Site of residual esophageal cancer: histopathological evaluation after neo-adjuvant chemoradiotherapy


31st European Congress of Pathology
08-09-2019

University of Groningen, University Medical Center Groningen, the Netherlands
Standard treatment: nCRT + surgery (CROSS)*

Response:
- pCR: 20-35% → Surgery?
- cCR ≠ pCR

After nCRT: “Watchful waiting strategy”?

Problem: residual esophageal cancer (60%)

Aim

- To determine the rate of residual EC after nCRT according to:
  - anatomical site
  - tumor target volumes
- To evaluate the impact of residual EC on treatment decisions
Methods

- Retrospective study: prospectively maintained database
  - period: 2009 - 2018
  - n = 386

- Uniform group: n = 151
  - staging: PET/CT + EUS
  - nCRT*: carboplatin / paclitaxel + 41.4 Gy RT
UMCG method: in- and ex-vivo determined tumor target volumes

Gross tumor volume (GTV)
Clinical tumor volume (CTV)
Planning target volume (PTV)

I: above the CTV
II: proximal to the CTV
III: GTV
IV: distal to the CTV
V: below the CTV

A: ex-vivo resected specimen inked after pinned directly on corkboard.
B: ex-vivo localized TV
C: in-vivo localized TV

Intraoperative: marked target volumes (TV) (preoperative landmarks)

Standard: ex-vivo pathologic evaluation of pinned and inked specimen on cork board

- From proximal to distal: sequence in toto sealed
- Mandard classification of TRG (response)
Results: standard pathology method

- Total group: resection with curative intent: n=151

- Radicality resection:
  - Complete (R0): n= 136 (90%)
  - Irradical microscopic (R1): n=15
Response rate: Ro-resections: n = 136

- Complete: pCR ~ 20%
- Partial: pPR: ~ 66%
- Non-respond: pNR ~ 14%
Residual tumor in TRG 2-5: n=109

- ypT0N+ n= 7
- ypT+N0 n= 63
- ypT+N+ n=39

Response rate: TRG1= pCR
Complete: ypToNo ~ 20%
Residual EC in esophageal layers
Ro group: Mandard TRG 2-5 (T+No/N+): n=94

Mucosa: ypT1a n=8 (7.3%)

Submucosa: ypT1b n=18 (16.5%)

Muscularis prop: n=21 (19.3%)

Adventitia: n=47 (43.1%)
Microscopic residual tumor partial responders (Mandard TRG 2-3): n=90

- **Mucosa**: ypT1a n=7 (7.8%)
- **Submucosa**: ypT1b n=11 (12.2%)
- **Muscularis prop**: n=11 (12.2%)
- **Adventitia**: n=22 (24.4%)
Residual EC regarding radiation fields in Mandard TRG 2-3 group: n=90

PRIMARY TUMOR

- Macroscopic residue outside GTV (III): 8.9%
- Microscopic residue outside CTV (II/IV): 16.7%
- Microscopic residue outside CTV only: 1.1%
Residual EC in LN regarding radiation fields

Mandard TRG 2-3 group: n=90

- Proximal to CTV (II/IV)
  n=2 (5.4%)

- Distal to CTV (II/IV)
  n=5 (13.5%)

- One ypToN+ outside CTV
Site of residual tumor:
- limited superficial (ypTo-1N+) and
- deeper layers (ypT1-4aN0/T2-4aN+) (p=0.002).
DFS and type of residual tumor

DFS in TRG 2-5 group (n=118) microscopic v.s. macroscopic residual tumor (p=0.022).
pCR ~ 20% and limited superficial residue (ypT1aN0) in 7.8% in Ro group

In pts with ypT0: ~ 6.4% had nodal (N+) residual disease cranial or caudal to the CTV

DFS significantly lower in macroscopic tumor detected outside the GTV and in partial responders with nodal residual disease
These pathological findings of residual disease emphasize:

- The limitations of clinical staging and subsequently the established radiation fields
- The potential limitations of a watch and wait policy