UNIVERSITÀ CATTOLICA del Sacro Cuore

I tumori della giunzione esofago-gastrica

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Premessa

Istologia prevalente nei tumori della Giunzione Esofago-Gastrica è l’adenocarcinoma (AGEG)

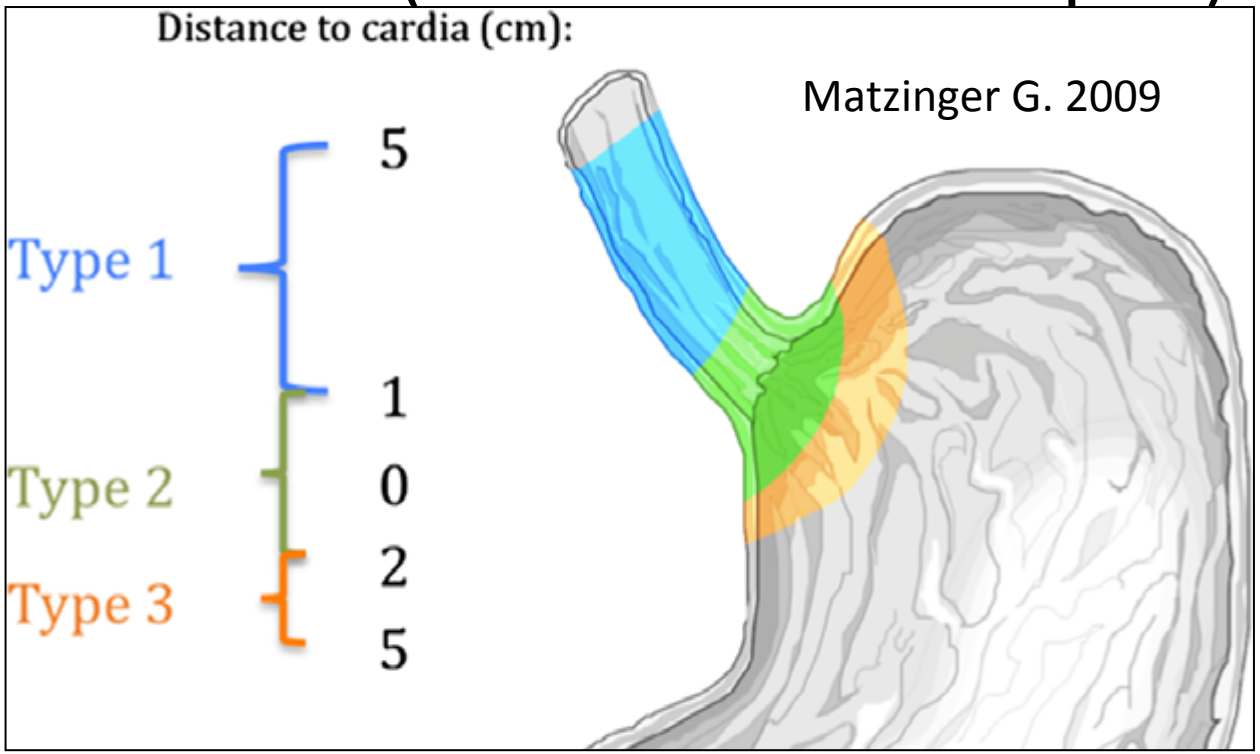
INDICE

- Classificazione dell'AGEG
- Problemi metodologici nell'inquadramento dell'AGEG
- Approccio terapeutico all' ADEG
- Prospettive future nella terapia dell'AGEG
- Note di tecnica radioterapica

INDICE

- Classificazione dell’AGEG

AGEG: Classificazione di Siewert (anatomia endoscopica)



GEG:"Upper end of the typical longitudinal fold of the gastric mucosa)

Siewert JR. B. J. Surg. 1998

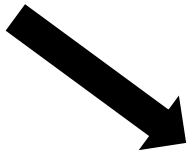
AGEG: problematiche di inquadramento

Approccio terapeutico
Carcinoma Esofago

Immagine esofago

Squamo-cellulare = Adenocarcinoma

Adenocarcinoma Cardias



Carcinoma Gastrico

Crehange G. Cancer Radiother. 2008

AGEG: entità specifica

Ca Esofago **Ca Gastrico**

AGEG

Epidemiologia
Patogenesi
Prognosi

AGEG: Epidemiologia

- L’ incidenza del AGEG è aumentata a partire dagli anni 70 (Nord America e Europa)

Botterweck et al. 2000

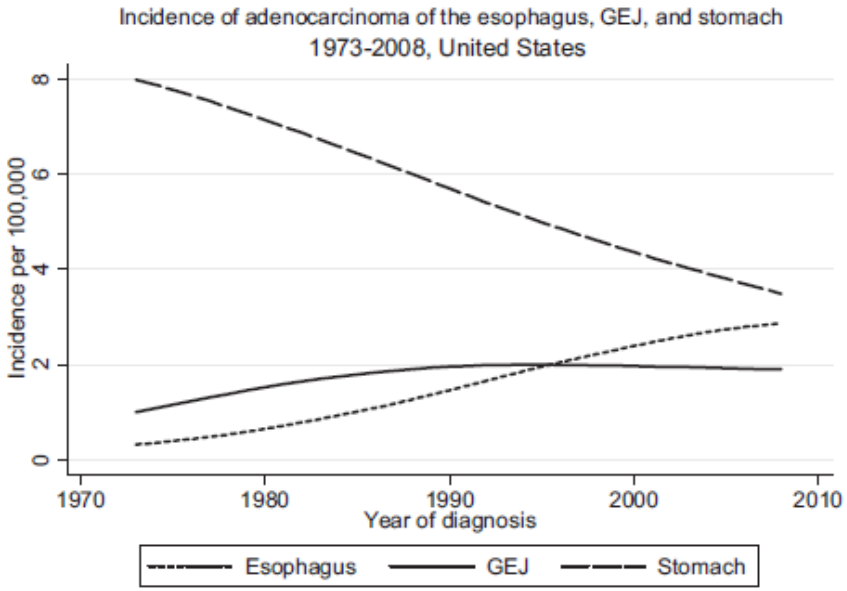


Figure 1 Trends in incidence of adenocarcinoma of the esophagus, gastroesophageal junction (GEJAC), and noncardia stomach in the United States, 1973-2008 (per 100,000, adjusted for age, race, and sex to the 2000 U.S. standard population, with lowess smoothing). Data from the National Cancer Institute's SEER Program (SEER* Stat Database: Incidence: SEER 9 Regs Public Use, November 2010 submission).

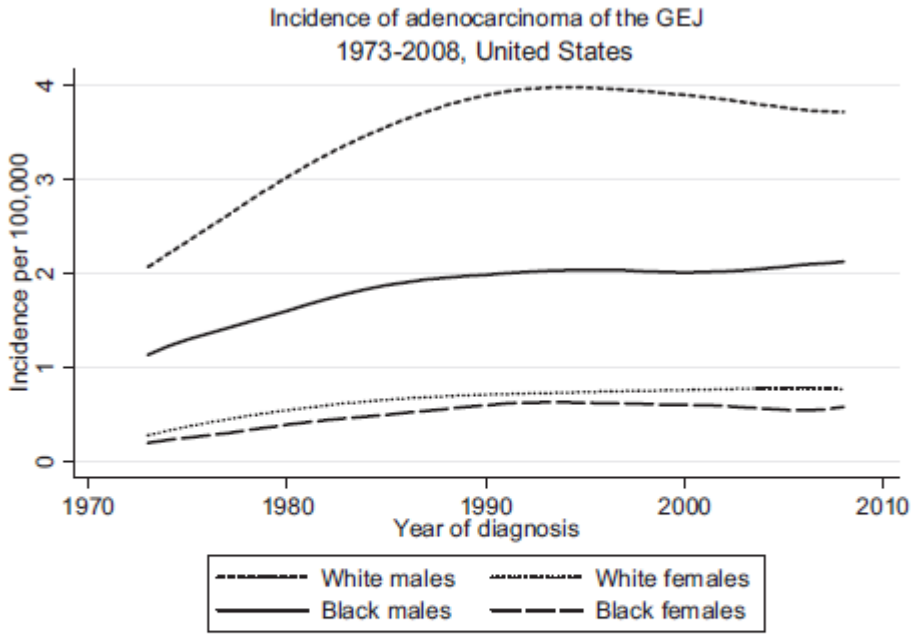
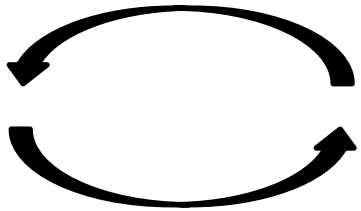


Figure 2 Trends in incidence of GEJAC in the United States by race and gender, 1973-2008 (per 100,000, age-adjusted to the 2000 U.S. standard population, with lowess smoothing). Data from the National Cancer Institute's SEER Program (SEER* Stat Database: Incidence: SEER 9 Regs Public Use, November 2010 submission).

Errori di registrazione

Ca Gastrico
Ca Esofogo



AGEG

Studio Svedese:
variazione incidenza AGEG da -15% a +45%

Ekstrom AM. J Nat. Cancer Inst 1999

AGEG: Fattori di rischio

FUMO → > rischio AGEG (ORs 2-4)

Laghergren J. Int. J. Cancer 2010
Cook M.B. J. Natl Cancer Inst 2010

'65-'70
% fumatori → **< Incidenza SCC Esofago/ Ca Gastrico no cardias**

'70 > incidenza AGEG

Holmes SR. Semin. Radiat Oncol 2007
Abrams JA. Cancer Epidemiol Biomarkers 2011

AGEG: Fattori di Rischio

Reflusso GE → > rischio AGEG (ORs 2-13)

Obesità → > rischio AGEG (ORs 2-3.6)

H. Pylori → < rischio AGEG (ORs 0.3-0.4)

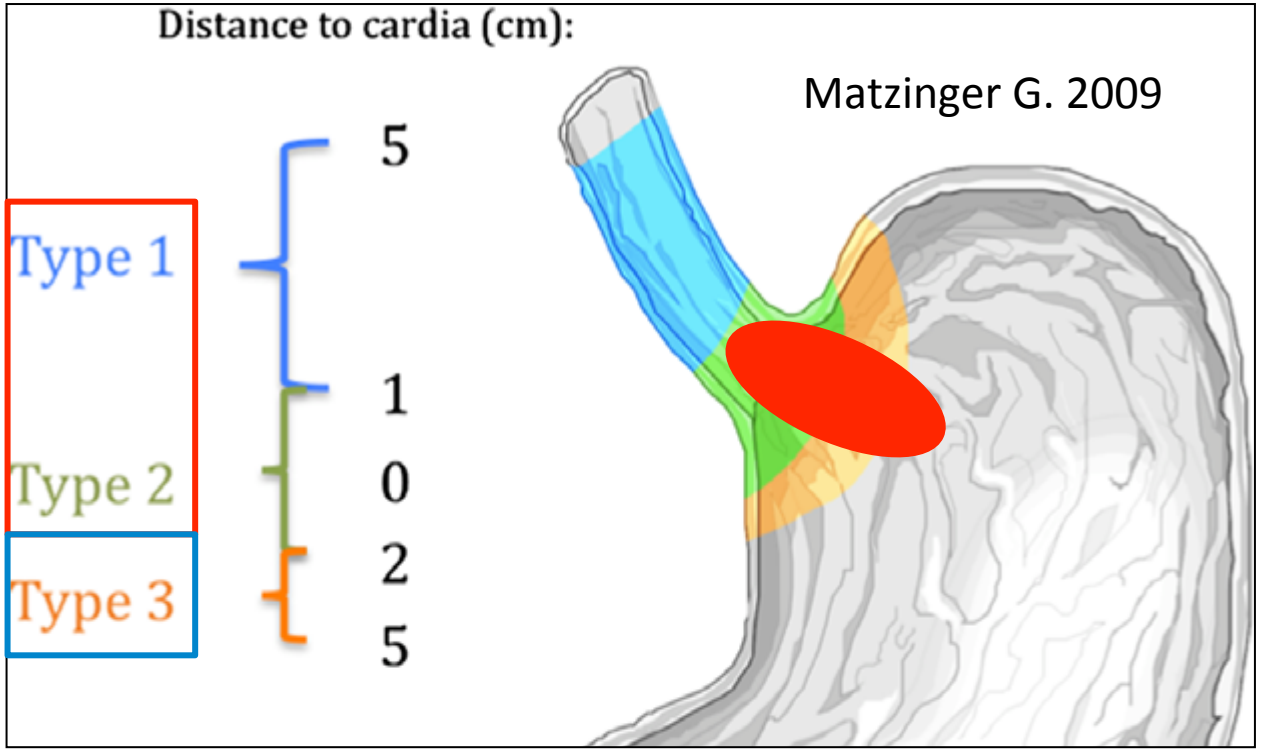
Witheman DC. Gut 2008
O'Doerthy MG Gut 2012
Kamangar F. J NatlCancer Inst 2006

AGEG e AED

Clinical charateristics, biologic behavior and survival after esophagectomy are similar for adenocarcinoma of the GEJ and the distal esophagus

Leers JM. J Thorac Cardiovasc Surg 2009

TNM – AJCC 7° EDITION 2010



Sottosede Tumore Esofageo ADCA

Sottosede Tumore Gastrico

INDICE

- Classificazione dell'AGEG
- Problemi metodologici nell'inquadramento dell'AGEG

AGEG: Problemi metodologici

Trials Clinici non idonei per definire un corretto standard terapeutico

Carcinoma Esofago: SCC e ADCA

Forme prossimali e distali

ADCA: mix

Esofago
AGEG

Gastrico no cardias

AGEG: Problemi metodologici

Trials Clinici non idonei per definire un corretto standard terapeutico

Carcinoma Esofago: SCC e ADCA

Forme prossimali e distali

ADCA: mix

Esofago

AGEG

Gastrico no cardias

Table 4 Selected Randomized Trials Including Patients with Distal and Gastroesophageal Junction Adenocarcinoma

Study	Percentage of Patients with Adenocarcinoma	Percentage of Patients with Distal Esophagus and GE Junction Tumors	
INT-113 (Kelsen et al[36,37])	53%	54%	I
MAGIC (Cunningham et al[12])	100%	26%	S
MRC OEO2[11,38]	66%	66%	S
FNCLCC-FFCD (Ychou et al[13])	100%	75%	S
German Oesophageal Cancer Study Group (Stahl et al[39])	100%	100%	S
Trinity College (Walsh et al[40])	76%	75%	I
Trans-Tasman and Australasian (Burmeister et al[41])	62%	62%	I
al[14,17])			
University of Amsterdam and Rotterdam (Hulscher et al[10])	100%	100%	S
JCOG 9502 (Sasako[32])	100%	96%	S
German Oesophageal Cancer Study Group (Stahl et al[39])	100%	100%	S
CROSS (Van Hagen et al[8])	75%	82%	S
ECOG 1201 (Kleinberg et al[15])	100%	89%	I

GE, gastroesophageal; 5-FU, fl

non informazioni sottogruppo AGEG

Kleinberg L. Semin. Radiat Oncol 2013

AGEG: Problemi metodologici

Futuro: trials disegnati per AGEG per migliorare le terapia e i risultati

Oggi: linee guida dai trials a disposizione

INDICE

- Classificazione dell'AGEG
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- Approccio terapeutico all' ADEG

AGEG: Approccio Terapeutico

Chirurgia:

stadi iniziali

Number of Nodes	Number of Patients	5-Year Survival	10-Year Survival
0	697	63%	51%
1-2	300	33%	22%
2-6	268	20%	12%
>6	466	8%	3%

Gertler R. Ann Surg 2011

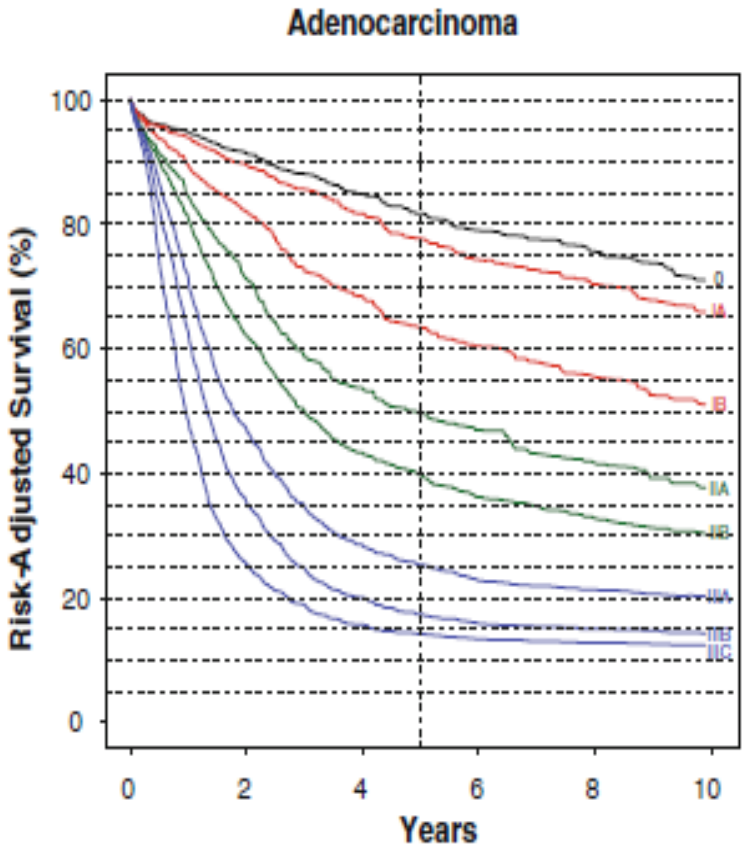


FIG. 1 Risk-adjusted survival for adenocarcinoma according to the American Joint Committee on Cancer *Cancer Staging Manual*, 7th edition, stage groups

Rice TW. Cancer 2010

AGEG: Approccio Terapeutico

Approccio multimodale:
N+ e T oltre la sottomucosa

Quando rispetto alla chirurgia ?

Neoadiuvante

Adiuvante

Quale terapia oltre la chirurgia ?

Chemioterapia

Radiochemioterapia

AGEG: Approccio Terapeutico

Table 4 Selected Randomized Trials Including Patients with Distal and Gastroesophageal Junction Adenocarcinoma

Study	Experimental Question	Published Eligibility for GE Junction	Percentage of Patients with Adenocarcinoma	Percentage of Patients with Distal Esophagus and GE Junction Tumors	Conclusions
INT-113 (Kelsen et al[36,37])	Benefit to neoadjuvant cisplatin/5-FU?	GE Junction allowed except tumors of gastric origin	53%	54%	No benefit to addition of cisplatin and 5-FU added to surgery alone
MAGIC (Cunningham et al[12])	Benefit to neoadjuvant cisplatin/5-FU?	Adenocarcinoma of lower third of esophagus and GE junction and stomach	100%	26%	Survival benefit with neoadjuvant cisplatin and 5-FU added to surgery alone
MRC OEO2[11,38]	Pre- and postoperative epirubicin, cisplatin, and 5-FU?	Included tumors of lower third of esophagus plus cardia (75%)	66%	66%	Survival benefit with neoadjuvant cisplatin and 5-FU added to surgery alone
FNCLCC-FFCD (Ychou et al[13])	Pre- and postoperative cisplatin, and 5-FU?	Lower third and GE junction (75%) and stomach	100%	75%	Survival benefit with neoadjuvant cisplatin and 5-FU added to surgery alone
German Oesophageal Cancer Study Group (Stahl et al[39])	Preoperative cisplatin, 5-FU, and radiation?	Lower third of esophagus and cardia (97/130)	100%	100%	Survival benefit with neoadjuvant chemoradiation added to surgery alone
Trinity College (Walsh et al[40])	Cisplatin, vinblastine, 5-FU, and radiation?	Esophageal cancer, GE junction allowed	76%	75%	Nonsignificant survival benefit with neoadjuvant chemoradiation
Trans-Tasman and Australasian (Burmeister et al[41])	Cisplatin, 5-FU, and radiation?	Included tumors involving cardia of primarily in the stomach	62%	62%	No benefit to this regimen added to surgery
CALGB 9781 (Tepper et al[15])	Cisplatin, 5-FU, and radiotherapy?	Esophageal cancer, including GE junction with <2-cm extension into cardia (not specified)	77%	75%	Benefit to addition of this therapy to surgery, but small number of patients enrolled
SWOG 0116 (Macdonald et al[14,17])	Adjuvant 5-FU, leucovorin, and radiotherapy?	Stomach and GE junction/ cardia (20%)	100%	20%	Benefit to this regimen when added postoperatively, largely enrolled patients with gastric cancer
University of Amsterdam and Rotterdam (Hulscher et al[10])	Surgery only, resection by thoracotomy vs transhiatal approach?	Mid to distal esophagus, including cardia, if also involves the distal esophagus	100%	100%	Similar survival with either surgical approach
JCOG 9502 (Sasako[32])	Surgery only, resection by thoracotomy vs transhiatal approach?	Gastric cardia and body involving GE junction, no >2 cm extension into esophagus	100%	96%	Similar survival with either surgical approach
German Oesophageal Cancer Study Group (Stahl et al[39])	Benefit to adding radiation to cisplatin, 5-FU, etoposide neoadjuvant chemotherapy?	Gastroesophageal junction adenocarcinoma, type I-III	100%	100%	Study closed owing to poor accrual. Benefit in response and R0 resection and nonsignificant survival benefit trend
CROSS (Van Hagen et al[6])	Preoperative paclitaxel, carboplatin, and radiation?	Esophagus or GE junction (tumors involving both cardia and esophagus)	75%	82%	Survival benefit to this neoadjuvant regimen
ECOG 1201 (Kleinberg et al[16])	Preoperative paclitaxel/cisplatin/ radiation or preoperative irinotecan/cisplatin/radiation?	Adenocarcinoma of the esophagus with no >2 cm extension into the cardia	100%	89%	No suggestion of superiority of either regimen

GE, gastroesophageal; 5-FU, fluorouracil.

Chemioterapia **Radiochemioterapia**

AGEG: Radiochemioterapia neoadiuvante

113 pz

100% Adenocarcinomi

Esofago medio 14.1%
Esofago distale e Siewert I-III 85.9%

	CH	Preop. RT-CT (CDDP/5-FU + 40Gy)
pCRR		25%
N+	82%	25%
SVV mediana	11 mesi	16 mesi
SVV 5 aa	6%	32%

Walsh TN. N Engl J med 1996

AGEG: Radiochemioterapia neoadiuvante

100 pz 75% Adenocarcinomi

	CH	Preop. RT-CT (CDDP/vinblastina + 45Gy)
pCRR		28%
SVV mediana	16.9 mesi	17.6 mesi
SVV 3 aa	16%	30%

Urba SG. J Clin Oncol. 2001

AGEG: Radiochemioterapia neoadiuvante

56 pz (chiuso per scarso arruolamento)

75% Adenocarcinomi 75% GEG

	CH	Preop. RT-CT (CDDP/5-FU + 50Gy)
SVV mediana	1.7 anni	4.48 anni
SVV 5 aa	16%	39%

Tepper J. J Clin Oncol. 2008

AGEG: Radiochemioterapia neoadiuvante

168 pz 75% Adenocarcinomi Esofago distale e GEG 82%

	CH	Preop. RT-CT (Carbo/Paclitaxel + 40Gy)
pCRR		23%
N+	75%	21%
R0	69%	92%
SVV mediana	24 mesi	47 mesi
SVV 5 aa	34%	47%

Van Hagen P. N Engl J Med 2012

AGEG: Radiochemioterapia neoadiuvante

Fase II 100% Adenocarcinomi

	Preop RTCT Irinot/CDDP + 45 Gy	Preop RTCT Paclitaxel/CDDP + 45 Gy
pCRR	15%	17%
SVV mediana	35 mesi	24 mesi
SVV 5aa	46%	34%

Kleinberg L. J Clin Oncol 2012 Abstract

AGEG: CT o RT-CT neoadiuvante

SVV a 5 aa

CH	16-39%
CT	23-36%
RT-CT	27-47%

Table 1 Selected Prospective Randomized Trials Reporting 5-Year Survival Results

	5 Year Survival	Median Survival (Months)
Surgery alone		
Van Hagen et al[8]	34%	24
Urba et al[9]	16%	18
Hulscher[10]—transhiatal	27%	18
Hulscher[10]—transthoracic	39%	24
MRC[11]	17%	13.3
Cunningham et al[12]/MAGIC	23%	NR
Ychou et al[13]	24%	NR
Macdonald et al[14]	25%	27
Tepper et al[15]	16%	21
Neoadjuvant chemotherapy		
MRC[11]	23%	16.8
Ychou et al[13,*]	38%	NR
Cunningham et al[12,*]	36%	NR
Neoadjuvant chemoradiation		
Van Hagen et al[8]	47%	49
Tepper et al[15]	39%	54
Kleinberg et al[16,*] Irinotecan/ cisplatins	46%	35
Kleinberg et al[16,*] Paclitaxel/ cisplatin	27%	21

Kleinberg L. Semin Radiat Oncol 2012

AGEG: CT o RT-CT neoadiuvante

- Metanalisi: 1932 pz SCC o ADCA Esofago/GEG

Table 5 Metanalysis of Trials of Neoadjuvant Therapy for Adenocarcinoma of Esophagus and GEJ[44]

Neoadjuvant Therapy	All Patients (HR, 95% CI)	Adenocarcinoma (HR, 95% CI)
Chemoradiation	0.78 (0.70-0.88) $P < 0.0001$	0.75 (0.59-0.95) $P = 0.02$
Chemotherapy	0.87 (0.79-0.96) $P = 0.005$	0.83 (0.71-0.95) $P = 0.01$
Chemoradiation vs chemotherapy	0.88 (0.76-1.01) $P = 0.07$	

GEJ, gastroesophageal junction; HR, hazard ratio; CI, confidence interval.

Sjoquist KM. Lancet Oncol 2011

AGEG: CT o RT-CT neoadiuvante

European Journal of Cancer (2013) 49, 3149–3158

Available at www.sciencedirect.com

SciVerse ScienceDirect

journal homepage: www.ejcancer.com

Preoperative chemo(radio)therapy versus primary surgery
for gastroesophageal adenocarcinoma: Systematic review with
me

14 RCT ADCA Esofago Stomaco Giunzione
2422 pz (43% dati singolo paziente)

Ulri
Meinhard Kieser [d], Tracy E. Slanger [e], Bryan Burmeister [f], David Kelsen [g],
Donna Niedzwiecki [h], Christoph Schuhmacher [i], Susan Urba [j], Cornelis van de Velde [k],
Thomas N. Walsh [l], Marc Ychou [m], Katrin Jensen [d]

Study or Subgroup	log[Hazard Ratio]	SE	peri-op chemo Total	surgery Total	Weight	Hazard Ratio IV, Random, 95% CI
Wang 2000	-0.24512	0.17991	30	30	7.2%	0.78 [0.55, 1.11]
Kobayashi 2000	0.098082	0.25277	91	80	3.8%	1.10 [0.67, 1.81]
Urba 2001	-0.2941	0.25115	37	39	3.9%	0.75 [0.46, 1.22]
Walsh 2002	-0.59222	0.21071	58	55	5.4%	0.55 [0.37, 0.84]
FAMTX 2004	0.33895	0.30025	27	29	2.8%	1.40 [0.78, 2.53]
TROG-AGITG 2005	-0.003	0.1806	80	78	7.1%	1.00 [0.70, 1.42]
Zhao 2006	-0.65	0.58	34	20	0.8%	0.52 [0.17, 1.63]
MAGIC 2006	-0.28768	0.1118	250	253	16.1%	0.75 [0.60, 0.93]
RTOG 8911 2007	-0.10951	0.14306	115	121	10.8%	0.90 [0.68, 1.19]
CALGB 9781 2008	-0.79199	0.40777	23	19	1.5%	0.45 [0.20, 1.01]
Feng 2008	-0.23111	0.16167	27	25	8.7%	0.79 [0.58, 1.09]
OE02 2009	-0.15082	0.099816	265	268	19.1%	0.86 [0.71, 1.05]
EORTC 40954 2010	-0.17847	0.24482	72	72	4.1%	0.84 [0.52, 1.35]
ACCORD 07 2011	-0.36157	0.16056	113	111	8.8%	0.70 [0.51, 0.95]
Total (95% CI)			**1222**	**1200**	**100.0%**	**0.81 [0.73, 0.89]**

Heterogeneity: Tau² = 0.00; Chi² = 14.45, df = 13 (P = 0.34); I² = 10%
Test for overall effect: Z = 4.15 (P < 0.0001)

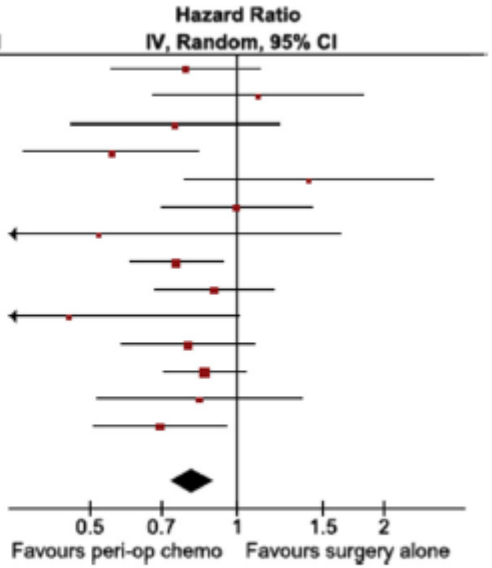
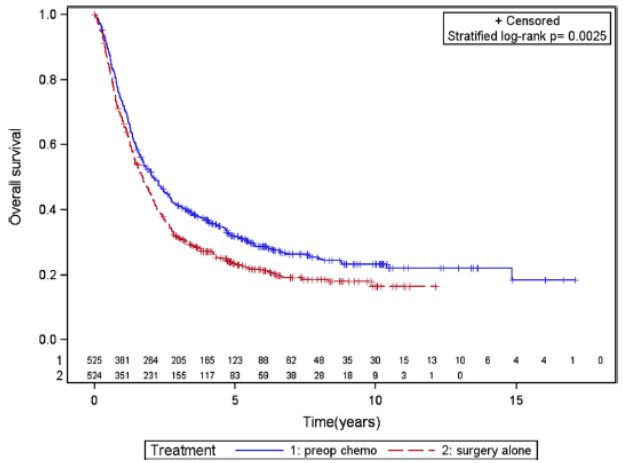


Fig. 2. Forest plot for the primary outcome overall survival (calculated using a random-effects model).



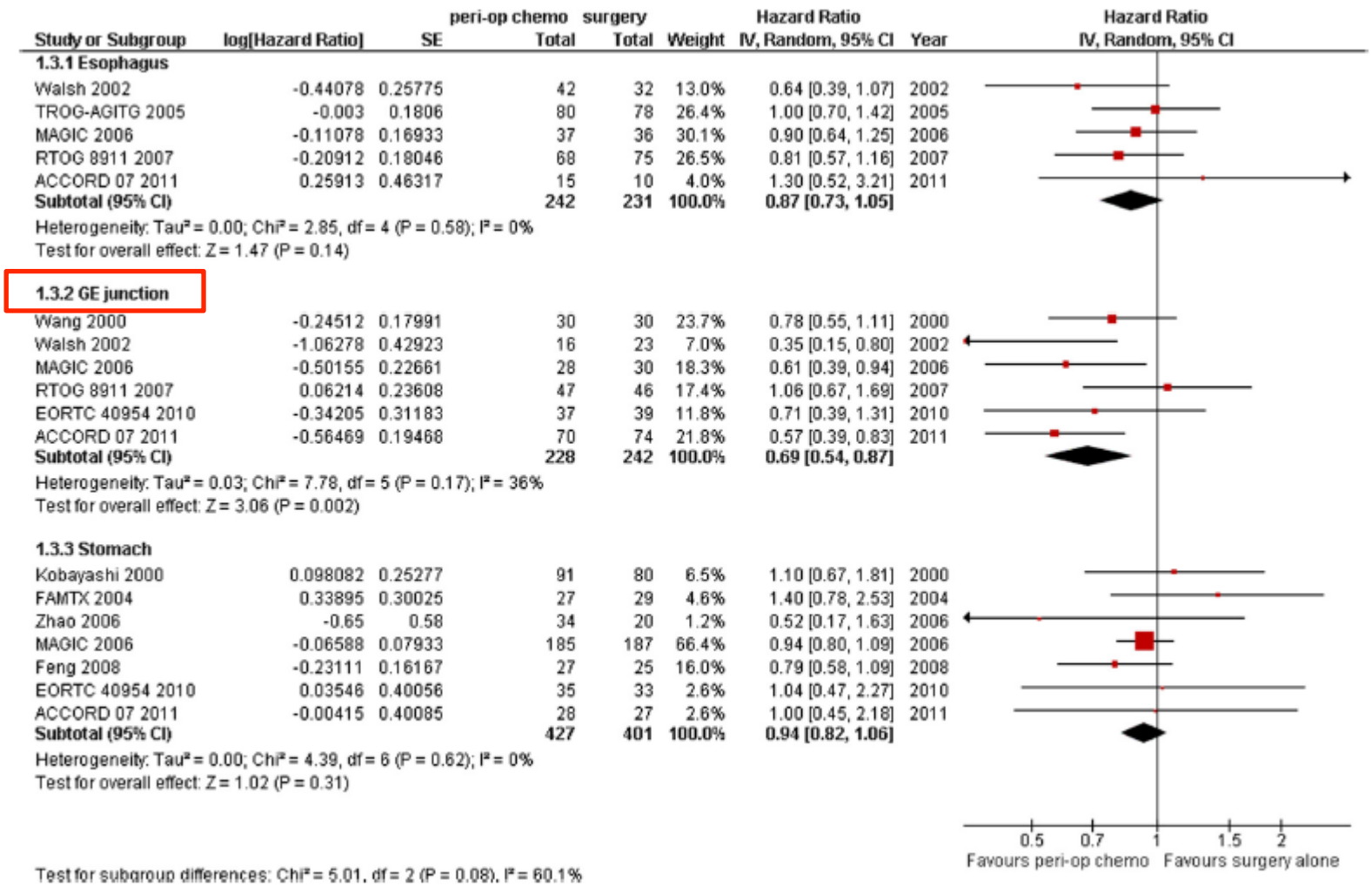
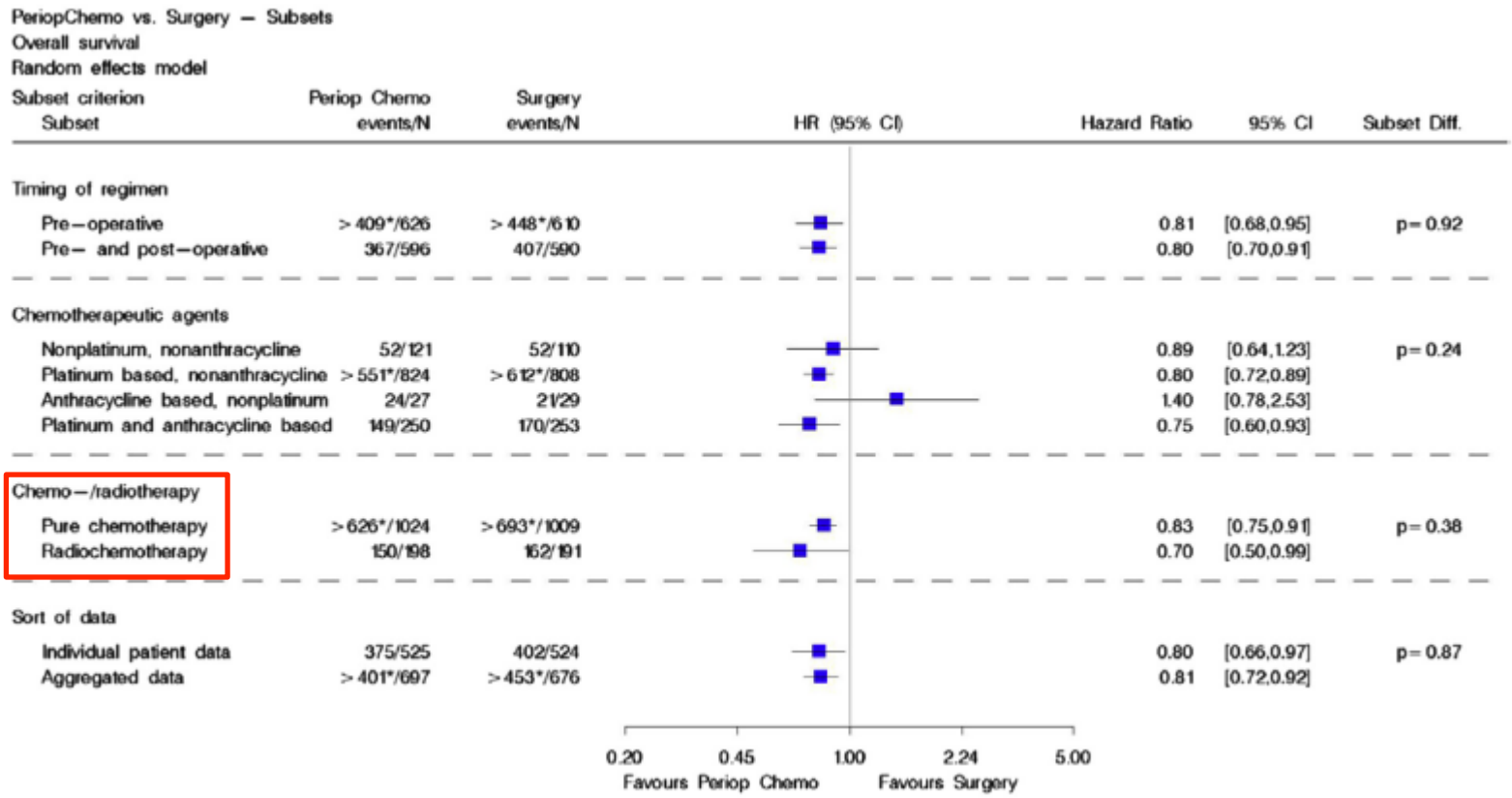


Fig. 5. Forest plot for overall survival by tumour site (calculated using random-effects models).


PeriopChemo vs. Surgery — Subsets
Overall survival
Random effects model
Subset criterion
Subset
Periop Chemo events/N
Surgery events/N
HR (95% CI)
Hazard Ratio
95% CI
Subset Diff.
Timing of regimen
Pre−operative >409*/626 >448*/610 0.81 [0.68,0.95] p=0.92
Pre− and post−operative 367/596 407/590 0.80 [0.70,0.91]
Chemotherapeutic agents
Nonplatinum, nonanthracycline 52/121 52/110 0.89 [0.64,1.23] p=0.24
Platinum based, nonanthracycline >551*/824 >612*/808 0.80 [0.72,0.89]
Anthracycline based, nonplatinum 24/27 21/29 1.40 [0.78,2.53]
Platinum and anthracycline based 149/250 170/253 0.75 [0.60,0.93]
Chemo−/radiotherapy
Pure chemotherapy >626*/1024 >693*/1009 0.83 [0.75,0.91] p=0.38
Radiochemotherapy 150/198 162/191 0.70 [0.50,0.99]
Sort of data
Individual patient data 375/525 402/524 0.80 [0.66,0.97] p=0.87
Aggregated data >401*/697 >453*/676 0.81 [0.72,0.92]
0.20
0.45
1.00
2.24
5.00
Favours Periop Chemo
Favours Surgery

AGEG: CT o RT-CT neoadiuvante

126/452 (chiuso per scarso arruolamento) 100% AGEG (Siewert I-III)

	Preop CT CDDP/5-FU	Preop CT-RTCT CDDP/5FU CDDP/etoposide + 45 Gy
pCRR	2%	16%
SVV mediana	28 mesi	48 mesi
SVV 3 aa	28%	48%

Sthal M. J Clin Oncol 2009

AGEG:Linee guida

NCCN	
T1bN+	**1° RT-CT preop.**
T2-T4a N0-N+	**2° CT preop.**
ESMO	
T1b-T2 N0	**1° CT preop.** **2° RT-CT preop.**
T2 N+	**1° RT-CT preop.**
T3-T4a N0-N+	**2° CT preop.**

AGEG: scelta terapia neoadiuvante

Presentazione
di malattia

PS
Comorbidità
Tossicità attesa

Monjazeb AM. Semin Radiat Oncol 2013

INDICE

- Classificazione dell'AGEG
- Problemi metodologici nell'inquadramento dell'AGEG
- Approccio terapeutico all' ADEG
- Prospettive future nella terapia dell'AGEG

AGEG: prospettive future

Targeted Therapies	ADCA esofago-gastrico M+	Risultati a favore della Targeted Therapies
Trastuzumab	(HER2+) CDDP/5FU +/- Transtuzumab	SVV mediana Tasso Risposta
Bevacizumab	CDDP/5-FU +/- Bevacizumab	NS
Cetuximab	ECF o IC o FOLFOX + Cetuximab	Tasso risposta ECF 57%
Panitumumab	EOC +/- panitumumab	Chiuso in anticipo

AGEG: prospettive future

Targeted Therapies	Radiochemioterapia in ADCA esogago-gastrico M0	Risultati a favore della Targeted Therapies
Trastuzumab Studio pilota	(HER2+) CDDP/Paclitaxel + 50 Gy + Transtuzumab per 1 anno	SVV 3 aa 47% No eventi avversi
Bevacizumab Fase II	Carbo/Paclitaxel/5-FU + 45Gy IC Bevacizumab + 45 Gy	pCRR 30% pCRR 12%
Cetuximab	CDDP/Paclitaxel +/- Cetuximab + 50 Gy	Chiuso in anticipo
Panitumumab	-	-

RTOG 1010: HER2+ , operabile, ADCA esofago e GEG
Carbo/Paclitaxel + 50 Gy +/- Trastuzumab

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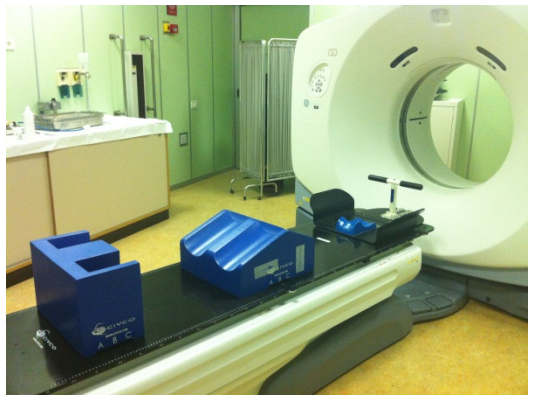
Tecnica Radioterapica

- Simulazione:
  - Immobilizzazione in posizione supina



  - Posizione prona migliora distanza midollo-esofago

Corn BW IJROBP 1991

Tecnica Radioterapica

- Simulazione:
  - Stomaco vuoto

Stomaco pieno non impatta su dose GTV 3DCRT o IMRT

Bouchard M. IJROBP 2010

- TC con mdc x os ed ev per definire alterazioni della superfice mucosa e stazioni linfonodali

Definizione del target

GTV

- Referto Endoscopia ed Ecoendoscopia
  (distanza da arcata dentale o giunzione esofago-gastrica)

- TC mdc torace-addome: limitata nel definire il GTV

Estensione del T corretta 42% Love VJ. Mol Imaging Biol 2005

Definizione del target

GTV

- PET: Estensione GTV correla con lunghezza T misurata all'esame istologico e con ecoendoscopia

Mamede M. Ann Nucl Med 2007
Jeganathan R. Eur J Nucl Med Mol Imaging 2011

- PET: Soglia SUV di 2.5 o metodo visivo correlano con estensione del GTV

Muijs CT. Radiother Oncol 2010
Jeganathan R. Eur J Nucl Med Mol Imaging 2011

- PET: modifica nel 69% dei pazienti il GTV definito alla TC di simulazione

Maureau L. IJROBP 2005

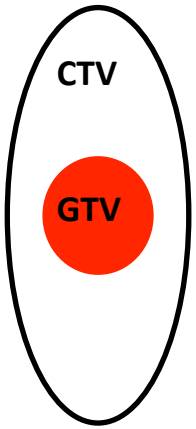
Definizione del target

CTV t

- Malattia microscopica:
  - 3 cm dal margine prossimale
  - 5 cm dal margine distale

Gao XS. IJROBP 2007

Margini CTV t
5 cm cc
1.5-2 cm radiali



Pepek JM. Semin Radiat Oncol 2013

Definizione del target

CTV n

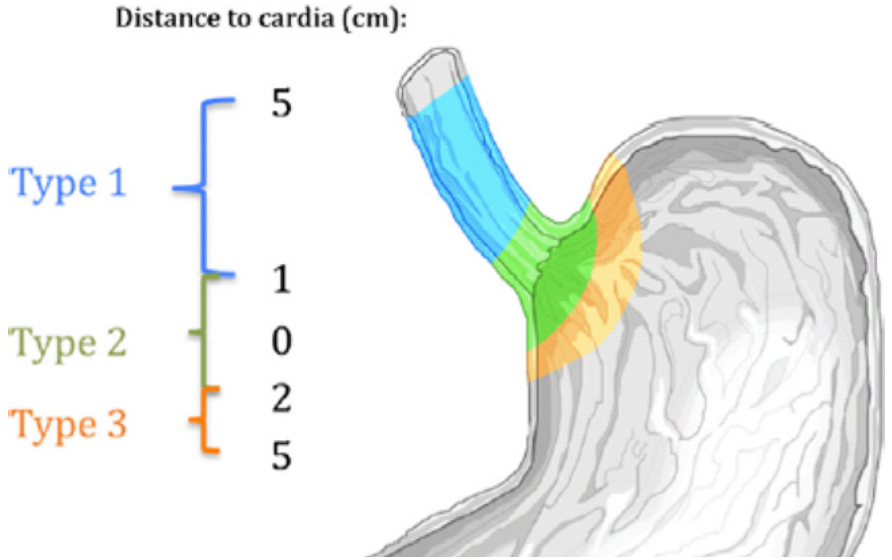
Interessamento linfonodale dopo chirurgia nel 70% dei pazienti con AGEG Tipo I-II

N mediastinici

- paraesofagei
- paraortici
- tracheobronchiali

N addominali

- paracardiali
- gastrici di sinistra
- piccola curvatura



Dresder SN. Surgery 2001

Radiotherapy and Oncology 92 (2009) 164–175

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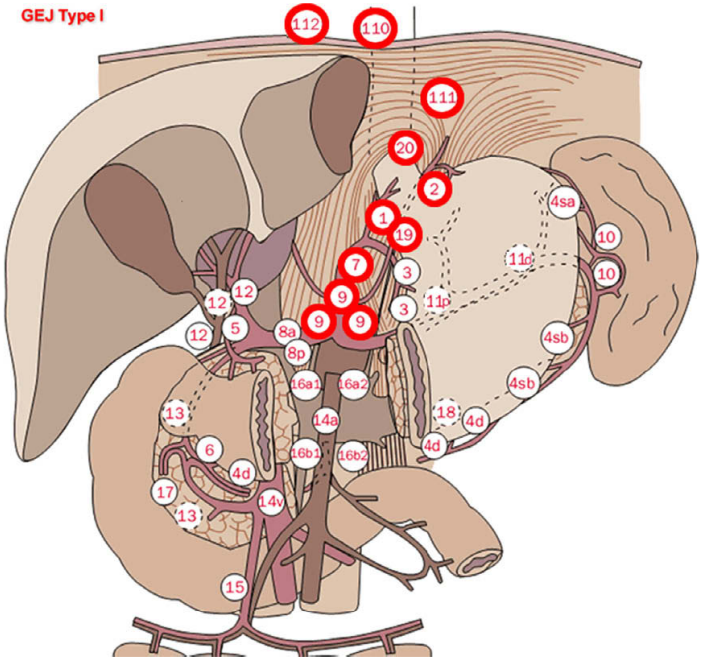
journal homepage: www.thegreenjournal.com

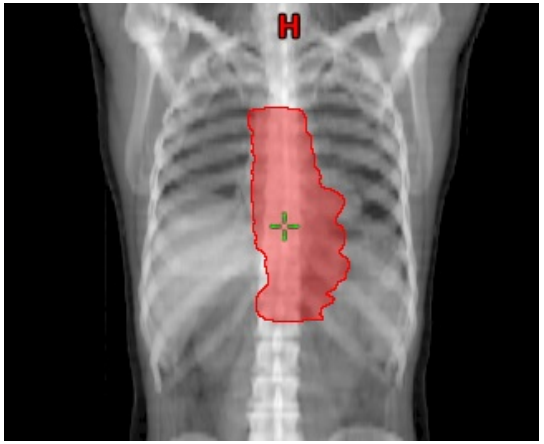
Guidelines

EORTC-ROG expert opinion: Radiotherapy volume and treatment guidelines for neoadjuvant radiation of adenocarcinomas of the gastroesophageal junction and the stomach

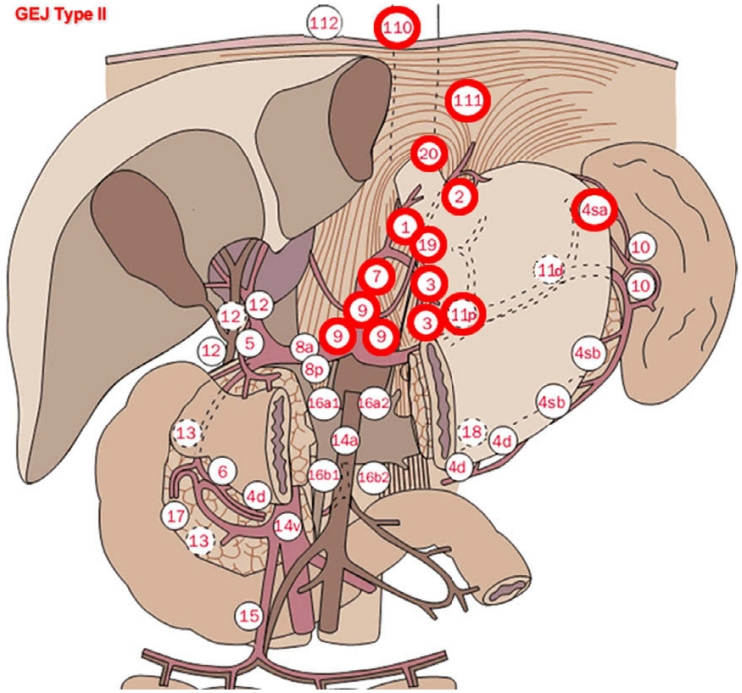
Oscar Matzinger [a,b,*], Erich Gerber [c], Zvi Bernstein [d], Philippe Maingon [e], Karin Haustermans [f], Jean François Bosset [g], Akos Gulyban [a], Philip Poortmans [h], Laurence Collette [a], Abraham Kuten [d]

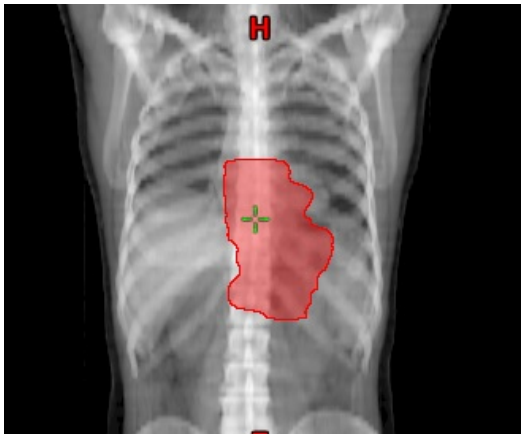
Tumour localization	Elective lymph node stations numbers and name	
GEJ type I	1	Right paracardial LN
	2	Left paracardial LN
(Figs. 3, 4 and 10)	7	LN along the left gastric artery
	9	LN around the celiac artery
	19	Infradiaphragmatic LN
	20	LN in the oesophageal hiatus of the diaphragm
	110	Paraoesophageal LN in the lower thorax
	111	Supradiaphragmatic LN
	112	Posterior mediastinal LN



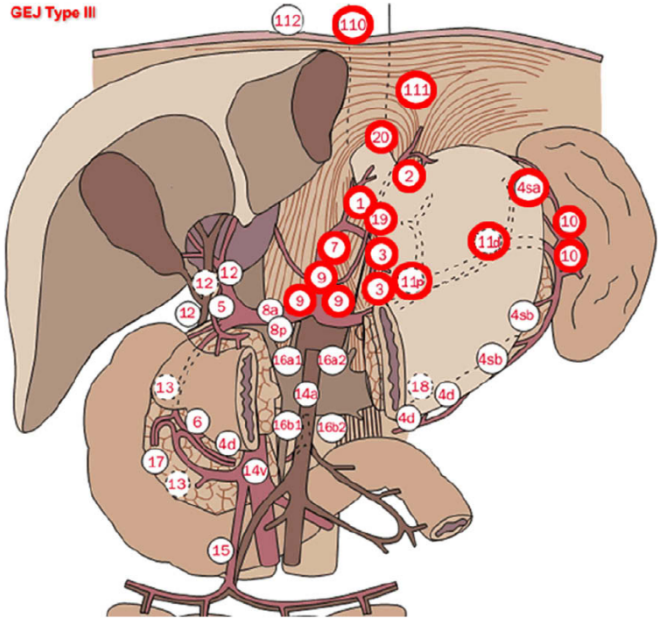


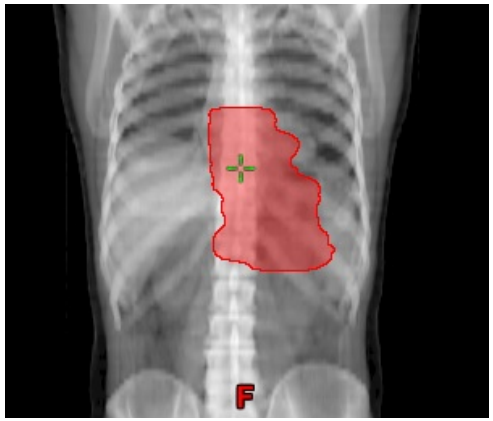
Tumour localization	Elective lymph node stations numbers and name	
GEJ type II	1	Right paracardial LN
	2	Left paracardial LN
(Figs. 3, 5 and 10)	3	LN along the lesser curvature
	4sa	LN along the short gastric vessels
	7	LN along the left gastric artery
	9	LN around the celiac artery
	11p	LN along the proximal splenic artery
	19	Infradiaphragmatic LN
	20	LN in the oesophageal hiatus of the diaphragm
	110	Paraoesophageal LN in the lower thorax
	111	Supradiaphragmatic LN





Tumour localization	Elective lymph node stations numbers and name	
GEJ type III	1	Right paracardial LN
	2	Left paracardial LN
(Figs. 3, 6 and 10)	3	LN along the lesser curvature
	4sa	LN along the short gastric vessels
	7	LN along the left gastric artery
	9	LN around the celiac artery
	10	LN at the splenic hilum
	11p	LN along the proximal splenic artery
	11d	LN along the distal splenic artery
	19	Infradiaphragmatic LN
	20	LN in the oesophageal hiatus of the diaphragm
	110	Paraoesophageal LN in the lower thorax
	111	Supradiaphragmatic LN





Definizione del target

Internal Margin

Esofago distale e GEG hanno un movimento respiratorio maggiore dell'esofago medio-prossimale in direzione CC

Studi con TC 4D:

movimento di lesioni GEG

< 0.75 cm radiale

< 1.5 cm CC

Yaremko BP. IJROBP 2008
Zhao KL. Radioth Oncol 2007
Wysocka B. IJROBP 2010

Definizione del target

Internal Margin

Studi con TC 4D:

Movimento N tripode celiaco

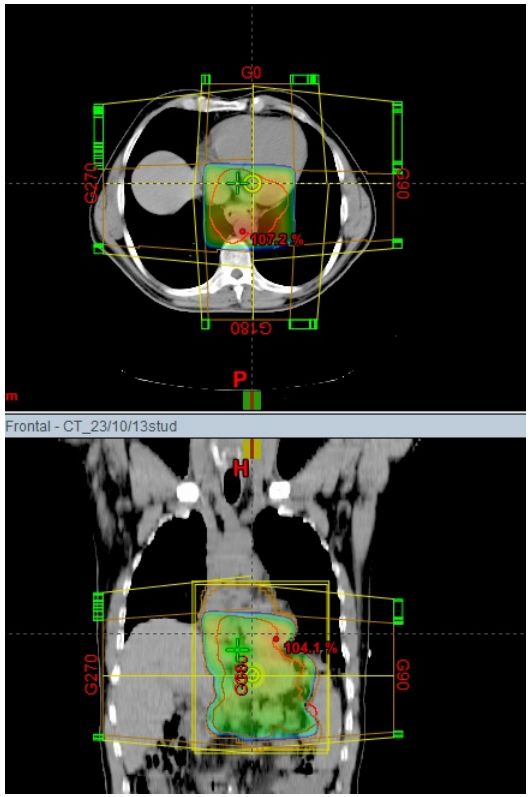
0.5 cm AP

1.5 cm CC

Patel AA. IJROBP 2009

3DCRT vs IMRT

3DCRT standard

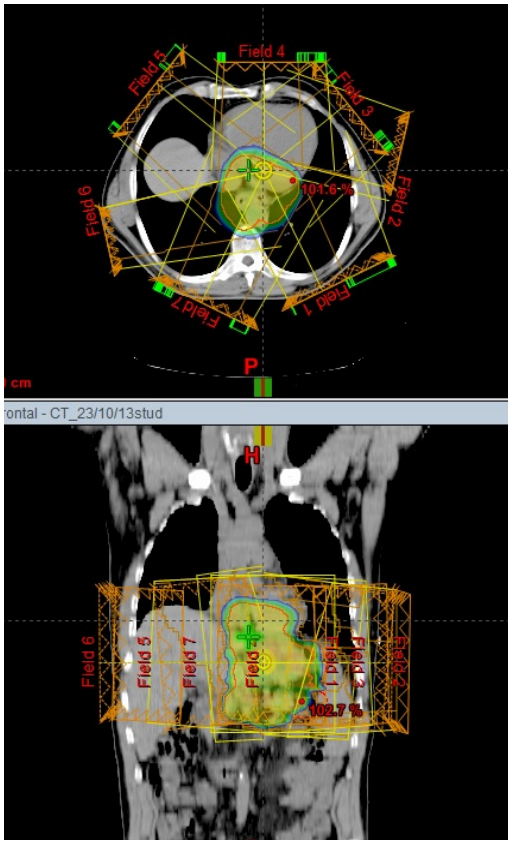


Minsky BD J Clin Oncol 2002

3DCRT vs IMRT

IMRT opzionale

< dose media cuore e coronaria destra
< dose media V10 e V20 polmone
< V30 fegato
< dose media reni



Kole TP. IJROBP 2012
Chen WJ Med Dos 2007
Chandra A. Radioth Oncol2005
Van der Geld YG. IJROBP 2007
Minn AY Cancer 2010

3DCRT vs IMRT

Rispettare i limiti di tolleranza degli OR

Cuore	**V40 < 30%**	**V25 < 50%**	
Polmoni	**V20 < 30-35%**	**dose media <20-23Gy**	**V5 < 60%**
Fegato	**V30 < 30%**		
Reni	**V30 <70%**	**dose media <18Gy**	

Hancock SL. Br J Radiol 1993
Matzinger O. Radiother Oncol 2009
Marks LB IJROBP 2010
Wang SL. IJROBP 2006
Tuker SL. IJROBP 2006
Dowson LA. IJROBP 2010

Conclusioni

- Classificazione dell'AGEG
- Problemi metodologici nell'inquadramento dell'AGEG
- Approccio terapeutico all' ADEG
- Prospettive future nella terapia dell'AGEG
- Note di tecnica radioterapica