



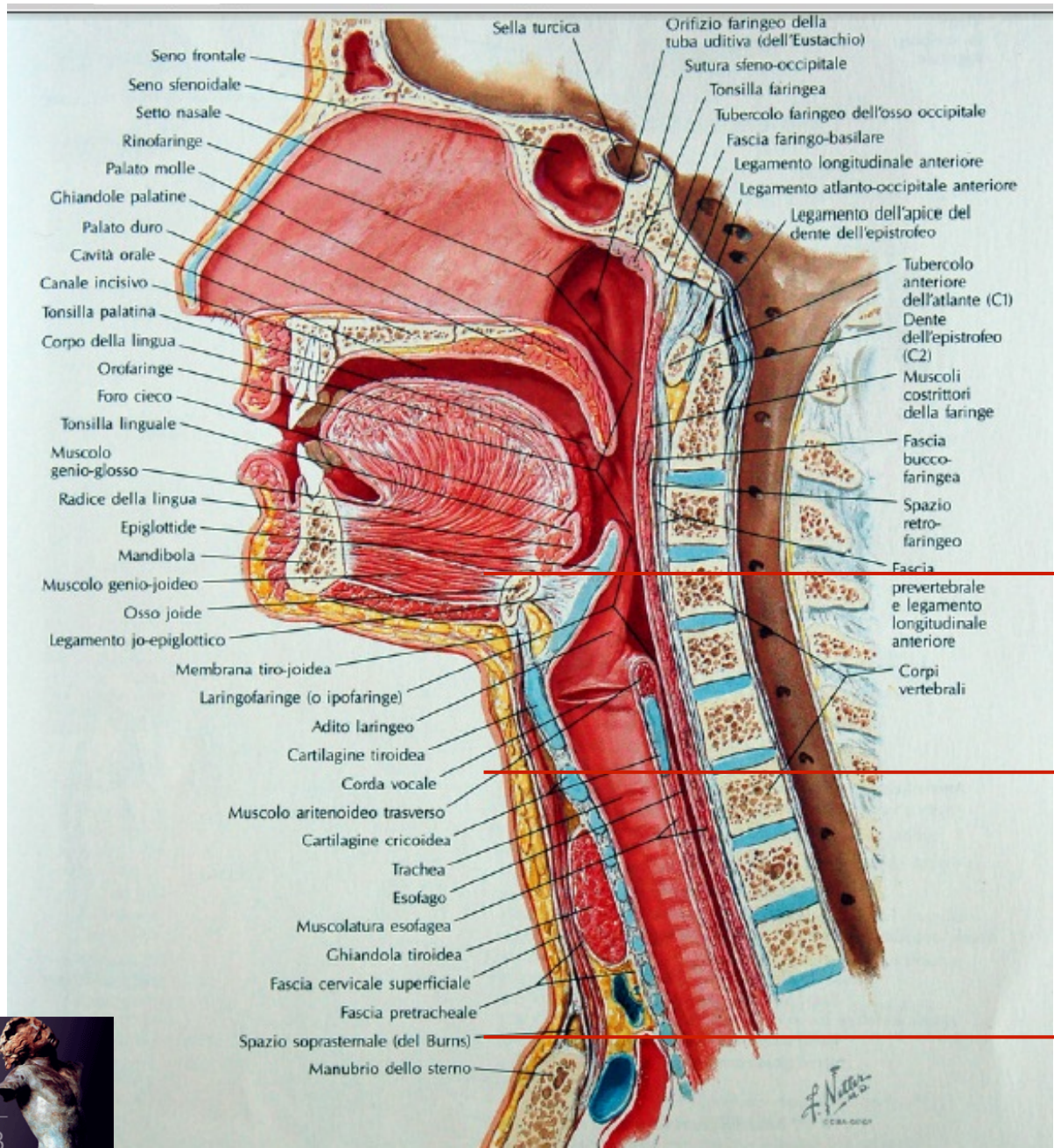
**Management diagnostico-terapeutico nei tumori dell'ipofaringe e esofago cervicale**

# Trattamenti integrati nella malattia localizzata

Stefano Pergolizzi



XXIII Congresso AIRO. Giardini Naxos (ME) 26-29 Ottobre 2013

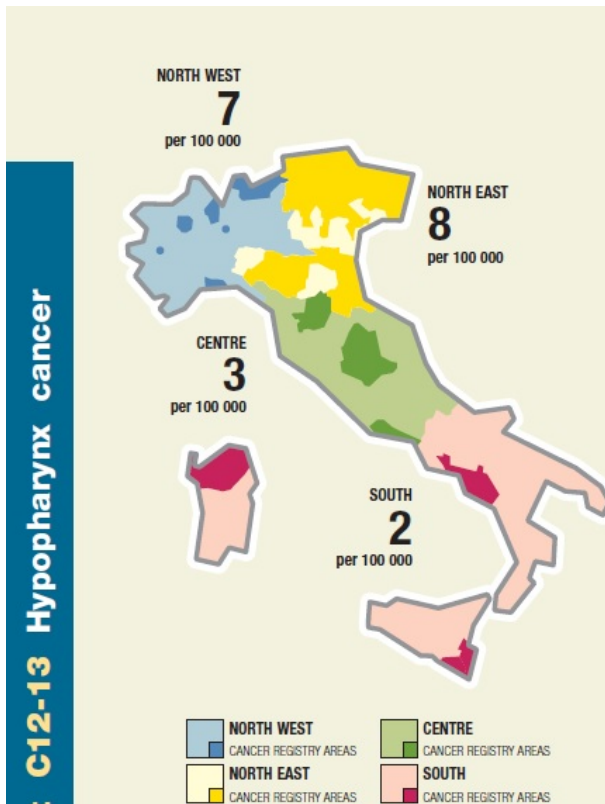


Ipofaringe

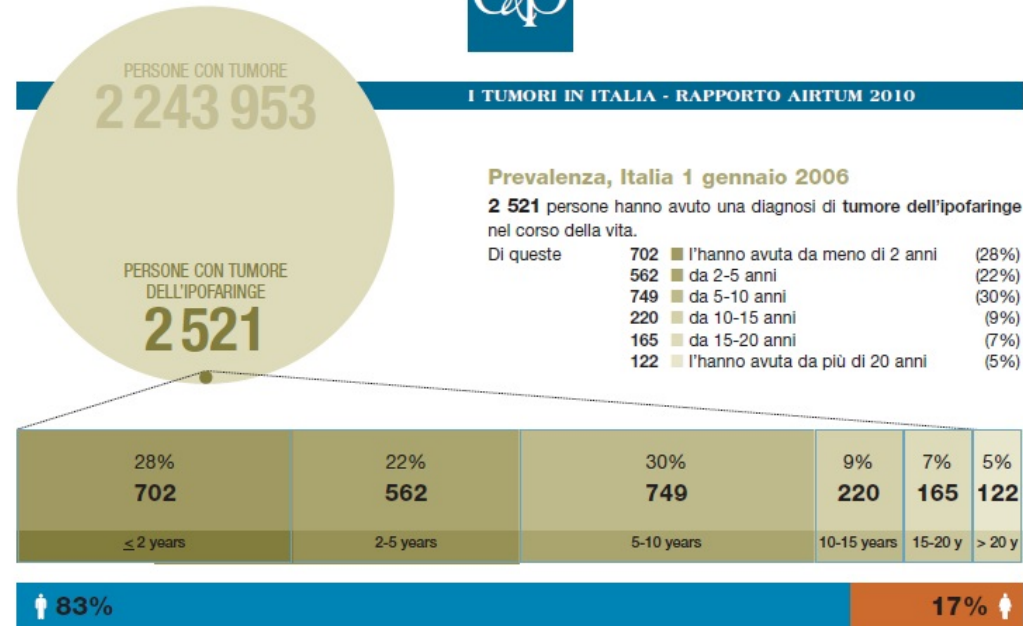
Esofago cervicale



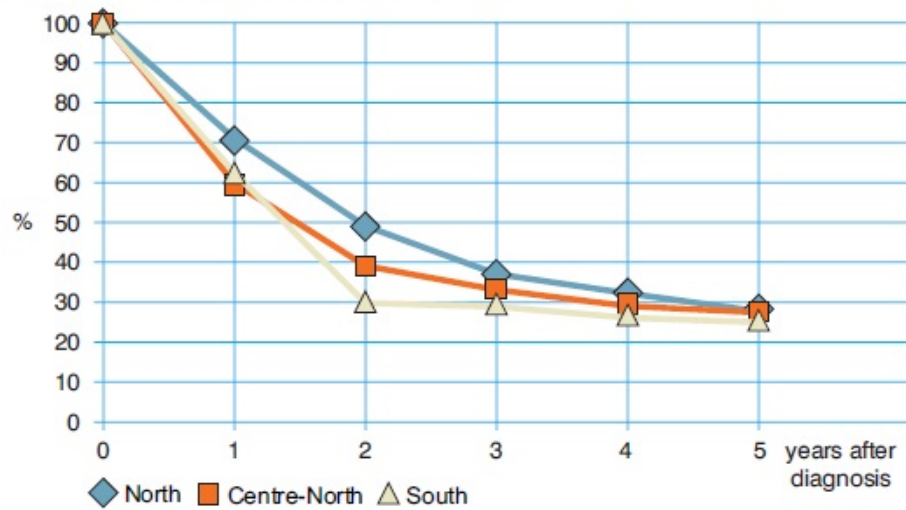
# Ipofaringe



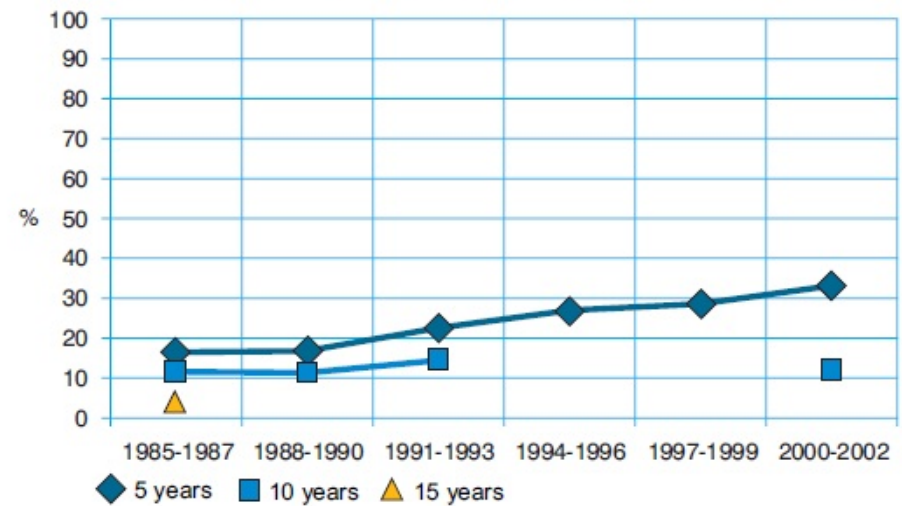
I TUMORI IN ITALIA - RAPPORTO AIRTUM 2010



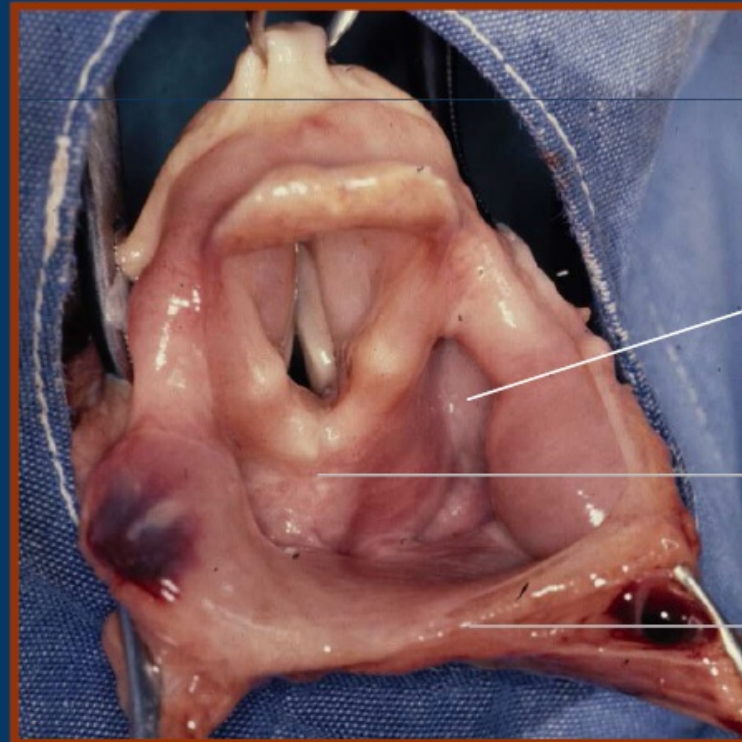
**Relative survival by Italian Areas**



**Trend of relative survival Pool of some Italian Registries**



- SOTTOSEDI



Seno piriforme

Area retrocricoidea

Parete posteriore  
del faringe



D. Alterio, Milano 22 Giugno 2013

## Hypopharynx

- |            |   |
|------------|---|
| <b>T1</b>  | Tumor limited to one subsite of hypopharynx and/or 2 cm or less in greatest dimension   |
| <b>T2</b>  | Tumor invades more than one subsite of hypopharynx or an adjacent site, or measures more than 2 cm but not more than 4 cm in greatest diameter without fixation of hemilarynx |
| <b>T3</b>  | Tumor more than 4 cm in greatest dimension or with fixation of hemilarynx or extension to esophagus   |
| <b>T4a</b> | Moderately advanced local disease<br>Tumor invades thyroid/cricoid cartilage, hyoid bone, thyroid gland, or central compartment soft tissue**                                 |
| <b>T4b</b> | Very advanced local disease<br>Tumor invades prevertebral fascia, encases carotid artery, or involves mediastinal structures  |



\*\*Note: Central compartment soft tissue includes prelaryngeal strap muscles and subcutaneous fat.

### Regional Lymph Nodes (N)†: Oropharynx and Hypopharynx

- |            |  |
|------------|--|
| <b>NX</b>  | Regional lymph nodes cannot be assessed  |
| <b>N0</b>  | No regional lymph node metastasis  |
| <b>N1</b>  | Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension  |
| <b>N2</b>  | Metastasis in a single ipsilateral lymph node, more than 3 cm but not more than 6 cm in greatest dimension, or in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension, or in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension |
| <b>N2a</b> | Metastasis in a single ipsilateral lymph node more than 3 cm but not more than 6 cm in greatest dimension  |
| <b>N2b</b> | Metastasis in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension  |
| <b>N2c</b> | Metastasis in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension  |
| <b>N3</b>  | Metastasis in a lymph node more than 6 cm in greatest dimension  |

†Note: Metastases at level VII are considered regional lymph node metastases.

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## Anatomic Stage/Prognostic Groups: Oropharynx, Hypopharynx

Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T3	N0	M0
	T1	N1	M0
	T2	N1	M0
	T3	N1	M0
Stage IVA	T4a	N0	M0
	T4a	N1	M0
	T1	N2	M0
	T2	N2	M0
	T3	N2	M0
	T4a	N2	M0
Stage IVB	T4b	Any N	M0
	Any T	N3	M0
Stage IVC	Any T	Any N	M1



# Prognosi peggiore tra tutti i ca. tratto aero-digestivo

-recidiva locale

-N+ alla diagnosi

-Metastasi sincrone o metacrone

-Secondi tumori in altre sedi tratto aero-digestivo

-Patologie correlate ad elevato consumo di alcool e tabacco





## Sopravvivenza % a 5 anni (3906 pz)

Seno Piriforme 33.6

Tutte le sottosedi 31.4

Hoffman HT

Laryngoscope 1997

Arch Otolaryngol Head and Neck Surg 1998



## Sopravvivenza % a 5 anni (1980-1985, 1295 pz)

Stadio I	63
Stadio II	58
Stadio III	42
Stadio IV	22

Hoffman HT

Laryngoscope 1997

Arch Otolaryngol Head and Neck Surg 1998



# Malattia in stadio iniziale

## 5yy OS (%)

RT +/- CT

52-77

Yoshimura RI IJROBP 2010

CH +/- RT +/- CT  
SCHLP-SGHLP

56-77

Laccourreye O Ann Otol Rhinol Laryngol 2005

MicroCH Laser +/- RT

70-73

Karatzanis AD J Surg Oncol 2010



## Sopravvivenza % a 3 anni (2000-2008, 103 pz)

Stadio I	100
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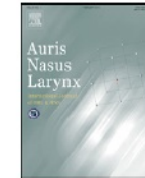
Stadio II	84
-----------	----

Stadio III	67
------------	----

Stadio IV	43-67
-----------	-------

Nakajima A Int J Radiat Oncol Biol Phys 2012





## Current management strategy of hypopharyngeal carcinoma

Jimmy Yu Wai Chan \*, William Ignace Wei

**Results:** In early-staged hypopharyngeal cancer, the overall and disease-specific survival rates after organ-preserving radiotherapy is comparable to that after surgery. However, for advanced staged disease, the results initial surgery with post-operative adjuvant radiotherapy was superior to chemoradiotherapy alone. The incidence of occult nodal metastasis is found to be more than 20%. Selective neck dissection removing cervical lymph node level II–IV is the procedure of choice for patients with clinically N0 neck. Contralateral nodal clearance may also be considered in tumors involving the medial wall of the pyriform recess, post-cricoid region or the posterior wall, and those with ipsilateral palpable nodal metastasis and clinical stage IV disease. Transoral robotic surgery (TORS) has the potential value as the minimally invasive procedure for the management of carcinoma of the hypopharynx.

**Conclusions:** The treatment strategy for carcinoma of the hypopharynx has been evolving with time. Organ preserving chemoradiotherapy has been the treatment of choice for early stage disease, with surgical resection and reconstruction reserved for advanced and recurrent tumors.



# Quale Target

## Stadio I-II

- E' necessario includere nel CTV Rinofaringe e basicranio?
- Quali livelli linfonodali irradiare profilatticamente



Table 2 Positive detection rate and invasion site of 186 patients with hypopharyngeal carcinoma

Invasion site	Primary subsite ( <i>n</i> , %)		
	Pyriiform sinus (142)	Pharyngeal wall (35)	Post-cricoid area (9)
Pyriiform sinus	142 (100)	33 (94.3)	7 (77.8)
Post-cricoid area	94 (66.2)	22 (62.9)	9 (100)
Posterior wall	119 (83.8)	35 (100)	3 (33.3)
Arytenoid	102 (71.8)	18 (51.4)	6 (66.7)
Aryepiglottic fold	134 (94.4)	24 (68.6)	7 (77.8)
Hyoid bone	15 (10.6)	3 (8.6)	0
Epiglottis	92 (64.8)	10 (28.6)	1 (11.1)
Pre-epiglottic space	77 (54.2)	3 (8.6)	1 (11.1)
Thyroid cartilage	70 (49.3)	14 (40)	2 (22.2)
Cricoid cartilage	27 (19)	7 (20)	2 (22.2)
Paraglotic space	113 (79.6)	11 (31.4)	3 (33.3)
Vocal cord	63 (44.4)	4 (11.4)	0
Ventricular bands	85 (59.2)	8 (22.9)	2 (22.2)
Anterior commissure	17 (12)	2 (5.7)	0
Esophagus	21 (14.8)	21 (60)	2 (22.2)
Thyroid gland	13 (9.2)	4 (11.4)	0
Pre-vertebral fascia	5 (10.6)	20 (57.1)	1 (11.1)
Oropharynx	61 (43)	16 (45.7)	0
→ Nasopharynx	0 (0)	1 (2.9)	0



Zheng WU A-P JCO 2012

**Table 3** Distribution of regional lymph node metastases of 186 patients with hypopharyngeal carcinoma

Level	Lymph node metastasis ( <i>n</i> , %)		
	PSC (142)	PWC (35)	PCC (9)
I	3 (2.1)	0 (0)	0 (0)
II	103 (72.5)	27 (77.1)	4/9 (44.4)
III	80 (56.3)	18 (51.4)	3/9 (33.3)
IV	25 (17.6)	9 (25.7)	0/9 (0)
V	7 (4.9)	2 (5.7)	0/9 (0)
VI	6 (4.2)	8 (22.9)	0/9 (0)
Retropharyngeal	15 (10.6)	12 (34.3)	2/9 (22.2)

PCC, post-cricoid carcinoma; PSC, pyriform sinus carcinoma; PWC, pharyngeal wall carcinoma.

Zheng WU A-P JCO 2012

Table 1  
Comparison between the TNM atlas terminology and the Robbins' classification of the lymph nodes of the neck

TNM atlas for lymph nodes of the neck		Robbins' classification	
Group number	Terminology	Level	Terminology
1	Submental nodes	Ia	Submental group
2	Submandibular nodes	Ib	Submandibular group
3	Cranial jugular nodes	II	Upper jugular group
4	Medial jugular nodes	III	Middle jugular group
5	Caudal jugular nodes	IV	Lower jugular group
6	Dorsal cervical nodes along the spinal accessory nerve	V	Posterior triangle group
7	Supraclavicular nodes	V	Posterior triangle group
8	Prelaryngeal and paratracheal nodes	VI	Anterior compartment group
9	Retropharyngeal nodes		
10	Parotid nodes		
11	Buccal nodes		
12	Retroauricular and occipital nodes		





# Quindi?

Rinofaringe

Potenzialmente No

Livelli II , III, IV

Si

Livello VI

Potenzialmente No

RPLN

Potenzialmente No

Seno Piriforme

Consigliabile

Parete Faringea  
Area postcricoidea





Contents lists available at SciVerse ScienceDirect

## Cancer Treatment Reviews

journal homepage: [www.elsevierhealth.com/journals/ctrv](http://www.elsevierhealth.com/journals/ctrv)



### Swallowing dysfunction in head and neck cancer patients treated by radiotherapy: Review and recommendations of the supportive task group of the Italian Association of Radiation Oncology

Elvio G. Russi <sup>a,\*</sup>, Renzo Corvò <sup>b</sup>, Anna Merlotti <sup>c</sup>, Daniela Alterio <sup>d</sup>, Pierfrancesco Franco <sup>e</sup>,  
Stefano Pergolizzi <sup>f</sup>, Vitaliana De Sanctis <sup>g</sup>, Maria Grazia Ruo Redda <sup>h</sup>, Umberto Ricardi <sup>i</sup>, Fabiola Paiar <sup>j</sup>,  
Pierluigi Bonomo <sup>k</sup>, Marco C. Merlano <sup>l</sup>, Valeria Zurlo <sup>m</sup>, Fausto Chiesa <sup>m</sup>, Giuseppe Sanguineti <sup>n</sup>,  
Jacques Bernier <sup>o</sup>

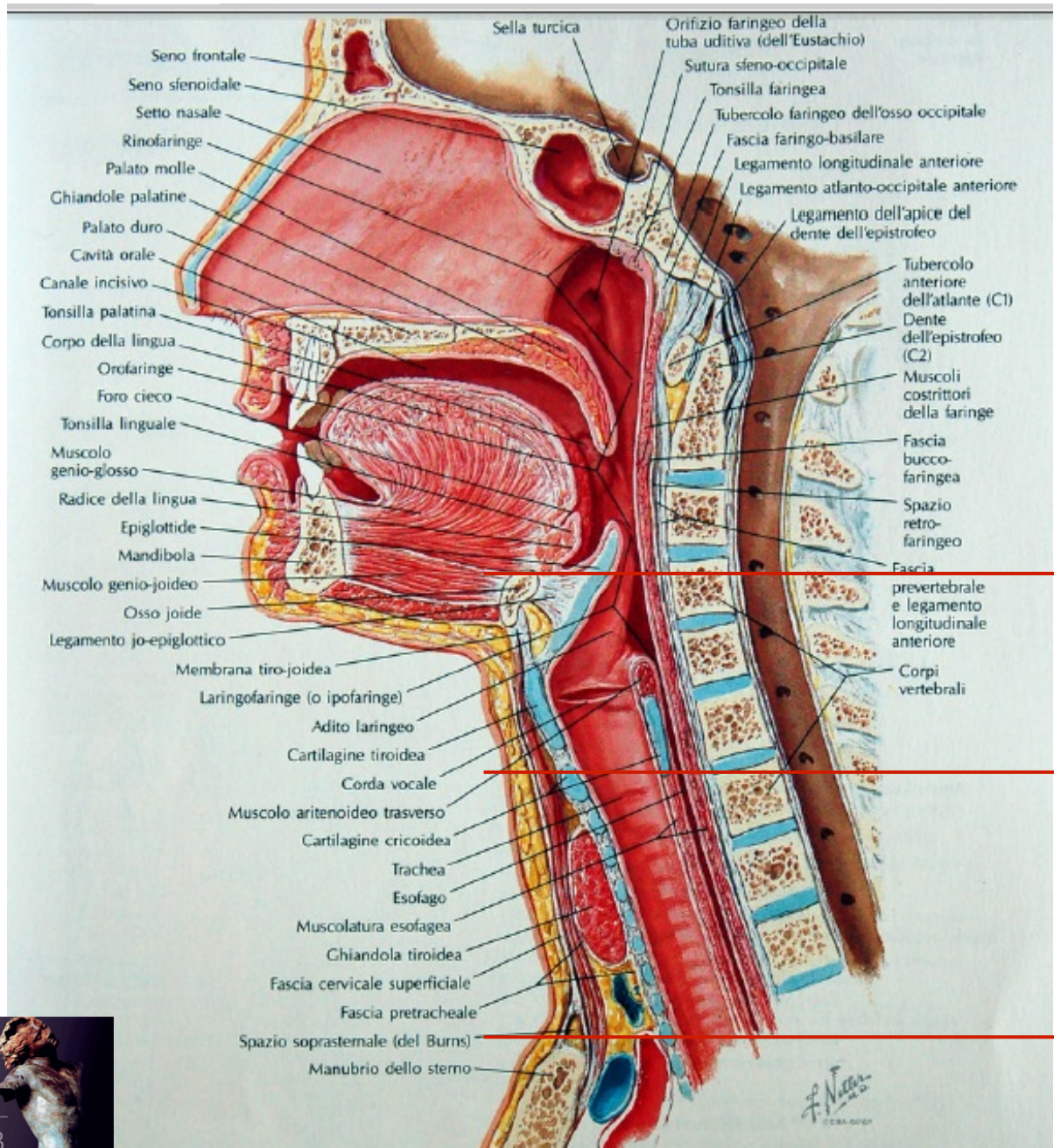
**Ch + RT**

“the summing effect of both therapies worsens swallowing uncoordination and may cause severe dysphagia and aspiration (if the larynx is preserved).”

**RT + CT**

“.....generalized weakness and un-coordination in deglutition. This could be due to the enhancement of radioinduced fibrosis of the musculature or added toxic effects on the neuromuscular junctions”



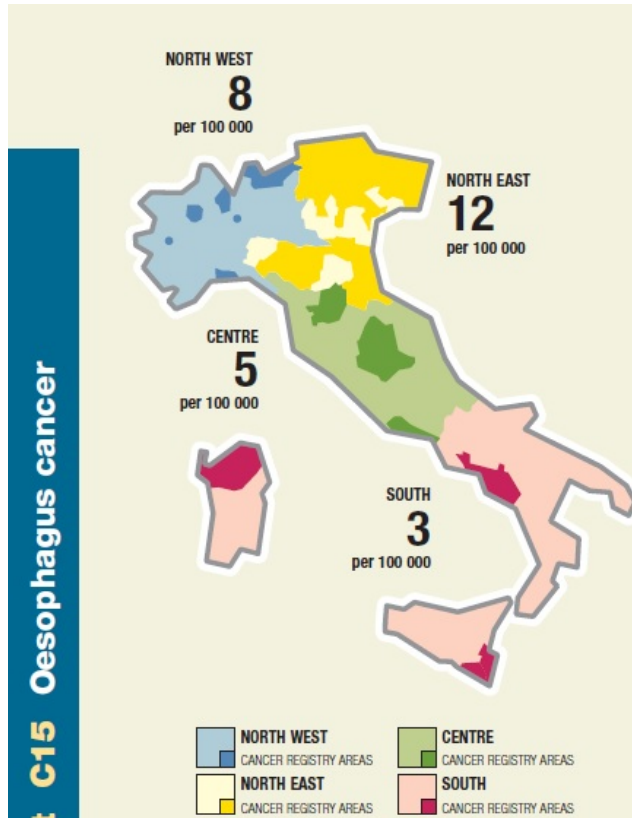


Ipofaringe

Esofago cervicale



# Esofago



PERSONE CON TUMORE  
**2 243 953**

I TUMORI IN ITALIA - RAPPORTO AIRTUM 2010

## Prevalenza, Italia 1 gennaio 2006

**3 737** persone hanno avuto una diagnosi di tumore dell'esofago nel corso della vita.

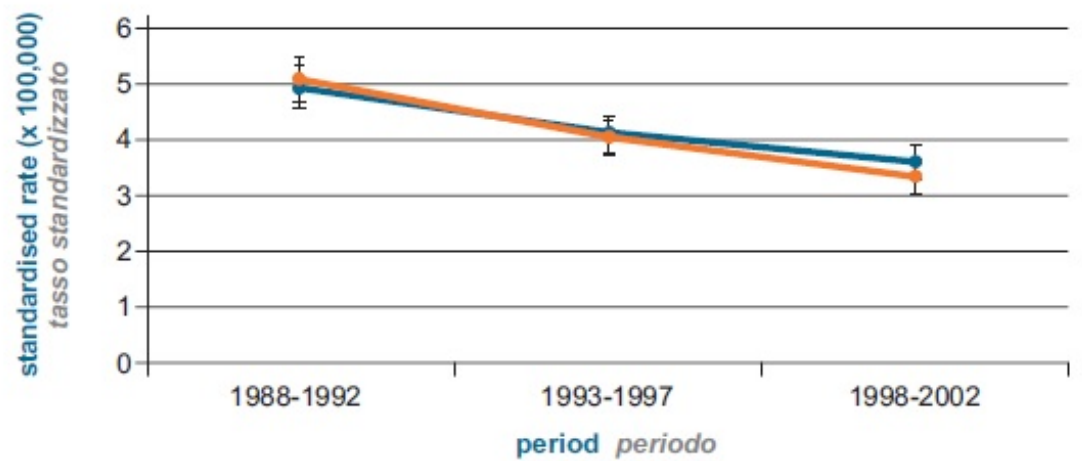
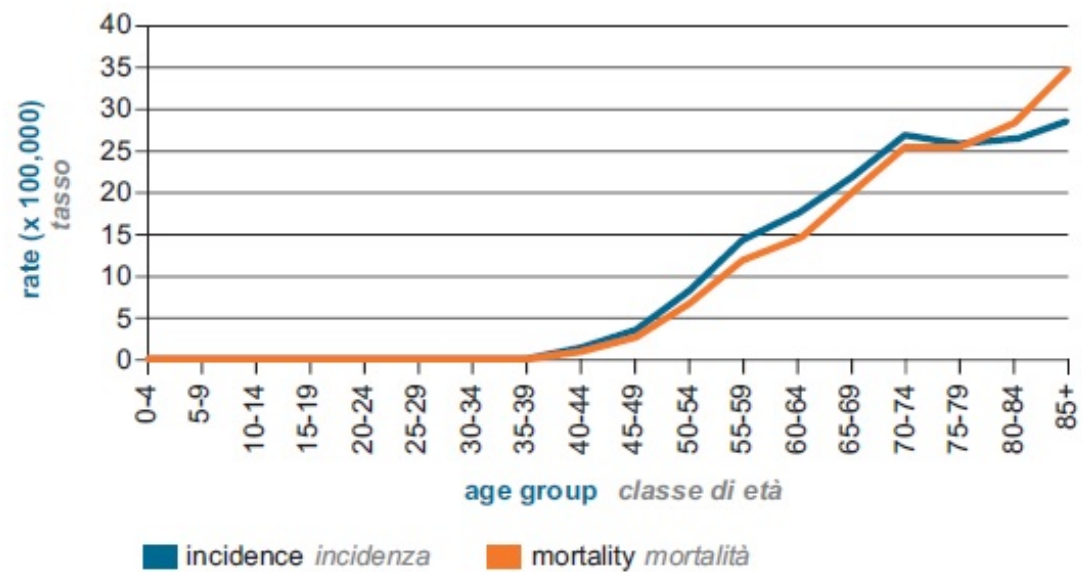
Di queste

1 727	l'hanno avuta da meno di 2 anni	(46%)
775	da 2-5 anni	(21%)
676	da 5-10 anni	(18%)
257	da 10-15 anni	(7%)
162	da 15-20 anni	(4%)
140	l'hanno avuta da più di 20 anni	(4%)

PERSONE CON TUMORE DELL'ESOFAGO  
**3 737**

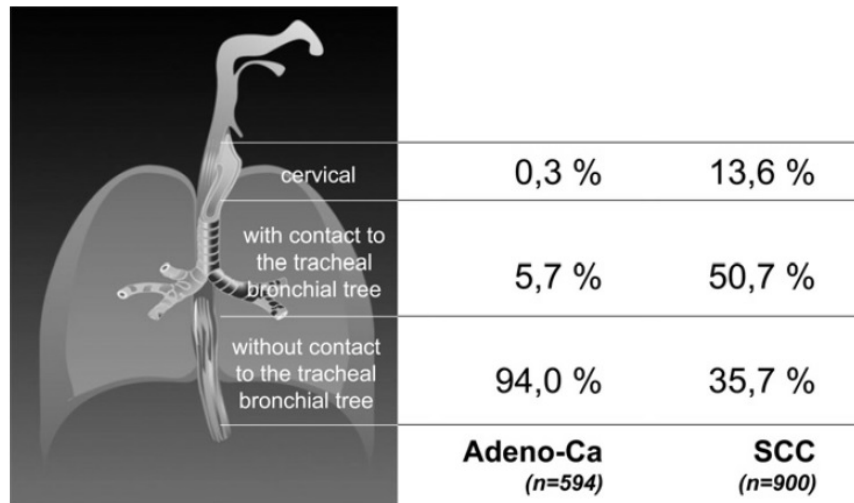
46%	21%	18%	7%	4%	4%	<b>162</b>
<b>1 727</b>	<b>775</b>	<b>676</b>	<b>257</b>			<b>140</b>
≤ 2 years	2-5 years	5-10 years	10-15y	15-20	> 20y	





## Squamous-Cell Cancer of the Esophagus

Median age	53.4 years
Male/female	7:1
Occupation (prevalence)	
Academics	20.8%
“White collar worker”	27.2%
“Blue collar worker”	52.2%
Alcohol abuse (prevalence)	69.7%
Nicotine abuse (prevalence)	69.3%
Malnutrition (prevalence)	24.1%
Pulmonary capacity (average FEV% compared with normal)	82.5%
Cardiovascular risk factors (prevalence)	19.5%
Impaired liver functioning (prevalence)	35.3%



**Figure 1** Differences in tumor location of squamous-cell cancer and adenocarcinoma of the esophagus.

XXIII Congresso AIRO. Giardini Naxos (ME) 26-29 Ottobre 2013



**Table 1**

**American Joint Committee on Cancer (AJCC)  
TNM Classification of Carcinoma of the Esophagus and  
Esophagogastric Junction (7th ed, 2010)**

**Primary Tumor (T)**

TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	High-grade dysplasia*
T1	Tumor invades lamina propria, muscularis mucosae, or submucosa
T1a	Tumor invades lamina propria or muscularis mucosae
T1b	Tumor invades submucosa
T2	Tumor invades muscularis propria
T3	Tumor invades adventitia
T4	Tumor invades adjacent structures
T4a	Resectable tumor invading pleura, pericardium, or diaphragm
T4b	Unresectable tumor invading other adjacent structures, such as aorta, vertebral body, trachea, etc.

\*High-grade dysplasia includes all noninvasive neoplastic epithelia that was formerly called carcinoma in situ, a diagnosis that is no longer used for columnar mucosae anywhere in the gastrointestinal tract.

**Regional Lymph Nodes (N)**

NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in 1–2 regional lymph nodes
N2	Metastasis in 3–6 regional lymph nodes
N3	Metastasis in seven or more regional lymph nodes

**Distant Metastasis (M)**

M0	No distant metastasis
M1	Distant metastasis

**Anatomic Stage/Prognostic Groups**

**Squamous Cell Carcinoma\***

Stage	T	N	M	Grade	Tumor Location**
Stage 0	Tis (HGD)	N0	M0	1, X	Any
Stage IA	T1	N0	M0	1, X	Any
Stage IB	T1	N0	M0	2–3	Any
	T2–3	N0	M0	1, X	Lower, X
Stage IIA	T2–3	N0	M0	1, X	Upper, middle
	T2–3	N0	M0	2–3	Lower, X
Stage IIB	T2–3	N0	M0	2–3	Upper, middle
	T1–2	N1	M0	Any	Any
Stage IIIA	T1–2	N2	M0	Any	Any
	T3	N1	M0	Any	Any
	T4a	N0	M0	Any	Any
Stage IIIB	T3	N2	M0	Any	Any
Stage IIIC	T4a	N1–2	M0	Any	Any
	T4b	Any	M0	Any	Any
	Any	N3	M0	Any	Any
Stage IV	Any	Any	M1	Any	Any

\*Or mixed histology including a squamous component or NOS.

\*\*Location of the primary cancer site is defined by the position of the upper (proximal) edge of the tumor in the esophagus.

[Continue...](#)



Cervical esophageal cancers are treated definitively with radiation doses, field design, and chemotherapy regimens similar to head and neck cancers.



Samuel Bak. BK1509 *Questionable*. Oil on canvas, 18" x 24".



*Neoadjuvant chemoradiotherapy followed by surgical resection is the current standard of care for localized cancer of the esophagus.*



## Radiation Therapy and Esophageal Cancer

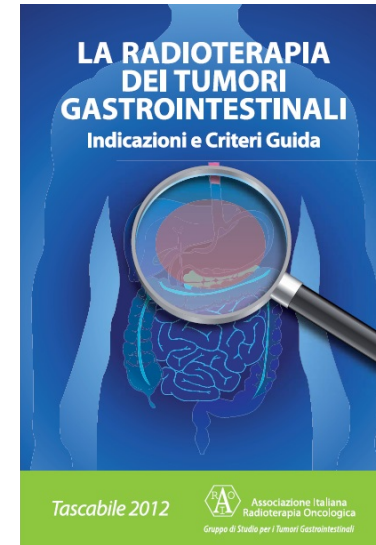
Ravi Shridhar, MD, PhD, Khaldoun Almhanna, MD, MPH, Kenneth L. Meredith, MD, FACS,  
Matthew C. Biagioli, MD, Michael D. Chuong, MD, Alex Cruz, and Sarah E. Hoffe, MD



## **Stadio IA (T1 N0 M0; G1-2 o Gx); Stadio IB (T1-T2 N0 M0 G1-2)**

### *Opzioni standard*

1. Resezione endoscopica mucosa per via endoscopica o ablazione (T1a) (9, 10) (**III; B**)
2. Esofagectomia (T1a- esofago toracico e giunzione esofago-gastrica) (9, 10) (**IIa; B**)
3. Esofagectomia (T1b-T2 esofago toracico e giunzione esofago-gastrica) (9, 10) (**IIa A**)
4. Radio-chemioterapia (50.4-64.8 Gy 1.8 Gy/die; CDDP e 5-FU) concomitante definitiva (T1b-T2 esofago cervicale; < 5 cm dal m. cricofaringeo) (11, 12) (**IIb; A**)
5. Radio-chemioterapia concomitante neoadiuvante (45-50.4 Gy 1.8 Gy/die; CDDP e 5-FU) (T2 esofago toracico e giunzione esofago-gastrica) (6, 13-16) (**Ia; A**)
6. Chemioterapia neoadiuvante (5FU e CDDP) (17-20) (T2 per tutte le sedi): riservato a pazienti non proponibili per la terapia concomitante o per controindicazioni alla Radioterapia (17-20) (**B**)
7. Radio-chemioterapia adiuvante in caso di R0 con N+ patologico, R1 ed R2 (esofago toracico distale e giunzione esofago-gastrica) (21-23) (**IIb; A**)

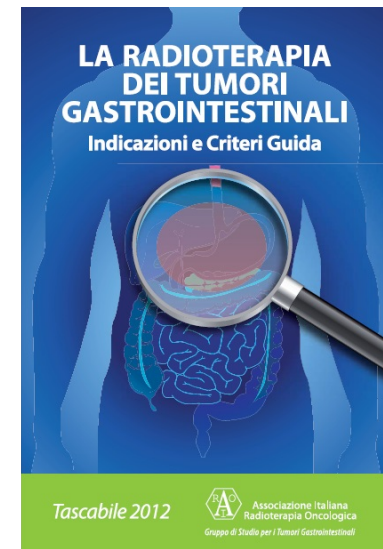
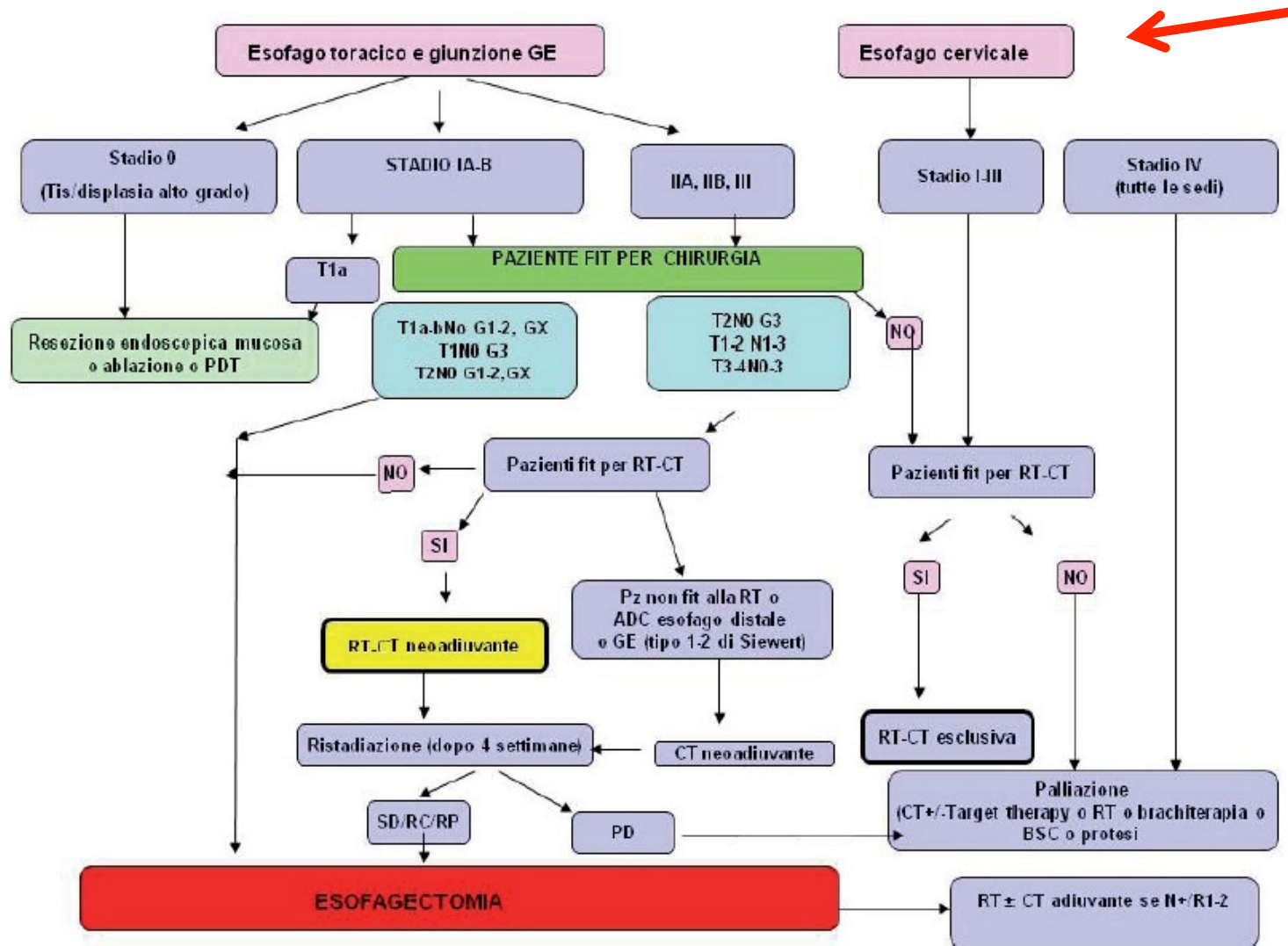


## **Stadio IIA (T2 N0 M0 G3) & Stadio IIB (T1-T2 N1 M0; T3 N0 M0)**

### *Opzioni standard*

1. Radio-chemioterapia concomitante neoadiuvante (45-50.4 Gy 1.8 Gy/die; CDDP e 5-FU) (esofago toracico e giunzione esofago-gastrica) (6, 13-16) (**Ia; A**)
2. Radio-chemioterapia (50.4-64.8 Gy 1.8 Gy/die; CDDP e 5-FU) concomitante definitiva (esofago cervicale; < 5 cm dal m. cricofaringeo) (11-12) (**IIb; A**)
3. Esofagectomia (esofago toracico e giunzione esofago-gastrica) (9, 10) (**IIa A**)
4. Chemioterapia neoadiuvante (5FU e CDDP) (17-20) (tutte le sedi): riservato a pazienti non proponibili per la terapia concomitante o per controindicazioni alla Radioterapia (17-20) (**B**)
5. Radio-chemioterapia adiuvante in caso di R0 con N+ patologico, R1 ed R2 (esofago toracico distale e giunzione esofago-gastrica) (21-23) (**IIb; A**)





#### PRINCIPLES OF SURGERY

- Prior to surgery, clinical staging should be performed to assess resectability with CT scan of the chest and abdomen, whole body PET (Integrated PET/CT is preferred) and endoscopic ultrasound.
- Prior to starting therapy all patients should be assessed by an esophageal surgeon for physiologic ability to undergo esophageal resection.<sup>1</sup> Esophageal resection should be considered for all physiologically fit patients with resectable esophageal cancer (> 5 cm from cricopharyngeus)
- Cervical or cervicothoracic esophageal carcinomas < 5 cm from the cricopharyngeus should be treated with definitive chemoradiation.



# RT-CT 50-50.4 Gy + 5FU & CDDP based schedule



# Quale Target

## CTV

-4cm craniale e caudale ; 1cm lateralm. al GTV

-I linfonodi sovraclaveari devono essere inclusi nel CTV

RTOG 0113

v. 2004

RTOG 0436

v. 2012



