

간문부 담관암

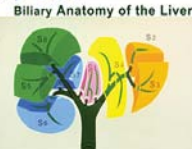
- 진단적 접근과 황달 치료 -

국립암센터 내과

이 우 진

Biliary Tract Cancer (BTC) [Cholangiocarcinoma, CC]

- 10–15% of hepatobiliary cancer
- Adenocarcinoma (cholangiocarcinoma)
- Intrahepatic cholangiocarcinoma (IH CC)
- Extrahepatic cholangiocarcinoma (EH CC)



Biliary Anatomy of the Liver

우간관, 좌간관, 총간관, 담낭관, 총담관, 원위부총담관

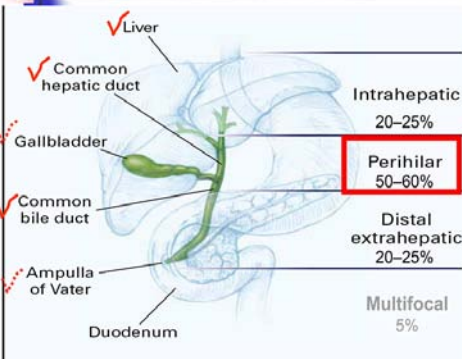
- Cure; only in curatively resected patients but high recurrence rate and poor prognosis
- Initially present with advanced disease
- Main causes of mortality
 - liver failure
 - recurrent sepsis due to biliary obstruction
 - cancer cachexia

Hilar Cholangiocarcinoma

- Most common cholangiocarcinoma
- Complicated strictures on complicated hilar region
- Late clinical presentation
- Usually locally advanced disease
- Poor prognosis
- To improve the survival
 - early diagnosis and complete extensive surgical resection but difficult to achieve

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Biliary Tract Cancer (BTC)



Intrahepatic (IH)

Intrahepatic 20–25%

Perihilar 50–60%

Extrahepatic (EH)

Distal extrahepatic 20–25%

Multifocal 5%

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Contents: Hilar CC

- I. Diagnostic approach
- II. Resectability
- III-1. Biliary drainage - Preoperative
- III-2. Biliary drainage - Palliative
(endoscopic bilateral metal stenting)

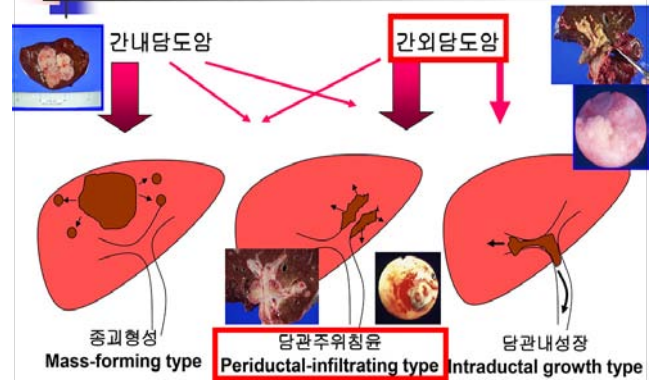
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I. Diagnostic approach

- US
 - CT
 - MRI (MRCP/MRA)
 - PET
 - PTC
 - ERC + brush, bx
 - EUS + FNA
 - PTCS + bx
 - IDUS
- Detection
 - Intraductal extent
 - Outer extent
 - Vascular Invasion
 - Global information

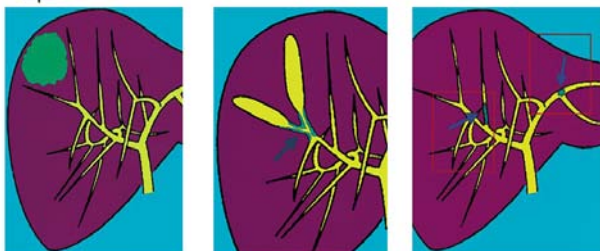
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Types of Cholangiocarcinoma



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Types of Cholangiocarcinoma-2



Mass forming type:
m.c. in intrahepatic CC
Capsular retraction
Delayed enhance of central portion

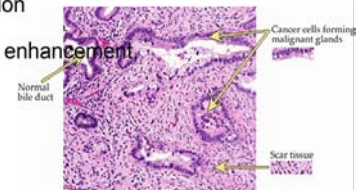
Periductal infiltrative type:
m.c. in extrahepatic CC
Periductal infiltration of tumor
Bile duct stricture
Delayed enhancement of bile duct wall

Intraductal growth type:
Rare
Good prognosis
Multiplicity.
Poor enhancement.
Mucin production

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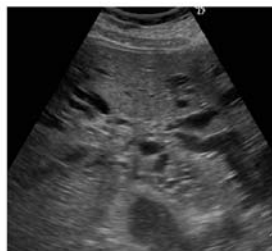
Periductal Infiltrative (PI) Type

- Perpendicular and longitudinal tumor growth
- Tumor growth along the bile duct wall
- Perivascular, perineural, lymphatic invasion
- Bile duct stenosis and obstruction
- Proximal bile duct dilatation
- Bile duct wall thickening, enhancement, periductal infiltration
- Focal or diffuse (5%)



US

- Mass itself hardly seen
- Bile duct dilatation and separation
- Wall thickening, mass formation
- Hepatic metastases



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MDCT-PI Type

- Extent of tumor
- Hilar vasculature
- LN, metastasis

Benefits of MDCT

- Thin section images, MPR, ↓ motion artifact
- More accurate diagnosis and staging

MDCT findings

- Bile duct wall thickening, lumen narrowing
- Ductal wall enhancement
 - Delayed enhancement due to fibrosis
- Proximal bile duct dilatation
- Hepatic metastases, LN enlargement
- Findings of vascular invasion-More than 95% accuracy
 - Lumen narrowing and irregularity
 - Tumor thrombus
 - Loss of fat plane, more than 180 degree
 - Collateral vessels and THAD



Lee HY, et al. Radiology 2006; 219: 100-106

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MDCT: PI Type-2

■ Diagnostic performance of MDCT

- Detection of perihilar CC
 - 100% (vs. 40-60% of conventional CT)
- Resectability
 - 75-92% (vs. 54% of conventional CT)

Choi JY. AJR 2008

■ Limitations of MDCT

- Longitudinal tumor extent
 - Microscopic extension
 - Dysplasia
- LN metastases

Lee HY. Radiology 2006, Chen HW. Hepatogastroenterol 2009



MRI-PI Type

- MRI, MRC, MRA; "all in one"
- Noninvasive

■ MR

- T1 low or iso, T2 high signal mass
- Enhancing wall thickening. Proximal duct dilatation

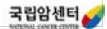
■ MRCP

- 71-96% accuracy in Dx. of tumor extent
- Proximal duct visualization (Better than ERCP)
- MRCP-guided biliary drainage

■ MR vs. MDCT

- Enhanced MR with MRCP vs. MDCT with direct cholangiography
 - Similar performance

Kim JY, et al. J Magn Reson Imaging 2007



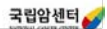
ERCP

- Early diagnosis
- Differentiation of benign from malignant strictures
- Tissue sampling for histopathologic diagnosis
- Assessment of resectability, extent of disease
- Assessment of longitudinal spreading
- Combined aid procedure- IDUS, POCS
- Therapeutic – decompression
- Problem- invasive, complication (esp. cholangitis)
- No information about local tumor extension, LN, vascular involvement



IDUS (Intraductal US)

- High frequency, wire-guided probe
- Provide accurate image of the bile duct wall
- Complements the role of ERCP
 - Improved accuracy in the diagnosis of biliary strictures
 - Differentiating between benign and malignant strictures
- Better in assessing T stage, compared with EUS
- Identifies tumor extension into adjacent organs/major blood vessels (RHA, PV, pancreas)
- Determines longitudinal tumor extent



EUS

- Less invasive
 - Visualization of the biliary tree
 - Providing information of the extent of disease by periductal/vascular invasion, L/N metastasis
 - FNA: variable yield (25-89%)
 - Limitations - Incomplete visualization of CHD, IHD
- Limited accuracy of local tumor staging



Cholangioscopy

- Direct visualization of the biliary tree and strictures with small caliber scope
- Improve ability to characterize strictures
- Additional diagnostic procedure
- Two kinds of systems
 - PTCS (percutaneous transhepatic cholangioscopy)
 - POCS (peroral cholangioscopy)
- PTCS ;drawbacks
 - Invasive
 - Need for mature transhepatic routes
 - Complications; bleeding, bile leakage
 - Time consuming
 - Discomfort to patients

Peroral Cholangioscopy

- "Mother" and "baby" scopes
- Ultra-slim upper endoscopes
- Spyglass direct visualization system
- Narrow band imaging
- Probe-based confocal laser endoscopy



Endoscopic procedures for hilar CC

- Differentiation of benign from malignant strictures- ERCP,EUS,IDUS,POC
- Tissue sampling for histopathologic diagnosis- ERCP,EUS,IDUS,POC
- Assessment of resectability-EUS,IDUS
- Assessment of longitudinal spreading -IDUS,POC
- Early diagnosis



Limitations of Endoscopic Dx

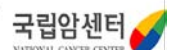
- Negative results in tissue sampling
 - Do not exclude the presence of a malignancy
- Dependent to operator
- Need expensive endoscopic equipment
- High level of skill
 - Always technically successful procedures?
- Worry about complication



II. Resectability

-Factors for Considering Resectability-

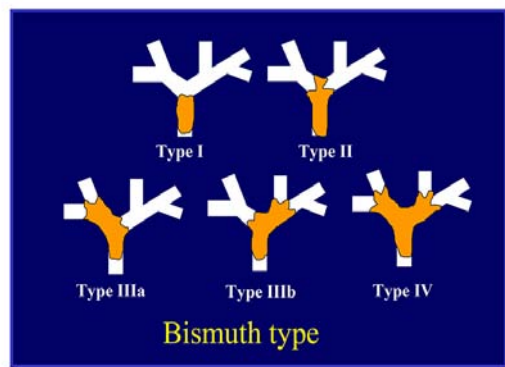
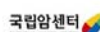
- Patient general condition; liver fn., cholangitis, co-morbidity
- ✓ Tumor extent
 - Longitudinal (intramural) spread
 - : extent of hepatic resection (+ caudate lobe resection)
 - : combined PPPD (= hepatopancreatoduodenectomy;HPD)
 - Radial (extramural) spread
 - : combined resection of PV, HA?
 - LN & distant metastasis : PET, staging laparoscopy
- Volume of future liver remnant (FLR) -20~40%
 - : portal vein embolization (PVE)
- Anatomy (normal variation) of BD, HA & PV



AJCC Staging 7th, 2010

PRIMARY TUMOR (T)	
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma in situ
T1	Tumor confined to the bile duct, with extension up to the muscle layer or fibrous tissue
T2a	Tumor invades beyond the wall of the bile duct to surrounding adipose tissue
T2b	Tumor invades adjacent hepatic parenchyma
T3	Tumor invades unilateral branches of the portal vein or hepatic artery
T4	Tumor 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
REGIONAL LYMPH NODES (N)	
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

0	Tis	N0	M0
I	T1	N0	M0
II	T2a-b	N0	M0
IIIA	T3	N0	M0
IIIB	T1-3	N1	M0
IVA	T4	N0-1	M0
IVB	Any T	N2	M0
	Any T	Any N	M1



- Guidance of therapy (resection or palliative)
- Inability of selection of surgical candidates
- No prognostic value

Summary

- Unilobar involvement with encasement of contralateral portal vein or hepatic artery
- Bilateral vascular involvement of HA, PV
- Distant metastases
- Underlying liver disease (advanced fibrosis, cirrhosis)
- FLR <20%~30% and no or poor response to PVE
- Severe co-morbidities
- Bismuth 4, PV invasion : **not contraindication for resection**
- Individualized decision
- Multi-disciplinary approach
between physician, surgeon and radiologist



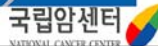
III. Bile Drainage

- Palliative; 수술과 비슷한 효과, 적은 합병증
ERBD (plastic, metal stent)
PTBD
- Preoperative
ENBD
ERBD (plastic stent)
PTBD



PTBD

- 외부 배액
- 침습적
- Entire liver can be drained by multiple catheter
- 금기; 심한 출혈소인, 심한 복수, 다발성 간종괴
- Tract 따라 seeding 위험성
- Tube 관리-소독, N/S 세척
- Malposition, oozing, obstruction
- Tube 교체 : 2-3개월
- PTBD 통한 내부 배액, 금속관 삽입



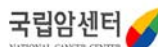
ENBD

- 임시적 배액
- 장점
 - 덜 침습적
 - 작은 구경 (5, 7 Fr)
 - F/U 담도조영 가능
 - 제거가 용이
- 단점
 - 환자 불편
 - 빠질 수 있으며 오래 갖고 있을 수 없다.
 - 외부 배액



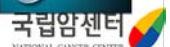
ERBD (내부 배액)

- 정상 장-간 순환; 감염, 심장, 신장, 간재생, 면역
- 수술, PTBD와 비슷한 효과, 적은 합병증(덜 침습적)
- 삶의 질
- Tube 관리가 필요 없다.
- Tube check, F/U 담도조영은 할 수 없다



ERBD (Plastic Stent)

- Polyethylene, polyurethane, teflon
- 5 Fr – 12 Fr, 3 cm-15 cm
- 10-11.5 Fr >> 7 Fr, straight >> pigtail
- 제거, 교체 가능
- 평균 개통기간; 3-4개월(clogging)
- Migration



Self Expanding Metal Stent

- Nitinol (nickel-titanium), Elgiloy (cobalt)
- 장점
 - 넓은 구경; 30Fr (10mm)
 - 평균 개통기간 6-9개월(ingrowth)
- 단점
 - 제거가 불가능(uncovered)
 - 수술에 방해(간문부 담관암)
 - 비용
- Uncovered vs. covered



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악성 담관 폐쇄에서 배액관의 비교

	plastic	metal
내경 Ø	2.1-3.6 mm	8-10 mm
교체	가능	불가능
가격	싸다	비싸다
합병증		비슷
성공률		비슷
막힘	오니 3-4개월	양조직 6-9개월

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Covered Metal Stent

- Coated by polyurethane or silicone
- tumor ingrowth 방지
- 평균 개통기간; 비슷
- Migration, cholecystitis, pancreatitis 우려



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Biliary Drainage in Malignant Biliary Strictures -Considering Factors-

- Setting; palliative / preoperative
- Do? Do not? - How long?; duration?
- Method?; ERBD / ENBD / PTBD
 - Physiologic?; internal / external / combined
 - Which stent?; plastic / metal stent
- ✓ Obstruction level?; distal / hilar
- ✓ Hilar; type, site, number, method

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- where to? how? what?
 - Right duct vs. left duct
 - Unilateral vs. bilateral- Extent of drainage
 - Radiologic vs. endoscopic- Type of approach
 - Plastic vs. metal stents- Type of stent
 - Double metal stents
 - Inside-stent vs. outside-stent
- The general condition of the patient
- The effectiveness of the various palliative therapies
- QoL
- Duration of survival
- The anatomy of obstruction
- The cost
- The risk of the procedure
- The expertise at a given institution

Comparison of PTBD, ENBD & ERBD

	PTBD	ENBD	ERBD stent
Tube size	large (8.5-16Fr)	small (7Fr)	medium (10Fr)
Physiologic	no (ext.)	no (ext.)	yes (int.)
Cholangiography	yes	yes	no
Pt. Convenience	not good	not good	good
Complication	hemobilia	pancreatitis	pancreatitis cholangitis
Contraindication	bleeding tendency	GI obstruction unstable vital	
Surgical field	clean	tolerable	inflammation

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III-1. Preoperative Biliary Drainage (PBD) for Hilar CC

Pros

- Resolve cholangitis, jaundice, pruritus
- Correct malnutrition and bleeding tendency
- Improve jaundice-related hepatic or renal insufficiency
- Diagnostic value- extent, resection line
- Improve hypertrophy of remnant liver with PVE

Cons

- Take > 6 weeks for normalization of liver function
- Increase inflammatory complication (cholangitis)
- Delay or prevent resection
- Cause periductal fibrosis (difficult to ddx. With cancer)
- Tract seeding

PBD Indication

- Presence of cholangitis
- To correct severe undernourishment or hypoalbuminemia
- To treat jaundice-induced liver or renal failure
- To prevent worsening during the waiting period
 - Need for neoadjuvant therapy
 - Expected delay in surgery
 - Refer to tertiary center
 - Correction of underlying co-morbid medical illnesses
- Severe, long-standing jaundice (pruritus) in old age?
 - Is bilirubin level important or not? >10? 20? 30? mg/dL
 - Any other reliable criteria? (prothrombin time, albumin..)
 - Maximum tolerable level of bilirubin for hepatectomy?
 - How long? (duration >4 weeks?)

PBD in Hilar CC

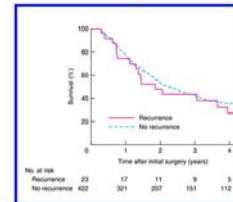
	PTBD	ERBD
Success rate	95%	> 80-90%
Accuracy of type	85%	> 65%
Selection of BD	relatively easy	> difficult
Reposition	possible	> impossible
Complication		
cholangitis	infrequent	< frequent
pancreatitis	no	< 5%
hemobilia	occasionally	> rare

- Safety, effectiveness, cost benefit, Dx value; $P > E$
- Compliance, comfortability; $P < E$
- Long-term effect? -survival, QoL

Percutaneous transhepatic biliary drainage catheter tract recurrence in cholangiocarcinoma

Takahashi Y. Br J Surg 2010;97:1860.

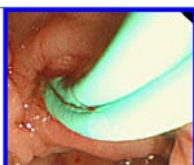
- PTBD tract recurrence ; 5.2%(23/445)
- Risk factors : PTBD >60 days, multiple PTBD, papillary type
- Poor survival of PTBD tract recurrence group (OS 27.3 month vs. 22.8 month, $P=0.095$)



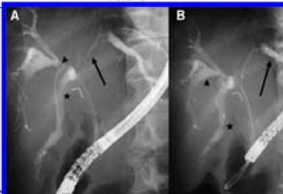
Endoscopic nasobiliary drainage is the most suitable preoperative biliary drainage method in the management of patients with hilar cholangiocarcinoma

Kawakami H. J Gastroenterol 2011;46:242-248.

	ENBD (n = 60)	EBS (n = 20)	PTBD (n = 48)	
Total	23 (38.3%)	13 (65%) ¹	15 (31.3%) ²	$p < 0.05^1$
Minor complications				
Tube occlusion with cholangitis	6 (10%)	12 (60%) ³	1 (2.1%)	$p < 0.0001^*$
Tube dislocation	9 (15%)	1 (5%)	7 (14.6%)	N.S.
Contralateral segmental cholangitis	6 (10%)	1 (5%)	4 (8.3%)	N.S.
Post-ERCP pancreatitis	2 (3.3%)	1 (5%)	-	
Major complications				
Total	1 (1.7%) ⁴	-	7 (14.6%) ⁵	$p < 0.01^4$
Retroperitoneal perforation	1 (1.7%)	-	-	
Injury of portal vein	-	-	4 (8.3%)	
Cancer dissemination	-	-	3 (6.3%)	



Kawakubo K. Dig Endosc 2013;25:76.



Summary

Proximal Obstruction

- Major hepatic resection mortality 3~5% (~10%) (liver failure)
 - Considering factors; liver function, cholangitis, PVE operation (Lt or Rt, trisectionectomy, vascular resection)
1. Is PBD necessary for hilar CC patients?
 - Still not enough evidence
 - Most high-volume centers do PBD for hilar CC
 2. What is the choice of PBD in hilar CC patients?
 - Paradigm shift? PTBD → ENBD?
 - Multiple separated bile ducts, long-term indwelling; PTBD >
 3. Unilateral or bilateral?
 - In principle, unilateral PBD in the future remnant lobe is enough
 - Bilateral; segmental cholangitis or slow-improving jaundice
- * Large multicenter RCT should be necessary

Conclusion; PBD

- I. Largely operator-dependent; local expertise and preference
- II. Multi-disciplinary approach
 - Biliary endoscopist, surgeon and radiologist
- III. Patient-by-patient basis; individualized decision
 - type, site, number and approach must be defined and tailored, according to the planned hepatic resection
- IV. Adequate PBD is the key
 - If PBD-induced cx. is removed from analysis → beneficial?
- V. **Make every effort not to provoke procedure-related cx!**

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III-2. Biliary Drainage – Palliative – Endoscopic Bilateral Metal Stenting–

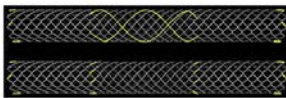
- Challenging and complex than distal CBD
- Vulnerable to cholangitis associated with procedures
- Ideal, physiologic goal to preserve functional liver volume
 - 25%?/ 50%?/ as much as possible?
- Bilateral metal stenting
 - To draining of adequate liver volume (>50%)
 - Techniques
 - Side by side (SBS) deployment-easier access, revision
 - Stent in stent (SIS) deployment-Ideal, physiologic method

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Metal stent, Type

Open-cell or Closed-cell type?

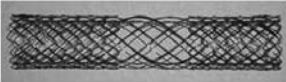
Technical success rates, 73.3 % ~ 100% in hilar obstruction.
However, no proven differences in patency or successful revision rates.



M-Hilar stent (BONA stent, Korea)



Niti-S large cell D-type stent (LCD; Taewoong)



Niti-S Y-type stent (Taewoong, Korea)



Zilver Biliary Self-Expanding Stent, Cook

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