Challenges in Cancer Staging after Neoadjuvant Treatment

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Neoadjuvant Treatment of Solid Tumors

- The clinical case for neoadjuvant treatment for solid tumors
- The problem
- Current trends and future possibilities
- What data needs collecting, how is it found?
- What is in our AJCC 8th Ed Cancer Staging Manual?
- Evaluation of response
- How is cTNM linked to yTNM?
- Case for collecting ycTNM when there is no ypTNM
The Clinical Case

• Life-threatening aspect of cancer is distant spread of disease
• Adjuvant chemotherapy after surgery given since 1970’s to improve survival
  – Cancer staging was only cTNM and pTMN after surgery, before adjuvant treatment given
  – However, survival curves included both surgery and adjuvant treatment (if given)
• Neoadjuvant systemic therapy began with treatment for locally advanced tumors
• Neoadjuvant radiation therapy +/- systemic therapy now standard for certain sites (rectal carcinoma)
Problems on Multiple Fronts

• Data not collected in CoC hospitals

• Fields don’t exist or poorly defined

• Registry community overwhelmed catching up on 2018 cases using 8th Ed

• Data not needed/used by surveillance community

• Neoadjuvant treatment increasing
Neoadjuvant Systemic Therapy

• Given with therapeutic intent before surgery:
  – Treats occult distant at earliest possible time
  – Reveals tumor sensitivity to systemic agent: responder or non-responder
  – Reduce local tumor burden to allow less surgery (sometimes no surgery)

• Usually infusional chemotherapy

• Oral hormonal therapy

• Future applications – oral targeted therapy or infusional immunotherapy
Neoadjuvant Radiation Therapy

- Neoadjuvant radiation therapy (usually combined with chemotherapy):
  - Reduces local tumor burden to allow less surgery (sometimes no surgery)
  - Improves final pathological surgical margins
  - Caution, radiation only provides local treatment
    - During this window of local tumor treatment
    - Occult distant disease may become overt
What is in AJCC 8th Ed Staging Manual?

- Majority of solid tumors (including lung, colorectal, prostate, most head and neck carcinomas)
  - Single prognostic stage group table
  - No separation of clinical and pathological stage groups

- Breast, melanoma, and Merkel cell carcinoma
  - Separate clinical and pathological stage group tables

- Esophageal & Stomach carcinomas
  - Separate clinical, pathological, and posttherapy (yp) stage group tables
Duration/Intent of Neoadjuvant Treatment

• Usually several months with short recovery period before definitive surgery

• Neoadjuvant treatment may terminate early due to
  – Toxicity of treatment or
  – Progression of disease

• A short run-in (days or weeks) course of chemo or hormone therapy
  – Looks for early markers of response
  – NOT considered or included as neoadjuvant treatment for staging purposes
Evaluation of Response

• Response of local regional tumor is complete (CR), partial (PR), no response (NR), or progression
  – Evaluation made by
    • Clinical exam
    • Serial imaging
    • Scopes and biopsies

• Response of occult distant metastases is progression or no progression
  – Evaluation made by
    • Symptoms/imaging
    • Rarely clinical exam
Neoadjuvant Complete Response

- cT2 cN1 cM0 invasive ductal carcinoma. Neoadjuvant chemo (completed planned 6 cycles) followed by MRM. Final pathology shows no residual tumor, 13 negative nodes.

- Neoadjuvant therapy destroyed all tumor, complete pathological response
  - ypT0 ypN0 cM0 stage 99
  - Entered into data item for posttherapy staging
  - Reminder - must meet criteria for neoadjuvant
Neoadjuvant - No Response

- cT2 (4.1 cm) cN0 cM0 invasive ductal carcinoma. Neoadjuvant chemo (completed planned 6 months). Post chemo imaging shows 6.5 cm ycT3 (no response). Pathology of mastectomy shows 7.7 cm residual tumor, 0/3 sentinel nodes, ypT3 ypN0.

- Assign posttherapy yp staging ypT3 ypN0 cM0
- Some patients do not respond to neoadjuvant therapy
- Currently, this is considered progressive disease and staging stops
  - Data collected now only includes cases that responded, resulting in skewed analysis
  - Overall effectiveness of neoadjuvant therapy is overestimated
Challenges of yc Classification

• yc not being collected
• yp will trump yc
  – Currently: ?80% patients receiving neoadjuvant treatment have yp, therefore yc not essential
  – Future: fewer patients have resection of primary tumor or regional nodes
• Timing of yc evaluation depends on specific treatment and response
• Clinical exam and imaging essential to evaluate response
  – Neither currently has synoptic reporting or defined data fields
• Number of expanded fields needed is not great, but complexity of accurate collection is great
https://cancerstaging.org

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- 7th Edition Forum will remain
- Located within CAanswer Forum
- Provides information for all
- Allows tracking for educational purposes

http://cancerbulletin.facs.org/forums/