Status of Surgical Treatment of Biliary Tract Cancer

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Key Words

Biliary tract carcinoma • Bile duct carcinoma, hilar, middle, distal • Gallbladder carcinoma • Papilla of Vater carcinoma • Biliary surgery, 5-year survival • Disease stage

Abstract

Complete surgical resection of biliary tract carcinoma remains the best treatment. The Japanese Society of Biliary Surgery has organized a registry project and established a classification of biliary tract carcinoma. We report here the status of biliary surgery in Japan. For hilar bile duct carcinoma, major hepatectomy is needed to increase the resection rate, and total caudate lobectomy is required for curative resection. The 5-year survival rate was 39.1%. Middle and distal bile duct carcinomas were treated with pancreatoduodenectomy (PD) or pylorus-preserving PD (PPPD) or bile duct resection alone. The 5-year survival rate was 44.0%. The treatment of gallbladder carcinoma with pT1 lesions is cholecystectomy. The treatment of pT2 lesions is extended cholecystectomy or various hepatectomy with or without extrahepatic bile duct resection along with lymphadenectomy. Treatment of pT3 and pT4 lesions includes hepatectomy with or without bile duct resection, combined with vascular re-

section, extended lymphadenectomy, and autonomic nerve dissection. Several groups in Japan have performed hepato-pancreatoduodenectomy. The 5-year survival rate of pT1, pT2, pT3, and pT4 were 93.7, 65.1, 27.3, and 13.8%. PD or PPPD is the standard operation for carcinoma of the papilla of Vater. The 5-year survival rate was 57.5%.

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Introduction

Complete surgical resection of biliary tract carcinoma remains the best treatment for long-term survival. In Japan, the Japanese Society of Biliary Surgery (JSBS) is organized into 225 institutions. It performs registration of biliary tract carcinomas as one of its projects. In this project, the society has established guidelines for the treatment of cancer of the biliary tract based on the extent of involvement at each site. A total of 3,518 cases of biliary tract carcinoma were registered between 1998 and 2002; the site of carcinoma was the bile duct in 1,669, the gallbladder in 1,345, and the papilla of Vater in 504 cases. These cases were analyzed with regard to patient survival. We report the status of biliary surgery in Japan.

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0253-4886/07/0242-0131\$23.50/0

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Classification of Biliary Tract Carcinoma

As noted above, the JSBS established guidelines for the treatment of cancer of the biliary tract based on the extent of involvement at each site, according to the Classification of Biliary Tract Carcinoma currently used in Japan, and the 2nd English edition was published in 2004 [1]. The guidelines promoted in Japan for the treatment of biliary tract carcinoma are divided into three anatomical regions: the biliary duct, gallbladder, and papilla of Vater.

Bile Duct Carcinoma

Staging

Extrahepatic carcinomas have been subdivided into proximal or hilar, middle, and distal subgroups. The histological extent of tumor invasion around the bile duct (t category) in the classification of biliary tract carcinoma of JSBS is defined as the degree of tumor extension. According to the currently used Japanese classification of tumor invasion into the bile duct wall, serosal invasion is histologically divided into 5 stages, m, fm, ss, se, and si, in anatomical fashion. Furthermore, various types of direct invasion of the carcinoma into four structures present around the bile duct, i.e., invasion of the hepatic parenchyma (hinf), pancreatic parenchyma (panc), portal venous system (p), and arterial system (a), are graded from 0 to 3. Nodal involvement of carcinoma is classified into four groups. The stages of biliary tract carcinoma of JSBS are classified into five groups [1].

Hilar Bile Duct Carcinoma

Long-term survival with hilar bile duct carcinoma depends critically on complete resection with negative margins. The resection rate increases with the performance of major hepatectomy, and the likelihood of negative margins by performing it rises in hilar bile duct carcinoma. In addition, total caudate lobectomy is required for curative resection since caudate branches join the hilar bile duct [2, 3]. However, the risk of developing hepatic failure as a postoperative complication increases when major hepatectomy is performed. Therefore, when major hepatectomy is planned, portal vein embolization (PVE) is performed in many Japanese institutions. The main purpose of PVE is to induce compensatory hypertrophy of the future remnant liver and thus minimize postoperative liver dysfunction. In the recent literature from high-volume centers in Japan [4–11], the mortality

Table 1. Surgical procedure for hilar bile duct carcinoma

Type of hepatectomy	Cases	With PD	With PV	With HA
Left hepatectomy	54	2	2	1
Extended left hepatectomy	66	9	6	3
Left trisegmentectomy	10	1	2	
Right hepatectomy	35	8	1	
Extended right hepatectomy	69	9	4	
Right trisegmentectomy	18	4	2	
Central bisegmentectomy	3			
Total	255	29	17	8

PD = Pancreatoduodenectomy; PV = resection and construction of the portal vein; HA = resection and construction of the hepatic artery.

rate ranged from 0 to 12%. The overall 3- and 5-year survival rates ranged from 26 to 54.8% and 23 to 40%, respectively. The proportion of stage IVa (5th edition of UICC) or over stage III (6th edition of UICC) ranged from 41 to 72%. A total of 255 cases of hilar bile duct carcinoma subjected to major hepatectomy were registered in the JSBS between 1998 and 2002 (table 1). The surgical procedure was left hepatectomy in 54 patients, extended left hepatectomy in 66 patients, left trisegmentectomy in 10 patients, right hepatectomy in 35 patients, extended right hepatectomy in 69 patients, right trisegmentectomy in 18 patients, and central bisegmentectomy in 3 patients. Bloc hepatic resection with pancreatoduodenectomy (HPD) was performed in 29 patients. Portal vein resection and reconstruction was performed in 167 patients. Resection of the right or left hepatic artery and reconstruction was performed in 78 patients. The overall the 1-, 2-, 3-, and 5-year survival rates of patients who underwent major hepatectomy were 77.3, 55.9, 46.7, and 39.1%, respectively. Patients were grouped according to the Japanese classification as stage I (n = 21, 8.2%), stage II (n = 45, 17.6%), stage III (n = 66, 25.9%), stage IVa (n = 86, 33.7%), or stage IVb (n = 37, 14.5%). The 5-year survival rate was 90.0% in stage I patients, 57.7% in stage II, 46.2% in stage III, 29.9% in stage IVa, and 17.0% in stage IVb patients (fig. 1). Compared with high-volume centers in Japan, the overall survival rate of the JSBS is good. This difference in survival rate is attributable to the higher percentage of cases of advanced cancer among those undergoing surgery at high-volume centers in Japan where aggressive surgery is often performed for advanced cancer.

Fig. 1. Survival rates of hilar bile duct carcinoma according to stage.

Fig. 2. Survival rates of middle and distal bile duct carcinoma according to stage.

Table 2. Studies of middle and distal bile duct carcinoma

Reference	Year	Location of tumor	Patients	3-Year survival, %	5-Year survival, %
Yamaguchi et al. [12]	1997	Distal	11	38	19
Yamaguchi et al. [12]	1997	Middle	11	33	11
Kayahara et al. [13]	1999	Middle and distal	50	47	35
Suzuki et al. [14]	2000	Middle and distal	99	50	37.4
Sasaki et al. [15]	2001	Middle and distal	59	42.6	33.6
Yoshida et al. [16]	2002	Distal	27	37	37
Sakamoto et al. [17]	2005	Middle and distal	55	52	24

Middle and Distal Bile Duct Carcinoma

Middle and distal bile duct carcinoma is treated with pancreatoduodenectomy (PD) or pylorus-preserving PD (PPPD) or bile duct resection alone. In Japan, some surgeons have advocated complete removal of the primary bile duct cancer with connective tissue clearance, including lymph nodes and neural plexus dissection. Recent results reported from high-volume centers in Japan are summarized (table 2) [12–17]. The overall 3- and 5-year survival rates ranged from 33 to 52% and 11 to 37.4%, respectively. 427 patients with middle and duct carcinoma, excluding those with insufficient data, who underwent PD or PPPD were registered in the JSBS between 1998 and 2002. The overall 1-, 2-, 3-, and 5-year survival rates were 83.5, 66.6, 57.9, and 44.0%, respectively. Patients were

grouped according to the Japanese classification as stage I (n = 36, 8.4%), stage II (n = 82, 19.2%), stage III (n = 134, 31.4%), stage IVa (n = 130, 30.4%), or stage IVb (n = 45, 10.5%). The 5-year survival rates were 64.8% in stage I patients, 56.9% in stage II, 45.6% in stage III, 36.8% in stage IVa, and 19.5% in stage IVb (fig. 2).

Gallbladder Carcinoma

Staging

The histological extent of tumor invasion around the gallbladder (t category) in the classification of gallbladder carcinoma of the JSBS is defined as the degree of tumor extension. According to the currently employed Japanese

Fig. 3. Survival rates of gallbladder carcinoma according to depth of invasion.

classification of tumor invasion into the bile duct wall, serosal invasion is histologically classified into five stages, m, mp, ss, se, and si, in accordance with the anatomical structure. Furthermore, various types of direct invasion of carcinoma into four structures present around the bile duct are distinguished, i.e., invasion of the hepatic parenchyma (hinf), hepatoduodenal ligament (binf), portal venous system (p), and arterial system (a), which are graded from 0 to 3. Nodal involvement of gallbladder carcinoma is classified into four groups. The stages of biliary tract carcinoma of the JSBS are classified into five groups [1].

Surgery

Most surgeons agree that pT1 tumors are effectively treated with cholecystectomy. The 1-, 2-, 3-, and 5-year survival rates of pT1 patients ($n = 160$) registered with the JSBS were 99.4, 97.8, 95.4, and 93.7%, respectively (fig. 3). pT2 tumors often exhibit lymph node metastases. 30% (93/306) of the T2 tumors registered with JSBS were associated with lymph node metastases. Lymph node dissection is thus necessary for pT2 gallbladder carcinoma. Extended cholecystectomy or various types of hepatectomy with or without extrahepatic bile duct resection have been performed for pT2 patients in Japan. The range of liver resection required as part of radical surgery is still controversial. The 1-, 2-, 3-, and 5-year survival rates of

Fig. 4. Survival rates of gallbladder carcinoma according to stage.

T2 patients ($n = 306$) registered with the JSBS were 89.8, 81.1, 75.2, and 65.1%, respectively (fig. 3). For pT3 and pT4 tumors, the surgical procedures currently used in Japan include various types of hepatectomy with or without bile duct resection, combined vascular resection, extended lymphadenectomy, and autonomic nerve dissection. Several surgical groups in Japan have performed HPD for locally advanced gallbladder carcinoma. The usefulness of extrahepatic bile duct resection as part of radical surgery for advanced gallbladder carcinoma is also still controversial, particularly when there is no apparent extrahepatic bile duct involvement. The 1-, 2-, 3-, and 5-year survival rates of pT3 patients ($n = 66$) registered with the JSBS were 57.7, 41.0, 27.3, and 27.3%, while those for pT4 patients ($n = 228$) were 53.6, 30.3, 19.5, and 13.8%, respectively (fig. 3).

760 patients with gallbladder carcinoma, excluding those with insufficient data, who underwent resection were registered in the JSBS between 1998 and 2002. The overall 1-, 2-, 3-, and 5-year survival rates were 78.2, 66.3, 58.9, and 52.6%, respectively. There are two papers concerning large numbers in Japan from different periods. The 5-year survival rate of 1,686 patients with resection between 1979 and 1988 was 30.1% [18], while that of 3,249 patients with resection between 1988 and 1998 (JSBS) was 42% [19]. Patients were grouped according to the Japanese classification as stage I ($n = 160$, 8.4%), stage II

Fig. 5. Survival rates of carcinoma of the papilla of Vater according to stage.

Table 3. Studies of carcinoma of the papilla of Vater

Reference	Year	Patients	3-Year survival, %	5-Year survival, %
Kawarada et al. [20]	1993	89	63.6	57.4
Nakao et al. [21]	1994	26	57.7	52.3
Shirai et al. [22]	1996	35	60	
Kayahara et al. [23]	1997	36	66	56
Tanaka et al. [24]	2002	16	58.9	55

(n = 208, 19.2%), stage III (n = 98, 31.4%), stage IVa (n = 152, 30.4%), or stage IVb (n = 142, 10.5%). The 5-year survival rate was 93.6% in stage I patients, 80.8% in stage II, 52.6% in stage III, 21.5% in stage IVa, and 6.5% in stage IVb (fig. 4).

Carcinoma of the Papilla of Vater

Staging

The histological extent of tumor invasion around the papilla of Vater (t category) in the classification of gallbladder carcinoma of the JSBS is defined as the degree of tumor extension. Various types of histologically direct invasion of the carcinoma into two structures present

around the papilla of Vater, i.e. the pancreatic parenchyma (panc) and duodenum (du), are graded from 0 to 3. Nodal involvement of gallbladder carcinoma is classified into four groups. The stages of biliary tract carcinoma of JSBS are classified into five groups [1].

Surgery

In most series, the resectability rate is higher than for other malignant tumors of the periampullary region. PD or PPPD is the standard operation for carcinoma of the papilla of Vater. Recent reports from high-volume centers in Japan are summarized (table 3) [20–24]. The overall 3- and 5-year survival rates ranged from 55 to 66% and from 40 to 60%, respectively. 404 patients with carcinoma of papilla of Vater, excluding those with insufficient data, who underwent PD or PPPD were registered in the JSBS between 1998 and 2002. The overall 1-, 2-, 3-, and 5-year survival rates were 89.3, 75.6, 66.0, and 57.5%, respectively. Patients were grouped according to the Japanese classification as stage I (n = 112, 27.7%), stage II (n = 65, 16.1%), stage III (n = 126, 31.2%), stage IVa (n = 64, 15.8%), or stage IVb (n = 37, 9.2%). The 5-year survival rates were 76.3% in stage I patients, 71.7% in stage II, 54.0% in stage III, 47.2% in stage IVa, and 7.4% in stage IVb (fig. 5).

Conclusion

We report the status of biliary surgery in Japan. Hilar bile duct carcinoma is one of the diseases on which Japanese biliary tract surgeons place particular emphasis. PVE performed during major hepatectomy and total caudate lobectomy have contributed to improving the outcome of treatment of hilar bile duct carcinoma. Middle and distal bile duct carcinomas are treated with PD or PPPD or bile duct resection alone. The treatment of gallbladder carcinoma with pT1 lesions is cholecystectomy. The treatment of pT2 lesions is extended cholecystectomy or various hepatectomy with or without extrahepatic bile duct resection, and lymphadenectomy. The treatment of pT3 and pT4 lesions includes various types of hepatectomy with or without bile duct resection combined vascular resection, extended lymphadenectomy, and autonomic nerve dissection. The usefulness of resection of the extrahepatic bile duct and the range of liver resection of gallbladder carcinoma are still controversial. Several groups in Japan perform HPD for locally advanced gallbladder carcinoma. PD or PPPD is the standard operation for carcinoma of the papilla of Vater.

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