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A New Clinical Classification of Hilar Cholangiocarcinoma (Klatskin Tumor)

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Abbreviations: MSKCC: Memorial Sloan Kettering Cancer Center, AJCC: American Joint Committee of Cancer; European HPBA: European Hepato-Pancreato-Biliary Association

Introduction

Altemeir first described hepatic hilar cholangiocarcinoma in 1957 [1]. In 1965, a series of 13 cases of hepatic hilar cholangiocarcinoma was reported by Klatskin [2]. This tumor makes up about 60% of all cholangiocarcinoma. Anatomically, this tumor situates at special site, i.e. hilar biliary bifurcation within a limited small space, close to vessels (portal vein, hepatic artery) and liver (especially caudate lobe). Biologically, it usually grows slowly and locally, with submucosal infiltration (up to 1.6 cm from gross margin of the tumor), neurovascular infiltration and lymphnode metastasis, but less often with distance metastasis. Therapeutically, its resection usually is difficult, especially to obtain R0 resection, while it does not respond well with chemo-and/or radiational therapy. Local recurrence is high (>50%), leading treatment failure and poor outcome [3].

Staging/Classification

Over years, there were a number of staging/classification system, including Bismuth/Corlette, Liver Cancer Study Group of Japan, MSKCC (Memorial Sloan Kettering Cancer Center), AJCC (American Joint Committee of Cancer), and most recently European HPBA (European Hepato-Pancreato-Biliary Association). The most well-known classification was from Dr. Henry Bisthmus (Figure 1) [4], who classified the tumor according to the anatomic locations:

a) Type 1 - tumor involves hepatic bile duct only;

b) Type 2 - tumor involves bile duct bifurcation;

c) Type 3a - tumor involves bile duct burfication and right hepatic bile duct;

d) Type 3b - tumor involves bile duct burfication and left hepatic bile duct;

e) Type 4 - tumor involves both sides of hepatic bile ducts. This system is used widely in clinical practice. It was based on anatomic level or involvment of the tumor to biliary tree. This does help in preparation of surgical plan. However, it does not describe the involvement status of vessels, status of liver parenchyma, metastasis and lymphnode. Therefore, it is not as helpful when liver resection and vascular resection/reconstruction are considered.

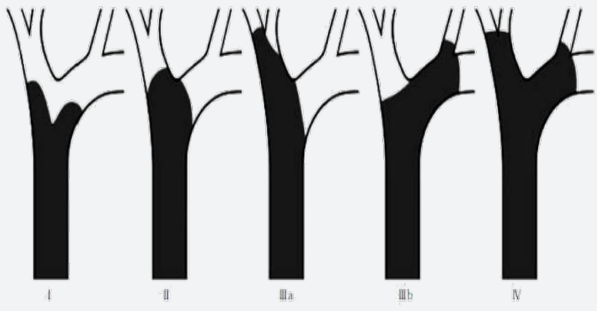

Figure 1: Bismuth/Corlette Classifiction.

In 2000, the Liver Cancer Study Group of Japan proposed a classification according cancer growing pattern, mass forming, periductal infitration and intraductal growing (Figure 2) [5]. This was more about cancer biological behaviour, with better prognosis of mass forming and intraductal growing. Preoperatively, the information about this classification would unlikely be obtained in detail. Further more, there was no description about vascular involvement and liver lobar status. Therefore, the value of this classification in surgical assessment regarding resectability was limited.

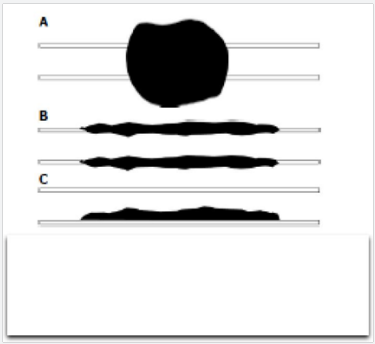

Figure 2: The Liver Cancer Study Group of Japan Classification. A: mass forming; B: periductal infiltration and C: intraducal growing.

Table 1: MSKCC Staging/Classification.

	Biliary involvement	PV invasion	Lobar atrophy
T1	hilus ± unilateral sectional bile ducts	no	no
T2	hilus ± unilateral sectional bile ducts	ipsilateral	±ipsilateral
T3	hilus+ bilateral sectional bile ducts	yes/no	yes/no
T3	hilus + unilateral sectional bile ducts	contralateral	yes/no
T3	hilus + unilateral sectional bile ducts	yes/no	contralateral
T3	hilus ± unilateral sectional bile ducts	bilateral	yes/no

MSKCC staging/classification took bile duct involvement, vascular involvement and liver atrophy into consideration (Table 1) [6]. It helps in preparation of liver resection in treatment of Klatskin tumor. However, this classification did not include lymphnode and metastasis status, and did not consider liver transplantation as option of treatment. The AJCC's TNM classification based on tumor, lymphnodes involvemen and distance metastasis [7] (Table 2). TNM is often used for most of the cancer staging. However, it is mostly appropriate for postoperative pathological staging, as some information such as tumor invasion, lymphnode metastasis, may not be accurately assessed before surgery.

Table 2: Perihilar bile duct tumors (American Joint Committee on Cancer) and Joint Commission on Cancer Staging 7th edition).

Tumor
T1 Tumor confined to bile duct histologically
T2a Tumor beyond the wall of bile duct into adjacent fat
T2b Tumor beyond the wall of bile duct into liver parenchyma
T3 Tumor invades ipsilateral portal vein (R or L) or hepatic artery (R or L)
T4 Tumor invades
(1) Main portal vein or its branches bilaterally (or)
(2) Common hepatic artery (or)
(3) The second-order biliary radicals bilaterally
(4) Unilateral second-order biliary radicals with contralateral portal vein or hepatic artery involvement
Node
Nx Regional lymph nodes cannot be assessed.
N0 No regional lymph node metastasis
N1 Regional lymph node metastasis (including nodes along the cystic duct, common bile duct, hepatic artery, and portal vein)
N2 Metastasis to periaortic, pericaval, superior mesenteric artery, and/or celiac artery lymph nodes
Metastasis
M0 No distant metastasis
M1 Distant metastasis
Tumor Stage
Stage 0: Tis, N0, M0
Stage I: T1, N0, M0
Stage II: T2a-b, N0, M0
Stage IIIa: T3, N0, M0
Stage IIIb: T1, T2 or T3, N1, M0
Stage IVa: T4, N0 or N1, M0
Stage IVb: Any T, N2, M0 or Any T, any N, M1

Table 3: Consensus classification (European Hepato-Pancreato-Biliary Association).

Bile duct (B)
B1 Common bile duct
B2 Hepatic duct confluence
B3 R Right hepatic duct
B3 L Left hepatic duct
B4 Right and left hepatic duct
Tumor size (T)
T1 < 1 cm
T2 1-3 cm
T3 ≥ 3 cm
Tumor form (F)
Sclerosing Sclerosing (or periductal)
Mass Mass-forming (or nodular)
Mixed Sclerosing and massforming

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Polypoid Polypoid (or intraductal)
Involvement (> 180°) of the portal vein (PV)
PV0 No portal involvement
PV1 Main portal vein
PV2 Portal vein bifurcation
PV3 R Right portal vein
PV3 L Left portal vein
PV4 Right and left portal veins
Involvement (> 180°) of the hepatic artery (HA)
HA0 No portal involvement
HA1 Proper hepatic artery
HA2 Hepatic artery bifurcation
HA3 R Right hepatic artery
HA3 L Left hepatic artery
HA4 Right and left hepatic artery
Liver remnant volume (V)
V0 No information on the volume needed (liver resection not foreseen)
V% Indicate segments Percentage of the total volume of a putative remnant liver after resection
Underlying liver disease (D) Fibrosis
Nonalcoholic steatohepatitis
Primary sclerosing cholangitis
Lymph nodes (N)
N0 No lymph node involvement
N1 Hilar and/or hepatic artery lymph node involvement
N2 Periaortic lymph node involvement
Metastases (M)
M0 No distant metastases
M1 Distant metastases (including liver and peritoneal metastases)

In 2011, an international working group based on a consensus from the European Hepato-Pancreato-Biliary Assoiation, published a new most complete staging/classification system [8] (Table 3) [16]. This is not only including information about bile duct, hepatic artery and portal vein, but also covering tumor biological growing form, liver resection related information such as liver volume, remnant volume and, background liver disease history. This system seems very complicated with some information not easily and accurately obtainable before resection.

Surgical management update

Original local resection of hilar cholangiocarcinoma (Klatskin tumor) had poor long term results with 5 year survival <7.3% [9]. In 1990's, more and more studies showed R0 resection resulted longer survival. Klatskin tumor is found to have relatively low distance metastasis and high local recurrences. Therefore, combining radical choledochectomy with liver lobectomy was promoted, especially including right hemi- or right extended hemihepatectomy plus caudate lobe resection [10,11]. The 5 year survival rate increased to over 30-40%. However, postoperative morbidity and mortality were as high as 59% and 11%. In 2009, Chen XP et al. [12] however, published a paper on British Journal of Surgery, suggesting minor limited hepatectomy for patients whose cancers were not involving vascular structures might not be necessarily worse in outcome, with 5-yr survival rate of 34%, while the postoperative morbidity and mortality from a major extended resection were greatly avoided [12].

Issue of vascular resection and reconstruction has been reviewed through a mega-analysis by Abass S and Sandrassi C [13]. There were 669 patients out of 2457 cases had vascular resection, 22-88% resected sample were found positive on pathology, 36-88% of patients achieved R0 resection while the morbidity and mortality were respectively 22-88% and 2-15%. Five year survival was 20-56%. In 2012, Jong MC et al. [14] reported a multi-institutional analysis of 305 cases [14], showing portal vein resection should be undertaken when necessary to extirpate all disease. Combined liver resection, extra-hepatice bile duct resection and portal vein resection can offer long-term survival in some patients with advanced hilar cholangiocarcinoma.

Liver transplantation for treatment of cholangiocarcinoma has been attempted for more than twenty years. Before 2000, however, five year survival was only 28%. With neo-adjuvant therapy, the results were gradually improving. In 2005, Rea SR et al. [15] from Mayo Clinic with tedious strict preoperative selecting and treatment protocol [15]. The results was significantly better, with 1, 3, 5 year survival as 92%, 82% and 82%. Liver transplantation as a treatment option though in a small highly-selected group of patient, achieves R0 resection more readily without concerning about lobar atrophy, intrahepatic bile duct or vascular involvment.

Proposal of New Clinical Classification

Former staging/classifications did not take fully consideration of therapeutic process and are limited on description of cancer status related surgical management. Any final results of a cancer patient treatment is actually determined by three parts [15]:

a) patient's systemic healthy with range of tolerance of therapeutic actions;

b) the cancer itself and its response to therapies; and

c) the therapies.

This new clinical classification is based on clinical therapeutic options according to patient's condition and cancer status. As therapeutic technologies including neoadjuvant therapy, chemo-radiation and transplantation, are continuously improving, with further advances in therapeutic technologies in the future, more

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patients will receive radical treatment with better final results. In order to take all present available therapeutic options into consideration, a new clinical therapeutic classification is here proposed (Table 4).

Table 4: Proposed New Clinical Classification.

Classification	BD, PV, HA & Lobar atrophy	Reconstructable BD, PV or HA	Possible Management
Resectable	Limited to one side	Yes	Resection, adjuvant chemoradiation
Marginally resectable	Both sides	Yes/No	Neo-adjuvant, lap, resection, adjuvant chemotherapy
Unresectable but Transplantable	Both sides	No	Neo-adjuvant, lap, LTX, adjuvant chemotherapy
Unresectable and untransplantable	Both sides	No	Chemoradiation; palliative care

BD: Bile Duct; PV: Portal Vein; HA: Hepatic Artery; lap: Exploratory Laparotomy; LXT: Liver Transplantation

This relatively simple classification is to help in making clinical decisions regarding therapeutic purpose. The patients with Klatskin tumor are classified in 4 groups: resectable, marginally resectable, unresectable but transplantable and, unresectable and untransplantatable. Surgical treatment of hilar cholangiocarcinoma is not only depending on resection, but also on reconstruction. We could do as much resection as possible, as long as vascular and biliary reconstruction is achievable. Liver transplantation is useful when reconstruction becomes not possible. However, in order to achieve long-term good outcome with liver transplantation, liver transplantation could only be used in highly-selected patient group without distance metastasis, at present i.e. biologically less aggressive with 3-months neoadjuvant therapy with no progress and pathologically localized tumor with exploratory laparotomy -finding of no positive lymphnode.

Conclusion

Advances in management of hilar cholangiocarcinoma (Klatskin Tumor) leads to a new clinical classification, which will facilitate in clinical therapeutic decision at present time.

References

1. Matras H (1970) Die Wirkungen verschiedener Fibrinpräparate auf Altemeier WA, Gal EA, Zinninger MM, Hoxworth PI (1957) Sclerosing Carcinoma of the Major Intrahepatic Bile Ducts. AMA Arch Surg 75(3): 450 - 461.
1. Klastskin G (1965) Adenocarcinoma of the hepatic duct at its bifurcation within the porta hepatis. Am J of Med 38(2): 241-258.
2. Soares KC, Kamel I, Cosgrove DP, Herman JM, Pawlik TM (2014) Hilar cholangiocarcinoma: diagnosis, treatment options, and management. Hepatobiliary surg Nutr 3(1): 18-24.
3. Bismuth H, Corlette MB (1975) Intrahepatic cholangioenteric anastomosis in carcinoma of the hilus of the liver. Surg Gynecol Obsstet 140(2): 170-178.
4. Liver Cancer Study Group of Japan (2000) The general rules for the clinical and pathological study of primary liver cancer, (4th edn.), Kanehara, Tokyo, 19(1): 98-129.
5. WR Jarnagin, Y Fong, RP DeMatteo, M Gonen, EC Burke, et al. (2001) Staging, resectability, and outcome in 225 patients with hilar cholangiocarcinoa. Ann Surg 234(4): 507-517.
6. Cancer Staging Manual (2010) (7th edn). American Joint Committee on Cancer. Springer, NY, USA.
7. Deoliveira ML, Schulick RD, Nimura Y, Rosen C, Gores G, et al. (2011) New-staging system and a registry for perihilar cholangiocarcinoma. Hepatology 53(4): 1363-1371.
8. Robert M Cannon, Guy Brock, Joseph F Buell (2012) Surgical resection for hilar cholangiocarcinoma: experience improves resectability. HPB 14(2): 142-149.
9. Neuhaus P, Jonas S, Bechstein WO, Lohmann R, Radke C, et al. (1999) Extened resections for hilar cholangiocarcinoma. Ann of Surg 230(6): 808 -819.
10. Dinant S (2005) The importance of complete excision of the caudate lobe in resection of hilar cholangiocarcinoma. HPB 7(4): 263-267.
11. Chen XP, Lau WY, Huang ZY, Zhang ZW, Chen YF, et al. (2009) Extent of liver resection for hilar cholangiocarcinoma. Br J of Surg 96(10): 1167-1175.
12. Abbas S and Sandroussi C (2013) Systemic review and meta-analysis of the role of vascular resection in the treatment of hilar cholangiocarcinoma. HPB 15(7): 492-503.
13. de Jong MC, Marques H, Clary BM, Bauer TW, Marsh JW, et al. (2012) The Impact of Portal Vein Resection on Outcomes for Hilar Cholangiocarcinoma A Multi-Institutional Analysis of 305 Cases. Cancer 118(19): 4737-4747.
14. Rea DJ (2005) Liver Transplantation with Neoadjuvant Chemoradiation is More Effective than Resection for Hilar Cholangiocarcinoma. Ann Surg 242: 451-461.
15. Kelsey Hinther, Sanji Ali, Jack Spiers, Bill Taylor, Roman Bacchus, et al. (2017) Preoperative Prognostic Features of Pancreatic Head Adenocarcinoma. Open Access J Surg 2(1): 1-5.
16. DeOliveira MI, Schulick RD, Nimura Y, et al. New Staging System and a Registry for Perihilar Cholangiocarcinoma. Hepatology 2011; 53: 1363 -1371

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