition.

2.3. Prognostic outcomes

For each patient, clinical data, including age, sex, origin of primary carcinoma, date of initial treatment, date of adrenalectomy, site of adrenal metastasis, metastatic adrenal tumor size, type of adrenalectomy, disease-specific interval (DSI), disease-specific recurrence-free survival (RFS), and overall survival (OS), were analyzed. DSI was defined as the time interval between the date of initial primary carcinoma treatment and the date of adrenalectomy. Disease-specific RFS was defined as the time interval between the date of adrenalectomy and the date of second recurrence (locoregional area and/or distant metastasis) after adrenalectomy. OS was defined as the time interval between initial primary carcinoma treatment and the last follow-up date. Factors related to second recurrence after adrenalectomy were analyzed.

2.4. Statistics

Continuous variables are presented as mean \pm standard deviation with ranges, and categorical variables are presented as percentages and absolute numbers. Univariate and multivariate Cox proportional hazards modeling analyses were performed to identify risk factors for second recurrence. Hazard ratios (HRs) with 95% confidence intervals (CIs) were calculated. For clinical applicability, the area under the curve (AUC) was calculated using receiver operating characteristic (ROC) curve analysis in order to evaluate the cutoff value for continuous variables with significance. Scatter plots with Pearson's correlation were used to show the main trend between DSI and

disease-specific RFS. Survival outcomes were analyzed using the Kaplan–Meier method and log-rank tests. P values of <0.05 were considered statistically significant. Analyses were performed using SPSS version 20.0 for Windows (SPSS Inc., Chicago, USA).

3. Results

A total of 30 patients with metachronous adrenal metastasis from solid primary carcinoma were included. The mean age was 54.3 years. The male:female ratio was 26:4. Hepatocellular carcinoma was the major primary carcinoma ($n = 19$; 63.3%), followed by lung carcinoma (LC; $n = 11$; 36.7%). Eighteen patients underwent surgical resection of the primary carcinoma with curative intent, whereas 12 patients received treatments other than surgery (chemoradiation, 3; transarterial chemoembolization, 9). The mean metastatic adrenal tumor size was 5.0 cm. In total, 19 (63.3%) patients underwent OA and 11 (36.7%) underwent LA. In terms of disease status at the time of adrenalectomy, 18 (60%) patients had no evidence of disease (NED) and 12 (40%) had persistent disease related to the primary carcinoma. The mean DSI was 23.2 months. Second recurrence (either in the locoregional area or distant metastasis) after adrenalectomy occurred in 26 (86.7%) patients, with a disease-specific RFS of 23.4 months (Table 1).

Factors related to second recurrence after adrenalectomy were analyzed (Table 2). There was a significant difference in patient age between the no second recurrence and second recurrence groups, with younger age found to be associated with second recurrence ($P = 0.036$). There was no statistical difference in metastatic adrenal tumor size, site of adrenal metastasis, type of adrenalectomy, and disease status at the time of adrenalectomy between the two groups ($P > 0.05$). There was no significant difference in DSI ($P = 0.055$); however, the mean interval between initial treatment of primary carcinoma and adrenalectomy appeared to be longer in the no second recurrence group compared to the second recurrence group (DSI, 41.3 vs 20.5 months, respectively). In univariate analysis, the metastatic adrenal tumor size ($P = 0.018$) was found to be associated with second recurrence (HR, 1.270; 95% CI, 1.04–1.55). The ROC curve was calculated and the cutoff value of the metastatic adrenal tumor

Table 1

Clinical characteristics of patients who underwent adrenalectomy for metachronous adrenal metastases from other primary carcinomas after initial treatment.

Characteristics	n = 30	% (range)
Age (years)	54.3 \pm 11.14	(36–75)
Sex		
Male	26	86.7%
Female	4	13.3%
Types of primary carcinoma		
Hepatocellular carcinoma	19	63.3%
Pulmonary carcinoma	11	36.7%
Primary carcinoma treatment		
Surgery	18	60.0%
Other treatment	12	40.0%
Size of metastatic adrenal tumor (cm)	5.0 \pm 2.23	(1.5–9.2)
Site of adrenal metastasis		
Left	18	60.0%
Right	12	40.0%
Type of adrenalectomy		
Open adrenalectomy	19	63.3%
Laparoscopic adrenalectomy	11	36.7%
Status at the time of adrenalectomy		
No evidence of disease	18	60.0%
Persistent disease	12	40.0%
Disease-specific interval (months)	23.2 \pm 20.28	(5–99)
Second recurrence after adrenalectomy	26	86.7%
Disease-specific recurrence-free survival (months)	23.4 \pm 28.53	(1–132)
Overall survival (months)	65.5 \pm 47.49	(13–182)

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