

**Is There a Role for Hepatic Pedicle Lymphadenectomy  
in Intrahepatic Cholangiocarcinoma?  
Review of a 17-years Experience  
in a Tertiary Institution.**

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# Backgrounds(1)

- Intrahepatic cholangiocarcinoma (ICC)
  - ✓ The second most common primary liver cancer next to hepatocellular carcinoma
- Complete surgical resection results to the most promising long term outcome in the treatment of ICC
- prognostic factors for survival after resection of ICC
  - ✓ Positive resection margin
  - ✓ Lymph node metastasis
  - ✓ Intrahepatic metastasis
  - ✓ Mass-forming type
  - ✓ Tumor multiplicity or size
  - ✓ Macroscopic vascular invasion



# Backgrounds(2)

- The value of lymph node dissection (LND) with liver resection is a controversial subject.
- Some investigators suggest that routine LND may result in decreased locoregional nodal recurrence and optimizes pathological staging.
- Others argued that routine LND is unnecessary as it did not contribute to improvement of survival of patients.
- There is no clear guideline on the role of LND in ICC.



# *Purpose*

- We aimed to examine the role of hepatic pedicle lymphadenectomy for ICC and to study the prognostic factors of survival.



# Methods(1)

## ➤ Patient selection

- ✓ From May 1995 to March 2012,
- ✓ There were 304 patients who underwent surgical resection with curative intent for intrahepatic cholangiocarcinoma (ICC) in Samsung Cancer Center

## ➤ Exclusion

- ✓ Patients with double primary cancer and other histologic type except for ductal adenocarcinoma
- ✓ Patients underwent neoadjuvant therapy, palliative resection

## ➤ Inclusion

- ✓ patients with adenocarcinoma arising from intrahepatic bile duct

: **226** patients who were suitable for analysis



**Total 304 patients**

**Palliative resection : 2 Pts**

**Neoadjuvant therapy : 2 Pts**

**Double primary cancer : 20 Pts**

Colorectum(8), Stomach(3),  
Lung(3), Breast(2), CBD(1),  
Nasopharygeus(1), Tongue(1),  
RCC(1)

**Other histologic type : 44 Pts**

IPNB(24)  
Adenosquamous type(5)  
Sarcomatous type(4)  
Biliary cystic neoplasm(1)  
Combined HCC-ICC(10)

**226 patients included**

# Methods(2)

## ➤ The criteria for resectability for ICC

- 1) Absence of distant metastasis on imaging scans
- 2) Absence of intrahepatic metastasis to the contralateral lobe of liver
- 3) Absence of clinically and/or radiologically evident lymphadenopathy in the para-aortic region
- 4) Adequate functional reserve of liver based on Child-Pugh scoring and Indocyanine-green retention (ICG) R15 test

## ➤ Surgical policy

- ✓ Three out of nine surgeons : lymphadenectomy for the hepatic pedicle might improve the long term outcome of patients with ICC
- ✓ Other six surgeons did not.
- ✓ Two distinct groups of patients with (LND (+)) or without (LND(-)) hepatic pedicle lymphadenectomy were formed.



# Methods(3)

## ➤ The steps of hepatic pedicle lymphadenectomy

- ✓ For lesions situated in the right liver lobe
  - lymph nodes along the hepatoduodenal ligament, common hepatic artery till celiac axis
- ✓ For lesions situated in the left hepatic lobe
  - Additionally, lesser omentum and its connective tissue with lymph nodes along the left gastric artery

## ➤ Tumor location

- ✓ Peripheral type : located anywhere from 2nd order branch of bile duct to peripheral
- ✓ Central type : involved 1st order branch of bile duct or expanded to the hilum nearly



# Results(1) – Surgical procedures

Variable	No. (%)
Type of hepatectomy (n=226patients)	
Minor resections	51 (22.6)
Wedge resection	4 (1.8)
Segmentectomies	11 (4.9)
Bisegmentectomy	36 (15.9)
Major resections (Right/Left)	129 (57.1)
Hemihepatectomies (+ S1)	127 (56.2)
Central bisectionectomy	2 (0.9)
Extended resections (Right/Left)	46 (20.3)
Extended hemihepatectomies (+ S1)	38 (16.8)
Trisectionectomy (+ S1)	8 (3.5)
Additional procedure	
Bile duct resection	23 (10.2)
vascular resection	7 (3.1)
Hepatic artery	1 (0.4)
Portal vein	6 (2.7)
Other organ resection	22 (9.7)
Radiofrequency ablation	1 (0.4)
Lymph node dissection	
Not done	103 (45.6)
Lymphadenectomy	106 (46.9)
Sampling	17 (7.5)



# Results(2) - Demographics and clinical features

	LND (-) (n = 120)	LND (+) (n = 106)	P
Age, years (range)	59.9(37-79)	59.36 (37-80)	0.642
Gender, n			0.053
Male	86 (71.7)	63 (59.4)	
Female	34 (28.3)	43 (40.6)	
Symptoms, n			0.113
Asymptomatic	59 (49.2)	41 (38.7)	
Symptomatic	61 (50.8)	65 (61.3)	
Risk factors			
Intrahepatic duct stone, n	15(12.5)	11 (10.4)	0.618
Clonorchis sinensis, n	6 (5.0)	5 (4.8)	0.934
Liver cirrhosis, n	18 (15.0)	3 (2.8)	0.002
Chronic hepatitis B infection, n	28(23.3)	16 (15.1)	0.119
Preoperative tumor marker levels			
CA 19-9, U/mol (range)	845.1 (0.2-17022.6)	4140.9 (1.8-129612.0)	0.002
CEA, U/mol (range)	12.8 (0.5-190.0)	1.9 (0.1-224.2)	0.101
PVE, n	5 (4.2)	4 (3.8)	0.880
Type of hepatectomy, n			<0.001
Minor resections	39 (32.5)	12 (11.3)	
Major resections	58 (48.3)	56 (52.8)	
Extended resections	23 (19.2)	38 (35.8)	
Adjuvant treatment, n	8 (6.7)	29 (27.4)	<0.001



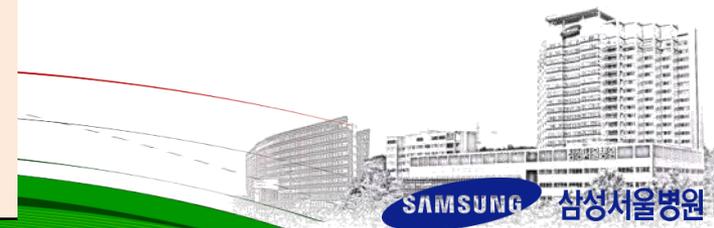
# Results(3) - Comparisons of pathologic characteristics

	LND (-) (n = 120)	LND (+) (n = 106)	P
Tumor size, cm (range)	4.7 (0.8-15.8)	5.2 (1.2-13.0)	0.089
<b>Tumor location</b>			<0.001
Peripheral	103 (85.8)	59 (55.7)	
Central	17(14.2)	47 (44.3)	
<b>T stage, n</b>			0.001
Tis	7 (5.8)	2 (1.9)	
T1	45 (37.5)	17 (16.0)	
T2a/T2b	26/11 (30)	28/10 (35.8)	
T3	28 (23.3)	36 (34.0)	
T4	4 (3.3)	13 (12.3)	
<b>Tumor differentiation, n</b>			0.049
Well	19 (15.8)	13 (12.3)	
Moderate	67 (55.8)	47 (44.3)	
Poorly	26 (21.7)	41 (38.7)	
NA	8 (6.7)	5 (4.7)	
<b>Macroscopic growth type, n</b>			0.001
Intraductal growth (IG)	13 (10.8)	5 (4.7)	
Mass-forming (MF)	95 (79.2)	71 (67.0)	
Periductal infiltrating (PI)	9 (7.5)	15 (14.2)	
Mixed forms (MF+PI)	3 (2.5)	15 (14.2)	
Multiple tumors, n	20 (16.7)	19 (17.9)	0.803
<b>Lymphovascular invasion, n</b>	25 (20.8)	40(37.7)	0.001
<b>Perineural invasion, n</b>	33 (27.5)	48 (45.3)	0.012
Adjacent organ invasion, n	14 (11.7)	5 (4.7)	0.060
Positive resection margin, n	8 (6.7)	12 (11.3)	0.219

## ❖ LND(+)

- mean number of lymph node harvested :  $12.8 \pm 8.1$  (4-51)
- mean number of lymph node involved :  $2.3 \pm 3.7$  (0-18)

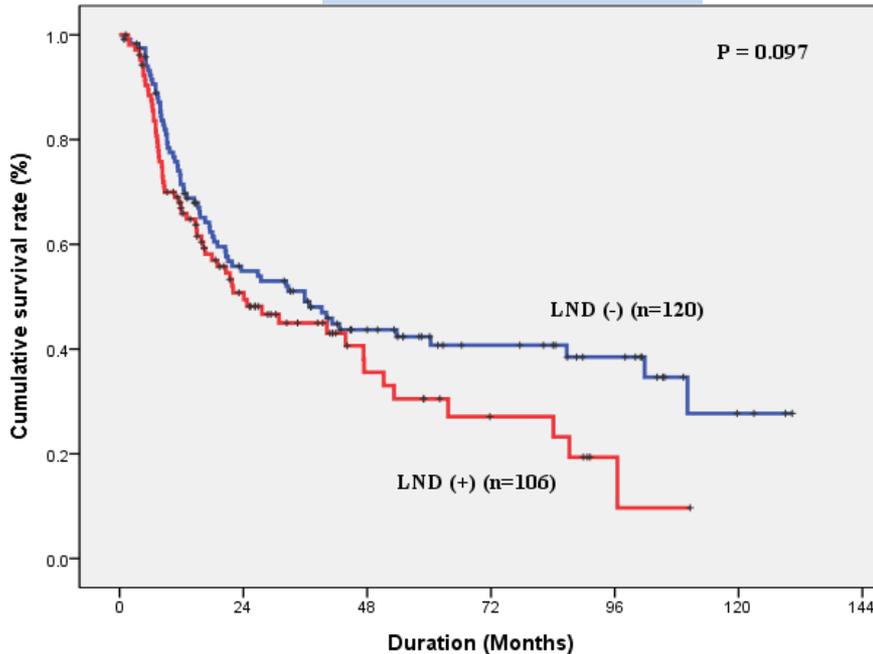
❖ 50.9% in LND (+) group (n = 54) : LN metastasis



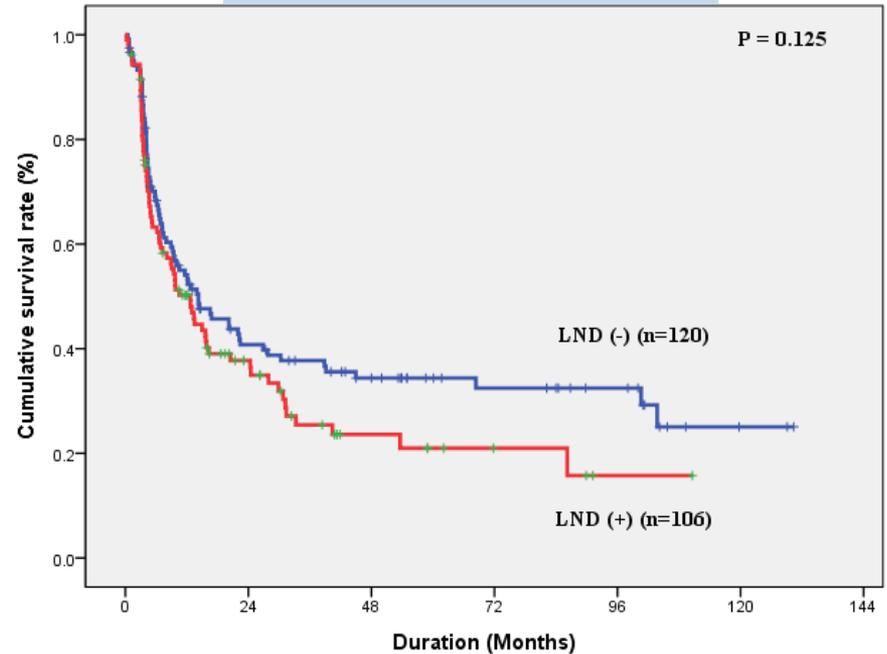
# Results(4)

- Kaplan-Meier analysis comparing the patients in the two groups

Overall survival



Disease-free survival

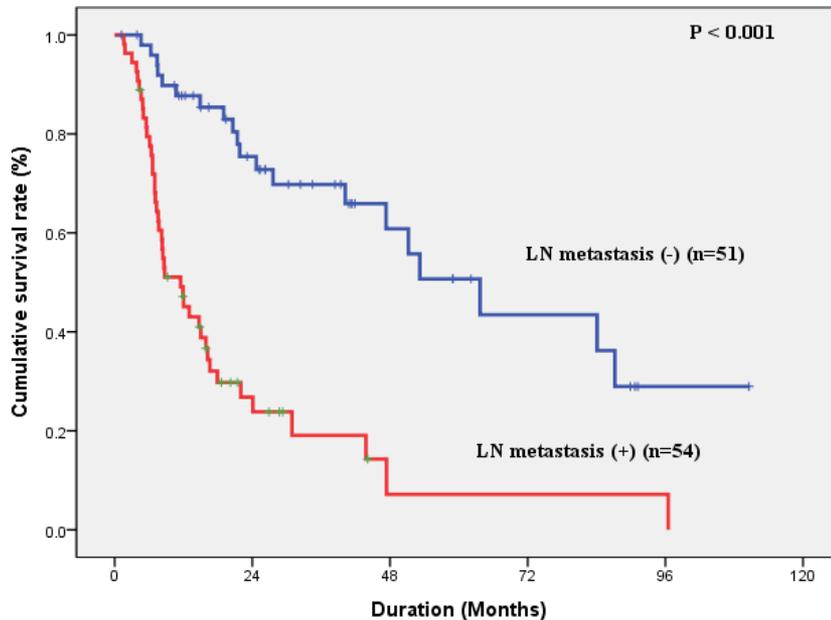


Lymph Node Dissection	Overall Survival		
	1-year	3-year	5-year
LND (-)	71.4%	49.1%	42.4%
LND (+)	65.9%	45.0%	30.5%

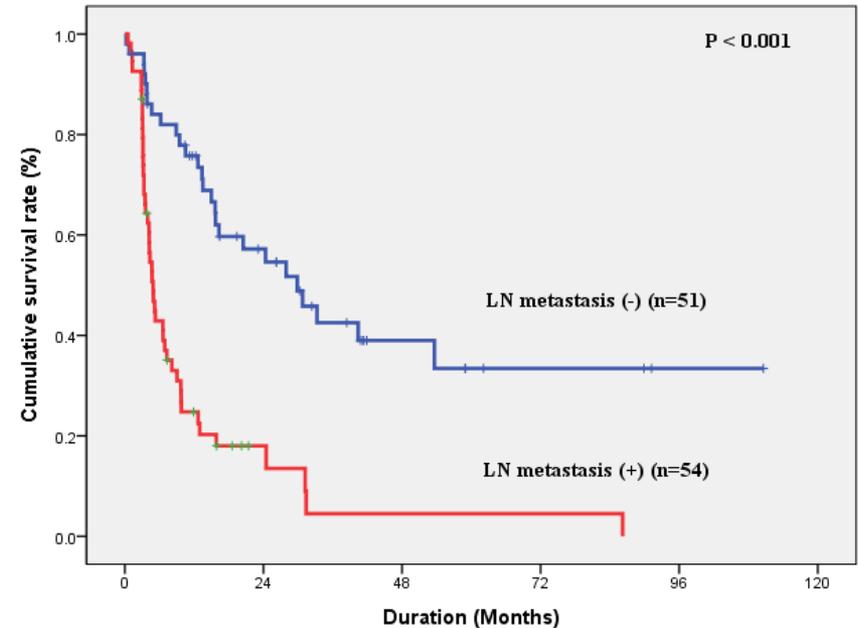
Lymph Node Dissection	Disease Free Survival		
	1-year	3-year	5-year
LND (-)	54.1%	37.7%	34.4%
LND (+)	50.2%	25.4%	21.0%

# Results(5)

- Survival of patients in LND (+) group, according to the presence of lymph node metastasis



Overall survival



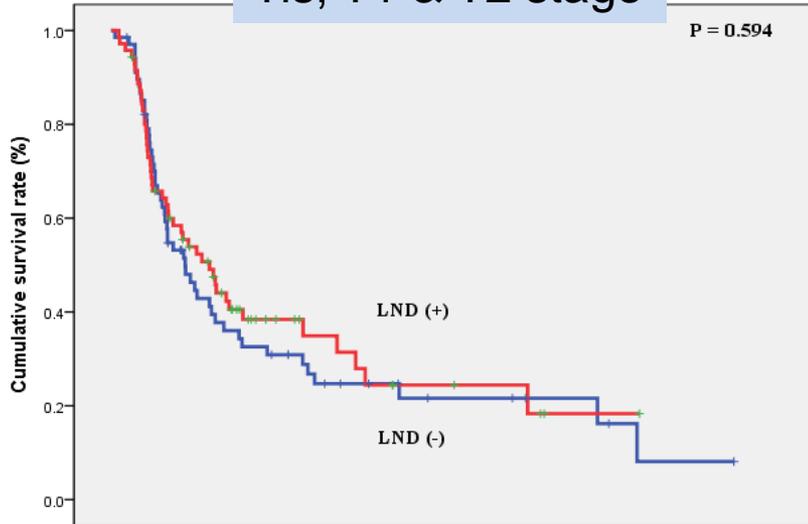
Disease-free survival



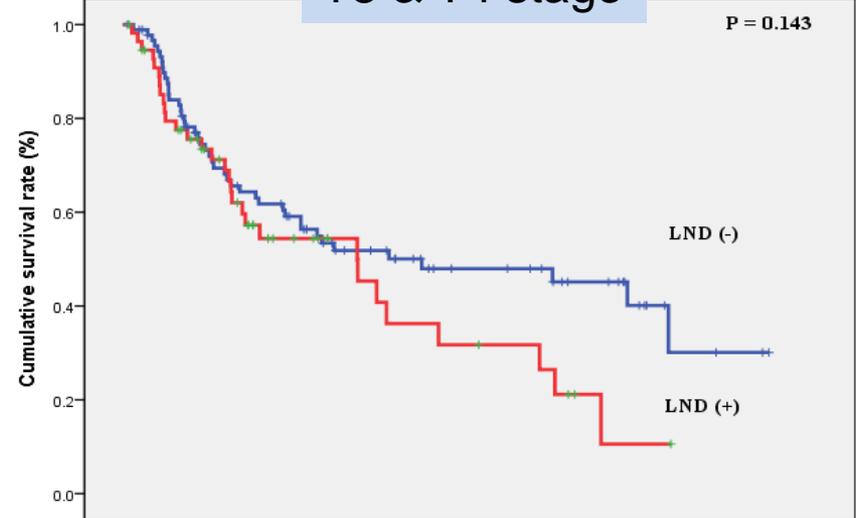
# Results(6)

– Survival comparing between LND (-) and LND (+) groups  
with stratified T-stage and tumor size

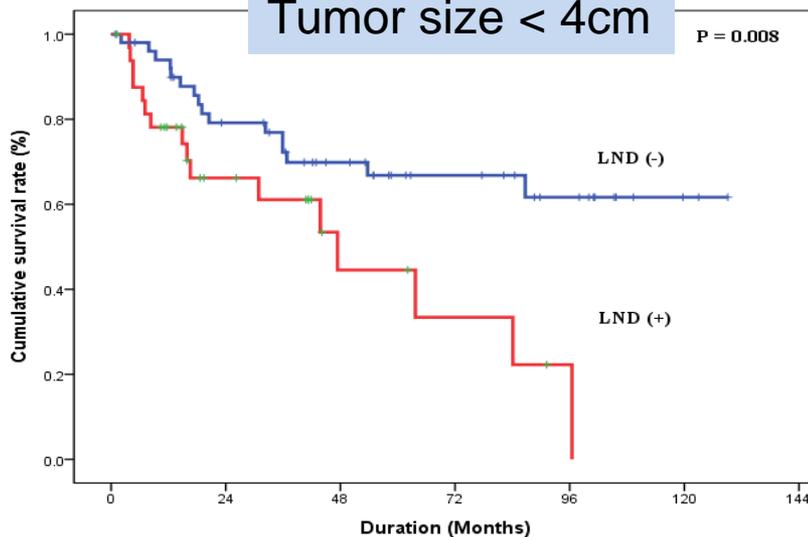
Tis, T1 & T2 stage



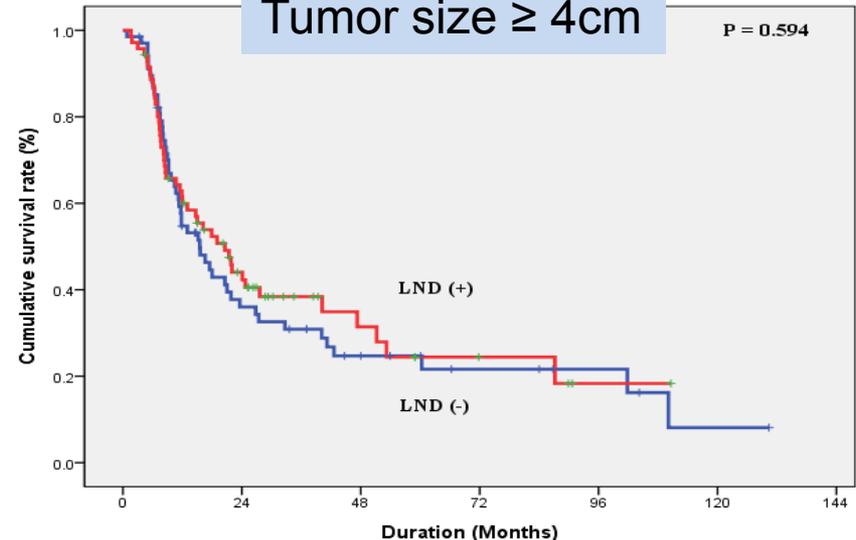
T3 & T4 stage



Tumor size < 4cm



Tumor size ≥ 4cm



# Results(7)

## - Univariate and multivariate analysis of prognostic factors for overall survival

	Univariate			Multivariate		
	HR	95% CI	P	HR	95% CI	P
LND (+)	1.34	0.95-1.90	0.098			
Tumor location						
Peripheral	1.00					
Central	1.15	0.78-1.71	0.471			
T stage						
Tis	1.00			1.00		
T1 & T2	8.33	1.16-60.10	0.035	0.24	0.01-4.59	0.345
T3 & T4	16.51	2.28-119.87	0.006	0.33	0.02-6.68	0.469
Tumor differentiation						
Well-Moderate	1.00			1.00		
Poorly	1.68	1.16-2.45	0.006	2.10	1.15-3.83	0.016
Tumor size > 4cm	2.71	1.81-4.06	<0.001	1.39	0.68-2.85	0.363
Macroscopic growth type						
Intraductal growth (IG)	1.00			1.00		
Mass-forming (MF)	6.39	2.02-20.24	0.002	2.50	0.31-19.94	0.387
Periductal infiltrating (PI), Mixed forms	5.74	1.74-19.22	0.005	1.90	0.22-16.65	0.561
Multiple tumors	2.16	1.43-3.26	<0.001	1.85	0.93-3.66	0.079
Lymphovascular invasion	1.91	0.99-3.67	0.053			
Adjacent organ invasion	1.58	0.89-2.81	0.120			
Positive resection margin	2.00	1.12-3.57	0.018	0.85	0.33-2.22	0.745
LN metastasis	4.56	2.64-7.90	<0.001	3.83	1.90-7.70	<0.001
Elevated CA 19-9 level	2.04	1.38-3.02	<0.001	0.92	0.49-1.70	0.785
Performed adjuvant treatment	1.98	1.27-3.09	0.003	0.89	0.46-1.71	0.726



# Discussion

- Patients with positive lymph node metastasis had significantly poorer overall survival with the mean overall survival of 20.3 months.
- Despite the debate of whether or not LND has a significant impact on survival, it remains clear that nodal status is one of the most important prognostic factors in ICC.
- LND was not associated with improvement of overall survival compared to those without LND in this study.
- Without LND, nodal assessment would be incomplete and the essential component of TNM staging would be compromised, required to decide on the best regimen of adjuvant therapy for the patients.



# Conclusion

- Presence of lymph node metastasis, together with poorly differentiated histologic grade were identified as independent prognostic factors for overall survival.
- Although routine hepatic pedicle lymphadenectomy in ICC did not show survival benefit, it may have a role in accurate pathological staging of ICC, which is important for prognostication and decision on adjuvant treatment.



*Thank you for your attention!*

