

# 간이식 전 발견된 조기위암

# Discussion

1. 간 경변 환자에서 ESD의 안전성 및 예후
2. 간 경변 환자에서 Non-curative ESD 후 STG 위험성
3. 제한적 림프절 절제와 감시림프절의 적용 가능성
4. 간 이식 후 면역억제 전략 및 위암 surveillance

# ESD in Liver cirrhosis

- **Excellent Short-term Outcomes & Safety**

- Comparable to non-cirrhotic patients: En-bloc (82.6–94.1%) & R0 resection rates (90–95.3%)

→ *No significant differences*

- Manageable complications: Bleeding (4.3–11.8%), Perforation (0–4.7%)

→ *Controlled via endoscopy*

**Table 3** Short-term outcomes of endoscopic submucosal dissection

Variable	LC group (n = 43)	LC-A group (n = 32)	LC-B group (n = 11)	CHB group (n = 47)	p value <sup>a</sup>	p value <sup>b</sup>
Procedure time, min, mean ± SD	50.2 ± 17.4	49.3 ± 18.2	52.8 ± 15.3	47.7 ± 11.1	0.419	0.564
Maximal diameter of resected specimens, cm, mean ± SD	4.3 ± 0.7	4.4 ± 0.8	4.2 ± 0.6	4.6 ± 0.6	0.046	0.449
<i>En bloc</i> resection, n (%)	42 (97.7)	31 (96.9)	11 (100)	46 (97.9)	1.000	1.000
R0 resection, n (%)	41 (95.3)	31 (96.9)	10 (90.9)	46 (97.9)	0.604	0.451
Bleeding after ESD, n (%)	4 (9.3)	3 (9.4)	1 (9.1)	3 (6.4)	0.705	1.000
Perforation after ESD, n (%)	2 (4.7)	1 (3.1)	1 (9.1)	1 (2.1)	0.604	0.451
Post-procedural mortality, n (%)	0 (0)	0 (0)	0 (0)	0 (0)	1.000	1.000
Hospital stay, days, mean ± SD	5.6 ± 1.5	5.4 ± 1.1	6.3 ± 2.1	5.0 ± 1.1	0.019	0.094
Worsening of CP score at 1 month after ESD, n (%)	0 (0)	0 (0)	0 (0)	0 (0)	1.000	1.000
Residual tumor at EGD surveillance, n (%)	0 (0)	0 (0)	0 (0)	0 (0)	1.000	1.000

CP score Child–Pugh score, CHB chronic hepatitis B, ESD endoscopic submucosal dissection, LC liver cirrhosis, SD standard deviation Choi et al. *Gut and liver* (2012) 6.1: 58.

<sup>a</sup>Comparison between LC and CHB groups

Kato et al. *Surgical endoscopy* (2015) 29.6: 1560-1566.

<sup>b</sup>Comparison between LC-A and LC-B groups

Choe et al. *Digestive diseases and sciences* (2018) 63.2: 466-473.

Kim et al. *Oncology Letters* (2022) 24.5: 404.

# ESD in Liver cirrhosis

- **Long-term Survival Dependent on Underlying Liver Function**

- Lower 5-year survival rate (~60%) vs. General population (91%)
- Primary cause of death: **Liver-related diseases (Liver failure, HCC, Variceal bleeding)** rather than gastric cancer
- Poor prognosis particularly in **Child-Pugh class B/C patients**

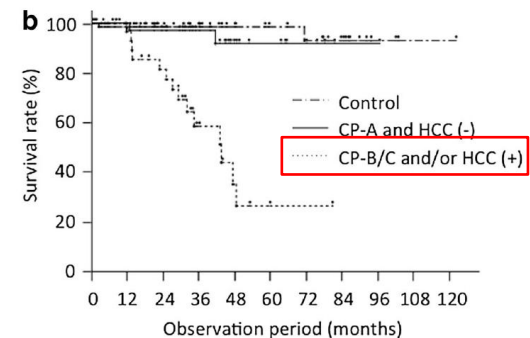
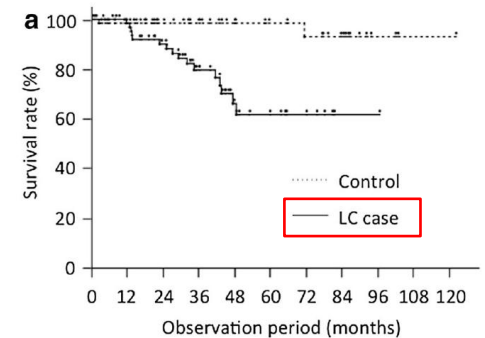
**Table 4** Long-term outcomes of endoscopic submucosal dissection

Variable	LC group	CHB group	<i>p</i> value
Observational periods, months, mean ± SD	64.8 ± 25.7	68.1 ± 24.4	0.540
Recurrence of gastric tumor <sup>a</sup> , <i>n/n</i> (%)	4/42 (9.5)	2/45 (4.4)	0.423
Local recurrence of gastric tumor, <i>n/n</i> (%)	1/42 (2.4)	0/45 (0.0)	0.483
Metachronous recurrence of gastric tumor <sup>b</sup> , <i>n/n</i> (%)	3/42 (7.1)	2/45 (4.4)	0.669
Metachronous recurrence of gastric cancer, <i>n/n</i> (%)	1/42 (2.4)	1/45 (2.2)	1.000
Metastasis of gastric tumor, <i>n/n</i> (%)	0/42 (0.0)	0/45 (0.0)	1.000
Occurrence of HCC	7/42 (16.7)	1/45 (2.2)	0.027
Recurrence of HCC [in patients with a past history of HCC], <i>n/n</i> (%)	5/7 (71.4)	1/1 (100.0)	1.000
Initial occurrence of HCC [in patients without a past history of HCC], <i>n/n</i> (%)	2/35 (5.7)	0/44 (0.0)	0.193
<b>Mortality cases, <i>n/n</i> (%)</b>	<b>8/42 (19.0)</b>	<b>2/45 (4.4)</b>	<b>0.045</b>
Cause of deaths, LC-related/EGC-related/others [in deaths], <i>n</i> (%)	7 (87.5)/0 (0.0)/1 (12.5)	1 (50.0)/0 (0.0)/1 (50.0)	0.378

CHB chronic hepatitis B, EGC early gastric cancer, ESD endoscopic submucosal dissection, HCC hepatocellular carcinoma, LC liver cirrhosis, SD standard deviation

<sup>a</sup>Recurrence of gastric tumor includes local recurrence, metachronous recurrence, and metastasis of gastric tumor

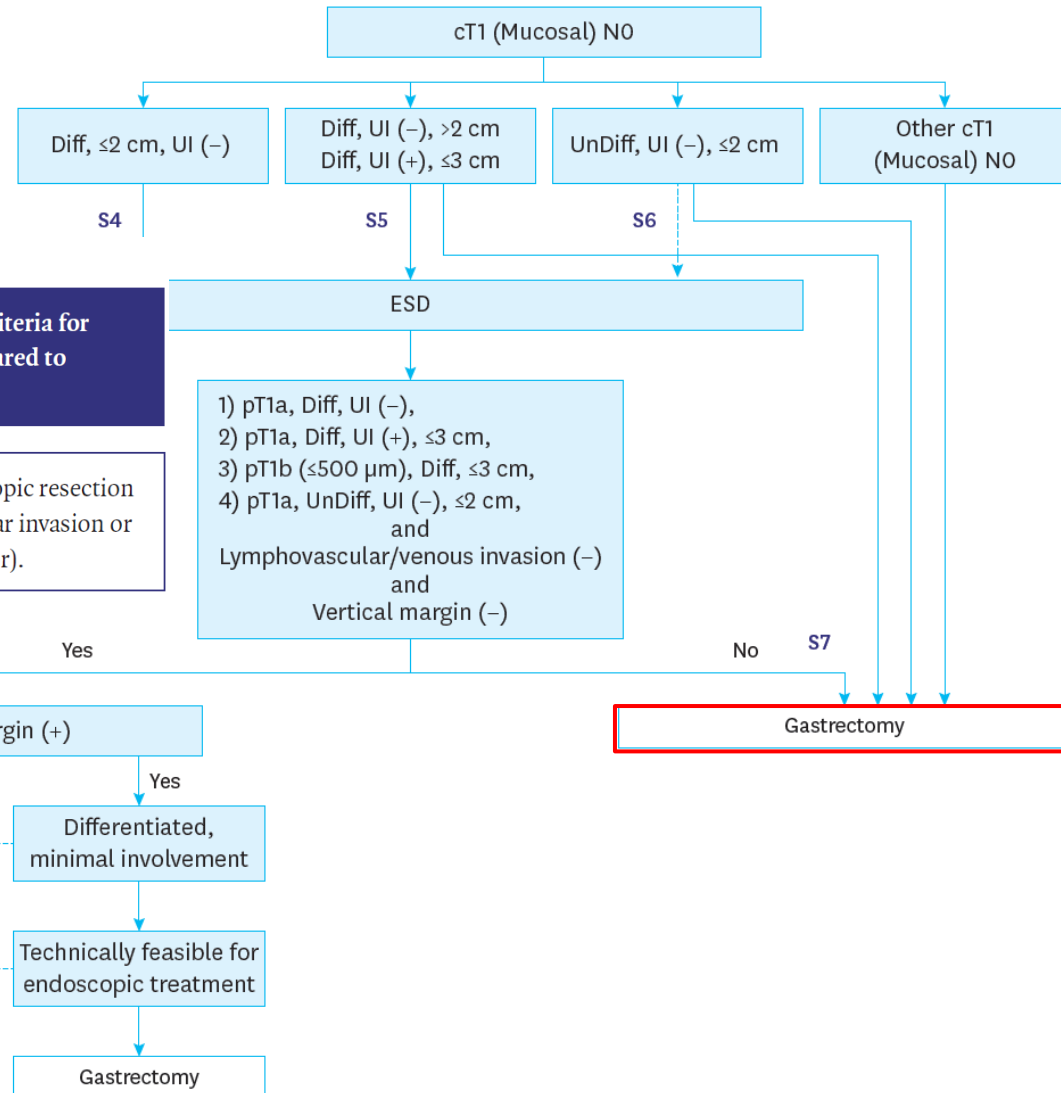
<sup>b</sup>Gastric tumor includes gastric dysplasia and gastric adenocarcinoma, whereas gastric cancer includes gastric adenocarcinoma



Kato et al. *Surgical endoscopy* (2015) 29.6: 1560-1566.

Choe et al. *Digestive diseases and sciences* (2018) 63.2: 466-473.

# Management after Non-curative ESD



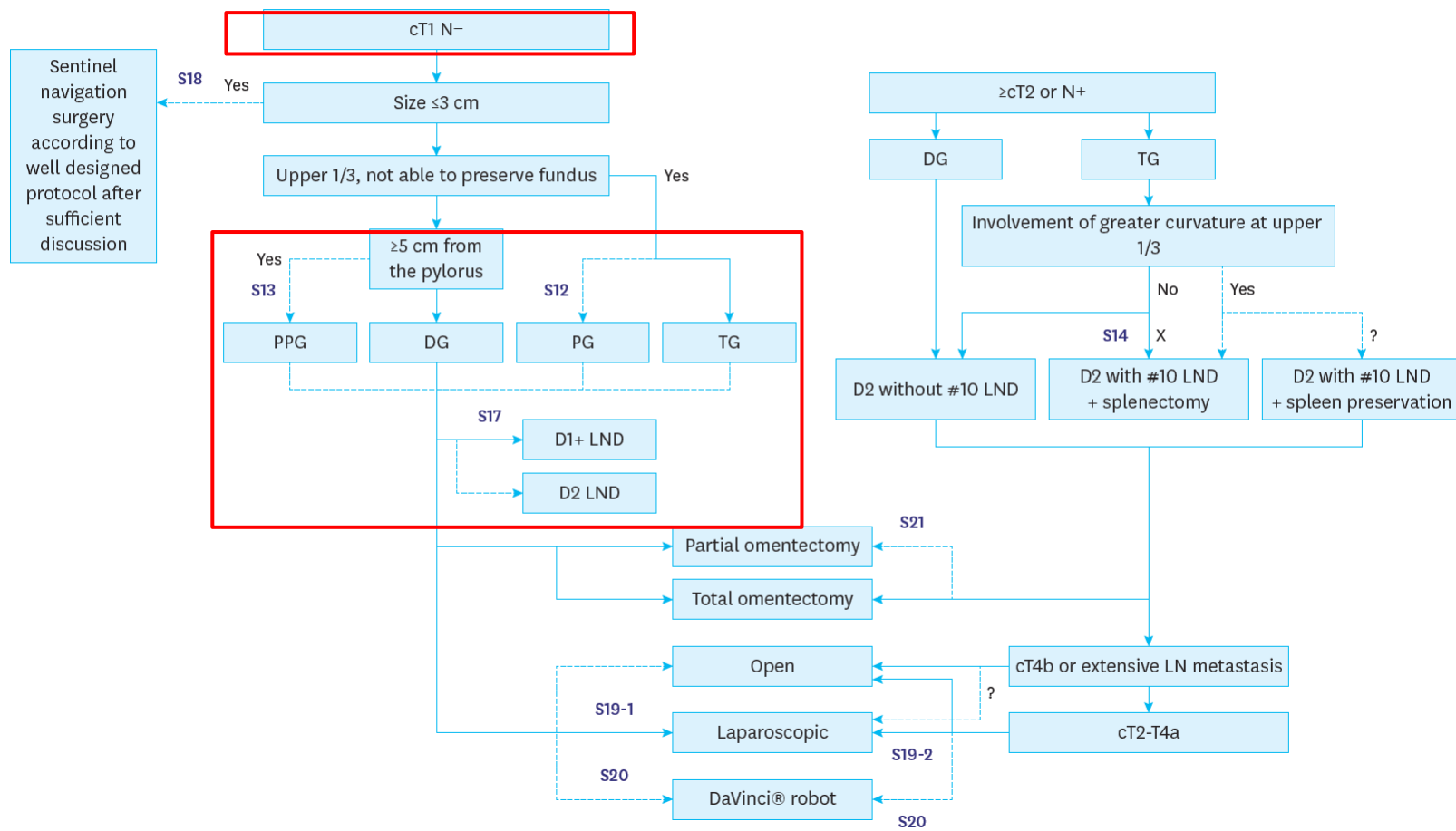
S7. Additional surgery after noncurative endoscopic resection for EGC

**KQ 7: When the results of endoscopic resection for EGC do not meet the criteria for curative resection, can additional surgery improve survival outcome compared to observation?**

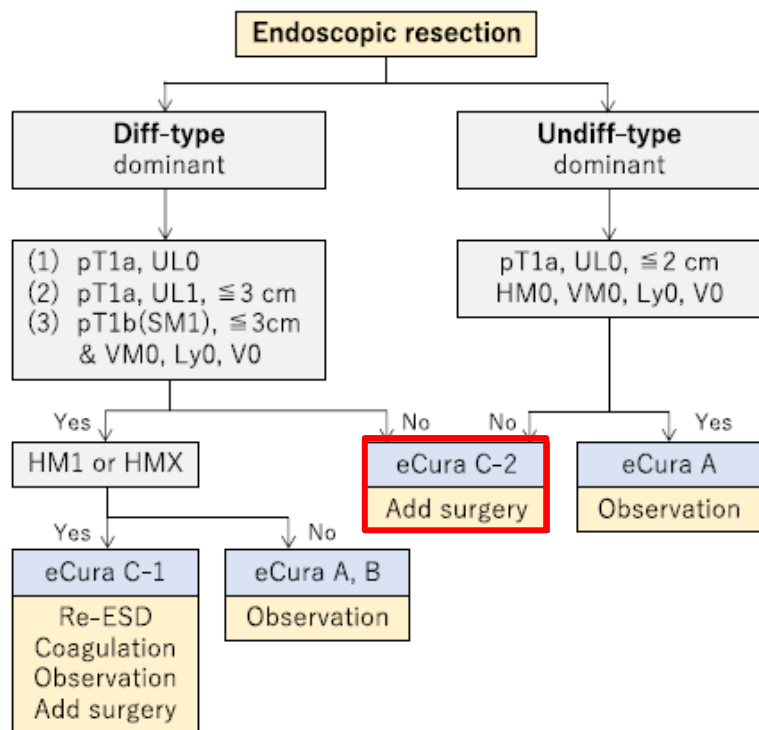
Statement 7: Additional surgery is recommended when the results of endoscopic resection for EGC do not meet the criteria for curative resection or when lymphovascular invasion or positive vertical margin is present (evidence: low, recommendation: strong for).

# Management after Non-curative ESD

## SURGICAL TREATMENT (Flowcharts 3-5)



# Management after Non-curative ESD



**Table 2** Incidence of nodal metastasis in various categories of early gastric cancer observed from surgically resected specimens operated at National Cancer Center Hospital and Cancer Institute Hospital [45]

Depth	Ulceration	Differentiated type		Undifferentiated type		
		Tumor diameter	≤ 2 cm	> 2 cm	≤ 2 cm	> 2 cm
M	UL0	Incidence of nodal metastasis	0% (0/437)	0% (0/493)	0% (0/310)	2.8% (6/214)
		95% confidence interval	0-0.7%	0-0.6%	0-0.96%	1.0-6.0%
	UL1	Incidence of nodal metastasis	0% (0/488)	3.0% (7/230)	2.9% (8/271)	5.9% (44/743)
		95% confidence interval	0-0.6%	1.2-6.2%	1.2-5.7%	4.3-7.9%
SM1	Tumor diameter	≤ 3cm	> 3cm	Any diameter		
	Incidence of nodal metastasis	0% (0/145)	2.6% (2/78)	10.6% (9/85)		
	95% confidence interval	0-2.6%	0.3-9.0%	5.0-19.2%		

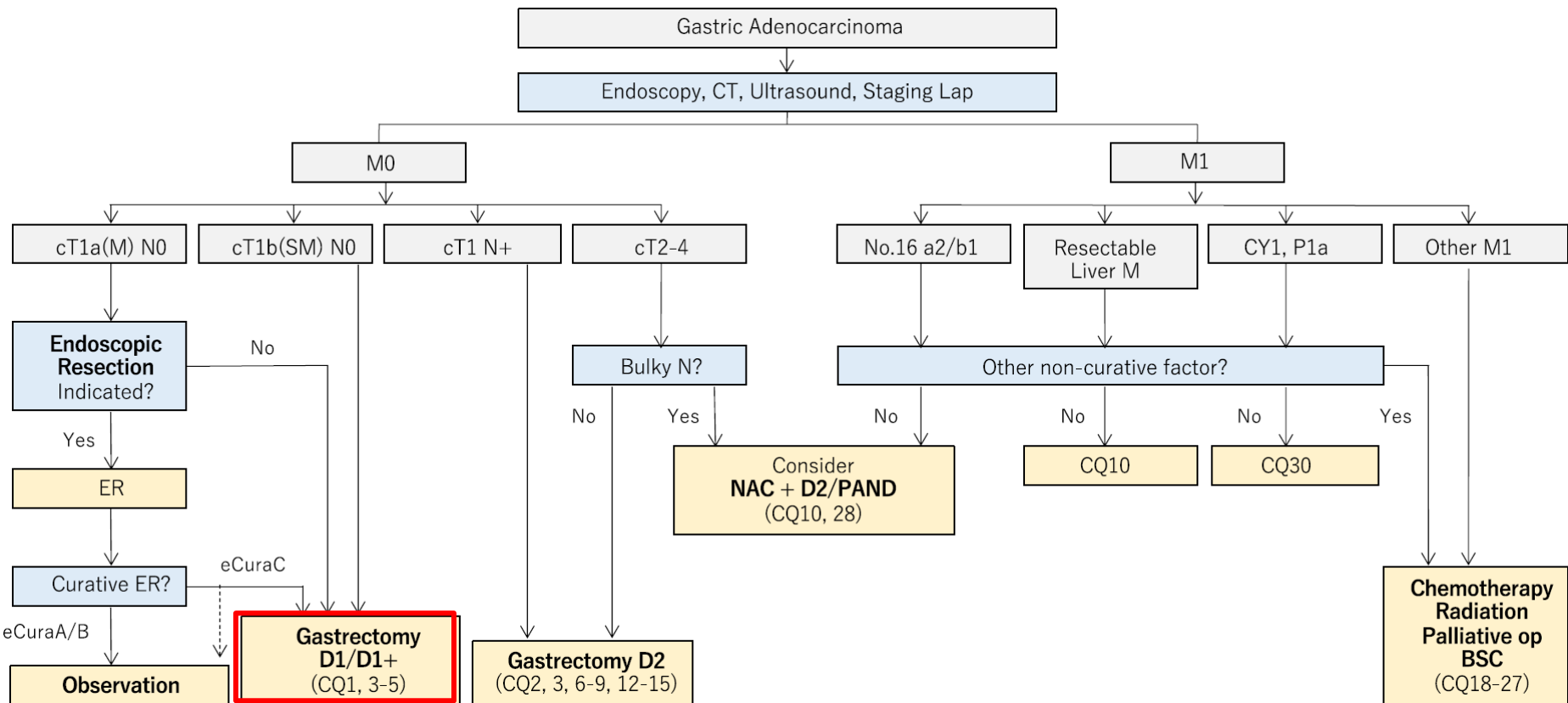
The green zone indicates the absolute indication for endoscopic resection, the yellow zone indicates the expanded indication, and the red zone indicates the relative indication

**Table 3** Incidence of nodal metastasis observed from the specimens of patients who underwent additional gastrectomy with lymphadenectomy after initial treatment with endoscopic resection

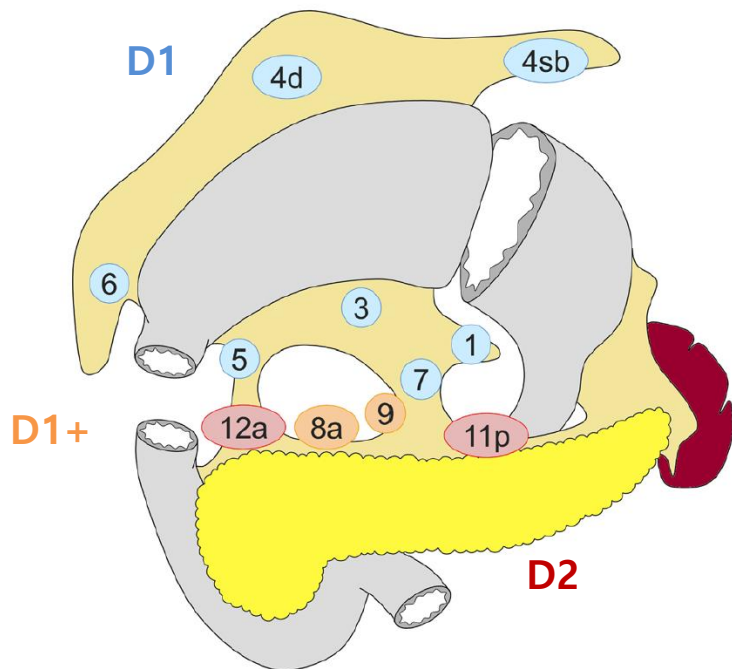
Total points	Number of patients (n=1101)	Number of patients with lymph node metastasis (n=94)	Incidence of nodal metastasis (%)(95% confidence interval)
0	62	1	1.6(0.0–8.7)
1	341	9	2.6(1.2–5.0)
2	185	9	4.9(2.3–9.0)
3	148	11	7.4(3.8–12.9)
4	132	11	8.3(4.2–14.4)
5	141	28	19.9(13.6–27.4)
6	77	21	27.3(17.7–38.6)
7	15	4	26.7(7.8–55.1)

Total points refer to the total of the following scoring scheme, with one point added for each of the following findings: diameter ≥ 3 cm, positive vertical margin, venous invasion, and depth ≥ SM2. Three points are added for a histopathological finding of lymphatic invasion [46]

# Management after Non-curative ESD



# D1+ vs. D2



**Fig. 3** Lymph node dissection in distal gastrectomy. Lymph node stations in blue need to be dissected in D1 dissection. In addition, lymph node stations in orange need to be dissected in D1+ dissection and lymph node stations in red as well in D2 dissection

## Indications for lymph node dissection

- **D1 lymphadenectomy**
  - cT1a tumors that do not meet the criteria for EMR/ESD
  - cT1bN0 tumors that are histologically of differentiated type and 1.5 cm or smaller in diameter
- **D1 + lymphadenectomy**
  - cT1N0 tumors other than the above
- **D2 lymphadenectomy**
  - potentially curable cT1N + , cT2–T4 tumors

# D1+ vs. D2

S17. D1+ dissection for EGC

**KQ 17: Can D1+ dissection show comparable survival outcomes for EGC (cT1N0) patients compared to D2 dissection?**

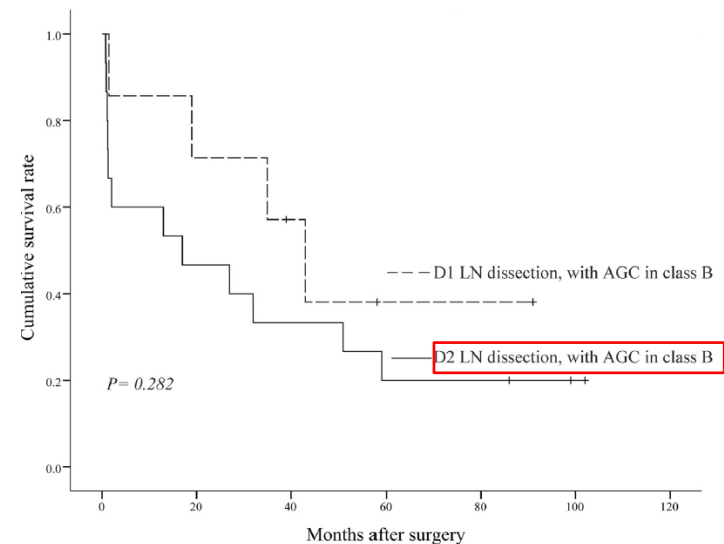
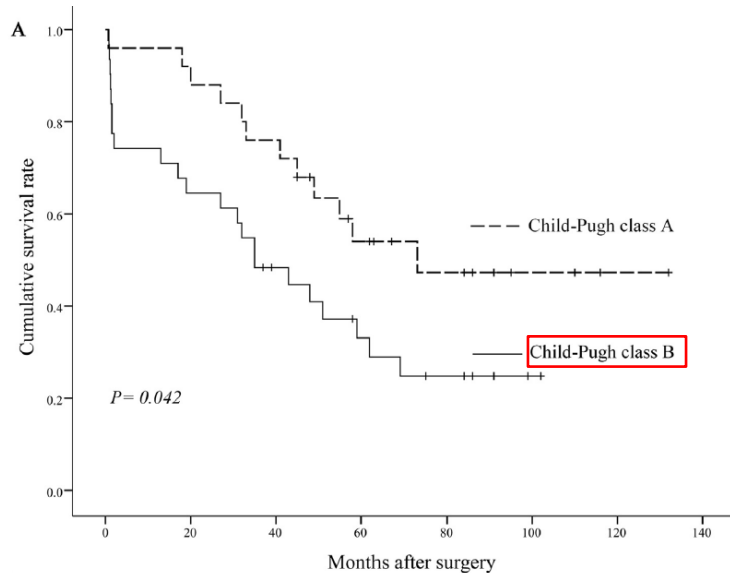
Statement 17: **D1+ dissection can be performed during surgery for EGC (cT1N0) patients in terms of survival outcomes (evidence: low, recommendation: strong for).**

- **D2 dissection** remains the global standard for gastric cancer based on the Dutch Trial long-term survival data.
- **Survival Equivalence:** In EGC patients, **10-year survival rates** show no significant difference
  - *D2 (95%) vs. D1 (87.5%) , P = 0.80*
- **Modified Approach:** Japanese reports indicate **10-year OS**
  - *D1+ (91%) is **identical** to standard D2 (91%)*
- **No metastasis found in second-tier LNs** for patients with cT1N0 or cT1N1

# Gastrectomy in Liver cirrhosis

**Table 2**  
Postoperative severe complications and mortality.

	Child-Pugh class A (n = 25)		Child-Pugh class B (n = 31)		Child-Pugh class C D1 (n = 2)	Total (n = 58)
	D1 (n = 10)	D2 (n = 15)	D1 (n = 14)	D2 (n = 17)		
Severe complication	2	8	7	15	2	34 (58.6%)
Massive ascites	1	8	6	15	2	32 (55.2%)
Postoperative bleeding	0	1	1	1	0	3 (5.2%)
Anastomosis leakage	0	0	0	1	0	1 (1.7%)
Pneumonia	1	2	2	3	1	9 (15.5%)
Hepatic failure	0	1	1	7	2	11 (19%)
Mortality	0	1	1	7	2	11 (19%)



**Table 3****Surgical outcomes of distal gastrectomy**

	Overall	Child–Pugh score				
		5	6	7	8	9
<b>Main outcome</b>						
Mortality (%)	702 (0.7)	266 (0.3)	247 (1.5)	163 (3.8)	19 (6.8)	7 (31.8)
Overall complications within 30 days, CD ≥3 (%)	5606 (5.3)	3946 (4.7)	1206 (7.5)	415 (9.7)	35 (12.5)	4 (18.2)
<b>Secondary outcome</b>						
SSI (%)	5570 (5.3)	4043 (4.8)	1102 (6.8)	400 (9.3)	24 (8.6)	1 (4.5)
Anastomotic leakage (%)	2395 (2.3)	1769 (2.1)	469 (2.9)	147 (3.4)	10 (3.6)	0 (0.0)
Liver failure-related complications (%)	136 (0.1)	66 (0.1)	38 (0.2)	23 (0.5)	7 (2.5)	2 (9.1)
Length of hospital stay [median (IQR)]	12.0 (9.0, 16.0)	11.0 (9.0, 15.0)	14.0 (10.0, 21.0)	17.0 (12.0, 30.0)	18.0 (12.0, 31.0)	19.5 (11.2, 32.0)

CD, Clavien–Dindo; IQR, interquartile range; SSI, surgical site infection.

**Table 5****ORs for short-term outcomes after distal gastrectomy according to Child–Pugh scores**

<b>Main outcome</b>	<b>Unadjusted OR</b>	<b>95% CI</b>	<b>P</b>	<b>Adjusted OR</b>	<b>95% CI</b>	<b>P</b>
<b>Child–Pugh score</b>						
<b>Outcome: Surgical mortality</b>						
5	Reference			Reference		
6	4.92	4.13–5.86	<0.001	2.46	2.03–2.99	<0.001
7	12.48	10.24–15.20	<0.001	4.23	3.34–5.37	<0.001
8	23.07	14.26–37.32	<0.001	6.76	4.02–11.38	<0.001
9	147.29	59.58–364.17	<0.001	64.80	23.64–177.65	<0.001
<b>Outcome: Complications within 30 days CD ≥3</b>						
5	Reference			Reference		
6	1.65	1.54–1.76	<0.001	1.29	1.20–1.39	<0.001
7	2.18	1.96–2.42	<0.001	1.53	1.36–1.72	<0.001
8	2.92	2.04–4.16	<0.001	1.89	1.31–2.72	<0.001
9	4.52	1.53–13.36	0.006	2.83	0.94–8.55	0.07
<b>Secondary outcome</b>						
<b>Outcome: SSI</b>						
5	Reference			Reference		
6	1.46	1.36–1.56	<0.001	1.21	1.13–1.31	<0.001
7	2.04	1.83–2.27	<0.001	1.60	1.42–1.81	<0.001
8	1.87	1.23–2.84	0.004	1.41	0.92–2.15	0.12
9	0.94	0.13–7.02	0.96	0.69	0.09–5.15	0.72
<b>Outcome: Anastomotic leakage</b>						
5	Reference			Reference		
6	1.40	1.26–1.55	<0.001	1.18	1.05–1.32	0.004
7	1.66	1.39–1.96	<0.001	1.35	1.12–1.63	0.002
8	1.73	0.92–3.26	0.09	1.35	0.71–2.57	0.36
9	0.00	CS		0.00	CS	
<b>Outcome: Liver failure-related complications</b>						
5	Reference			Reference		
6	3.02	2.02–4.50	<0.001	3.21	2.07–4.96	<0.001
7	6.88	4.27–11.07	<0.001	8.48	4.93–14.60	<0.001
8	32.82	14.92–72.17	<0.001	41.51	17.83–96.64	<0.001
9	127.51	29.22–556.50	<0.001	110.99	23.09–533.45	<0.001

CD, Clavien–Dindo; CI, confidence interval; CS, complete separation; OR, odds ratio; SSI, surgical site infection.

# Management after Non-curative ESD : eCura system

**Table 3.** Distribution of risk scores and risk classification for LNM in the development cohort

(A)				
Total points	Patients (n=1,101)	LNM (n=94)	Rate of LNM (%)	
0	62	1	1.6	
1	341	9	2.6	
2	185	9	4.9	
3	148	11	7.4	
4	132	11	8.3	
5	141	28	19.9	
6	77	21	27.3	
7	15	4	26.7	
(B)				
Risk category	Total points	Patients (n=1,101)	LNM (n=94)	Rate of LNM (%)
Low	0-1	403	10	2.5
Intermediate	2-4	465	31	6.7
High	5-7	233	53	22.7

LNM, lymph node metastasis.

- **Five risk factors for LNM**

- **3 points** for lymphatic invasion
- **1 point** each
  - : tumor size >30 mm,
  - positive vertical margin,
  - venous invasion,
  - SM invasion  $\geq 500 \mu\text{m}$

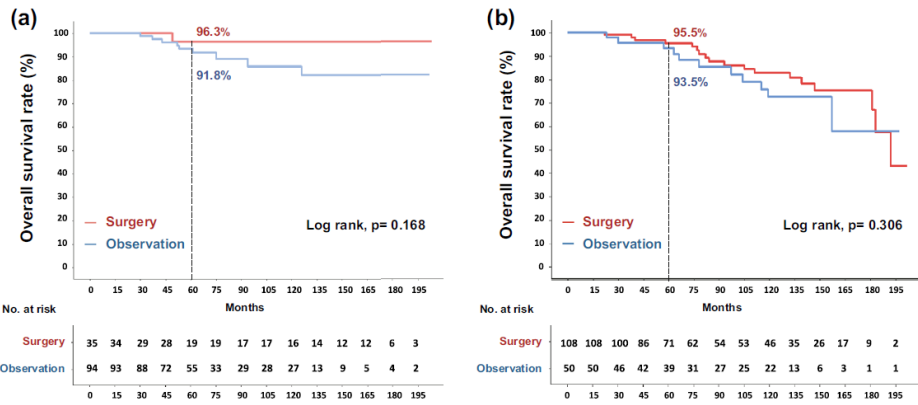
**< Case patient >**

- Size: 26mm (0)
- Negative margin (0)
- **SM invasion 629 $\mu\text{m}$  (1)**
- **LVI positive (3)**

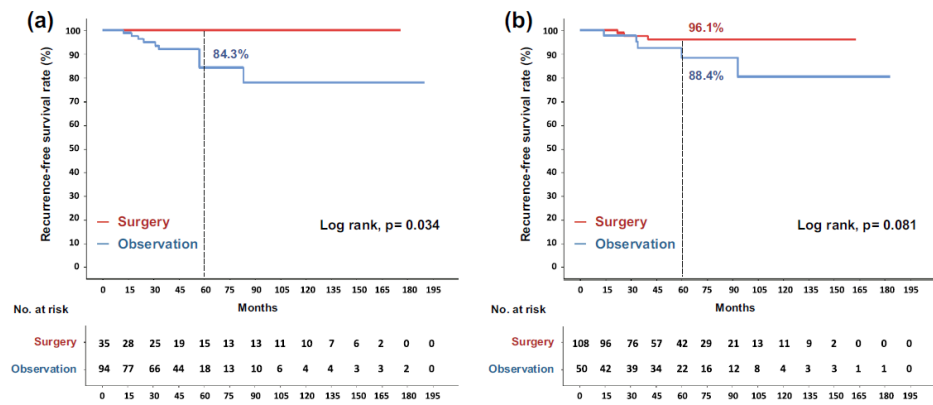


# Management after Non-curative ESD : eCura system

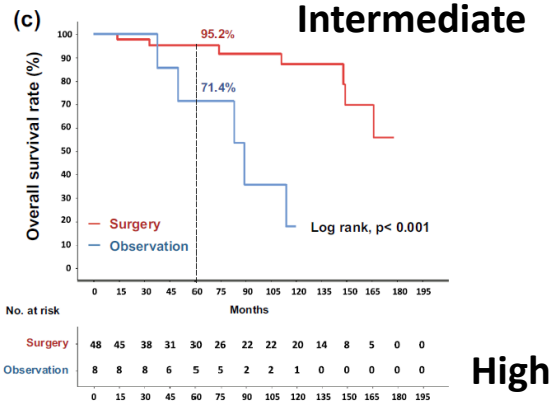
## <Overall survival>



## <Recurrence-free survival>

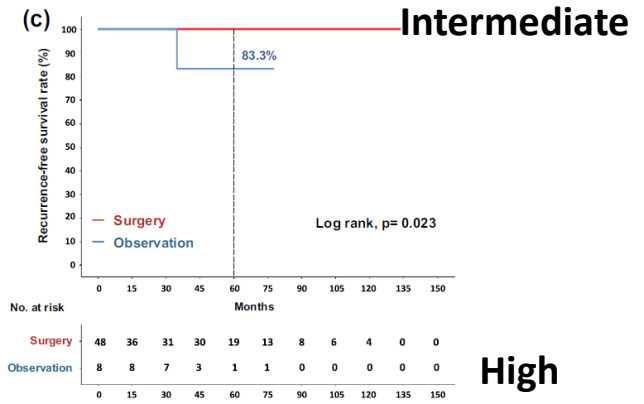


Low



High

Low



High

Fig. 2 Overall survival curves between surgery group and observation group according to risk categories of the eCura system. a Low-risk category. b Intermediate-risk category. c High-risk category

Fig. 3 Recurrence-free survival curves between surgery group and observation group according to risk categories of the eCura system. a Low-risk category. b Intermediate-risk category. c High-risk category

➔ Follow-up without additional surgery after non-curative ESD can be a reasonable option for low-risk and even intermediate-risk patients according to the eCura system

# Limited LN Dissection and Applicability of SNNS

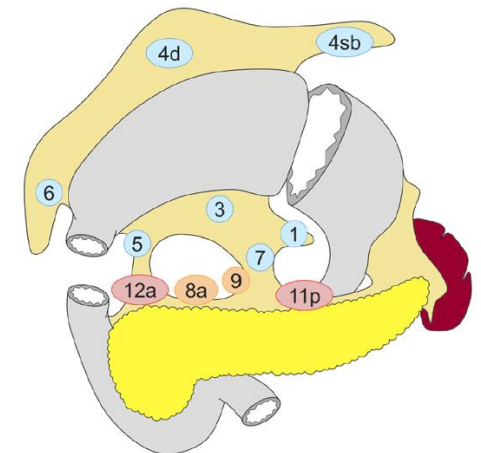
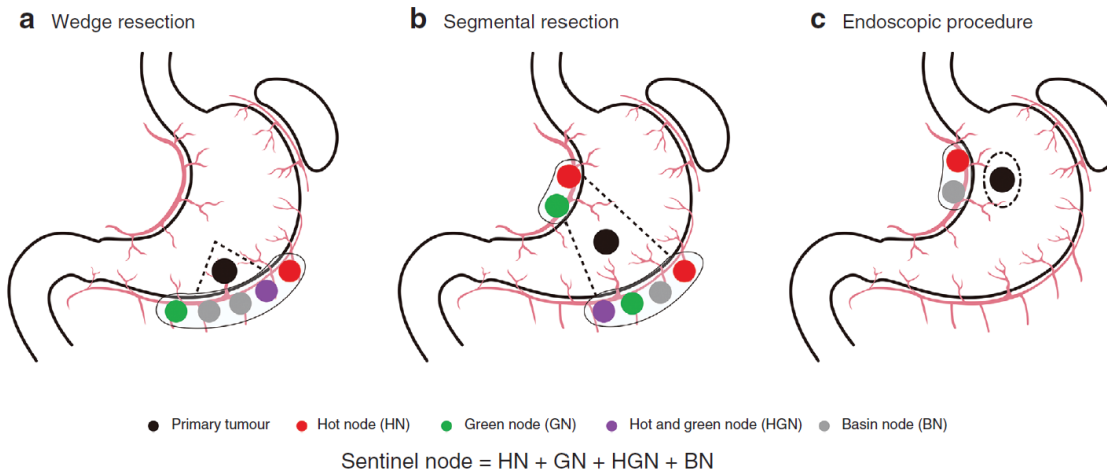
S18. Sentinel node navigation surgery (SNNS)

**KQ 18: Can SNNS be considered a treatment option compared to conventional laparoscopic gastrectomy (LG) regarding survival, nutritional outcomes and QOL?**

Statement 18: SNNS implemented by well-designed protocols and follow-up plans could be considered as a treatment option for cT1N0 and  $\leq 3$  cm gastric cancers in terms of better nutritional outcomes and QOL. Treatment decisions should be made after sufficient discussion with the patient regarding the possibility of metachronous cancer and rescue surgery (evidence: moderate, recommendation: conditional for).

**\*\*본 증례는 이중 추적자(Dual-tracer)를 이용한 정식 SNNS가 아니라 육안적 판단에 의존한 경험적 국소 절제를 시행**

Fig. 1 Laparoscopic sentinel node navigation surgery involving sentinel basin dissection and stomach-preserving surgery



a Wedge resection, b segmental resection and c endoscopic submucosal dissection or endoscopic full-thickness resection.

# Immunosuppression and GC Surveillance

- Risk of developing DNM (De novo malignancy)
  - **2 to 3-fold higher** in transplant recipients than in age- and sex matched healthy controls
  - **Gradually increase** starting from the first post-transplant year and appears highest at 6–10 y of follow-up
- The overall incidence of DNMs : **3.1-14.4%**
- **Korean population** showed that the **most frequent post-transplant DNM** was **stomach cancer (25%)**

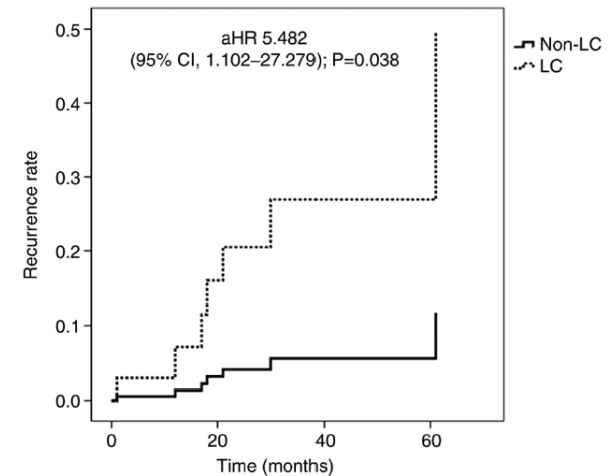


Figure 1. Recurrence of GC following ESD. Increased GC recurrence following ESD was observed in patients with LC (adjusted hazard ratio, 5.482; 95% confidence interval, 1.102-27.279; P=0.038). GC, gastric cancer; ESD, endoscopic submucosal dissection; LC, liver cirrhosis; HR, hazard ratio.

# Immunosuppression and GC Surveillance

- Optimization of immunosuppressive regimen

*Is there a specific immunosuppressive regimen for patients at high risk of cancer after LT?*

## Recommendations

- Exposure to CNIs should be minimised by employing combined immunosuppressive regimens, preferably an mTORi in the case of high risk of hepatic or extrahepatic cancer recurrence (**LoE 2, strong recommendation, strong consensus**).
- An mTORi-based immunosuppression regimen is strongly recommended in patients with history of recurrent/*de novo* non-melanoma skin cancer (**LoE 2, strong recommendation, strong consensus**).

- Strict follow-up protocol for EGC

: EGD & Abdominal CT (every 6 month, at least 3–5 years post-operation)

→ for monitoring local/metachronous recurrence, extragastric recurrence

**Thank you for your attention**