Adjuvant Chemoradiation Therapy in Gallbladder Cancer

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- ABSTRACT –

Adjuvant Chemoradiation Therapy in Gallbladder Cancer

Gallbladder cancer is a relatively uncommon gastrointestinal malignancy. Indications for adjuvant chemoradiation therapy after surgical resection have not yet been determined. We aimed this study to elucidate the effectiveness of adjuvant chemoradiation therapy according to TNM stage for gallbladder cancer. Between March 2001 and March 2009, 100 patients with gallbladder cancer underwent surgical resection. We divided the patients according to TNM stage, and subdivided further according to whether adjuvant chemoradiation therapy was added or not. The clinicopathologic factors, recurrence and survival were retrospectively analyzed. Patients with gallbladder cancer at T2N0M0, T2N1M0, T3N0M0 and T3N1M0 stages were enrolled in this study. Among the 4 stages, the 2 lymph node-negative stages (T2N0M0 and T3N0M0) did not show any gain in survival by adding adjuvant chemoradiation therapy. Conversely, the remaining lymph node-positive stages (T2N1M0 and T3N1M0) showed gain in disease-free survival, and the lymph node-positive T2 stage (T2N1M0) showed gain in disease-specific survival. In patients with lymph node-positive T2/T3 GB cancers, adjuvant chemoradiation therapy was an independent prognostic factor for survival. Adjuvant chemoradiation therapy is recommended for lymph node-positive T2/T3 gallbladder cancer following surgical resection.

Key words: gallbladder cancer, resection, adjuvant therapy, TNM stage, prognosis.

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

ABBREVIATION

GB, gallbladder;

CRTx, adjuvant chemotherapy with or without radiation therapy;

NCRTx, no adjuvant chemoradiation therapy;

DFS, disease-free survival;

DSS, disease-specific survival;

CA19-9, carbohydrate antigen 19-9

I. INTRODUCTION

Though it is the most common cancer of the biliary tree, gallbladder (GB) cancer is a relatively uncommon gastrointestinal tract malignancy worldwide, and it has been known to be a lethal malignancy (Henson et al., 1992; Furlan et al., 2008; Jemal et al., 2009).

Complete surgical resection still remains the only curative measure for GB cancer (de Aretxabala et al., 2006; Duffy et al., 2008; Furuse, 2008). However, recurrence is common, if it happens, it is considered to be fatal. Some auxiliary treatments, such as neoadjuvant or adjuvant chemotherapy and radiation therapy, have been introduced to enhance survival of patients with GB cancer. However, there is no established regimen for such measures (Murakami et al., 2009). In addition, indications for adjuvant chemoradiation therapy have not yet been determined.

To the best of our knowledge, there have been few published reports on TNM stage-specific comparative analysis of the effectiveness of adjuvant chemoradiation therapy. The aim of this study was to elucidate the effectiveness of adjuvant chemoradiation therapy according to TNM stage after surgical resection in patients with GB cancer.

II. MATERIALS AND METHODS

A. Materials

Between March 2001 and March 2009, 100 patients with GB cancer underwent surgical resection with curative intent at the National Cancer Center of Korea. Our center policy for GB cancer has been as follows: simple cholecystectomy for T0 (carcinoma *in situ*)/T1 cancer (invasion to the lamina propria or muscle layer) and extended cholecystectomy for T2N0M0 and more advanced stages. For extended cholecystectomy, a combination of liver resection with a more than 2-cm margin from the GB bed, cholecystectomy, and dissection of lymph node stations 8, 12 and 13 have been performed.

Adjuvant chemotherapy with or without radiation therapy (CRTx) was administered according to an interdisciplinary decision of a clinical oncologist and a surgeon after surgery. If the patient's general condition was tolerable, adjuvant concurrent chemoradiation therapy was applied to a patient with T2N0M0, T2N1M0, T3N0M0 or T3N1M0 stage, but in more advanced stages, only chemotherapy was applied without radiation therapy.

Among the 100 patients, 68 (68.0%) had T2N0M0, T2N1M0, T3N0M0 or T3N1M0 stage. We compared clinicopathologic factors and the survival rates between patients with (CRTx group) and without adjuvant CRTx (group) according to tumor stage: T2N0M0 (n = 18), T2N1M0 (n = 20), T3N0M0 (n = 10) and T3N1M0 (n = 20).

B. Methods

For the comparative analysis of the 2 groups in each stage, the following factors were analyzed: age, gender, tumor marker, blood transfusion, differentiation, vascular invasion, lymphatic invasion, perineural invasion, and resection margin. Comparisons of nominal and continuous variables were made using the Fisher's exact test (two-sided) and Mann-Whitney U test, respectively. The cumulative survival rate was calculated by the Kaplan-Meier method. For the evaluation of prognostic factors, the following factors were analyzed: age, gender, tumor marker, blood transfusion, T-classification, differentiation, vascular invasion, lymphatic invasion, perineural invasion, resection margin, and adjuvant chemoradiation therapy. We performed the Cox proportional hazard regression analyses both in the univariate and multivariate settings. A P value < 0.05 was considered statistically significant.

III. RESULTS

For the 68 patients, the 1-, 3- and 5-year disease-free survival (DFS) rates were 75.7%, 49.6% and 49.6%, respectively, and the 1-, 3- and 5-year disease-specific survival (DSS) rates were 81.0%, 61.9% and 58.7%, respectively. Both DFS (P = 0.018) and DSS (P = 0.006) were significantly different between TNM stages (Fig. 1).

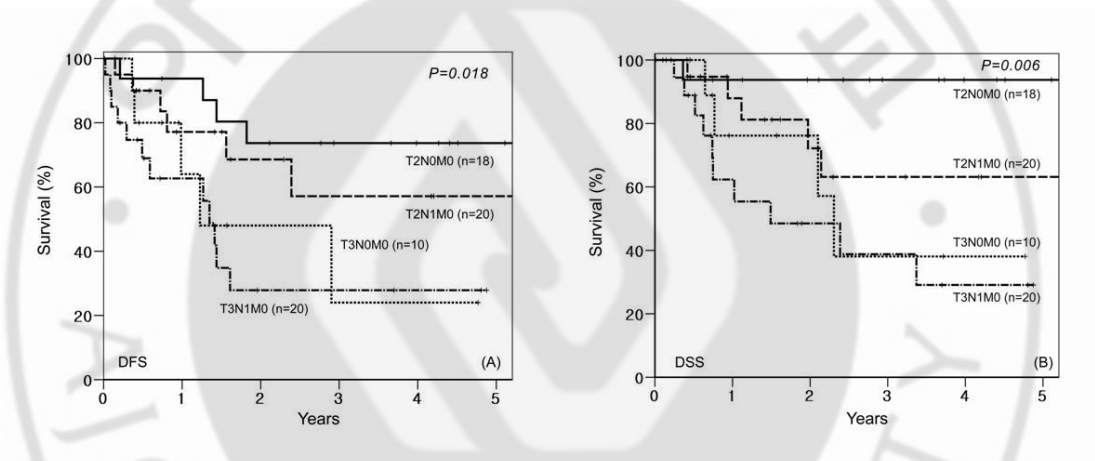

Fig. 1. Survival curves according to tumor stage in 68 patients with T2N0M0, T2N1M0, T3N0M0 or T3N1M0 stage. (A) disease-free survival (DFS). (B) disease-specific survival (DSS).

Among the 68 patients with T2/T3 classifications, 40 (58.8%) received adjuvant chemotherapy (5-fluorouracil in 35 patients [87.5%]; cisplatin + capecitabine in 3 patients [7.5%]; gemcitabine in 2 patients [5.0%]) concurrently with radiation therapy (dosage, 45 Gy in 25 fractions for 25 days). For 5-fluorouracil-based regimen which was the most commonly used radiosensitizer in our study, 5-fluorouracil was administered intravenously

on days 1, 2, 3 and on days 23, 24, 25 at a fixed dose of 500 mg/m^2 during radiation therapy period.

A. Comparative analysis of 18 patients with T2N0M0 stage

(NCRTx, n = 11; CRTx, n = 7)

Clinicopathologic factors did not show any significant differences between the 2 groups (Table 1).

Recurrence developed in 4 of the 18 patients with T2N0M0 stage; 2 (18.2%) of the 11 patients from the NCRTx group (2 recurrences in the liver, 3 and 23 months after surgery, respectively) and 2 (28.6%) of the 7 patients from the CRTx group (2 recurrences in peritoneum, after 16 and 18 months after surgery, respectively), but the DFS rate showed no statistical significance between the 2 groups ($P = 0.687$).

The DSS rate showed no statistical significance either because there was only 1 disease-specific death in the NCRTx group ($P = 0.439$).

Table 1. Comparative analysis of clinicopathologic factors in the patients with T2N0M0 stage.

Factors		NCRTx (n = 11)	CRTx (n = 7)	*P* value
		n (%)	n (%)	
Age	Median (range)	64.0 (56-70)	65.0 (45-75)	0.860
Gender	Male	8 (72.7)	4 (57.1)	0.627
	Female	3 (27.3)	3 (42.9)	
CA19-9*	≤ 37 U/ml	9 (90.0)	7 (100)	1.000
	> 37 U/ml	1 (10.0)	0 (0.0)	
Blood transfusion	No	11 (100)	6 (85.7)	0.389
	Yes	0 (0.0)	1 (14.3)	
Differentiation†	Well/Moderate	9 (90.0)	6 (85.7)	1.000
	Poor/Undifferentiated	1 (10.0)	1 (14.3)	
Vascular invasion	Negative	10 (90.9)	7 (100)	1.000
	Positive	1 (9.1)	0 (0.0)	
Lymphatic invasion	Negative	8 (72.7)	6 (85.7)	1.000
	Positive	3 (27.3)	1 (14.3)	
Perineural invasion	Negative	11 (100)	6 (85.7)	0.389
	Positive	0 (0.0)	1 (14.3)	
Resection margin	Free (R0)	10 (90.9)	6 (85.7)	1.000
	Involved (R1)	1 (9.1)	1 (14.3)	
Recurrence	case number	2	2	
(disease-free survival)	*P* value			0.687
Disease-specific death	case number	1	0	
(disease-specific survival)	*P* value			0.439

Abbreviation: NCRTx, no adjuvant chemoradiation therapy; CRTx, adjuvant chemoradiation therapy.

* Preoperative CA19-9 level (reference, ≤ 37 U/ml) of 1 patient in the NCRTx group was not available.

† The differentiation of 1 patient in the NCRTx group was not available because initial simple cholecystectomy was performed at other hospital, followed by additional extended resection at our institute.

B. Comparative analysis of 20 patients with T2N1M0 stage

(NCRTx, n = 7 and CRTx, n = 13)

Clinicopathologic factors did not show any significant differences between the 2 groups (Table 2).

Recurrence developed in 6 of the 20 patients with T2N1M0 stage; 3 (42.9%) of the 7 patients from the NCRTx group (1 recurrence in the peritoneum, 2 months after surgery; 2 recurrences in the lymph nodes, 5 and 9 months after surgery, respectively) and 3 (23.1%) of the 13 patients from the CRTx group (1 recurrence in the lymph nodes, 19 months after surgery; 2 recurrences in the peritoneum, 10 and 29 months after surgery, respectively). The DFS rate was higher in the CRTx group than in the NCRTx group ($P = 0.008$) (Fig. 2A).

There were 5 disease-specific deaths; 3 (50.0%) of the 6 patients from the NCRTx group (5, 14 and 24 months after surgery, respectively) and 2 (14.3%) of the 14 patients from the CRTx group (12 and 26 months after surgery, respectively). The DSS rate was also higher in the CRTx group than in the NCRTx group ($P = 0.003$) (Fig. 2B).

Table 2. Comparative analysis of clinicopathologic factors in the patients with T2N1M0 stage.

Factors		NCRTx (n = 7)	CRTx (n = 13)	*P* value
		n (%)	n (%)	
Age	Median (range)	67.5 (61-72)	59.5 (37-77)	0.056
Gender	Male	2 (28.6)	6 (46.2)	0.642
	Female	5 (71.4)	7 (53.8)	
CA19-9*	≤ 37 U/ml	4 (57.1)	10 (83.3)	0.305
	> 37 U/ml	3 (42.9)	2 (16.7)	
Blood transfusion	No	3 (42.9)	11 (84.6)	0.122
	Yes	4 (57.1)	2 (15.4)	
Differentiation†	Well/Moderate	6 (85.7)	6 (50.0)	0.173
	Poor/Undifferentiated	1 (14.3)	6 (50.0)	
Vascular invasion	Negative	6 (85.7)	11 (84.6)	1.000
	Positive	1 (14.3)	2 (15.4)	
Lymphatic invasion	Negative	4 (57.1)	7 (53.8)	1.000
	Positive	3 (42.9)	6 (46.2)	
Perineural invasion	Negative	5 (71.4)	7 (53.8)	0.642
	Positive	2 (28.6)	6 (46.2)	
Resection margin	Free (R0)	7 (100)	13 (100)	N-S‡
	Involved (R1)	0 (0.0)	0 (0.0)	
Recurrence	case number	3	3	
(disease-free survival)	*P* value			**0.008**
Disease-specific death	case number	3	2	
(disease-specific survival)	*P* value			**0.003**

Abbreviation: NCRTx, no adjuvant chemoradiation therapy; CRTx, adjuvant chemoradiation therapy.

* Preoperative CA19-9 level (reference, ≤ 37 U/ml) of one patient in CRTx group was not available.

† The differentiation of 1 patient in the CRTx group was not available because initial simple cholecystectomy was performed at other hospital, followed by additional extended resection at our institute.

‡ N-S: No statistics are computed.

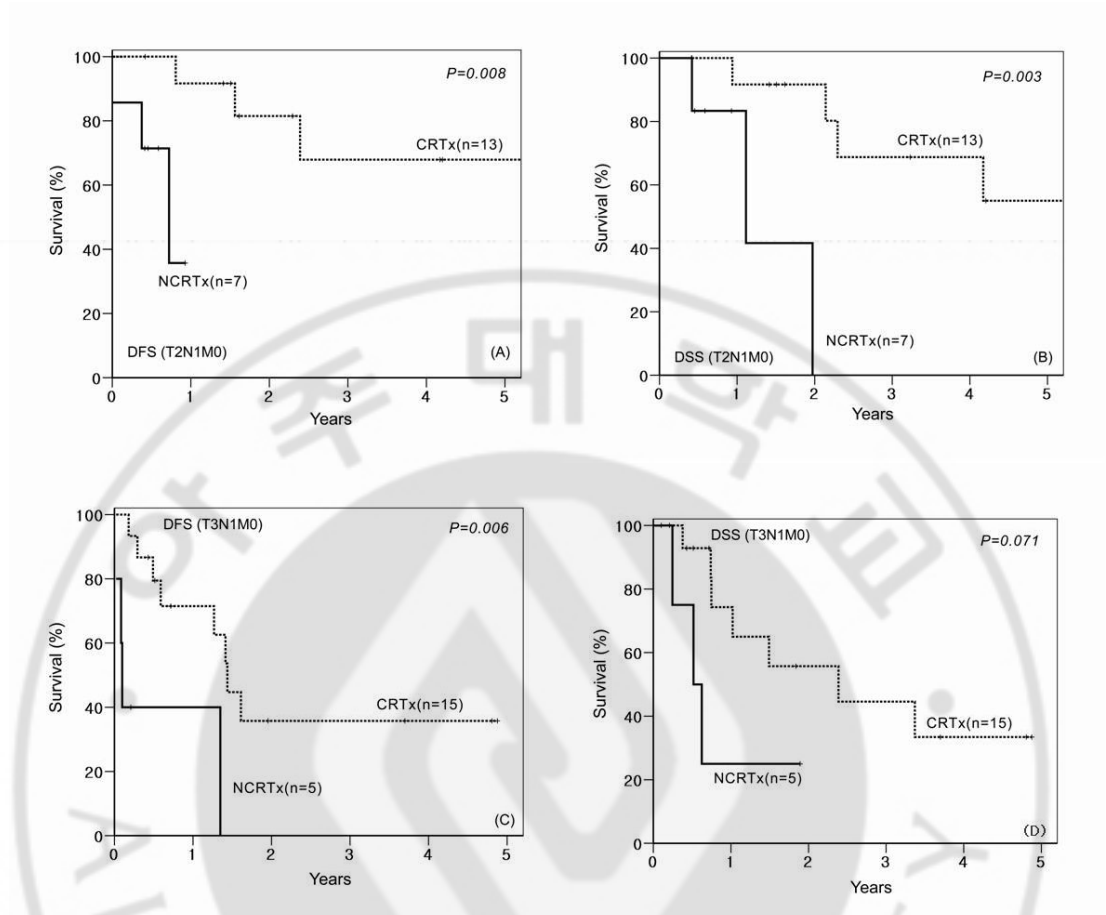

Fig. 2. Survival differences according to adjuvant chemoradiation therapy. (A) Disease-free survival (DFS) and (B) disease-specific survival (DSS) of the 20 patients with T2N1M0 stage (NCRTx, n = 7; CRTx, n = 13). (C) Disease-free survival (DFS) and (D) disease-specific survival (DSS) of the 20 patients with T3N1M0 stage (NCRTx, n = 5; CRTx, n = 15).

C. Comparative analysis of 10 patients with T3N0M0 stage

(NCRTx, n = 5 and CRTx, n = 5)

Clinicopathologic factors did not show any significant differences between the 2 groups (Table 3).

Recurrence developed in 5 of the 10 patients with T3N1M0 stage; 2 (40.0%) of the 5 patients from the NCRTx group (2 recurrences in the liver, 15 and 36 months after surgery, respectively) and 3 (60%) of the 5 patients from the CRTx group (1 recurrence in the peritoneum, 12 months after surgery; 2 recurrences in the liver, 5 months after surgery, respectively), but the DFS rate showed no statistical significance between the 2 groups (P = 0.144).

There were 4 disease-specific deaths; 1 (20.0%) out of the 5 patients from the NCRTx group (26 months after surgery) and 3 (75%) out of the 5 patients from the CRTx group (8, 10 and 28 months after surgery, respectively) but, the DSS rate showed no significant difference between the 2 groups (P = 0.104).

Table 3. Comparative analysis of clinicopathologic factors in the patients with T3N0M0 stage.

Factors		NCRTx (n = 5)	CRTx (n = 5)	*P* value
		n (%)	n (%)	
Age	Median (range)	71 (63-84)	61.0 (52-84)	0.310
Gender	Male	3 (60.0)	3 (60.0)	1.000
	Female	2 (40.0)	2 (40.0)	
CA19-9*	≤ 37 U/ml	3 (60.0)	1 (20.0)	0.524
	> 37 U/ml	2 (40.0)	4 (80.0)	
Blood transfusion	No	4 (80.0)	5 (100)	1.000
	Yes	1 (20.0)	0 (0.0)	
Differentiation	Well/Moderate	3 (60.0)	4 (80.0)	1.000
	Poor/Undifferentiated	2 (40.0)	1 (20.0)	
Vascular invasion	Negative	5 (100)	4 (80.0)	1.000
	Positive	0 (0.0)	1 (20.0)	
Lymphatic invasion	Negative	3 (60.0)	3 (60.0)	1.000
	Positive	2 (40.0)	2 (40.0)	
Perineural invasion	Negative	2 (40.0)	2 (40.0)	1.000
	Positive	3 (60.0)	3 (60.0)	
Resection margin	Free (R0)	4 (80.0)	4 (80.0)	1.000
	Involved (R1)	1 (20.0)	1 (20.0)	
Recurrence	case number	2	3	
(disease-free survival)	*P* value			0.144
Disease-specific death	case number	1	3	
(disease-specific survival)	*P* value			0.104

Abbreviation: NCRTx, no adjuvant chemoradiation therapy; CRTx, adjuvant chemoradiation therapy.

* Preoperative CA19-9 level (reference, ≤ 37 U/ml).

D. Comparative analysis of 20 patients with T3N1M0 stage
(NCRTx, n = 5 and CRTx, n = 15)

Clinicopathologic factors did not show any significant differences between the 2 groups (Table 4).

Recurrence developed in 12 of the 20 patients with T3N1M0 stage; 4 (80.0%) of the 5 patients from the NCRTx group (2 recurrences in the liver, both 1 month after surgery, respectively; 1 recurrence in the peritoneum, 2 months after surgery; and 1 recurrence in the lung, 17 months after surgery) and 8 (53.3%) of the 15 patients from the CRTx group (4 recurrences in the liver, 3, 8, 16 and 18 months after surgery, respectively; 3 recurrences in the lymph nodes, 4, 6 and 20 months after surgery, respectively; and 1 recurrence in the peritoneum, 18 months after surgery). The DFS rate was higher in the CRTx group than in the NCRTx group ($P = 0.006$) (Fig. 2C).

There were 10 disease-specific deaths; 3 (60.0%) out of the 5 patients from the NCRTx group (3, 7 and 8 months after surgery, respectively) and 7 (46.7%) out of the 15 patients from the CRTx group (5, 9, 10, 13, 19, 29 and 41 months after surgery, respectively), but the DSS rate showed no statistical significance between the 2 groups ($P = 0.071$) (Fig. 2D).

Table 4. Comparative analysis of clinicopathologic factors in the patients with T3N1M0 stage.

Factors		NCRTx (n = 5)	CRTx (n = 15)	*P* value
		n (%)	n (%)	
Age	Median (range)	63.0 (61-71)	61.0 (38-75)	0.395
Gender	Male	4 (80.0)	6 (40.0)	0.303
	Female	1 (20.0)	9 (60.0)	
CA19-9*	≤ 37 U/ml	3 (60.0)	8 (53.3)	1.000
	> 37 U/ml	2 (40.0)	7 (46.7)	
Blood transfusion	No	3 (60.0)	10 (66.7)	1.000
	Yes	2 (40.0)	5 (33.3)	
Differentiation	Well/Moderate	2 (40.0)	10 (66.7)	0.347
	Poor/Undifferentiated	3 (60.0)	5 (33.3)	
Vascular invasion	Negative	1 (20.0)	4 (26.7)	1.000
	Positive	4 (80.0)	11 (73.3)	
Lymphatic invasion	Negative	2 (40.0)	4 (26.7)	0.613
	Positive	3 (60.0)	11 (73.3)	
Perineural invasion	Negative	3 (60.0)	4 (26.7)	0.290
	Positive	2 (40.0)	11 (73.3)	
Resection margin	Free (R0)	4 (80.0)	14 (93.3)	0.447
	Involved (R1)	1 (20.0)	1 (6.7)	
Recurrence	case number	4	8	
(disease-free survival)	*P* value			0.006
Disease-specific death	case number	3	7	
(disease-specific survival)	*P* value			0.071

Abbreviation: NCRTx, no adjuvant chemoradiation therapy; CRTx, adjuvant chemoradiation therapy.

* Preoperative CA19-9 level (reference, ≤ 37 U/ml).

E. Prognostic factor analysis for lymph node negative T2/T3 stage (T2/T3N0, n = 28)

For the prognostic factor analysis of DFS in patients with lymph node negative T2/T3 GB cancer, lymphatic invasion (P = 0.005) and perineural invasion (P = 0.013) were significant in univariate analysis. NCRTx did not attain significance (P = 0.314). By multivariate analysis, the 2 factors were also proved to be independent prognostic factors (Table 5).

For the prognostic factor analysis of DSS, T3-classification (P = 0.048), differentiation (P = 0.016), lymphatic invasion (P = 0.041) and perineural invasion (P = 0.030) were significant in univariate analysis. NCRTx did not attain significance (P = 0.342). By multivariate analysis, only differentiation was proved to be an independent prognostic factor (Table 5).

F. Prognostic factor analysis for lymph node positive T2/T3 stage (T2/T3N1, n = 40)

For the prognostic factor analysis of DFS in patients with lymph node positive T2/T3 GB cancer, age > 60 (P = 0.039), T3-classification (P = 0.047) and NCRTx (P < 0.001) were significant by univariate analysis. By multivariate analysis, T3-classification and NCRTx were proved to be independent prognostic factors (Table 6).

For the prognostic factor analysis of DSS, age > 60 (P = 0.047) and NCRTx (P = 0.003) were significant by univariate analysis. By multivariate analysis, only NCRTx was proved to be an independent prognostic factor (Table 6).

Table 5. Significant factors for disease-free and disease-specific survival of T2/T3N0 GB cancer by multivariate analysis.

	Factors		Number	%	HR (95% CI)	*p* value
DFS	Lymphatic invasion	-	20	71.4	10.221	**0.009**
		+	8	28.6	(1.810-57.725)	
	Perineural invasion	-	21	75.0	5.252	**0.036**
		+	7	25.0	(1.116-24.713)	
DSS	Differentiation*	Well/Moderately	22	81.5	10.519	**0.033**
		Poorly/Undifferentiated	5	18.5	(1.212-91.302)	

Abbreviation: DFS, Disease-free survival; DSS, Disease-specific survival; HR, Hazard ratio; CI, Confidence interval.

*Tumor differentiation of 1 patient was not available.

Table 6. Significant factors for disease-free and disease-specific survival of T2/T3N1 GB cancer by multivariate analysis.

	Factors		Number	%	HR (95% CI)	*p* value
DFS	T-classification	T2	20	50.0	2.835	**0.040**
		T3	20	50.0	(1.046-7.658)	
	Adjuvant CRTx	Yes	11	27.5	6.245	**0.003**
		No	29	72.5	(1.836-21.243)	
DSS	Adjuvant CRTx	Yes	11	27.5	3.970	**0.032**
		No	29	72.5	(1.127-13.993)	

Abbreviation: DFS, Disease-free survival; DSS, Disease-specific survival; CRTx, Chemoradiation therapy; HR, Hazard ratio; CI, Confidence interval.

IV. DISCUSSION

Even after radical resection of GB cancer, not only locoregional recurrence but also distant metastasis is common, especially in advanced stages (Kresl et al., 2002; Jarnagin et al., 2003; de Aretxabala et al., 2006; Gourgiotis et al., 2008; Hueman et al., 2009). Thus, the multidisciplinary approach in addition to surgical resection may be necessary to treat advanced GB cancers. For these reasons, a combination of adjuvant systemic chemotherapy with radiation therapy is mandatory to decrease locoregional recurrence and distant metastasis after surgical resection of GB cancer.

In a previous retrospective analysis of the SEER database, adjuvant radiation therapy was associated with good survival only in patients with locally advanced GB cancer or GB cancer accompanied by a regional disease (Mojica et al., 2007). Another study of SEER database made a prediction model which predicts that adjuvant radiation therapy provides a survival benefit in node-positive or ≥ T2 GB cancer (Wang et al., 2008). Some previous studies on concurrent chemoradiation therapy for GB cancer have been reported (Kresl et al., 2002; Czito et al., 2005; Gold et al., 2009). However, there is still no established standard regimen of adjuvant chemotherapy for GB cancer (Treadwell and Hardin, 1976; Smoron, 1977; Hanna and Rider, 1978; Kopelson and Gunderson, 1983). Traditionally, 5-fluorouracil-based chemotherapy regimen has been used as an adjuvant therapy for biliary tract malignancies including GB cancer (Kresl et al., 2002; Takada et al., 2002; de Aretxabala et al., 2006; Reid et al., 2007). Recently, gemcitabine-, capecitabine, or S-1-based regimens have been tried, and several studies have demonstrated somewhat promising

results from GB cancer (Penz et al., 2001; Ueno et al., 2004; Alberts et al., 2005; Knox et al., 2005; Koeberle et al., 2008). However, few comparative analyses of treatments between detailed TNM stages of GB cancer have been reported. Well designed prospective randomized case-control studies are needed to confirm the results of these new trials.

Because of a relative paucity of GB cancer and lack of specific symptoms or signs in its early stage of it, surgical resection was performed on only 100 patients for 9 consecutive years at the National Cancer Center of Korea. Patients with stages less than T2N0M0 did not undergo adjuvant therapy. None of the patients with T1 classification showed lymph node metastasis in our series, and the number of patients with stages more than T3N1M0 was too small to be enrolled for this comparative analysis. Sixty-eight patients (68.0%) showed T2 or T3 classification without distant metastasis.

We evaluated patients' survival using disease-specific survival rather than overall survival to minimize selection bias effect from the following characteristics: (1) most of GB cancers developed in patients at an old age, (2) many of them had comorbidities such as other malignancies, cardiovascular disease and/or diabetes mellitus, and (3) the candidates for adjuvant CRTx should be under an appropriate general condition in order to receive this cytotoxic therapy. For the evaluation of prognostic factors, the TNM-specific 4 stages (T2N0, T2N1, T3N0 and T3N1) were reassembled into 2 stages according to the lymph node metastasis regardless of T-classification (T2/T3N0 and T2/T3N1), since the numbers of patients in each stage were relatively small. In patients with lymph node-positive T2/T3 (T2/T3N1) GB cancers, adjuvant chemoradiation therapy was an independent prognostic

factor for both DFS and DSS, while adjuvant chemoradiation therapy did not gain any survival benefit in lymph node negative T2/T3 (T2/T3N0) GB cancers.

Although T3N0M0 tumors belong to stage IIA of the sixth AJCC/UICC staging system and T2N1M0 tumors belong to stage IIB, the overall prognosis was poorer for T3N0M0 tumors (stage IIA) than for T2N1M0 tumors (stage IIB) in our series.

Neither DFS nor DSS showed any significant difference between the 2 groups in lymph node-negative T2N0M0 and T3N0M0 stages (Tables 1 and 3). For T2N1M0 stage, both DFS (P = 0.001) and DSS (P = 0.002) were higher in the CRTx group than in the NCRTx group (Table 2). However, for T3N1M0 stage, only DFS was higher in the CRTx group than in the NCRTx group (P = 0.006), and DSS did not show significant difference (P = 0.071) (Table 4).

Clinicopathologic profiles were not different between the 2 groups in any stage (Tables 1, 2, 3 and 4). Our study demonstrated that adjuvant chemoradiation therapy conferred no DFS or DSS benefit on patients with lymph node-negative T2 or T3 GB cancer. However, adjuvant chemoradiation therapy conferred DFS benefit on patients with lymph node-positive T2 and T3. Our adjuvant therapy reduced recurrences of GB cancer following resection in lymph node–positive patients. However, adjuvant chemoradiation therapy conferred DSS benefit on patients with T2N1M0 tumors but not on those with T3N1M0 tumors.

V. CONCLUSION

In summary, effective adjuvant therapy is necessary to improve treatment outcome of GB cancer following resection. Most patients (87.5%) in this study received 5-fluorouracil-based chemotherapy. The results of this study suggest that adjuvant chemoradiation therapy may be effective in the treatment of lymph node-positive T2/T3 GB cancers after surgical resection. Further randomized controlled studies with a larger sample size and with a new chemotherapy regimen are needed to confirm similar therapeutic effects on other stage tumors.

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– 국문요약 –

담낭암의 보조 화학방사선치료

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담낭암은 위장관계에서 상대적으로 드문 암이다. 수술적 절제 후 보조 화학방사선치료의 지침이 아직도 정립되지 않았다. 본 연구의 목표는 담낭암의 TNM 병기에 따른 보조 화학방사선치료의 효과를 밝혀보고자 함이다. 2001 년 3 월부터 2009 년 3 월까지 100 명의 담낭암환자가 수술적 절제를 받았다. 환자들을 TNM 병기에 따라 분류하였고, 보조 화학방사선치료 여부에 따라 더 세분하였다. 임상/병리적 인자들, 재발 그리고 생존에 대한 후향적 연구를 시행하였다. T2N0M0, T2N1M0, T3N0M0 와 T3N1M0 병기의 환자들이 본 연구에 등록되었다. 그 4 병기들 중 임파선전이가 없는 병기(T2N0M0 와 T3N0M0)에서는 보조 화학방사선치료를 시행하는 것이 생존에 이득이 없었다. 반면에, 임파선전이가 있는 병기(T2N1M0 와 T3N1M0)에서는 무병생존율에서, 그리고 그 중 T2N1M0 병기에서는 질병특이생존에서 이득을 보였다. 임파선전이가 있는 T2/T3 담낭암에서 보조 화학방사선치료가 생존의 독립적인 예후인자였다. 보조 화학방사선치료는 임파선전이가 있는 T2/T3 담낭암환자의 수술 후 추천되는 치료방법이라 할 수 있다.

핵심어 : 담낭암, 절제술, 보조 치료, TNM 병기, 예후