

## 제 8차 연례 위암 교육 심포지움

# 위암: 무엇이 새로 밝혀졌나

## 크피르 벤-데이비스 박사

마운트 사이나이 메디칼 센터

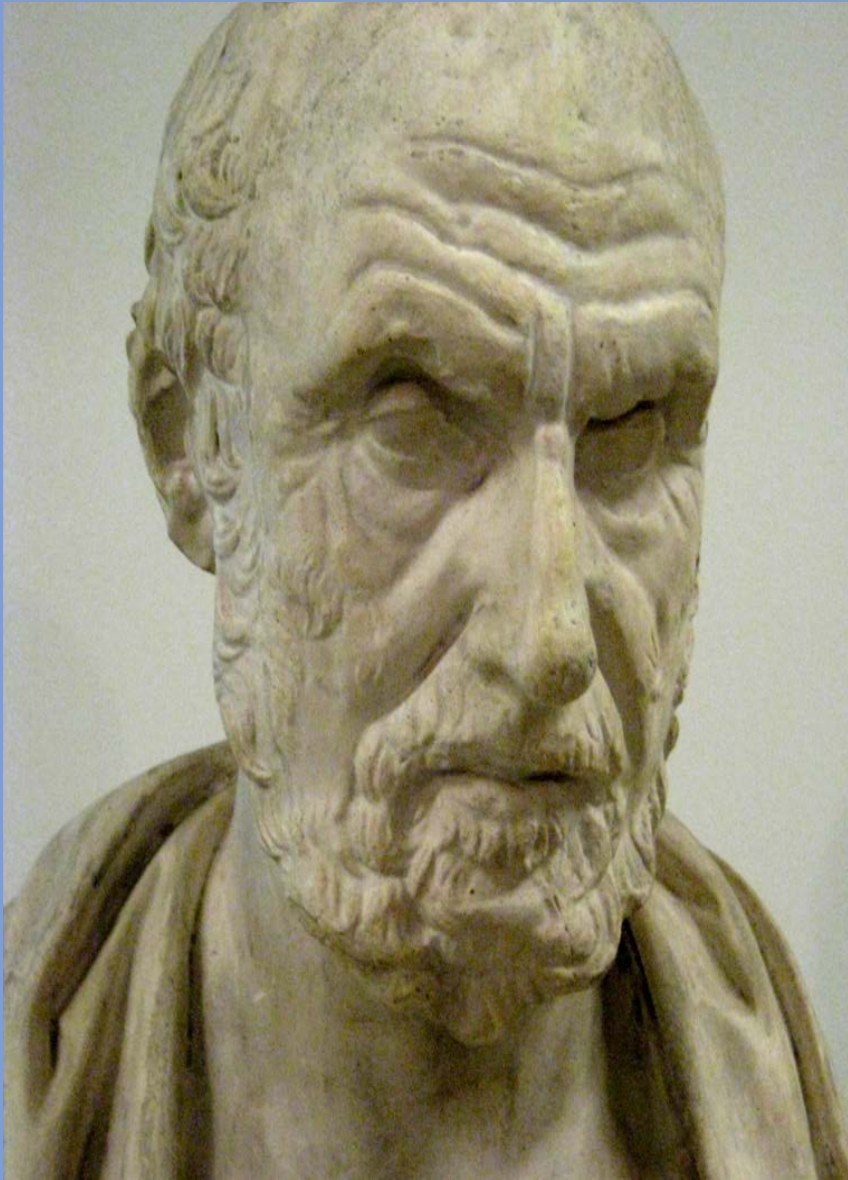
위암 외과 치프

외과 프로그램 디렉터

외과 부과장

# 디스클로저

- 없음



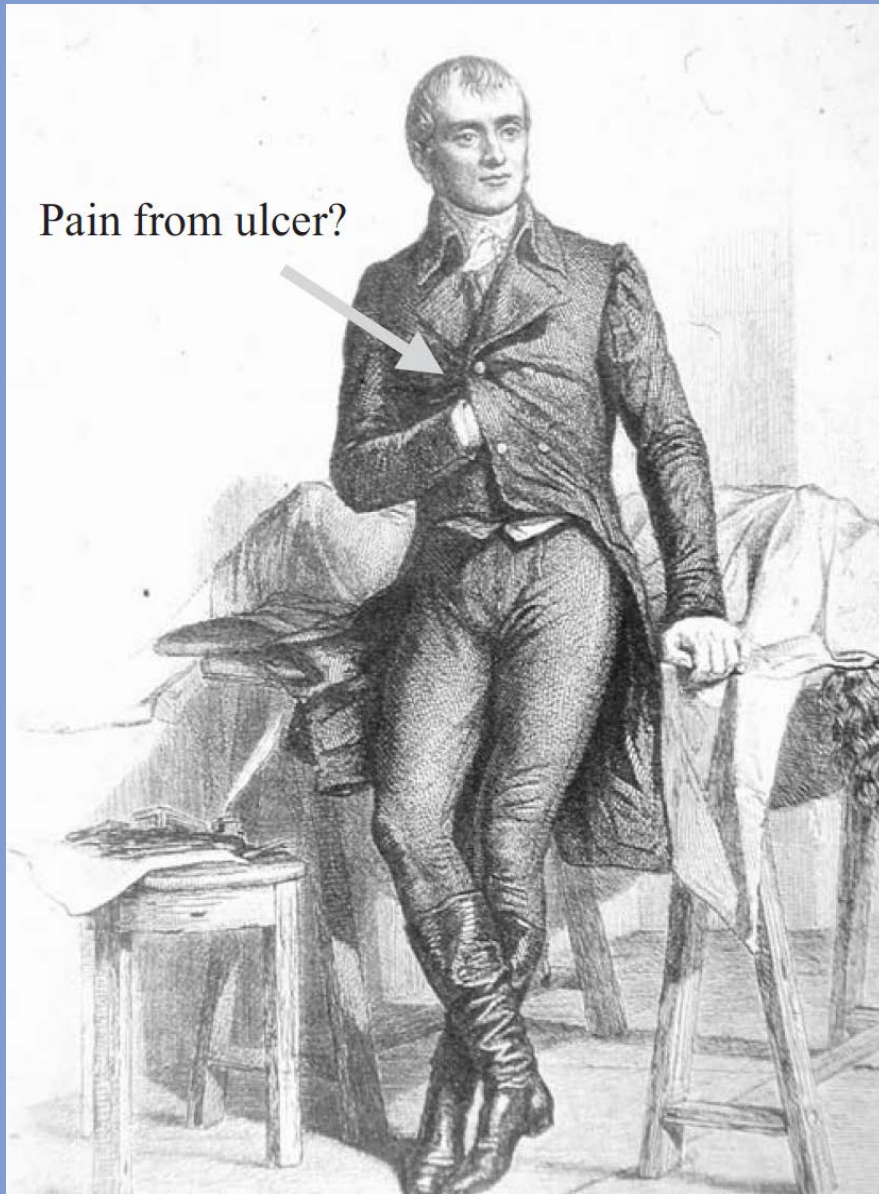
- 18 세기 에스크리푸스 후계자
- 최초로 암, 종양 을 사용
- 암이 피부를 통해 내장으로 침투한다고 믿음
- 이집트 로마 그리스: 시체가 해부에 쓰일 수 없었음

히포크라테스



- 1835년 최초 양성 음성 위  
궤양을 언급.
- 페릴 박사와 암의 원인  
가설 변형.
- 새로운 종양학 시대의  
시작.

진 크루베일허



나폴레옹 보나파르테

- 1821년 의심스런 죽음
- 1819년: 열, 복통, 계속되는 딸꾹질, 구토.
- 1821년 4월 28일: 사망 후 해부, 위를 검사.
- 부검 보고서를 아들에게 주라고 함.

# 부검 보고서

“ . . . the volume of the stomach was small, its anterior surface seems to be normal but on the right side exists a close adhesion with the inferior face of the left liver. Near the small curvature there was a hard area, perforated in the center. The perforation was closed by the liver adhesion. On opening the organ along its large curvature its capacity appeared filled with a considerable quantity of matters mixed with a liquid resembling the sediment of coffee. The internal surface of the stomach was occupied by a cancerous ulcer whose center was on the lesser curve and the digitations were extended from the cardias 'till 1 or 2 centimetres before the pylorus, with a scirrhus thickening of the wall.”

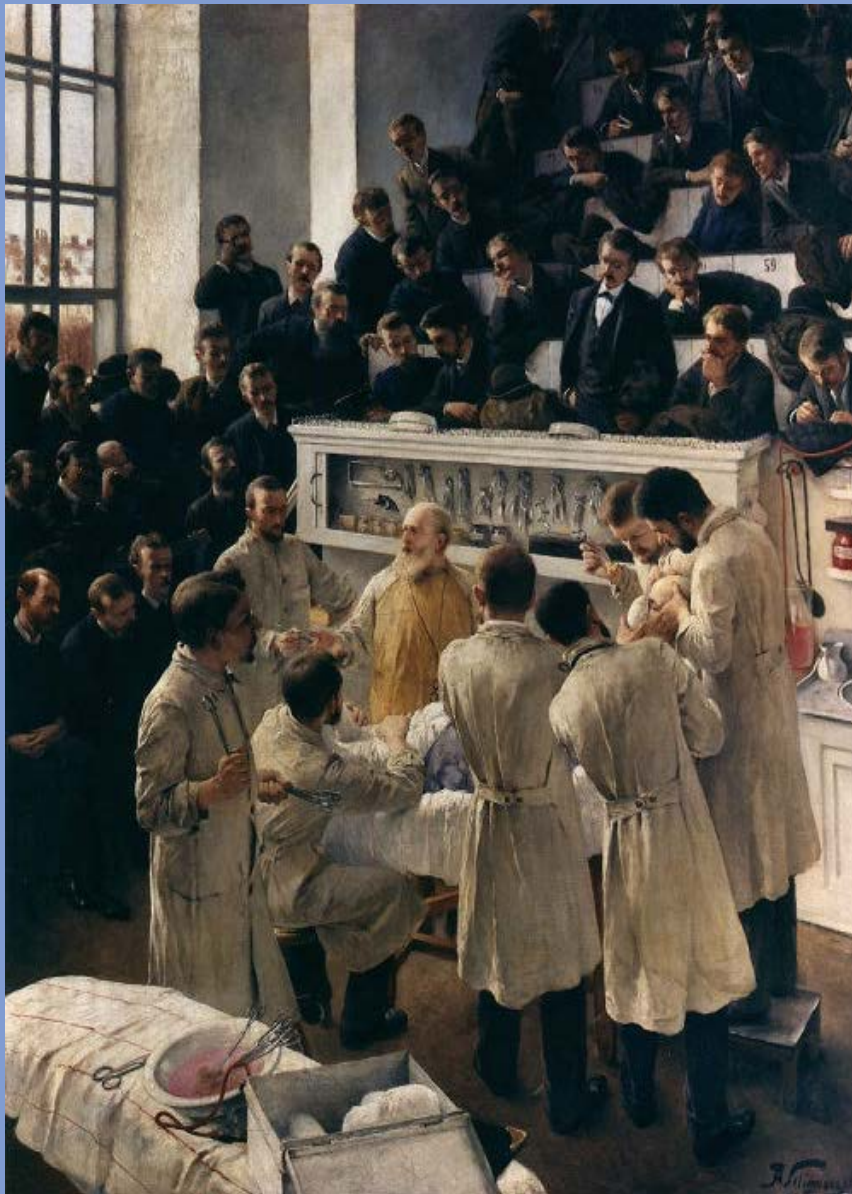
# 수술 시도



- 1879년 4월 9일: 최초 수술 시도. 사망.
- 1880년 11월 6일: 루드위그 본 라이디기어. 수술의 사망 권리.

JULES EMILE PEAN

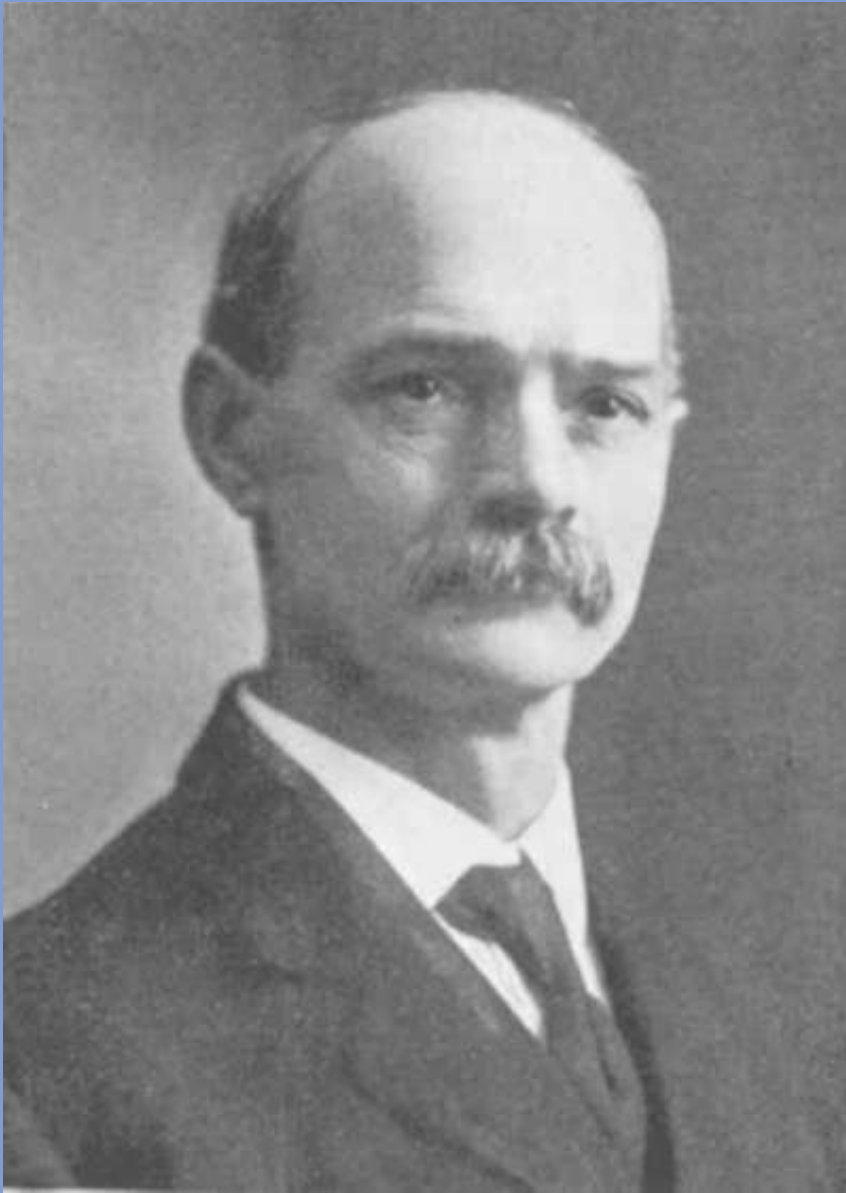




THEODOR BILLROTH

- 계속되는 위 수술 시도
- Jan 22 1881: Subtotal resection with gastroduodenostomy.
- Therese Heller mother of 8, with nausea vomiting and palpable epigastric mass.
- Stomach irrigated with 14 L water. 10 cm xiphoid incision.
- 14 cm long specimen. (T3N1)
- 54 sutures used for anastomosis.
- Discharged on POD 26.
- Died 4 months later from recurrence.





- 1897년 쥘리히: 최초 위 절제술.
- 환자는 병원에서 14달 머뭄. 위 생존 연구.
- 1년 후, 찰스 브링엄이 미국 최초 위 절제술.

칼 슈라터

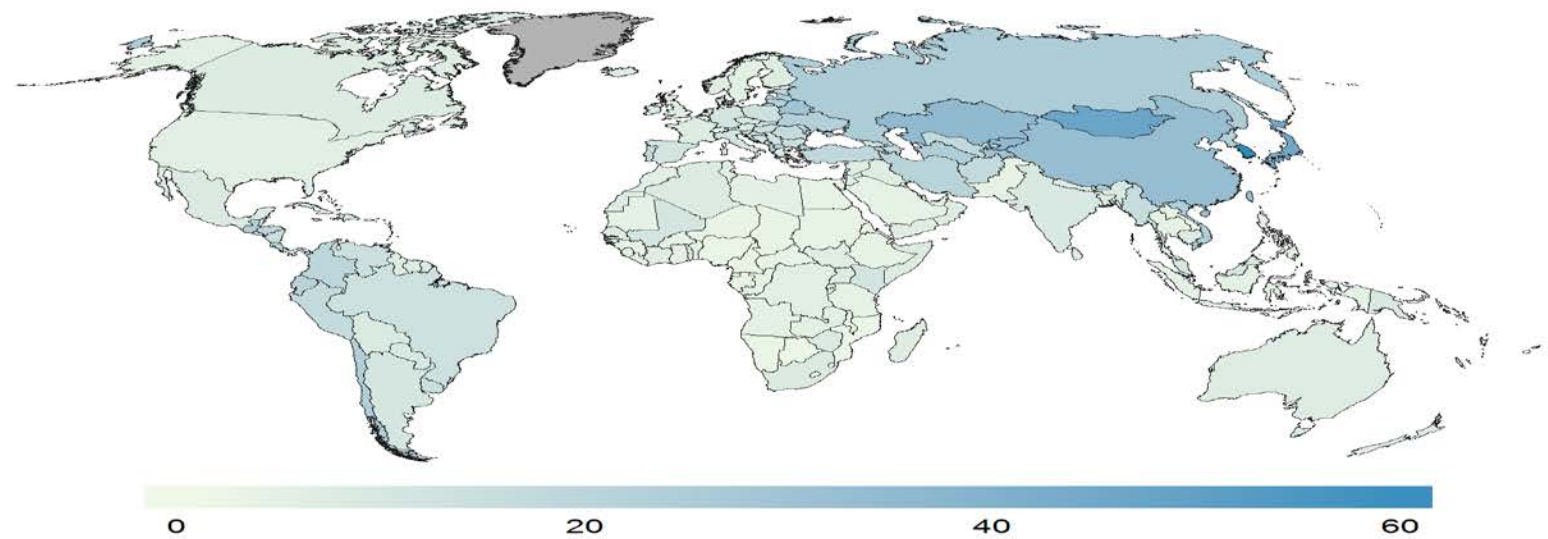
# 위암의 역학

- 5 번째 흔한 암. 100만명
- 3번째 암 사망률
- 남자 사망률이 두배.

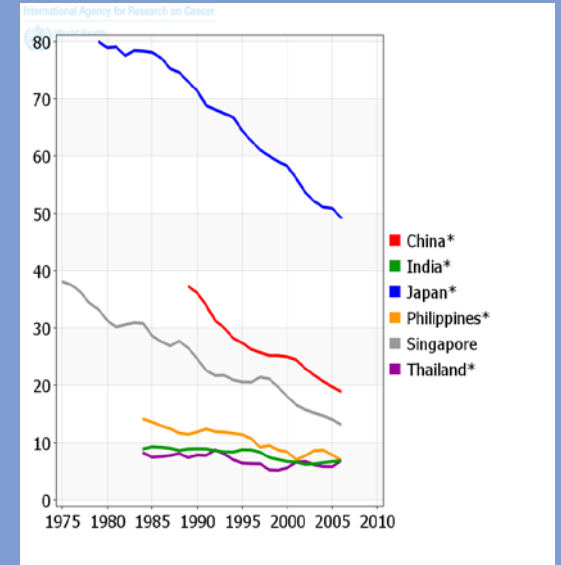
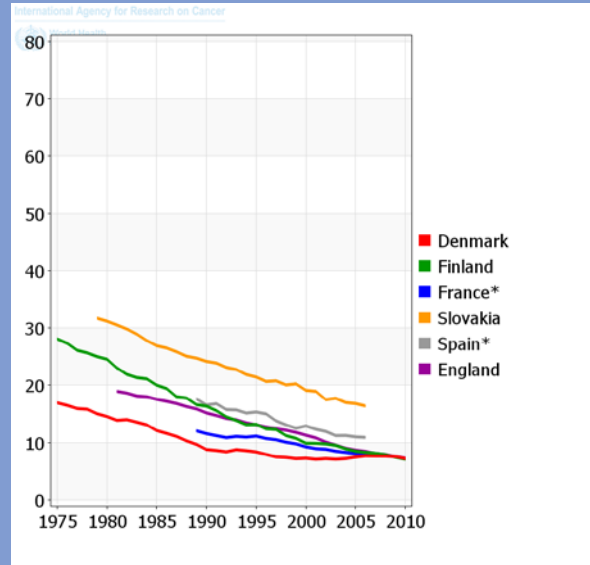
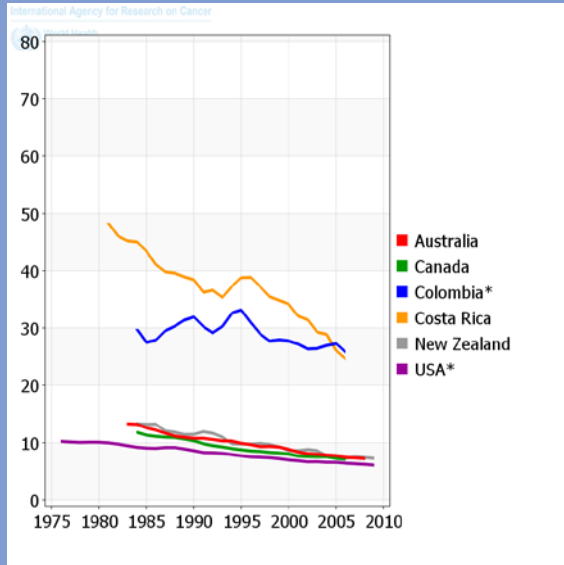
# 위암의 역학

- 2018년 새 진단 26,240
- 2018년 사망 10,800
- 5년 생존률 (2008-15) 31.0%

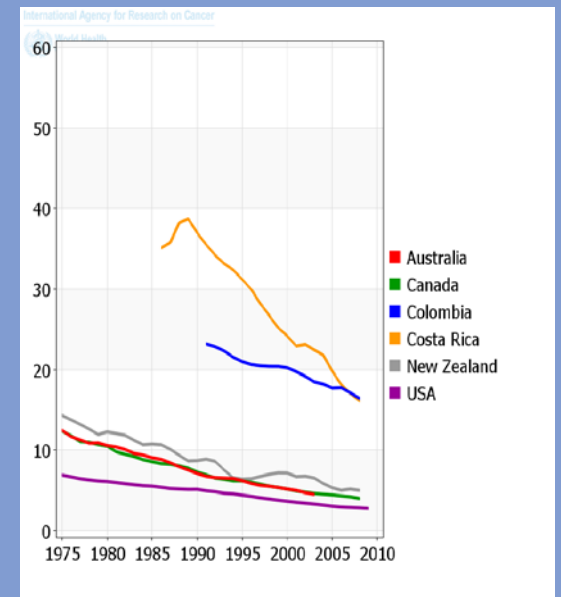
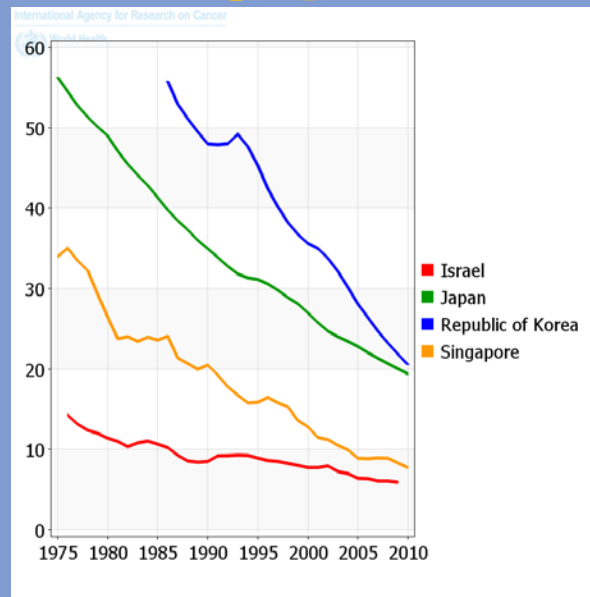
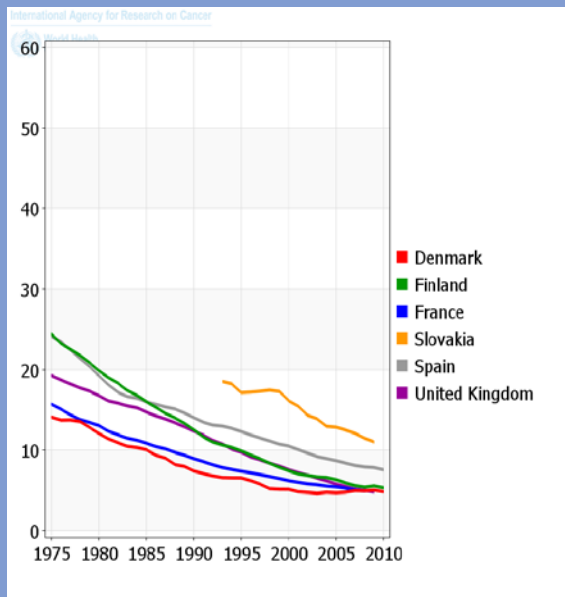
# 역학



# 발병률



# 사망률

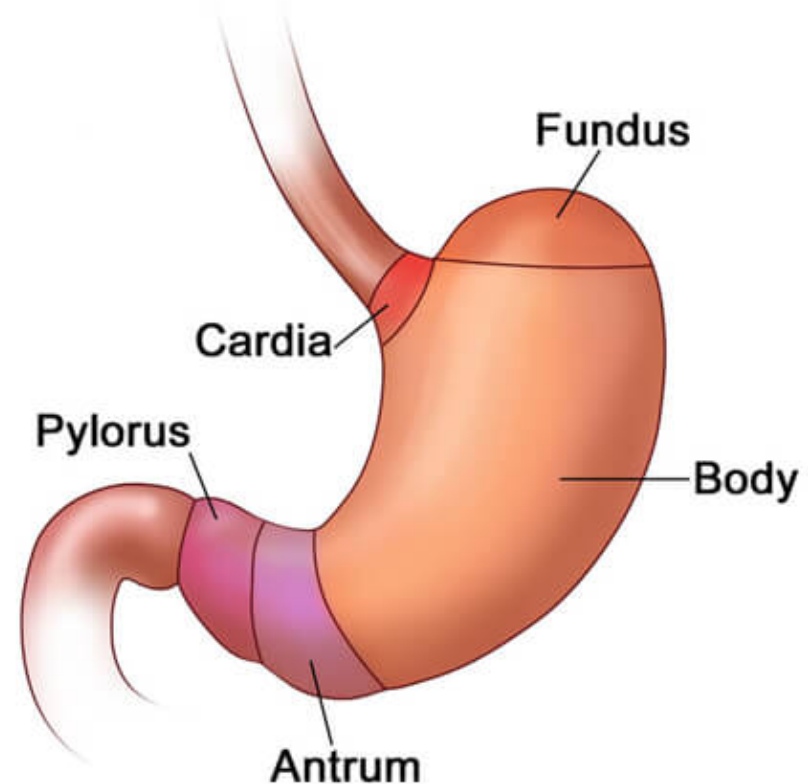


## 하위암 발병률이 젊은 미국인에게 증가

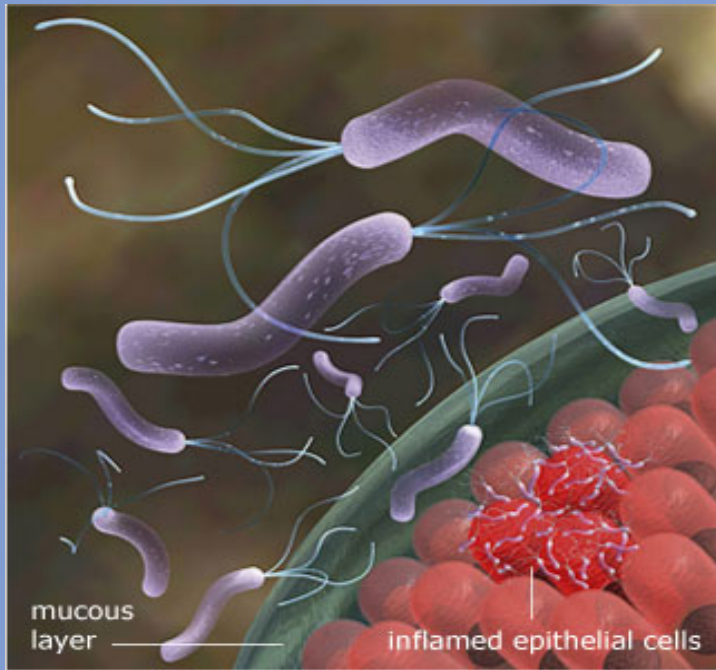
하위암 – 위의 밑쪽 부분 -  
발병률이 50세 이하 젊은  
미국인에게 증가.

보통의 발병률은 감소.

두가지 요인은  
헬리코 박터 감염 과  
자가 면역 위염.



# 헬리코 박터 감염



- 세계적으로 모든 암의 5.5% 에 해당
- 헬리코 박터 없으면, 75% 위암이 없음
- 감염 위험이 사회경제 정도와 연관
- 헬리코 박터 감염률이 미국에서 낮아지는 경향



정상  
위점막

Normal  
gastric  
mucosa



Chronic  
*H. pylori*  
gastritis

헬리코 박터 감염  
위염



Genomic instability  
DNA methylation  
유전자  
메틸화

Atrophic  
gastritis

위염

↘  
Intestinal  
metaplasia

장 전이



Mutation :  
*APC*, *TP53*

돌연변이

Dysplasia

이형성증



Mutation:  
*TP53*, *KRAS*  
LOH:  
*TP53*, *APC*, *DCC*

돌연변이

Intestinal-  
type  
carcinoma

# 위험인자

**Table 2**  
**Main risk factors for gastric cancer by anatomic location**

Risk Factor	Noncardia (Distal) Gastric Cancer RR (95% CI)	Cardia Gastric Cancer RR (95% CI)	Source of Data
<i>Helicobacter pylori</i> serology			
IgG antibodies positive	<b>2.97 (2.34–3.77)</b>	0.99 (0.72–1.35)	Pooled analysis of nested case-control studies HCCG 2001
IgG-positive and serum drawn >10 y before cancer	<b>5.93 (3.41–10.3)</b>	<b>0.46 (0.23–0.90)</b>	
Higher socioeconomic status			
University degree vs lowest education level (adjusted for <i>H pylori</i> infection)	1.51 (0.81–2.78)	<b>2.38 (1.12–5.0)</b>	EPIC study Nagel et al, <sup>39</sup> 2007
Cigarette smoking			
Current vs never	<b>1.60 (1.41–1.80)</b>	<b>1.87 (1.31–2.67)</b>	Meta-analysis Ladeiras-Lopes et al, <sup>40</sup> 2008
Alcohol drinking			
Current vs never	1.07 (0.91–1.26)	0.94 (0.78–1.13)	Meta-analysis Tramacere et al, <sup>44,45</sup> 2012
Heavy vs never	1.17 (0.78–1.75)	0.99 (0.67–1.47)	
Obesity			
BMI 25 to 30	1.16 (0.94–1.43)	<b>1.40 (1.16–1.68)</b>	Meta-analysis Yang et al, <sup>58</sup> 2009
BMI >30	1.26 (0.89–1.78)	<b>2.06 (1.63–2.61)</b>	
Diet			
Fruits (highest vs lowest category)	<b>0.61 (0.44–0.84)</b>	<b>0.58 (0.38–0.89)</b>	Meta-analysis Lunet et al, <sup>48</sup> 2007
Vegetables (highest vs lowest category)	<b>0.75 (0.59–0.95)</b>	<b>0.63 (0.50–0.79)</b>	

# 헬리코 박터 박멸

- 임상 실행 어려움: 암화에 시간이 많이 걸림.
- 상동 인터벤션 임상시험 : 15년 f/u 이 위암 발병률 감소.
- 로에슬러 연구 : 위암이 전암 단계에서 암이 되는 시점은 헬리코 박터 박멸이 소용없음
- 헬리코 박터의 위암 예방 효과
- 헬리코 박터 박멸에 대한 가이드라인은 없음.

Roesler BM, Costa SC, Zeitune JM. Eradication treatment of helicobacter pylori infection: its importance and possible relationship in preventing the development of gastric cancer. ISRN Gastroenterol 2012;2012:935410

Ma JL, Zhang L, Brown LM, et al. Fifteen-year effects of Helicobacter pylori, garlic, and vitamin treatments on gastric cancer incidence and mortality. J Natl Cancer Inst 2012;104:488-92.

# 분류

다른 분류 법



해부학적



침습 깊이

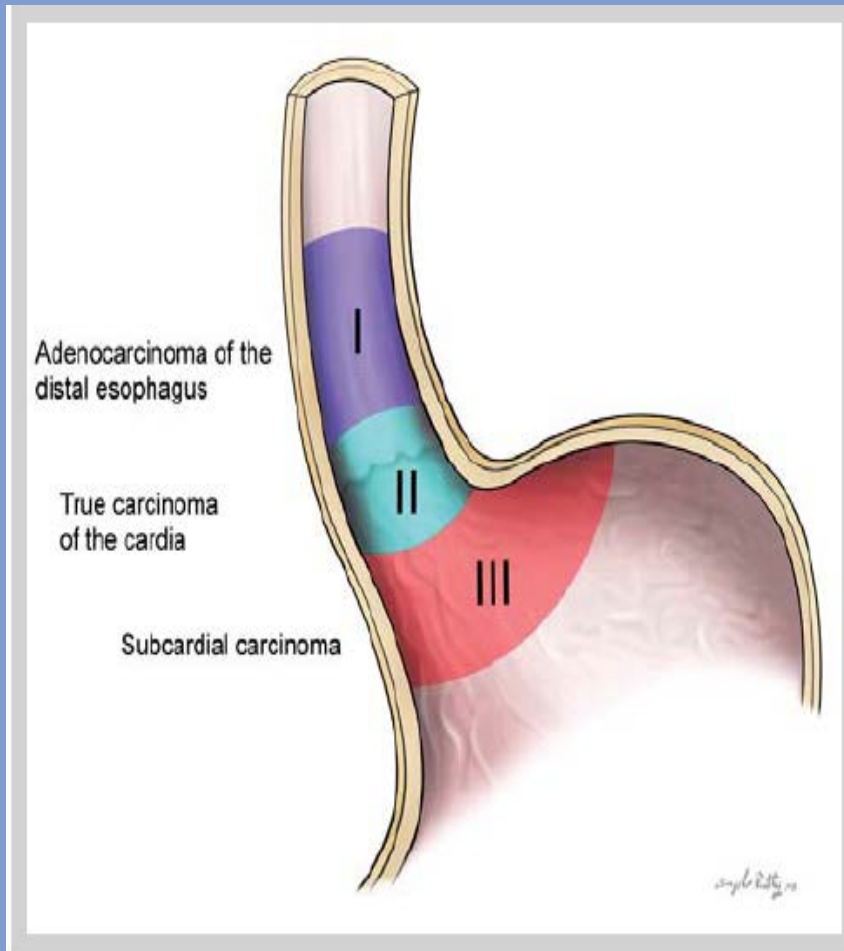


조직학적

# 위식도접합 암 GEJ???

## 시워트 분류

- I 형 : 해부학적으로 GEJ 위 1-5cm.
- II 형 : GEJ 위 1cm 밑 2cm 안에.
- III 형 : GEJ 밑 2-5cm



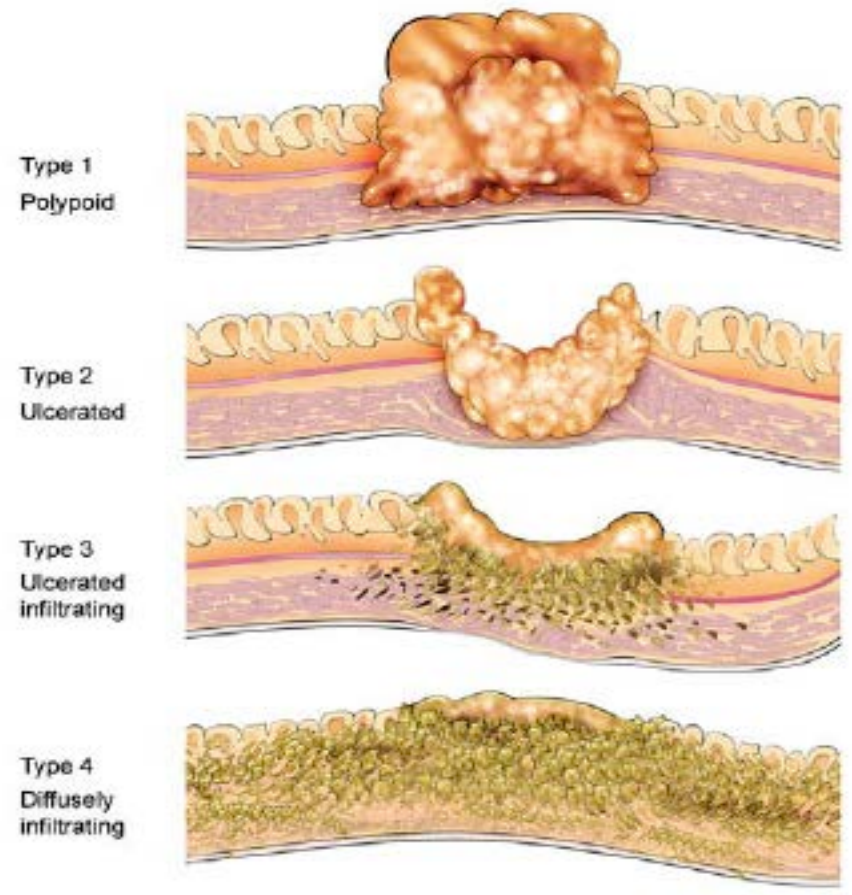
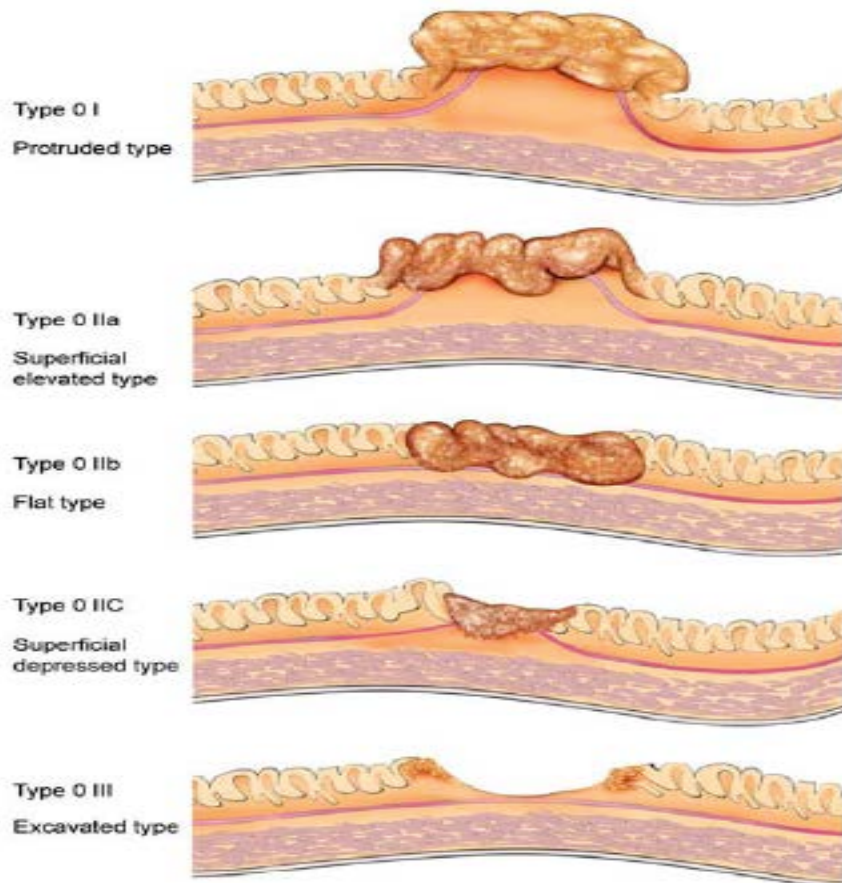
# 위식도암 접합부분암 **GEJ 암???**

미 암 분류 커미션 (7차):

- GEJ 암과 근처 위쪽 5 cm : 식도암
- 위식도암 접합부분암 5 cm 안 쪽 암 (식도쪽 뿐 아니라)
- 위식도암 접합부분암에서 5 cm 떨어진 병변 : 위암

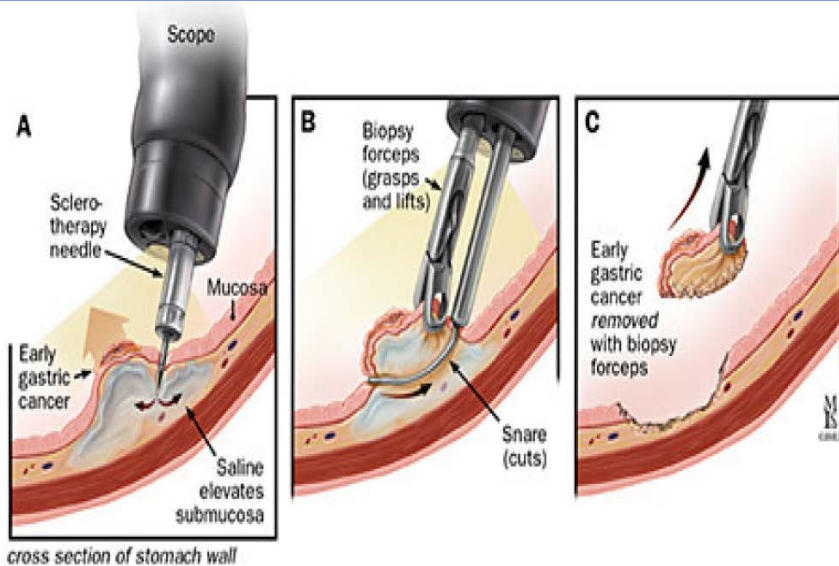
# 침습의 깊이

## 초기 대 진전된 위암



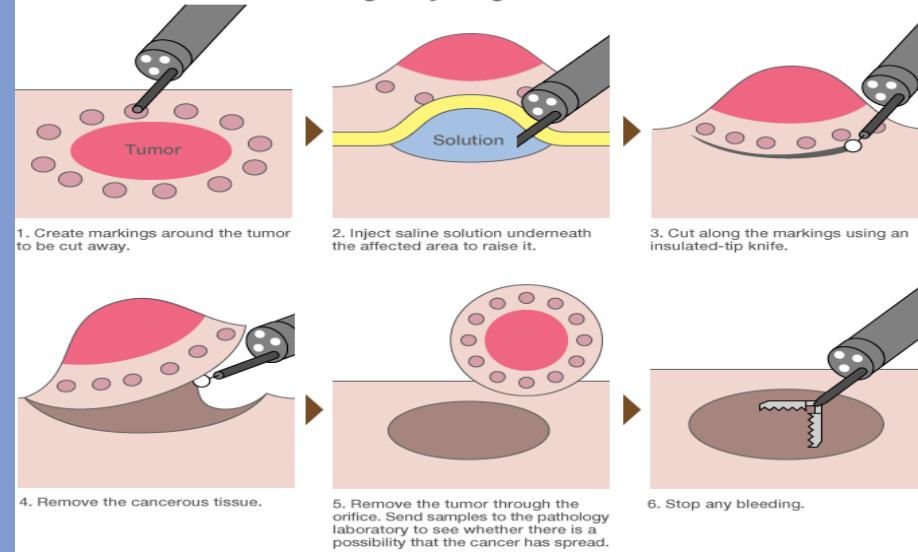


# 초기 대 진전된 위암



- 서구의 15% 이하의 발병률
- 일본은 57% 발병률
- 내시경 사용

## ESD: More Effective at Treating Early-Stage Cancer



# 조직학적 분류

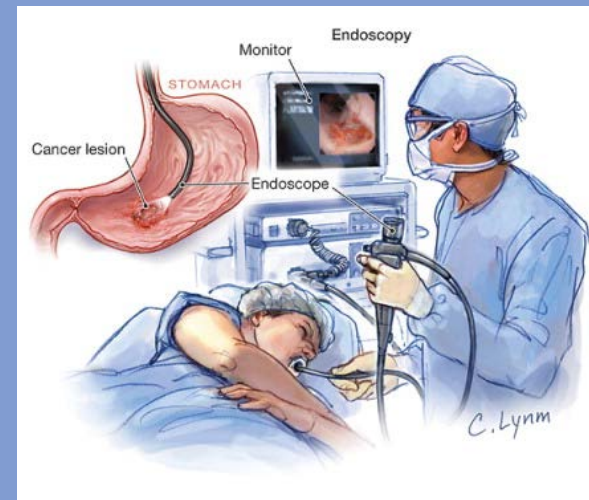
- 라우린 분류법:
  - 장 (53%): 선 형성.
  - 디퓨즈 (33%): 시그렛 링 세포
  - 미분류 (14%)

# 증상

- 몸무게 감소 (62%)
- 복부 고통 (52%)
- 메스꺼움 (34%)
- 소화기 출혈

# 진단

- 위쪽 내시경이 일반적인 방법
- 병변의 5%가 음성
- 모든 병변은 생검과 조직검사로 평가 ( 6-9 생검으로 90% 민감성)
- 위쪽 내시경이 단단한 가족같은 플라스크 형태의 위의 코니스트없는 확장성을 가진 환자에게 유용. 가족같은 플라스크 는 방사선 연구에서 더욱 뚜렷

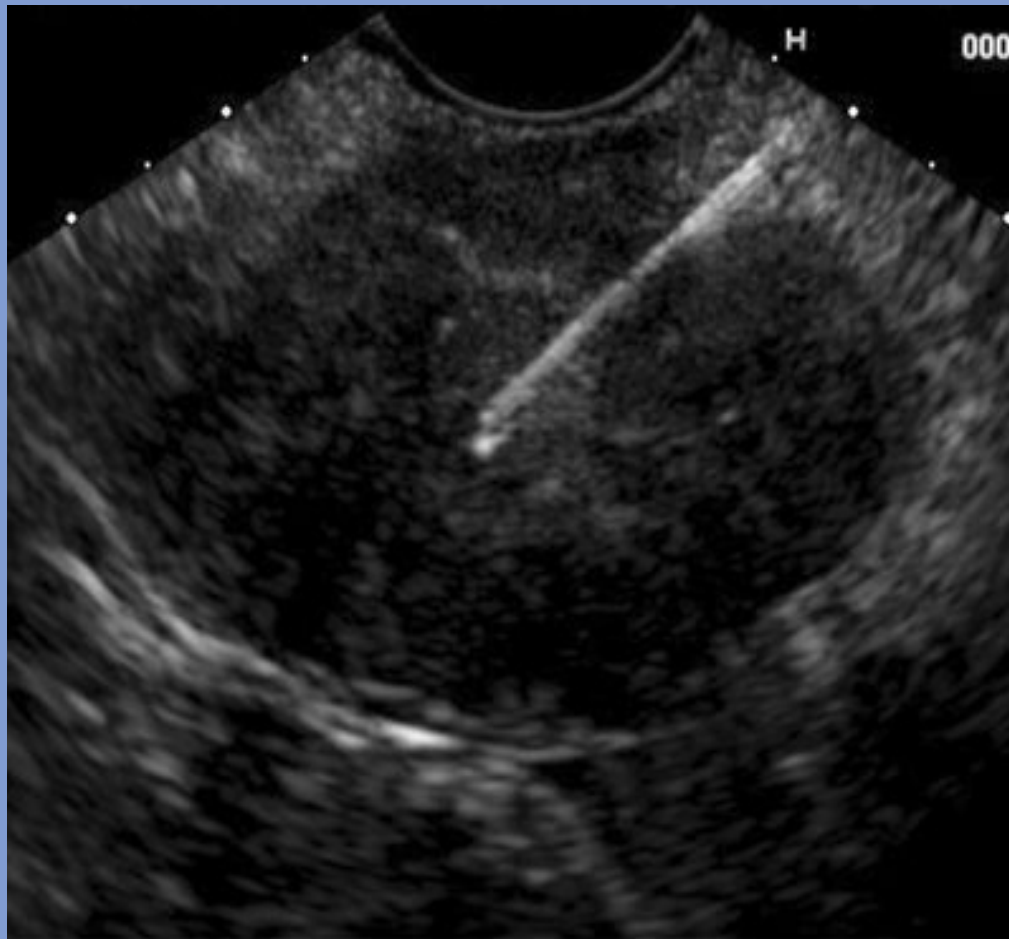


# 병기

- TNM 분류 - AJCC 암 병기 메뉴얼
- T, N 상태
- 흉 복부 골반 CT 스캔
- 복강경

전 이  
제 외

# EUS



- 분화시 정확도
- T1-T4: 77-93%
- 예상도: T,N이 CT 스캔보다 나음
- 이점: 의심스런 림프 절

# CT-복강경

- 전이를 배제하기 위해 쓰임.
- 복막 전이는 5mm 보다 작으면 CT 로 놓침
- 벌크 연구:

103 위암 환자

CT 스캔 음성 - 복강경 수술

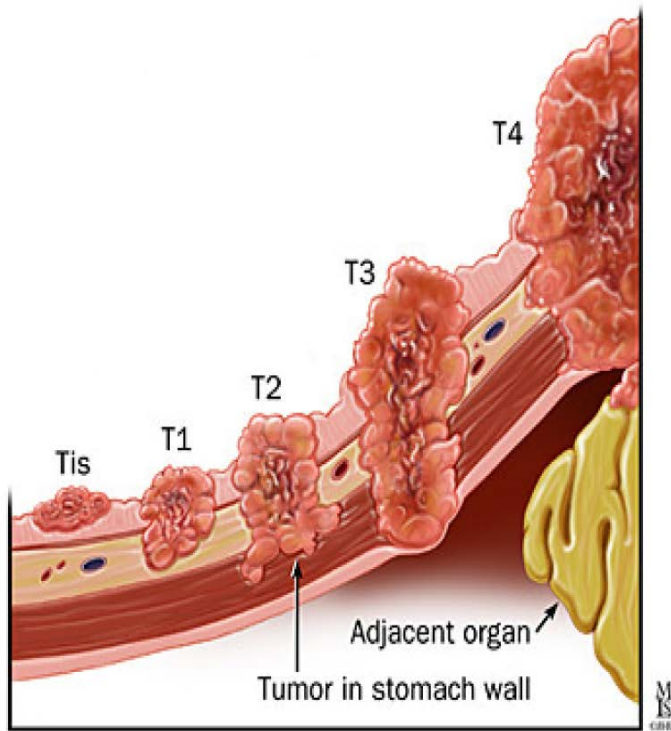
31% 복강경이 전이 생검을 밝힘



# CT-복강경

- 카라니코라스 연구: SEER 데이터 베이스
- 1998-2005년 사이 복강경이 얼마나 자주 쓰였는지 리뷰.
  - 6388 환자 – 8% 만이 병기 복강경
- 작년에 많이 증가. 아직도 복강경은 많이 안 쓰임

# 병기



## Primary tumor (T)

TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma in situ: intraepithelial tumor without invasion of the lamina propria
T1	Tumor invades lamina propria, muscularis mucosae, or submucosa
T1a	Tumor invades lamina propria or muscularis mucosae
T1b	Tumor invades submucosa
T2	Tumor invades muscularis propria
T3	Tumor penetrates subserosal connective tissue without invasion of visceral peritoneum or adjacent structures
T4	Tumor invades serosa (visceral peritoneum) or adjacent structures
T4a	Tumor invades serosa (visceral peritoneum)
T4b	Tumor invades adjacent structures

## Regional lymph nodes (N)

NX	Regional lymph node(s) cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in 1-2 regional lymph nodes
N2	Metastasis in 3-6 regional lymph nodes
N3	Metastasis in seven or more regional lymph nodes
N3a	Metastasis in 7-15 regional lymph nodes
N3b	Metastasis in 16 or more regional lymph nodes

## Distant metastasis (M)

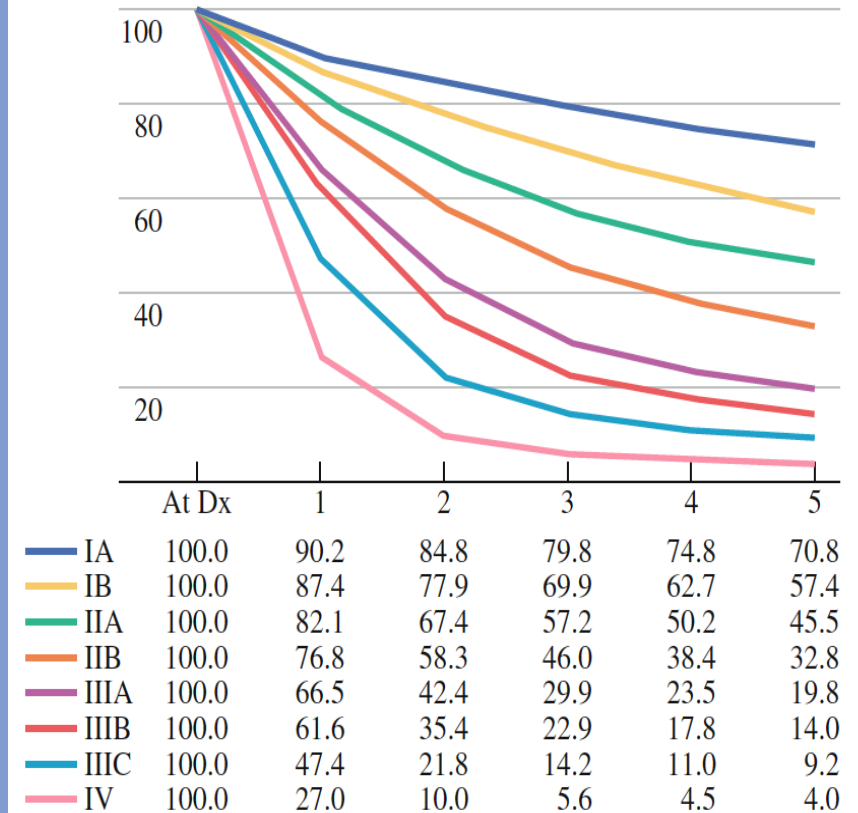
M0	No distant metastasis
M1	Distant metastasis

# 병기

**TABLE 3** Anatomic stage/prognostic groups, gastric cancer

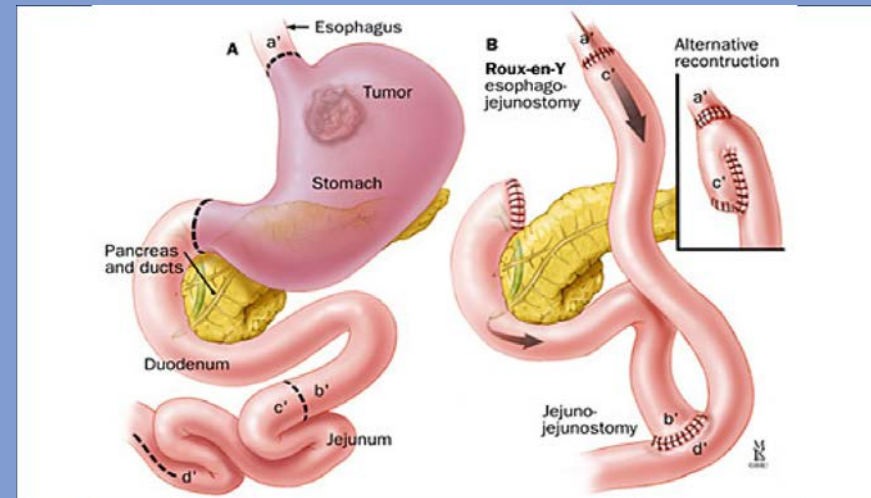
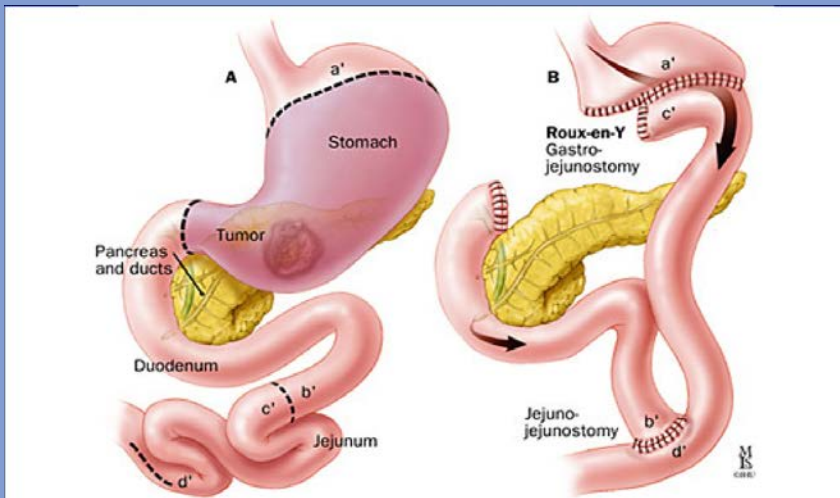
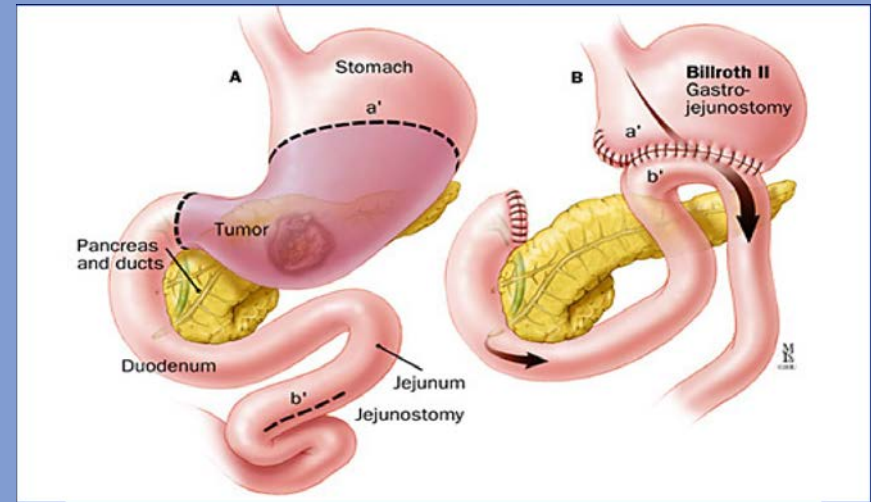
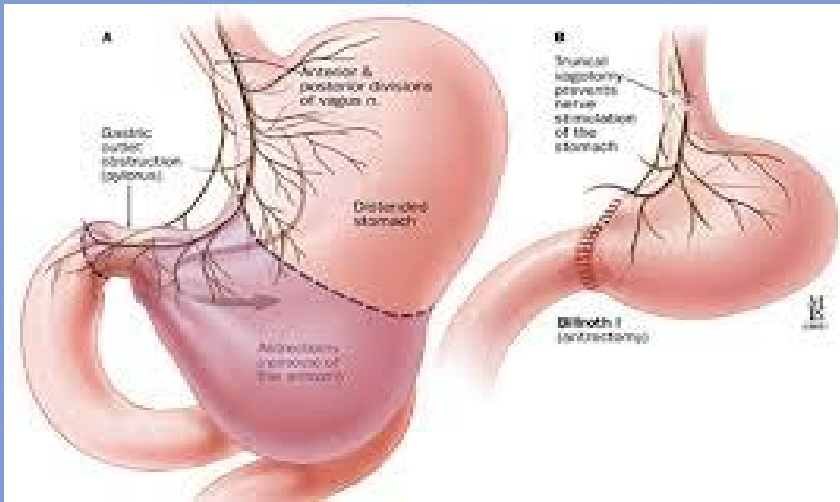
Stage 0	Tis	N0	M0
Stage IA	T1	N0	M0
Stage IB	T2	N0	M0
Stage IIA	T1	N1	M0
	T3	N0	M0
	T2	N1	M0
Stage IIB	T1	N2	M0
	T4a	N0	M0
	T3	N1	M0
	T2	N2	M0
Stage IIIA	T1	N3	M0
	T4a	N1	M0
	T3	N2	M0
	T2	N3	M0
Stage IIIB	T4b	N0 or N1	M0
	T4a	N2	M0
	T3	N3	M0
	T4b	N2 or N3	M0
Stage IIIC	T4a	N3	M0
	Any T	Any N	M1

**Survival  
rate**



# 절제 정도

## LESIONS OF THE DISTAL STOMACH

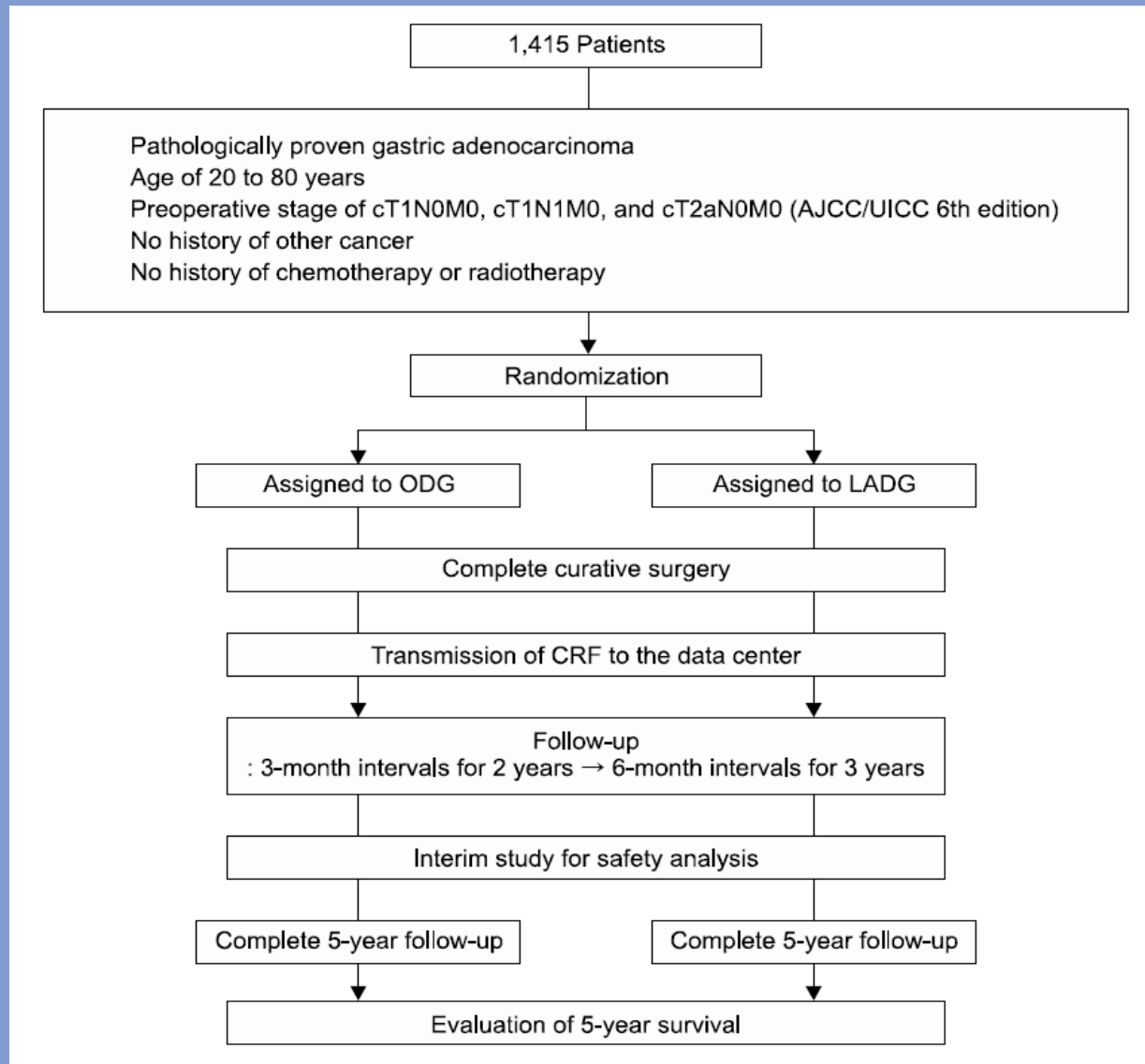


# 복강경 대 개복 수술

- 카타노가 첫 복강경 위 절제술을 한 이후로 많은 연구 (그러나 작은) 가 있었음.
- 결과는 비슷.
- 수술시 출혈이 적음.
- 병원에 머무는 시간이 짧고, 보통 음식으로 빨리 전환 가능

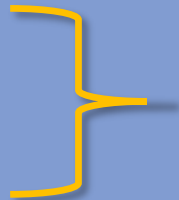
Hayashi et al. Prospective randomized study of open versus laparoscopy-assisted distal gastrectomy with extraperigastric lymph node dissection for early gastric cancer. Surg Endosc 2005; 19:1172-1176.  
Huscher et al. Laparoscopic versus open subtotal gastrectomy for distal gastric cancer: five-year results of a randomized prospective trial. Ann Surg 2005; 241: 232-237.  
Lee JH, Han HS, Lee JH. A prospective randomized study comparing open vs laparoscopy-assisted distal gastrectomy in early gastric cancer: early results. Surg Endosc 2005; 19:168-173.

# 클래스 임상시험



# 클래스 임상시험

- 2010년 중간 결과 보고.
- 병적 상태 : 복강경 10.5% 대 개복 수술 14.7% ( $p=0.137$ )
- 사망률: 복강경 1.1% 대 개복 수술 0% ( $p= 0.497$ )
- 삶의 질: 복강경 이 나음.
  - 내부 출혈 감소
  - 수술 후 무통
  - 수술 후 병원 머무르는 시간 줄

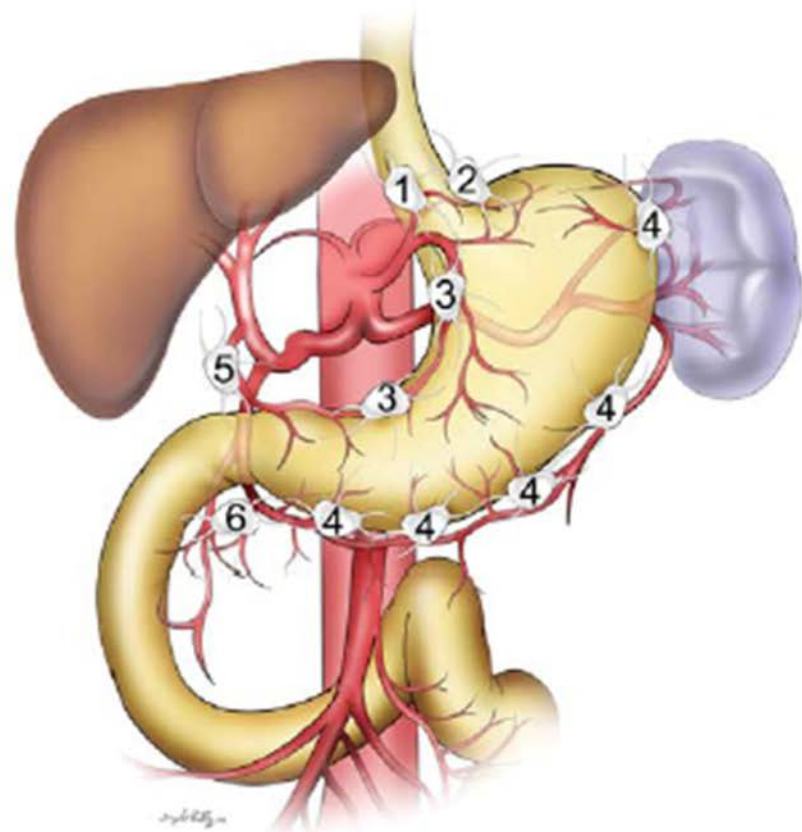




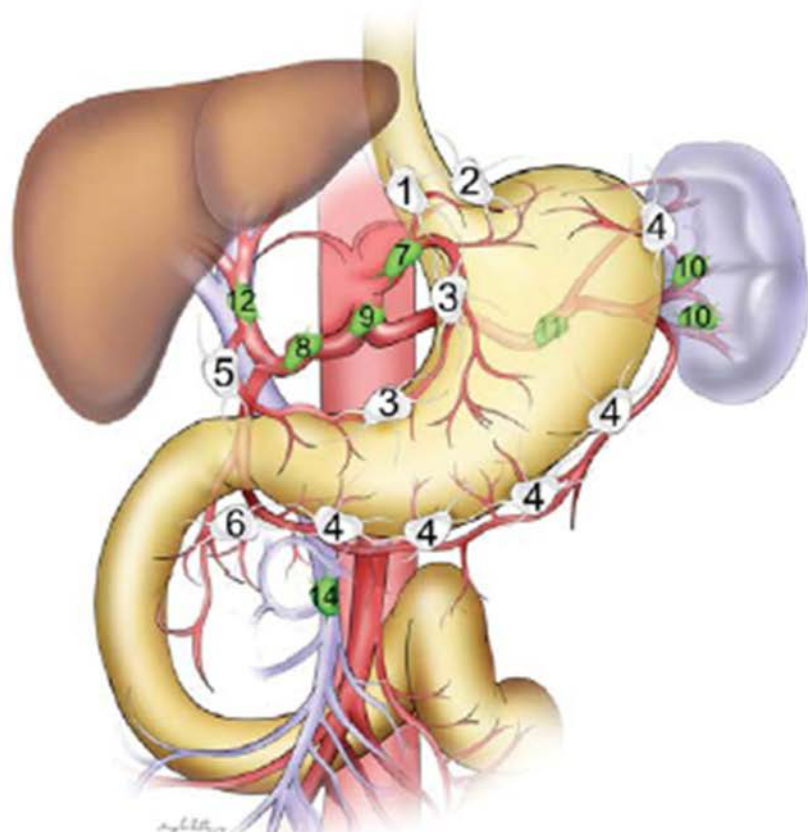
# 클래스 임상시험

- 복강경을 이용한 절제술과 개복 수술을 비교
- 위암 1기 환자
- 3상의 큰 연구
- 여러 센터. 무작위 선정. 프로스펙티브한 연구
- 5년 생존률 관찰.
- 위암 1기 환자에게 복강경 수술은 안전하고  
혜택이 많다.

# 림프 절제 정도



D1 lymphadenectomy



D2 lymphadenectomy

# 림프 절제 정도

- D2에 논의:
  - 림프절 더 많고
  - 1/3 환자에게서 림프 절제 어려움
  - 정확한 병기 어려움

Roukos DH, Kappas AM. Targeting the optimal extent of lymph node dissection for gastric cancer. J Surg Oncol 2002; 81:59.

Bunt et al. Surgical/pathologic-stage migration confounds comparisons of gastric cancer survival rates between Japan and Western countries. J Clin Oncol 1995; 13:19.

De Manzoni et al. The new TNM classification of lymph node metastasis minimises stage migration problems in gastric cancer patients. Br J Cancer 2002; 87:17

# 림프 절제 정도

- D2에 논의:
  - 병기나 사망률 더 높음
  - 더 큰 연구에서는 생존률에 도움이 된다는 증거 부족

Jiang Let al. Survival and recurrence free benefits with different lymphadenectomy for resectable gastric cancer: a meta-analysis. J Surg Oncol 2013; 107:807.

Dent DM, Madden MV, Price SK. Randomized comparison of R1 and R2 gastrectomy for gastric carcinoma. Br J Surg 1988; 75:110.

Cuschieri et al. Postoperative morbidity and mortality after D1 and D2 resections for gastric cancer: preliminary results of the MRC randomised controlled surgical trial. The Surgical Cooperative Group. Lancet 1996; 347:995.

Bonenkamp et al. Extended lymph-node dissection for gastric cancer. N Engl J Med 1999; 340:908.

# **Patient survival after D<sub>1</sub> and D<sub>2</sub> resections for gastric cancer: long-term results of the MRC randomized surgical trial**

A Cuschieri<sup>1</sup>, S Weeden<sup>2</sup>, J Fielding<sup>3</sup>, J Bancewicz<sup>4</sup>, J Craven<sup>5</sup>, V Joypaul<sup>1</sup>, M Sydes<sup>2</sup> and P Fayers<sup>2</sup>, for the Surgical Co-operative Group

- 400명 환자 D1 or a D2 림프 절제
- D2 에서 병기 더 높음 (46 Vs 28%)
- D2 에서 사망률 더 높음 (13 Vs 6%)
- 5년 생존률 비슷 (33 Vs 35%)

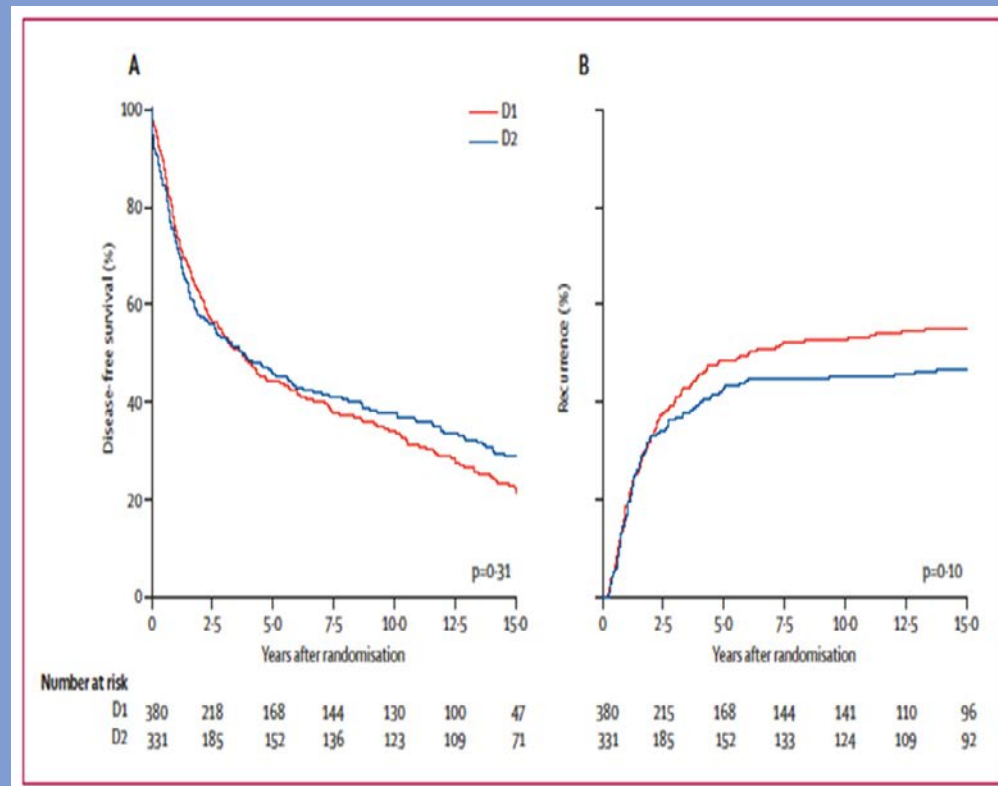
# 더치 임상시험

- 711명 환자 무작위로 선정 - D1 나 D2
- D2 에서 병기 더 높음 (43 Vs 25%) 사망률 더 높음 (10 Vs 4%)

	D1 group (n=380)	D2 group (n=331)	p value
Alive	82 (22%)	92 (28%)	0.34*
Deaths from gastric cancer	182 (48%)	123 (37%)	0.01†
Deaths from other causes	116 (31%)	116 (35%)	0.12†
Other diseases	94 (25%)	77 (23%)	..
Toxicity treatment	15 (4%)	32 (10%)	..
Unknown	7 (2%)	7 (2%)	..

Data are number of patients (%) or p value. D1=standardised limited lymphadenectomy. D2=standardised extended lymphadenectomy. \*Log-rank p value. †Gray's test p value.

Table 4: Causes of death



# 더치 임상시험

- 오류:

- 림프 절제가 생존률을 20에서 32%로 올린다는 추측에 근거함
- 40% 환자는 초기 위암
- 숫자가 적어 통계학적 의미 부여 어려움

# NCCN 가이드라인

“D2 림프 절제가 D1 림프 절제보다 권장됨.  
그러나, 무작위 임상시험 결과 수술 사망률이  
높다고 보고됨. 임상 의사들에서도 같은 의견.”



복강경을 이용한 절제술과 개복 수술을 비교  
(D2 진행된 위암)  
COACT 1001 임상시험 결과.

- 3상.
- 무작위
- 여러 센터
- 복강경 수술이 진행된 위암에 쓸 수 있다는 결론.



## HOW I DO IT

# Laparoscopic Distal, Subtotal Gastrectomy for Advanced Gastric Cancer

Kfir Ben-David · Rebecca Tuttle · Moshim Kukar ·  
Jacqueline Oxenberg · Steven N. Hochwald

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**Abstract** The objective of this study was to show laparoscopic subtotal, distal gastrectomy with D2 lymphadenectomy as a safe and appropriate method for the resection of advanced gastric cancer. This study was conducted at a designated NCI Cancer Center. Subjects of the study were patients with advanced gastric malignancy, including transmural penetration of the tumor and/or nodal disease, requiring subtotal, distal gastrectomy. The main outcome measure is a description of the technique of a laparoscopic subtotal, distal gastrectomy for antral and distal body tumors. In conclusion, the laparoscopic approach to advanced gastric malignancy with a subtotal, distal gastrectomy and D2 lymphadenectomy is a safe, oncologically appropriate procedure which provides excellent outcomes.

**Keywords** Laparoscopic gastrectomy · Advanced gastric cancer

## Introduction

There has been significant debate over the use of laparoscopic resection for the management of advanced gastric cancer. Laparoscopic surgery appears as a favorable approach given the previously reported decrease in postoperative pain, pulmonary complications, and hospital lengths of stay.<sup>1,2</sup> The reluctance to widely adopt this technique is over the concern for the oncologic completeness of the laparoscopic approach and the complexity of the procedure. Splenic-preserving D2 lymphadenectomy should be performed for appropriate patients undergoing resection for advanced gastric cancer given the reported decreased locoregional recurrence rates and gastric cancer-related deaths.<sup>3</sup> We describe our preferred

approach for a laparoscopic distal, subtotal gastrectomy with D2 lymphadenectomy and a Billroth II reconstruction for advanced T stage (T3) and/or node-positive disease.

## Methods

The standard workup for evaluation and staging of gastric cancer is utilized including endoscopic ultrasound (EUS) and CT scans.<sup>4</sup> Diagnostic laparoscopy and peritoneal washings should be considered for locoregionally advanced disease prior to the initiation of neoadjuvant therapy.<sup>5</sup> Neoadjuvant therapy is performed for T3–T4 and/or node-positive, M0 malignancy.<sup>6</sup> Following the completion of neoadjuvant therapy, patients are restaged with CT imaging. Surgery is offered to those patients who are medically fit and in whom no evidence of metastatic disease is identified. Laparoscopic subtotal, distal gastrectomy with Billroth II reconstruction is our standard approach for tumors of the antrum and distal body. Details of positioning and required equipment are described (Table 1).

## Operative Description

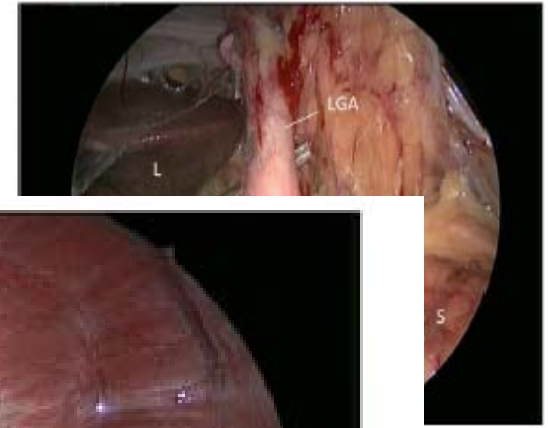
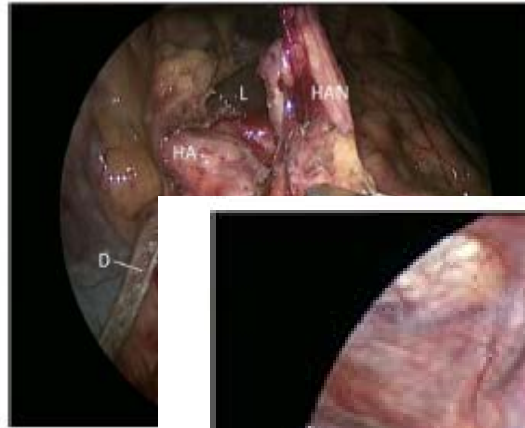
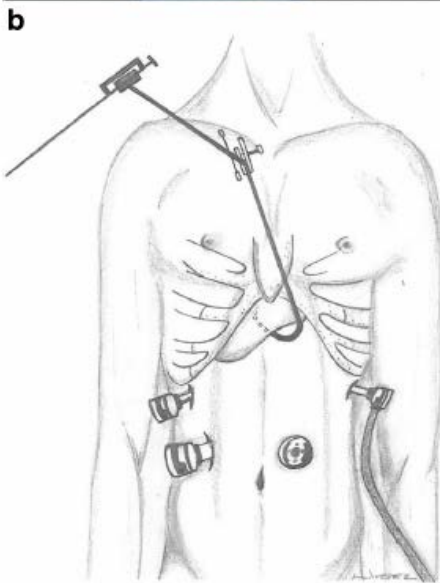
### Positioning

The patient is positioned supine on the operating room table. Standard anesthesia techniques are utilized. An 18-gauge

Kfir Ben-David and Rebecca Tuttle contributed equally to this publication.

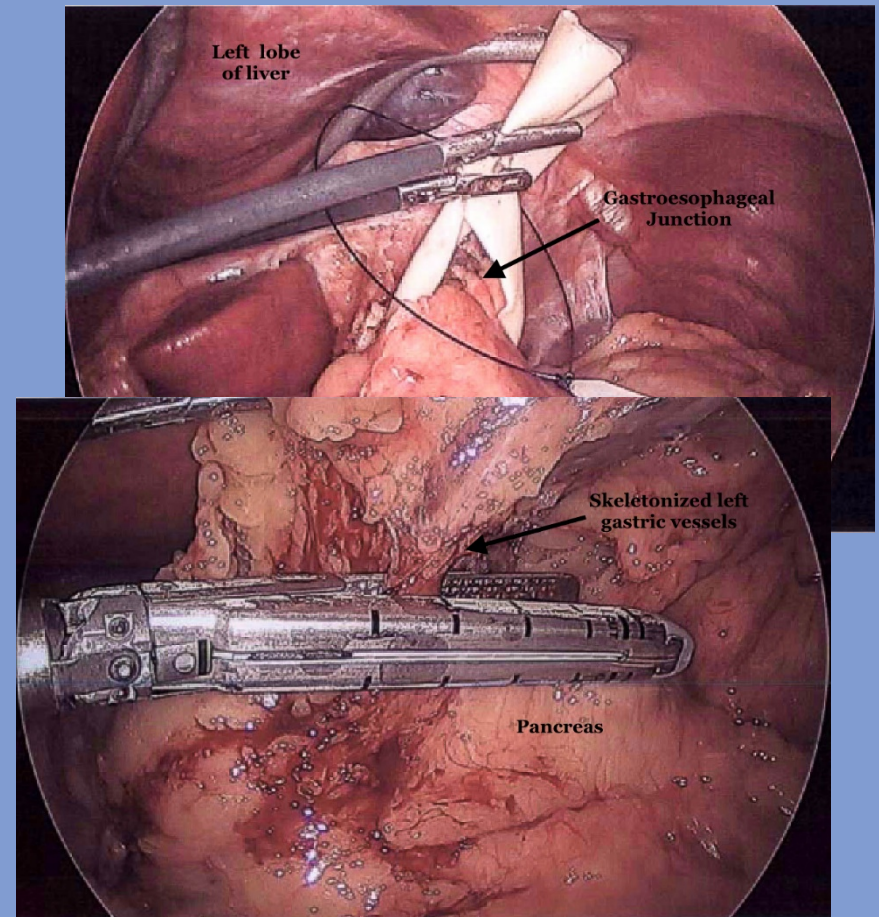
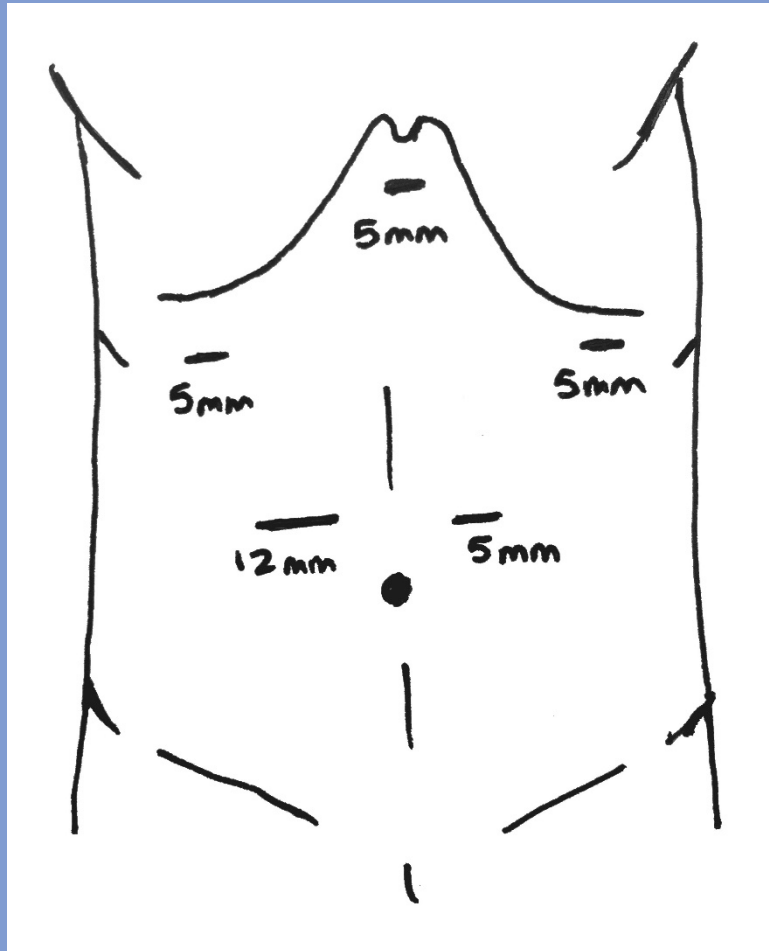
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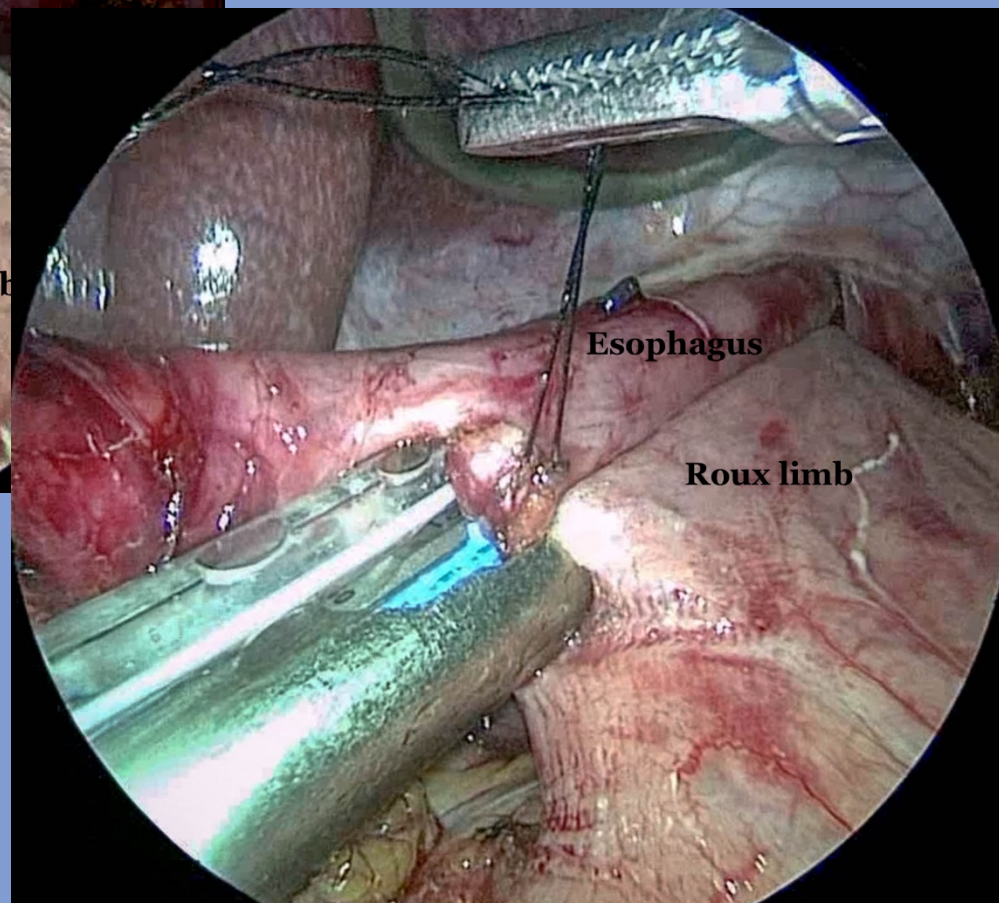
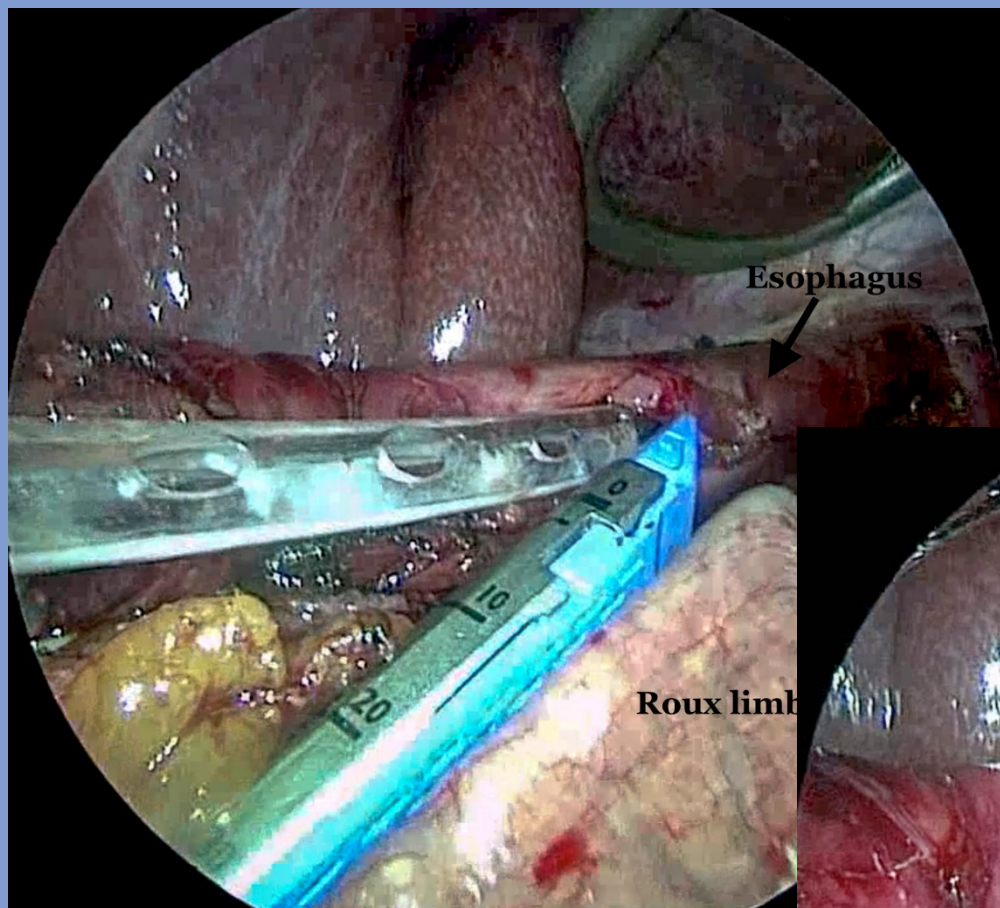


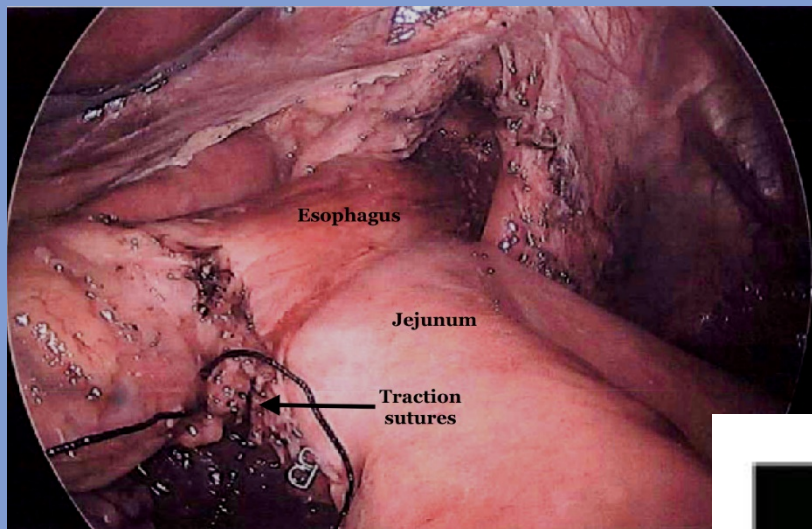
- 림프절 23개
- 병원 체류 중간 값 6일
- 수술 후 병원에서의 사망 없음

# 복강경을 이용한 절제술과 식도 절제 수술









## 복강경을 이용한 절제술 (진행된 위암) 은 안전하고 가능하다.

- 2010 – 2014년 68명 진행된 위암 환자가 ( $\geq T3$  혹은  $\geq N1$ ) 복강경 절제술 받음
- 수술 후, 초기 암 특이 진행 추이가 좋음
- 서구에서 보통 쓸 수 있는 방법으로 추천 됨

감사합니다