Tumori esofagei cervicali

Renato Romagnoli
Chirurgia 2U – Trapianto Fegato
Città della Salute e della Scienza - Torino

Introduzione

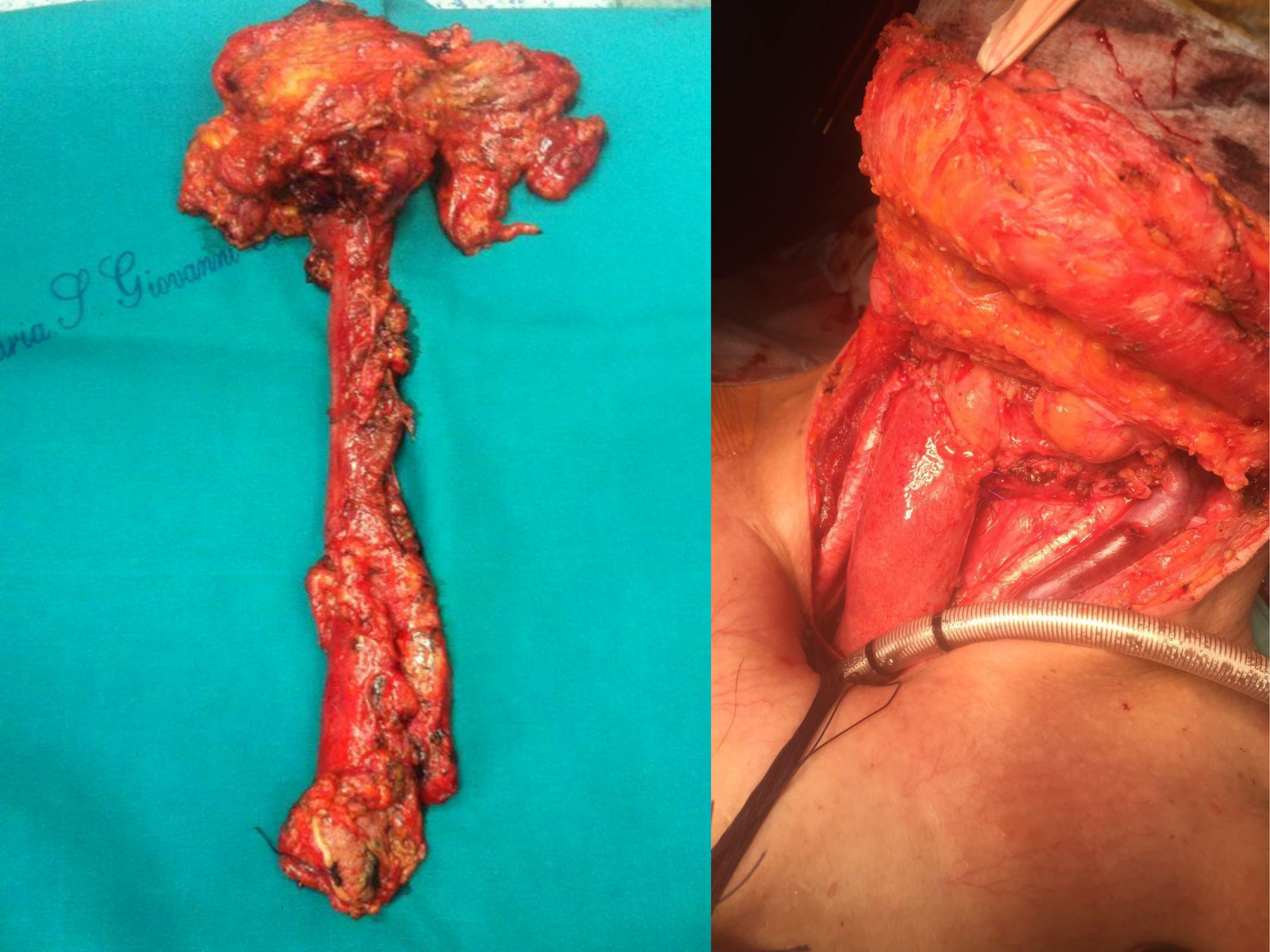
- Definizione: UES-stretto toracico superiore
- 5% dei tumori esofagei
- Carcinomi squamosi
- Tumori localmente avanzati alla diagnosi
- Tumore esofageo o dell’ipofaringe? Spesso difficile distinguere

Introduzione

- Necessari interventi ampiamente demolitivi
- Trattamenti CRT come alternativa alla chirurgia (preservazione laringe-esofago)
- CRT e/o chirurgia: in che ordine e con quali indicazioni?
  - (Chirurgia)
  - (Chirurgia – CT-CRT adiuvante)
  - CT-CRT neoadiuvante – chirurgia
  - CRT definitiva – chirurgia solo di salvataggio

Quale chirurgia?

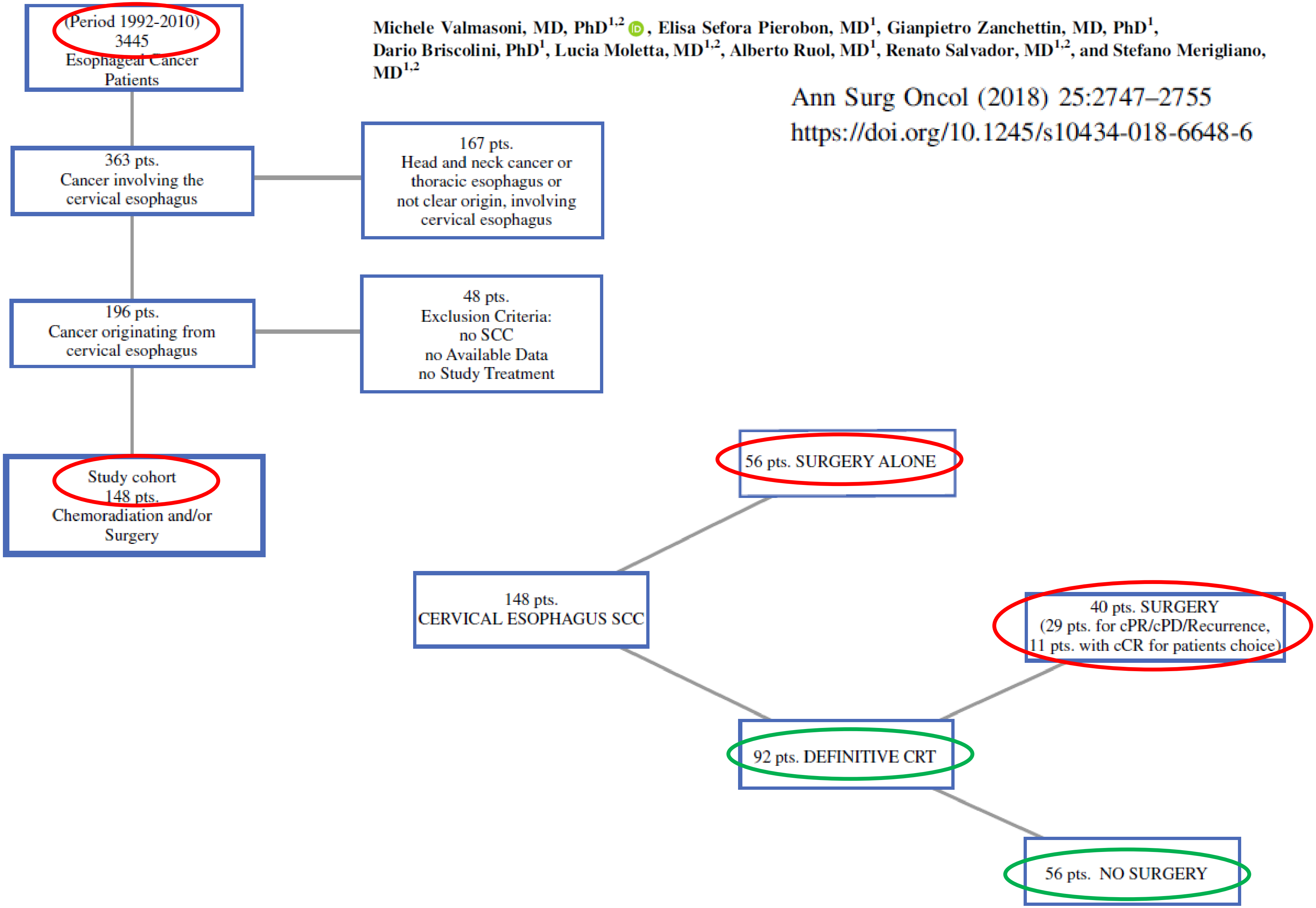
- UES infiltrato:
  - Ipofaringo-laringo-esofagectomia totale
    - Tubulo gastrico o colon
  - Esofagectomia parziale-laringectomia
    - Ansa digiunale «libera», lembi
- UES non infiltrato
  - Esofagectomia totale
    - Tubulo gastrico o colon
  - Esofagectomia parziale
    - Ansa digiunale «libera», lembi
- *la diagnosi di infiltrazione dell'UES talora è difficile…*


aria S. Giovanni

Cervical Esophageal Cancer Treatment Strategies: A Cohort Study Appraising the Debated Role of Surgery

Michele Valmasoni, MD, PhD[1,2], **Elisa Sefora Pierobon, MD**[1], **Gianpietro Zanchettin, MD, PhD**[1], **Dario Briscolini, PhD**[1], **Lucia Moletta, MD**[1,2], **Alberto Ruol, MD**[1], **Renato Salvador, MD**[1,2], **and Stefano Merigliano, MD**[1,2]

Ann Surg Oncol (2018) 25:2747–2755
https://doi.org/10.1245/s10434-018-6648-6



(Period 1992-2010)
3445
Esophageal Cancer
Patients

363 pts.
Cancer involving the
cervical esophagus

167 pts.
Head and neck cancer or
thoracic esophagus or
not clear origin, involving
cervical esophagus

196 pts.
Cancer originating from
cervical esophagus

48 pts.
Exclusion Criteria:
no SCC
no Available Data
no Study Treatment

Study cohort
148 pts.
Chemoradiation and/or
Surgery

148 pts.
CERVICAL ESOPHAGUS SCC

56 pts. SURGERY ALONE

92 pts. DEFINITIVE CRT

40 pts. SURGERY
(29 pts. for cPR/cPD/Recurrence,
11 pts. with cCR for patients choice)

56 pts. NO SURGERY

Cervical Esophageal Cancer Treatment Strategies: A Cohort Study Appraising the Debated Role of Surgery

Michele Valmasoni, MD, PhD[1,2], Elisa Sefora Pierobon, MD[1], Gianpietro Zanchettin, MD, PhD[1], Dario Briscolini, PhD[1], Lucia Moletta, MD[1,2], Alberto Ruol, MD[1], Renato Salvador, MD[1,2], and Stefano Merigliano, MD[1,2]

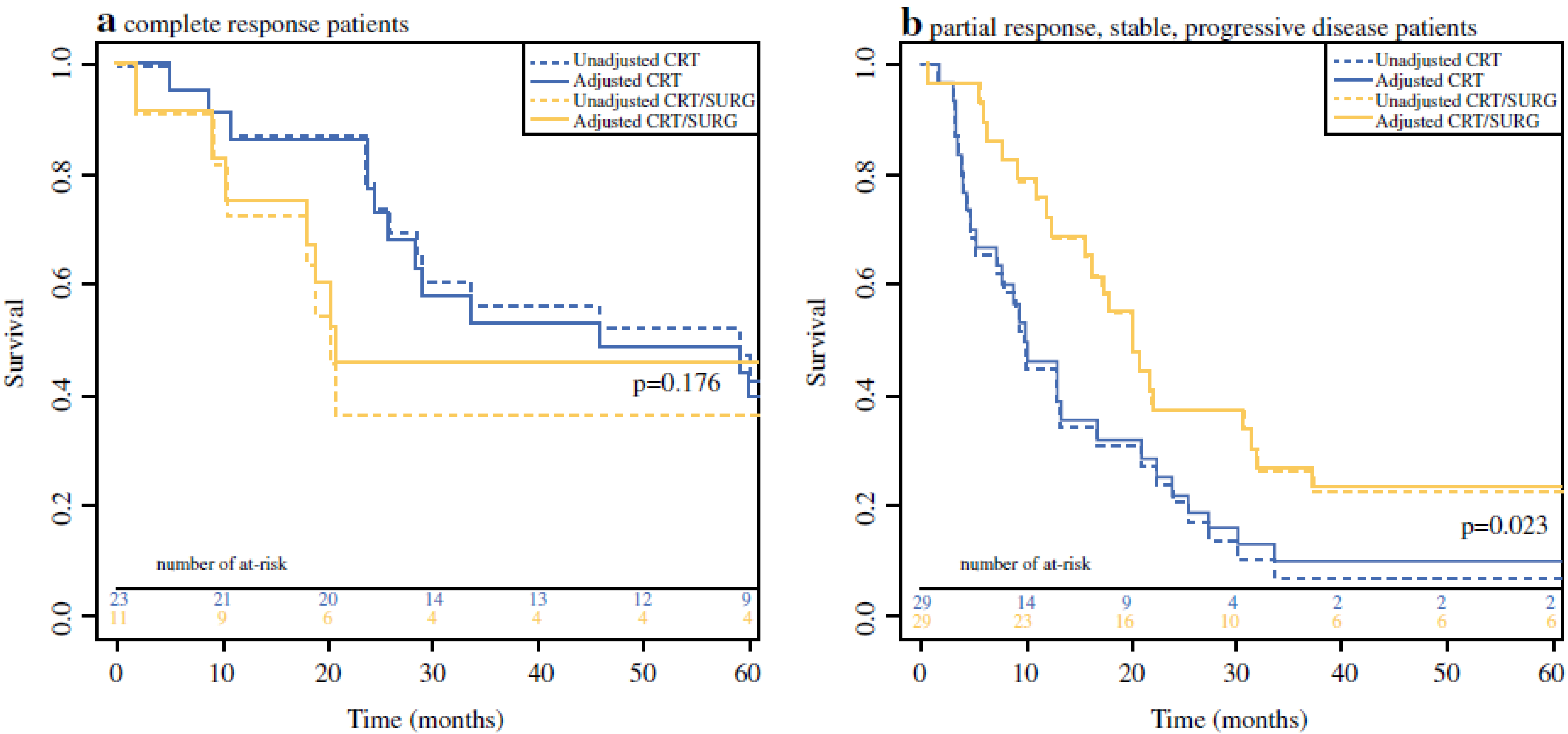
Ann Surg Oncol (2018) 25:2747–2755
https://doi.org/10.1245/s10434-018-6648-6

TABLE 3 Results of surgery

	SURG total ($n = 96$)	SURG ($n = 56$)	CRT + SURG ($n = 40$)	p value
Surgical radicality				
R0	69 (71.87)	41 (73.21)	28 (70)	0.668
R1–2	27 (28.13)	15 (26.79)	12 (30)	
Type of reconstruction				
EGP	47 (48.95)	25 (44.64)	22 (55)	0.156
ECP	2 (2.08)	0 (0)	2 (5)	
PGP	28 (29.1)	19 (33.36)	9 (22.5)	
PCP	11 (11.45)	6 (10.71)	5 (12.5)	
Jejunal interposition	2 (2.08)	2 (3.58)	0 (0)	
No reconstruction	6 (6.25)	4 (7.14)	2 (5)	
Pharyngo-laryngectomy				
No	51 (58.62)	25 (51.02)	22 (64.71)	0.214
Yes	36 (41.38)	24 (48.98)	12 (35.29)	
Intraoperative complications				
No	75 (79.79)	42 (77.78)	33 (82.5)	0.504
Recurrent nerve lesion	11 (11.7)	7 (12.96)	4 (10)	
Tracheal lesion	1 (1.06)	0 (0)	1 (2.5)	
Other	5 (5.32)	4 (7.4)	1 (2.5)	
Harvested lymph nodes				
Mean nodes [SD]	13.4 [9.02]	12.55 [8.92]	14.65 [9.16]	0.293
Mean positive nodes [SD]	1.04 [2.19]	0.88 [1.61]	1.28 [2.87]	0.458
Negative	58 (60.42)	34 (60.71)	24 (60)	0.943
Positive	38 (39.58)	22 (39.29)	16 (40)	
Vascular invasion				
No	20 (42.55)	13 (44.83)	7 (36.8)	0.484
Yes	27 (57.45)	15 (51.72)	12 (63.16)	
Postoperative complications				
No	44 (47.83)	24 (42.86)	20 (55.56)	0.233
Yes	48 (52.17)	32 (57.14)	16 (44.44)	
Anastomotic leak				
No	82 (86.32)	46 (83.64)	36 (90)	0.365
Yes	13 (13.68)	9 (16.36)	4 (10)	
Anastomotic stenosis				
No	79 (83.16)	44 (80)	35 (87.5)	0.328
Yes	16 (16.84)	11 (20)	5 (12.5)	

Statistical difference expressed as p for SURG versus CRT + SURG

SD standard deviation, *SURG* surgery alone, *CRT + SURG* chemoradiation followed by surgery, *EGP* esophago-gastroplasty, *ECP* esophago-coloplasty, *PGP* pharyngo-gastroplasty, *PCP* pharyngo-coloplasty

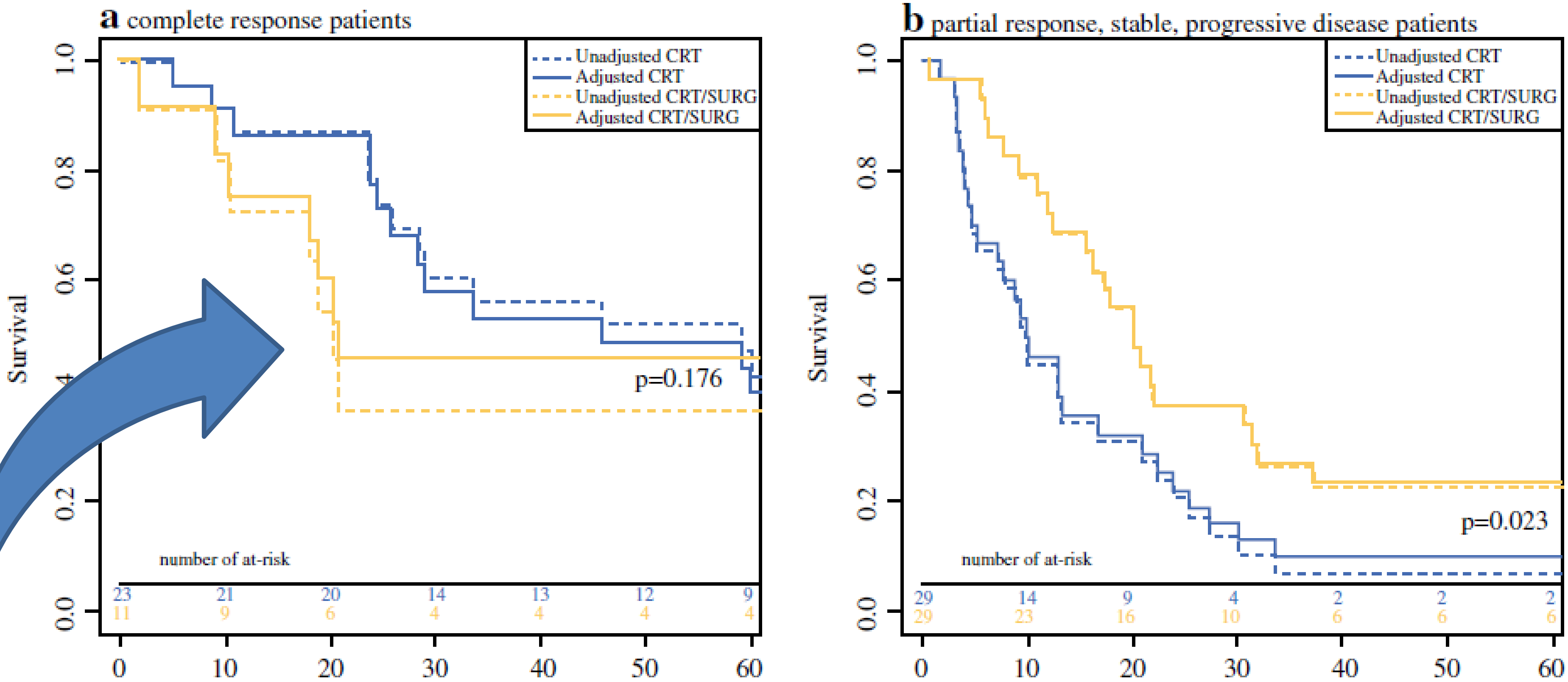


The overall survival rate was 21.8%. No significant differences were noted in the 5-year overall survival rates according to the treatment plan (SURG group: 12.6%; CRT group: 26.7%; CRT + SURG group: 30.7%; $p = 0.088$).

Considering patients with complete clinical response after CRT, there was no significant difference in survival in the CRT + SURG group compared with the CRT group ($p = 0.176$) (Fig. 2a).

For patients with partial response, stable disease, or progressive disease, the CRT + SURG group had a significantly higher survival compared with the CRT group ($p = 0.023$) (Fig. 2b).

patients in the CRT group with complete response and patients in the SURG group with R0 resection showed a significantly better survival for the CRT group ($p = 0.001$).



Among our patients, some strongly preferred to undergo surgery even after obtaining a complete response, but, interestingly, our study showed that adding surgery to the treatment options can have a negative impact on survival (Fig. 2a). Morbidity and mortality due to surgery is not counterweighted by a sufficient survival benefit. In contrast, for patients with partial or no response to CRT, surgery adds a significant survival benefit (Fig. 2b). Given these results, we no longer offer surgery as an option after achieving a clinical complete response with CRT.

Clinicopathological Features of Cervical Esophageal Cancer

Retrospective Analysis of 63 Consecutive Patients Who Underwent Surgical Resection

*Hiroshi Saeki, MD, PhD, FACS,[*] Satoshi Tsutsumi, MD,[*] Takafumi Yukaya, MD,[*] Hirotada Tajiri, MD,[*]
Ryosuke Tsutsumi, MD,[*] Sho Nishimura, MD,[*] Yu Nakaji, MD,[*] Kensuke Kudou, MD,[*] Shingo Akiyama, MD,[*]
Yuta Kasagi, MD,[*] Yuichiro Nakashima, MD, PhD,[*] Masahiko Sugiyama, MD, PhD,[*]
Hideto Sonoda, MD, PhD,[*] Kippei Ohgaki, MD, PhD,[*] Eiji Oki, MD, PhD, FACS,[*]
Ryuji Yasumatsu, MD, PhD,[†] Torahiko Nakashima, MD, PhD,[†] Masaru Morita, MD, PhD, FACS,[‡]
and Yoshihiko Maehara, MD, PhD, FACS[*]*

Annals of Surgery • Volume 265, Number 1, January 2017

The participants of this study were 1040 patients who underwent esophagectomy for esophageal cancer between 1980 and 2013,

main lesion was located in the cervical esophagus of 63 patients and in the thoracic or abdominal esophagus of 977 patients. In this study,

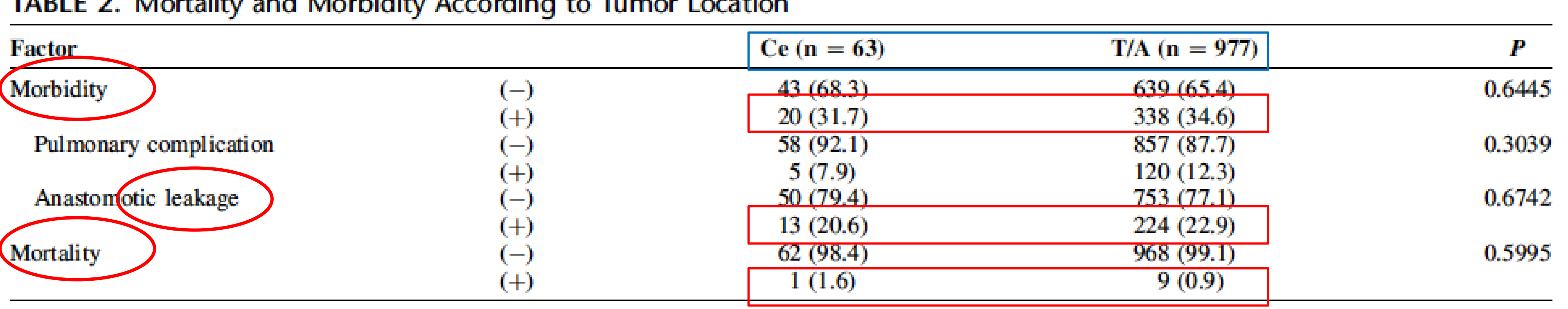


TABLE 2. Mortality and Morbidity According to Tumor Location

Factor		Ce (n = 63)	T/A (n = 977)	*P*
Morbidity	(−)	43 (68.3)	639 (65.4)	0.6445
	(+)	20 (31.7)	338 (34.6)	
Pulmonary complication	(−)	58 (92.1)	857 (87.7)	0.3039
	(+)	5 (7.9)	120 (12.3)	
Anastomotic leakage	(−)	50 (79.4)	753 (77.1)	0.6742
	(+)	13 (20.6)	224 (22.9)	
Mortality	(−)	62 (98.4)	968 (99.1)	0.5995
	(+)	1 (1.6)	9 (0.9)	

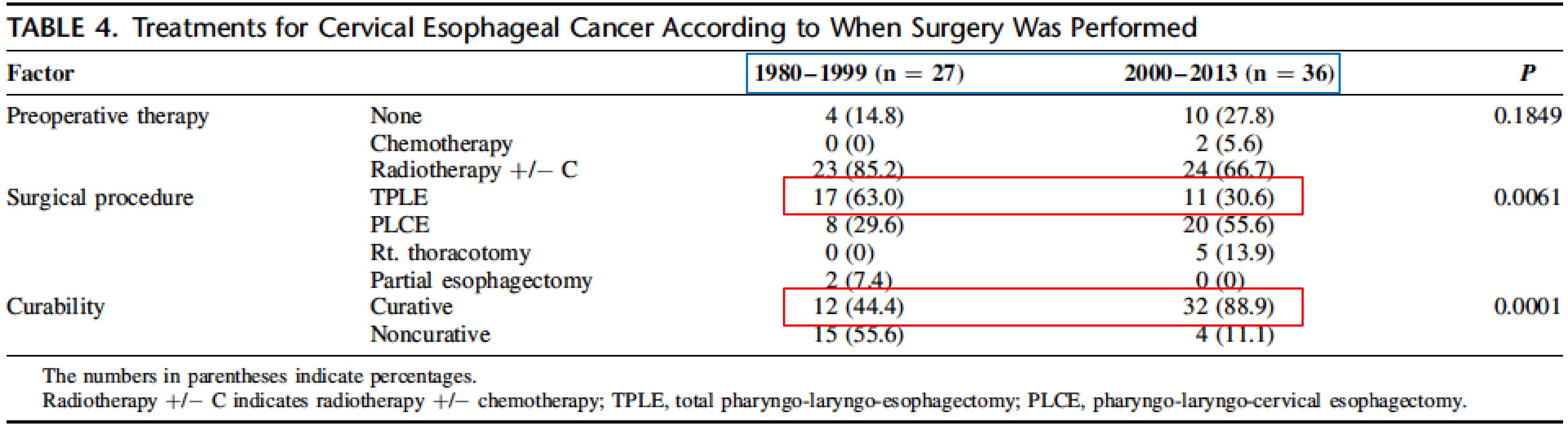


TABLE 4. Treatments for Cervical Esophageal Cancer According to When Surgery Was Performed

Factor		1980–1999 (n = 27)	2000–2013 (n = 36)	*P*
Preoperative therapy	None	4 (14.8)	10 (27.8)	0.1849
	Chemotherapy	0 (0)	2 (5.6)	
	Radiotherapy +/− C	23 (85.2)	24 (66.7)	
Surgical procedure	TPLE	17 (63.0)	11 (30.6)	0.0061
	PLCE	8 (29.6)	20 (55.6)	
	Rt. thoracotomy	0 (0)	5 (13.9)	
	Partial esophagectomy	2 (7.4)	0 (0)	
Curability	Curative	12 (44.4)	32 (88.9)	0.0001
	Noncurative	15 (55.6)	4 (11.1)	

The numbers in parentheses indicate percentages.
Radiotherapy +/− C indicates radiotherapy +/− chemotherapy; TPLE, total pharyngo-laryngo-esophagectomy; PLCE, pharyngo-laryngo-cervical esophagectomy.

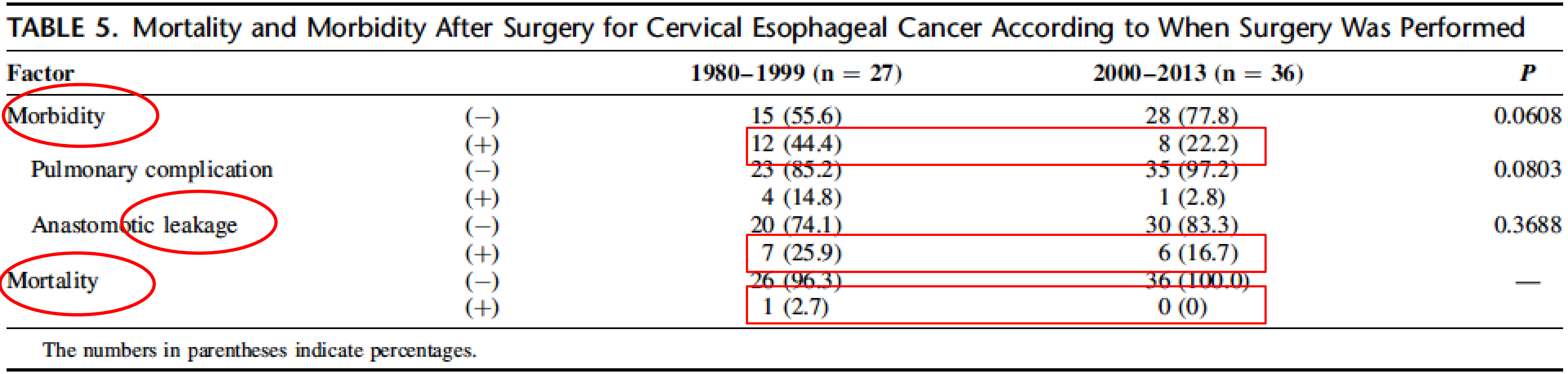
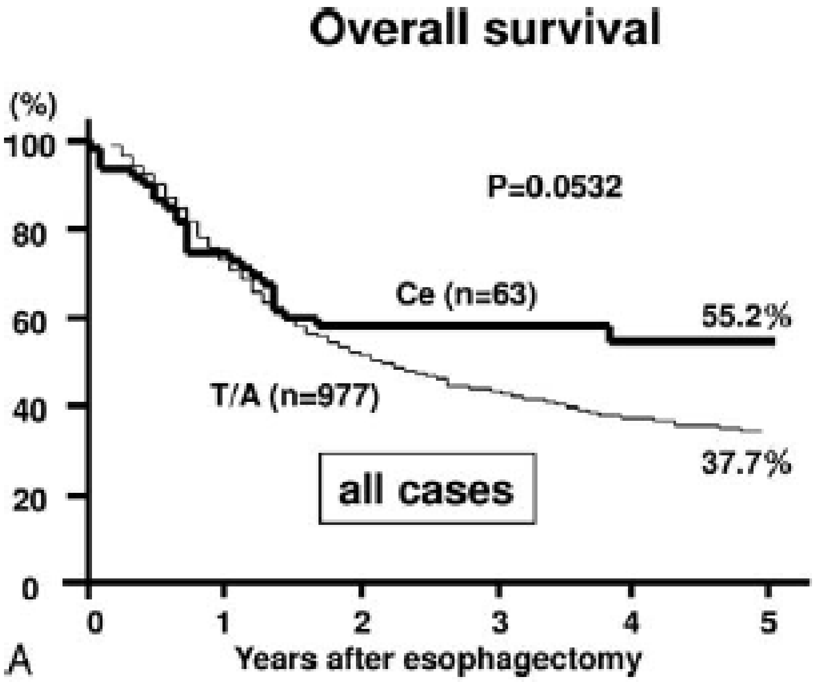
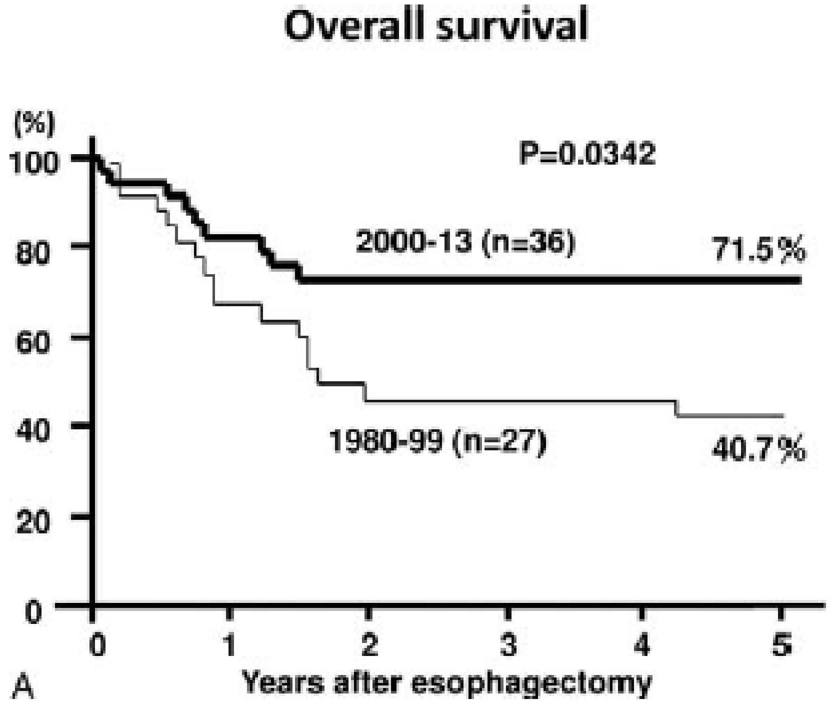


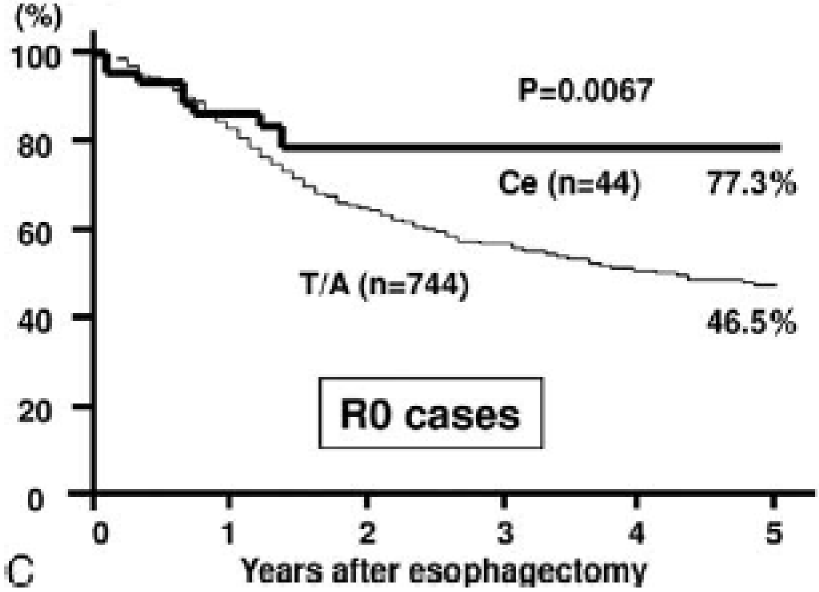
TABLE 5. Mortality and Morbidity After Surgery for Cervical Esophageal Cancer According to When Surgery Was Performed

Factor		1980–1999 (n = 27)	2000–2013 (n = 36)	*P*
Morbidity	(−)	15 (55.6)	28 (77.8)	0.0608
	(+)	12 (44.4)	8 (22.2)	
Pulmonary complication	(−)	23 (85.2)	35 (97.2)	0.0803
	(+)	4 (14.8)	1 (2.8)	
Anastomotic leakage	(−)	20 (74.1)	30 (83.3)	0.3688
	(+)	7 (25.9)	6 (16.7)	
Mortality	(−)	26 (96.3)	36 (100.0)	—
	(+)	1 (2.7)	0 (0)	

The numbers in parentheses indicate percentages.



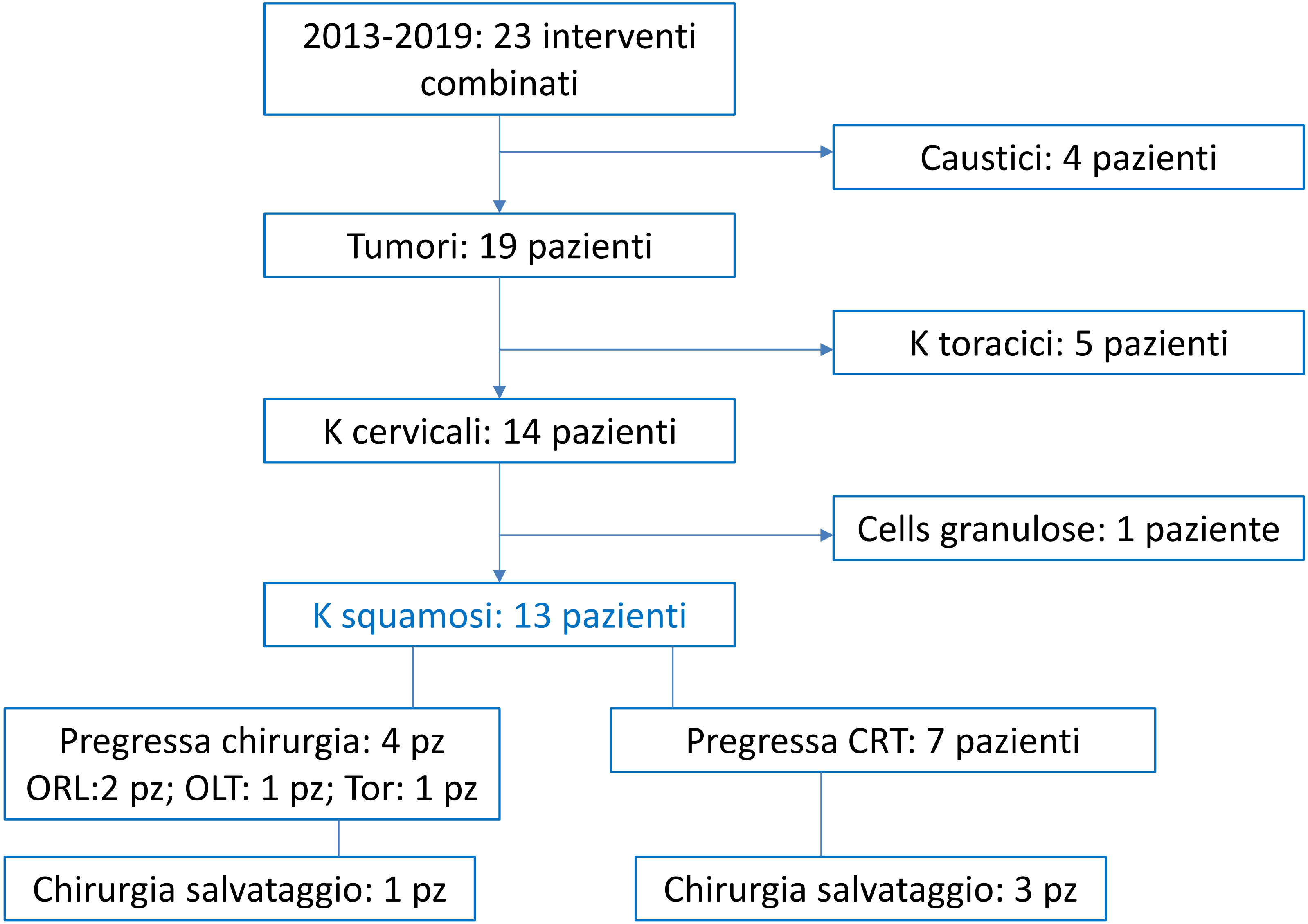




In our study, the 5-year overall survival rate of 55.2% for all Ce patients and 77.3% for Ce patients undergoing surgery after 1999 might be related to the high percentage of patients receiving curative resection and the low postoperative mortality rate. Importantly, the 5-year overall and disease-specific survival rates of Ce patients who underwent curative resection were significantly better than the survival rates of the corresponding T/A patients ($P = 0.0135$), although there was no difference in the percentage of advanced cases in the 2 patient groups. To the best of our knowledge, this is the first study that clearly demonstrates that the malignant potential of cervical esophageal cancer is not higher than that of other esophageal cancers. We

after 1999, the rate of curative resection for cervical esophageal cancer was significantly increased, and TPLE was less frequently performed, although there was no difference in the percentage of advanced cases between the earlier and later time periods (Table 3).

Esperienza Chirurgia 2U-IRCCS



2013-2019: 23 interventi combinati

Caustici: 4 pazienti

Tumori: 19 pazienti

K toracici: 5 pazienti

K cervicali: 14 pazienti

Cells granulose: 1 paziente

K squamosi: 13 pazienti

Pregressa chirurgia: 4 pz
ORL:2 pz; OLT: 1 pz; Tor: 1 pz

Chirurgia salvataggio: 1 pz

Pregressa CRT: 7 pazienti

Chirurgia salvataggio: 3 pz

Chirurgia: risultati

	Letteratura	**Chir 2U-IRCCS**
Mortalità precoce	1-6% (9% 90gg)	0%
Morbidità	22-57%	85% (≥3: 38%)
Fistole	10-21%	8%
Stenosi	17%	15%
Radicalità (R0)	69-89%	84%
Laringectomia	35-93%	46%

Torino: carcinomi squamosi

(n=103; 1998-2019)	Squamosi cervicali (N=13)	Squamosi toraco-cardiali (N=90)
Sesso (M:F)	11:2 (84.6%:15.4%)	56:34 (62.2%:37.8%)
Età	65 (53-76)	65 (37-83)
BMI	25 (20-34)	22 (13-35)
PS ECOG		
0	2 (15.4%)	26 (28.8%)
1	6 (46.2%)	32 (35.6%)
2	4 (30.8%)	32 (35.6%)
3	3 (23.1%)	0
ASA Score		
1	0	1 (1.1%)
2	3 (23.1%)	24 (26.7%)
3	7 (53.8%)	60 (66.7%)
4	3 (23.1%)	5 (5.5%)
Alcol	8 (61.5%)	40 (44.4%)
Fumo	11 (84.6%)	55 (61.1%)
Pregressa chirurgia	4 (30.8%)	10 (11.1%)

(n=103; 1998-2019)	Squamosi cervicali (N=13)	Squamosi toraco-cardiali (N=90)
pT		
0	1 (7.7%)	10 (11.1%)
1	3 (23.1%)	11 (12.2%)
2	1 (7.7%)	11 (12.2%)
3	3 (23.1%)	49 (54.4%)
4	5 (38.4%)	9 (10%)
pN		
0	4 (30.8%)	36 (40%)
1	6 (46.2%)	29 (32.2%)
2	1 (7.7%)	16 (17.8%)
3	2 (15.4%)	9 (10%)
pM		
0	12 (92.3%)	81 (90%)
1	1 (7.7%)	9 (10%)
Linfonodi asportati	37 (10-73)	24 (0-81)
Terapia neoadiuvante	7 (53.8%)	20 (22.2%)
Durata intervento (min)	707 (488-942)	555 (335-943)
Sacche trasfuse	0 (0-3)	0 (0-2)

(n=103; 1998-2019)	Squamosi cervicali (N=13)	Squamosi toraco-cardiali (N=90)
Viscere trasposto		
stomaco intero	0	23 (25.6%)
tubulo gastrico	13 (100%)	58 (64.4%)
ansa	0	6 (6.7%)
colon	0	3 (3.3%)
Livello anastomosi		
cervicale	13 (100%)	58 (64.4%)
intratoracica	0	32 (35.6%)
Radicalità		
R0	11 (84.6%)	70 (77.8%)
R1	1 (7.7%)	3 (3.3%)
R2	1 (7.7%)	17 (18.9%)
Giorni ventilazione	5 (1-36)	1 (0-80)
Giorni RIA	11 (3-38)	4 (0-103)
Giorni degenza	41 (21-73)	19 (10-186)
Complicanze post-op	11 (84.6%)	49 (54.4%)
Clavien-Dindo ≥ 3	5 (38.5%)	24 (26.7%)
Mortalità i.o.	0	0
Mortalità entro 90 giorni	0	8 (8.9%)

Chirurgia: risultati

- Sopravvivenza 5 aa gruppo giapponese 55% globale, 72% dal 1999 vs 22% del gruppo di Padova
- K cervicali sopravvivenze migliori dei toraco-addominali (studio giapponese)
- Torino:
  - FU mediano 13 mesi (4-71 mesi)
  - Vivi 4/12 (33%; 1 pz perso al FU)
  - Recidiva 6/12 (50%). 2 pz deceduti senza recidiva (ab ingestis, IMA)

Chirurgia: discussione

Studio Padova

- dopo CRT: 37% risposta completa, per questi sopravvivenza 5 aa 43% (vs 16%)
- Se risposta completa la chirurgia può impattare negativamente sulla sopravvivenza
- Migliore controllo locale della malattia dopo chirurgia (recidiva locale: 84% CRT vs 50% SURG e 55% CRT+SURG)

⬇

- CRT definitiva (con platinoidi e almeno 50.4 Gy), chirurgia solo di salvataggio (se non risposta completa)

Chirurgia: discussione

Studio giapponese (CRT neaodiuvante + chirurgia)

- Elevata sopravvivenza >1999 (72% a 5 aa)
  - elevata percentuale di R0 (89%)
  - bassa mortalità post-operatoria (0%)
- Sopravvivenza significativamente migliore dei tumori T/A (pur con simile percentuale di localmente avanzati nei due gruppi)
- >1999: ↑R0 (44%->89%) e ↓TPLE (63%->31%; laringectomie 93%->86%) pur con simile frequenza di localmente avanzati:
  - Diagnostica preoperatoria più accurata
  - Trattamento neoadiuvante più efficace
- Tumori cervicali biologicamente meno aggressivi (?)
- Resezione R0 fattore prognostico più importante

Chirurgia: discussione

Chirurgia 2U-IRCCS

- mortalità e morbidità in linea con letteratura
- Laringectomia necessaria quando si sacrifica UES (accurato studio pre-operatorio!)
- Chirurgia di salvataggio più difficoltosa:

⬇

- CRT neoadiuvante + chirurgia (CRT definitiva e chirurgia di salvataggio come seconda opzione)

Conclusioni

- Ruolo della chirurgia ancora dibattuto
- Necessarie competenze specifiche di chirurgia esofagea e ORL
- Chirurgia R0 e laringectomia (se UES sacrificato: 30-80%) sono fattori determinanti per la sopravvivenza
- Rispetto ai tumori toracici interventi più complessi e con maggior morbidità (ma con la stessa mortalità)