2007

Esophageal Cancer

Edward Yu
University of Western Ontario, edward.yu@lhsc.on.ca

ESOPHAGEAL CANCER

Dr. Edward Yu

A. **Incidence**: <5/100,000 in U.S. ; <10/100,000 in Canada.
gastroesophageal cancer of adenocarcinoma is on the rise as compare to squamous cell carcinoma of the esophagus.

B. **Risk factors**: Tylosis, Plummer-Vinson Syndrome, Caustic Injury, Achalasia, Smoking, Alcohol.

C. Basic patient **Work Up** requires the following:
History & Physical
Barium swallow
Endoscopy
CBC, Blood chemistry
Chest x-ray , Chest /Abdominal CT
Endoscopic U/S
Pathology

X-ray of a patient with lower third esophageal cancer.(barium filling defects)

D. Esophageal cancer **staging** uses TNM system:

Staging (TNM):

- T_1 Tumor invades lamina propria or submucosa.
- T_2 Tumor invades muscularis propria.
- T_3 Tumor invades adventitia.
- T_4 Tumor invades adjacent structures.
- N_1 Regional nodes mets.

Staging (TNM):

stage I T_1, N_0
stage II A- T_{2-3}, N_0 ; B-T_{1-2}, N_1
stage III T_{3-4}, N_1
stage IV M_1 (including Celiac nodes involvement).

E. Esophageal cancer **management** modality options:

1. **Surgery**:
   - Aim is to achieve R0 resection (complete resection of tumor).
   - The 5 yr. survival after R0 resection is 15-20%.
   - The median survival is about 18 months.

2. **Radiation Therapy**:
   - Randomized prospective trial (Radiation Therapy Oncology Group-RTOG 8501) showed that radiation alone of 64Gy at 2Gy/fx, 3yr. survival rate is zero.
   - Radiation therapy alone reserved for palliation or for medically unable to receive chemotherapy.
   - Pre-op. or post-op. radiation therapy has been shown to have no survival benefit.
   - Post-op radiation therapy can offer local control benefit in high risk patients.(Fok et al,Surg 1993,Teniere et al., Surg Gyn 1991).

3. **Chemoradiation**:
   - Randomized prospective trial (RTOG 8501) also showed that combined chemo (5FU/Cisp) + radiation therapy (50Gy) has survival benefit over radiation therapy (64Gy) alone.
   - The 5 yr. overall survival (OS) of combined modality is superior (27%) than radiation therapy alone (0%) , median survival 14 mos.(month) of combined versus (VS) 9 mos. of radiation alone.
   - Local failure rate of combined chemoradiation is also superior (47%) over radiation alone(65%).
   - Higher dose of radiation therapy (64.8Gy) with same chemo showed no additional benefit : median OS with higher radiation dose of 13 mos VS standard 50 Gy of 18.1 mos. not-significance (

NS), 2 yr. OS of 31% VS 40% (NS), and local/regional failure of 56% VS 52% (NS).

- Presently research focus on new investigational agents : paclitaxel- based, docetaxel-based, or irinotecan-based chemotherapy to improve overall survival.

Randomized Control Trials (RCTs)comparing pre-op chemoradiation therapy(**Trimodality**) with surgery alone .

- Although the concept is reasonable, confirmatory result is still pending.

(Urba et al, JCO 2001; Walsh et al, NEJM 1997; Bosset et al, NEJM 1997; Burmeister et al, Proc.ASCO 2002 ; Malthaner et al, BMC Cancer 2004).

4. **Brachytherapy**:
   - It is used mainly for palliation when given alone.
   - It has local control of 25-35%, median OS of 5 mos.

RTOG 9207 combined modality(5FU/Cisp/50Gy) followed by intra-luminal brachytherapy boost, local failure rate of 27%; acute toxicity Grade 3-5 58%, 26%, 8% ,respectively; fistula rate of 18%/yr. ; therefore , at the present time brachytherapy is not recommended by the American Brachytherapy Society as a boost when using with high dose rate concurrent with chemotherapy.

5. **Chemotherapy**:

- It is used mainly for palliation when given alone.
- Pre-op chemotherapy may provide small benefit in survival over surgery alone. Confirmative result is pending (Int.0113 study, Thirion et al , Proc ASCO , 2007) .
- Chemotherapy agents for esophageal cancer include : Cisplatinum, most active, >20% response rate. Others include 5FU, Mitomyc. Bleomyc, Doxorub, Vind, Paclit, Vinorel.

  5FU + Cisp combination has response rate of 20-50%.

6. **Endoscopic palliation**:

- Laser
- Ballon dilation
- Photodynamic
- Intracavitary irradiation and plastic or expandible metal prothesis,

all of above is for symptom control only.

MANAGEMENT SUMMARY :
Trimodality management of resectable esophageal cancer is evolving, many cancer centers favour the neoadjuvant management (chemoradiation followed by surgery) although final confirmative result is pending.

There is no clinical trial comparing the benefit of neoadjuvant VS adjuvant resectable esophageal cancer.

At London Regional Cancer Program (LRCP) :

Esophageal cancer that is operable, resectable T_1-T_3
The recommended management is:

- Esophagectomy
- After complete resection:
    - If N_0, the management is observation only.
    - If N_1, (or resection margins involvement) the recommended management is post -op chemoradiation.

Esophageal cancer that is operable, resectable T_1-T_3
It is not unreasonable to offer concurrent chemotherapy (5FU/Cisp) + radiation therapy (50Gy) as an alternative treatment option besides surgery (RTOG 8501). Survival can approach that of surgery alone in some circumstances.

Esophageal cancer that is inoperable T_4, or surgery refusal
The recommended management is concurrent chemoradiation .

Inoperable disease and patient is unable to tolerate chemotherapy , the management can be best supportive care.

Best supportive care includes the following:

- Obstruction-stent, laser, photodynamic therapy.
- Radiation therapy (xrt)(external beam, brachytherapy).
- Nutrition - external feeding(J-tube).
- Pain control - xrt/medications.
- Bleeding - xrt/surgery/endoscopic therapy.