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Research Article

A Retrospective Analysis of The Long-Term Operative Outcomes for T2 Carcinoma of Gallbladder

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Abstract

Background: Different treatments have been applied for T2 Gallbladder Carcinoma (GBC) ranging from simple cholecystectomy to extended resection which includes liver resection and lymph node dissection. The treatment outcomes of different operative approaches still need further evaluation.

Methods: This was a retrospective study to evaluate the long-term operative outcomes of different surgical treatments for T2 GBC, addressing the impact of different components of surgery, with special regard to T2a and T2b subgroups.

Results: Between April 2003 and February 2022, 42 consecutive histologically proven T2 GBC (21 T2a and 21 T2b) were identified. Six patients received cholecystectomy only,12 patients received extended resection after initial cholecystectomy and 24 patients received single stage extended resection. Patients with cholecystectomy only had significantly more recurrent disease and worse 5-Year Disease-Free Survival (DFS) as compared with patients with extended surgery (P=0.023 and 0.007 respectively). There was no difference in disease recurrence and survival outcomes whether the extended resection was done as second stage or as single stage. The incidence of liver micrometastasis was 2.8% for those who had liver resection done. Lymph node metastasis occurred in 25.0% of patients and was associated with worse 5-year DFS (14.8% vs 62.1%, P=0.009). Multivariable Cox regression analysis showed that lymph node metastasis and extended resection were predictors for DFS.

Conclusion: Extended resection instead of cholecystectomy alone is necessary for both T2a and T2b GBC to achieve long term survival. Lymph node dissection is essential whilst the role of liver resection for T2a tumours deserves more investigation.

Keywords: Gallbladder Carcinoma; Liver Resection; Lymph Node Dissection; T2 Stage

Introduction

Gallbladder Carcinoma (GBC) remains a rare disease except in some geographical areas like central and south America, central and eastern Europe, and Japan [1]. Patients with GBC usually present late as symptoms usually occur at advanced stage. Earlier disease is usually detected incidentally on imaging or after cholecystectomy for other indications commonly gallstone disease. Incidentally detected GBC after routine cholecystectomy was reported to be 0.6-1.6% [2,3]. The disease is regarded as early if the cancer cells are limited to the lamina propria (T1a) or just invade to the muscle layer (T1b) [4]. T2 disease implies the tumour has invaded through the muscle layer to reach the perimuscular connective tissue. Recently T2 is further classified to T2a if tumour locates at peritoneal side while T2b for tumour locates at liver side [5,6]. If tumour perforates the serosa or directly invades the liver, it becomes T3 stage. In T4 disease, the tumour invades to main portal vein or hepatic artery or 2 or more extrahepatic organs. T3 and T4 disease carry a dismal prognosis as even en bloc adjacent organ resection is permissible, this is not associated with improved long-term survival [7]. It is the tumour biology and stage rather than the extent of resection more important predictors for survival [8]. Curative surgery is only possible for earlier stage disease. Currently, simple cholecystectomy is considered as an adequate treatment for T1a disease. For T1b disease that is discovered after cholecystectomy, it is still controversial whether reoperation for liver resection and porta lymph node dissection is beneficial for survival. For T2 disease, reoperation is recommended to achieve disease clearance and to prolong survival. Study has shown that T2a had better prognosis than T2b [9]. Whether T2a disease desires reoperation after previous cholecystectomy yet to be answered. This study aims to assess the long-term operative outcomes for T2 GBC, with special reference to any difference in survival between cholecystectomy alone and extended surgery which includes liver resection, Lymph Node (LN) dissection with or without bile duct resection. Subgroup analysis is also made between T2a and T2b disease to evaluate any prognostic difference.

Methods

This was a retrospective study based on the pathological diagnosis of GBC on resected specimens from two hospitals (Prince of Wales Hospital and North District Hospital within the New Territories East Cluster of Hong Kong). The study period was between April 2003 and February 2022. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki. Informed consent was waived due to retrospective nature of study. Patient confidentiality and privacy rights were all protected. During the study period, 83 consecutive patients were identified to have GBC on resected specimens, which were all only surgically treated histologically confirmed cases of GBC. The number of patients in different T and M staging was as follows: 4 T1a, 5 T1b, 21 T2a, 21 T2b, 20 T3, 3 T4 and 9 M1 disease. T2 stage was the commonest stage for operated GBC in our centre and formed the patient cohort for the present study.In case of uncertainty of histological diagnosis or T staging of disease, the histology slides would be reviewed by a designated pathologist (HHWL) who was specialised on hepatobiliary pathology. Only T2 stage GBC was included in this study to make interpretation of result and recommendation of treatment for this intermediate stage of disease more precise. Besides, this was also the commonest stage of disease in GBC. The demographic data, operation details and follow-up outcomes were retrieved from a prospectively collected electronic database. No patient was lost to follow-up. Missing data was drop out for analysis. The study was approved by the Joint Chinese University of Hong Kong - New Territories East Cluster Clinical Research Ethics Committee (CREC Ref No. 2022.320).

Surgical Approach

For patients with suspected GBC, pre-operative imaging including Computed Tomography (CT) and Positron Emission Tomography (PET) were performed for delineation of lesion and staging of disease. During surgery, diagnostic laparoscopy was performed first to rule out liver or peritoneal metastasis before contemplating radical resection. Usually gallbladder would be removed first and together with the cystic duct margin these were sent for frozen section. Extended resection was defined as including liver resection (gallbladder fossa wedge resection or segment 4b/5 resection) and porta LN dissection (resection of cystic LNs, common bile duct LNs, LNs around hepatoduodenal ligament and the posterior superior pancreaticoduodenal LNs). It was performed if GBC stage T1b or above was found. Bile duct resection with Roux-en-Y hepatojejunostomy reconstruction was performed if the cystic duct margin close to common duct was involved. Occasionally pancreaticoduodenectomy was required if gross peripancreatic head LN involvement was noted. For patients who were found to have incidental GBC stage T1b or above after cholecystectomy, staging of disease was performed with PET CT. If there was no distant metastasis, surgery which included diagnostic laparoscopy, liver resection, cystic duct stump or bile duct resection with porta LN dissection was offered. If previous cholecystectomy was done laparoscopically, port site excision was also performed.Adjuvant chemotherapy was not given for T2 disease. Patients were regularly follow-up in outpatient clinic. Ultrasound (USG) was performed every 6 months for first two years and then yearly. Tumour markers including CEA and CA19.9 were monitored regularly. CT or PET would be performed when recurrent disease was suspected. Patients would be referred to oncologist for consideration of systemic chemotherapy if recurrent disease was diagnosed.

Statistical Analysis

Continuous variables were expressed as median (range), whilst categorical variables were presented in number (percentage). Mann-Whitney U test was used in continuous variable, Chi-square test or Fisher's exact test was used in categorical variable. Overall Survival (OS) was calculated from time of last operation to date of death or last available follow-up. Disease-Free Survival (DFS) was calculated from time of last surgery to date of diagnosis of first disease recurrence or last available follow-up. Survival curves were calculated by Kaplan-Meier method and was compared with the log-rank test. Univariate and multivariable analysis were performed by Cox regression to identify the risk factors of OS and DFS, with proportional hazards assumptions assessed. Those variables with *P*-values less than 0.1 in univariate analysis were used in multivariable analysis. IBM SPSS version 27 was used for statistical analysis, $P< 0.05$ was considered as statistically significant.

Results

Out of the 42 patients with T2 GBC, 6 patients had just cholecystectomy done while 36 patients had extended resection. Two patients had bile duct resection and hepaticojejunostomy due to involvement of cystic duct margin by tumour. Two other patients had primary diagnosis of choledochal cyst requiring bile duct resection and hepaticojejunostomy. Two further patients had pancreaticoduodenectomy done due to massive peripancreatic head lymphadenopathy. The follow-up period was 36.8 months (1.1-121.8) for cholecystectomy alone group versus 44.8months (0.2-252.7) for extended resection group (P=0.408). Out of the 36 patients with extended surgery, 12 patients had the extended resection done at second operation after initial cholecystectomy showing T2 disease. For the 6 patients with only cholecystectomy done, 5 patients were considered too old or too high risk for extended surgery while one patient refused re-operation. The patient demographics, pathology finding and survival outcomes of these 6 patients were compared with the 36 patients who had extended surgery (Table 1). Patients with cholecystectomy only were older and as expected had less LNs removed. They had significantly more recurrent disease (83.3% vs 30.6%, P=0.023) and worse 5-year DFS (16.7% vs 58.9%, P=0.007) as compared with patients with extended surgery. There was no difference on site of recurrent disease. When separate analysis was done for T2a and T2b subgroups, cholecystectomy alone still had worse 5-year DFS in T2a and more recurrent disease in T2b subgroups (P<0.001 and =0.035 respectively) (Table 2). On the contrary, there was no difference in disease recurrence and survival outcomes between the 24 patients with single stage extended surgery and the 12 patients with second stage extended surgery after previous cholecystectomy (Table 3).When the 21 patients with T2a disease were compared with the other 21 patients with T2b disease, there was no difference in patient demographics and disease characteristics (Table 4). One patient (2.8%) was found to have residual disease in liver after extended surgery following cholecystectomy showing T2b GBC. The recurrence rate for T2a disease was 28.6%, which was lower than T2b disease (47.6%), but it was not statistically significant (P=0.204). The 5-year OS and DFS for T2a were 63.5% and 58.7% respectively, while the corresponding values were 52.9% and 47.1% for T2b, there was no significant difference (P= 0.429 and 0.224 respectively) (Table 4 and Figure 1). Nine patients (25.0%) had LN metastasis for those with LN dissection performed. All of them had either one or two positive LNs (all N1 stage). Three patients had positive nodes along hepatoduodenal ligament only, five patients had further nodal involvement in posterosuperior pancreatic head and one last patient had further LN spread along coeliac trunk and superior mesenteric artery. When the nine patients with LN metastasis compared with 33 patients without LN metastasis, there was no difference in patient demographics, tumour size and biology. There was no difference in tumour recurrence and OS but node positive group had significantly worse 5-year DFS (14.8% vs 62.1%, P=0.009) (Figure 2). On univariate and multivariable analysis for OS and DFS, no predictor for OS was found. For DFS, LN metastasis was a negative predictor while extended resection was a positive predictor for survival (Table 5). T2a and T2b stages were not predictors for both OS and DFS.

	Cholecystectomy only (n = 6)	Extended resection	P-value
Age	84 (72 - 88)	68 (40 - 87)	0.002*
Sex (M : F)	3 (50.0%) : 3 (50.0%)	10 (27.8%) : 26 (72.2%)	0.353
ASA 1 2 3	0 (0.0%) 6 (100.0%) 0 (0.0%)	5 (13.9%) 25 (69.4%) 6 (16.7%)	>0.999 0.172 0.569
Pre-op INR	1.01 (0.92 - 1.10)	0.99 (0.86 - 1.29)	0.586
Pre-op albumin	34 (31 - 44)	39 (12 - 48)	0.235
Pre-op bilirubin	6.5 (3 - 29)	9.5 (5 - 181)	0.332
Pre-op creatinine	90.5 (62 - 114)	71 (46 - 163)	0.12
Coexist gallstone	4 (66.7%)	24 (66.7%)	>0.999
Size of tumor (cm)	2.8 (1.6 - 6.5)	3.5 (0.6 - 10.0)	0.594
Stage T2a T2b	2 (33.3%) 4 (66.7%)	19 (52.8%) 17 (47.2%)	0.663 0.663
Differentiation Well Moderate Poor N/A	1 (16.7%) 4 (66.7%) 0 (0.0%) 1 (16.7%)	3 (8.3%) 26 (72.2%) 2 (5.6%) 5 (13.9%)	0.474 >0.999 >0.999 >0.999
LVI (Yes)	2 (33.3%)	7 (19.4%)	0.593
PNI (Yes)	2 (33.3%)	6 (16.7%)	0.319
Liver micro metastasis No Yes	N/A	35 (97.2%) 1 (2.8%)	>0.999 >0.999
LN metastasis	0 (0.0%)	9 (25.0%)	0.312
Number of LN resected	0 (0 - 2)	4 (1 - 14)	<0.001*
Number of LN metastasis	0 (0 - 0)	0 (0 - 2)	0.35
90-day mortality	1 (16.7%)	2 (5.6%)	0.378
Morbidity	2 (33.3%)	11 (30.6%)	>0.999
Follow-up (months)	36.8 (1.1-121.8)	44.8 (0.2-252.7)	0.408
Recurrence	5 (83.3%)	11 (30.6%)	0.023*
Site of recurrence Liver Lymph node Peritoneum Lung Adnexa Bone	3 (50.0%) 3 (50.0%) 2 (33.3%) 0 (0.0%) 0 (0.0%) 0 (0.0%)	6 (16.7%) 6 (16.7%) 2 (5.6%) 2 (5.6%) 1 (2.8%) 1 (2.8%)	0.101 0.101 0.091 >0.999 >0.999 >0.999
Overall survival 1-yr 3-yr 5-yr	66.7% 50% 33.3%	86% 74.6% 62.5%	0.083
Disease-free survival 1-yr 3-yr 5-yr	50% 16.7% 16.7%	74.8% 62.9% 58.9%	0.007*

Table 1: Patient demographics, histology finding and survival outcome between patients with cholecystectomy alone and patients with extended resection.

ASA: American Society of Anaesthesiologists; N/A: not available; LVI: lympho vascular invasion; PNI: perineural invasion; LN: lymph node; * Statistically significant

	T2a GBC			T2b GBC		
	Cholecystectomy only (n = 2)	Extended resection (n = 19)	P-value	Cholecystectomy only (n = 4)	Extended resection (n = 17)	P-value
Recurrence	1 (50.0%)	5 (26.3%)	0.5	4 (100.0%)	6 (35.3%)	0.035*
Site of recurrence Liver Lymph node Peritoneum Lung Adnexa Bone	0 (0.0%) 0 (0.0%) 1 (50.0%) 0 (0.0%)	2 (10.5%) 4 (21.1%) 1 (5.3%) 1 (5.3%)	>0.999 >0.999 0.186 >0.999	3 (75.0%) 3 (75.0%) 1 (25.0%) 0 (0.0%) 0 (0.0%) 0 (0.0%)	4 (23.5%) 2 (11.8%) 1 (5.9%) 1 (5.9%) 1 (5.9%)	0.088 0.028* 0.352 >0.999 >0.999 >0.999
Follow-up (months)	32.7 (1.2 - 64.3)	40.5 (6.9 - 252.7)	0.4	36.8 (11.3 - 121.8)	51.8 (0.2 - 215.2)	0.635
Overall survival 1-yr 3-yr 5-yr	50% 50% 50%	89.5% 72.7% 64.6%	0.443	75% 50% 25%	82.4% 76.5% 60.2%	0.152
Disease-free survival 1-yr 3-yr 5-yr	0% 0% 0%	84.2% 73% 64.9%	<0.001*	75% 25% 25%	64.7% 52.3% 52.3%	0.304

Table 2: Survival outcome between patients with cholecystectomy alone and patients with extended resection stratified to T2a and T2b diseases; * Statistically significant

	Single stage (n = 24)	Two-stage (n = 12)	P-value
Recurrence	9 (37.5%)	2 (16.7%)	0.268
Site of recurrence Liver Lymph node Peritoneum Lung Adnexal Bone	4 (16.7%) 5 (20.8%) 2 (8.3%) 2 (8.3%) 1 (4.2%) 1 (4.2%)	2 (16.7%) 1 (8.3%) 0 (0.0%) 0 (0.0%) 0 (0.0%) 0 (0.0%)	>0.999 0.64 0.543 0.543 >0.999 >0.999
Follow-up time (months)	31.3 (0.2 - 172.0)	73.7 (8.3 - 252.7)	0.057
Overall survival 1-yr 3-yr 5-yr	66.7% 58.3% 47.1%	100% 100% 88.9%	0.121
Disease-free survival 1-yr 3-yr 5-yr	64.7% 52.3% 52.3%	91.7% 82.5% 82.5%	0.225

Table 3: Survival outcome between patients with single stage extended resection and second stage extended resection after previous cholecystectomy alone.

	T2a (N = 21)	T2b (N = 21)	P-value
Age	71 (46 - 88)	69 (40 - 87)	0.588
Sex (M : F)	7 (33.3%) : 14 (66.7%)	6 (28.6%): 15 (71.4%)	0.739
ASA 1 2 3	4 (19.0%) 15(71.4%) 2(9.5%)	1 (4.8%) 16 (76.2%) 4 (19.0%)	0.343 0.726 0.663
Pre-op INR	0.98 (0.86 - 1.20)	1.01 (0.88 - 1.29)	0.166
Pre-op Albumin	39 (32 - 48)	39 (12 - 46)	0.613
Pre-op Bilirubin	8 (5 - 148)	9 (3 - 181)	0.405
Pre-op Creatinine	74 (56 - 163)	72 (46 - 129)	0.85
Liver micro metastasis No Yes No liver resection	19(90.5%) 0(0.0%) 2(9.5%)	16 (76.2%) 1(4.8%) 4(19.0%)	0.41 >0.999 0.663
Coexist gallstone	14 (66.7%)	14 (66.7%)	>0.999
Size of tumor (cm)	3.5 (0.6 - 7.0)	3.5 (0.6 - 10.0)	0.891
Differentiation Well Moderate Poor NA	3(14.3%) 13(61.9%) 1(4.8%) 4(19.0%)	1(4.8%) 17(81.0%) 1(4.8%) 2(9.5%)	0.606 0.172 >0.999 0.663
LVI (Yes)	4 (19.0%)	5 (23.8%)	>0.999
PNI (Yes)	3 (14.3%)	5 (23.8%)	0.697
LN metastasis	5 (23.8%)	4 (19.0%)	>0.999
Number of LN resected	4 (0 - 14)	2 (0 - 7)	0.071
Number of LN metastasis	0 (0 - 2)	0 (0 - 2)	0.686
Recurrence	6 (28.6%)	10 (47.6%)	0.204
Site of recurrence Liver Lymph node Peritoneum Lung Adnexal Bone	2(9.5%) 4(19.0%) 2(9.5%) 1(4.8%) 0(0.0%) 0(0.0%)	7 (33.3%) 5 (23.8%) 2 (9.5%) 1 (4.8%) 1 (4.8%) 1 (4.8%)	0.13 >0.999 >0.999 >0.999 >0.999 >0.999
Follow-up (months)	40.5 (1.2 - 252.7)	49.8 (0.2 - 215.2)	0.97
Overall survival 1-yr 3-yr 5-yr	85.7% 70.6% 63.5%	81% 71.4% 52.9%	0.429
Disease-free survival 1-yr 3-yr 5-yr	76.2% 66% 58.7%	66.7% 47.1% 47.1%	0.224

Table 4: Patient demographics, histology finding and survival outcome between patients with T2a and T2b tumors.

	Univariate		Multivariable	
Variable	Hazard ratio (95% confidence interval)	P-value	Hazard ratio (95% confidence interval)	P-value
Age	1.026 (0.983, 1.072)	0.234		
Sex M F (reference)	 1.758 (0.756, 4.086) -	 0.19		
Diabetes mellitus Yes No (reference)	0.833 (0.301, 2.307) -	 0.726		
ASA ≥ 3 < 3 (reference)	 0.842 (0.245, 2.886) -	 0.784		
T stage T2a T2b (reference)	 0.598 (0.258, 1.382) -	 0.229		
Size of tumor (cm)	0.845 (0.643, 1.110)	0.226		
Differentiation Well Moderate/Poor (reference)	 0.685 (0.156, 2.995) -	 0.615		
LVI Yes No (reference)	 1.130 (0.418, 3.053) -	 0.81		
PNI Yes No (reference)	 1.725 (0.636, 4.682) -	 0.284		
LN metastasis Yes No (reference)	 3.284 (1.280, 8.426) -	 0.013*	 4.886(1.762,13.549) -	 0.002*
Extended resection Yes No (reference)	 0.298 (0.117, 0.762) -	 0.011*	 0.195(0.070,0.543) -	 0.002*-

Table 5: Univariate and multivariable analysis for disease-free survival. LVI: lymphovascular invasion; PNI: perineural invasion; LN: lymph node; *Statistically significant

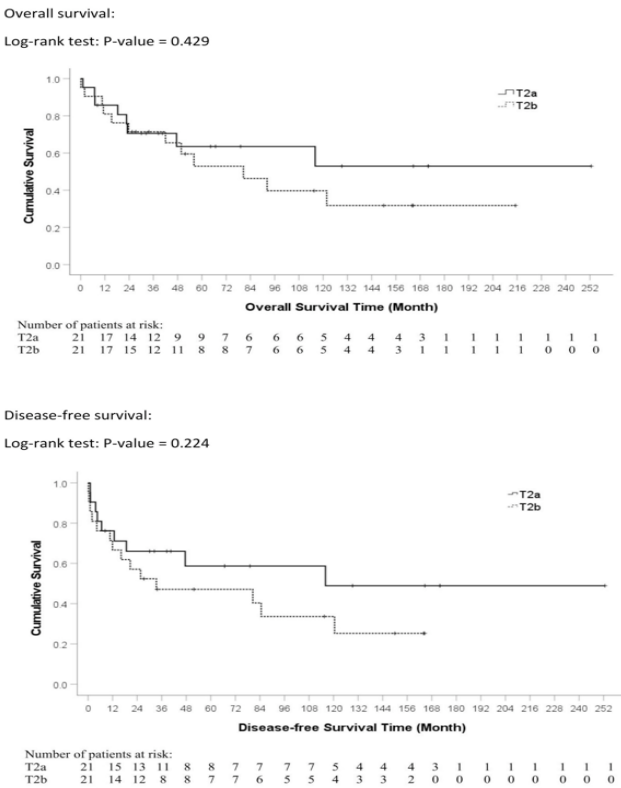


Figure 1: Overall and disease-free survival between T2a and T2b disease after surgery.

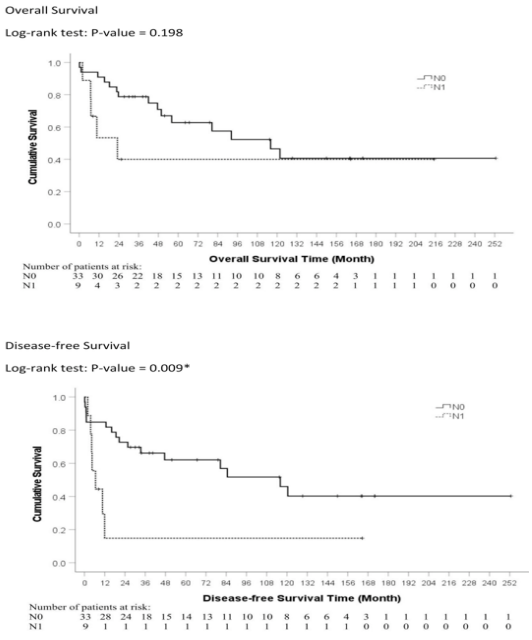


Figure 2: Overall and disease-free survival between patients with or without lymph node metastasis.

Discussion

For early GBC, simple cholecystectomy has been regarded as an adequate treatment for T1a disease, as the likelihood of residual disease or lymph node metastasis was exceedingly small (<5%) [10,11]. The optimal surgical extent for T1b remains controversial, while some studies showed a survival benefit with extended resection [12,13] some other studies showed no difference in survival after cholecystectomy alone versus extended surgery [14,15]. Currently the United States National Comprehensive Cancer Network (NCCN) guidelines indorse radical resection with portal lymph node dissection for T1b tumour whereas the Japanese guidelines recommend simple cholecystectomy [16,17]. A recent meta-analysis showed that simple and extended cholecystectomy showed comparable survival outcomes in T1b GBC [18]. While the value of extended resection for T1b tumour is still under question, this study showed that simple cholecystectomy appeared not enough for clearance of disease in T2 GBC. Despite a comparable biological behaviour of tumour which included tumour size, proportion of T2a and T2b tumours, grade of differentiation of tumour, presence of lymphovascular invasion and perineural invasion between patients with cholecystectomy alone and those with extended surgery, patients with extended surgery demonstrated significantly less tumour recurrence and better 5-year DFS (Table1). The group with cholecystectomy alone was significantly older (84 years vs 68 years), this just revealed the fact that younger patients were more readily offered repeated extended surgery. This implies that repeated radical surgery should by all means be offered to patients if feasible for the survival benefit. Such benefit was comparable to patients who had single stage extended resection (Table 3). The survival and oncological benefits were seen in both T2a and T2b diseases (Table 2), thus even T2a stage should receive extended resection.As part of the extended resection, LN dissection is essential as the incidence of LN metastasis occurred in one quarter of patients. This was comparable with a figure of 31% as found by another study [19]. Of note, apart from usual nodal involvement in hepatoduodenal ligament, further LN metastasis was found in peripancreatic head region and one patient at coeliac trunk and superior mesenteric artery. Kishi et al has already pointed out that posterior superior pancreatic head LNs were most frequently involved nodes outside hepatoduodenal ligament [20]. Thus routine resection of LNs at peripancreatic head region should also be performed.On the other hand, the incidence of liver micrometastasis was only 2.8% who had liver resection done. This occurred in a patient with T2b tumour. This is in contrary to another study that the incidence was reported to be as high as 33%.9 Whilst most surgeons would include liver resection as part of extended resection for T2 tumours, many others advocated this might not be necessary in T2a tumour as they could not show any survival benefit [21-24]. One study showed that liver resection had marginally superior 5-year DFS than simple cholecystectomy in both T2a and T2b disease [25], a more recent meta-analysis showed that the perioperative and long-term outcomes of hepatectomy and no hepatectomy approaches were comparable in T2 GBC [26]. A more recent retrospective study even suggested that liver resection has limited prognostic value for T2 GBC even for T2b tumors [27]. It appears that LN clearance is a more important element than liver resection in extended resection to provide survival benefit.The latest AJCC 8th edition staging for GBC has subdivided previous T2 stage into T2a and T2b,5 when we analysed the operative outcomes between T2a and T2b subgroups in this study, there was no significant difference in tumour recurrence or OS and DFS between the two groups. The small sample size might have limited the determination of any significant difference. However, recent studies also could not observe any significant survival difference between T2a and T2b tumors [25,28]. Similarly in this study, there was no difference between the two groups in terms of tumour size, degree of tumour differentiation, incidence of LN metastasis, lymphovascular invasion or perineural invasion. This was in contrary to the finding by Shindoh et al that tumours in hepatic side had higher vascular and neural invasion and nodal metastasis [9]. An interesting finding in the present study was that for recurrent tumour, LN recurrence is the commonest for T2a tumour while it was liver recurrence for T2b tumour, though the difference was again not significant (Table 2). This finding correlated with the observation by Endo et al that microscopic liver metastases were frequently detected in patients with T2 tumour on the hepatic side that had invaded the subserosa for more than 3cm [29]. Hence, liver resection is probably only beneficial for T2b tumors [21-24]. The avoidance of liver resection may make old patients with T2a tumours after cholecystectomy more feasible for repeated extended surgery.

Limitations

Given the rarity of the disease in this locality, the power of the present study was limited by the small number of patients included. Thus any significant difference in long term outcomes especially between T2a and T2b tumours might not be shown up and the study result should be interpreted with caution. The retrospective nature of study also involved bias in patient selection for surgery. The inclusion of only patients who have undergone surgery with histologically proven GBC would also unavoidably omitted patients with radiological or even biopsy proven GBC but no operation done due to various reasons, so the study population could not represent the main cohort of patients with same disease. Besides, the median number of LN retrieval in this study was four, which was below the desired number of six and might lead to inadequate or understaging of LN involvement [30]. The lack of a standardized LN dissection protocol might also alert the effectiveness of LN dissection.

Conclusion

The result of present study has provided some hints that extended resection provided survival benefit for T2 GBC, no matter it was T2a or T2b, while there was no difference in long-term outcomes between T2a and T2b tumours after surgery. LN dissection should be an essential part of extended surgery whilst the role of liver resection for T2a tumours deserves more investigation.

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