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MINI REVIEW ARTICLE

Liver transplantation for intrahepatic and hilar cholangiocellular carcinoma: Most recent updates in the literature

Susumu Eguchi | Masaaki Hidaka | Takanobu Hara | Hajime Matsushima | Akihiko Soyama

Department of Surgery, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan

Correspondence
Susumu Eguchi, Department of Surgery, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Sakamoto 1-7-1, Japan.
Email: sueguchi@nagasaki-u.ac.jp

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Abstract

Liver transplantation (LT) for non-hepatocellular carcinoma is still a debatable indication. Recently, hilar cholangiocellular carcinoma (hCCC) has attracted interest as a new indication for LT, but LT in this case should be carefully considered. Based on the recent meta-analysis for intrahepatic CCC (IHCCC) and our results from incidental IHCCC transplanted for other diseases such as primary sclerosing cholangitis, the indication for LT for IHCCC should be limited to a single tumor less than 2 cm. For hCCC, with pre-transplant chemoradiotherapy and careful selection criteria, long-term survival after LT could be attained. In order to improve the results of LT for intrahepatic and hCCC, further studies are required on the ingenuity of immunosuppressive therapy combined with chemotherapy, and optimal treatment methods to prevent recurrence, as well as initial case selection.

KEYWORDS
cholangiocellular carcinoma, hilar, intrahepatic, liver transplantation, resection

1 | INTRODUCTION

According to the national registration in Japan, reported by the Japanese Liver Transplantation Society, 14 cholangiocellular carcinoma (CCC) were performed in Japan from 1992 to the end of 2019 because of out-of-pocket health insurance coverage and relative contraindication.[1] However, in recent years, relatively good prognoses in patients receiving liver transplantation (LT) for hilar CCC (hCCC) have been reported after intensive pretransplant chemoradiotherapy and by carefully selecting cases using deceased donor livers.[2-4] In general, it is not easy to distribute deceased donor organs to patients in Japan, where the number of brain-dead donors is significantly limited compared to other countries. As a result, living-donor LT is often the only option, despite not being covered by health insurance. Intrahepatic CCC (IHCCC) had been considered a contraindication for LT because of poorer outcomes. However, with recent advances in chemotherapy, an indication for LT for IHCCC is becoming an important topic, but no definitive results have yet been shown. This paper introduces updated results and progress of LT for CCC stratified by intrahepatic and hilar methods.

Susumu Eguchi and Masaaki Hidaka are equally contributed on this manuscript as a first author.

2 | LT FOR INTRAHEPATIC CHOLANGIOCELLAR CARCINOMA (IHCCC)

2.1 | Indications and results of LT for IHCCC

Intrahepatic CCC is on the rise, accounting for 6.4% of primary liver cancer in Japan.[5] Surgical treatment is the only curative treatment, but there are many unresectable cases, and LT has been attempted since the 1980s for such cases.[6] However, due to the high recurrence rate and poor prognosis, LT is not indicated or IHCCC in many institutions. However, in recent years, better results have been reported than earlier due to the selection of cases.

Intrahepatic CCC that can be the target of LT falls into three categories: (1) those that can be resected (primary resectable); (2) those that are complicated by liver cirrhosis and cannot be resected due to liver dysfunction (unresectable due to poor liver functional reserve); and (3) those in which the tumor can be resected only by total hepatectomy due to tumor progression (far advanced). Table 1 summarizes the recent reports of LT for IHCCC.

2.1.1 | Primary resectable IHCCC

The advantages of performing LT for primary resectable cases are to secure a surgical margin and remove occult lesions in the liver. A recent study comparing the results of LT and hepatectomy by propensity score matching using the American National Cancer database showed no difference in survival rate between the hepatectomy group and the LT group even when the backgrounds are matched.[7] The overall results are poor because there are various T stages (tumor sizes) and N stages (degree of lymph node spread). In addition, immunosuppressive therapy needs to be administered after LT, which could increase the incidence of tumor recurrence.[8] Therefore, currently, hepatectomy is the best choice for resectable cases.

2.1.2 | Unresectable IHCCC due to poor liver function

Next, we consider IHCCC associated with cirrhosis. A multicenter study in Spain reported in 2014 examined the prognosis of 29 patients with cirrhosis, including cases of accidental IHCCC that were first diagnosed with resected liver at the time of LT.[9] When grouped according to tumor diameter and number, LT results tended to be better for early IHCCC of 2 cm or less than for those without this characteristic. In addition, there was no recurrence after LT in the early IHCCC (2 cm or less) group. Risks for recurrence were tumor diameter, lymph-vascular invasion, and degree of differentiation. Based on these results, the findings of the international multicenter joint research study by the same group was reported in 2016.[10] In that study of 48 patients with cirrhosis, LT results were significantly better for single IHCCC of 2 cm or less, and the 5-year overall survival (OS) was 65%. The recurrence rate was only 18%, compared to 61% for those with advanced IHCCC. In multivariate analysis, lymph-vascular invasion and degree of differentiation were seen as risk factors. The meta-analysis published last year contained 66% cases of cirrhosis. The 5-year OS was 71%, and the 5-year recurrence-free survival (RFS) rate was 67% for single-shot tumors of 2 cm or less.[11] About 70% of the 5-year OS with HCC in Japan are comparable.[5]

A Phase 2 study is currently underway to assess whether the prognosis after LT for single IHCCC of 2 cm or less associated with cirrhosis is really good. The indications are for 1) patients with liver cirrhosis who cannot be resected due to decreased liver function, 2) patients who have been shown to have IHCCC by liver biopsy, 3) a single tumor of size 2 cm or less, and 4) have neither vascular invasion nor intrahepatic lesion on the image.[12] The upper limit of tumor markers was also set to 100 ng/mL for CA19-9. The primary outcome was the 5-year OS, and the results after a few years are awaited. Based on the above information, patients with IHCCC associated with decompensated cirrhosis may have an indication for LT when appropriate tumor conditions are set.

2.1.3 | Unresectable IHCCC because of far advanced tumor

Finally, we discuss LT for unresectable IHCCC. Unresectable IHCCC includes at least 5 cm in diameter (locally advanced cancers), bilobed multiple tumors, hilar extension, involvement of a major branch of the portal vein or hepatic artery or adjacent organs other than the gall bladder. Lymph node metastases are excluded because they are extrahepatic lesions. Multidisciplinary approaches, including chemotherapy, have been reported for multiple or locally advanced cancers, as in the case of hepatectomy. A study including hilar cholangiocarcinoma was reported by the UCLA group published in 2011.[13] One-year RFS was approximately 70% after LT (n = 25) and 60% after hepatectomy (n = 12), while 5-year RFS was around 40% after LT and 10% after hepatectomy without statistical significance. For LT patients, neo-adjuvant and adjuvant chemotherapy were given for 36% and 28% of LT patients, respectively, while adjuvant chemotherapy was only given in 42% of hepatectomy patents. The usefulness of LT for advanced IHCCC was not shown even with additional chemotherapy.

Previously, unresectable IHCCC was treated with preoperative chemotherapy or a combination of chemoradiotherapy and adjuvant therapy during the perioperative period.[13] The group treated before and after LT had the best prognosis. Tumor recurrence in the chemo-treated group was 28%. From the report of the Mayo group in 2019, LT had been performed in nine cases for advanced IHCCC, including six cases with multiple tumors, and three cases recurred after LT.[14] Eighty-three per cent of LT patients attained 5-year OS.

However, preoperative chemotherapy for IHCCC is still controversial, and reports on preoperative/perioperative chemotherapy are limited. Thus far, there is no fixed regimen or treatment period. The International Liver Transplantation Society (ILTS) consensus conference issued a recommendation in 2020, but the effectiveness

TABLE 1 Updated studies of liver transplantation for intrahepatic cholangiocellular carcinoma

	First author	Report year	Country	Study design		Patient number	Median OS	Notes
Resectable IHCCC	Hue et al	2021	USA	Retrospective	LT	n = 50	36.1 months	Propensity score matched
				Naional Cancer database	Resection	n = 46	33.6 months	NAC 70.3% in LT, 12.8% in Resection group
							n.s.	

	First author	Report year	Country	Study design			5 years OS (%)	5 years RFS (%)	
Decompensated liver cirrhosis	Hara et al	2021	Japan	Retrospective	LT	n = 19	46%	45%	
32% misdiagnosed as HCC				Japanese multicenter	single and ≤2 cm	n = 5	60%	75%	
68% incidental ICC					multiple or >2 cm	n = 14	41%	36%	
							n.s.	n.s.	
Decompensated liver cirrhosis	Ziogas et al	2020	18 papers	Meta-analysis	LT	n = 48			
66% liver cirrhosis					single and ≤2 cm	n = 15	71%	82%	
30% incidental ICC					multiple or >2 cm	n = 33	48%	33%	
							$P < 0.001$	$P < 0.001$	
Advanced IHCCC	Lunsford et al	2018	USA	Prospective	LT	n = 9	83%	50%	NAC with Gemcitabin + cisplatin or capecitabine
Multiple or single≥5 cm									

	First author	Report year	Country	Study design			5 years OS	5 years Recurrence Rate	
Decompensated liver cirrhosis	Sapisochin et al	2016	Spain	Retrospective	LT	n = 48			mictrovascular invation, poor differentiation
very early stage IHCCC				International multicenter	single and <2 cm	n = 15	65%	18%	
					multiple or >2 cm	n = 33	33%	61%	
							$P = 0.02$	$P = 0.01$	
Decompensated liver cirrhosis	Sapisochin et al	2014	Spain	Retrospective	LT	n = 29			

TABLE 1 (Continued)

	First author	Report year	Country	Study design			5 years OS	5 years Recurrence Rate	
				Spanish multicenter	single and ≤2 cm	n = 8	73%	0%	size, mictrovascular invation, poor differentiation
					multiple or >2 cm	n = 21	34%	42%	
							n.s.	$P = 0.05$	
Advanced IHCCC									
61% ≥5 cm	Hong et al	2011	USA	Retrospective	LT	n = 25			
60% multiple				Single center	NAC + adjuvant	n = 9	47%	50%	
					adjuvant	n = 7	33%	28%	
					none	n = 9	20%	40%	

of preoperative chemotherapy was only a conditional recommendation.[15] Thus, there is no established LT and adjuvant therapy for unresectable IHCCC cases at this moment, but recently developed selective fibroblast growth factor receptor 2 inhibitor could play a potential role for adjuvant or recurrent IHCCC following LT.[16]

3 | LT FOR INCIDENTAL INTRAHEPATIC CHOLANGIOCELLAR CARCINOMA (Table 1)

Incidental IHCCC in the explanted liver has been reported due to the difficulty of obtaining an accurate diagnosis in cirrhotic livers on preoperative imaging. Previously, we conducted a nationwide survey to analyze the incidence of incidental IHCCC and outcomes after LT in Japan.[8]

Forty-five of 64 institutions (70%) responded to our initial survey. Between January 2001 and December 2015, 6627 LTs were performed, with 19 cases (0.3%) of incidental IHCCC reported from 12 LT centers. Six cases were diagnosed as HCC preoperatively. The 1-, 3-, and 5-year RFS rates were 79%, 45%, and 45%, respectively. Tumor recurrence after LT was found in 10 patients (53%). The 1-, 3-, and 5-year OS rates were 79%, 63%, and 46%, respectively. According to the gross tumor type, the 5-year RFS rate in patients with the periductal infiltrating tumor type was only 25%, which was worse than those for the intraductal growth tumor type (67%) and the mass-forming tumor type (57%). All periductal infiltrating type cases recurred as extrahepatic lesions. The 1-, 3-, and 5-year RFS rates were worse in patients with positive microvascular invasion compared with patients without microvascular invasion (93%, 46%, and 46% vs 25%, 25%, and 0%, respectively). The pattern of post-LT incidental IHCCC recurrence presents as extrahepatic in most cases. IHCCC with LT is associated with a high risk of recurrence and poor prognosis, even these tumors are detected incidentally in the explanted liver.

4 | LT FOR HILAR CHOLANGIOCELLULAR CARCINOMA (hCCC)

Complete resection is the only treatment for hCCC. Since the 1970s, Japanese liver surgeons have introduced extensive hepatectomy using portal vein embolization, combined resection of blood vessels,[17] which has dramatically improved the prognoses. The Nagoya University group, a world famous leading center for resection, reported recently that the OS of patients who underwent resection for hCCC without combined vascular resection was a median of 61 months.[18] However, if the tumor was unresectable, the 5-year survival rate remained less than 10% or a median OS of 10 months.[18]

In the 1990s, the Mayo Clinic established a protocol for LT after chemoradiotherapy for unresectable hCCC and reported good long-term prognoses.[19] Based on those results, LT has been the usual indication for unresectable hCCC in the United States since 2010.[20,21] Criteria for LT include unresectable hCCC due to extensive local

TABLE 2 Updated studies of liver transplantation for hilar cholangiocellular carcinoma

First author	Report year	Country	Study design	Patient number	Medican Age (years)	PSC (%)	Tumor size (cm)	LDLT/DDLT/ DLT	Median OS (months)	1 year OS (%)	3 years OS (%)	5 years OS (%)	Recurrence rate (%)	Mortality
Single-centre studies														
Dondorf et al	2018	Germany	retrospective	n = 22	52.5 (30-71)[a]	2 (6%)	3.8 (1.6-8.5)[a]	9/12/1	28.7 (4.8-154.7)[a]	78.2	32.1	24.1	N/A	13.6% (30-day)
Loveday et al	2017	Canada	retrospective	n = 6	53.9	N/A	N/A	3/3/0	N/A	83.3	N/A	N/A	1/6 (16%)	N/A
Rosen	2012	USA	retrospective	n = 136	(26.7-62.8)[a] N/A	87 (64%)	N/A	45/90/1	N/A	92	81	74	29/136 (21.3%)	N/A
Multicentric studies														
Ethun et al	2017	USA	retrospective, multi center	n = 41	54 (43-62)[a]	25 (61%)	2.5 (1.1-5.0)[a]	N/A	N/A	93	72	64	10/41 (24%)	4.8% (90-day)
Kaiser et al	2008	Germany	retrospective, multi center	n = 47	N/A	8 (17%)	N/A	N/A	35.5	61	31	22	16/47 (34%)	25.5% (30-day)
Robles et al	2004	Spain	retrospective, multi center	n = 36	44 (20-63)[a]	3 (8%)	N/A	N/A	55 ± 11	82	53	30	19/36 (53%)	8.3% (90-day)
										79	40.3	38	45/124 (36.3%)	13.70%
Registry study														
Salgia et al	2013	USA	retrospective, multi center	n = 359	49 (18-71)[a]	84 (23%)	N/A	40/319/0	65(2-251)[a]	85.8	63.5	51.4	N/A	N/A

Abbreviations: N/A, not available; OS, overall survival.

[a]Median value (Minimum value - Maximum value).

progression, insufficient residual liver volume, concern about postoperative liver and tumor diameter of 3 cm or less, no intrahepatic/extrahepatic metastasis, and it is imperative that preoperative treatment be given. Results from 12 US centers, including the Mayo Clinic, were reported in 2012, with a 5-year RFS rate of 65% for 214 patients who underwent LT after preoperative treatment for unresectable hilar CCC.[22] Furthermore, the expansion of LT indications for resectable lesions has been discussed in Europe and the United States,[23-25] and randomized controlled trials are underway in France. In February 2019, the first international consensus conference on transplant oncology (a concept that develops treatment and research for intractable and advanced cancers through the fusion of oncology and transplant medicine) was held in Rotterdam, the Netherlands. LT after preoperative chemoradiotherapy for unresectable hCCC was designated as a "moderate recommendation."[26] Updated results are summarized in Table 2. In Japan, Professor Taizo Hibi (Kumamoto University) has made considerable contribution to the discussion while representing Japan.

A previous report indicated that LT is more effective and achieved better survival and less recurrence than surgical resection, and that the indications for LT and neoadjuvant treatment (chemotherapy + local radiation therapy) should be advocated for in resectable hCCC patients. According to these favorable findings, physicians have advocated for this viewpoint for patients with hCCC-associated primary sclerosing cholangitis (PSC) and have performed LT on such patients at many transplant centers.[27,28]

Liver transplantation in combination with neoadjuvant treatment can attain outcomes similar to surgical resection for unresectable early-stage hCCC patients arising in the setting of PSC.[29,30] Recently, programmed cell death protein-1 inhibitors have also been noted as a promising therapeutic option for treatment of CCC.[31] In addition, chimeric antigen receptor T cells, oncolytic viruses, cancer vaccines, and bispecific antibodies show a remarkable ability to achieve satisfactory results.

It has been shown that longer time elapsing between neoadjuvant therapy and LT results in reduced local recurrence.[32,33] Selection of patients with prolonged intervals and better oncologic biography, who are less susceptible to their disease progression following neoadjuvant treatment with chemo-radiotherapy, are less prone to develop recurrence post-LT. However, radiation-induced fibrosis and longer intervals can significantly complicate the staging and transplant operations. Living donor LT (LDLT) may solve these problems by removing the need to wait for a deceased donor and help physicians provide optimal timing of LT. Recent findings based on clinical study demonstrated that LDLT and deceased donor LT (DDLT) outcomes for hCCC-associated PSC are similar. In addition, LDLT for occult de novo hCCC shows a recurrence tendency and slightly worse OS compared to DDLT.[8]

5 | CONCLUSIONS

We have introduced the current state of LT for intra and hilar CCC.[34] At present, it is realistic to discuss the expansion of LT indications for patients with decompensated cirrhosis who have single IHCCC of 2 cm or less localized in the liver, and the results of prospective studies are awaited.[35] The long-term outcome of LT for IHCCC should be comparable to LT for HCC, in the face of the current shortage of deceased donations worldwide.[36,37] Realistically, all of the factors related to the poor prognosis (size of the tumor, vascular/lymph invasion, differentiation of the tumor) were all obtained from the liver sample after LT, so that it would be difficult to establish definite preoperative guidelines, not like HCC. This is especially true in the case of LDLT, which poses a risk to healthy donors. Going forward, further studies are thus called for concerning case selection criteria, selection of immunosuppressive therapy, and combined use with adjuvant therapy.[38-40]

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ORCID

Susumu Eguchi https://orcid.org/0000-0002-7876-0152
Masaaki Hidaka https://orcid.org/0000-0001-8191-6405
Hajime Matsushima https://orcid.org/0000-0002-1577-6587
Akihiko Soyama https://orcid.org/0000-0003-2932-4300

REFERENCES

1. Umeshita K, Eguchi S, Egawa H, et al. Liver transplantation in Japan: registry by the Japanese liver transplantation society. Hepatol Res. 2019;49:964–80.
2. Tan EK, Taner T, Heimbach JK, et al. Liver transplantation for perihilar cholangiocarcinoma. J Gastrointest Surg. 2020;24:2679–85.
3. Mueller M, Breuer E, Mizuno T, et al. Perihilar cholangiocarcinoma - novel benchmark values for surgical and oncological outcomes from 24 expert centers. Ann Surg. 2021;274:780–8.
4. Kitajima T, Hibi T, Moonka D, et al. Center experience affects liver transplant outcomes in patients with hilar cholangiocarcinoma. Ann Surg Oncol. 2020;27:5209–21.
5. Kudo M, Izumi N, Kokudo N, et al. Report of the 22nd nationwide follow-up survey of primary liver cancer in Japan (2012–2013). Hepatol Res. 2022;52:5–66.
6. Muhlbacher F, Rockenschaub SR. Transplantation for metastases. In: Busuttil RW, Klintmalm GBG, (eds). Transplantation of the Liver, 3rd edn. Elsevier. 2015;p. 214-7.
7. Hue JJ, Rocha FG, Ammori JB, et al. A comparison of surgical resection and liver transplantation in the treatment of intrahepatic cholangiocarcinoma in the era of modern chemotherapy: an analysis of the national cancer database. J Surg Oncol. 2021;123(4):949–56.
8. Hara T, Eguchi S, Yoshizumi T, et al. Incidental intrahepatic cholangiocarcinoma in patients undergoing liver transplantation: a multi-center study in Japan. J Hepatobiliary Pancreat Sci. 2021;28:346–52.

9. Sapisochin G, de Sevilla EF, Echeverri J, Charco R. Management of "very early" hepatocellular carcinoma on cirrhotic patients. World J Hepatol. 2014;6:766–75.
10. Sapisochin G, Facciuto M, Rubbia-Brandt L, et al. Liver transplantation for "very early" intrahepatic cholangiocarcinoma: international retrospective study supporting a prospective assessment. ICCA International consortium. Hepatology. 2016;64:1178–88.
11. Ziogas IA, Giannis D, Economopoulos KP, et al. Liver transplantation for intrahepatic cholangiocarcinoma: a meta-analysis and meta-regression of survival rates. Transplantation. 2021;105:2263–71.
12. Moeckli B, Ivanics T, Claasen M, et al. Recent developments and ongoing trials in transplant oncology. Liver Int. 2020;40:2326–44.
13. Hong JC, Jones CM, Duffy JP, et al. Comparative analysis of resection and liver transplantation for intrahepatic and hilar cholangiocarcinoma: a 24-year experience in a single center. Arch Surg. 2011;146:683–9.
14. Lunsford KE, Javle M, Heyne K, et al. Liver transplantation for locally advanced intrahepatic cholangiocarcinoma treated with neoadjuvant therapy: a prospective case-series. Lancet Gastroenterol Hepatol. 2018;3:337–48.
15. Sapisochin G, Javle M, Lerut J, et al. Liver transplantation for cholangiocarcinoma and mixed hepatocellular cholangiocarcinoma: working group report from the ILTS transplant oncology consensus conference. Transplantation. 2020;104:1125–30.
16. Tsimafeyeu I, Temper M. Cholangiocarcinoma: an emerging target for molecular therapy. Gastrointest Tumors. 2021;8:153–8.
17. Mizuno T, Ebata T, Nagino M. Advanced hilar cholangiocarcinoma: an aggressive surgical approach for the treatment of advanced hilar cholangiocarcinoma: perioperative management, extended procedures, and multidisciplinary approaches. Surg Oncol. 2020;33:201–6.
18. Mizuno T, Ebata T, Yokoyama Y, et al. Combined vascular resection for locally advanced perihilar cholangiocarcinoma. Ann Surg. 2022;275:382–90.
19. Rea DJ, Heimbach JK, Rosen CB, et al. Liver transplantation with neoadjuvant chemoradiation is more effective than resection for hilar cholangiocarcinoma. Ann Surg. 2005;242:451–8.
20. Darwish Murad S, Kim WR, et al. Efficacy of neoadjuvant chemoradiation, followed by liver transplantation, for perihilar cholangiocarcinoma at 12 US centers. Gastroenterology. 2012;143:88–98. e3.
21. Loveday BPT, Knox JJ, Dawson LA, et al. Neoadjuvant hyperfractionated chemoradiation and liver transplantation for unresectable perihilar cholangiocarcinoma in Canada. J Surg Oncol. 2018;117:213–9.
22. Rosen CB, Darwish Murad S, Heimbach JK, Nyberg SL, Nagorney DM, Gores GJJ. Neoadjuvant therapy and liver transplantation for hilar cholangiocarcinoma: is pretreatment pathological confirmation of diagnosis necessary? Am Coll Surg. 2012;215(1):31–8; discussion 38–40.
23. Robles R, Figueras J, Turrión VS, et al. Spanish experience in liver transplantation for hilar and peripheral cholangiocarcinoma. Ann Surg. 2004;239:265–71.
24. Duignan S, Maguire D, Ravichand CS, et al. Neoadjuvant chemoradiotherapy followed by liver transplantation for unresectable cholangiocarcinoma: a single-centre national experience. HPB. 2014;16:91–8.
25. Croome KP, Rosen CB, Heimbach JK, et al. Is liver transplantation appropriate for patients with potentially resectable de novo hilar cholangiocarcinoma? J Am Coll Surg. 2015;221:130–9.
26. Kaiser GM, Sotiropoulos GC, Jauch KW, et al. Liver transplantation for hilar cholangiocarcinoma: a German survey. Transplant Proc. 2008;40:3191–3.
27. Safarpour AR, Askari H, Ejtehadi F, et al. Cholangiocarcinoma and liver transplantation: what we know so far? World J Gastrointest Pathophysiol. 2021;12:84–105.
28. Sapisochin G, Muaddi H, Baxter NN, et al. Implementation of critical care response teams in Ontario: impact on the outcomes of surgical patients. Ann Surg. 2020. [Online ahead of print]
29. Gringeri E, Gambato M, Sapisochin G, et al. Cholangiocarcinoma as an indication for liver transplantation in the era of transplant oncology. J Clin Med. 2020;9:1353.
30. Murad SD, Kim WR, Harnois DM, et al. Efficacy of neoadjuvant chemoradiation, followed by liver transplantation, for perihilar cholangiocarcinoma at 12 US centers. Gastroenterology. 2012;143:88–98.
31. Ito T, Butler JR, Noguchi D, et al. A 3-decade, single-center experience of liver transplantation for cholangiocarcinoma: impact of era. Tumor size: location, and neoadjuvant therapy. Liver Transpl. 2021;28(3):386–96.
32. Guo X, Shen W. Latest evidence on immunotherapy for cholangiocarcinoma. Oncol Lett. 2020;20:381.
33. Salgia RJ, Singal AG, Fu S, et al. Improved post-transplant survival in the United States for patients with cholangiocarcinoma after 2000. Dig Dis Sci. 2014;59:1048–54.
34. Heimbach JK, Gores GJ, Haddock MG, et al. Predictors of disease recurrence following neoadjuvant chemoradiotherapy and liver transplantation for unresectable perihilar cholangiocarcinoma. Transplantation. 2006;82:1703–7.
35. Ethun CG, Lopez-Aguiar AG, Anderson DJ, et al. Transplantation versus resection for hilar cholangiocarcinoma: an argument for shifting treatment paradigms for resectable disease. Ann Surg. 2018;267:797–805.
36. Sapisochin G, Ivanics T, Heimbach J. Liver transplantation for intrahepatic cholangiocarcinoma: ready for prime time? Hepatology. 2022;75(2):455–72.
37. Mazzaferro V, Gorgen A, Roayaie S, et al. Liver resection and transplantation for intrahepatic cholangiocarcinoma. J Hepatol. 2020;72:364–77.
38. Schaefer B, Zoller H, Schneeberger S. Con: liver transplantation for expanded criteria malignant diseases. Liver Transpl. 2018;24:104–11.
39. Dondorf F, Uteβ F, Fahrner R, et al. Liver transplant for perihilar cholangiocarcinoma (Klatskin Tumor): the essential role of patient selection. Exp Clin Transplant. 2019;17:363–9.
40. Sapisochin G, Hibi T, Toso C, et al. Transplant oncology in primary and metastatic liver tumors: principles, evidence, and opportunities. Ann Surg. 2021;273:483–93.

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