Multidisciplinary management of Locally advanced gastric cancer: challenges for the surgeon

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Frame

- **Multidisciplinary approach**
  - Digestive tumor board
- **Locally advanced gastric cancer**
- **Prognosis**
- **Correct Staging**
- **Treatment Standards**
- **To what extend extensive surgery**
  - DI, II, III, more. . .
  - Multiorgan resection
  - R0, RI, RII,
- **Peritoneal recurrence**
  - HIPEC/Cytoreductive surgery

Locally advanced gastric cancer

Tumors infiltrating or adherent to adjacent organs and/or structures with or without lymph node involvement in patients without distant metastasis.

- **Gastric carcinomas are considered unresectable**
  - peritoneal involvement,
  - distant metastases,
  - locally advanced disease
    - invasion or encasement of major blood vessels.

- Long-term survival of patients with invasion to adjacent organs is poor.

- For locally advanced gastric cancer with adjacent organ infiltration, extended resection including the invaded organ is required to achieve R0 resection with negative surgical margins

5 year surviaval rates after R0 Gastrectomy,

Concer, 2000

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

TNM Staging, Gastric Cancer

Table 2
TNM staging of gastric cancer (7th Edition of AJCC/UICC guidelines) [6,7].

Primary tumour (T)		Regional lymph nodes (N)		Distant metastasis (M)	
TX	Primary tumour cannot be assessed	NX	Regional lymph node(s) cannot be assessed	MX	Distant metastasis cannot be assessed
T0	No evidence of primary tumour	N0	No regional lymph node metastasis	M0	No distant metastasis
Tis	Carcinoma in situ: intraepithelial tumour without invasion of the lamina propria	N1	Metastasis in 1–2 regional lymph nodes	M1	Distant metastasis or positive peritoneal cytology
T1a	Tumour invades lamina propria or muscularis mucosae	N2	Metastasis in 3–6 regional lymph nodes		
T1b	Tumour invades submucosa	N3	Metastasis in 7 or more regional lymph nodes		
T2	Tumour invades muscularis propria				
T3	Tumour penetrates subserosal connective tissue without invasion of visceral peritoneum or adjacent structures*				
T4a	Tumour invades serosa (visceral peritoneum)				
T4b	Tumour invades adjacent structures**				

Edge SB, Byrd DR, Compton CC, eds. AJCC Cancer Staging Handbook, 7th ed. New York, NY: Springer, 2010. Used with the permission of the American Joint Committee on Cancer (AJCC), Chicago, Illinois. The original source for this material is the AJCC Cancer Staging Handbook, Seventh Edition (2010) published by Springer Science and Business Media LLC, www.springer.com.

* T3 tumours also include those extending into the gastrocolic or gastrohepatic ligaments, or into the greater or lesser omentum, without perforation of the visceral peritoneum covering these structures.

** Adjacent structures include the spleen, transverse colon, liver, diaphragm, pancreas, abdominal wall, adrenal gland, kidney, small intestine and retro-peritoneum.

Staging and treatment principles

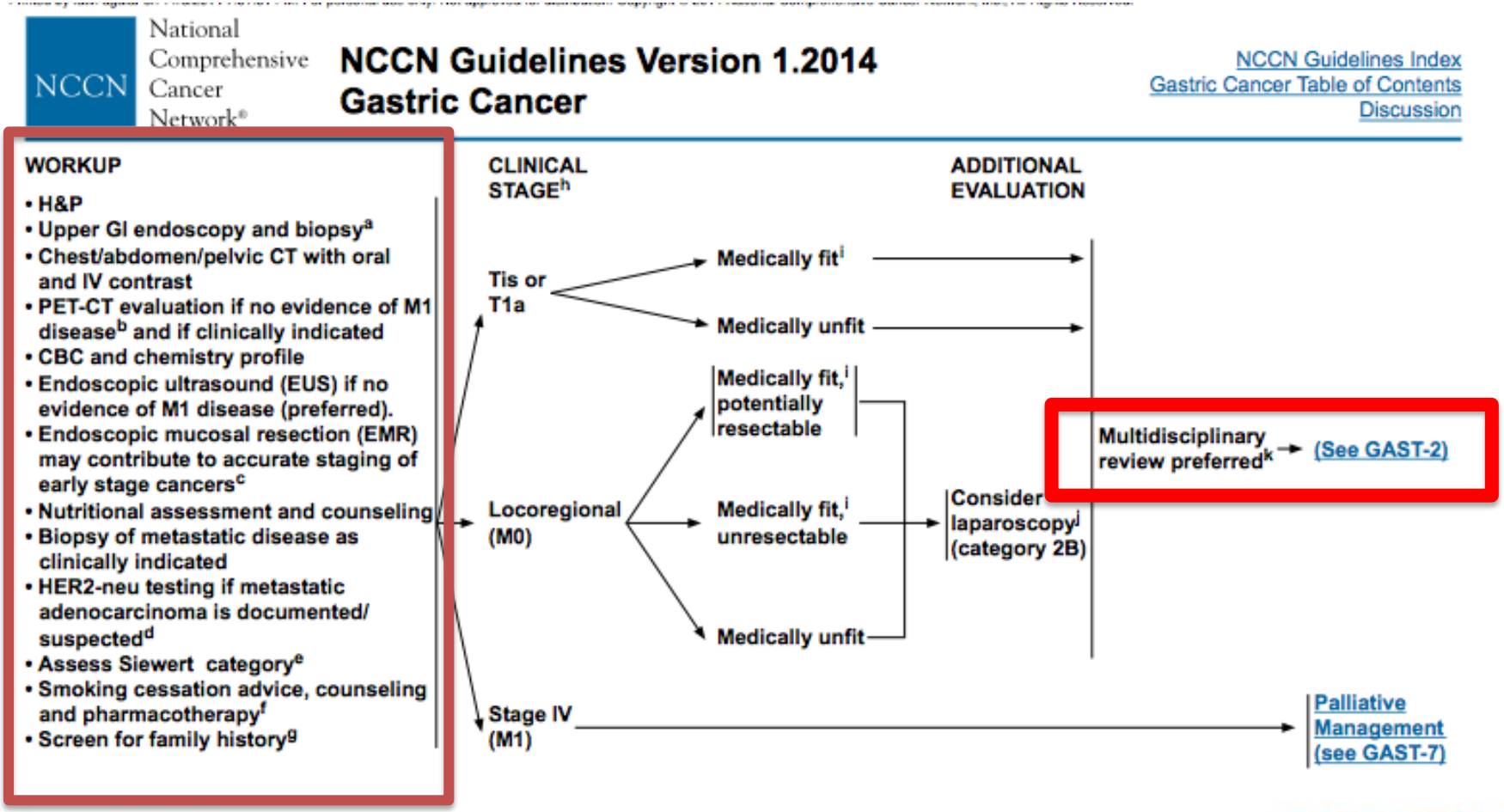
NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

Gastric Cancer

Version 1.2014

NCCN.org

STAGING

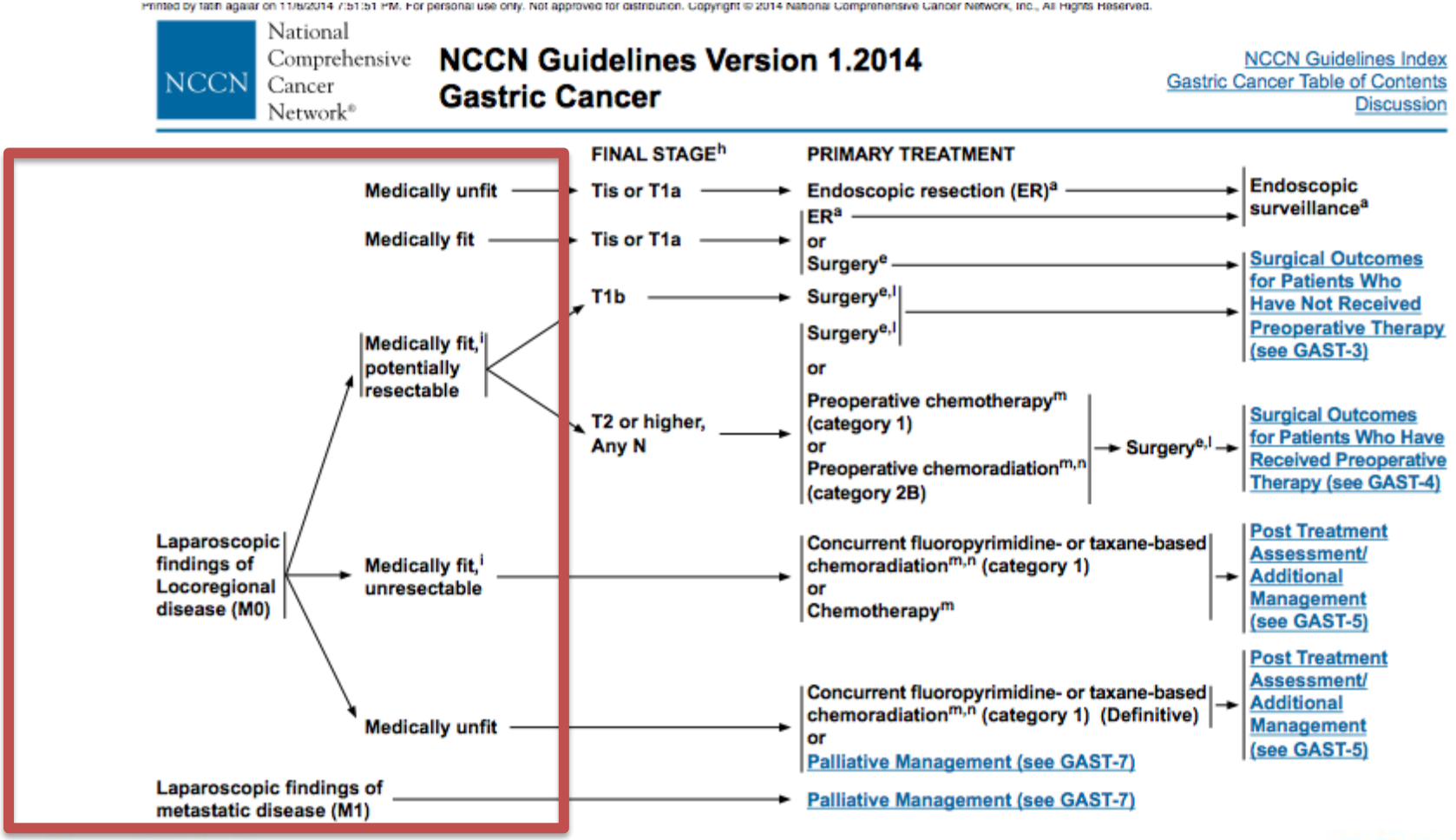


'Sağlığın Merkezi'

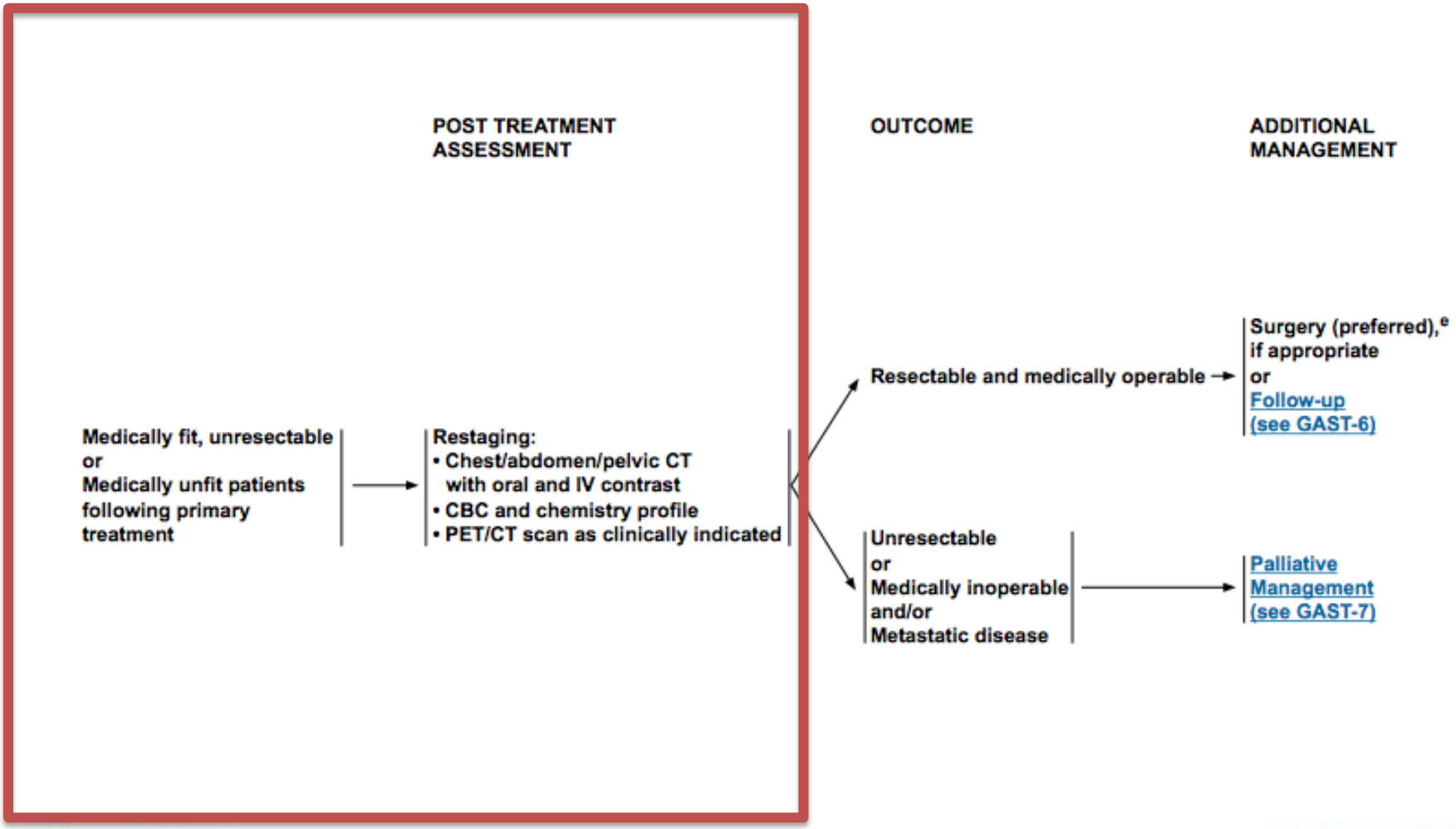
ANADOLU

In Affiliation with JOHNS HOPKINS MEDICINE

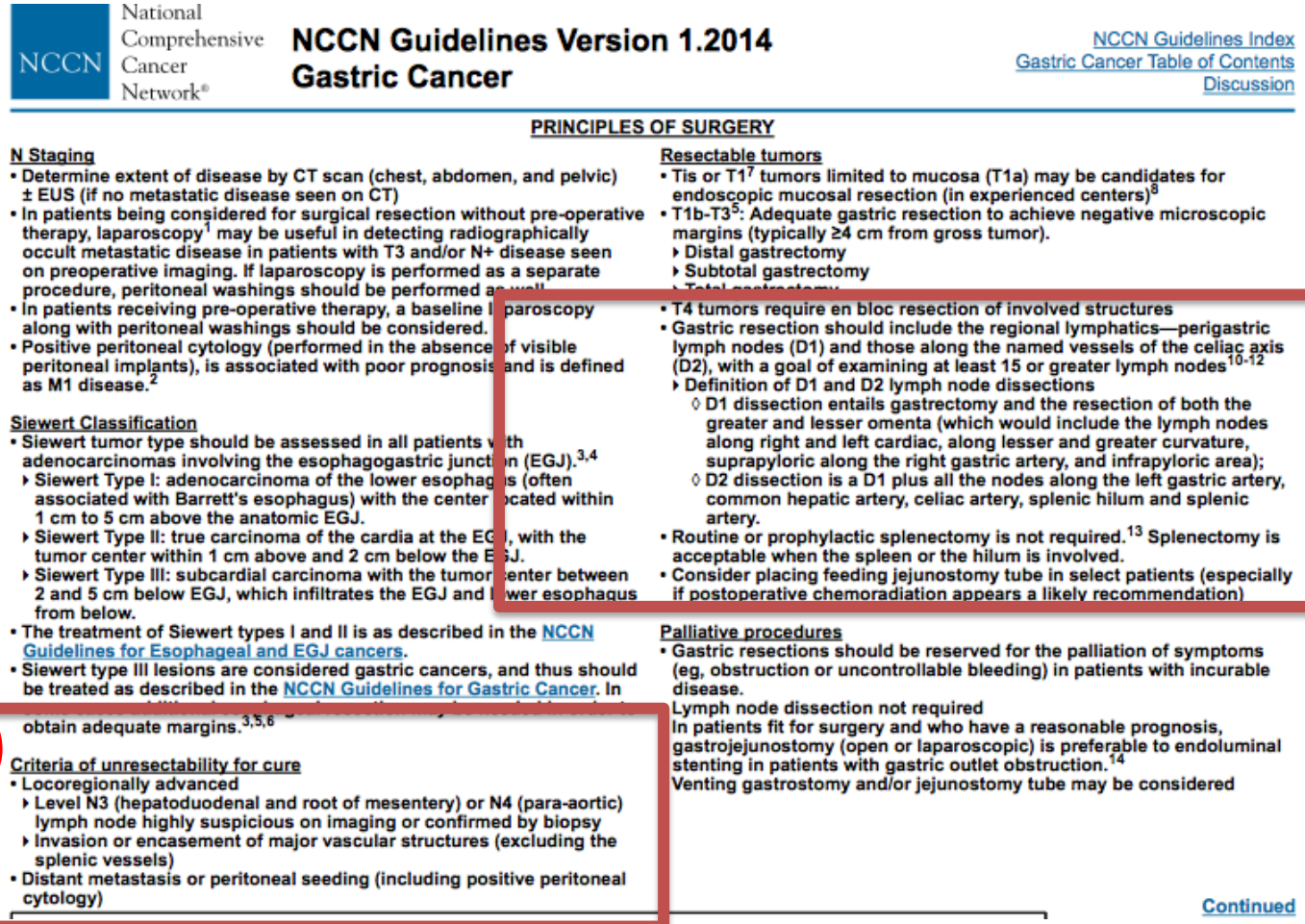
STAGING LAPAROSCOPY



RE-STAGING after neoadjuvant therapy



D2 dissection



National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2014
Gastric Cancer

NCCN Guidelines Index
Gastric Cancer Table of Contents
Discussion

PRINCIPLES OF SURGERY

N Staging
- Determine extent of disease by CT scan (chest, abdomen, and pelvic) ± EUS (if no metastatic disease seen on CT)
- In patients being considered for surgical resection without pre-operative therapy, laparoscopy[1] may be useful in detecting radiographically occult metastatic disease in patients with T3 and/or N+ disease seen on preoperative imaging. If laparoscopy is performed as a separate procedure, peritoneal washings should be performed as well.
- In patients receiving pre-operative therapy, a baseline laparoscopy along with peritoneal washings should be considered.
- Positive peritoneal cytology (performed in the absence of visible peritoneal implants), is associated with poor prognosis and is defined as M1 disease.[2]

Siewert Classification
- Siewert tumor type should be assessed in all patients with adenocarcinomas involving the esophagogastric junction (EGJ).[3,4]
  - Siewert Type I: adenocarcinoma of the lower esophagus (often associated with Barrett's esophagus) with the center located within 1 cm to 5 cm above the anatomic EGJ.
  - Siewert Type II: true carcinoma of the cardia at the EGJ, with the tumor center within 1 cm above and 2 cm below the EGJ.
  - Siewert Type III: subcardial carcinoma with the tumor center between 2 and 5 cm below EGJ, which infiltrates the EGJ and lower esophagus from below.
- The treatment of Siewert types I and II is as described in the NCCN Guidelines for Esophageal and EGJ cancers.
- Siewert type III lesions are considered gastric cancers, and thus should be treated as described in the NCCN Guidelines for Gastric Cancer. In obtain adequate margins.[3,5,6]

Criteria of unresectability for cure
- Locoregionally advanced
  - Level N3 (hepatoduodenal and root of mesentery) or N4 (para-aortic) lymph node highly suspicious on imaging or confirmed by biopsy
  - Invasion or encasement of major vascular structures (excluding the splenic vessels)
- Distant metastasis or peritoneal seeding (including positive peritoneal cytology)

Resectable tumors
- Tis or T1[7] tumors limited to mucosa (T1a) may be candidates for endoscopic mucosal resection (in experienced centers)[8]
- T1b-T3[5]: Adequate gastric resection to achieve negative microscopic margins (typically ≥4 cm from gross tumor).
  - Distal gastrectomy
  - Subtotal gastrectomy
  - Total gastrectomy
- T4 tumors require en bloc resection of involved structures
- Gastric resection should include the regional lymphatics—perigastric lymph nodes (D1) and those along the named vessels of the celiac axis (D2), with a goal of examining at least 15 or greater lymph nodes[10-12]
  - Definition of D1 and D2 lymph node dissections
    - ◊ D1 dissection entails gastrectomy and the resection of both the greater and lesser omenta (which would include the lymph nodes along right and left cardiac, along lesser and greater curvature, suprapyloric along the right gastric artery, and infrapyloric area);
    - ◊ D2 dissection is a D1 plus all the nodes along the left gastric artery, common hepatic artery, celiac artery, splenic hilum and splenic artery.
- Routine or prophylactic splenectomy is not required.[13] Splenectomy is acceptable when the spleen or the hilum is involved.
- Consider placing feeding jejunostomy tube in select patients (especially if postoperative chemoradiation appears a likely recommendation)

Palliative procedures
- Gastric resections should be reserved for the palliation of symptoms (eg, obstruction or uncontrollable bleeding) in patients with incurable disease.

Lymph node dissection not required
In patients fit for surgery and who have a reasonable prognosis, gastrojejunostomy (open or laparoscopic) is preferable to endoluminal stenting in patients with gastric outlet obstruction.[14]
Venting gastrostomy and/or jejunostomy tube may be considered

Continued

?

- **Dutch RCT**: D1 vs D2 lymphadenectomy
  - significant reduction in the proportion of locoregional recurrence and cancer-related death after a long follow-up.

- **Taiwanese RCT:**
  - significant survival benefit of D2 or more extensive lymphadenectomy compared with D1 lymphadenectomy

- **European Society for Medical Oncology Guideline** for gastric cancer and the **National Comprehensive Cancer Network Guideline** for gastric cancer, now recommend an **extended D2 lymphadenectomy** as in the Japanese guidelines.

WHEN YOU HAVE TO SHOOT, SHOOT. DON'T TALK!
Eli Wallach.

From: (very) GOOD, (never) Bad, and (Occasionaly) UGLY

Standard treatment ?

- NCCN
- Japanese
- ESMO

- SWOG, 0116
- MAGIC
- French trial
- Newer ones
- Ongoing trials. . .

Japanese Standard

Table 6 – Recommendations given by the Japanese Gastric Cancer Treatment Guidelines (3rd edition) 2010

	N0	N1 (1-2)	N2 (3-6)	N3 (>7)
T1a	ESD (well diff. <2 cm)	D1+8a, 9 (<2 cm) D2 (>2.1 cm)	D2	D2
T1b	D1 (well diff. <1.5 cm) D1+8a, 9	D1+8a, 9 (<2 cm) D2 (>2.1 cm)	D2	D2
T2	D2	D2+CT adjuv.	D2+CT adjuv.	D2+CT adjuv.
T3	D2+CT adjuv.	D2+CT adjuv.	D2+CT adjuv.	D2+CT adjuv.
T4a	D2+CT adjuv.	D2+CT adjuv.	D2+CT adjuv.	D2+CT adjuv.
T4b	D2+CT adjuv.	D2+CT adjuv.	D2+CT adjuv.	D2+CT adjuv.
	+ combined resection	+ combined resection	+ combined resection	+ combined resection

Any M1: chemotherapy, palliative surgery, palliative treatments.

European Standard

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journal homepage: www.thegreenjournal.com

Guidelines

Gastric cancer†: ESMO–ESSO–ESTRO Clinical Practice Guidelines for diagnosis, treatment and follow-up

Tom Waddell [a], Marcel Verheij [b], William Allum [c], David Cunningham [d], Andrés Cervantes [e], Dirk Arnold [f,*]

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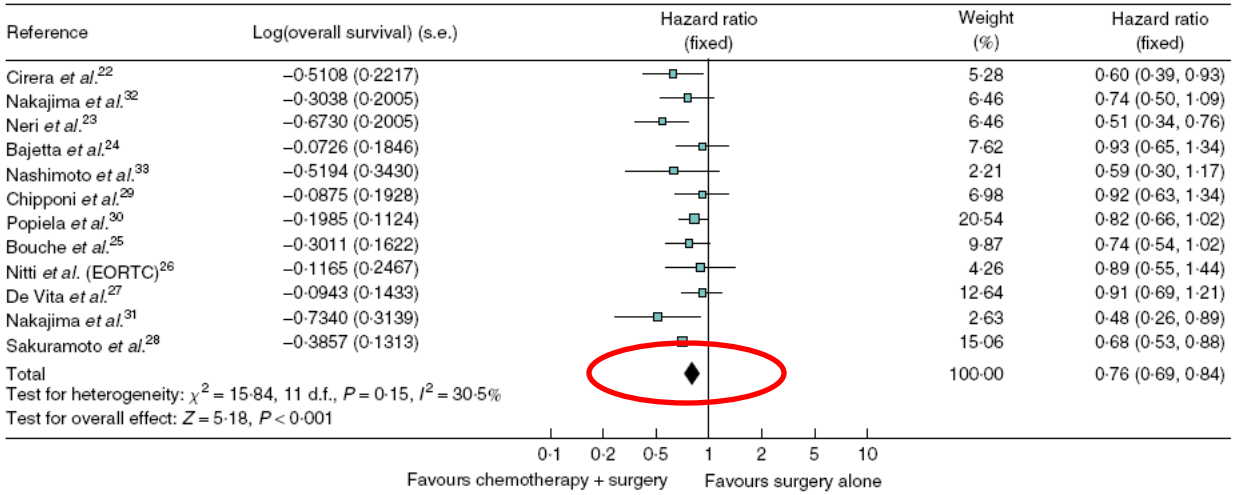
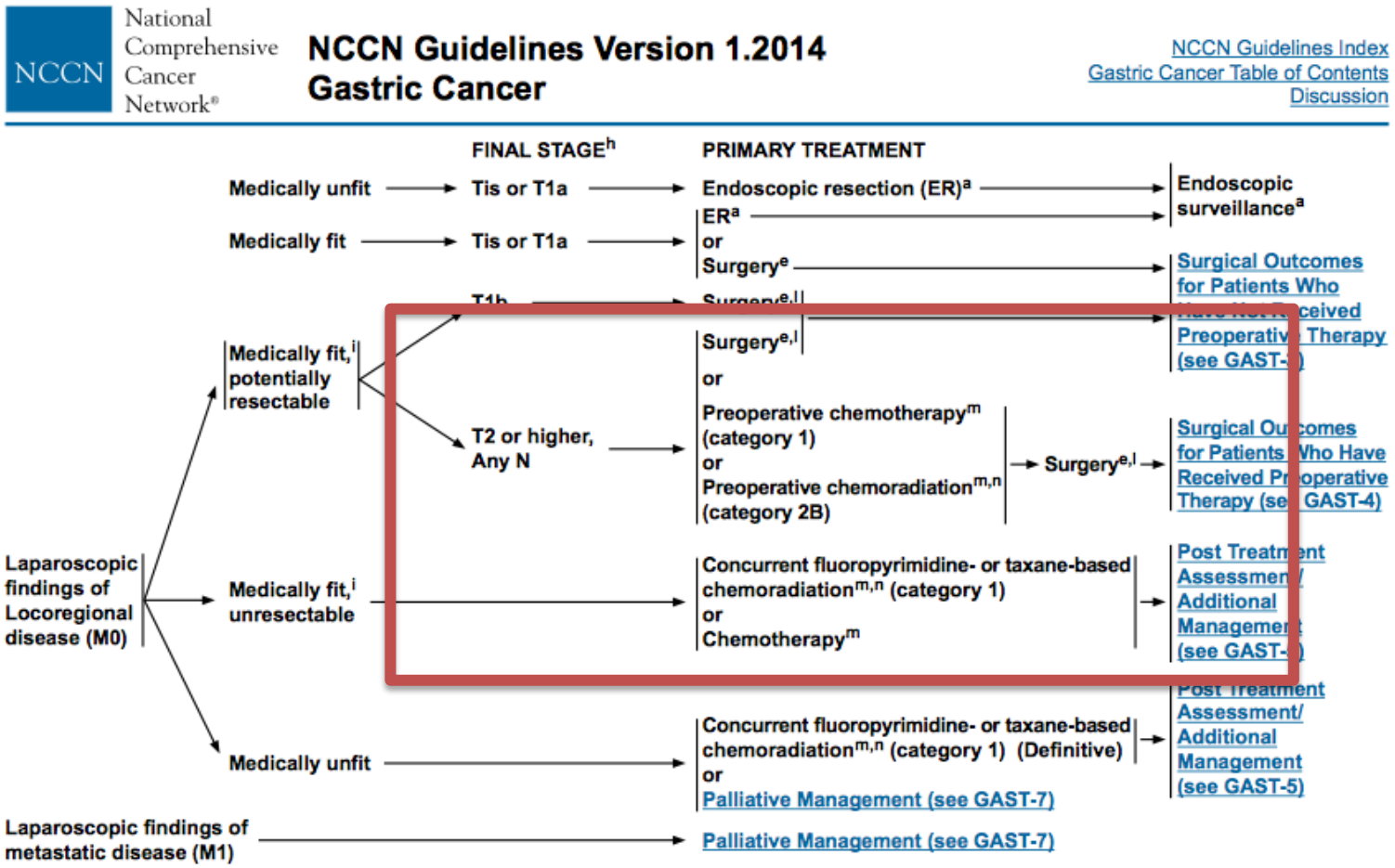


Fig. 4 Meta-analysis of overall survival in randomized clinical trials comparing chemotherapy plus surgery with surgery alone, after exclusion of the International Collaborative Cancer Group trial reported by Nitti and colleagues[26]. Hazard ratios are shown with 95 per cent confidence intervals. EORTC, European Organization for Research and Treatment of Cancer

Adjuvant radiotherapy is beneficial after curative surgery for locally advanced gastric cancer

NCCN Treatment recommendations Preoperative chemotherapy/ chemoradiation



- **Extended Surgery in Gastric Cancer**

Surgeon is there where the action is!

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JULY 31, 2008 VOL. 359 NO. 5

D2 Lymphadenectomy Alone or with Para-aortic Nodal Dissection for Gastric Cancer

Mitsuru Sasako, M.D., Takeshi Sano, M.D., Seiichiro Yamamoto, Ph.D., Yukinori Kurokawa, M.D., Atsushi Nashimoto, M.D., Akira Kurita, M.D., Masahiro Hiratsuka, M.D., Toshimasa Tsujinaka, M.D., Taira Kinoshita, M.D., Kuniyoshi Arai, M.D., Yoshitaka Yamamura, M.D., and Kunio Okajima, M.D., for the Japan Clinical Oncology Group

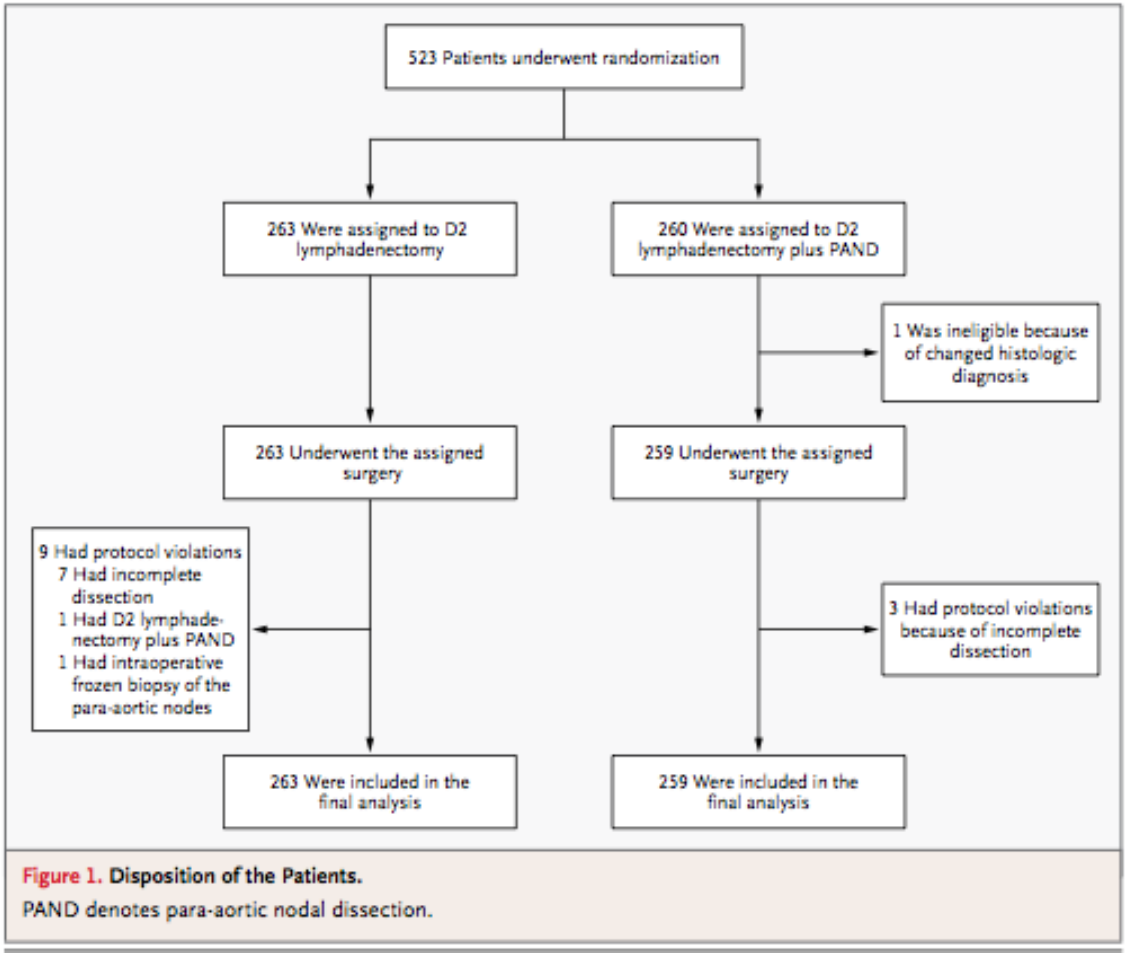


Figure 1. Disposition of the Patients.

PAND denotes para-aortic nodal dissection.

Table 2. Site of First Tumor Recurrence.*

Site	D2 Lymphadenectomy Alone (N=109)	D2 Lymphadenectomy plus PAND (N=106)
	no. (%)	
Peritoneum	43 (39.4)	39 (36.8)
Lymph nodes	24 (22.0)	23 (21.7)
Liver	21 (19.3)	24 (22.6)
Others	21 (19.3)	20 (18.9)

* In nine patients in the group assigned to D2 lymphadenectomy alone and seven patients in the group assigned to D2 lymphadenectomy plus para-aortic nodal dissection (PAND), more than one site was involved at the time of first recurrence.

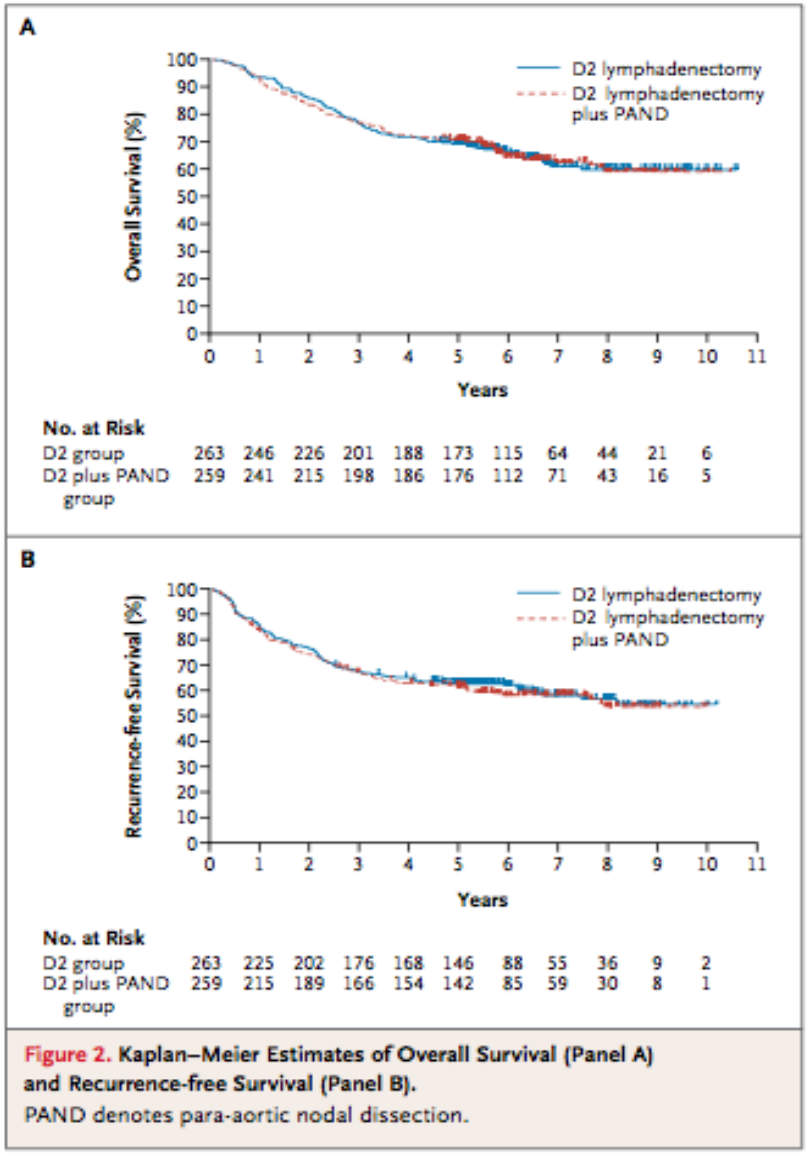


Figure 2. Kaplan–Meier Estimates of Overall Survival (Panel A) and Recurrence-free Survival (Panel B).
PAND denotes para-aortic nodal dissection.

ORIGINAL ARTICLE

Multivisceral Resection for Locally Advanced Gastric Cancer

JAMA Surg. 2013;148(4):353-360

An Italian Multicenter Observational Study

Fabio Pacelli, MD; Giacomo Cusumano, MD; Fausto Rosa, MD; Daniele Marrelli, MD; Mariantonietta Dicosmo, MD; Chiara Cipollari, MD; Alberto Marchet, MD; Stefano Scaringi, MD; Stefano Rausei, MD; Alberto di Leo, MD; Franco Roviello, MD; Giovanni de Manzoni, MD; Donato Nitti, MD; Francesco Tonelli, MD; Giovanni Battista Doglietto, MD; for the Italian Research Group for Gastric Cancer (IRGGC)

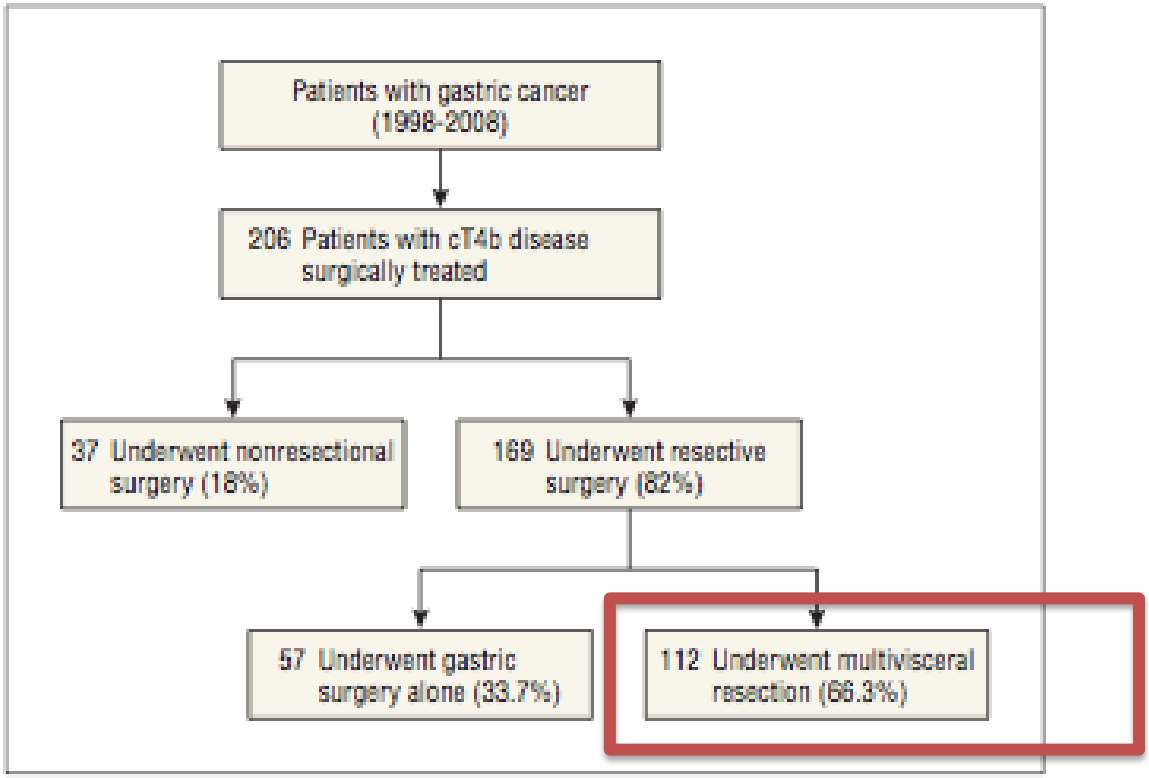


Figure 1. Consort diagram of the study.

Table 1. Postoperative Outcomes

	No./No.			
	Nonresectional Surgery	Gastrectomy Alone	Multiorgan Resection	*P* Value
Postoperative mortality	0/7	3/7	4/7	.55
Major complications	9/65	18/65	38/65	.38
Sepsis	1/11	5/11	5/11	.36
Anastomotic leak	1/14	5/14	8/14	.50
Bowel infarction	0/4	2/4	2/4	.47
Pancreatic complications[a]	1/18	3/18	14/18	.50
Respiratory complications[b]	0/6	5/6	1/6	.26
Cardiac complications[c]	1/4	3/4	0/4	.06
Other[d]	2/8	2/8	4/8	.90

[a] Pancreatic fistula, acute pancreatitis, pancreatic necrosis, and pancreatic abscess.
[b] Pneumonia and postoperative respiratory insufficiency.
[c] Myocardial infarction, arrhythmia, and cardiogenic shock.
[d] Ictus cerebri, renal failure, and hepatic dysfunction.

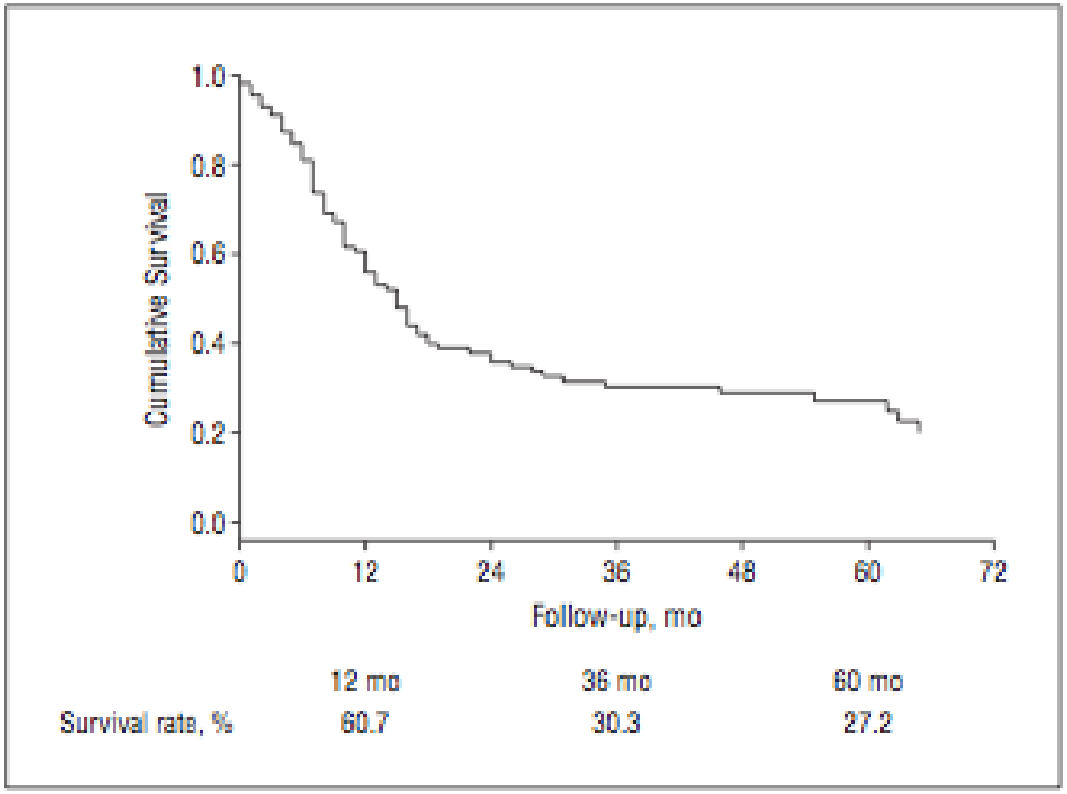
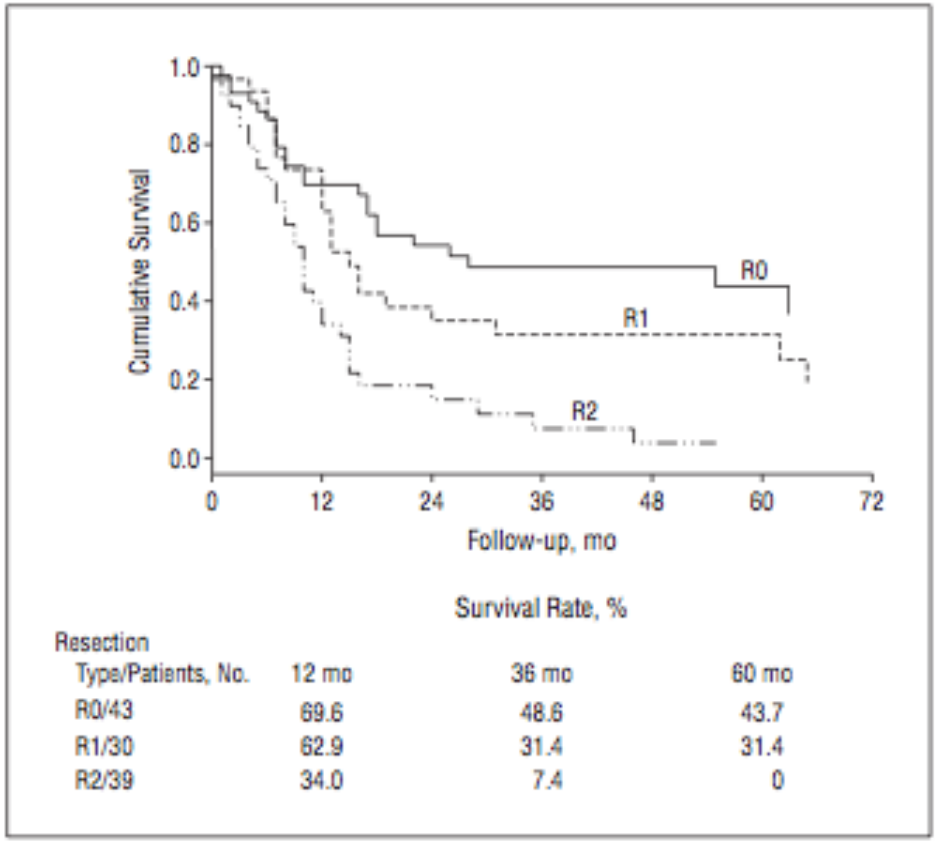


Figure 2. Overall survival curve.

R0, R1, RII survival

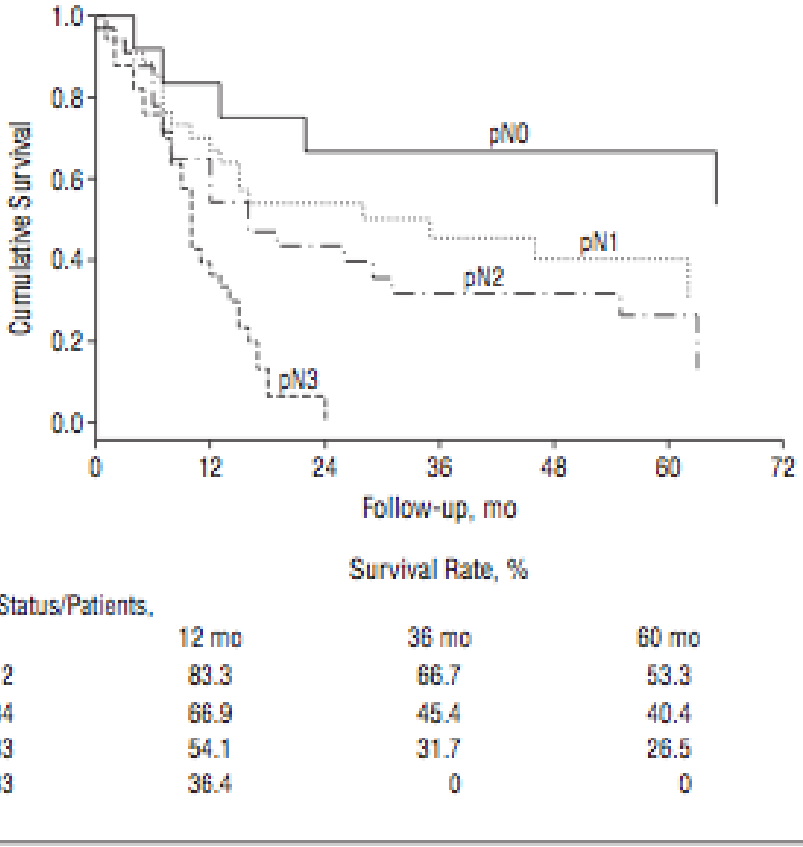


Survival Rate, %

Resection Type/Patients, No.	12 mo	36 mo	60 mo
R0/43	69.6	48.6	43.7
R1/30	62.9	31.4	31.4
R2/39	34.0	7.4	0

Figure 3. Survival rate according to the completeness of resection.

N status and survival



Survival Rate, %

Nodal Status/Patients, No.	12 mo	36 mo	60 mo
N0/12	83.3	66.7	53.3
N1/34	66.9	45.4	40.4
N2/33	54.1	31.7	26.5
N3/33	36.4	0	0

Figure 4 Survival rate according to the nodal status

Multivariate regression

Table 4. Cox Univariate and Multivariate Regression Hazard Models

Feature	Cox Univariate Regression Model, HR (95% CI)	*P* Value	Cox Multivariate Regression Model, HR (95% CI)	*P* Value
Sex	1.01 (0.99-1.03)	.29		
Age ≥65 y	0.97 (0.60-1.55)	.89		
Site of tumor	0.99 (0.81-1.21)	.94		
Bormann classification	1.19 (0.76-1.90)	.44		
Lauren classification	0.73 (0.42-1.26)	.26		
Multiple resection	1.22 (0.76-1.95)	.39		
Spleen	1.48 (0.94-2.35)	.09		.49
Colon	0.78 (0.49-1.22)	.28		
Pancreas	1.04 (0.66-1.63)	.85		
Liver	0.73 (0.40-1.38)	.35		
Peritoneum	1.78 (1.02-3.10)	.04		.71
Diaphragm	0.52 (0.16-1.65)	.27		
Other organs	1.10 (0.53-2.32)	.78		
Tumor size, cm				
< 7	1.74 (1.01-1.14)	.02		.39
>7	0.04 (0.38-3.01)	.04		
pT	0.71 (0.38-1.32)	.28		
pN	1.83 (1.42-2.36)	< .001	1.77 (1.28-2.43)	< .001
No. of lymph nodes	1.00 (0.99-1.01)	.87		
No. of pathologic lymph nodes				
<15	1.02 (1.01-1.03)	<.001		.92
>15	2.08 (1.30-3.33)	<.002		
Type of lymphadenectomy	1.00 (0.71-1.40)	>.99		
R (R0, R1, and R2)	1.81 (1.36-2.39)	<.001	1.64 (1.15-2.34)	.006
Cytology	1.35 (1.01-1.83)	.04		

Abbreviation: HR, hazard ratio.

- **Patients undergoing extended resections experience acceptable postoperative morbidity and mortality rates**
- **En-bloc multi-visceral resection should be performed**
  - complete resection can be realistically obtained
  - when lymph node metastasis is not evident

Achieving R0 Resection for Locally Advanced Gastric Cancer: Is It Worth the Risk of Multiorgan Resection? Martin RG er al. Journal of the American College of Surgeons, 2002

- 337=single additional organ resected
- 63=2 additional organ
- 18=3 additional organ

- 580 complications: 33% of patients
- Perioperative mortality: 4%

- **The number of resected organs (RR 3.8) is a major risk factor for severe complications**

Prognostic factors, multivisceral resection

Table 5 Prognostic factors determined by multivariate analysis

Variables	OR	95% CI	*P*
Age >70 y	3.32	1.37–8.08	.008
Lymph node metastasis	11.48	2.48–53.10	.002
Number of organs resected	2.65	1.30–5.42	.007

R1 resection, positive resection margin

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EJSO

the Journal of Cancer Surgery

EJSO 39 (2013) 229–234

www.ejso.com

Prognostic improvement of reexcision for positive resection margins in patients with advanced gastric cancer

J.-D. Chen [a], X.-P. Yang [b], J.-G. Shen [a], W.-X. Hu [a], X.-M. Yuan [a], L.-B. Wang [a,*]

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[b] *Department of General Surgery, Taizhou Central Hospital, Taizhou, Zhejiang 318000, PR China*

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- **Retrospective:**
- N:222 (with positive margins who underwent potentially curative resection for locally advanced GC).
- 50 patients (re-excised to a negative resection margin)
- 72 patients who were left with a positive resection margin were compared using univariate and multivariate analyses.

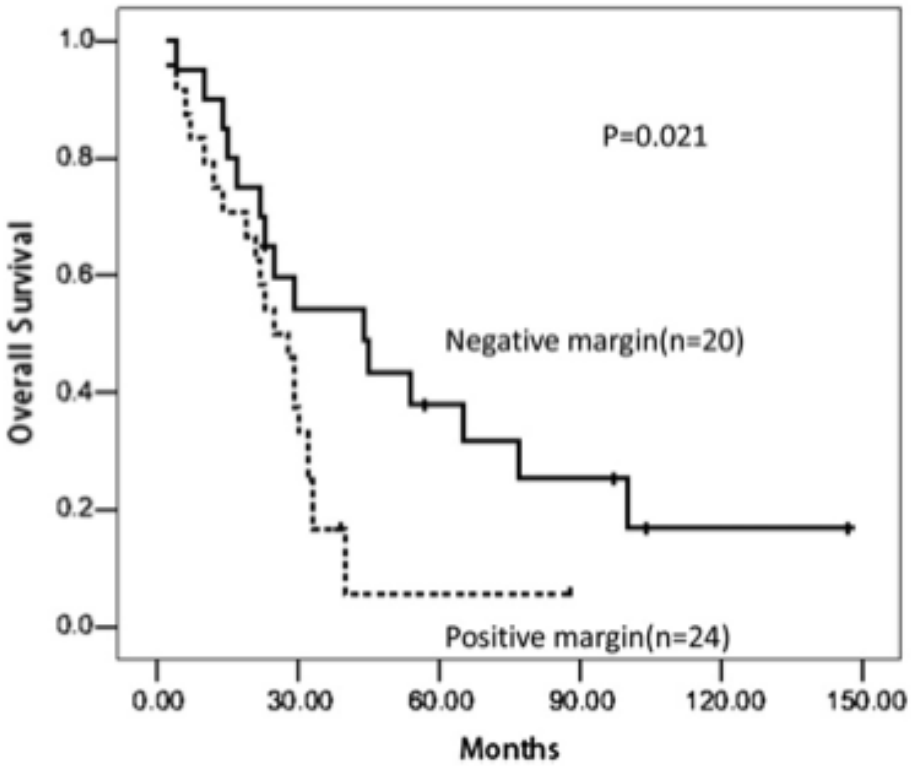

Figure 2. Survival curves for ≤pN2-category patients with either negative margins or positive margins at final histological analysis.

Table 2
Univariate and multivariate analyses of factors influencing overall survival.

Factor	Univariate	Multivariate
	p Value	*p* Value
Type of lymphadenectomy	0.006	0.002
Positive resection margin	0.019	0.048
pN-category	0.042	0.011
pTNM stage	0.043	0.932

Gastrectomy in Advanced Gastric Cancer Effectively Palliates Symptoms and May Improve Survival in Select Patients. Collins A. J Gastrointest Surg (2014)

- Incomplete (i.e., R2) gastrectomy in advanced gastric cancer (?)

Retrospective:

- n: 210 locally advanced or metastatic gastric cancer pts (1992–2008).
- Three groups:
  - Gastrectomy (N = 99),
  - Exploration without resection (N = 66),
  - No surgery (N = 45).

- Symptom resolution after gastrectomy: 48%
- Complication rate: 32%
- Mortality: 6%
- Overall median survival: 6.2 months
  - 10.0 months after gastrectomy,
  - 4.1 months after exploration without resection
  - 5.3 months for no surgery ($p<0.001$).

Peritoneal Recurrence

- Survival is poor
- Despite adjuvant chemotherapy, AGC patient often develop recurrence
- Peritoneum is the most common site of recurrence
- intraperitoneal chemotherapy has been proposed as a treatment option

Factors predicting peritoneal recurrence in advanced gastric cancer: implication for adjuvant intraperitoneal chemotherapy HEE JL, Gastric Cancer (2014)

- N: 805 AGC, curative D2 gastrectomy (2003- 2009)
- 5-year peritoneal recurrence-free survival was 79.3%.
- Recurrence = 245 patients (30.4%).
- Risk factors for peritoneal recurrence=
  - Depth of tumor invasion CT3
  - Extensive lymph node metastasis (N3)
  - Borrmann type 4
  - Venous invasion

HIPEC

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EJSC
the Journal of Cancer Surgery

EJSO 40 (2014) 12–26

www.ejso.c

Review

Intraperitoneal chemotherapy in advanced gastric cancer. Meta-analysis of randomized trials

. Coccolini [a,b,*], E. Cotte [b], O. Glehen [b], M. Lotti [a], E. Poiasina [a], F. Catena [c], Y. Yonemura [d], L. Ansaloni [a]

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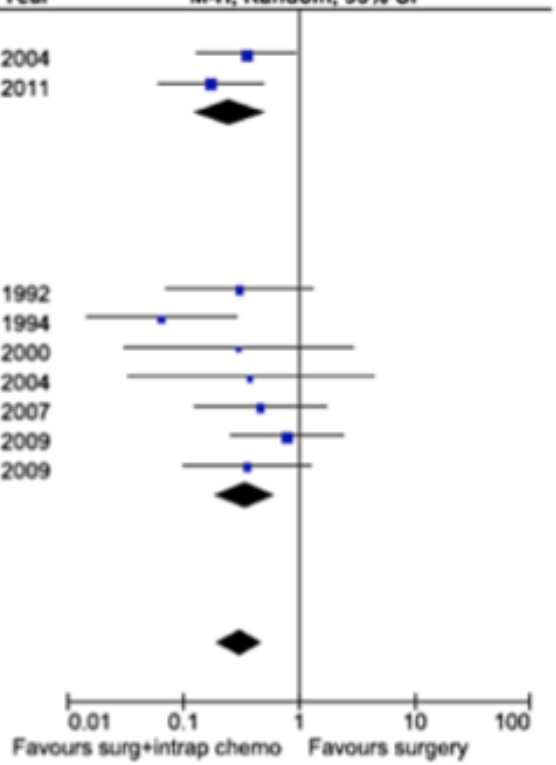
Accepted 23 October 2013

Overall mortality at one year

A

Study or Subgroup	Surgery+intrap chemother Events	Total	Surgery Events	Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
1.1.1 Treatment of Peritoneal carcinosis							
Sautner 2004	11	33	20	34	18.9%	0.35 [0.13, 0.95]	2004
Yang 2011	10	34	24	34	17.4%	0.17 [0.06, 0.49]	2011
Subtotal (95% CI)		**67**		**68**	**36.3%**	**0.25 [0.12, 0.51]**	
Total events	21		44				
Heterogeneity: Tau² = 0.00; Chi² = 0.91, df = 1 (P = 0.34); I² = 0%							
Test for overall effect: Z = 3.77 (P = 0.0002)							
1.1.2 Prophylaxis of Peritoneal carcinosis							
Hagiwara 1992	3	24	8	25	9.1%	0.30 [0.07, 1.32]	1992
Fujimura 1994	3	40	10	18	8.8%	0.06 [0.01, 0.29]	1994
Tan 2000	1	22	4	29	3.9%	0.30 [0.03, 2.87]	2000
Zuo 2004	1	46	2	36	3.4%	0.38 [0.03, 4.34]	2004
Ding 2007	4	41	7	37	11.2%	0.46 [0.12, 1.73]	2007
Kuramoto 2009	10	59	6	29	15.1%	0.78 [0.25, 2.41]	2009
Deng 2009	4	44	9	41	12.1%	0.36 [0.10, 1.26]	2009
Subtotal (95% CI)		**276**		**215**	**63.7%**	**0.34 [0.18, 0.62]**	
Total events	26		46				
Heterogeneity: Tau² = 0.10; Chi² = 7.05, df = 6 (P = 0.32); I² = 15%							
Test for overall effect: Z = 3.48 (P = 0.0005)							
Total (95% CI)		**343**		**283**	**100.0%**	**0.31 [0.19, 0.48]**	
Total events	47		90				
Heterogeneity: Tau² = 0.03; Chi² = 8.44, df = 8 (P = 0.39); I² = 5%							
Test for overall effect: Z = 5.10 (P < 0.00001)							
Test for subgroup differences: Chi² = 0.39, df = 1 (P = 0.53), I² = 0%							



Overall mortality at two years

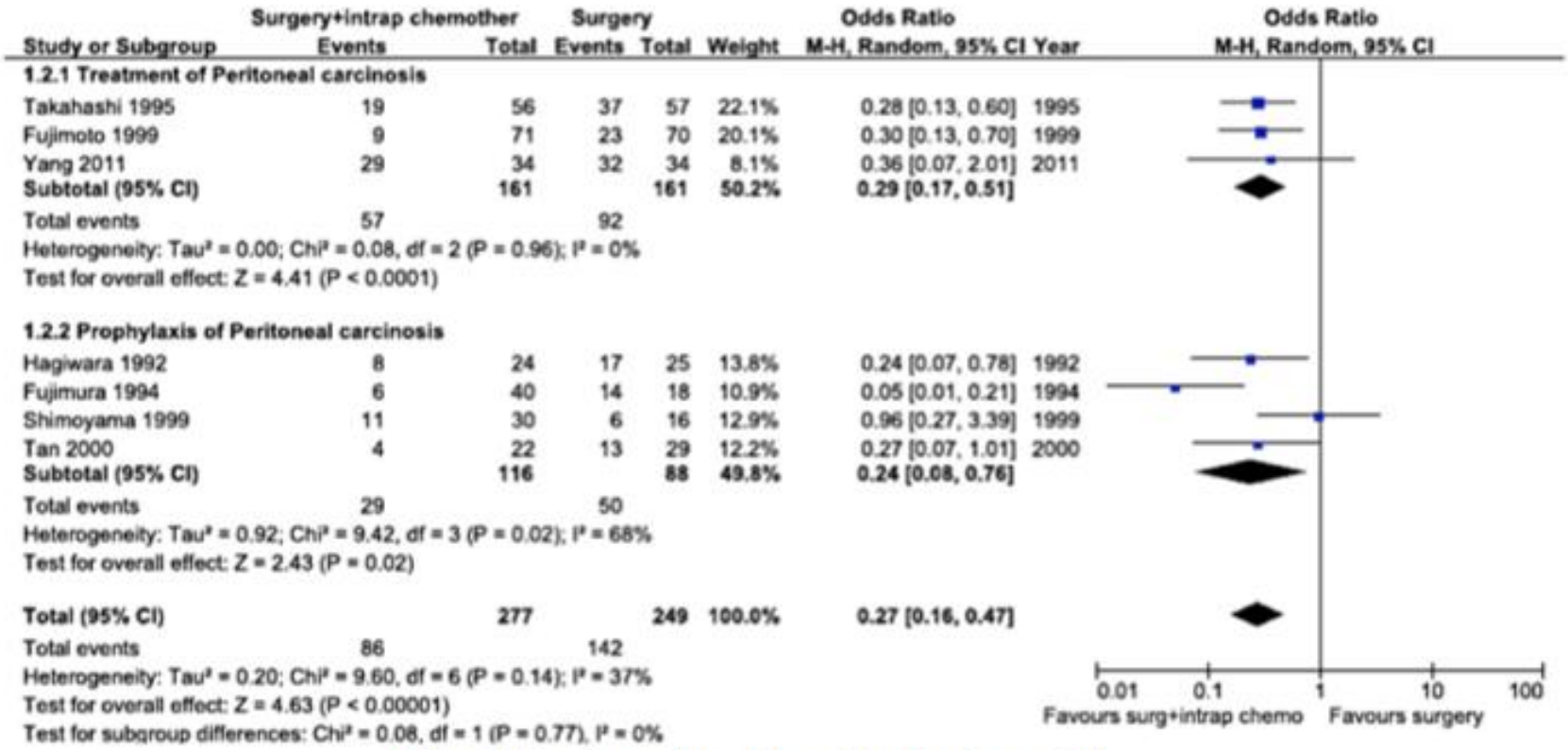


Figure 1. Overall mortality at 1 year (A) and at 2 years (B).

Overall mortality at 5 years

D

Study or Subgroup	Surgery+intrap chemother Events	Total	Surgery Events	Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
1.4.1 Treatment of Peritoneal carcinosis							
Sautner 2004	26	33	26	34	7.8%	1.14 [0.36, 3.61]	2004
Miyashiro 2011	54	135	52	133	34.6%	1.04 [0.64, 1.69]	2011
Subtotal (95% CI)		**168**		**167**	**42.3%**	**1.05 [0.67, 1.65]**	
Total events	80		78				
Heterogeneity: Tau² = 0.00; Chi² = 0.02, df = 1 (P = 0.88); I² = 0%							
Test for overall effect: Z = 0.23 (P = 0.82)							
1.4.2 Prophylaxis of Peritoneal carcinosis							
Hamazoe 1993	18	42	21	40	13.0%	0.68 [0.28, 1.62]	1993
Ikeguchi 1995	38	78	51	96	25.1%	0.84 [0.46, 1.52]	1995
Yonemura 2001	44	92	17	47	18.2%	1.62 [0.79, 3.33]	2001
Kuramoto 2009	50	59	29	29	1.3%	0.09 [0.01, 1.60]	2009
Subtotal (95% CI)		**271**		**212**	**57.7%**	**0.89 [0.49, 1.63]**	
Total events	150		118				
Heterogeneity: Tau² = 0.16; Chi² = 5.49, df = 3 (P = 0.14); I² = 45%							
Test for overall effect: Z = 0.37 (P = 0.71)							
Total (95% CI)		**439**		**379**	**100.0%**	**0.99 [0.71, 1.37]**	
Total events	230		196				
Heterogeneity: Tau² = 0.02; Chi² = 5.61, df = 5 (P = 0.35); I² = 11%							
Test for overall effect: Z = 0.09 (P = 0.93)							
Test for subgroup differences: Chi² = 0.19, df = 1 (P = 0.67), I² = 0%							

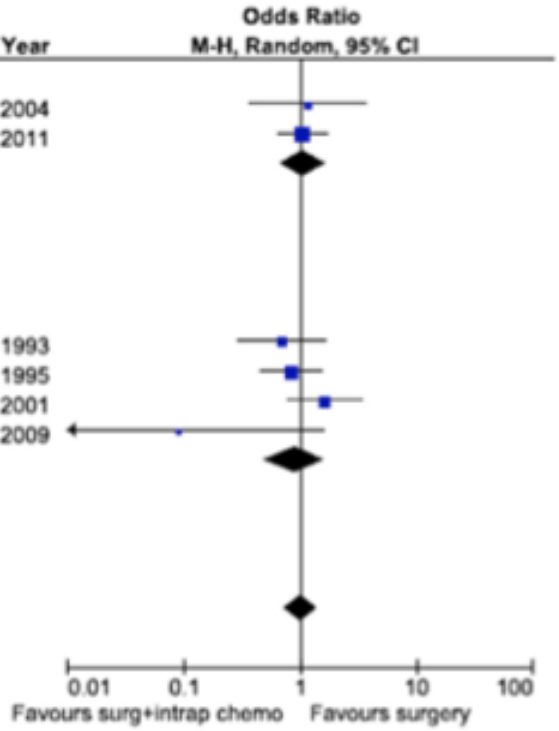


Figure 2. Overall mortality at 3 years (C) and at 5 years (D).

Peritoneal recurrencerate

B

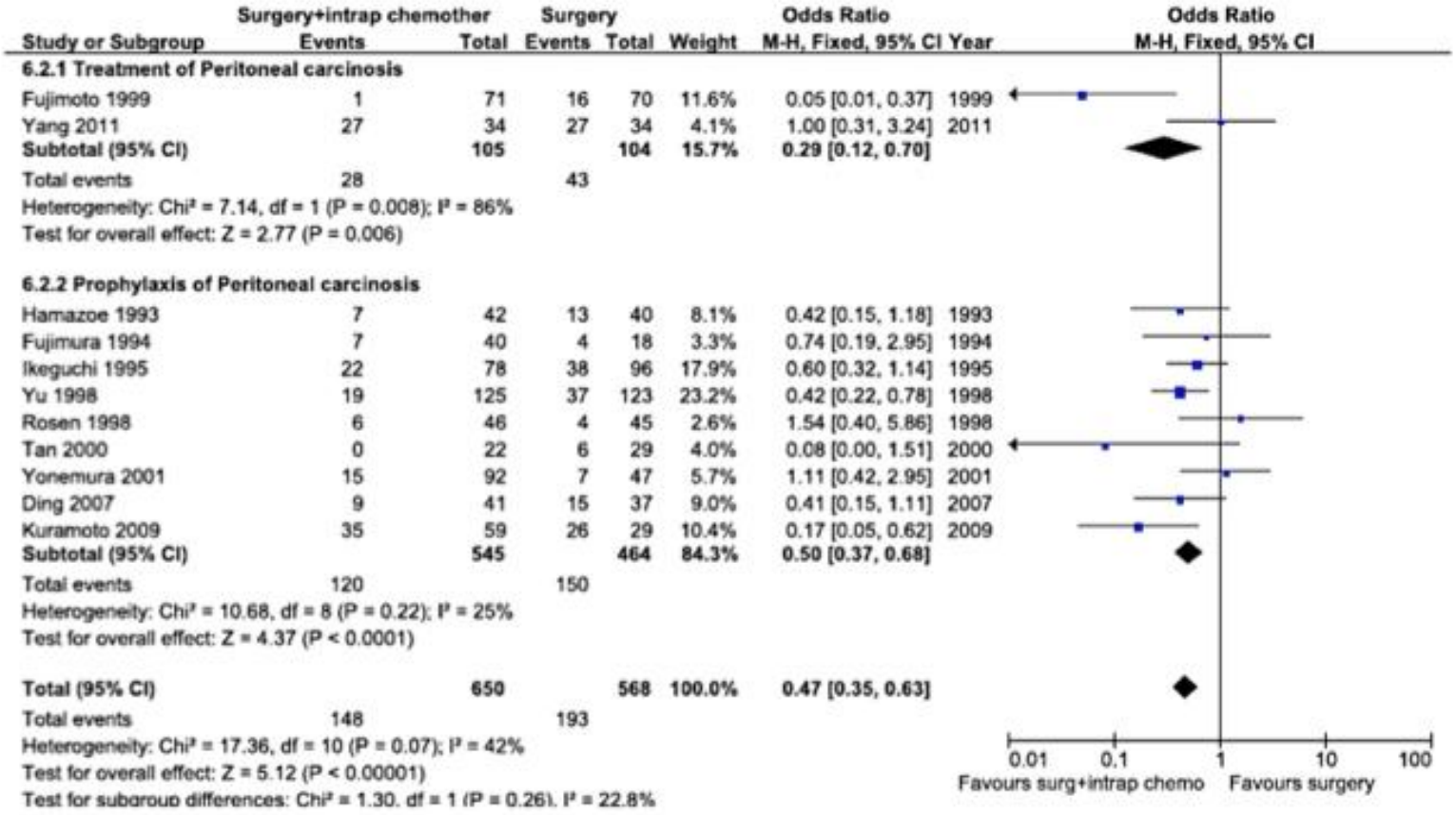


Figure 3. Recurrence rate: overall (A) and peritoneal (B).

HIPEC

- 1, 2 and 3-year overall survival is incremented by the IPC.
- A positive effect of IPC has been found on overall and peritoneal recurrence and on distant metastasis.
- Morbidity rate is incremented by IPC.
- Loco-regional lymph-nodes invasion in patients affected by advanced gastric cancer is not a contraindication to IPC.

Assessment of Response Following Neoadjuvant Therapy-Biopsy

- **Endoscopic biopsy after CRT has been used to determine response**
- N: 156 patients (MSKCC), CRT for local-regionally advanced esophageal cancer -> biopsy -> resection
- **118 patients had no tumor identified on endoscopic biopsy:**
  - 69% had local disease at time of surgery
  - Negative biopsy better predicted a pCR for squamous cell carcinoma versus adenocarcinoma (54.3% vs 13.6% P<0.001).
  - Nodal status of surgical specimens did not correlate
  - Survival was equivalent
- **CONCLUSION: A negative endoscopic biopsy is not a useful predictor of a pCR after CRT, final nodal status, or overall survival**

Sarkaria IS, et al. Ann Surg. 2009.

Assessment of Response Following Neoadjuvant Therapy

- PET is useful in restaging after CRT to exclude distant metastasis
- Multiple studies are looking at prognostic value after CRT or chemotherapy
- Preliminary results suggest that PET/CT can potentially be a prognosticator for OS, but data on meaningful prediction of response are lacking

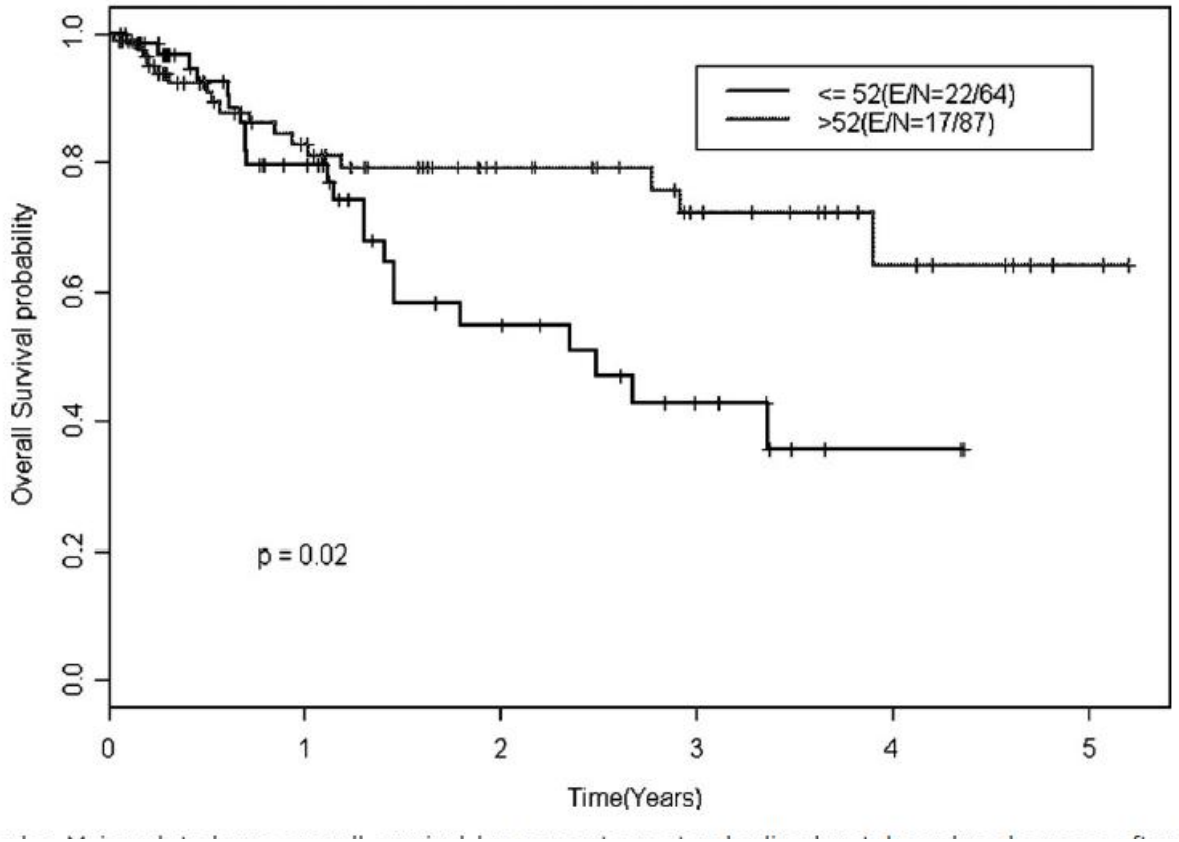
Assessment of Response Following Neoadjuvant Therapy

- Retrospective analysis
- n:152 (Esoph/GEJ ACA) CRT and surgery
- >52% SUV decrease was associated with improved OS (43% vs 72% at 3 y)
- Pathologic response with <50% residual cancer associated with longer OS

- **SUV decrease is the only prognostic factor of OS** (multivariate analysis)

Javeri H et al. Cancer. 2009

Assessment of Response Following Neoadjuvant Therapy-PET/CT



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Javeri H et al. Cancer. 2009

Original Article

A Prospective Evaluation of the Utility of 2-Deoxy-2-[^{18}F]Fluoro-D-Glucose Positron Emission Tomography and Computed Tomography in Staging Locally Advanced Gastric Cancer

Elizabeth Smyth, MD[1]; Heiko Schöder, MD[2]; Vivian E. Strong, MD[3]; Marinela Capanu, PhD[4]; David P. Kelsen, MD[1]; Daniel G. Coit, MD[3]; and Manish A. Shah, MD[1]

Cancer November 15, 2012

Aim: to prospectively examine, the potential added benefit of FDG-PET/CT to modern gastric cancer staging paradigms.

Table 1. Patient Characteristics

Characteristic (n = 113)		Value
Sex		
Male	68	(60%)
Female	45	(40%)
Median age, y	61	(range: 25-83 y)
Site		
Gastric	71	(63%)
Proximal/gastroesophageal junction	42	(37%)
Lauren's Classification		
Intestinal	38	(34%)
Diffuse	52	(46%)
Mixed	12	(11%)
Not reported	11	(9%)
Differentiation		
Moderate	25	(22%)
Moderate-poor	11	(10%)
Poor	77	(68%)
Stage		
≥T3[a]	112	(99%)
≥N1	70	(62%)

[a] 1 patient with T1N1 tumor on endoscopic ultrasound.

Table 4. PET/CT Sensitivity and Specificity Among the Subset of Patients With Gastric Cancer Who Have Fluorodeoxyglucose-Avid Primary Tumors (n = 76)

	Metastatic Cancer Confirmed			Positive Predictive Value
	Yes	No	Total	
PET/CT-Positive	11	1	12	91.7% (95% CI: 62%-99.8%)
PET/CT-Negative	11	53	64	
Total	22	54	76	

CI indicates confidence interval; PET/CT, positron emission tomography/computed tomography.
Sensitivity for M1 50% (95% CI: 28%-72%) Specificity for M1 98% (95% CI: 90%-100%)

Table 5. PET/CT Sensitivity and Specificity Among the Subset of Patients With Gastric Cancer Who Have a Negative Laparoscopy

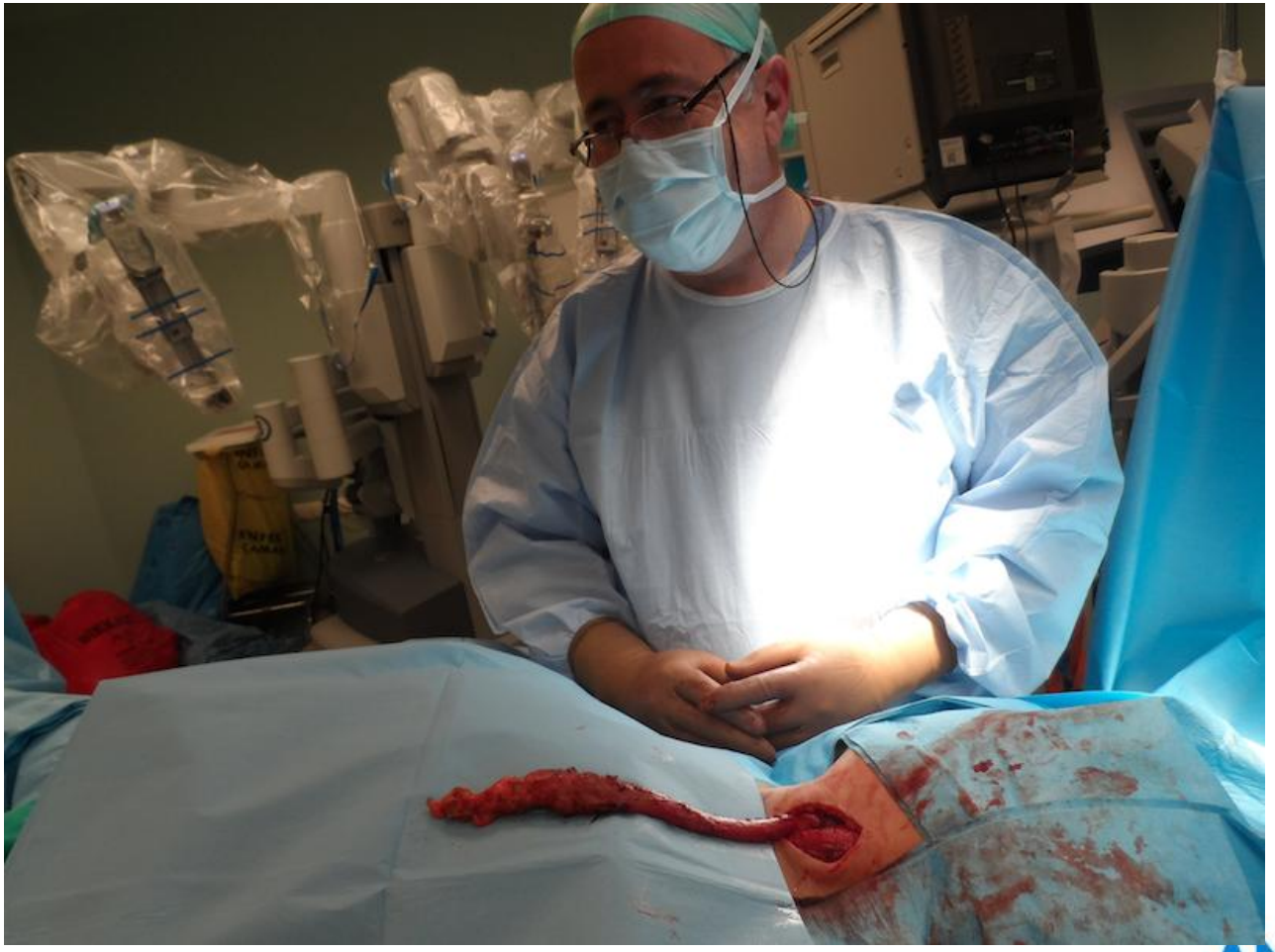
	Metastatic Cancer Confirmed			Positive Predictive Value
	Yes	No	Total	
PET/CT-Positive	10	1	11	90.9% (95% CI: 66%-90.9%)
PET/CT-Negative	0	81	81	
Total	10	82	92	

CI indicates confidence interval; PET/CT, positron emission tomography/computed tomography.
Sensitivity for M1 100% (95% CI: 73%-100%) Specificity for M1 99% (95% CI: 96%-99%)

- **PET CT can spare 27% of patients from unnecessary surgery.**

- The use of FDG- PET/CT appears to add significantly to clinicans ability to correctly stage locally advanced gastric cancer prior to surgery

Happyme



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