6 ulusal CERRAHİ ONKOLOJİ KONGRESİ

24 - 27 Şubat 2022 | Gloria Golf Resort – ANTALYA

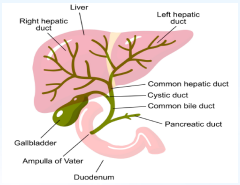
DOÇ. DR. GÖKHAN AKKURT

ANKARA ŞEHİR HASTANESİ CERRAHİ ONKOLOJİ KLİNİĞİ

Nüks safra yolu tümörlerinde cerrahi şansı yok mu?

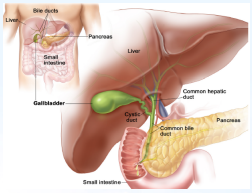
Safra Yolu Tümörleri (BTC):

- *Kolanjiokarsinom*
- *Safra Kesesi Kanseri*
- *Ampulla Vateri Kanseri*



Kolanjiokarsinom anatomik olarak;

- *İntrahepatik kolanjiokarsinom (ICC)*
- *Ekstrahepatik kolanjiokarsinom (ECC)*
  - *Hiler kolanjiokarsinom (Klatskin Tm)*
  - *Distal kolanjiokarsinom*



İntrahepatik kolanjiokarsinom (ICC)

- ICC insidansı son birkaç yılda dünya çapında artmaktadır.
- ICC'da kür sağlamanın tek yolu cerrahidir.
- Cerrahi rezeksiyon ➡ 3 yıllık sağkalım ***%40-50***
- Hiler safra kanalı, vasküler invazyon nedeniyle ***kombine hepatektomi + safra kanalı rezeksiyonu*** gerekir.

Unrezektabl lokal ileri CCA

⬇

Neoadjuvan kemoterapi

⬇

Tümör boyutunda küçülme ve/veya evre düşmesi

⬇

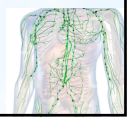
Rezeksiyon şansı

Lenfadenektominin sağkalım üzerine faydası **net değil**

Rezeksiyon sonrası nüks *%46 ile %65*

	8th Edition[1]	7th Edition[10]
T category (pT)		
Tis	Carcinoma in situ (intraductal tumor)	Carcinoma in situ (intraductal tumor)
T1	Solitary, without vascular invasion	Solitary, without vascular invasion
T1a	Solitary, ≤5 **cm** without vascular invasion	
T1b	Solitary, >5 **cm** without vascular invasion	
T2	Solitary, with vascular invasion; or multiple, with or without vascular invasion	
T2a		Solitary, with vascular invasion
T2b		Multiple, with or without vascular invasion
T3	Perforating the visceral peritoneum	Perforating the visceral peritoneum or involving local extrahepatic structures by direct invasion
T4	**Involving local extrahepatic structures by direct invasion**	Periductal invasion
N category (pN)		
N0	No regional lymph node metastasis	No regional lymph node metastasis
N1	Regional lymph node metastasis	Regional lymph node metastasis
AJCC stage groupings		
IA	**T1a N0 M0**	
IB	**T1b N0 M0**	
I		T1 N0 M0
II	T2 N0 M0	T2 N0 M0
IIIA	T3 N0 M0	
IIIB	**T4 N0 M0; any T N1 M0**	
III		T3 N0 M0
IV	Any T any N M1	
IVA		T4 N0 M0; any T N1 M0
IVB		Any T any N M1

- **AJCC 8th ed; ICC için 17 bölgesel lenf nodu (LN) tanımlanmıştır.**
- **Sağ karaciğer ICC için,**
  - *hiler (ortak safra kanalı, hepatik arterler, portal ven ve sistik kanal),*
  - *periduodenal ve peripankreatik LN*
- **Sol karaciğer ICC için,**
  - *infra-frenik, hiler ve gastrohepatik LN*
- Çölyak ve/veya periaortik ve kaval LN uzak metastaz (M1).



Tsuji T, Hiraoka T, Kanemitsu K, Takamori H, Tanabe O, Tashiro S. Lymphatic spreading pattern of intrahepatic cholangiocarcinoma. Surgery. 2002;129:407.

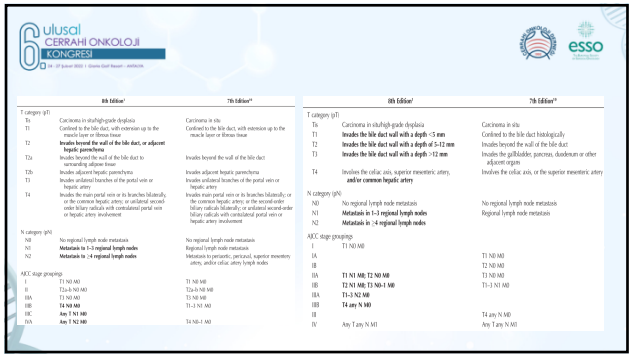
Ekstrahepatik kolanjiokarsinom (ECC)

Gelişmiş görüntüleme yöntemleri

Cerrahi teknikler

➡ Küratif rezeksiyon oranı giderek artmakta

- **Nüks safra yolu tümörleri;**
  - *lokal yetmezlik*
  - *karaciğer metastaz*
  - *LN metastazı*
  - *peritoneal metastaz*
- Marjin (-) rezeksiyon sonrası nükslerin çoğu ***lokorejyonel olmakta***



	8th Edition[1]	7th Edition[9]
T category (pT)		
Tis	Carcinoma in situ/high-grade dysplasia	Carcinoma in situ
T1	Confined to the bile duct, with extension up to the muscle layer or fibrous tissue	Confined to the bile duct histologically
T2	**Invades beyond the wall of the bile duct, or adjacent hepatic parenchyma**	Invades beyond the wall of the bile duct
T2a	Invades beyond the wall of the bile duct to surrounding adipose tissue	
T2b	Invades adjacent hepatic parenchyma	Invades adjacent hepatic parenchyma
T3	Invades unilateral branches of the portal vein or hepatic artery	Invades unilateral branches of the portal vein or hepatic artery
T4	Invades the main portal vein or its branches bilaterally; or the common hepatic artery; or unilateral second-order biliary radicals with contralateral portal vein or hepatic artery involvement	Invades main portal vein or its branches bilaterally; or the common hepatic artery; or the second-order biliary radicals bilaterally; or unilateral second-order biliary radicals with contralateral portal vein or hepatic artery involvement
N category (pN)		
N0	No regional lymph node metastasis	No regional lymph node metastasis
N1	**Metastasis to 1–3 regional lymph nodes**	Regional lymph node metastasis
N2	**Metastasis to ≥4 regional lymph nodes**	Metastases to periaortic, pericaval, superior mesentery artery, and/or celiac artery lymph nodes
AJCC stage groupings		
I	T1 N0 M0	T1 N0 M0
II	T2a-b N0 M0	T2a-b N0 M0
IIIA	T3 N0 M0	T3 N0 M0
IIIB	**T4 N0 M0**	T1–3 N1 M0
IIIC	**Any T N1 M0**	
IVA	**Any T N2 M0**	T4 N0–1 M0

	8th Edition[1]	7th Edition[9]
T category (pT)		
Tis	Carcinoma in situ/high-grade dysplasia	Carcinoma in situ
T1	**Invades the bile duct wall with a depth <5 mm**	Confined to the bile duct histologically
T2	**Invades the bile duct wall with a depth of 5–12 mm**	Invades beyond the wall of the bile duct
T3	**Invades the bile duct wall with a depth >12 mm**	Invades the gallbladder, pancreas, duodenum or other adjacent organs
T4	Involves the celiac axis, superior mesenteric artery, **and/or common hepatic artery**	Involves the celiac axis, or the superior mesenteric artery
N category (pN)		
N0	No regional lymph node metastasis	No regional lymph node metastasis
N1	**Metastasis in 1–3 regional lymph nodes**	Regional lymph node metastasis
N2	**Metastasis in ≥4 regional lymph nodes**	
AJCC stage groupings		
I	T1 N0 M0	
IA		T1 N0 M0
IB		T2 N0 M0
IIA	**T1 N1 M0; T2 N0 M0**	T3 N0 M0
IIB	**T2 N1 M0; T3 N0–1 M0**	T1–3 N1 M0
IIIA	**T1–3 N2 M0**	
IIIB	**T4 any N M0**	
III		T4 any N M0
IV	Any T any N M1	Any T any N M1

Safra Kesesi Kanseri

Safra kesesi kanserinde (GBC) prognoz;

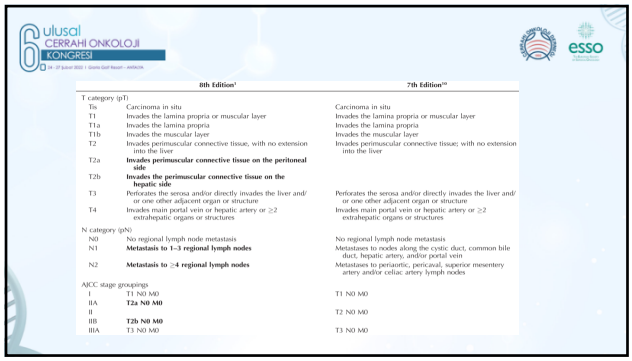
- *Evreye bağlı değişkenlik*
- *Cerrahi rezeksiyon sonrası kötü prognoz*

%30-65 oranında nüks

- *lenf nodu metastazı*
- *pozitif rezeksiyon sınırı*
- *orta veya az diferansiasyon*
- *karaciğer ve safra kanalında tm*

Kim WS, Choi DW, Yoo DO, Ho CY, Heo JS, Choi SH. Risk factors influencing recurrence, patterns of recurrence, and the efficacy of adjuvant therapy after radical resection for gallbladder carcinoma. J Gastrointest Surg. 2010;14:679–87.

Margonis GA, Gani F, Buettner S, et al. Rates and patterns of recurrence after curative intent resection for gallbladder cancer: a multi-institution analysis from the US extra-hepatic biliary malignancy consortium. HPB (Oxford). 2016;18:872–9.



	8th Edition[1]	7th Edition[10]
T category (pT)		
Tis	Carcinoma in situ	Carcinoma in situ
T1	Invades the lamina propria or muscular layer	Invades the lamina propria or muscular layer
T1a	Invades the lamina propria	Invades the lamina propria
T1b	Invades the muscular layer	Invades the muscular layer
T2	Invades perimuscular connective tissue, with no extension into the liver	Invades perimuscular connective tissue; with no extension into the liver
T2a	**Invades perimuscular connective tissue on the peritoneal side**	
T2b	**Invades the perimuscular connective tissue on the hepatic side**	
T3	Perforates the serosa and/or directly invades the liver and/or one other adjacent organ or structure	Perforates the serosa and/or directly invades the liver and/or one other adjacent organ or structure
T4	Invades main portal vein or hepatic artery or ≥2 extrahepatic organs or structures	Invades main portal vein or hepatic artery or ≥2 extrahepatic organs or structures
N category (pN)		
N0	No regional lymph node metastasis	No regional lymph node metastasis
N1	**Metastasis to 1–3 regional lymph nodes**	Metastases to nodes along the cystic duct, common bile duct, hepatic artery, and/or portal vein
N2	**Metastasis to ≥4 regional lymph nodes**	Metastases to periaortic, pericaval, superior mesentery artery and/or celiac artery lymph nodes
AJCC stage groupings		
I	T1 N0 M0	T1 N0 M0
IIA	**T2a N0 M0**	
II		T2 N0 M0
IIB	**T2b N0 M0**	
IIIA	T3 N0 M0	T3 N0 M0

Ampulla Vateri Kanseri

- Primer ampullar karsinomlar nadir görülen maligniterlerdir (Gastrointestinal kanserler <%1).

Ampullar kanser ➡ *ampulla vater*

Periampuller tümörler *safra kanalı, bağırsak* veya *pankreas*

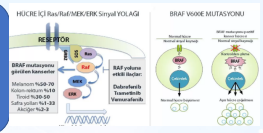
- Ampuller kanser, pankreas kanseri cerrahi rezeksiyon sonrası ***5 yıllık sağkalım (%37-68/%10-30).***
- Küratif rezeksiyon sonrası ***%50 nüks***

Morris-Stiff G, Alabraba E, Tan YM, et al. Assessment of survival advantage in ampullary carcinoma in relation to tumor biology and morphology. Eur J Surg Oncol. 2009;35:746–50.

Konstantinidis IT, Warshaw AL, Allen JN, et al. Pancreatic ductal adenocarcinomas: is there a survival difference for R1 resection versus locally advanced unresectable tumors? What is a true R0 resection? Ann Surg. 2013;257:731–6.

	8th Edition[1]	7th Edition[19]
T category (pT)		
Tis	Carcinoma in situ	Carcinoma in situ
T1	Limited to ampulla of Vater or sphincter of Oddi **or invades into the duodenal submucosa**	Limited to ampulla of Vater or sphincter of Oddi
T1a	**Limited to ampulla of Vater or sphincter of Oddi**	
T1b	**Invades beyond the sphincter of Oddi and/or into the duodenal submucosa**	
T2	Invades into the **muscularis propria** of the duodenum	Invades duodenal wall
T3	Invades the pancreas **or extends into peripancreatic/ periduodenal tissue or duodenal serosa**	Invades pancreas
T3a	**Invades the pancreas (<0.5 cm)**	
T3b	**Invades the pancreas (>0.5 cm) or peripancreatic/ periduodenal tissue or duodenal serosa**	
T4	**Involves the celiac axis, superior mesenteric artery, and/or common hepatic artery**	Invades peripancreatic tissues or other adjacent organs or structures
N category (pN)		
N0	No regional lymph node metastasis	No regional lymph node metastasis
N1	**Metastasis to 1–3 regional lymph nodes**	Regional lymph node metastasis
N2	**Metastasis to ≥4 regional lymph nodes**	
AJCC stage groupings		
IA	**T1a N0 M0**	T1 N0 M0
IB	**T1b–2 N0 M0**	T2 N0 M0
IIA	**T3a N0 M0**	T3 N0 M0
IIB	**T3b N0 M0**	T1–3 N1 M0
IIIA	**T1a–3b N1 M0**	
IIIB	**T4 any N M0; any T N2 M0**	

- *Fibroblast büyüme faktörü reseptörü (FGFR)*
- *İzositrat dehidrojenaz inhibitörler (IDH)*
- *Anti- Human epidermal büyüme faktörü reseptörü-2 (HER2)*
- *MEK inhibitörleri*
- *BRAF inhibitörleri*



Wei Zhang, Hongyuan Zhou, Yingying Wang, Zewu Zhang, Guangtai Cao, Tiangiang Song, Ti Zhang, Qiang Li. Systemic treatment of advanced or recurrent biliary tract cancer. BioScience Trends. 2020; 14(5):328-341.

- Günümüzde nüks BTC için cerrahiye giderek artan ilgi var.
- ***Nüks paternlerinin değişkenlik göstermesinden*** dolayı bazı hastaların ameliyattan fayda görme olasılığı yüksek
- Nüks BTC nedeniyle ameliyat olan hastalarda ***sağkalım avantajı gösterilmiştir.***
- *Hala belirsizlik mevcut*
- *Çalışmaların çoğunluğu tek merkezli*

Takahashi Y, Ebata T, Yokoyama Y, Igami T, Sugawara G, Mizuno T et al. (2015) Surgery for recurrent biliary tract cancer: a single-center experience with 74 consecutive resections. Ann Surg 262:121–129.

ORIGINAL ARTICLE

Surgery for Recurrent Biliary Tract Cancer

A Single-center Experience With 74 Consecutive Resections

Yu Takahashi, MD, Tomoki Ebata, MD,* Yukihiro Yokoyama, MD,* Tsuyoshi Igami, MD,* Gen Sugawara, MD,* Takashi Mizuno, MD,* Yuji Nimura, MD,† and Masato Nagino, MD**

Objective: To review our experiences with surgery for recurrent biliary tract cancer (BTC).
Background: Few studies have reported on surgical procedures for recurrent BTC; therefore, it is unclear whether this surgery has survival benefit.
Methods: Between 1991 and 2010, 606 patients had recurrences after resection of BTC (gallbladder cancer, n = 135; cholangiocarcinoma, n = 471). 74 patients underwent resection for recurrence, whereas the remaining 532 did not. The medical records were retrospectively reviewed.

Only 1 original study (n = 27)[9] and several small case series[10–12] have been published on surgery for recurrent CC. To date, we have aggressively performed surgical resections for recurrent BTC when the surgery is technically feasible and could offer a better chance of long-term survival.

The aim of the present study was to review our experiences with surgical treatment of recurrent BTC and to evaluate whether aggressive surgical approaches have beneficial effects.

- 1991- 2010 yılları arasında 606 BTC hastası rezeksiyon sonrası nüks
  - *135 hasta GBC*
  - *471 hasta CCA*
- **74 hasta nüks nedeniyle rezeksiyon**
  - *Daha az ilerlemiş kanser*
  - *Nüks etme süreleri daha uzun (1.4-0.8 yıl; P < 0.001)*
- Toplam 89 cerrahi prosedür
  - 63 hastada 1
  - 11'de ≥2 kez
- Nüks sonrası sağkalım ***rezeksiyon grubunda daha iyiydi*** (3 yılda ***%32'ye karşı %3;*** P < 0,001).

- Bazı çalışmalar da; soliter nüks ICC için ***tekrar hepatektomiler sonrası iyi prognoz***
- ***Spolverrato ve ark***. ICC için küratif amaçlı karaciğer rezeksiyonu sonrası,

210 hasta (%53) destek tedavi,
190 hasta (%48)

- *sadece sistemik kemoterapi (%24)*
- *tekrarlayan karaciğere yönelik tedavi ve sistemik kemoterapi (%76).*
  - *tekrarlayan hepatik rezeksiyon ± ablasyon (28.5 %)*
  - *sadece ablasyon (18.7 %)*
  - *intra-arteriyal terapi (52.8 %)*

Masaru Miyazaki, Hiroaki Shimizu, Hideyuki Yoshitomi, Atsushi Kato, Katsunori Furukawa, Tsukasa Takayashiki, Satoshi Kubota, Shigetsugu Takano, Masayuki Ohtsuka. Clinical implication of surgical resection for recurrent biliary tract cancer: Does it work or not? Ann Gastroenterol Surg. 2017;1:164–170.

- Rezeksiyon yapılan nüks vakalarda medyan sağkalım ***26.7 ay***
- ICC rezeksiyonu sonrası hastaların ***üçte ikisinde nüks***
- Nüks olduğunda prognoz kötü
- %10 hastada nüks sonrası ***tekrar karaciğer rezeksiyonu*** olasılığı
- Mütevazı bir hayatta kalma avantajı sağladı

Spolverato G, Kim Y, Alexandrescu S, et al. Management and outcomes of patients with recurrent intrahepatic cholangiocarcinoma following previous curative-intent surgical resection. Ann Surg Oncol. 2016;23:235–43.

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Surgical re-resection for recurrence of ICC after initial hepatectomy

Author	Year	n	Re-surgery	Prognosis
Yamamoto et al.[13]	2001	4/25	Hepatectomy	17-155 mo (range)
Ohtsuka et al.[22]	2009	9/37	Hepatectomy	Median 22 mo
Ercolani et al.[23]	2010	6/39	Hepatectomy	56% at 3 y
Kamphues et al.[24]	2010	13/71	Hepatectomy+Ablation	Median 51 mo
Salura et al.[19]	2011	4/25	Hepatectomy	43% at 5 y
		1/25	Pneumonectomy	137 mo alive
Song et al.[25]	2011	5/74	Hepatectomy	6.8-58.5 mo
Sulpice et al.[26]	2012	4/45	Hepatectomy	100% at 5 y
Takahashi et al.[27]	2015	2/47	Hepatectomy	NA
		3/47	Pneumonectomy	NA
		2/47	Locoregional	NA
Souche et al.[28]	2016	10/76	Hepatectomy	Median 25 mo
Miyazaki et al.[29]	2017	9/36	Hepatectomy	Median 28.5 mo (uncertain)
Spolverato et al.[30]	2016	41/400	Hepatectomy	Median 26.7 mo

ICC, intrahepatic cholangiocarcinoma; mo, months; n, no. patients for re-surgery/recurrence; NA, not available; y, years.

Masaru Miyazaki, Hiroaki Shimizu, Hideyuki Yoshitomi, Atsushi Kato, Katsunori Furukawa, Tsukasa Takayashiki, Satoshi Kuboki, Shigetsugu Takano, Masayuki Ohtsuka. Clinical implication of surgical resection for recurrent biliary tract cancer: Does it work or not? Ann Gastroenterol Surg. 2017;1:164–170.

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- ***Çoklu primer tümör*** (n = 1 [%6.7] n = 31 [%33.3], p = 0.037)
- ***Erken nüks*** (≤ 1 yıl; n = 4 [%26.7] ve n = 62 [%66.7], p = 0.003)
- Nüks sonrası sağkalım ***cerrahi uygulanan hastalarda daha iyiydi***

(91.6/10.4 ay ve 3 yıllık sağ kalım: %86,7/%8,7, p<0,001)

Tomoaki Yoh[1] · Etsuro Hatano[2] · Satoru Seo[1] · Yukihiro Okuda[1] · Hiroaki Fuji[1] · Yoshinobu Ikeno[1] · Kojiro Taura[1] · Kentaro Yasuchika[1] · Hideki Ogiso[1] · Toshimi Kaido[1] · Shinji Uemoto[1]

1993-2015 yılları arasında

üks ICC'u olan 108 hasta

5 hasta tekrar ameliyat edildi

ntrahepatik 7/29, ekstrahepatik rekürrensli 8/44 hasta ameliyat için müsaitti

- Cerrahi yapılanlarda düşük lenf nodu metastazı oranı vardı (n = 0 [%0] n = 47 [%50.5], p<0.001)

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Multicenter Study

Repeated re… cholangioc… multicentre…

Fabian Bartsch [1], Joh… Nadja Lehwald-Tywuschik [1], Felix Oldhafer [2], Markus Dienes [2], Ariane… Tobias Keck [3], Helmut Friess [3], Bertram… Andreas Schnitzbauer [3], Hauke Lang [3]

Affiliations + expand

PMID: 32997886 DOI: 10.1111/ivs.1468

Tekrarlayan rezeksiyon yapılanlarda medyan **GS 65.2 ay** (1,3 ve 5 yıllık GS; %98, %78 ve %57)

Tekrarlanan rezeksiyon gününden itibaren medyan **GS 36.8 ay** (1,3 ve 5 yıllık GS; %86, %51 ve %34)

%27 minör morbidite (grade I-II), %20 grade IIIa-IVb morbidite, %3,5 mortalite

…inden ***nüks ICC*** …oplandı.

…nünden itibaren nükssüz

- ICC'un tekrarlayan rezeksiyonu ***kabul edilebilir morbidite ve mortaliteye sahip***
- ***İyileştirilmiş uzun süreli sağkalım*** ile ilişkili görünmekte
- Bu hastaların erken teşhisi için ***rezeksiyonu sonrası yakın takip önemli***

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- Ekstrahepatik safra kanalının orta kısmından kaynaklı ECC;
  - İlk ameliyatta → *Safra kanalı rezeksiyonu*
  - Nüks → *PD veya hepatektomi*
- LN tutulumu yoksa iyi, göğüs ve abdominal duvar tutulumu ***kötü prognoz***

Nodal durum
İlk nüks yeri
→ Bağımsız prediktif faktör

- ***Tekrarlayan rezeksiyonlar güvenli ve sağkalım da etkili***

Takahashi Y, Ebata T, Yokoyama Y, et al. Surgery for recurrent biliary tract cancer: a single-center experience with 74 consecutive resections. Ann Surg. 2015;262:125–8.

ulusal CERRAHİ ONKOLOJİ KONGRESİ

Surgical re-resection for recurrence of extrahepatic bile duct cancer after initial resection

Author	Year	n	Initial surgery	Re-surgery	Prognosis
Targarona et al.[39]	1993	1/?	BDR	Hepatectomy	10 mo alive
Yoon et al.[40]	2005	1/?	BDR	Hepatectomy	46 mo alive
		1/?	Hepatectomy	BDR	9 mo alive
Hibi et al.[41]	2006	1	PD	Hepatectomy	8 mo alive
Hwang et al.[42]	2010	2/?	BDR	PD	37 and 65 mo alive
Song et al.[25]	2011	10/242	BDR	PD, LN dissection, 4-101 mo (range)	
		10/242	BDR, PD	Metastasectomy	
Kureosaki et al.[28]	2011	7/37	PD	Hepatectomy	Median 14 mo
Noji et al.[43]	2015	18/114	NA	NA	23.5% at 5 y
Lee et al.[44]	2015	6/?	BDR	PD	Median 16 mo
Takahashi et al.[27]	2015	47/424	Hepatectomy, PD	PD, Hepatectomy	32% at 3 y
Miyazaki et al.[29]	2017	4/60	PD, hepatectomy	Hepatectomy	19% at 5 y

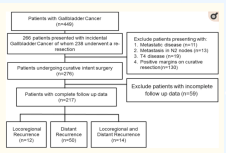
BDR, bile duct resection; HPD, hepatopancreaticoduodenectomy; LN, lymph nodes; mo, months; n, no. patients for re-surgery/recurrence; NA, not available; PD, pancreaticoduodenectomy; y, years.

Masaru Miyazaki, Hiroaki Shimizu, Hideyuki Yoshitomi, Atsushi Kato, Katsunori Furukawa, Tsukasa Takayashiki, Satoshi Kuboki, Shigetsugu Takano, Masayuki Ohtsuka. Clinical implication of surgical resection for recurrent biliary tract cancer: Does it work or not? Ann Gastroenterol Surg. 2017;1:164–170.

ulusal CERRAHİ ONKOLOJİ KONGRESİ

Margonis ve ark.

- GBC için küratif rezeksiyon sonrası ***nüks oranları*** ve ***paternleri*** bildirmiş
  - *ABD Ekstrahepatik Biliyer Malignite Konsorsiyum*
- 76 hasta (%35) nüks
  - *yalnızca bölgesel %12*
  - *yalnızca uzak %66*
  - *bölgesel ve uzak %18*
- *Nüks sonrası adjuvan tedavi* ***iyileştirilmiş genel sağkalım ile ilişkiliydi***
  - *1 yıl GS 91% vs 69%*
  - *3-yıl GS 79% vs 29%*
  - *5-yıl GS 76% vs 16%*



Margonis GA, Gani F, Buettner S, et al. Rates and patterns of recurrence after curative intent resection for gallbladder cancer: a multi-institution analysis from the US extra-hepatic biliary malignancy consortium. HPB (Oxford). 2016;18:872–8.

- ***Nüks safra kesesi kanserinde*** cerrahinin rolü hakkında çok az veri var
- Lokal ve/veya sistemik tedavi yetersiz
- **Takahashi ve ark.**
  - *Nüks GBC nedeniyle 20 hastayı ameliyat etmiş*
  - *%35.6* ➡ 3 yıllık sağkalım

Takahashi Y, Ebata T, Yokoyama Y, Igami T, Sugawara G, Mizuno T et al. (2015) Surgery for recurrent biliary tract cancer: a single-center experience with 74 consecutive resections. Ann Surg 262:121–128.

Surgical re-resection for recurrence of gallbladder carcinoma after initial resection

Author	Year	n	Initial surgery	Re-surgery	Prognosis
Noji et al.[43]	2015	9/36	NA	NA	23.5% at 5 y
Takahashi et al.[27]	2015	20/135	CHX-HPD	NA	6% at 5 y
Miyazaki et al.[29]	2017	1/11	NA	NA	Median 28.5 mo

CHX, cholecystectomy; HPD, hepatopancreaticoduodenectomy; mo, months; n, no. patients for re-surgery/recurrence; NA, not available; y, years.

Surgical re-resection for the recurrence of ampullary cancer after initial resection

Author	Year	n	Initial surgery	Re-surgery	Prognosis
Kurosaki et al.[38]	2011	6/22	PD	Hepatectomy	8-75 mo (range)
Miyazaki et al.[29]	2017	1/11	NA	NA	NA

mo, months; n, no. patients for re-surgery/recurrence; NA, not available; PD, pancreaticoduodenectomy.

Masaru Miyazaki, Hiroaki Shimizu, Hideyuki Yoshitomi, Atsushi Kato, Katsunori Furukawa, Tsukasa Takayashiki, Satoshi Kuboki, Shigetsugu Takano, Masayuki Ohtsuka. Clinical implication of surgical resection for recurrent biliary tract cancer: Does it work or not?. Ann Gastroenterol Surg. 2017;1:164–170.

Multicenter Study > HPB (Oxford). 2021 Sep;23(9):1371-1382. doi: 10.1016/j.hpb.2021.01.007. Epub 2021 Jan 22.

Oncological outcomes of surgery for recurrent biliary tract cancer: who are the best candidates?

Jun Sakata [1], Tatsuya Nomura [2], Takashi Aono [3], Chie Kitami [4], Naoyuki Yokoyama [5], Masahiro Minagawa [6], Kazuyasu Takizawa [7], Kohei Miura [8], Yuki Hirose [9], Hiroshi Ishikawa [10], Masayuki Nagahashi [11], Yoshifumi Shimada [12], Takashi Kobayashi [13], Toshifumi Wakai [14]

Affiliations + expand

PMID: 33558069 DOI: 10.1016/j.hpb.2021.01.007

- **Nüks BTC olan 178 hasta, tek merkez**
  - *24 hasta ameliyat*
  - *85 hasta kemoterapi*
  - *69 hasta destekleyici bakım*
- **Nüks BTC nedeniyle ameliyat olan 52 hasta, çok merkez**
  - *safra kesesi kanseri (%39)*
  - *distal kolanjiokarsinom (%27)*
  - *perihilar kolanjiokarsinom (%21)*
  - *intrahepatik kolanjiokarsinom (%13)*

Tek merkezli çalışmada;

- Nüks sonrası 3 yıllık sağkalım;
  - *cerrahi uygulanan hastalarda %53,*
  - *kemoterapi alanlarda %4*
  - *destekleyici bakım alan hastalarda %0 idi (p < 0.001).*
- Cerrahi ***bağımsız bir prognostik faktördü*** (p < 0,001).

Çok merkezli serilerde,

- 52 hastada nüks nedeniyle cerrahi sonrası 3 ve 5 yıllık sağkalım %50 ve %29 idi.
- ***İlk nüks bölgesi*** tek bağımsız prognostik faktördü (p = 0.019).

Tek uzak	Multifokal uzak	Lokorejyonel nüks	(Cerrahi sonrası beş yıllık sağkalım)
⬇	⬇	⬇	
%51	%0	%0	

Univariate and multivariate analyses of cancer-specific survival after surgery for recurrence in 52 patients with recurrent biliary tract cancer

Variable	No. of patients	Survival rate (%)			Univariate analysis	Multivariate analysis	
		1-year	3-year	5-year	p-value	Hazard ratio (95% CI)	p-value
Age at surgery for recurrence, years					0.300		
< 65	16	75	56	32			
≥ 65	36	80	47	29			
Sex					0.671		
Male	27	74	52	16			
Female	25	83	48	37			
Site of primary tumor					0.764		
Gallbladder	20	79	59	33			
Perihilar bile ducts	11	91	62	0			
Distal bile duct	14	62	34	17			
Intrahepatic bile ducts	7	86	86	51			
Adjuvant chemotherapy for primary tumor					0.904		
Absent	30	77	54	21			
Present	20	80	44	33			
pT classification*					0.226		
pT1plus pT2	29	85	52	40			
pT3 plus pT4	23	73	47	21			
pN classification*					0.982		
pN0	32	84	45	30			
pN1 plus pN2	20	73	58	37			
pM classification*					0.618		
pM0	47	78	46	28			
pM1	5	80	80	40			

Variable	No. of patients	Survival rate (%)			Univariate analysis	Multivariate analysis	
		1-year	3-year	5-year	p-value	Hazard ratio (95% CI)	p-value
Initial site of recurrence					0.032		
Locoregional	17	77	49	0		0.540 (0.229–1.315)	0.178
Single distant	24	92	68	51		0.256 (0.108–0.612)	0.019
Multifocal distant	11	55	18	0		1.000	
Time to recurrence, years					0.336		
< 2	27	70	37	31			
≥ 2	25	87	64	26			
Preoperative chemotherapy for recurrence					0.428		
Absent	41	76	53	30			
Present	11	91	35	23			
Postoperative chemotherapy for recurrence					0.722		
Absent	19	84	44	29			
Present	33	76	62	28			
Complications† after surgery for recurrence					0.969		
Lower than IIIa	42	80	51	29			
IIIa or higher	10	70	48	32			
Residual tumor classification (R)* for recurrence					0.001		
R0	39	87	56	40		1.000	
R1 plus R2	13	54	31	0		1.886 (0.817–4.407)	0.136

CI, confidence interval; pT classification, pathological primary tumor classification; pN classification, pathological regional lymph nodes classification; pM classification, pathological distant metastasis classification.
* According to UICC TNM staging system.[14]
† Other histological types included adenosquamous carcinoma (n = 3), small cell carcinoma (n = 1).
‡ According to Clavien-Dindo classification.[15]

Tek uzak nüks bölgeleri:

- *Karaciğer (n = 13, %54)*
- *Uzak lenf nodları (tümü GBC, n = 7, % 29)*
- *Akciğer (n = 2, % 9)*
- *Periton (n = 1, %4)*
- *Karın duvarı (n = 1, %4)*

***Sonuçta** Nüks BTC de;*

- daha az agresif tümör biyolojisi

- tek uzak nüks olan hastalarda

cerrahi etkili bir seçenek

- Unrezektabl CCA da ***karaciğer transplantasyonu (LT)*** bir seçenek olarak kabul edilebilir.

  - pozitif cerrahi sınır
  - yetersiz karaciğer volümü
  - altta yatan sklerozan kolanjit gibi primer hastalık

- Geçmişte, ***yüksek nüks*** oranı nedeniyle LT etkisiz olarak kabul edildi

1993 yılında Nebraska Üniversitesi

Mayo Klinik Karaciğer Nakli Merkezi

➡ Neoadjuvan protokol

Gringeri E, Gambato M, Sapisochin G, Ivanics T, Lynch EN, Mescoli C et al. Cholangiocarcinoma as an Indication for Liver Transplantation in the Era of Transplant Oncology. J. Clin. Med. 2020, 9, 1353

Mayo Clinic Protocol

Mayo Clinic Protocol	External beam radiation therapy (45 Gy in 30 fractions, 1.5 Gy twice daily) Brachytherapy (20 Gy at 1 cm in approximately 20–25 h)—administered 2 weeks following completion of external beam radiation therapy Capecitabine—administered until the time of transplantation, held during perioperative period for staging Abdominal exploration for staging—as time nears for deceased donor transplantation or else prior to living donor transplantation Liver transplantation
Inclusion Criteria	Diagnosis of pCCA (transcatheter biopsy or brush cytology, CA 19–9 > 100 mg/mL and/or a mass on cross-sectional imaging with a malignant appearing stricture on cholangiography) Unresectable tumor above cystic duct (pancreatoduodenectomy for microscopic involvement of CBD, resectable pCCA arising in PSC) Radial tumor diameter 3 cm Absence of intrahepatic and extrahepatic metastases Candidate for liver transplantation
Exclusion Criteria	Intrahepatic cholangiocarcinoma Uncontrolled infection Prior radiation or chemotherapy Prior biliary resection or attempt resection Intrahepatic metastases Evidence of extrahepatic disease History of other malignancy within 5 years Transperitoneal biopsy (including percutaneous and EUS-guided FNA)

pCCA: perihilar cholangiocarcinoma; PSC: primary sclerosis cholangitis, CA19-9: Carbohydrate Antigen 19-9; CBD: common bile duct; EUS: endoscopic ultrasound; FNA: guided fine-needle aspiration.

PROTOCOL FOR LIVER TRANSPLANTATION IN HILAR CHOLANGIOCARCINOMA

STEPS FOR LT IN hCCA	
LT centers	Specialized centers selected by SNT
LT standardization	Performed based on a protocol under SNT supervision in order to evaluate the outcomes
LT approval	Approval in a multidisciplinary meeting at local institution with mandatory presence of a radiologist, clinical oncologist, hepatopancreatobiliary surgeon and transplantation surgeon
LT notification	All cases must be referred to the SNT for evaluation and final approval.

LT INDICATION	
Patient selection	Indication for hCCA with unlikely R0 resection and/or unresectable hCCA due to chronic liver disease (primary sclerosing cholangitis or other causes of chronic liver disease)
Official authorization	After SNT approval, patients will be included in the list for LT with a special MELD score (MELD 30)*
LDLT	Follow the same inclusion and exclusion criteria of DDLT They will only have coverage by the Brazilian Ministry of Health if meeting the established criteria
Neoadjuvant chemotherapy and radiotherapy	For tumors ≤ 3 cm, there is a recommendation of performing at least one type of neoadjuvant chemotherapy and one radiotherapy modality (external radiotherapy or brachytherapy). In such cases, DDLT and LDLT will be allowed.
	For tumors > 3 cm and < 4 cm, there is a recommendation of performing at least one type of neoadjuvant chemotherapy and one radiotherapy modality (external radiotherapy or brachytherapy). In such cases, only LDLT will be allowed.

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LIVER TRANSPLANT ONCOLOGY (C QUINTINI AND C MILLER, SECTION EDITORS)

New Breakthroughs for Liver Transplantation of Cholangiocarcinoma

Robert R. McMillan[1] · Ashish Saharia[1] · Maen Abdelrahim[2] · R. Mark Ghobrial[1]

Accepted: 7 January 2021 / Published online: 2 February 2021

Abstract
Purpose Liver transplantation (LT) has gained ground as a treatment for cholangiocarcinoma. LT has achieved an established role as curative treatment for unresectable hilar cholangiocarcinoma (hCCA), and there are emerging data supporting its use in select patients with intrahepatic cholangiocarcinoma (iCCA). This review explores the current frontiers and future directions of LT for CCA.
Recent Findings Results of retrospective studies support randomized trials of LT for resectable hCCA. Select patients with iCCA who have small tumors or favorable disease biology, as demonstrated by response to neoadjuvant therapy, have long-term survival after LT. Discoveries in the biology of iCCA show patients with *FGFR* and other genetic abnormalities have improved outcomes and may benefit from targeted therapies.
Summary The outcomes of LT for CCA support its increased utilization. Policies should be considered to increase accessibility of donor organs for patients with iCCA.

Transplantasyon;

- *CCA için bir tedavi olabilir*
- *LT'nin hCCA için faydaları iyi bilinmekte*
- *Seçilmiş hastalarda iCCA da uygulanabilir*
- *Moleküler patogenez önemli*

> Lancet Gastroenterol Hepatol. 2018 May;3(5):337-348. doi: 10.1016/S2468-1253(18)30045-1. Epub 2018 Mar 13.

Liver transplantation for locally advanced intrahepatic cholangiocarcinoma treated with neoadjuvant therapy: a prospective case-series

Keri E Lunsford [?], Milind Javle [?], Kirk Heyne [?], Rachna T Shroff [?], Reham Abdel-Wahab [?], Nakul Gupta [?], Constance M Mobley [?], Ashish Saharia [?], David W Victor [?], Duc T Nguyen [?], Edward A Gravius [?], Ahmed O Kaseb [?], Robert S McFadden [?], Thomas A Aloia [?], Claudius Conrad [?], Xian C Li [?], Howard P Monsour [?], A Osama Gaber [?], Jean-Nicolas Vauthey [?], R Mark Ghobrial [?], Methodist-MD Anderson Joint Cholangiocarcinoma Collaborative Committee (MMAJCCC)

Affiliations + expand
PMID: 29548617 DOI: 10.1016/S2468-1253(18)30045-1

- Ocak 2010-Aralık 2017 6 hastaya ICC nedeniyle ***karaciğer nakli*** yapıldı.
- Tanıdan transplantasyona medyan süre 26 ay (IQR 17-33)
- Transplantasyondan sonra ***medyan takip süresi*** 36 ay (29-51)
- **Genel sağkalım;**
  - *1. yılda %100*
  - *3 yılda %83.3*
  - *5. yılda %83.3*

- CCA da ***R0 rezeksiyonu*** mümkün olduğunda en iyi seçenektir.
- Unrezektabl tümörlerde %65'ten fazla 5 yıllık sağkalım avantajı nedeniyle ***LT tercih edilebilir.***
- Sistemik neoadjuvan rejimler
- Deneyimli merkez

Sonuç olarak:

- *Nüks BTC için ameliyat;*
- *Dikkatle seçilmiş hastaların multimodal yönetiminde,*
- ***Uzun süreli sağkalım şansını arttıran <u>etkili bir seçenek olabilir.</u>***

teşekkürler…