original article

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# Survival benefit of combined curative resection of the stomach (D2 resection) and liver in gastric cancer patients with liver metastases

S. H. Cheon[1], S. Y. Rha[1], H.-C. Jeung[1], C.-K. Im[1], S. H. Kim[2], H. R. Kim[1], J. B. Ahn[1], J. K. Roh[1], S. H. Noh[3] & H. C. Chung[1]*

[1]*Department of Internal Medicine, Cancer Metastasis Research Center, Yonsei Cancer Center, Yonsei University College of Medicine;* [2]*Graduate School of East-West Medical Science, Kyung Hee University, Gyeonggi-do;* [3]*Department of Surgery, Cancer Metastasis Research Center, Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, South Korea*

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**Background:** The benefit of surgical resection of liver metastases from gastric cancer has not been well established. The aim of this study was to evaluate the rationale for hepatic resection in patients with hepatic metastases from gastric cancer.

**Methods:** Among 10 259 patients diagnosed with gastric adenocarcinoma in the Yonsei University Health System from 1995 to 2005, we reviewed the records of 58 patients with liver-only metastases from gastric cancer who underwent gastric resection regardless of hepatic surgery.

**Results:** The overall 1-year, 3-year, and 5-year survival rates of 41 patients who underwent hepatic resection with curative intent were 75.3%, 31.7%, and 20.8%, respectively, and three patients survived >7 years. Of the 41 patients, 22 had complete resection and 19 had palliative resection. Between the curative and palliative resections, survival rates after curative intent were not different. The number of liver metastasis (solitary or multiple) was a marginally significant prognostic factor for survival.

**Conclusions:** Surgery for liver metastases arising from gastric adenocarcinoma is reasonable if complete resection seems feasible after careful preoperative staging, even if complete resection is not actually achieved. Hepatic resection should be considered as an option for gastric cancer patients with hepatic metastases.

**Key words:** curative intent, gastric cancer, hepatic resection, liver metastases



## introduction

The optimal treatment of gastric cancer with liver metastases without peritoneal dissemination or other distant metastases remains a matter for debate. In such patients, the continuing question is whether it is beneficial to resect both the primary gastric cancer and hepatic metastases as the only potential opportunity for a cure.

Around 5%–14% of patients who undergo surgery for gastric cancer develop liver metastases synchronously or metachronously [1–5]. Long-term survival is usually hard to achieve following metastatic liver involvement from gastric cancer with a median survival of ∼6 months, even with palliative chemotherapy [4, 6, 7]. Many studies have reported on the benefit of hepatic resection for metastatic tumors from colorectal cancer [8–12]. In contrast, the significance of hepatic resection for gastric metastases has been controversial [2–4, 9, 13–16]. A number of studies have found that the effect on survival of hepatic resection for hepatic metastases from gastric cancer is doubtful [17–20], while others indicate that only hepatic resection leads to long-term survival [2, 5, 12–16, 21–26]. These reports describe that ∼5%–30% of enrolled patients survive for >5 years after hepatic surgery.

In Western countries, hepatic resection in gastric cancer patients is seldom indicated because of the presence of multiple tumors or associated peritoneal dissemination [4, 13, 27]. Peritoneal metastases are recognized in 40% of gastric cancer patients with liver metastases. For these reasons, most surgeons hesitate to perform hepatic resection, even if only a solitary hepatic metastasis may be involved. However, because one of the most important factors in the prognosis of gastric cancer is liver metastasis, complete surgical resection of the primary gastric tumor and liver metastases appears to be the only chance to cure this disease. One possible explanation for the persistent controversy may be the lack of sufficient data in a relatively large number of patients undergoing hepatic resection for gastric cancer metastases. To our best knowledge,

**Correspondence to:* Dr H. C. Chung, Department of Internal Medicine, Cancer Metastasis Research Center, Yonsei Cancer Center, Yonsei University College of Medicine, 134, Shinchon-Dong, Seodaemoon-gu, Seoul 120-752, South Korea. Tel: +82-2-2228-8132; Fax: +82-2-393-3652; E-mail: unchung8@yuhs.ac

only one report has included >40 patients [13]. In addition, all previous reports have been retrospective analyses of heterogeneous patients. Thus far, little is known about prognostic factors in patients with liver surgery for gastric cancer metastases.

We evaluated the possible beneficial effect of hepatic resection on survival in gastric cancer with hepatic metastases and identified patients who might benefit from combined curative surgery.

## patients and methods

### patients

From January 1995 to December 2005, 10 259 patients were diagnosed with gastric adenocarcinoma in the Yonsei University Health System, South Korea. Of these 10 259 patients, 1013 patients (9.9%) had synchronous or metachronous liver metastases. Among these 1013 patients, 84 underwent gastric resection. Fifty-eight patients with liver-only metastases among these 84 patients who underwent gastric resections regardless of hepatic operation were included in this study (Figure 1). This study included patients who underwent hepatic surgical resection including radiofrequency ablation (RFA) and those who did not undergo hepatic resection for metastatic hepatic tumors but did surgical treatment of the gastric cancer. Patients who received prior chemotherapy before surgery were excluded. The median follow-up period was 15.5 months (range 0.5–106.8 months).

### methods

*evaluation of clinical and tumor characteristics.* The following demographic and clinicopathological information was retrospectively obtained from patient records: age, gender, interval between gastrectomy and hepatic surgery, types of surgical procedures, characteristics of primary gastric cancer and liver metastases, postoperative chemotherapy, and relapse pattern. Characteristics of the primary gastric cancer included depth of invasion, extent of lymph node metastasis, pathologic type, tumor differentiation, tumor location, tumor size, and surgical margin. Characteristics of hepatic metastases included the number, size, lobar distribution, time to liver metastasis, and surgical margin of the resected tumors. Pathological staging was determined according to American Joint Committee on Cancer criteria (6th edition, 2002).

*definition of curative gastric surgery (D2 surgery).* Curative gastric resection included the absence of residual tumor, both macroscopically and microscopically, by D2 lymphadenectomy with omentectomy and splenectomy. For D2 lymphadenectomy, all perigastric lymph nodes, those along the left gastric, common hepatic, celiac arteries, and retropancreatic lymph nodes were removed. Splenectomy was carried out only in cases of documented lymph node enlargement at the splenic hilum.

*indications of hepatic surgery or RFA.* Curative hepatic resection was defined as macroscopically and microscopically undetectable tumors. Indications for resection of hepatic metastases included (i) no signs of peritoneal dissemination or any other distant metastases on preoperative imaging, (ii) feasibility of complete tumor resection including primary gastric cancer and hepatic metastases, and (iii) acceptable hepatic function on the basis of serum liver function test panel. Patients with hepatic metastases from gastric cancer who seemed to be inappropriate candidates for curative hepatic resection due to the number, size, and location of hepatic tumors were evaluated for RFA. Indications of RFA included (i) no signs of peritoneal dissemination or any other extrahepatic distant metastasis on preoperative imaging, (ii) probably impossible hepatic resection on the basis of the location, size, or number of hepatic metastases, (iii) unresectability as determined by the surgeon based upon intraoperative

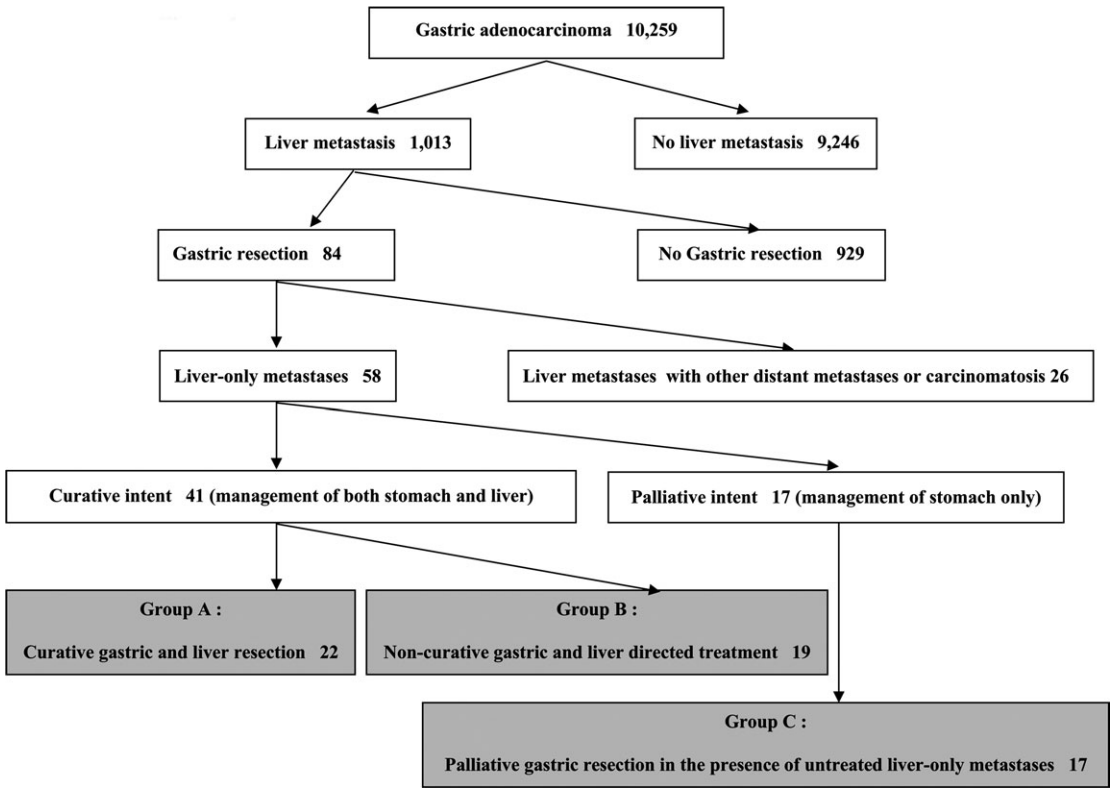


**Figure 1.** Grouping of enrolled patients.

findings of number, size, and location of tumors as well as comorbid conditions, and (iv) presence of hepatic tumors ≤5 cm.

*patient groups.* We classified the patients into three groups. Group A included patients who underwent combined curative resection of gastric cancers and hepatic metastases ($n = 22$). Group B patients underwent both gastric and hepatic surgery with curative intent, but at least one surgery was ultimately palliative due to microscopically or macroscopically residual disease ($n = 19$). Group B included nine patients treated with RFA, eight resection margin-positive patients, and two patients with residual cancer. RFA was carried out with curative intent but was ultimately defined as a palliative intervention. Among the eight resection margin-positive patients, seven had residual microscopic cancer cells at the hepatic resection margin and one at the stomach. The two patients with residual cancer were considered for curative resection on initial preoperative examination, but surgery revealed too many liver metastases, making curative resection impossible. Group C included patients who underwent gastric resection in the presence of untreated liver-only metastases ($n = 17$) (Figure 1).

*follow-up.* Overall survival after hepatic metastases was defined as the time from diagnosis of liver metastases in both synchronous and metachronous types to death from any cause or last follow-up. Relapse-free survival in the curatively resected group (Group A, $n = 22$) was defined as the time from diagnosis of liver metastases to the first documentation of recurrence or last follow-up.

*statistics.* Data related to patient characteristics were compared among the three groups using an analysis of variance for continuous variables and the chi-square test or Fisher's exact test for categorical end points. Data on patients who were alive or lost to follow-up were censored. Data on patients who were alive and free of recurrent disease were censored at the time of the last follow-up visit.

Survival curves were estimated by the Kaplan–Meier method, and the differences in survival curves among groups were compared with the log-rank test. In order to adjust for confounding variables, we used Cox proportional hazards models to estimate the simultaneous effects of prognostic factors on survival. Hepatic resection margins were not included in this analysis because some of the margins were not recorded on a numeric scale (millimeter), but rather as presence of tumor cells (negative or positive). All statistical tests were two sided, and $P < 0.05$ was considered statistically significant. SAS software (version 9.1, SAS Inc., NC) was used for statistical analysis.

## results

### patient characteristics

The baseline characteristics of eligible patients are presented in Table 1. There were 49 men and 9 women with a median age of 61 (range 36–74) years. There were no major imbalances between groups in terms of characteristics of primary gastric cancer except with regard to the number and distribution of hepatic metastases. The number of patients with a solitary metastasis was 18 (81.8%) in group A, 10 (52.6%) in group B, and 1 (5.9%) in group C, respectively ($P < 0.0001$). In group A, the location of the tumors was unilobar in 21 patients (95.5%) and bilobar in 1 (4.5%). In groups B and C, the proportion of patients with bilobar distribution of hepatic metastases was 21.1% and 64.7%, respectively. Patients with unresected hepatic metastases (group C) showed more multiple hepatic metastases and bilobar distribution. Hepatic metastases were detected synchronously in 18 patients and metachronously in 4 patients in group A.

In patients who underwent metachronous liver resection, the median interval between gastric resection and the diagnosis of hepatic metastases was 19.1 months in total (range 8.0–38.2 months), 12.8 months in group A (range 8.9–19.1 months), and 25.9 months (range 8.0–38.2 months) in group B.

**Table 1.** Patient characteristics

| Characteristics | Number of patients (%) | | | *P* value |
|---|---|---|---|---|
| | Group A ($n = 22$) | Group B ($n = 19$) | Group C ($n = 17$) | |
| Sex | | | | |
| Male | 18 (81.8) | 16 (84.2) | 15 (88.2) | 0.9047 |
| Female | 4 (18.2) | 3 (15.8) | 2 (11.8) | |
| Age (median years) | 59 (40–74) | 60 (36–70) | 61 (52–74) | 0.3693 |
| Primary gastric cancer | | | | |
| Serosal invasion | | | | |
| Absent | 3 (13.6) | 3 (15.8) | 2 (11.8) | 1.0000 |
| Present | 19 (86.4) | 14 (73.7) | 15 (88.2) | |
| NA | – | 2 (10.5) | – | |
| Lymph node metastasis | | | | |
| Absent | 3 (13.6) | 3 (15.8) | 2 (11.8) | 1.0000 |
| Present | 19 (86.4) | 14 (73.7) | 15 (88.2) | |
| NA | – | 2 (10.5) | – | |
| Histologic grade | | | | |
| Poorly differentiated | 9 (40.9) | 5 (26.4) | 9 (52.9) | 0.3391 |
| Moderately differentiated | 12 (54.5) | 10 (52.6) | 8 (47.1) | |
| Well differentiated | 1 (4.6) | 2 (10.5) | 0 (0) | |
| NA | – | 2 (10.5) | – | |
| Tumor location | | | | |
| Upper body | 5 (22.7) | 4 (21.1) | 4 (23.5) | 0.8135 |
| Mid-body | 2 (9.1) | 4 (21.1) | 2 (11.8) | |
| Lower body | 15 (68.2) | 9 (47.3) | 11 (64.7) | |
| NA | – | 2 (10.5) | – | |
| Tumor size (mean cm ± SD) | 5.7 ± 2.4 | 6.6 ± 3.1 | 6.1 ± 2.3 | 0.5754 |
| Hepatic metastasis | | | | |
| Number | | | | |
| Solitary | 18 (81.8) | 10 (52.6) | 1 (5.9) | <0.0001 |
| Multiple | 4 (18.2) | 9 (47.4) | 16 (94.1) | |
| Metastatic type | | | | |
| Synchronous | 18 (81.8) | 12 (63.2) | 12 (70.6) | 0.4049 |
| Metachronous | 4 (18.2) | 7 (36.8) | 5 (29.4) | |
| Distribution | | | | |
| Unilobar | 21 (95.5) | 15 (78.9) | 6 (35.3) | <0.0001 |
| Bilobar | 1 (4.5) | 4 (21.1) | 11 (64.7) | |
| Tumor size (mean cm ± SD) | 2.4 ± 1.7 | 2.1 ± 1.4 | NA | 0.6387 |

Group A: combined curative resection of gastric cancers and hepatic metastases. Group B: gastric and hepatic resection with curative intent, where at least surgery was ultimately only palliative. Group B includes radiofrequency ablation for hepatic metastases. Group C: palliative gastric resection in the presence of untreated liver-only metastases.
NA, not applicable; SD, standard deviation.

## treatments

Fifteen and eleven partial gastrectomies and seven and eight total gastrectomies were carried out with curative intent in groups A and B, respectively. In group C, 11 patients underwent partial gastrectomies and 6 patients total gastrectomies. In terms of the type and extent of hepatic resection, wedge resection was done in 59.1% of cases in group A and 42.1% of cases in group B. RFA was carried out in 47.4% of cases and lobectomy was not carried out in group B. Table 2 details the type of hepatic surgery in each group. Overall postoperative hospital mortality was 1.72% (1 of 58). Excluding patients who underwent RFA, complete resectability of surgical procedures was 68.8% (22 of 32).

A total of 51 patients (87.9%) received postoperative chemotherapy. Among those who underwent curatively intended gastric and hepatic surgery ($n = 41$), 37 (90.2%) received postoperative chemotherapy. Anthracycline- and cisplatin-based chemotherapies were the most common chemotherapy regimens.

## recurrence

Cancer recurred in 14 (63.6%) of the 22 group A patients who underwent curative resection. The most common site of initial recurrence after hepatic resection was the liver ($n = 11$; 78.6%). Relapse pattern is summarized in Table 3. Median relapse-free duration of the curatively resected group was 13.3 months (Figure 2A). We evaluated the potential effect of prognostic factors known to influence recurrence in the

**Table 2.** Type of hepatic surgery

| Type of hepatic surgery | Number of patients (%) | |
|---|---|---|
| | Group A ($n = 22$) | Group B ($n = 19$) |
| Wedge resection | 13 (59.1) | 8 (42.1) |
| Segmentectomy | 6 (27.3) | 2 (10.5) |
| Lobectomy | 3 (13.6) | 0 (0) |
| Radiofrequency ablation | 0 (0) | 9 (47.4) |

Group A: combined curative resection of gastric cancers and hepatic metastases. Group B: gastric and hepatic resection with curative intent, where at least surgery was ultimately only palliative. Group B includes radiofrequency ablation for hepatic metastases.

**Table 3.** Relapse patterns in 22 curatively resected patients (group A)

| | Number | (%) |
|---|---|---|
| Relapse | 14 | (63.6) |
| Local relapse only | 0 | |
| Systemic relapse only (except liver) | 3 | |
| Intrahepatic relapse only | 6 | |
| Intrahepatic and systemic relapse | 5 | |
| Relapse free | 8 | (36.4) |

Group A: combined curative resection of gastric cancers and hepatic metastasis.

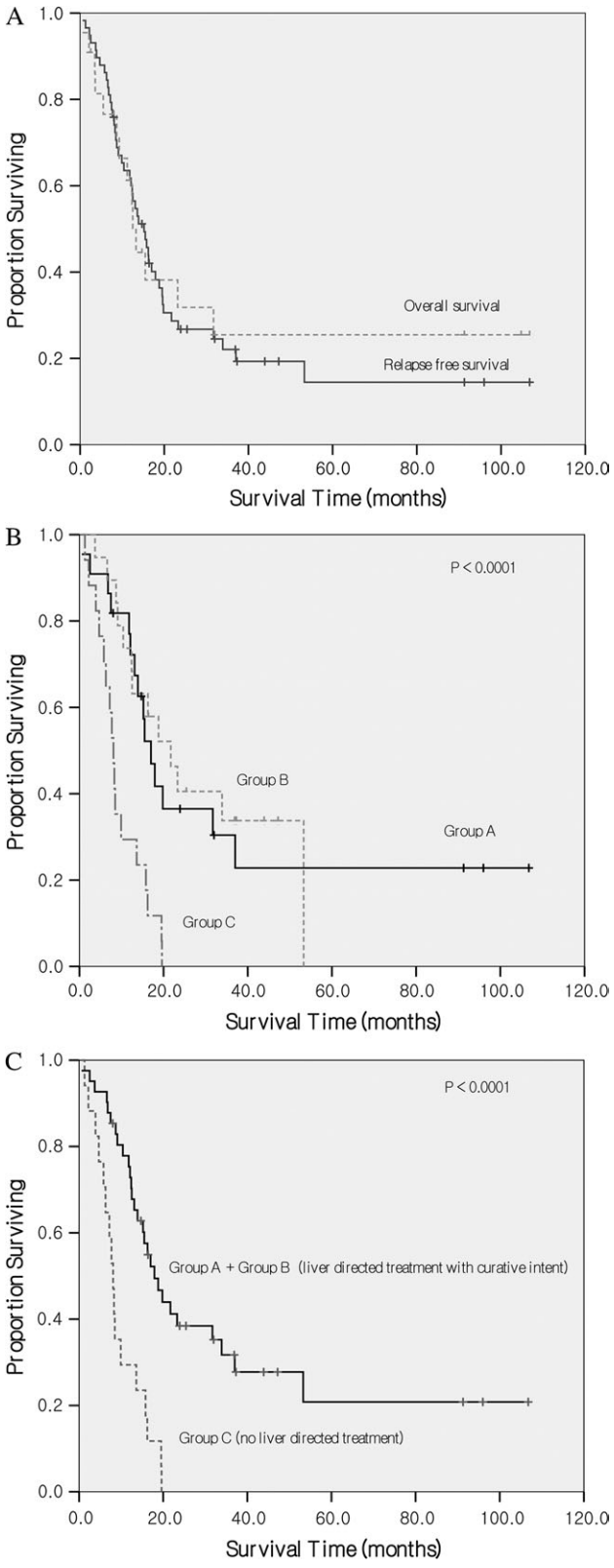


**Figure 2.** (**A**) Relapse-free survival of patients receiving curative resection (group A) and overall survival of all patients. (**B**) Overall survival of each group (A, B, and C). (**C**) Overall survival comparing patients who underwent hepatic resection with curative intent (groups A and B) with patients who underwent palliative gastrectomy without hepatic resection (group C).

curatively resected group and found no significant relationships (data not shown).

The most common site of recurrence in the nine patients that received RFA was also the liver ($n = 7$; 77.8%). Site of recurrence could not be evaluated in six of eight patients who had a positive resection margin due to follow-up loss. Of the remaining two patients, one had liver recurrence and the other had systemic recurrence.

## survival

We examined survival in two different ways. First, we compared the overall survival of groups A, B, and C. Second, we compared the survival of patients who received hepatic resection with curative intent regardless of actual curative or palliative outcome to those who were unresected.

The median overall survival of patients in groups A, B, and C was 17 months (range 0.6–106.8 months), 21.7 months (range 3.7–53.3 months), and 8.1 months (range 1.3–19.6 months), respectively. Adjustment for sex, age, number of liver metastases (solitary versus multiple), and hepatic metastatic type (synchronous versus metachronous) resulted in hazard ratios for death of 0.512 ($P = 0.1963$) in group A and 0.309 ($P = 0.01$) in group B compared with group C (Table 4). The 1-year, 3-year, and 5-year survival rates were 77%, 30.4%, and 22.8% in group A; 73.7%, 33.8%, and 0% in group B; and 29.4%, 0%, and 0% in group C, respectively. There was no statistically significant difference in survival rate at 1 and 3 years between groups A and B (Figure 2B), but there were long-term survivors in group A on the basis of 5-year survival rates. Three out of 22 patients in group A survived >7 years.

Next, we classified the patients into two groups (groups A and B versus group C) on the basis of the curative or palliative intent of the surgical resection, namely whether liver directed treatment or not. The 1-year, 3-year, and 5-year survival rates in the hepatic resection group with curative intent (groups A and B including RFA) were 75.3%, 31.7%, and 20.8%, respectively, while in the hepatic unresected group (group C) the rates were 29.4%, 0%, and 0%, respectively ($P < 0.0001$) (Figure 2C). The survival benefit of groups A and B (that underwent hepatic surgery with curative intent) was a 20.8% improvement in the 5-year survival rate compared with group C, corresponding to a 64.0% reduction in the risk of death after adjusting for sex, age, number of liver metastases (solitary versus multiple), and hepatic metastatic type (synchronous versus metachronous) (Table 5).

RFA also showed comparable outcomes to curative resection (Figure 3). There was one cancer-unrelated mortality in group A in a patient who died of septic shock not related to surgery or chemotherapy.

**Table 4.** Multivariate analysis of hazard ratio for death in each group ($n = 58$)

| Variable | *P* value | Hazard ratio |
|---|---|---|
| Sex | 0.6837 | 1.199 |
| Age | 0.1846 | 1.027 |
| Group A[a] | 0.1963 | 0.512 |
| Group B[b] | 0.0103 | 0.309 |
| Hepatic tumor number (solitary versus multiple) | 0.0814 | 2.171 |
| Hepatic metastatic type (synchronous versus metachronous) | 0.4437 | 1.320 |

Group A: combined curative resection of gastric cancers and hepatic metastases. Group B: gastric and hepatic resection with curative intent, where at least surgery was ultimately only palliative. Group B includes radiofrequency ablation for hepatic metastases. Group C: palliative gastric resection in the presence of untreated liver-only metastases.
[a]Group A versus group C.
[b]Group B versus group C.

**Table 5.** Multivariate analysis of hazard ratio for death in patients who underwent surgical procedures with curative intent (groups A and B) compared with palliative intent (group C) ($n = 58$)

| Variable | *P* value | Hazard ratio |
|---|---|---|
| Sex | 0.6024 | 1.261 |
| Age | 0.1774 | 1.028 |
| Curative intent (liver directed treatment versus untreated liver metastases)[a] | 0.0184 | 0.360 |
| Hepatic tumor number (solitary versus multiple) | 0.1563 | 1.767 |
| Hepatic metastatic type (synchronous versus metachronous) | 0.6218 | 1.190 |

Group A: combined curative resection of gastric cancers and hepatic metastases. Group B: gastric and hepatic resection with curative intent, where at least surgery was ultimately only palliative. Group B includes radiofrequency ablation for hepatic metastases. Group C: palliative gastric resection in the presence of untreated liver-only metastases.
[a]Groups A and B versus group C.

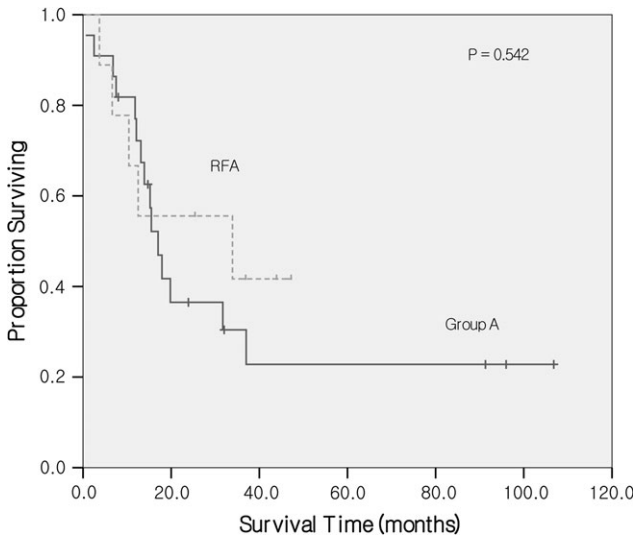


**Figure 3.** Overall survival of patients treated with radiofrequency ablation (RFA) compared with curative resection (group A).

### prognostic factors

In the present study, although the total number of patients was small, only the number of liver metastases (single versus multiple) was a marginally significant prognostic factor for survival after hepatic surgery with curative intent ($P = 0.052$) (Table 6). The presence of metachronous hepatic metastases was not a significant determinant for favorable prognosis after hepatic resection in our study.

## discussion

Previous studies describe the incidence of gastric cancers metastasizing to the liver as 5%–14% [1–5]. In our series of 10 259 patients diagnosed with gastric adenocarcinomas, 1013 patients (9.9%) had liver metastases over the past decade. Among them, 84 patients (8.3%) underwent gastric surgical resections. As gastric cancer is still a major concern in Asian nations, proper treatment strategy development for such patients with metastases is necessary.

Among several approaches such as systemic chemotherapy, radiation therapy, and surgical therapy, the effectiveness of hepatic resection for metastases from gastric cancer has not been well defined [2–4, 13–16]. In reality, very few patients with gastric hepatic metastases are potential candidates for hepatic resection because of multiple bilateral metastases or extrahepatic diseases such as simultaneous peritoneal dissemination or extensive lymph node metastases [2, 4, 27]. Hepatic resection, a potentially curative approach for patients with liver metastases from colorectal carcinoma, carries a 5-year survival rate of 30%–50%. In contrast, hepatic resection from gastric carcinoma metastases has highly variable results and a median survival time of 5–31 months, with 15%–77% survival at 1 year and 0%–38% survival at 5 years [2, 3, 5, 9, 15–17, 26]. While the reasons for the differences in survival rates are not clear, possible explanations include differences in patient selection, screening programs, adjuvant chemotherapy, and surgical techniques such as D2 versus D1 dissection. Thus, the clinical benefit of resection of hepatic metastases from gastric carcinoma is not widely accepted and remains controversial. However, as nonsurgical treatments such as systemic or hepatic artery infusion chemotherapy also do not achieve satisfactory results [2, 6, 7], the effort to evaluate the potential role of hepatic resection is worthwhile.

In this retrospective study, we observed a survival benefit of hepatic surgery (including RFA) with curative intent (groups A and B) as compared with group C, as evidenced by an improvement of 20.8% in the 5-year survival rate, corresponding to a 64.0% reduction in the risk of death. Even with incomplete resections in these patients, we found that the survival rate was not significantly different from that of the curatively resected patients. These results have the limitation of patient selection bias because patients undergoing surgical resection with curative intent would be expected to have relatively good health and better prognosis. Even so, there were no significant differences in characteristics of primary gastric cancers, and the survival benefit was consistently found even after adjusting for multiple confounding factors that might affect survival. The median survival duration of patients who received RFA for hepatic metastases was 33.9 months, which was longer than previously reported. Moreover, the median survival duration in patients who had a positive surgical margin after hepatic surgery was 19.5 months.

Seventeen patients with liver-only metastases in group C did not receive hepatic surgery even in the absence of distant metastases or peritoneal seeding, usually due to the surgeon's decision that the hepatic metastases could not be resected curatively. One patient had a single hepatic metastasis metachronously at liver segment 6 after curative gastric resection and adjuvant chemotherapy. He was treated with second-line chemotherapy instead of hepatic resection. When the survival of groups A and B versus C was analyzed after adjusting for sex, age, number of liver metastases (solitary versus multiple), and hepatic metastatic type (synchronous versus metachronous), the hazard ratio for death was 0.360 in groups A and B compared with group C. These results indicate the survival benefit of hepatic resection.

Compared with previous studies, our report is one of the largest on surgical treatment of liver metastases in gastric adenocarcinoma including both curatively and palliatively resected patients. Five-year survival rates and median survival time in our study were similar to those of other reports showing the best results. Even though we included patients with incomplete resections, we observed a longer median survival compared with previous studies (Table 7). Roh et al. [27] observed favorable results in patients who had a solitary lesion in the liver. Sakamoto et al. and Okano et al. [3, 2] also found favorable results when evaluating only curatively resected patients. In contrast, Zacherl et al. [4] showed disappointing results in their analysis of 15 patients who underwent hepatic resection with curative intent. They found that only 10 patients received a curative resection, showing a significant survival benefit in curatively resected patients compared with palliatively resected patients.

The clinicopathological characteristics related to the prognosis of gastric cancer with hepatic metastases have not

**Table 6.** Variables affecting survival following hepatic resection with curative intent (groups A and B) ($n = 41$)

| Variable | *P* value | Hazard ratio |
|---|---|---|
| Hepatic tumor number (solitary versus multiple) | 0.0519 | 2.311 |
| Age | 0.4617 | 1.016 |
| Sex | 0.8126 | 0.879 |
| Hepatic metastatic type (synchronous versus metachronous) | 0.7241 | 0.830 |
| Hepatic operation type (including RFA) | 0.8130 | 0.957 |

Group A: combined curative resection of gastric cancers and hepatic metastases. Group B: gastric and hepatic resection with curative intent, where at least surgery was ultimately only palliative. Group B includes radiofrequency ablation for hepatic metastases. Group C: palliative gastric resection in the presence of untreated liver-only metastases.
RFA, radiofrequency ablation.

**Table 7.** Comparison of reports of liver surgery for metastases originating from gastric adenocarcinoma

| Reference | Nation | Enroll period (years) | Patient number (*n*) | Synchronous (*n*) | Metachronous (*n*) | Median survival duration (months) | Overall survival (%) | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | 1 year | 2 years | 3 years | 5 years |
| Zacherl et al. [4] | Austria | 1980–1999 (20) | 15 | 10 | 5 | 8.8 (4–51) | 35.7 | 28.6 | 14.3 | 0.0 |
| Sakamoto et al. [3] | Japan | 1985–2001 (17) | 22 | 12 | 10 | 21.0 (1.4–71) | 73.0 | – | 38.0 | 38.0 |
| Okano et al. [2] | Japan | 1986–1999 (14) | 19 | 13 | 6 | 21.0 | 77.0 | – | 34.0 | 34.0 |
| Roh et al. [27] | Korea | 1988–1996 (9) | 11 | 8 | 3 | 19.0 | 72.7 | – | – | 27.3 |
| Imamura et al. [9] | Japan | 1990–1997 (8) | 17 | 7 | 10 | – | 60.0 | 25.0 | 25.0 | 0.0 |
| Ambiru et al. [13] | Japan | 1975–1999 (25) | 40 | 18 | 22 | 12.0 (1–206) | – | 27.0 | – | 18.0 |
| Shirabe et al. [26] | Japan | 1979–2001 (23) | 36 | 16 | 20 | – | 64 | 43 | 26 | 26 |
| Sakamoto et al. [5] | Japan | 1990–2005 (16) | 37 | 16 | 21 | 31 | – | – | – | 11 |
| Cheon et al (current study) | Korea | 1995–2005 (11) | 41 | 30 | 11 | 17.9 (0.6–106.8) | 75.3 | 38.4 | 31.7 | 20.8 |

been comprehensively identified [4, 5, 9, 16, 25, 26, 28]. Whether surgical margin is a prognostic factor of survival in patients with metastatic liver tumors remains controversial [9, 13, 15], whereas resection margin is a significant prognostic factor in colorectal metastatic cancer patients undergoing hepatic resection [10, 29, 30]. In our study, positive surgical margin did not greatly affect patient survival negatively in agreement with the findings of Sakamoto [5]. This result indicates that an extensive safety resection margin may not be essential for better outcomes of hepatic resection in gastric cancer. Positive surgical margins should be avoided if possible, however, because long-term survival was not found in margin-positive patients.

In the present study, although the total number of patients was small, the number of liver metastases was a marginal prognostic factor for survival after hepatic surgery with curative intent ($P = 0.0519$). Okano et al. [2] reported 3-year survival rates of 56% for a single metastasis and 0% for multiple metastases, and the number of liver metastases is a significant prognostic factor in other reports as well [3, 15]. In contrast, the number of colorectal liver metastases is no longer considered an important predictor of long-term survival [11]. The different results between colorectal and gastric metastases are thought to reflect the aggressively infiltrative biologic behavior of gastric cancer [2]. Our findings indicate that surgical resection should be considered first for solitary liver metastasis from gastric cancer.

Ambiru et al. [13] reported significantly longer survival in patients with metachronous metastases (5-year survival, 29%) than in those with synchronous disease (5-year survival, 6%). Other authors have also reported favorable outcomes in patients with metachronous metastases [2, 9]. We observed no significant difference in survival between synchronous and metachronous metastases in groups A and B ($P = 0.7241$).

Few reports have revealed patterns of recurrence after hepatic resection for gastric metastases [5, 26]. Recurrence was documented in 63.6% of the patients in the curatively resected group. Relapse developed most commonly in the liver (78.6%), indicating that the remaining liver should be a focus for relapse monitoring. A sensible strategy for improving survival would be close observation for a second relapse in the liver and adjuvant chemotherapies after surgery. We were unable to draw any conclusions about adjuvant chemotherapy, and a multi-institutional prospective randomized trial will be needed for this issue. Sex, age, number of liver metastases (solitary versus multiple), hepatic metastatic type (synchronous versus metachronous), and surgical type of hepatic resection did not affect relapse-free survival.

In conclusion, our results show that surgery for liver metastases arising from gastric adenocarcinoma is reasonable if complete resection seems feasible after careful preoperative staging, even if complete resection is not actually achieved. Hepatic resection should be therefore being considered as an option for patients who had gastric cancer with hepatic metastases.

## funding

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