Università di Verona
Dipartimento di Chirurgia
Divisione di Chirurgia dell'Esofago e dello Stomaco

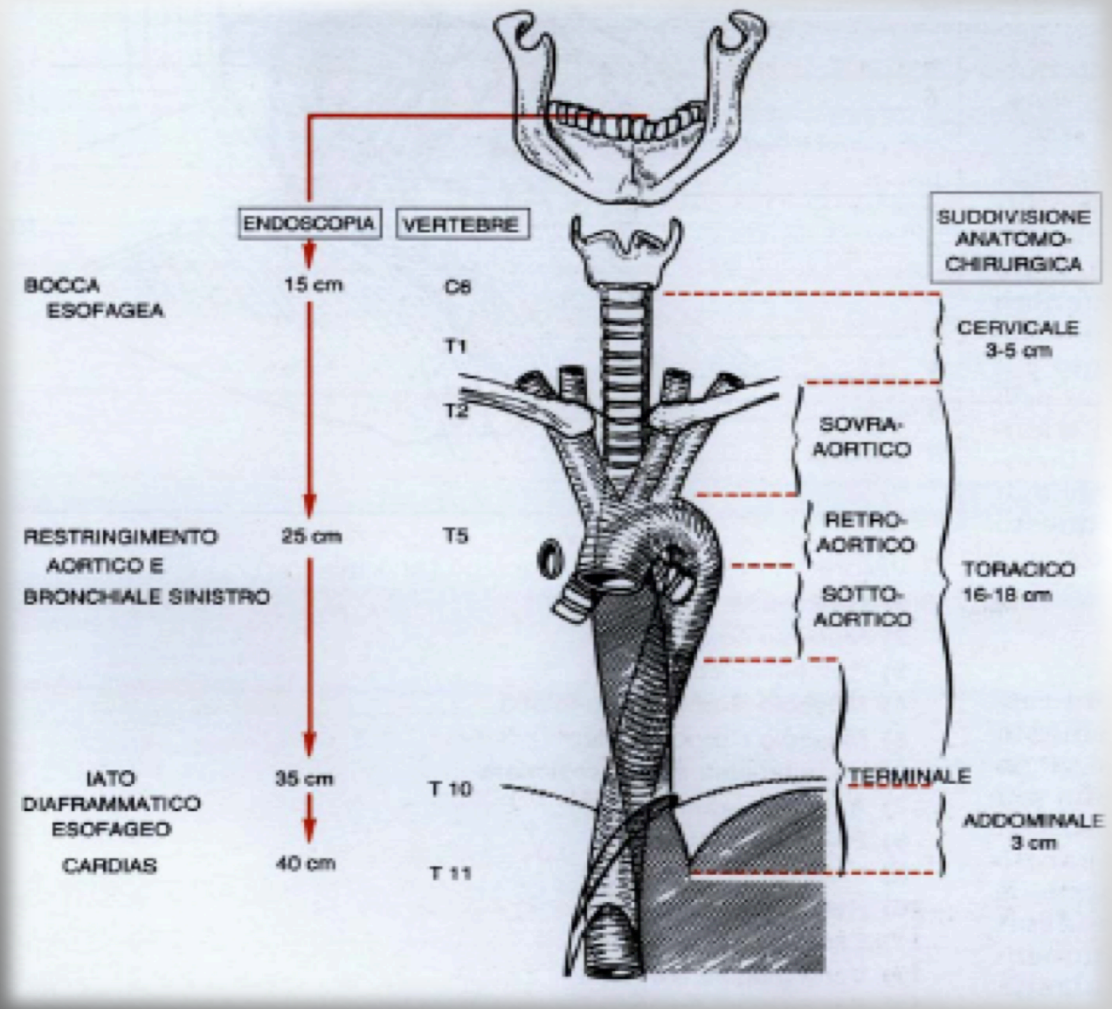
MANAGEMENT DIAGNOSTICO-TERAPEUTICO NEI TUMORI DI IPOFARINGE E ESOFAGO CERVICALE

Indicazioni e Risultati del Trattamento Chirurgico

Prof. G. de Manzoni

Giardini Naxos-Taormina, 27 ottobre 2013

Anatomy



3-5 cm

Epidemiology

"Carcinoma of the cervical esophagus is rare, accounting for only 2% to 10% of carcinomas of the esophagus…"

HIROYUKI DAIKO, MD,et al *Surgical Management of Carcinoma of the Cervical Esophagus* Journal of Surgical Oncology 2007;96:166–172

At our Institution from 2000

2000-2013
22/267 cervical scc/total scc
8.3%

…in the past

Primary carcinoma of the hypopharynx and cervical esophagus: evolution of surgical therapy.

Laterza E, Mosciaro O, Urso US, Inaspettato G, Cordiano C.

Hepatogastroenterology. 1994 Jun;41(3):278-82.

1973-1992: 37/167: 22%

5 y OS: 16.6% surgery alone

Procedure: pharyngolaryngo-esophagectomy with gastric pull-up

Open problems…

1. **Few studies (no randomized trials)**
2. **Studied with hypopharynx**

Study with hypopharynx

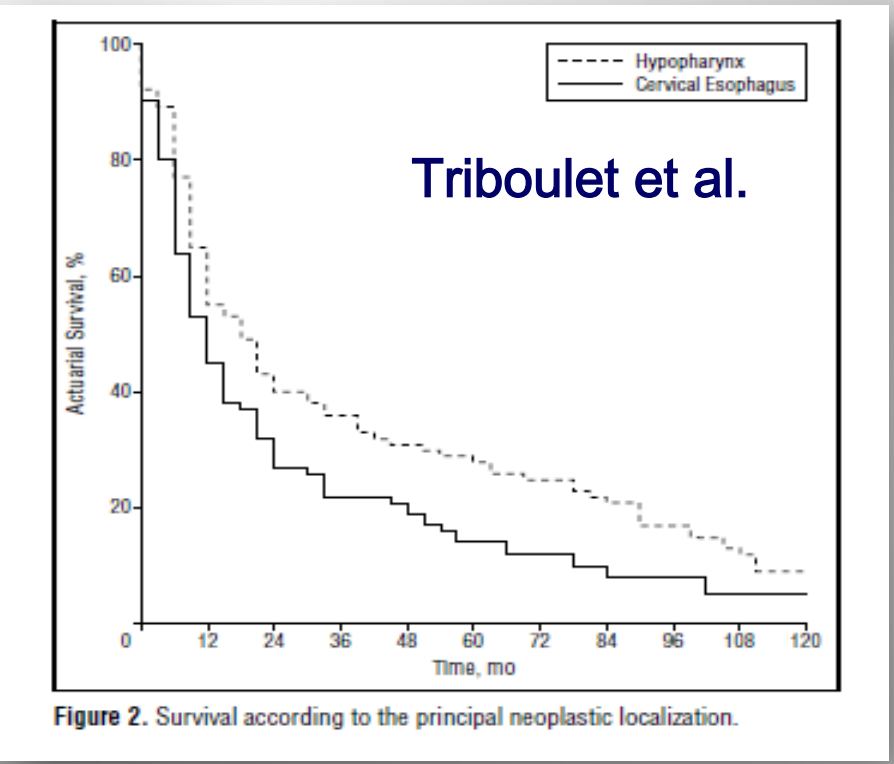
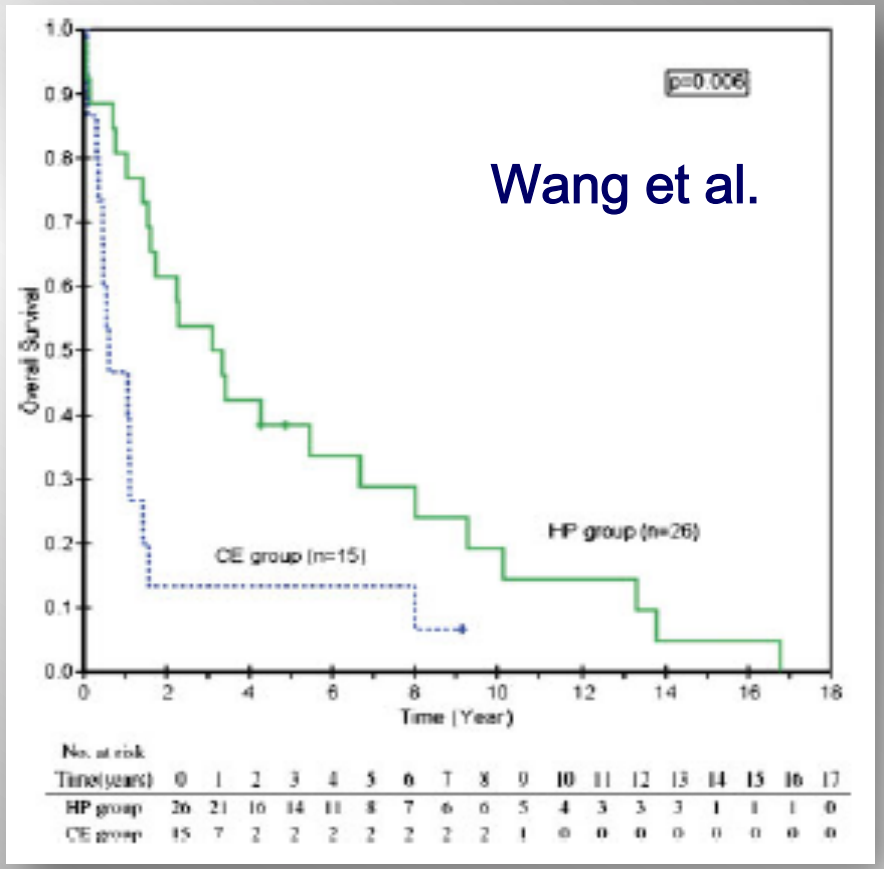


Figure 2. Survival according to the principal neoplastic localization.

HP 5 y OS: 38%
CE 5 y OS: 13%



HP 5 y OS: 29%
CE 5 y OS: 14%

Therapeutic Strategy

1. Type of surgery
2. Type of reconstruction
3. Type of lymphadenectomy
4. Multimodal therapy

1. Type of surgery

Total esophagectomy with gastric tube reconstruction

VS

Cervical esophagectomy with free jejunal graft

With or without Laryngectomy

1. Type of surgery

Current status of surgery for carcinoma of the hypopharynx and cervical esophagus*

A. Peracchia,[1] L. Bonavina,[1] M. Botturi,[2] M. Pagani,[1] A. Via,[1] G. Saino[1]

Larynx preservation may be indicated in selected patients with cancer of the distal cervical esophagus in whom it is possible to obtain a 2-cm margin above the tumor, or when a downstaging has been obtained with radiochemotherapy.

World J Surg (2013) 37:551–557
DOI 10.1007/s00268-012-1875-7

World Journal of Surgery

Larynx-Preserving Limited Resection and Free Jejunal Graft For Carcinoma of the Cervical Esophagus

Hiroshi Miyata · Makoto Yamasaki · Tsuyoshi Takahashi · Yukinori Ku
Kiyokazu Nakajima · Shuji Takiguchi · Masaki Mori · Yuichiro Doki

the indications for the larynx-pres… in our institution are as follows: (1) …tumor does not invade the trachea; (2) ther… recurrent nerve palsy; (3) the distance bet… …dge of the primary tumor and the inferior bo… cricoid cartilage is >1.0 cm.

After neoadjuvant treatment!

1. Type of surgery

	Nr of patients	Pure cervical	Total esophagectomy	Cervical esophagectomy
Triboulet et al. 2001	209 (1982-1999)	78	PLE: 132	L: 77
			L-P: 0	L-P: 0
Wang et al. 2006	41 (1984-2002)	15	PLE:41	L: 0
				L-P: 0
Daiko et al. 2007				L: 55
				L-P: ?
Ferahkose et al. 20				L: 22
				L-P: 30
Ott et al. 2009				L: 20
				L-P: 89
Kadota et al. 2009	32 (1984-2002)	17	PLE: 0	L: 0
			L-P: 0	L-P: 32
Tong et al. 2011	76 (1995-2008)	76	PLE: 70	L: 0
			L-P: 6	L-P: 0
Miyata et a. 2013	58 (1994-2010)	58	PLE: 0	L: 25
			L-P: 0	L-P: 33

Mind the gap…
Neoadjuvant CRT sometimes used…

1. Type of surgery

	Nr of patients	Neoadjuvant treatment	Surgery alone	Adjuvant treatment
Triboulet et al. 2001	209 (1982-1999)	22 CRT 15 CT 5 RT	22	45 RT
Wang et al. 2006	41 (1984-2002)	6 RT	14	21 RT
Daiko et al. 2007	74 (1982-2002)	-	58	11 RT 5 CT
Ferahkose et al. 2007	52 (1996-2006)	n.d.	n.d.	n.d.
Ott et al. 2009	109 (1986-2006)	94 CRT	15	-
Kadota et al. 2009	32 (1984-2002)	4 previous RT	23	2 RT 3 CT
Tong et al. 2011	76 (1995-2008)	6 CRT 3 RT	29	31 RT 7 CRT
Miyata et a. 2013	58 (1994-2010)	40 CRT 5 CT	13	-

1. Type of surgery

At our Institution from 2000

1/19 previous Laryngectomy:

Neoadjuvant CRT used as standard of care

12/19 without Laryngectomy: 63%

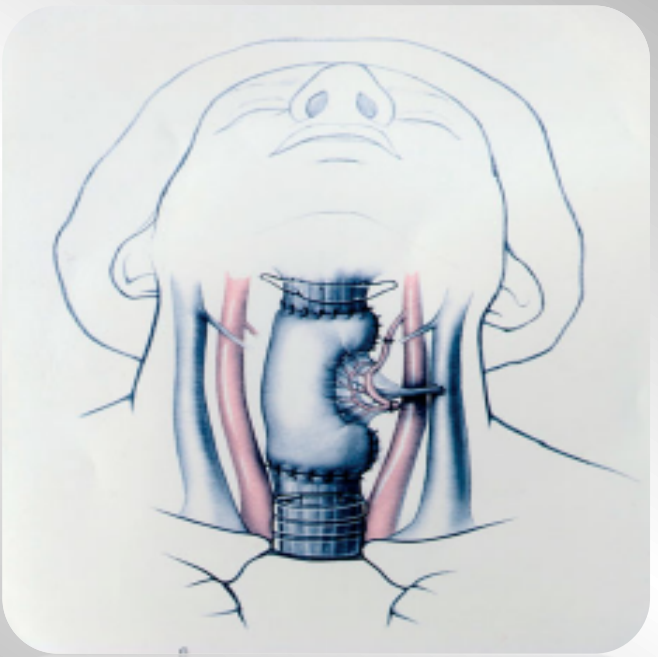
6/19 with Laryngectomy: 32%

2. Type of reconstruction

Gastric Pull-up

VS

Free Jejunal Graft



2. Type of reconstruction

Gastric Pull-up

VS

Free Jejunal Graft

Advantages:

1. Only one anastomosis
2. No problem of vascularization
3. No problem of distal margin
4. Possible mediastinal lymphadenectomy (?)

2. Type of reconstruction

Gastric Pull-up

VS

Free Jejunal Graft

Disadvantages:

1. **Highly destructive surgery**
2. **Cardio-pulmonary morbidity**

2. Type of reconstruction

Gastric Pull-up

VS

Free Jejunal Graft

Advantages:

1. **Limited resection**
2. **Better functional outcomes**
3. **Less destructive surgery**

2. Type of reconstruction

Gastric Pull-up

VS

Free Jejunal Graft

Disadvantages:

1. 3 visceral anastomoses
2. 2 microvascular anastomoses
3. High risk of leak and necrosis
4. High risk of R+ on the proximal margin

2. Type of reconstruction

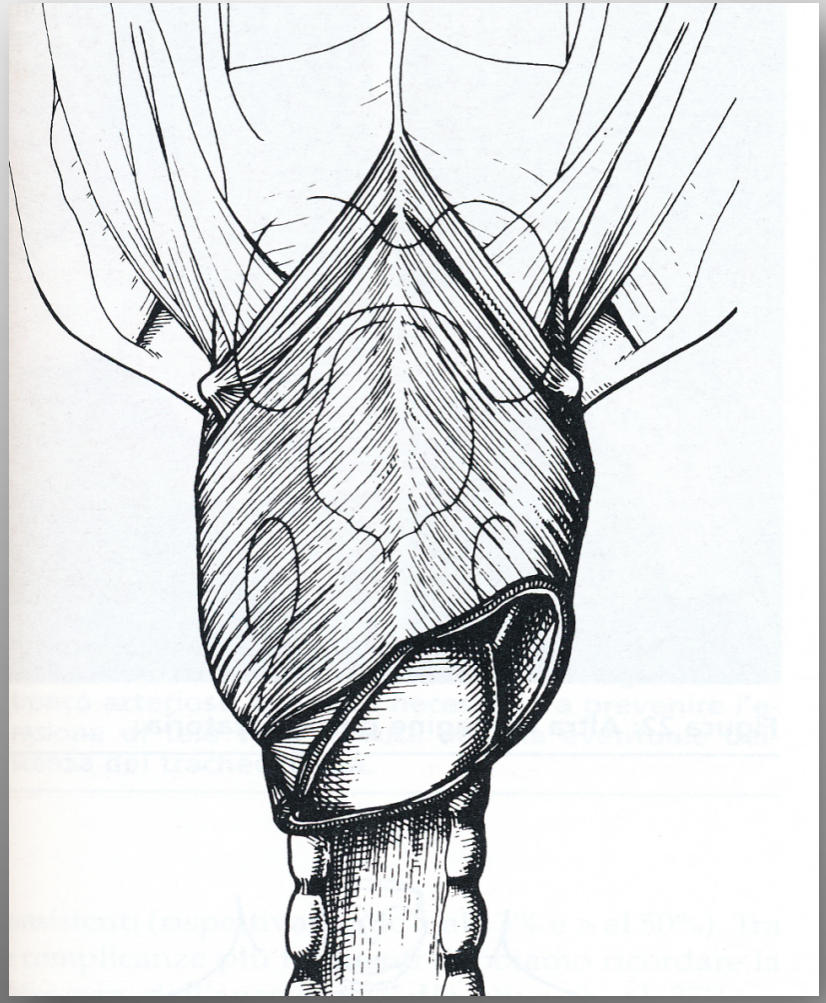
	Nr of patients	Gastric Pull-up	Free Jejunal graft	Others (colon graft, flaps, etc.)
Triboulet et al. 2001	209 (1982-1999)	127	77	5
Wang et al. 2006	41 (1984-2002)	39	-	2
Daiko et al. 2007	74 (1982-2002)	19	50	5
Ferahkose et al. 2007	52 (1996-2006)	38	14	-
Ott et al. 2009	109 (1986-2006)	-	109	-
Kadota et al. 2009	32 (1984-2002)	-	32	-
Tong et al. 2011	76 (1995-2008)	?	-	?
Miyata et a. 2013	58 (1994-2010)	-	58	-

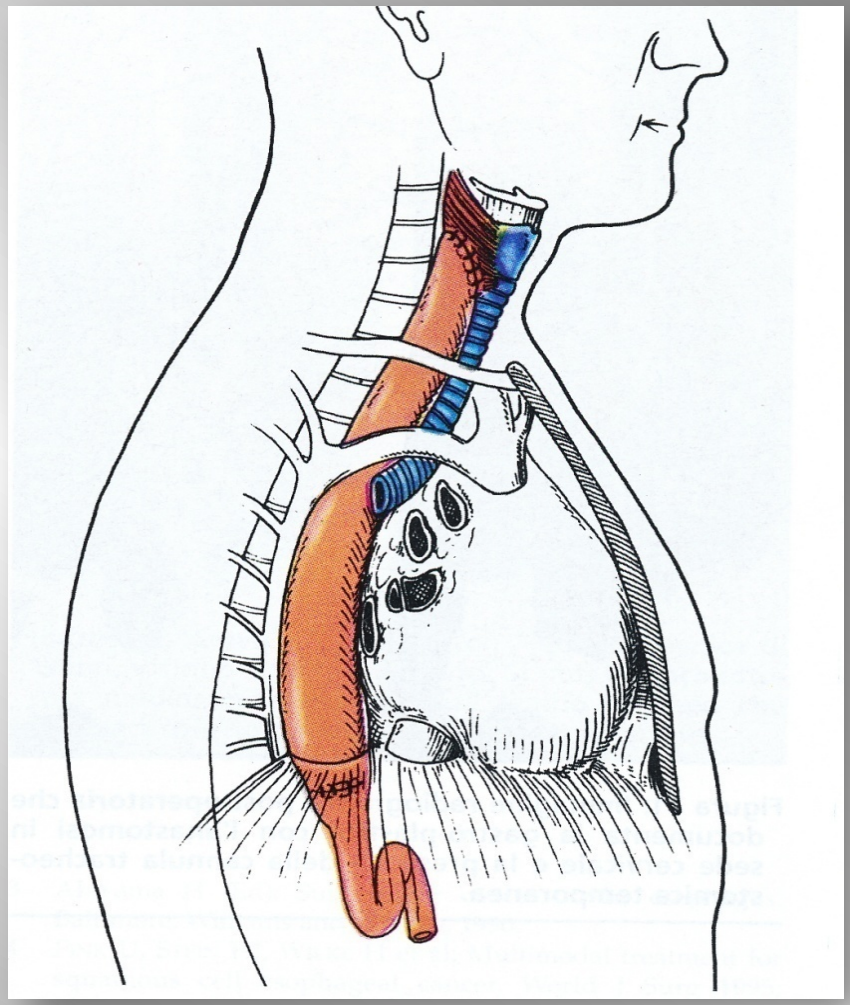
2. Type of reconstruction

At our Institution

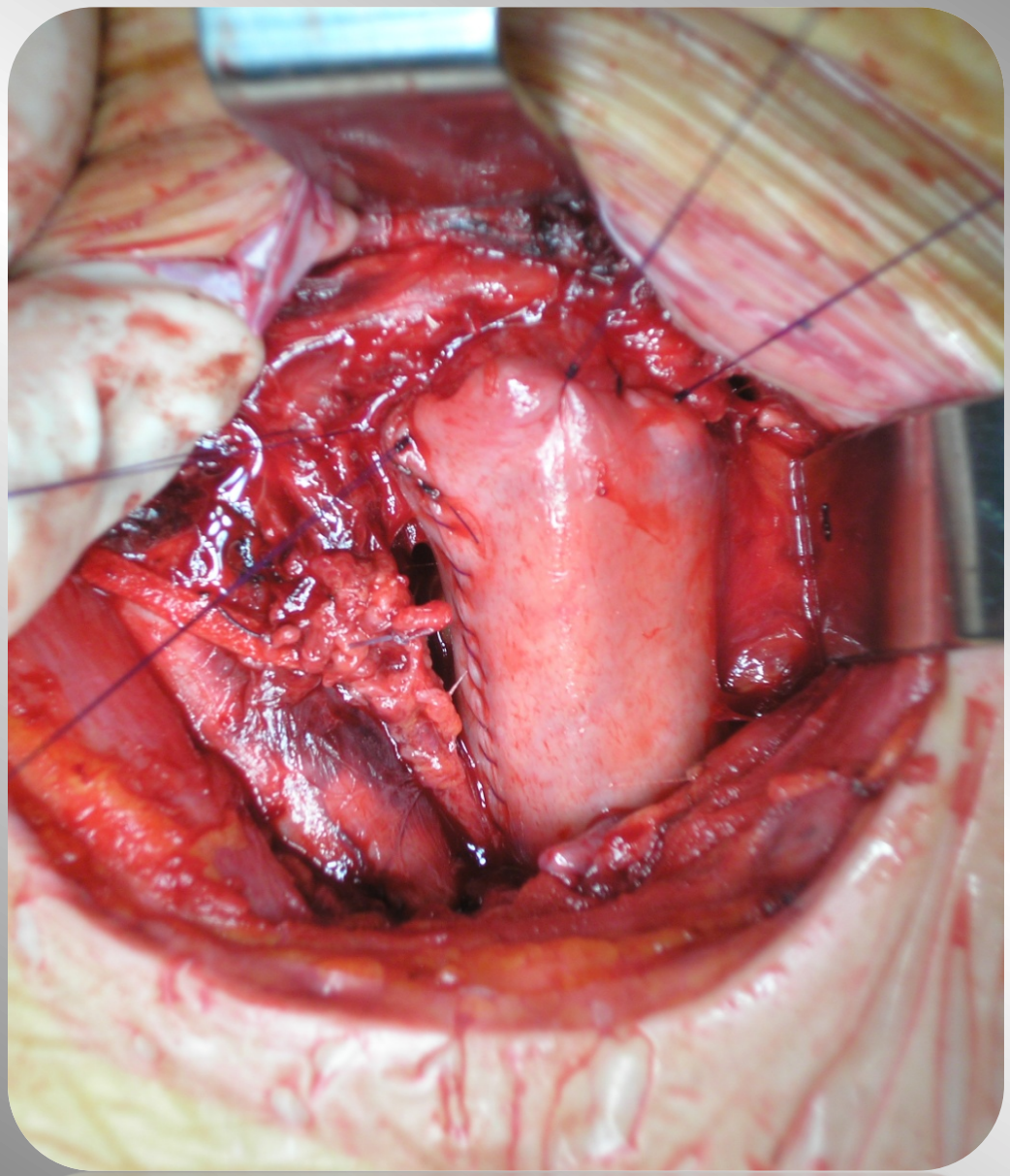
Gastric Pull-up used as standard of care

Gastric pull-up and larynx preservation

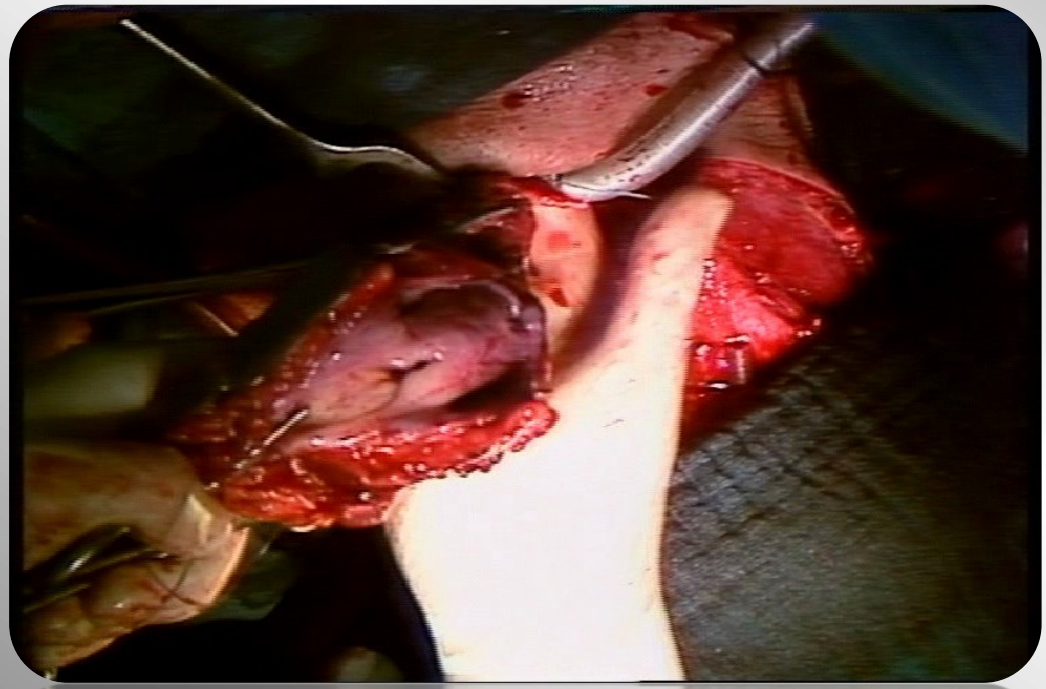


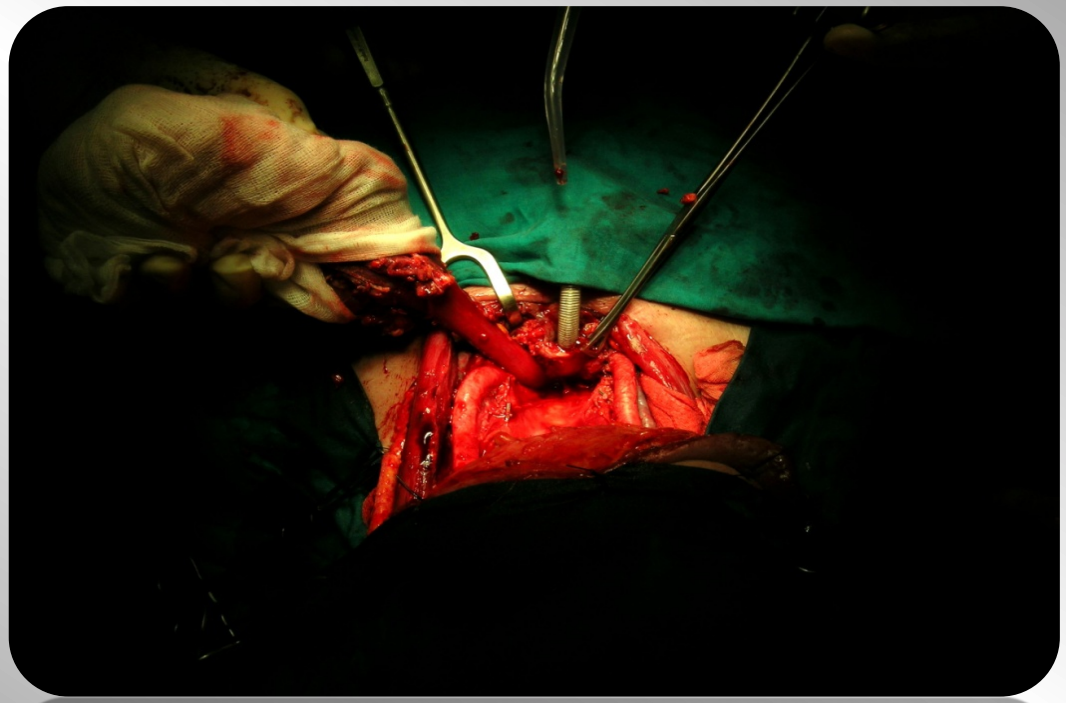


Gastric pull-up and larynx preservation

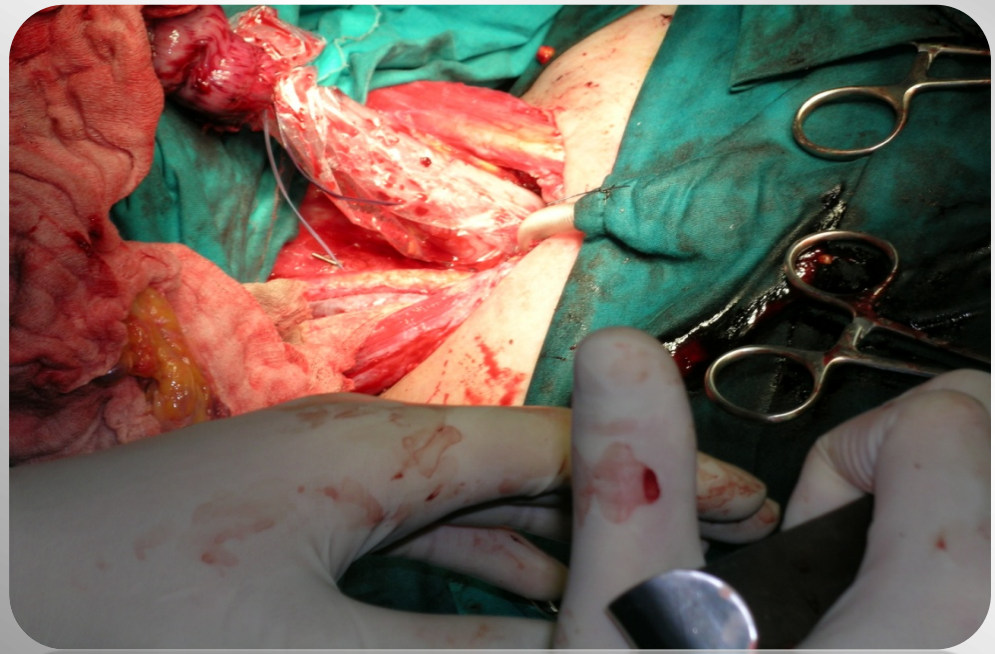


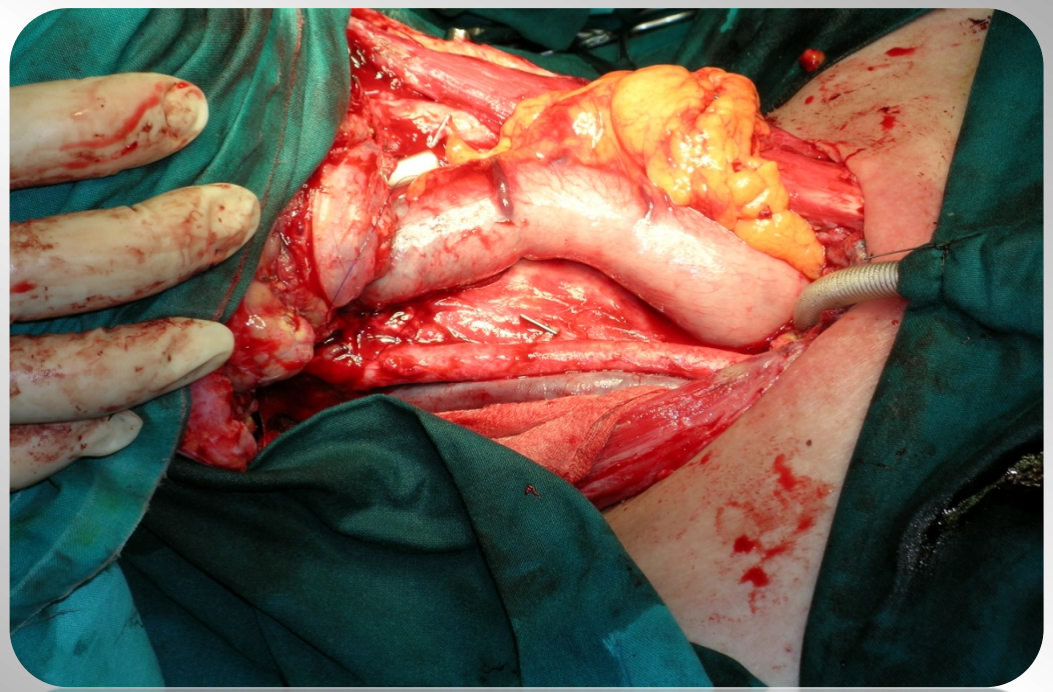
Gastric pull-up after PLE





Gastric pull-up after PLE





Morbidity-Mortality

	Nr of patients	Morbidity (% total)				Mortality
		Anastomotic leak		Graft necrosis		
		GP	FJG	GP	FJG	
Triboulet et al. 2001	209 (1982-1999)	80 (38.3%)				10 (4.8%)
		20 /127(16%)	25/77 (32%)	2/127 (1.7%)	5/77 (6%)	
Wang et al. 2006	41 (1984-2002)	19 (46.3%)				4 (9.8%)
		9/39 (23%)	-	1/39 (3%)	-	
Daiko et al. 2007	74 (1982-2002)	25 (34%)				3 (4%)
		2/19 (10%)	2/50 (4%)	2/19 (10%)	3/50 (6%)	
Ferahkose et al. 2007	52 (1996-2006)	27 (51.9%)				3 (5.7%)
		1/38 (3%)	0/14 (0%)	2/38 (6%)	1/14 (7%)	
Ott et al. 2009	109 (1986-2006)	81 (74.3%)				3 (2.8%)
		-	29/109 (27%)	-	26/109 (24%)	
Kadota et al. 2009	32 (1984-2002)	16 (50%)				0 (0%)
		-	4/32 (12%)	-	0/32 (0%)	
Tong et al. 2011	76 (1995-2008)	40 (51%)				5 (7.1%)
		7/76 (10%)		3/76 (4.3%)		
Miyata et a. 2013	58 (1994-2010)	31 (53.4%)				3 (5.1%)
			10/58 (17%)		3/58 (5.1%)	

Morbidity-Mortality

At our Institution from 2000

Anastomotic leak:
4/19
21%

Mortality:
1/19
5.2%

sis:
0/19
0%

3. Type of lymphadenectomy

TNM 7th ed.

Esophagus 7th edition, TNM definitions: AJCC = UICC

Tis	Carcinoma in situ /High grade dysplasia
T1	Lamina propria or submucosa
T1a	Lamina propria or muscularis mucosae
T1b	Submucosa
T2	Muscularis propria
T3	Adventitia
T4	Adjacent structures
T4a	Pleura, pericardium, diaphragm, or adjacent peritoneum
T4b	Other adjacent structures, e.g., aorta, vertebral body, trachea

N0	No regional lymph node met.
N1	1 to 2 regional lymph nodes
N2	3 to 6
N3	> 6

[N1 was site dependent]

M0	No distant metastasis
M1	Distant metastasis

[M1a, b were site dependent]

Changes from 6th ed

TNM 7th ed.

Oesophagus: New Definition of the Regional Lymph Nodes

The regional lymph nodes, irrespective of the site of the primary tumour, are those in the oesophageal drainage area including coeliac axis nodes and paraoeso-phageal nodes in the neck but not supraclavicular nodes.

Lymphatic diffusion of cervical esophagus

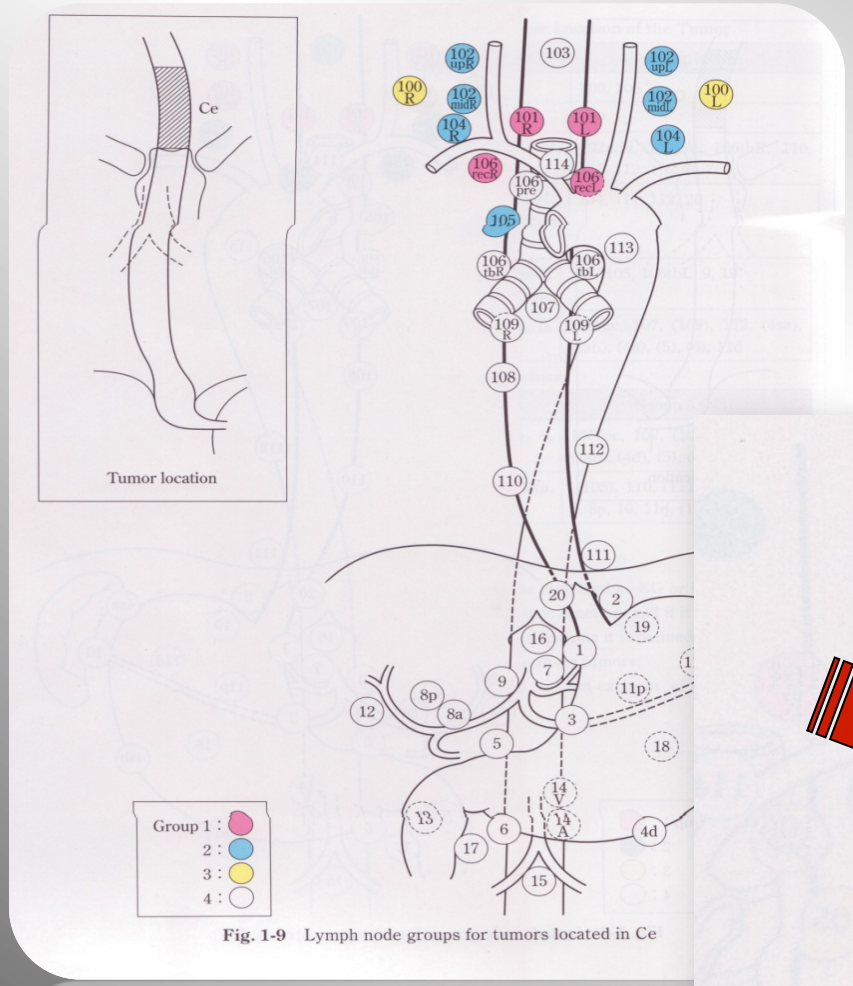
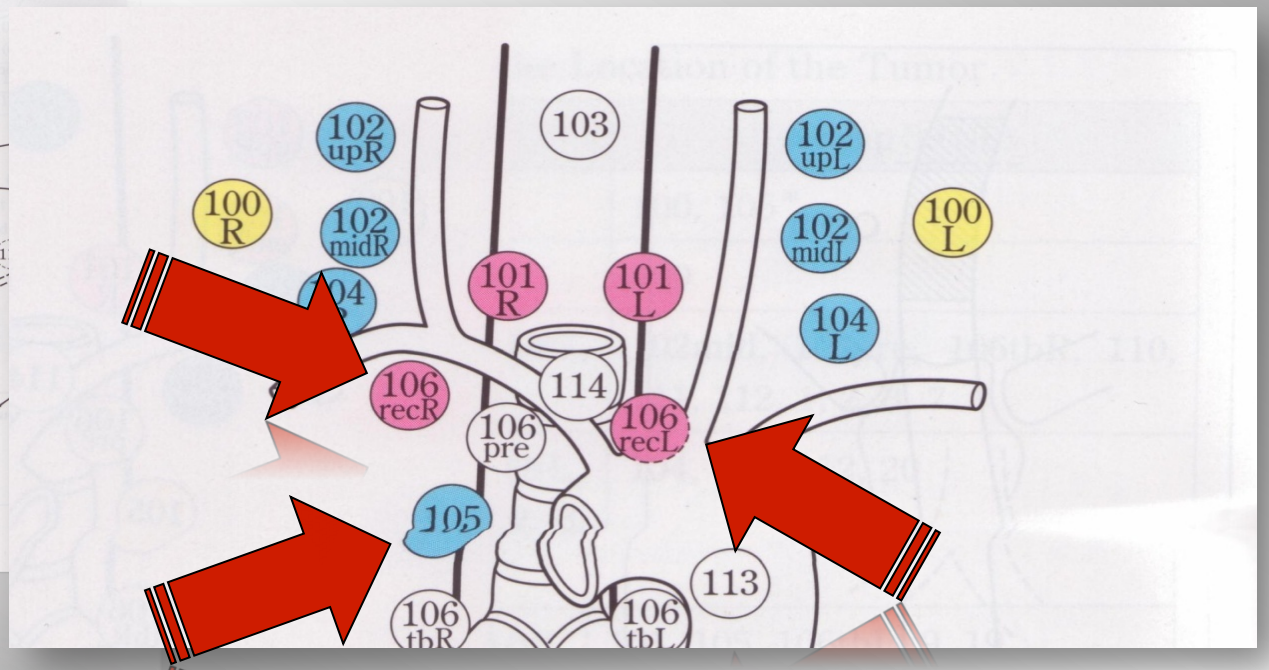


Fig. 1-9 Lymph node groups for tumors located in Ce

Japanese Classification of Esophageal Cancer
Tenth ed.



3. Type of lymphadenectomy

	Nr of patients	Neck Dissection	Mediastinal dissection	pN+
Triboulet et al. 2001	209 (1982-1999)	n.d.	n.d.	n.d.
Wang et al. 2006	41 (1984-2002)	28 68%	-	26 93%
Daiko et al. 2007	74 (1982-2002)	74 100%	-	50 67.5%
Ferahkose et al. 2007	52 (1996-2006)	52 100%	-	n.d.
Ott et al. 2009	109 (1986-2006)	67 61%	n.d.	21 31%
Kadota et al. 2009	32 (1984-2002)	29 91%	-	n.d.
Tong et al. 2011	76 (1995-2008)	20 28.6%	n.d.	n.d.
Miyata et a. 2013	58 (1994-2010)	58 100%	24 41%	22 38%

3. Type of lymphadenectomy

Annals of Otology, Rhinology & Laryngology 116(4):290-296.

Upper Mediastinal Node Dissection for Hypopharyngeal and Cervical Esophageal Carcinomas

Shigeru Hirano, MD, PhD; Kunihiko Nagahara, MD, PhD; Sueyoshi Moritani, MD; Morimasa Kitamura, MD; Shin-ichi Takagita, MD, PhD

21 pz
pure cervical

33.3 % mediastinal pN+

3. Type of lymphadenectomy

At our Institution from 2000

15/19 cervical & mediastinal dissection: 79%

4/19 previous node dissection in the neck

3. Type of lymphadenectomy

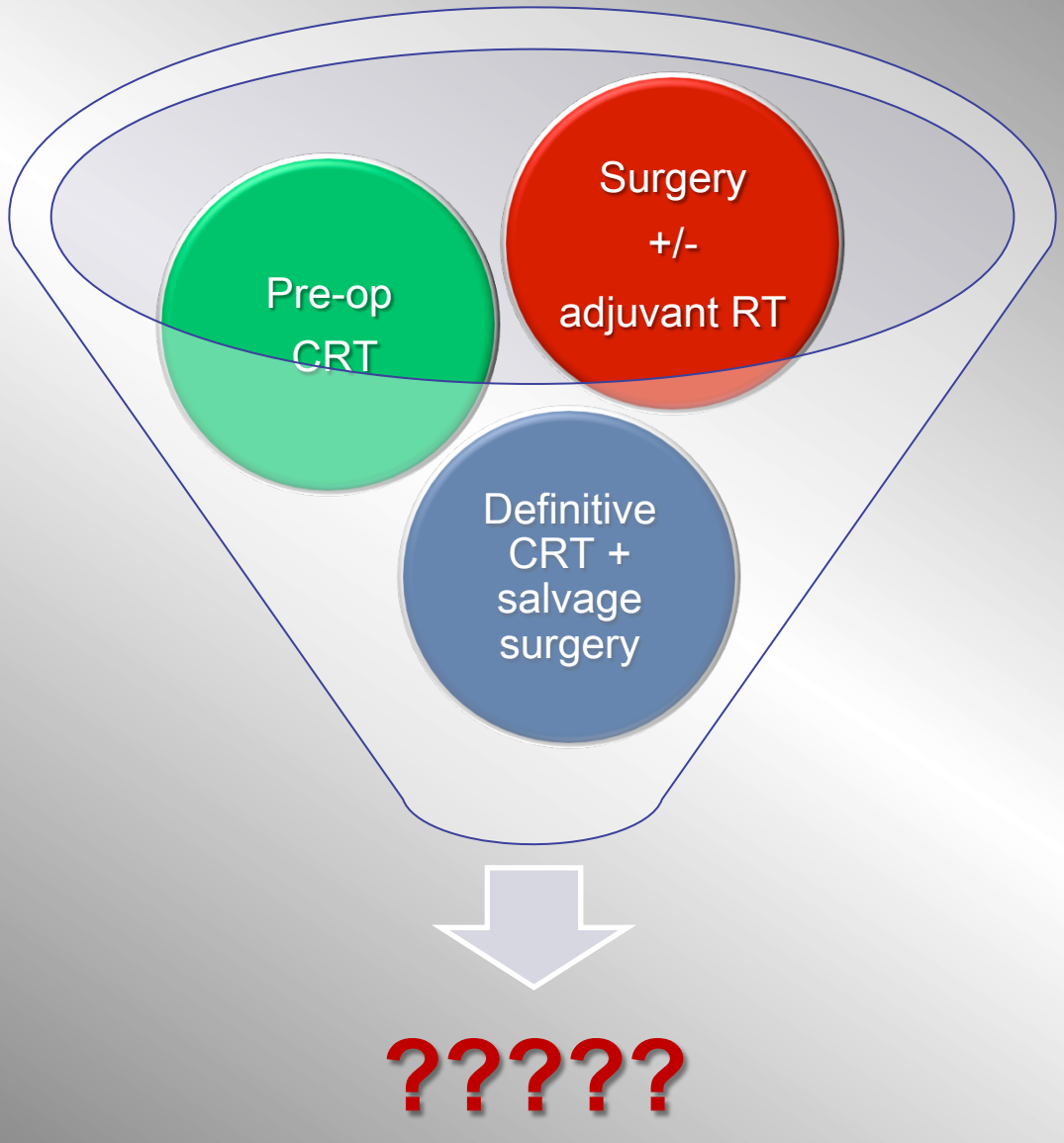
At our Institution from 2000

7/19 pN+
37

Cervical & Mediastinal node dissection used as standard of care

mediastinal nodes: 21%

4. Multimodal therapy



4. Multimodal therapy

	Nr of patients	Neoadjuvant treatment	Surgery alone	Adjuvant treatment
Triboulet et al. 2001	209 (1982-1999)	22 CRT 15 CT 5 RT	22	45 RT
Wang et al. 2006	41 (1984-2002)	6 RT	14	21 RT
Daiko et al. 2007	74 (1982-2002)	-	58	11 RT 5 CT
Ferahkose et al. 2007	52 (1996-2006)	n.d.	n.d.	n.d.
Ott et al. 2009	109 (1986-2006)	94 CRT	15	-
Kadota et al. 2009	32 (1984-2002)	4 previous RT	23	2 RT 3 CT
Tong et al. 2011	76 (1995-2008)	6 CRT 3 RT	29	31 RT 7 CRT
Miyata et a. 2013	58 (1994-2010)	40 CRT 5 CT	13	-

4. Multimodal therapy

At our Institution from 2000

15/19 treated with neoadjuvant CRT

Our CRT: 5FU+Cisplatin+Docetaxel+ 50 Gy RT

NCCN Guidelines – Esophagus and Esophagogastric Junction Cancer

NCCN guidelines 2013

Squamous cell carcinoma T1b,N+ or T2-4,N0-N+ definitive chemoradiation recommended for cervical esophagus

Salvage surgery

Watch & Wait:

CRT
&
Salvage Surgery

Salvage surgery

Review

Salvage oesophagectomy after local failure of definitive chemoradiotherapy

British Journal of Surgery 2007; **94**: 1059–1066

J. Gardner-Thorpe,

Recurrence rate:
40-60%
within 1 year

The emerging role of salvage esophagectomy.

Lee D, Chiu L, Kim JY.

Department of Surgery Michael E. DeBakey VA Medical Center Baylor College of Medicine, Houston, TX, USA.

Salvage surgery

1. **Difficult choice of candidates for a salvage surgery:**

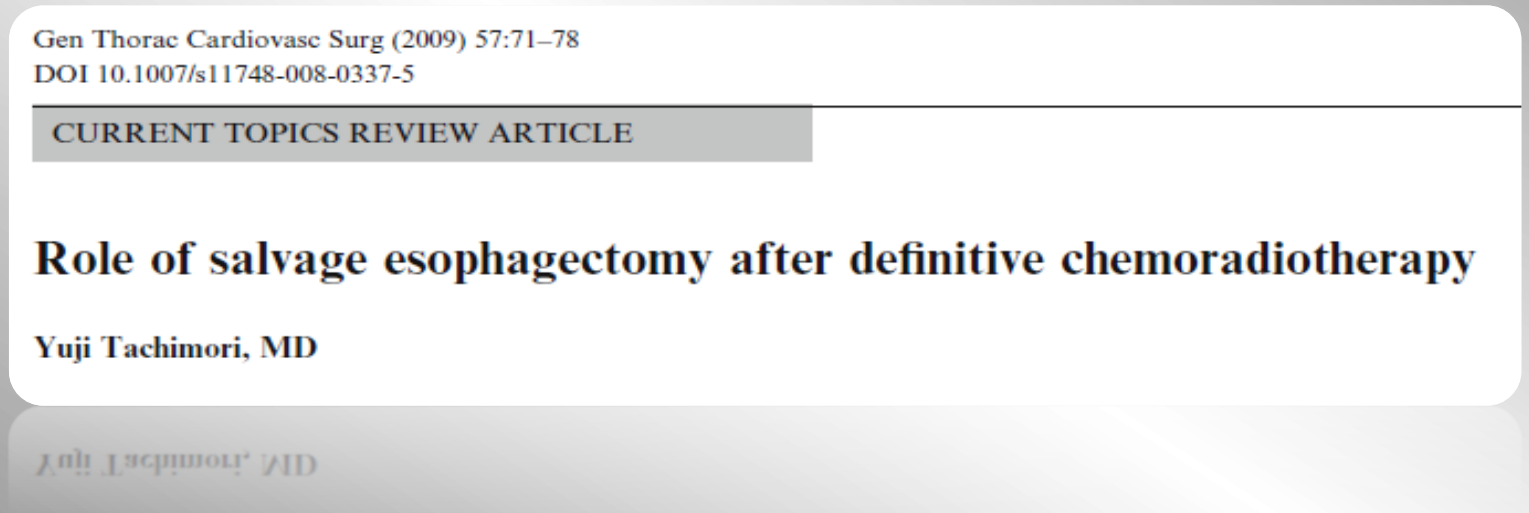
   - **Risk of *progression* if follow-up not effective**

   - **Risk of *overtreatment* in patients with pCR for low sensibility and specificity of endoscopy and imaging**

Dis Esophagus. 2013 Aug 29.
Clinical tools do not predict pathological complete response in patients with esophageal squamous cell cancer treated with definitive chemoradiotherapy.
Molena D, Sun HH, Badr AS, Mungo B, Sarkaria IS, Adusumilli PS, Bains MS, Rusch VW, Ilson DH, Rizk NP.
Division of Thoracic Surgery, Department of Surgery, Johns Hopkins Medicine, Baltimore, Maryland

Salvage surgery

2. Surgical technical difficulties for inflammation and fibrosis with risk of high morbidity and mortality


Gen Thorac Cardiovasc Surg (2009) 57:71–78
DOI 10.1007/s11748-008-0337-5

CURRENT TOPICS REVIEW ARTICLE

Role of salvage esophagectomy after definitive chemoradiotherapy

Yuji Tachimori, MD

Salvage surgery

Reference	Histological type	Location			Stage				
		Upper	Middle	Lower	0	I	II	III	IV
Meunier *et al.*[21]	SCC	1	5	0	0	0	5	0	1
Murakami *et al.*[11]	SCC	n.r.	n.r.	n.r.	0	1	3	0	0
Wilson *et al.*[5]	SCC/adeno	n.r.	n.r.	n.r.	0	0	10	6	0
Swisher *et al.*[22]	SCC/adeno	4	3	6	0	9	0	3	1
Gotohda *et al.*[23]	SCC	1	3	2	3	0	3	0	0
Nakamura *et al.*[3]	SCC	4	17	6	0	0	0	19	8
Tomimaru *et al.*[24]	SCC	5	13	6	0	4	7	11	2

Few cases in general and in particular for cervical and upper esophagus

Salvage surgery

Table 4 Morbidity and mortality of salvage esophagectomy

Study	No. of patients	Morbidity (%)	Leakage (%)	Pulmonary complication (%)	Hospital stay (days)	30-Day mortality (%)	Hospital mortality (%)	Cause of hospital mortality
Meunier[29]	6	50	33	16	47 (mean)		16	Necrosis of the gastric tube
Wilson[27]	16		6		14 (median)	6	6	Intraoperative hemorrhage
Swisher[30]	13	77	38	38	29.4 (mean)	15	15	ARDS, leakage
Nakamura[31]	27		22	11	39.9 (mean)	4	7	ARDS, leakage
Tomimaru[32]	24	50	21	21		4	12	Peritonitis, hemoptysis
Oki[33]	14	50	36	21			7	Bleeding from tumor
Smithers[28]	14	79	14	57	31.5 (median)	7	7	
Nishimura[34]	46	54	22	9	47 (mean)	9	15	Leakage, pneumonia, arterial bleeding, tracheal necrosis, pneumonitis, cardiac
Chao[35]	27		15	33	22.4 (mean)	19	22.2	Leakage, ARDS

ARDS, acute respiratory distress syndrome

High morbidity and mortality

Salvage surgery

Table 5 Survival after salvage esophagectomy

Study	No. of patients	Survival (%)	Median survival (months)
Meunier[29]	6	0 (5 years)	7
Wilson[27]	16	37 (3 years)	16

It can be considered in selected cases

Despite morbi-mortality, it can achieve prolonged survival

Survival

	Nr of patients	Overall survival	Only cervical carcinomas
Triboulet et al. 2001	209 (1982-1999)	24% 5 y	14% 5 y
Wang et al. 2006	41 (1984-2002)	31.5% 5 y	13.3% 5 y
Daiko et al. 2007	74 (1982-2002)	33% 5 y	n.d.
Ferahkose et al. 2007	52 (1996-2006)	n.d.	n.d.
Ott et al. 2009	109 (1986-2006)	47% 5 y	47% 5 y
Kadota et al. 2009	32 (1984-2002)	n.d.	45.9% 5 y
Tong et al. 2011	76 (1995-2008)	n.d.	n.d.
Miyata et a. 2013	58 (1994-2010)	45% 5y	45% 5y

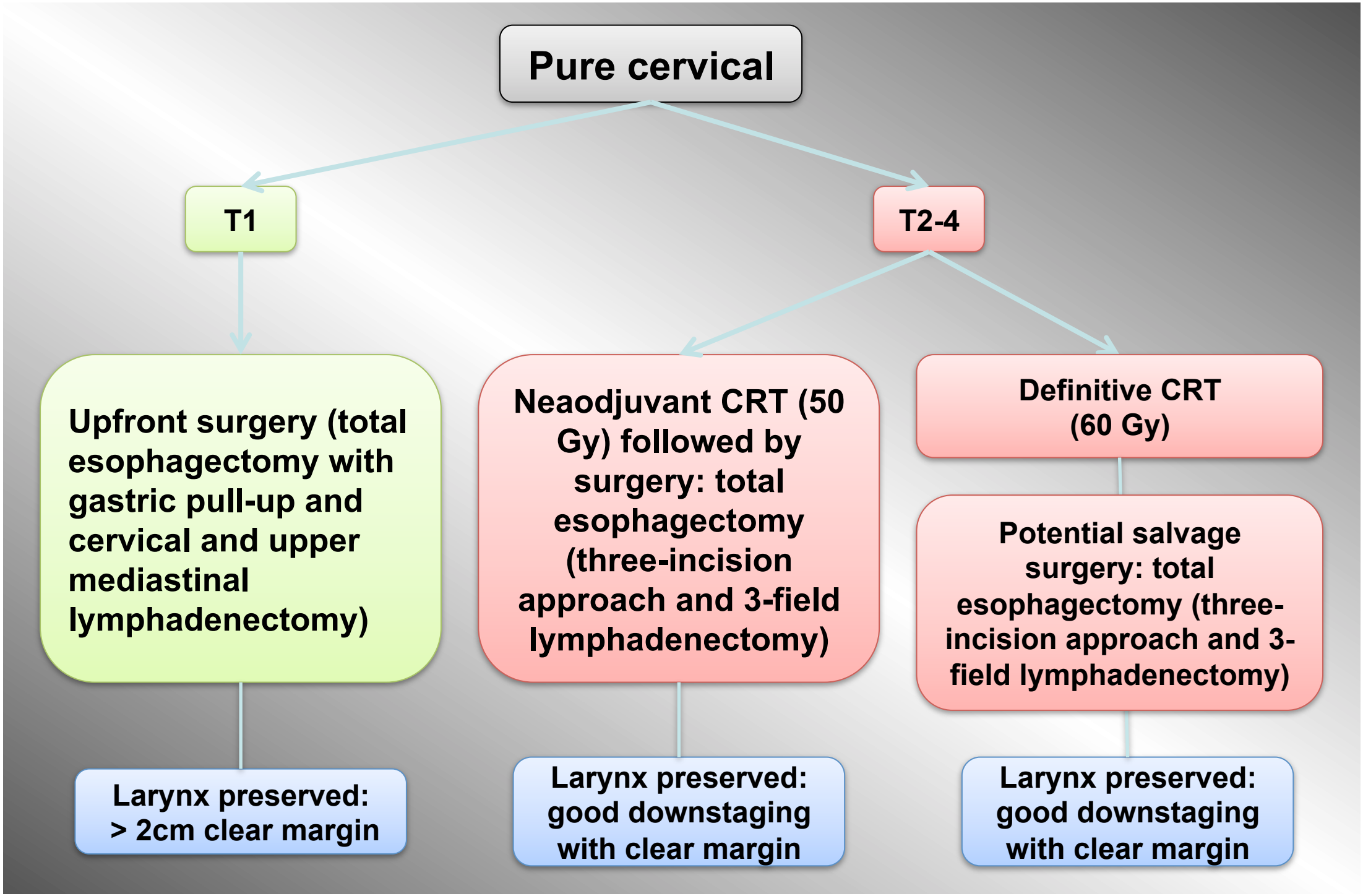
Survival

At our Institution from 2000

8/19 died during follow up
42%

KM curves not yet performed for the low number of cases

11 alive, with median follow-up of 38 months


Pure cervical
T1
T2-4
Upfront surgery (total esophagectomy with gastric pull-up and cervical and upper mediastinal lymphadenectomy)
Neaodjuvant CRT (50 Gy) followed by surgery: total esophagectomy (three-incision approach and 3-field lymphadenectomy)
Definitive CRT (60 Gy)
Potential salvage surgery: total esophagectomy (three-incision approach and 3-field lymphadenectomy)
Larynx preserved: > 2cm clear margin
Larynx preserved: good downstaging with clear margin
Larynx preserved: good downstaging with clear margin

Grazie per l'attenzione!