



Mide kanseri cerrahisinde yeni ne var?

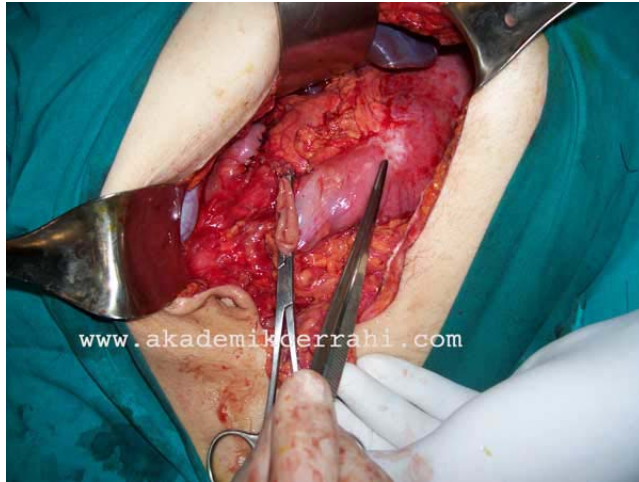
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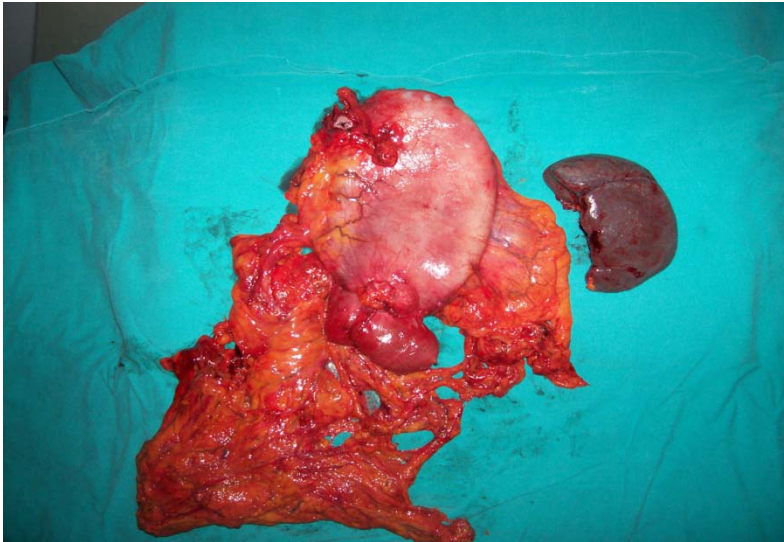


Radikal gastrektomi



Lokalizasyon ve onkolojik gereksinim nedeni ile splenektomi yapıyoruz

Remnant kanseri



Kardiya kanseri



Meta-analysis of adjuvant chemotherapy after radical surgery for advanced gastric cancer. P. Sun, BJS. 2009

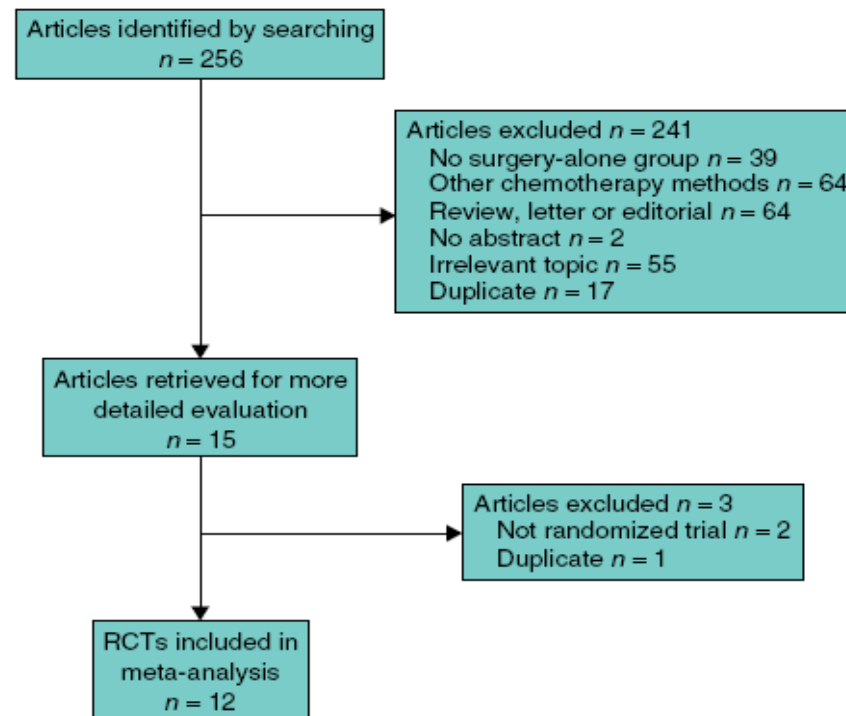


Fig. 1 Process of selection of articles for analysis. RCT, (randomized clinical trial)

Meta-analysis of adjuvant chemotherapy after radical surgery for advanced gastric cancer. P. Sun, BJS. 2009

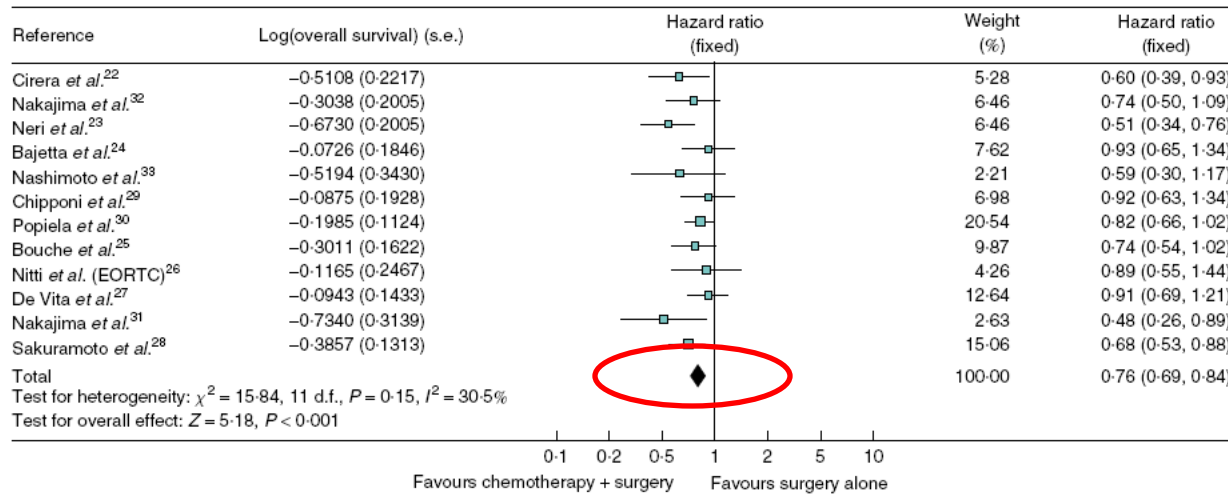


Fig. 4 Meta-analysis of overall survival in randomized clinical trials comparing chemotherapy plus surgery with surgery alone, after exclusion of the International Collaborative Cancer Group trial reported by Nitti and colleagues²⁶. Hazard ratios are shown with 95 per cent confidence intervals. EORTC, European Organization for Research and Treatment of Cancer

**İleri evre mide kanserinde
küratif cerrahi sonrası kemoterapi
sağkalımda faydalıdır**

Meta-analysis of laparoscopic and open distal gastrectomy for gastric carcinoma

**Muhammed Ashraf Memon · Shahjahan Khan ·
Rossita Mohamad Yunus · Richard Barr ·
Breda Memon**

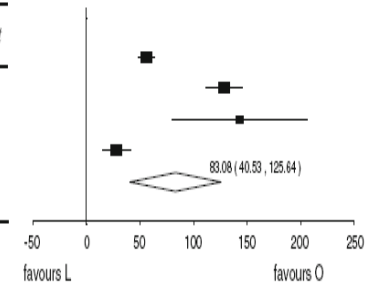
- 5 RKÇ, n=82/80
- Parameteler:
 - Ameliyat süresi
 - Kanama miktarı
 - Lenf nodu sayısı
 - Oral alıma başlama günü,
 - Hastanede kalış süresi
 - Kompliksasyonlar
 - Rekürrens
 - Mortalite

Meta-analysis of laparoscopic and open distal gastrectomy for gastric carcinoma

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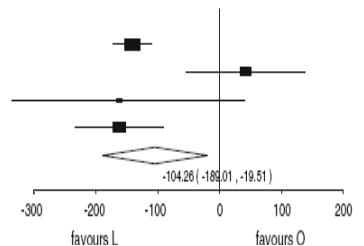
Laparoskopik DG de
1. Sure daha uzun
2. Kanama daha az
3. Lenf nodu sayisi daha az

Authors	Pt	LADG	Pt	ODG	MD (95% c.i.)	weight
Kitano et al	14	227 (7)	14	171 (13)	56 (48.27, 63.73)	0.28
Lee et al	24	319 (16.2)	23	190.4 (39.1)	128.6 (111.36, 145.84)	0.27
Hayashi et al	14	378 (97)	14	235 (71)	143 (80.03, 205.97)	0.17
Huscher et al	30	196 (21)	29	168 (29)	28 (15.04, 40.96)	0.28
<i>Pooled</i>	82	268.37 (1817.68)	80	186.69 (1643.58)	83.08 (40.53, 125.64)*	1



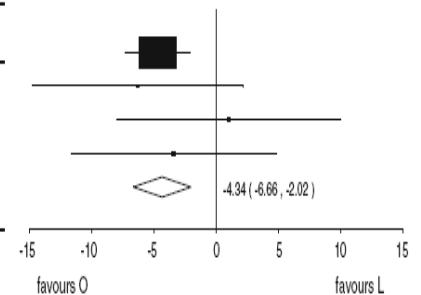
Mean of blood loss in mls (standard deviation)

Authors	Pt	LADG	Pt	ODG	MD (95% c.i.)	weight
Kitano et al	14	117 (30)	14	258 (53)	-141 (-172.90, -109.10)	0.35
Lee et al	24	336 (180)	23	294 (156)	42 (-54.35, 138.35)	0.25
Hayashi et al	14	327 (245)	14	489 (301)	-162 (-365.30, 41.30)	0.12
Huscher et al	30	229 (144)	29	391 (136)	-162 (-233.45, -90.55)	0.29
<i>Pooled</i>	82	258.04 (27449.42)	80	357.10 (29864.09)	-104.26 (-189.01, -19.51)*	1



Mean of lymph nodes harvested (standard deviation)

Authors	Pt	LADG	Pt	ODG	MD (95% c.i.)	weight
Kitano et al	14	20.2 (3.6)	14	24.9 (3.5)	-4.7 (-7.33, -2.07)	0.78
Lee et al	24	31.8 (13.5)	23	38.1 (15.9)	-6.3 (-14.75, 2.15)	0.08
Hayashi et al	14	28 (14)	14	27 (10)	1 (-8.01, 10.01)	0.07
Huscher et al	30	30 (14.9)	29	33.4 (17.4)	-3.4 (-11.68, 4.88)	0.08
<i>Pooled</i>	82	28.51 (171.11)	80	32.14 (203.93)	-4.3 (-6.66, -2.02)*	1



Meta-analysis of laparoscopic and open distal gastrectomy for gastric carcinoma

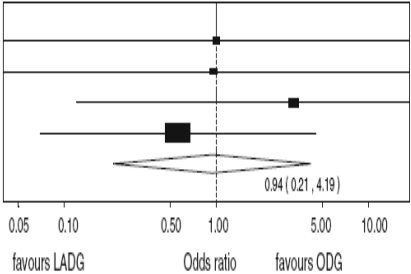
Muhammed Ashraf Memon · Shahjahan Khan ·
Rossita Mohamad Yunus · Richard Barr ·
Breda Memon

1. Mortalite riski farklı degil

2. Tümör rekurrensi farklı degil

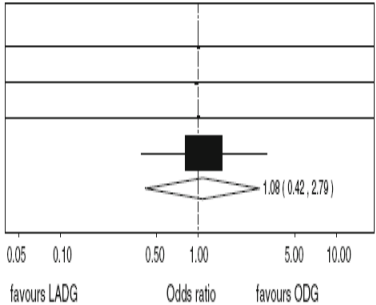
Odds ratio for mortality

Authors	LADG	ODG	OR (95% c.i.)	weight
Kitano et al	0 of 14	0 of 14	1(0.02,53.89)	0.14
Lee et al	0 of 24	0 of 23	0.96(0.02,50.35)	0.14
Hayashi et al	1 of 14	0 of 14	3.22(0.12,86.10)	0.21
Huscher et al	1 of 30	2 of 29	0.56(0.07,4.52)	0.51
Pooled	2 of 82	2 of 80	0.94(0.21,4.19)	1

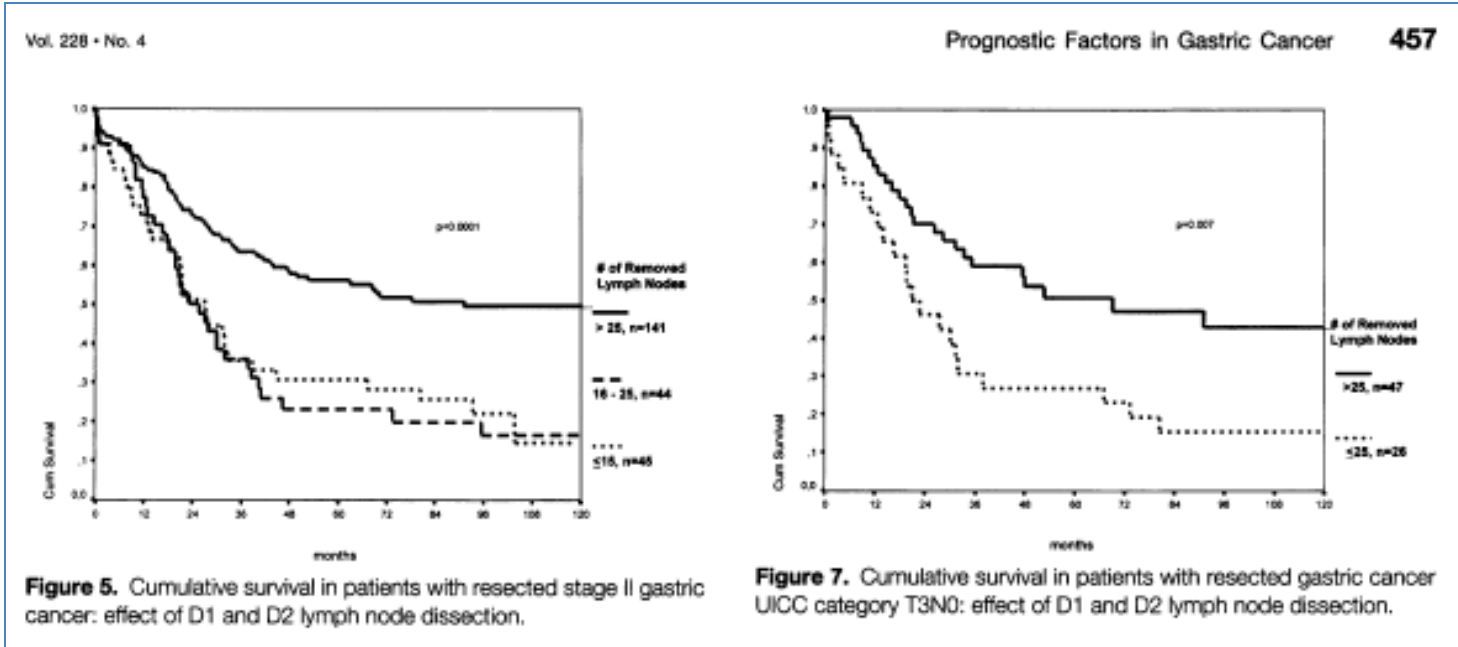


Odds ratio for tumour recurrence

Authors	LADG	ODG	OR (95% c.i.)	weight
Kitano et al	0 of 14	0 of 14	1.00(0.02,53.89)	0.06
Lee et al	0 of 24	0 of 23	0.96(0.02,50.35)	0.06
Hayashi et al	0 of 14	0 of 14	1.00(0.02,53.90)	0.06
Huscher et al	11 of 30	10 of 29	1.10(0.38,3.12)	0.83
Pooled	11 of 82	10 of 80	1.08(0.42,2.79)	1



Siewert,RJ et al. Relevant Prognostic Factors in Gastric Cancer Ten-Year
Results of the German Gastric Cancer Study.
ANNALS OF SURGERY 1998



D2 diseksiyonu
Hem erken hem ileri evrede
1. Daha iyidir
veya
2. Evre spesifik sag kalımı artırmaktadır

Siewert,RJ et al. Relevant Prognostic Factors in Gastric Cancer Ten-Year
Results of the German Gastric Cancer Study.
ANNALS OF SURGERY 1998

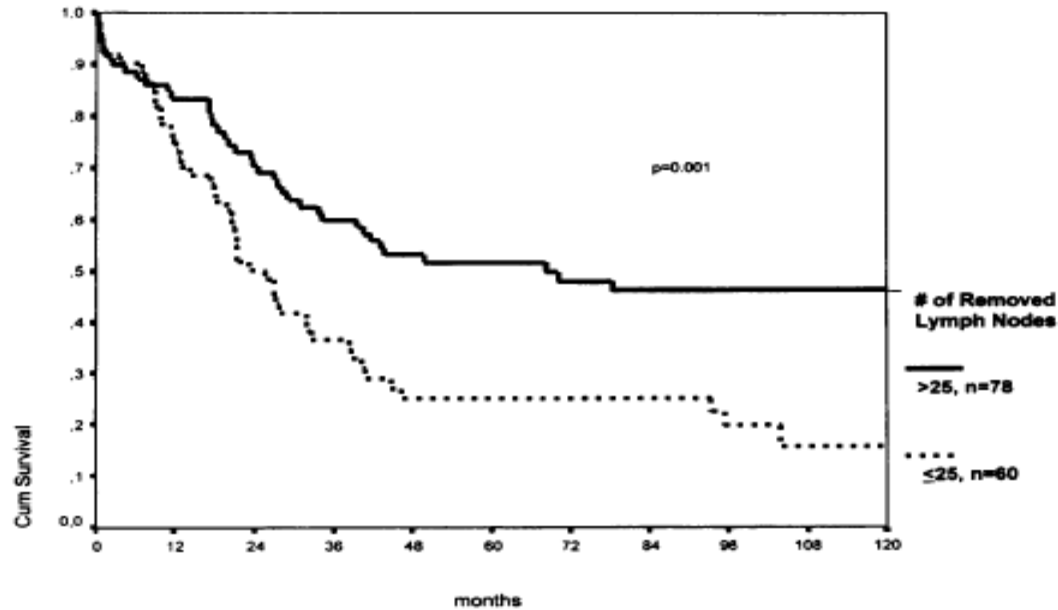


Figure 6. Cumulative survival in patients with resected gastric cancer UICC category pT2N1: effect of D1 and D2 lymph node dissection.

pT2N1 de D2 sağkalım avantajı sağlar

Siewert,RJ et al. Relevant Prognostic Factors in Gastric Cancer Ten-Year
Results of the German Gastric Cancer Study.
ANNALS OF SURGERY 1998

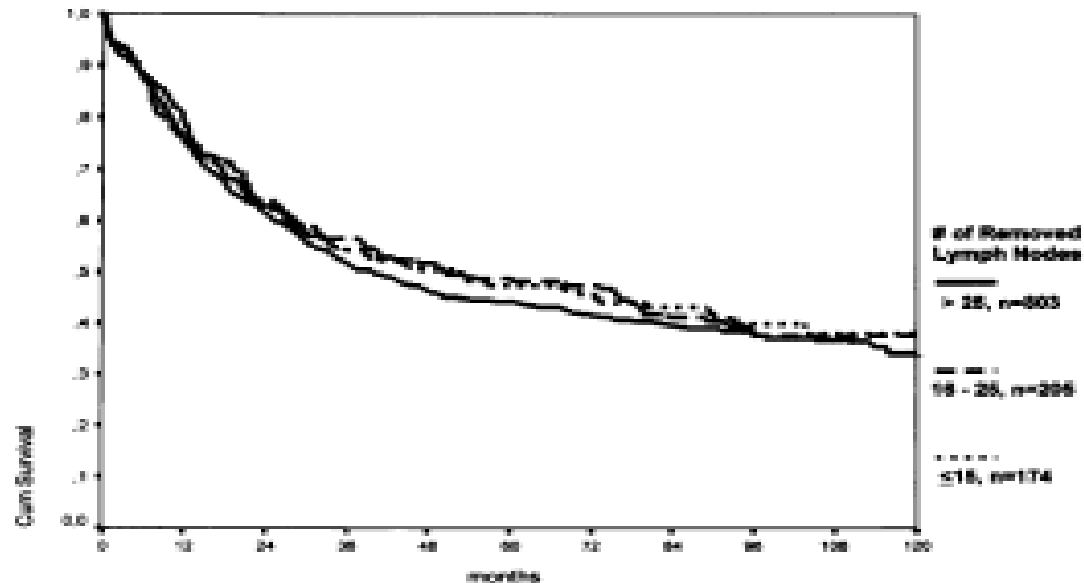


Figure 4. Cumulative survival in patients with R0 resection: effect of D1 and D2 lymph node dissection.

**R0 rezeksiyon yapildiginda
D1ve D2 diseksiyonlari
genel sag kalim oranlari farksizdir**

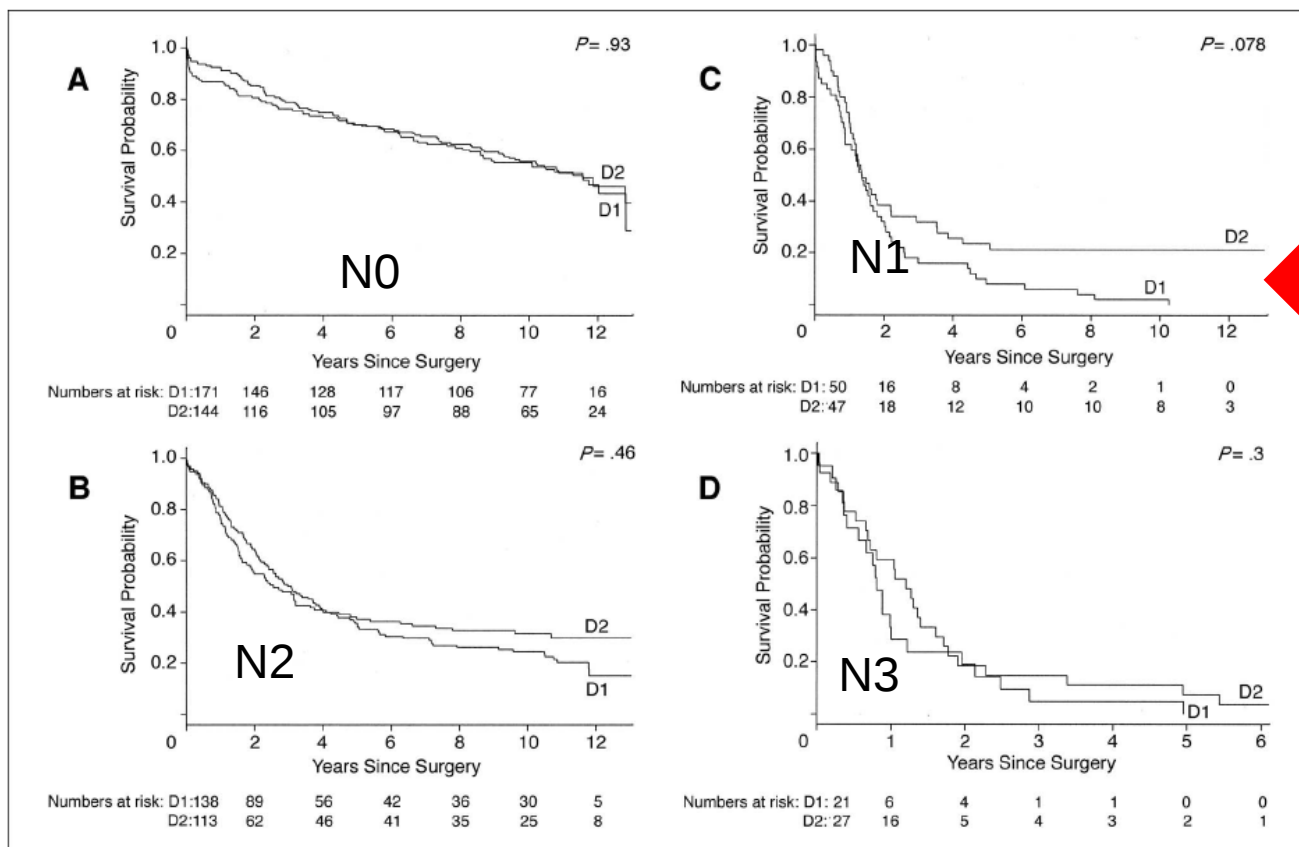


Fig 3. Survival of patients treated with curative intent according to N stage. (A), N0; (B), N1; (C), N2; (D), N3. D1, limited lymph node dissection group; D2, extended lymph node dissection group.

Erken gastrik kanser

Tüm gastrik kanserler içinde insidens

Batı ülkeleri= % 6-16

Japonya= % 50-60

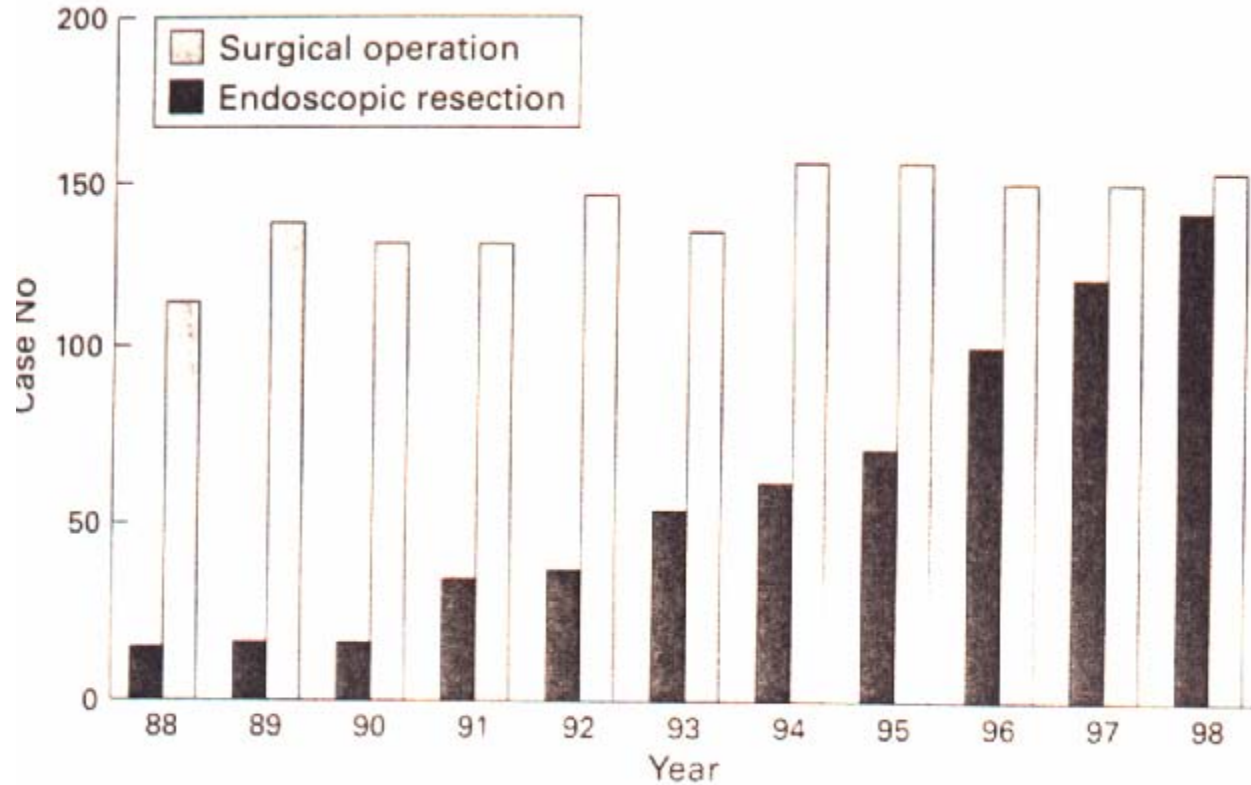
Erken gastrik kanserde tedavi yönelimi Japonya ve batıda farklı

Agresif

Konservatif



Erken gastrik kanser konservatif girişim



Milli kanser hastanesi TOKYO

Erken Gastrik Kanser

Daha sınırlı cerrahi?

- * Endoskopik mukozal rezeksiyon (EMR)
- * Lokal rezeksiyon + regioner lenfadenektomi
- * Laparoskopik wedge rezeksiyon veya intragastrik mukozal rezeksiyon.
- * Proximal gastrektomi jejunal poş interpozisyon
- * Pilor koruyucu gastrektomi (PPG)

EMR

23 yıldır uygulanmakta (in 1987)

Bazı sorunları var:

- Endikasyon
- Teknik
- Kürabilite için preoperatif değerlendirme (EUS, Laparoskopi..)
- Takip biçimi

EMR

Tümör çapı ?

< 3cm

> 3cm orta – iyi diferansiye

“superficial elevated”

depressed (tip I, IIa, and IIc) ülserasyonsuz

Lezyon > 3 cm komplet rezeksiyon oranı= 38%

EMR

Rezeksiyon sınırı ?

- Komplet rezeksiyon – lokal nüks %2
- Komplet rezeksiyon (parça parça çıkarılırsa)
 - 4. ayda lokal nüks %18

Nüks olduğunda: cerrahi

Mukozal kanserde lenf nodu metastazı

- Ülseri olmayan mukozal kanser

Lenf nodu metastazı

<u>Çap</u>	<u>İyi diferansiye</u>	<u>kötü diferansiye</u>	
$\leq 10\text{mm}$	0 / 163 (%0)	0 / 43 (%0)	
$\leq 20\text{mm}$	0 / 274 (%0)	0 / 98 (%0)	
$\leq 30\text{mm}$	2 / 305 (%0.5)	2 / 117 (%1.7)	
$> 31\text{mm}$	4 / 187 (%1.4)	4 / 97 (%4.1)	
Toplam	6 / 929 (%0.5)	6 / 355 (%1.7)	

(The guideline of gastric cancer treatment, Japanese Cancer)

EGK de lokal rezeksiyon ve rejyoner lenfadenektomi

Laparoskopi veya laparotomi

- Boyanın endoskopik sub - mukozal injeksiyonu
- Boyanın tutulduğu perigastrik nodların (sentinel nod) çıkarılması ve diğer alan LN'dan örnekleme
- LN FS - analizi
 - LN + → Gastrektomi + lenf nodu diseksiyonu
 - LN - → Lokal rezeksiyon

Erken gastrik kanser tedavisi sonuç

- Sınırlı cerrahi yalnızca mukozal EGK de önerilmelidir
- Submukozal plana ilerlemiş EGK de ileri lenf adenektomi sağkalımı artırmaktadır.
 - Perigastrik lenf nodları dışındaki nodlarına skip mikrometastaz %7'dir.
 - Avrupa ve ABD de sınırlı cerrahi sadece çok yüksek riskli hastalara uygulanmaktadır

Will Rogers fenomeni - Stage Migrasyon

- Daha geniş lenfadenektomi= Daha doğru evreleme
- “Upstaging”
- D2-3 rezeksiyonlar evre spesifik sağkalımı artırır
 - D2 – 2 0%
 - D3 – 4 3%

Sasagawa (Costa Rica): 2008, Am J Surg11

- n=199 (CR), n=497 (Japanese Cohort)
- All received D2 resection
- F/U not specified
- Japanese surgeon assisted with all operations

Evreleme: AJCCS

“American Joint Committee on Cancer System”

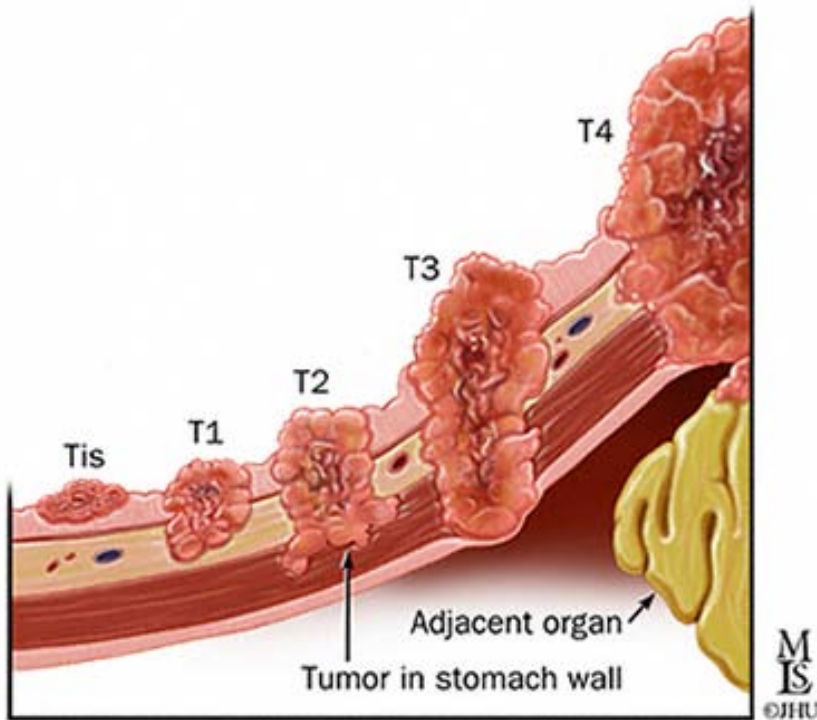


Figure 18. TNM staging of tumor by depth of invasion.

No-	Primer tumor yok
Tis-	intraepitelyal tumor lamina propria invaze degil
T1-	Lamina propria veya submukoa invaze
T2-	Muskularis propria tutulmus
T3-	Tumor serosaya ilerlemis organ invazyonu yok
T4-	Tumor bitisik organlari tutmus

Evreleme: AJCCS

“American Joint Committee on Cancer System”

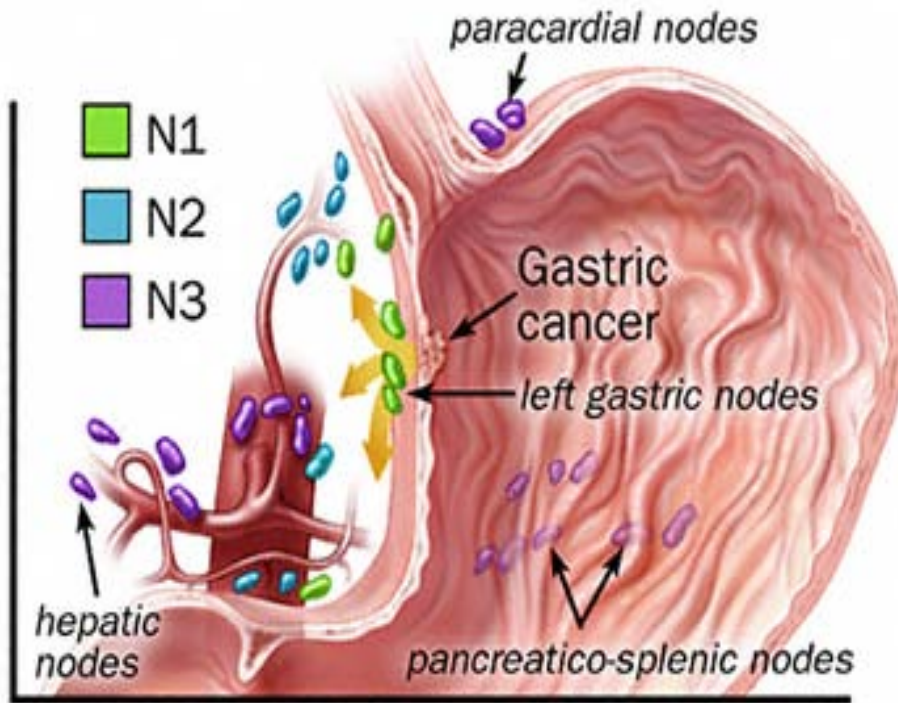


Figure 19. TNM staging for lymph node involvement.

Tutulan lenf nodu sayısı evrelemede önemlidir. En az 15 lenf nodu çıkarılmalıdır.

Lenf nodu bölgesi önemli değildir.

N1: 1-6 nod +

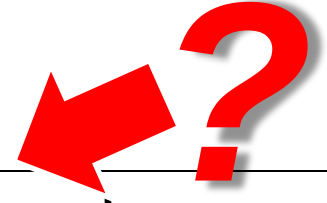
N2: 7-15 nod +

N3: > 15 nod +

M1: Uzak metastaz veya Rejyoner lenf nodları dışındaki lenf nodu tutulumları

R0 Gastrektomi sonrasında 5 yıllık sağkalım oranları

(*Cancer 2000, 88:921-32*)



AJCC evre	U.S.A	Japonya	Japon-göçmenler
IA	78%	95%	95%
IB	58%	86%	75%
II	34%	71%	46%
IIIA	20%	59%	48%
IIIB	8%	35%	18%
IV	7%	17%	5%
Overall	28%	NR	42%

Gastrik Kanser için adjuvan tedavi

Radyoterapi:

- Gastrik kanser sıklıkla resistandır
- Lokal rekürrens:
 - palyatiftir
- Radikal cerrahi sonrası adjuvan radyoterapinin sağkalıma etkisi yoktur

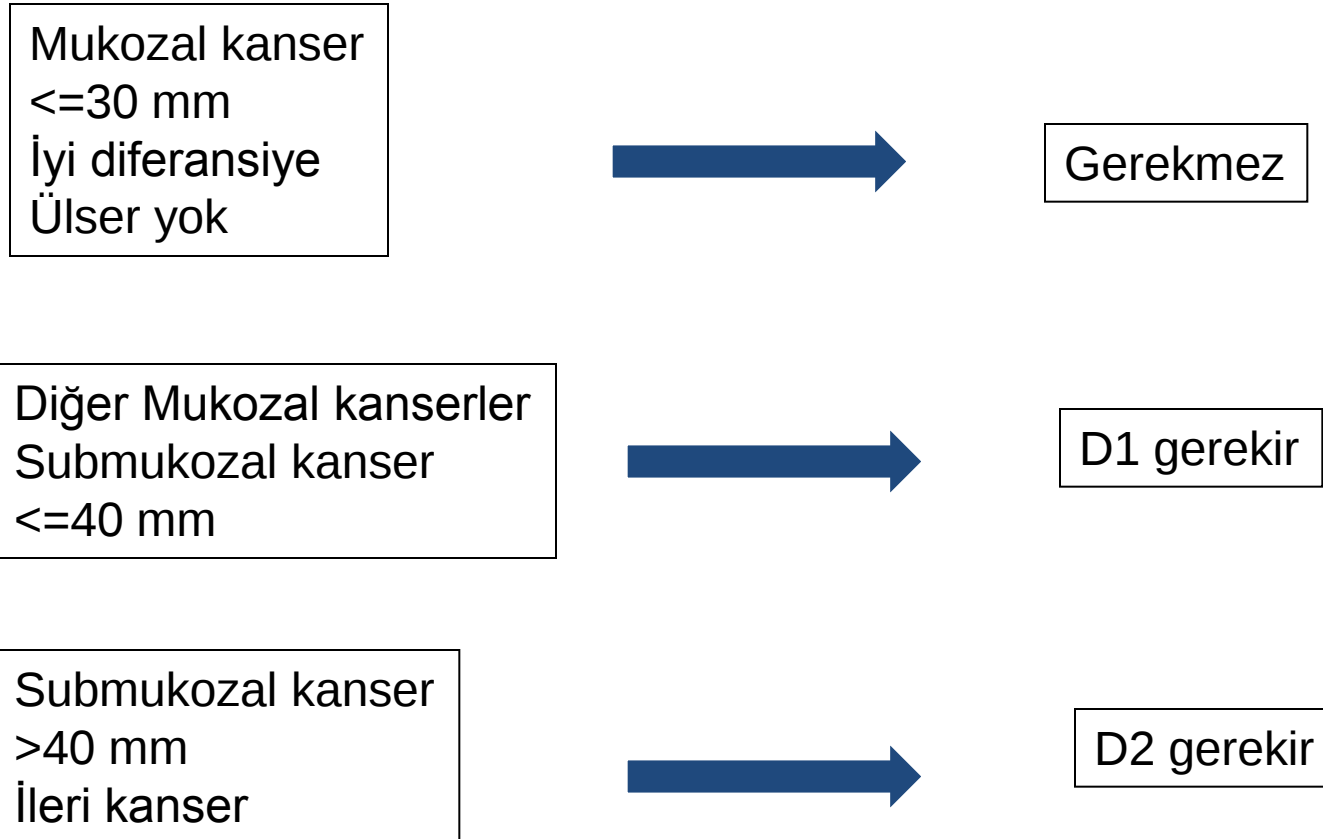
Kemoterapi:

- 5-FU'ya cevap= %20
- Mitomisin, sisplatin, doxorubisin, methotrexat, CPT-11, paklitaxel, taxotere
- Küratif rezeksiyon sonrası kemoterapi sadece rezeksiyona göre orta düzeyde sağkalım avantajı sağlar.

Neoadjuvant Kemoterapi

- İngiliz (Medical Research Council “MAGIC”) çalışması
- N=503 olgu, Stage II and III gastrik kanser
- Randomizasyon: Cerrahi veya 3 kür preop epirubisin, sisplatin, and fluorourasil (ECF) sonra cerrahi sonra 3 kür tekrar ECF
- T1/T2 tumor sık olduğu için resektabilite yüksek bulunmuş (%79 vs %69)
- 2-yıllık sağkalım=
 - Neoadjuvant group % 48
 - Cerrahi = %40 (p=0.063)

Optimal lenf nodu diseksiyonu



Gastrik kanserde adjuvan kemoterapi - metaanalizler

Table 2. Meta-analyses on randomized adjuvant chemotherapy studies in gastric cancer

Meta-analysis (First author; ref. #)	No. studies	No. patients	Odds ratio (CI)
Hermans 1993 [46]	11	2096	0.88 (0.78–1.08)
Earle 1999 [45]	13	1990	0.80 (0.66–0.97)
Mari 2000 [47]	21	3658	0.82 (0.75–0.89)
Janunger 2002 [44]	21	3962	0.84 (0.74–0.96)

CI, confidence interval

	Adjuvant (<i>n</i> = 281)	Surgery alone (<i>n</i> = 275)	<i>P</i> value
Median duration of survival	36 months	27 months	0.005
Three-year survival rate	50%	41%	
Hazard ratio for death	1.0	1.35 (95% CI 1.09–1.66)	0.005
Median relapse-free survival	30 months	19 months	0.001
Three-year relapse-free survival	48%	31%	
Hazard ratio for relapse	1.0	1.52 (95% CI 1.23–1.86)	0.001

Adjuvan kemoterapi

Hem genel sağkalımda,

Hem de hastalıksız sağkalımda avantaj sağlamaktadır

Hollanda çalışması

Benenkamp et al. New England Journal of Medicine 1999

80 merkez, D-1 (n:380) - D-2 (n:331)

- **D-2 diseksiyonun komplikasyonu fazla**
% 43 vs. % 25 $P < 0.001$
- **D-2 diseksiyonun perioperatif mortalitesi fazla**
% 10 vs. % 4 $P = 0.004$
- **D-2 diseksiyon hastanede kalış süresini uzatır**

medyan 16 vs. 14 gün $P < 0.001$

D-2 Lenfadenektomi

sağkalım farklı değil

yayın	N	sağkalım	P
Dent	D-1 n = 35	68%	NS
	D-2 n = 31	67%	
Robertson	D-1 n = 25	45%	NS
	D-2 n = 30	35%	
Bonenkamp	D-1 n = 380	45%	NS
	D-2 n = 331	47%	
Cuschieri	D-1 n = 200	35%	NS
	D-2 n = 200	45%	

Lenf nodu evrelemesi



UICC / AJCC

- “N0” demek için en az 15 lenf nodu değerlendirilmelidir

Özet

- * R0 rezeksiyon amaçtır
- * Distal tümörlerde distal subtotal gastrektomi tercih edilmelidir
- * Onkolojik gereksinim dışında splenektomi pankreatektomi yapılmamalıdır
- * Cerrahi işlem ve patolojik incelemede minimum 15 lenf nodu amaçlanmalıdır

THE BRITISH MRC GASTRIC CANCER SURGICAL TRIAL

- Dizayn: prospektif randomize klinik araştırma
- karşılaştırma: D1 vs D2
- N: 200 D1, 200 D2

	<u>D2</u>	<u>D1</u>
Postoperatif mortalite:	%13	%6.5 (p<0.001)
Anastomoz kaçağı:	%26	%11
Kardiak sorun:	%8	%2
5 yıllık sağkalım:	%33	%35

Status of Extended Lymph Node Dissection: Locoregional Control Is the Only Way to Survive Gastric Cancer

HENK H. HARTGRINK* AND CORNELIS J.H. VAN DE VELDE

Department of Surgery, Leiden University Medical Centre, Leiden, The Netherlands

TABLE V. Analysis of the Group Treated With Curative Intent, Without 165 Patients Who had a Splenectomy and Without 108 Patients Who had a Pancreatectomy

	D1	D2	<i>P</i> -value
No splenectomy (n = 546)			
Morbidity (%)	23	35	0.001
Mortality (%)	3.8	6.3	0.19
Survival 11-years (%)	32	43	0.015
No pancreatectomy (n = 603)			
Morbidity (%)	23	39	0.0001
Mortality (%)	3.5	9.0	0.004
Survival 11-years (%)	31	42	0.02

From Hartgrink et al. [8].

Long term Outcomes of Early-Stage Gastric Carcinoma Patients Treated with Laparoscopy-Assisted Surgery Fujiwara M J Am Coll Surg 2008

sağkalımı etkileyen faktörler

Diyabet
kötü yönde etkiliyor

İleri yaş
kötü yönde etkiliyor

**Lenf nodu metastazı
varlığı**
kötü yönde etkiliyor

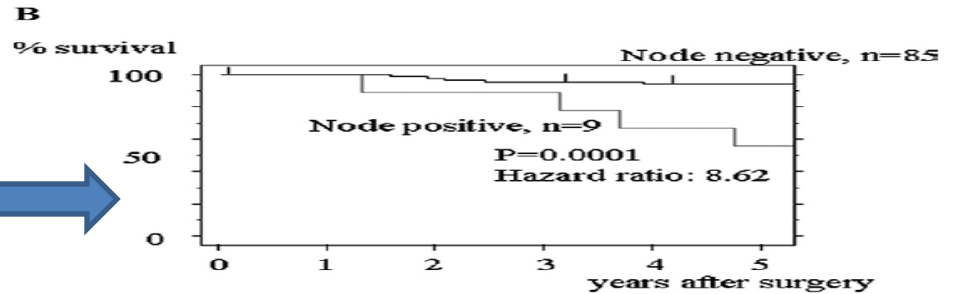
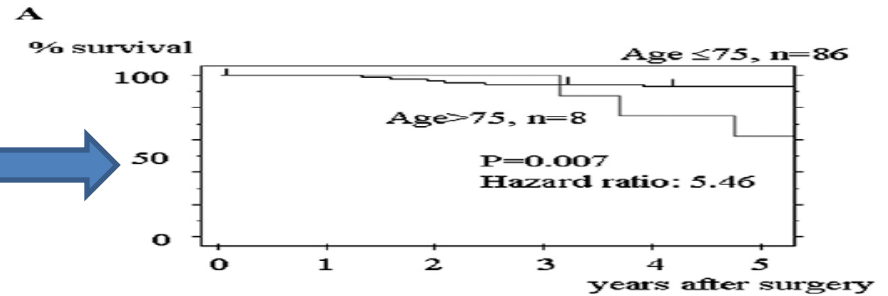
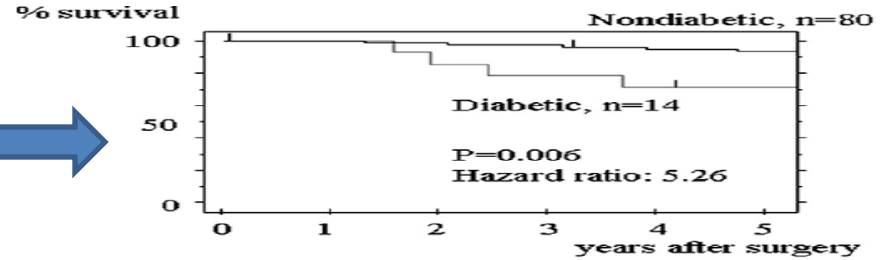


Figure 3. Survival of patients stratified by three significant prognostic factors: (A) comorbidity (diabetes mellitus), (B) age, and (C) nodal status; p values are from log-rank test, and hazards ratios were calculated in the univariate analysis. These do not retain significance in the multivariable model.

Impact of Total Lymph Node Count on Staging and Survival After Gastrectomy for Gastric Cancer: Data From a Large US-Population Database *Smith D. et al*
JOURNAL OF CLINICAL ONCOLOGY , 2005

Daha fazla lenf nodu çıkarılmış olması evre spesifik sağkalımı veya evreleme doğruluğunu artırmaktadır

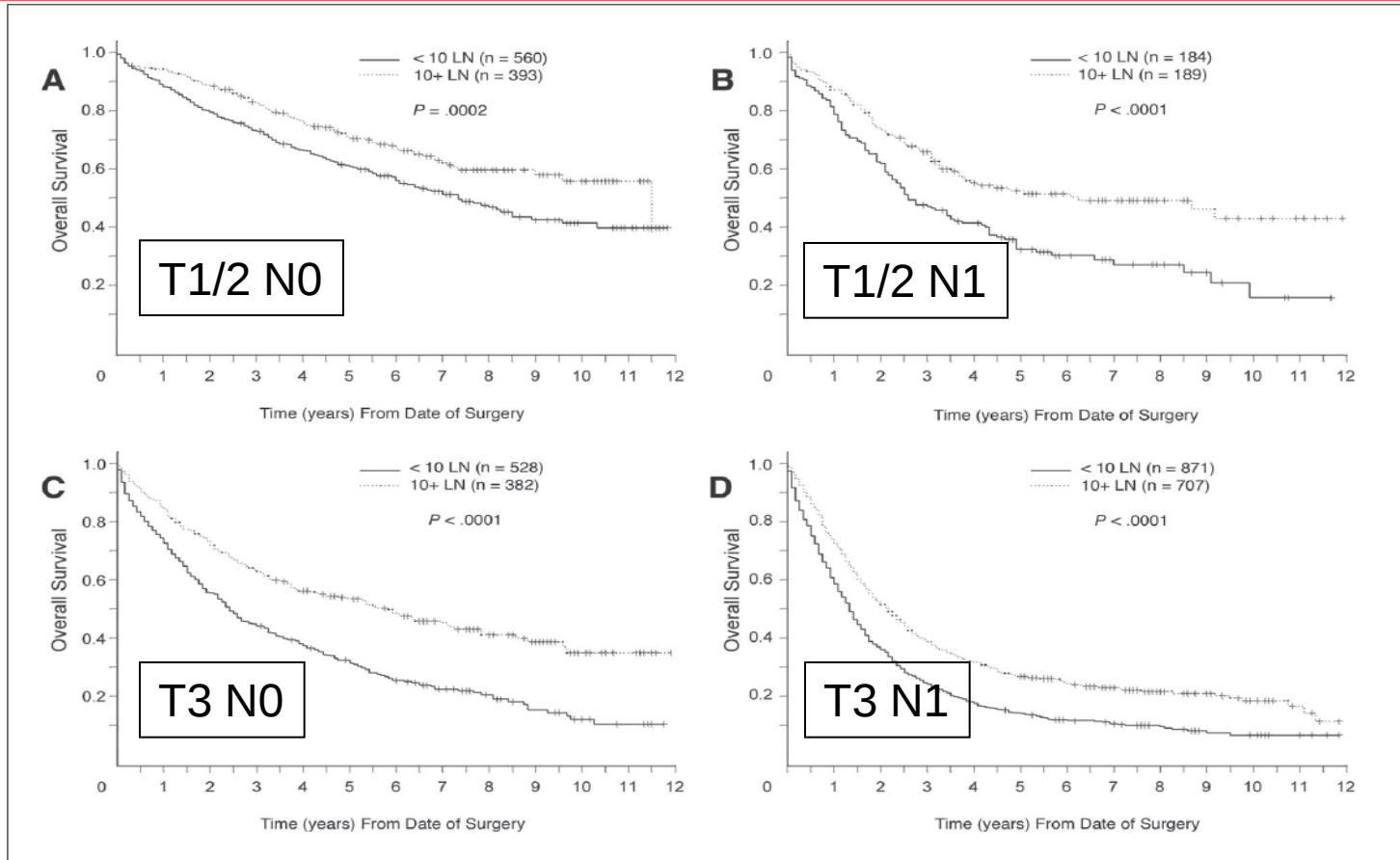


Fig 3. Actuarial overall survival curves, according to stage subgroup, comparing patients with fewer than 10 lymph nodes (LN) examined to those with 10 or more lymph nodes examined. (A) T1/2N0; (B) T1/2N1; (C) T3N0; (D) T3N1.



Lymphatic mapping and sentinel node biopsy in gastric cancer

Xiangyang Song, M.D., Ph.D.^a, Linbo Wang, M.D., Ph.D.^a, Wenjun Chen, M.D.^a,
Tao Pan, M.D.^a, Hongbo Zhu, M.D.^a, Jinyao Xu, M.D.^b, Mei Jin, M.D.^b,
Robert K. Finley III, M.D.^c, Jinmin Wu, M.D.^{a,*}

- Sentinal nod navigasyon cerrahisi ile lenfadenektominin boyutuna karar verilebilir.

<u>Teknik</u>	<u>% sensitivite</u>
Indocyanin green	90
Technetium-99 m kolloid	91.7
Isosulfan blue	100

Lymph node dissection around the splenic artery and hilum in advanced middle third gastric carcinoma C. Li et al. / EJSO (2008)

**İleri evre gövde
gastrik kanserlerinde
10 ve 11 nolu lenf
nodu metastazı
varlığında
sağkalım daha
kötüdür**

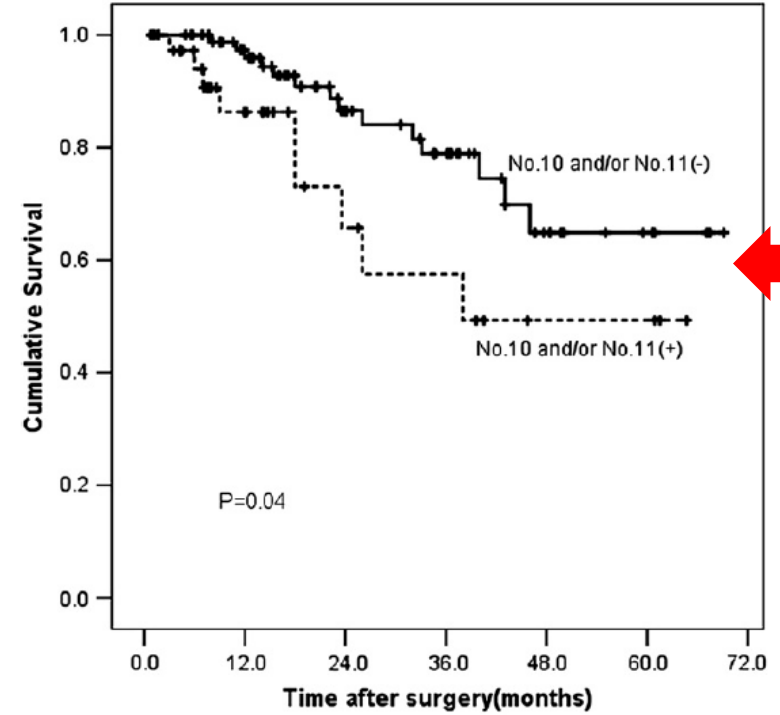


Figure 1. Cumulative survival curves for patients with advanced middle third gastric carcinoma with or without No. 10 and/or No. 11 lymph node metastasis. No. 10 and/or No. 11 lymph node negative patients showed significantly better survival than No. 10 and/or No. 11 lymph node positive patients ($p = 0.04$).

Lymph node dissection around the splenic artery and hilum in advanced middle third gastric carcinoma C. Li et al. / EJSO (2008)

Proksimal gastrik kanserlerde 10 ve 11 no'lu gruba metastaz için bağımsız risk faktörü= **çap>5 cm** ise splenik arter civarı ve splenik hilumda lenf nodu metastaz riskini belirlemek için sağ parakardiak ve çöliak lenf nodlarına frozen section önerilmelidir

Erken mide kanserlerinde lenf nodu mikrometastaz riski ?

n: 90

anticytokeratin immunohistokimya boyama,
70 aylık takip

Sonuçlar:

- 1. Nod negatif erken mide kanserlerinde lenf nodlarında immün boyama ile mikrometastaz varlığı %10'dur.**
- 2. Lenfatik invazyon ve tümör çapı mikrometastaz oluşumu için bağımsız risk faktörüdür.**
- 3. EMR ve ESD için kesin kontrendikasyon lenf nodu metastazı varlığıdır**
- 4. Rekürrens yok**

Lymph node micrometastasis in node negative early gastric cancer J.J. Kim, K.Y. Song, EJSO (2008)

The New England Journal of Medicine **EXTENDED LYMPH-NODE DISSECTION FOR GASTRIC
CANCER** J.J. BONENKAMP et al. 1999

**Küratif cerrahi yapılanlarda
uzun dönem sağkalımda
D2 nin D1 diseksiyona
bir avantajı saptanmamıştır**

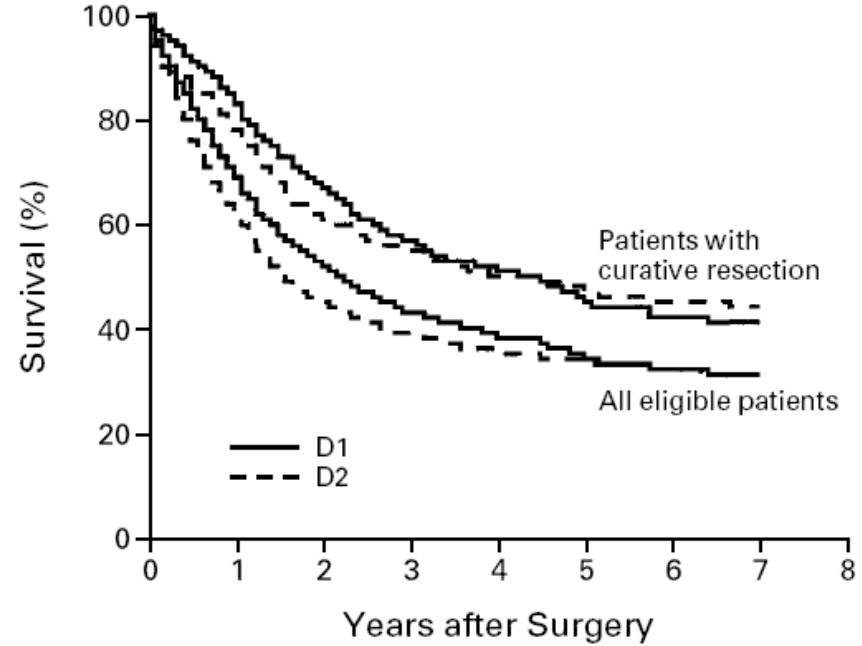


Figure 1. Survival among All Eligible Patients and Those Treated with Curative Intent.

Of the 996 patients eligible for participation, 513 underwent D1 dissection and 483 underwent D2 dissection. Of the 711 patients treated with curative intent, 380 underwent D1 dissection and 331 underwent D2 dissection.

The New England Journal of Medicine **EXTENDED LYMPH-NODE DISSECTION FOR GASTRIC
CANCER** J.J. BONENKAMP et al 1999

Prospektif randomize mide kanseri
D1-D2 karşılaştırma çalışmalarında
deneyimsiz merkezler için çok önemli
iki sorun vardır.

KONTAMİNASYON
NON-KOMPLİANS

TABLE 5. ADHERENCE TO THE PROTOCOL FOR LYMPH-NODE
DISSECTION IN THE 711 PATIENTS WHO UNDERWENT RESECTION
WITH CURATIVE INTENT.

TYPE OF PROTOCOL VIOLATION	DISSECTION	
	D1 (N=380)	D2 (N=331)
	no. of patients affected (%)	
Contamination (proof of lymph nodes from more than two lymph-node stations that were not supposed to be harvested)	22 (6)	23 (7)
Noncompliance (absence of lymph nodes from more than two lymph-node stations that were supposed to be harvested)	137 (36)	169 (51)

Improved survival after resectable non-cardia gastric cancer in the Netherlands:

The importance of surgical training and quality control

P. Krijnen et al. EJSO (2009)

2009 yılına gelindiğinde; Hollandalılar D2 diseksiyonunu öğrendikçe Mide kanserinde sağkalım oranlarımız artıyor diyorlar

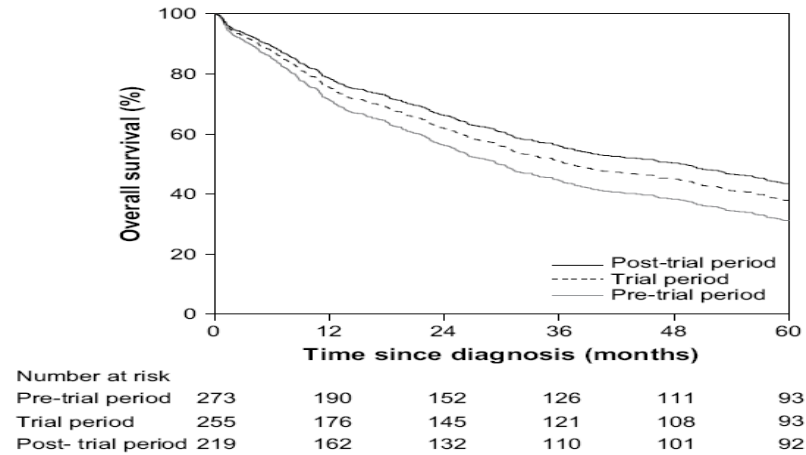


Figure 1. Overall survival after resectable non-cardia gastric cancer by period of diagnosis, adjusted for age, gender, tumour site, pT-stage, pN-stage and hospital volume.

Bu üç dönem içinde çıkarılan lenf nodu sayısında da artış var.
İki anlamı var:

1. Fazla lenf nodu çıkarılması sağkalımı artırır.
2. "Stage migration"

Muratore A et al., Low rates of loco-regional recurrence following extended lymph node dissection for gastric cancer. Eur J Surg Oncol (2009)

- **Amaç: D2 diseksiyonu ile radyoterapi + cerrahi tedavinin nüks açısından karşılaştırılması.**
- **Dizayn:** Retrospektif araştırma (2000-2006), n: 200 olgu.
- **Nüks:**
 - lokorejyoner,
 - peritoneal
 - uzak
- **Bulgular:**
 - Perioperatif mortalite= %1
 - Ortalama lenf nodu sayısı= 26
 - Genel 5 yıllık sağkalım= %61
- **SONUÇ: d2 diseksiyon güvenilir bir yöntem olup, düşük loko-rejyoner nüks oranlarına sahiptir.**

Rejyoner lenf bezlerindeki metastatik hastalık D2 diseksiyonu ile mi yoksa kemoradyoterapi ile mi daha iyi kontrol edilebilir?

MacDonald et al. (Southwest Oncology Group/Intergroup 0116 trial)

- **Dizayn:** RKÇ, Cerrahi vs cerrahi+kemoradyoterapi
- Olguların çoğu D0 diseksiyon

<u>Yöntem</u>	<u>Lokal nüks</u>
Cerrahi	%29
Cerrahi+ kemoradyoterapi	%19

- Bu çalışmadan sonra ABD de resektabl gastrik kanser tedavi standardı değişmiştir.

MacDonald JS, Smalley S, Benedetti J, et al. Chemoradiotherapy after surgery compared with surgery alone for adenocarcinoma of the stomach or gastroesophageal junction. N Engl J Med 2001;345:725–30

The Prognostic Analysis of Lymph Node-Positive Gastric Cancer Patients Following Curative Resection. Jingyu Deng, et al J surg res 2009

**Çok yönlü analizlerde
Metastatik lenf nodu sayısı ve
Metastik lenf nodu oranı önemli
bulunmuştur**

TABLE 2

Multivariate Analysis of Factors Affecting Overall Survival of 196 Positive Node Metastatic Patients

Variable	Hazard ratio	95% CI	<i>P</i>
Number of metastatic lymph nodes (<i>n</i> stage)*	1.768	1.407–2.223	<0.001
Ratio of metastatic lymph nodes	1.936	1.418–2.644	<0.001

95% CI indicates 95% confidence interval.

*According to pTNM classification of UICC.

The influence of stage migration on the comparison of surgical outcomes between D2 gastrectomy and D3 gastrectomy (para-aortic lymph node dissection): a multi-institutional retrospective study. Kunisaki C The American Journal of Surgery (2008)

Amaç: İleri evre gastrik kanserlerde D2 –D3 diseksiyon tekniklerinin “Stage Migration” üzerine etkilerini incelemek.

Metod: D2 (n= 430) gastrektomi vs. D3 (n=150) gastrektomi

	%
N-stage migrasyon	22.7
Patolojik stage migrasyon	20.7

<u>Evre spesifik stage migrasyon</u>	<u>p</u>
simüle D2 vs D2 gastrektomi	>0.05
5 vs 10 cm çaplı pN2 tümörlerde	
D2 vs D3 diseksiyon	<0.05
D2 vs simüle D2	>0.05

Sonuç: 1. D3 diseksiyonda “stage migrasyon” fazla oranda oluşmaktadır.
2. Evre IV kanserlerde D2 ve D3 diseksiyon arasında sağkalım farkı bulunmaktadır (*P*: .0471).

Modified radical lymphadenectomy (D1.5) for T2–3 *gastric cancer*. Ichikura T Langenbecks Arch Surg (2005)

Table 2 Surgical procedure, postoperative morbidity and mortality, and number of retrieved nodes

	Group A	Group B	Group C	
Number of patients	123	145	148	
Surgical procedure ^a				
Total gastrectomy	38 (31%)	54 (37%)	56 (38%)	
With splenectomy	30	50	53	*
With distal pancreatectomy	5	15	12	NS
Distal gastrectomy ^b	85 (69%)	91 (63%)	92 (62%)	
Postoperative complications				NS
Cardiopulmonary complications	5	3	3	
Anastomotic leakage	4	4	4	
Pancreatic fistula	2	2	1	
Intraperitoneal infection	3	5	2	
Intestinal obstruction	1	1	1	
Reoperation	1	1	1	
Operative mortality ^a	1	0	1	NS
Number of retrieved nodes ^c				
Perigastric nodes	25±13	26±12	27±12	NS
#7+#8a+#9+#11 ^d	6±4	8±6	10±6	*, **
Total	32±15	37±15	39±16	*, **

NS Not significant

^aNumber of patients with percentage in parentheses

^bNo patients underwent splenectomy or pancreatectomy

^cMean±standard deviation

^d#7, lymph nodes along the left gastric artery; #8a, lymph nodes along the common hepatic artery; #9, lymph nodes along the celiac artery; #11, lymph node along the splenic artery

* $p<0.05$, group A vs group C

** $p<0.05$, group A vs group B

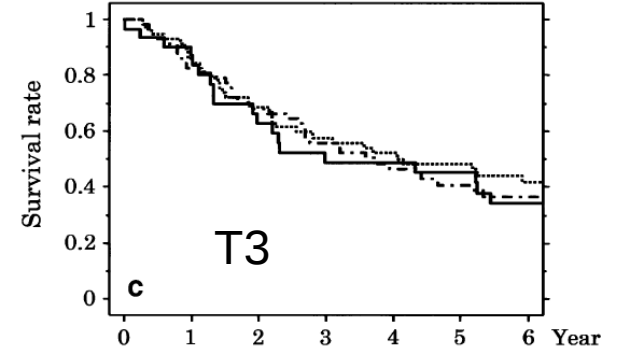
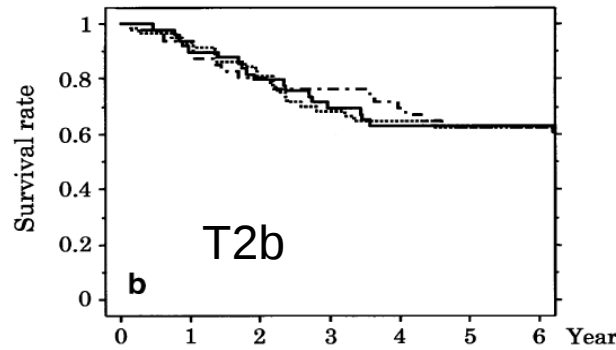
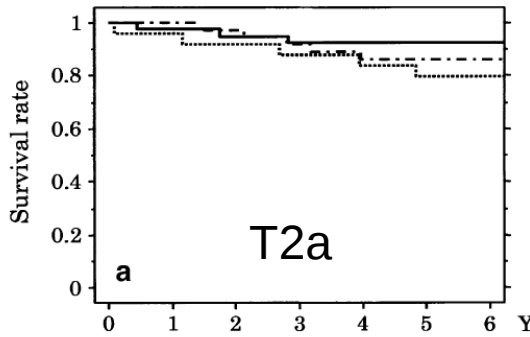
Mortalite ve komplikasyonlar açısından hiçbir fark yok !

Grup A: D1 (perigastrik + sol gastrik + hepatik arter civarı)

Grup B: D1+perigastrik + sol gastrik + hepatik arter civarı+ Çöliak arter parsiyel diseksiyonu

Grup C: D2 veya>D2 diseksiyon

Modified radical lymphadenectomy (D1.5)
for T2–3 gastric cancer. Ichikura T. Langenbecks Arch Surg (2005)



**Hastaların yapılan cerrahiye göre, evre spesifik
sağkalım oranlarında fark yok**

Grup A: D1 (perigastrik + sol gastrik + hepatik arter civarı)

Grup B: D1+perigastrik + sol gastrik + hepatik arter civarı+ Çöliak arter parsiyel diseksiyonu

Grup C: D2 veya >D2 diseksiyon

Modified radical lymphadenectomy (D1.5)
for T2–3 *gastric cancer*. Ichikura T. Langenbecks Arch Surg (2005)

**D2 ile D1.5
diseksiyonlar arasında
sağkalım farkı yoktur**

Table 4 Multivariate survival analysis using Cox's proportional hazard model

Variables	Hazard ratio	95% Confidence interval	<i>p</i> Value
Age	1.016	1.003–1.029	0.014
T category ^a			
T2b	2.067	1.253–3.409	0.0044
T3	2.530	1.526–4.193	0.0003
T4	2.915	1.361–6.243	0.0059
N category ^b			
N1	1.301	0.825–2.052	0.26
N2	3.527	2.198–5.661	<0.0001
N3	8.181	4.786–13.984	<0.0001
Tumor location ^c			
Whole stomach	1.912	1.102–3.319	0.021
Upper	1.890	1.322–2.703	0.0005
Surgeons ^d			
Group A	1.033	0.713–1.496	0.89
Group B	0.946	0.671–1.333	0.86

^aVs T2a

^bVs N0

^cVs middle or lower stomach

^dVs group C

Sentinal nod mikrometastazının immünohistokimya ve RT - PCR ile saptanması

N: 61

Olgular: T1-T2 (cT1-T2) ve N0 (cN0)

Girişim: Standart radikal gastrektomi+lenf nodu diseksiyonu.

Bulgular:

Sentinal nod saptanması : %100

<u>Metastaz saptanması:</u>	Hematoksilen- eosin	% 8.2
	IHC	%13.1
	IHC ile metastaz yok RT-PCR (+)	%23

Sonuç:

- RT-PCR ile saptanan mikrometastaz oranları yüksektir
- cT1 and cN0 'da Tanısal doğruluk oranı %100

Prognostic Factors for Patients With Node-Negative Gastric Cancer: Can Extended Lymph Node Dissection Have a Survival Benefit? PARK SS. Journal of Surgical Oncology 2006

Amaç: Mide kanserinde D2 diseksiyonun sağkalıma etkisini incelemek.

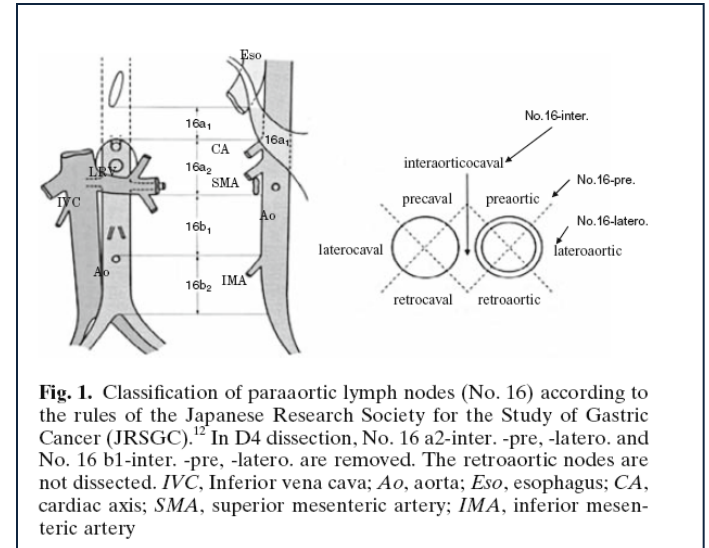
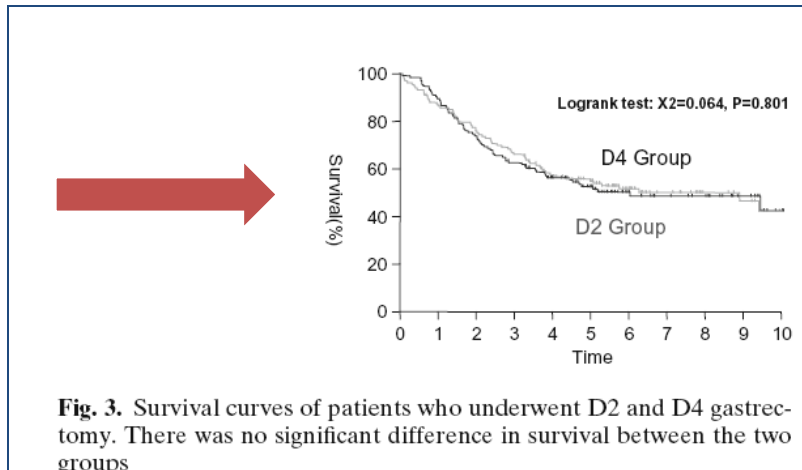
Metod: nod negatif 506 olgu retrospektif olarak incelendi.

Sonuç:

- **Yaş ve T evre** önemli prognostik faktörler olarak bulunmuştur.
- **D2 lenfadenektominin prognostik değeri sadece T3 tümörlerde ortaya çıkmıştır.**
- Node negatif gastrik kanserlerde D2 diseksiyonun T1ve T2 evrelerde sağkalıma etkisi bulunmamaktadır.

Randomized clinical trial of D2 and extended paraaortic lymphadenectomy in patients with gastric cancer **Yonemura Y . Int J Clin Oncol (2008)**

- **Dizayn: Çok merkezli RKÇ D2 vs D4 (d2+paraaortik diseksiyon).**
- **İleri evre potansiyel kur olabilen gastrik kanserli hastalar n: 269 (135 D2 vs 134 D4)**
- **Sonuç: Kür potansiyeli olan ileri evre mide kanserinde profilaktik D4 diseksiyon uygun değildir.**



Prospektif gözlem çalışması

Yıl: 1985 - 2000,

Bulgular:

Mide+tek organ rezeksiyonu: 337

Mide+2 organ rezeksiyonu: 63

Mide+3 organ rezeksiyonu: 18

Komplikasyon: %33 (n:580). Perioperatif mortalite: 4% (n: 48). **Yaş (RR:1.57), ikiden çok organ rezeksiyonu (RR:3.57) komplikasyon oranını artırmaktadır (Logistic regression)**

.

Table 5. Organs Resected

Organ resected	Number of organs
Spleen any	251
Spleen only	186
Spleen/pancreas	47
Spleen with other	18
Pancreas any	65
Pancreas only	18
Colon	36
Liver	33
Lung	20
Gallbladder	27
Small bowel	27
Other	40
Total	517

Achieving R0 Resection for Locally Advanced Gastric Cancer:
Is It Worth the Risk of Multiorgan Resection? Martin R. J Am Coll Surg 2002

Achieving R0 Resection for Locally Advanced Gastric Cancer: Is It Worth the Risk of Multiorgan Resection? Martin R. J Am Coll Surg 2002

Kombine organ rezeksiyonlarında kardiyak komplikasyonlar ve anastomoz sorunları sıktır

Table 6. Total Complications in 404 Patients

Complication	No. of complications	%
Cardiac	88	15
Pneumonia	85	14
Anastomotic leak	80	14
Wound infection	69	12
Abscess	41	7
Fistula	23	4
Hemorrhage	22	4
Pulmonary embolism	20	4
Sepsis	19	3
Total	580	

Table 7. Primary Cause of 48 Perioperative Deaths

Cause of death	n
Anastomotic leak	15
Cardiac arrhythmia/ischemia	13
Pneumonia	8
Pulmonary embolism	4
Hemorrhage	2
Gastric perforation	3
Duodenal stump leak	1
Colon perforation	1
Renal failure	1

n: 1,283

Gastrektomi ile birlikte en az bir organın rezeksiyonu: %33 (n: 418).

Yalnız gastrektomi: %68 (n: 826),

Gastrektomi yapılamayan olgular: %3 (n: 39)

2008 e gelindiğinde;

**Mide kanseri cerrahisinde iyi bir lokal kontrol için
radoterapi veya D2 diseksiyon gerektiği çok açıktır**

- D2 diseksiyonu
 - Volümü yüksek merkezlerde düşük morbidite ile yapılabilir
 - sağkalım avantajı sağlar
- >D2 diseksiyonu morbiditeyi artırır
- Profilaktik >D2 lenfadenektomi uygun değildir.
- Adjuvan tedavi ülkelere göre değişiktir
 - Avrupada - Neoadjuvant + post-operatif kemoterapi
 - ABD - Postoperatif adjuvant kemoterapi
 - Japonya - Postoperative S-1 monoterapi

MM ın klinik anlamı için daha fazla bilgiye ihtiyaç var

- Lenf nodunda MM ve ITH olması lokorejyoner nüksü artırır
 - Doekhie FS, Mesker WE, van Krieken JH, Kok NF, Hartgrink HH, Kranenbarg EK, et al. Clinical relevance of occult tumor cells in lymph nodes from gastric cancer patients. Am J Surg Pathol 2005;29:1135e44
- Lenf nodunda immünohistokimya ile farkedilen MM'in sağkalıma etkisi yoktur.
 - Fukagawa T, Sasako M, Mann GB, Sano T, Katai H, Maruyama K, et al. Immunohistochemically detected micrometastases of the lymph nodes in patients with gastric carcinoma. Cancer 2001;92:753e60

Detection of micrometastases in sentinel nodenavigation surgery for gastric cancer
Selection of tracer for sentinel node detection, Yanagita S. et al Surgical Oncology (2008)

SN navigasyon cerrahisi

1. Radioisotope (RI)-işaretli kolloid (99mTc)

- 99mTc-tin colloid, 99mTc-sulfur colloid, 99mTc-serum albumin and 99mTc-phytate [31e34]

2. Boya kılavuzluğunda

- Patent blue Tanısal doğruluk : 98%
- Indocyanine green (ICG)
- infrared elektronik endoskopi ve ICG boyama

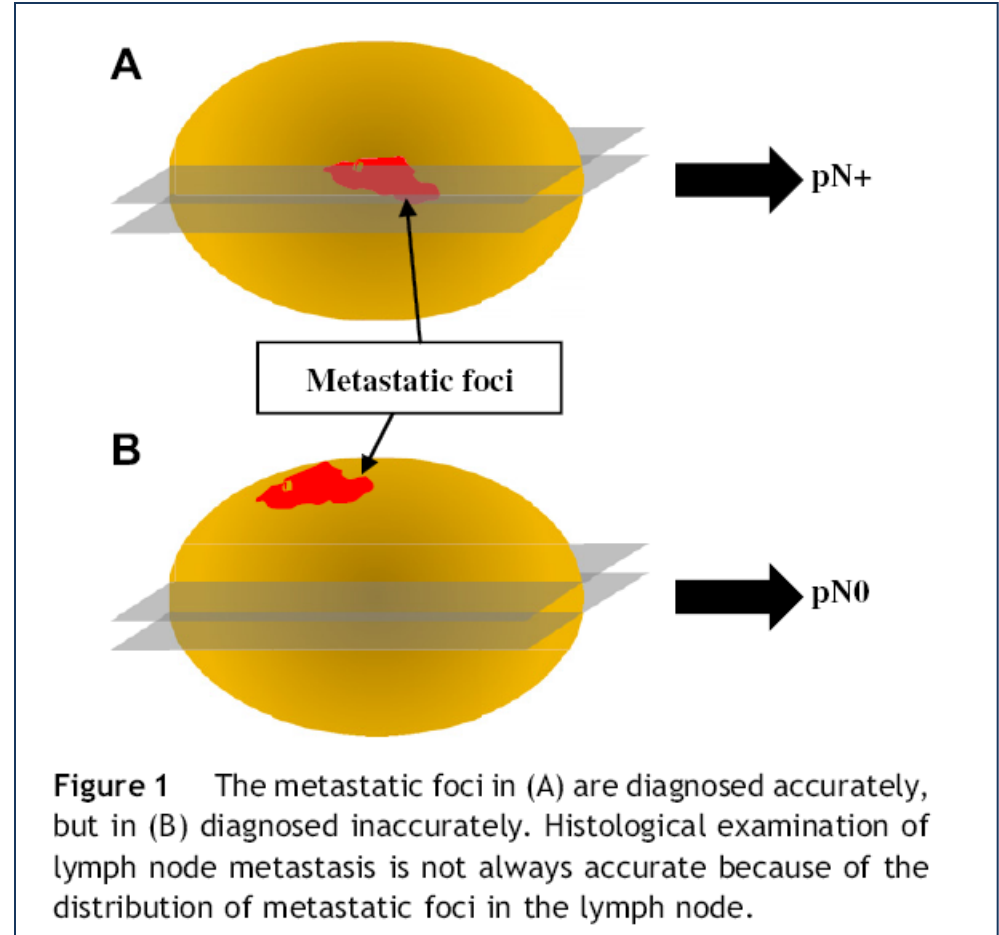
3. Her ikisi birden kullanılarak.

4. SN saptanabilme oranı: **98% (136/139)**

- Mide için en uygun partikül boyutu: 100 nm

Detection of micrometastases in sentinel nodenavigation surgery for gastric cancer
Selection of tracer for sentinel node detection, Yanagita S. et al Surgical Oncology (2008)

**Doğru tanı patoloğun
nereye baktığı ile
ilişkilidir
Mikrometastazda,
geleneksel patolojik
incelemede yalancı
negatiflik oranı fazladır**



Surgical Outcomes in Patients with T4 Gastric Carcinoma

Kunisaki C. J Am Coll Surg 2006

- T4 gastrik kanserler için en iyi tedavinin ne olduğu belli değildir.
- Dizayn: retrospektif, n:117 T4 olgu
- Bulgular: Küratif rezeksiyon: n= 38 (%32.4)
- En sık rezeke edilen organ: Pankreas.
- 5 yıllık genel sağkalım: %16,
- Median sağkalım: 11 ay.
- Küratif rezeksiyon sonrası 5 yıllık sağkalım: %32
- Tümör çapı <10 cm, <6 lenf nodu metastazı bağımsız prognostik parametrelerdir.
- Sonuç: **Çapı 10 cm'den küçük tümörlü T4 gastrik kanserlerde agresif cerrahiden kaçınılmamalıdır.**

Table 2. Combined Resection

Organs	Curative resection*		Non-curative resection†	
	n	%	n	%
Pancreas body, tail and spleen	17	44.7	15	19.0
Transverse colon or mesocolon	15	39.5	19	24.1
Liver	3	7.9	7	8.9
Diaphragm or abdominal wall	2	5.3	4	5.1
Partial resection of pancreas head	2	5.3	4	5.1
Spleen	2	5.3	2	2.5
Pancreas head and duodenum	1	2.6	0	
Small intestine	0		2	2.5

*n = 38.

†n = 79.

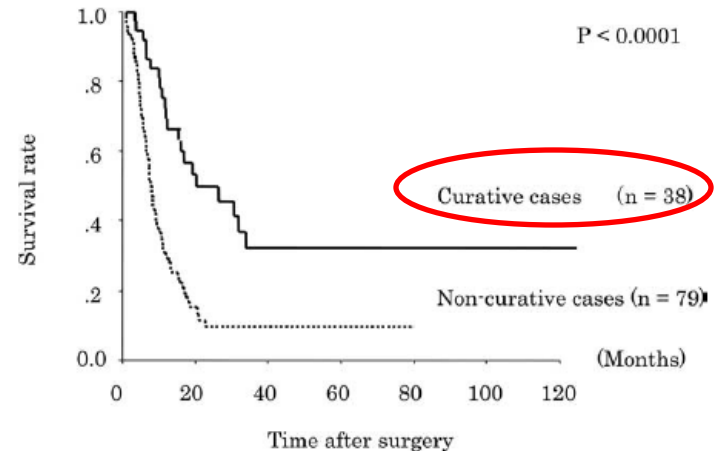


Figure 2. Survival curves of patients according to curability. There was a substantial difference in survival between patients after curative and noncurative resections ($p < 0.0001$).

Extended Lymph Node Dissection Without Routine Spleno-Pancreatectomy for Treatment of Gastric cancer: Low Morbidity and Mortality Rates in a Single Center Series of 250 Patients. Biffi R et al. Journal of Surgical Oncology, 2006

- Metod: İtalyada 250 ardışık olguya dalak ve pankreas korunarak, radikal gastrektomi ve D2 diseksiyon yapılmıştır (1994–2002)
- Bulgular: Total gastrektomi (n=140) , subtotal (n=110)
- Splenektomi: 8, spleno-pancreatectomy: 15.
- Hastanede kalış süresi: 14.8 (medyan) gün.
- Morbidite: %18, Mortalite: %1.2
- Sonuç: **Tecrübeli merkezlerde D2 diseksiyon D1 diseksiyon kadar güvenli bir şekilde yapılabilir.**

An evidence-based medicine review of lymphadenectomy extent for gastric cancer

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KEYWORDS:

Gastric neoplasm;
D1, D2, D3;
Meta-analysis;
Randomized
controlled trials

Abstract

BACKGROUND: Several studies in the literature have investigated the possible role of the extent of lymphadenectomy in gastric cancer treatment failure. The current study attempted to determine the effectiveness and safety of lymphadenectomy with gastrectomy for the treatment of gastric cancer.

METHODS: Randomized controlled trials (RCTs) were identified by means of MEDLINE, EMBASE, Cochrane Controlled Trials Register databases, and Chinese Biomedical Database, as well as by selecting references from relevant articles.

RESULTS: Overall, 14 RCTs (3,432 patients) were included in the meta-analysis. Of the D1 and D2 surgery groups, the operative mortality and postoperative morbidity were higher in the D2 group than in the D1 group, but the 3- and 5-year survival rates were not statistically different. Also the operative time was shorter in D1 compared to D2. In the D2 versus the D3 surgical group, the operative mortality, percentage of postoperative complications, operative time, and hospital stay were not significantly different.

CONCLUSIONS: The results suggest that D2 and D3 surgery may not offer specific advantages for gastric cancer and instead may lead to disadvantages for patient outcomes.

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An evidence-based medicine review of lymphadenectomy extent for gastric cancer. Sun Hu Yang et al. The American Journal of Surgery (2009)

Table 1 Characteristics of included studies

Study	Country	Patients (n)	Intervention	Design	Randomization procedure	Allocation concealment	Blinding	Groups comparable	Chemotherapy or radiotherapy	intention to treat
Bonenkamp JJ, 1995 ¹⁵	Dutch	711 (380/331)	D1 vs D2	RCT	Adequate	Adequate	Not stated	Not stated	Not stated	Not stated
Bonenkamp JJ, 1999 ²⁰	Dutch	711 (380/331)	D1 vs D2	RCT	Adequate	Adequate	Not stated	Not stated	Not stated	Not stated
Cuschieri A, 1996 ¹⁶	UK	400 (200/200)	D1 vs D2	RCT	Adequate	Adequate	Not stated	Not stated	Not stated	Not stated
Cuschieri A, 1999 ²¹	UK	400 (200/200)	D1 vs D2	RCT	Adequate	Adequate	Not stated	Not stated	Not stated	Not stated
Degiuli M, 2004 ²²	Italy	162 (76/86)	D1 vs D2	RCT	Not stated	Unclear	Not stated	Not stated	Not stated	Not stated
Liu J, 2001 ²³	China	60 (30/30)	D1 vs D2	RCT	Adequate	Unclear	Not stated	Not stated	Not stated	Not stated
Bunt AMG, 1995 ²⁴	Netherlands	473 (253/220)	D1 vs D2	RCT	Not stated	Unclear	Not stated	Not stated	Not stated	Not stated
Dent DM, 1988 ²⁵	South Africa	43 (22/21)	R1† vs R2*	RCT	Adequate	Adequate	Not stated	Yes	Not stated	Yes
Bonenkamp JJ, 1992 ²⁶	Netherlands	131 (64/67)	R1† vs R2*	RCT	Not stated	Unclear	Not stated	Not stated	Not stated	Not stated
Wu CW, 2006 ²⁷	Taiwan	221 (110/111)	D1 vs D3*	RCT	Adequate	Unclear	Not stated	Not stated	Yes	Not stated
Wu CW, 2004 ²⁸	Taiwan	221 (110/111)	D1 vs D3*	RCT	Adequate	Unclear	Not stated	Not stated	Yes	Not stated
Robertson CS, 1994 ²⁹	Hong Kong	54 (25/29)	R1† vs R3*	RCT	Adequate	Adequate	Not stated	Yes	Not stated	Not stated
Kodera Y, 2005 ³⁰	Japan	523 (263/260)	D2 vs D3	RCT	Adequate	Adequate	Not stated	Not stated	Not stated	Not stated
Sano T, 2004 ³¹	Japan	523 (263/260)	D2 vs D2+‡	RCT	Adequate	Adequate	Not stated	Yes	Not stated	Not stated
Maeta M, 1999 ³²	Japan	70 (35/35)	D3* vs D4‡	RCT	Not stated	Unclear	Not stated	Yes	Not stated	Not stated
Kulig J, 2007 ³³	Poland	275 (141/134)	D2 vs D2+‡	RCT	Adequate	Unclear	Not stated	Yes	Yes	Not stated
Yonemura Y, 2006 ³⁴	Japan	256 (128/128)	D2 vs D4‡	RCT	Not stated	Unclear	Not stated	Yes	Not stated	Not stated
Jiang B, 2000 ³⁵	China	53 (32/21)	D2 vs D4‡	RCT	Not stated	Unclear	Not stated	Not stated	Not stated	Not stated

*Japanese classification of gastric carcinoma, 2nd English edition D2.

†Japanese classification of gastric carcinoma, 2nd English edition D1.

‡Japanese classification of gastric carcinoma, 2nd English edition D3.^{9,10}

**An evidence-based medicine review of lymphadenectomy
extent for gastric cancer. Sun Hu Yang et al. The American Journal of Surgery (2009)**

Metaanaliz (MEDLINE, EMBASE, Cochrane Controlled Trials veri tabanı, and Çin biyomedikal veritabanı)

- N: 14 RKÇ (3432 olgu)
- D1-D2 –D3 karşılaştırması
- D1 vs. D2: D2'nin morbidite ve mortalite yüksek
3 ve 5 yıllık sağkalımlar farklı değil
- D2 vs. D3: mortalite, morbidite, ameliyat hastanede
yatış süresi farklı değil.

D2-3 diseksiyonun sağaltımda yeri olmayabilir

Düşük Maruyama Index cerrahisi

- Intergroup 01116 postoperatif kemoradyoterapi çalışması ve
- Hollanda D1-2 çalışması bulguları “Maruyama index of unresected disease” e göre yeniden değerlendirilmiş
- Sonuç: Düşük Maruyama Index’ li amaliyetlerde ($MI < 5$) hastalıksız ve genel sağkalım daha iyi

Scandinavian Journal of Surgery 95: 243–248, 2006 **Low Maruyama Index surgery for gastric cancer SA Hundahl**

Hollanda çalışmasında 11 yıl izlenen ve ölen olguların otopsi bulgularına göre MI'ı lokal rekürrensi riskini kestirimde çok faydalıdır

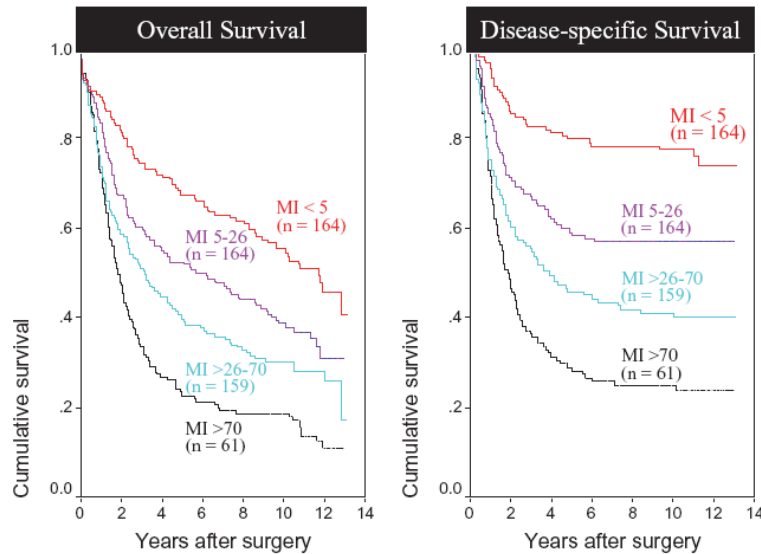


Table 1. Failure analysis by Maruyama Index (MI), as shown by autopsy

	MI < 5 n (%)	MI ≥ 5 n (%)
Died, no recurrence	44 (59)	110 (30)
Regional recurrence	6 (8)	78 (21)
Regional + distant	14 (19)	130 (36)
Distant only	11 (15)	48 (13)
Total	75 (100)	366 (100)

P < 0.001. There is a significant difference in the pattern of failure. See text for details

Fig. 1. Overall survival (*left*) and disease-specific survival (*right*), from date of surgery, by Maruyama Index (MI) quartiles (log-rank *P* < 0.01 for both graphs). *Top line* reflects the MI < 5 quartile

Maruyama bilgisayar programı

- 7 parametre
 1. Cinsiyet
 2. Yaş
 3. Borman
 4. Lokasyon
 5. Histoloji
 6. Derinlik
 7. Çap
- Verdiği sonuç= **#1 - #16 lenf grubunda** % metastaz olma ihtimali
- Rekürrens ve sağkalımı tahmin ediyor

The volume-outcome conundrum. Kizer KW. *N Engl J Med* 2003;

Mesaj

Bu hastalığa yakalananların bu alanda tecrübeli birini YAKALAYIP ona ameliyat olması gerekir

2009'a gelindiğinde,
En çok okunanlar listesinin başında belki de
“DUTCH Gastric Cancer Trial” vardır ama;
sınır komşusunun kılavuzunda D2 diseksiyon standart
işlem olarak önerilmektedir

