



Long term outcome after resection of liver metastases from squamous cell carcinoma

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Accepted 1 September 2017

Available online ■ ■ ■

Abstract

Background: Squamous cell carcinoma (SCC) liver metastases still remains a difficult challenge and the effectiveness of resection for SCC liver metastases is unclear. The aim of this study was to analyze long-term outcomes of surgically treated patients with SCC liver metastases.

Methods: The clinicopathological characteristics, overall survival (OS), and recurrence free survival (RFS) of all patients with SCC liver metastases resected between 1998 and 2015, were analyzed.

Results: Among 28 patients who met inclusion criteria, there were 19 patients with anal cancer metastases (68%), 2 (7%) with cervix cancer metastases, 2 (7%) with tonsil cancer metastases, 2 (7%) with lung cancer metastases, 2 (7%) with primary unknown cancer metastases and 1 (4%) with vulvar cancer metastases. Four (14%) patients underwent major hepatectomy. There were no liver insufficiency cases or 90-day mortality. Cumulative 3- and 5-year OS rates were 52% and 47%. Cumulative 1- and 3-year RFS rates were 50% and 25%.

Conclusions: Long-term outcomes after resection of SCC liver metastases compare favorably with those of colorectal or neuroendocrine liver metastases. Liver resection can be an effective treatment option for SCC liver metastases in appropriately selected patients after systemic therapy.

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Keywords: Liver metastases; Squamous cell carcinoma; Liver resection; Overall survival; Recurrence free survival

Introduction

Surgical resection of colorectal or neuroendocrine liver metastases is a well-established and effective therapeutic modality [1–5]. In contrast, the outcomes hepatectomy of non-colorectal, non-neuroendocrine liver metastases is not well described due to the rarity of resectable cases.

About 20% of patients with anal squamous cell carcinoma (SCC) had liver metastases, which are the most frequent site of distant metastases [6]. It is also common that patients with SCC of the head and neck [7], esophagus [8], and lung [9] have liver metastases. Although primary SCC is often sensitive to multimodality treatment with

chemoradiation [10,11], the 5-year overall survival (OS) of patients with metastatic anal SCC was only 19% from the National Cancer Database [12], and the 5-year OS of patients treated with chemotherapy for advanced anal SCC was 15% [13]. Furthermore, the 5-year OS of patients with resection of SCC liver metastases has been reported to be approximately 20% [14,15]. Hence, the efficacy of resecting SCC liver metastases remains controversial. In the era of improving multimodality treatment, the validation of resecting SCC liver metastases is needed.

In this context, the primary aim of this study was to analyze the long-term survival outcomes of surgically treated patients with SCC liver metastases.

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Patients and methods

Study population and review of patient records

MD Anderson Cancer Center Institutional Review Board approval was obtained for this retrospective study (PA17-0392). From a prospectively maintained database, we identified 28 consecutive patients who underwent liver resection for histologically confirmed SCC liver metastases between January 1998 and September 2015, with follow-up through April 2017.

All patients were evaluated preoperatively with a baseline history and physical examination. Decisions about the treatment were made collectively at a multidisciplinary liver tumor conference. Following preoperative chemotherapy, patients were re-staged and surgical resection was offered to those for whom tumors were considered resectable. SCC liver metastases were deemed resectable when a hepatic resection could achieve a negative margin while preserving adequate standardized future liver remnant, sparing 2 continuous hepatic segments, and maintaining vascular inflow and outflow and biliary drainage [16]. In patients with an anticipated insufficient future liver remnant, preoperative portal vein embolization was performed before hepatectomy [17].

The following data were recorded from the electronic medical record: sex, age, diagnosis, preoperative chemotherapy cycles and regimens, perioperative outcomes (estimated blood loss, blood transfusion, operative time, and surgical procedure) and tumor characteristics (largest metastasis diameter and number of lesions). Postoperative complications were defined and classified according to the Clavien-Dindo classification, and grade IIIa or higher complications were defined as major complications [18]. Postoperative hepatic insufficiency (PHI) was defined as a postoperative peak serum total bilirubin level >7 mg/dL, as previously validated [19]. Death from liver failure was calculated at 90 days after surgical resection or during index admission.

Statistical analyses

Continuous variables were compared using the Wilcoxon rank-sum test, and categorical variables were compared using the χ^2 test. OS was measured from the date of hepatic resection until the date of death or last follow-up. RFS was measured from the date of hepatic resection until the date of radiographic detection of recurrence or last follow-up. Survival curves were generated using the Kaplan-Meier method, and differences between curves were evaluated with the log-rank test. All tests were two-sided, and $P < 0.05$ was considered significant. Factors associated with OS and RFS were examined using Cox regression analyses. Factors influencing OS and RFS were reported with hazard ratio (HR) and the 95% confidence intervals (CI). Statistical analyses were performed with JMP software (version 12.1.0; SAS Institute Inc, Cary, NC).

Results

Patient characteristics

Among 28 patients who met inclusion criteria, there were 19 patients with anal cancer metastases (68%), 2 (7%) with cervix cancer metastases, 2 (7%) with tonsil cancer metastases, 2 (7%) with lung cancer metastases, 2 (7%) with primary unknown cancer metastases and 1 (4%) with vulvar cancer metastases. Clinicopathologic characteristics are summarized in Table 1. Of 28 patients, 9 patients (32%) had primary lymph node metastases and 14 patients (50%) had synchronous liver metastases. One patient (4%) had lung metastases at the time of hepatectomy, and underwent lung resection three months after hepatectomy. Except for the patients who had liver metastases from unknown primary, the patients underwent chemo-radiation ($n = 20$, 71%), operation ($n = 5$, 18%), and radiation ($n = 1$, 4%) for the primary lesions.

Perioperative characteristics are summarized in Table 2. Of 28 patients, 22 patients (79%) underwent preoperative chemotherapy. In terms of operative extent, only 4 patients (14%) underwent major hepatectomy. There were no liver insufficiency cases and deaths within 90 days of surgery. On final pathology, the margin status was microscopically positive (R1) in only one patient. Of 28 patients, 12 patients (43%) had hepatic recurrence only.

Survival outcomes and univariate analysis

With a median follow-up of 34.4 months from hepatic resection, 19 patients (68%) developed a recurrence. Of 19 patients, the recurrence sites were liver only ($n = 8$),

Table 1
Patient clinicopathologic characteristics.

Total, n	28
Demographic	
Gender (M: F)	6: 12
Age, y ^b	57 (39–74)
Body mass index (kg/m ²) ^b	25.4 (19.8–59.0)
Primary tumor site	
Anal	19 (68%)
Cervix	2 (7%)
Tonsil	2 (7%)
Lung	2 (7%)
Primary unknown	2 (7%)
Vulvar	1 (4%)
Primary T stage (T1/T2/T3/T4) ^a	3/12/11/0
Primary N stage (N0/N1/N2) ^a	17/3/6
Therapy at primary tumor ^a	
Chemotherapy + Radiation	20 (71%)
Chemotherapy + Radiation + Surgery	2 (7%)
Surgery	2 (7%)
Radiation	1 (4%)
Radiation + Surgery	1 (4%)
Synchronous/Metachronous	14/14

^a Exclude Primary unknown.

^b Median (range).

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