



Original research

Hepatectomy for liver metastases in non-colorectal, non-neuroendocrine cancer patients. The survival benefit in primary unresectable cases



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HIGHLIGHTS

- Retrospective analysis of 59 patients underwent hepatectomy for non-colorectal, non-neuroendocrine liver metastases.
- The 5-year overall survival rate after hepatectomy was 30%.
- The 5-year disease-free survival rate after hepatectomy was 28%.
- The presence of bilateral liver metastases was an independent poor prognostic factor.
- The survival rate of the conversion cases was not inferior to primary resectable cases.

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ABSTRACT

Background: Although liver resection is widely accepted as a potentially curative treatment for colorectal liver metastases, there is an ongoing debate on the indications for hepatectomy for the treatment of liver metastases from non-colorectal primary tumors. The number of candidates for hepatectomy for non-colorectal liver metastases may increase due to advances in chemotherapy; however, the factors related to prognosis after hepatectomy for non-colorectal liver metastases have yet to be clearly elucidated.

Methods: The clinical outcomes of 59 patients who underwent hepatectomy for non-colorectal liver metastases at a single institute were retrospectively analyzed.

Results: The 5-year overall survival rate after hepatectomy for non-colorectal, non-neuroendocrine liver metastases was 30%, and 8 patients (gastric cancer (n = 2), ovarian cancer (n = 2), uterine cancer (n = 2) and breast cancer (n = 2)) survived for 5 years. The 5-year disease-free survival rate after hepatectomy was 28%. The postoperative morbidity rate was 25%; however, there were no cases of in-hospital mortality and no patients suffered liver failure. The presence of bilateral liver metastases was identified to be an independent predicting factor for poor prognosis by a multivariate analysis (P = 0.049). The survival rate of the conversion cases (initially unresectable and converted to resection after chemotherapy) was not inferior to that of primary resectable cases in terms of either overall survival or disease-free survival.

Conclusion: The present study demonstrates that hepatectomy for liver metastases from non-colorectal tumors is safe and that it may be a promising strategy for prolonging survival and achieving a cure.

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1. Introduction

Liver resection is now widely accepted as a potentially curative treatment of colorectal liver metastases and neuroendocrine

carcinoma liver metastases with reported 5-year survival rates of 40–50% [1–4] and 63–74% [5,6], respectively. In contrast, the significance of surgical resection for non-colorectal and non-neuroendocrine liver metastases remains controversial. Although there are some reports regarding hepatectomy for non-colorectal liver metastases, the results and the prognostic factors differ according to the backgrounds of the patients in each report, since groups of patients with liver-limited metastases from non-

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colorectal tumors are generally small in number and very heterogeneous due to the variety of primary tumors.

The present study aimed to clarify the outcomes of surgical resection for non-colorectal, non-neuroendocrine liver metastases and the prognostic factors after hepatectomy.

2. Patients and methods

From 1997 to 2014, 59 patients underwent hepatectomy for non-colorectal, non-neuroendocrine liver metastases with macroscopically curative intent at Hokkaido Cancer Center, Sapporo. A retrospective analysis was conducted for these patients. This study was approved by the ethical committee of the hospital and informed consent was obtained from all of the patients.

The indications for hepatectomy in non-colorectal, non-neuroendocrine liver metastases were as follows: the possibility of a macroscopically curative resection (or ablation) of all lesions, the sufficiency of the remnant liver parenchyma (>30% of the normal liver parenchyma), and the consensus of a multidisciplinary team. Hepatectomy was performed for all of the liver metastases that were diagnosed to be technically resectable, even if the liver metastases were multiple or large in size. Thus, the number and size of the liver metastases were not included in indications for hepatectomy. Even if extra-hepatic metastases were present, hepatectomy was indicated when all of the extra-hepatic lesions had been controlled by either resection or chemotherapy. Chemotherapy was administered for initially unresectable cases or marginally resectable cases. Partial resection with a free margin of >1 cm was preferred, and anatomical resection was selected when needed. All detectable lesions were resected to achieve an R0 resection, and ablation therapy (MCT; microwave coagulation therapy or RFA; radiofrequency ablation) were also used in some cases for small nodules (<5 mm) that were located deeper in the liver.

The following clinicopathological factors were analyzed for their impact on overall survival and disease-free survival: age, gender, location of the primary tumor, pathological diagnosis, interval

between primary tumor resection and the appearance of liver metastases, the number and maximum diameter of the liver metastases, type of hepatectomy, preoperative chemotherapy, and postoperative complications.

The cumulative survival curves from the date of hepatectomy were estimated using the Kaplan–Meier method, and were analyzed using the log-rank test. A p value of <0.05 was considered to be statistically significant. A univariate analysis was performed and parameters with a p value of <0.2 were selected as candidate prognostic factors and entered into a Cox proportional hazards regression model to identify the independent predictors of survival. All statistical analyses were performed using the EZR statistical software program [7].

3. Results

3.1. Patient demographics

Fifty-nine patients underwent hepatectomy for non-colorectal, non-neuroendocrine metastatic liver tumor. The clinical and pathological features of the patients are shown in Table 1. The primary sites of the liver metastases were as follows: gastrointestinal cancer in 30 cases (the stomach (n = 19), the esophagus (n = 4), the biliary tract (n = 4), the pancreas (n = 2) and the omentum (n = 1)), gynecological cancer in 15 cases (the ovary (n = 10), the uterus (n = 5)), urogenital cancer in 6 cases (the testicle (n = 3), the kidney (n = 1), the ureter (n = 1), and the adrenal gland (n = 1)), breast cancer in 6 cases, soft tissue tumor in 1 case, and lung cancer in 1 case. The pathological diagnoses of the primary sites were as follows: adenocarcinoma (n = 39), squamous cell carcinoma (n = 5), germ cell tumor (n = 4), sarcoma (n = 2), granulosa cell tumor (n = 2) and other (n = 7). The 59 cases were composed of 31 females and 28 males with median age of 63 years (range; 8–88 years). In 32 cases, liver resection was performed for a single liver metastasis, while 9 cases had two liver metastases and 18 cases had ≥3 liver metastases. The maximum size of the liver

Table 1
Clinical and pathological features of the patients who underwent liver resections for metastases.

Primary site		Number of liver metastases	
Gastrointestinal	30	1	32
Esophagus	4	2	9
Stomach	19	3–4	9
Pancreas	2	5 or more	9
Biliary tract	4		
Omentum	1		
Gynecological	15	Diameter of largest liver metastases	48
Ovary	10	≤5 cm	11
Uterus	5		
Urogenital	6	Distribution of metastases	
Breast	6	Bilateral	14
Othres	2	Unilateral	45
Histology of the primary tumors		Presentation	
Adenocarcinoma	39	Synchronous liver metastases (<12 months)	36
Squamous cell carcinoma	5	Metachronous liver metastases	23
Germ cell tumor	4		
Sarcoma	2	Extrahepatic metastases	
Granulosa cell tumor	2	Present	19
Others	7	Absent	40
Age		Preoperative chemotherapy	
Average	60.5 (8–88)	Performed	27
		Not performed	32
Gender		Effects of chemotherapy	
Female	31	CR or PR	7
Male	28	SD or PD	16
		Not evaluated	4

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