Cancer

Cancer is characterized by:

- uncontrolled, rapid cell growth
- avoidance of programmed cell death (apoptosis)
- ability to signal vessel growth (angiogenesis)
- invasion of adjacent structures, including nodes
- metastasis to distant organs

Staging is a way of describing the spread of disease within a cancer patient at the time of diagnosis through grouping patients with similar cancer characteristics, based on the experience and outcomes of prior patients.
TNM Staging and Importance

2 Major Staging Systems

AJCC/UICC (TNM) Stage
- Detailed, narrower categories, developed for clinicians, critical for cancer care delivery and research

Summary Stage
- Broad categories, most general, excellent for surveillance, monitoring trends

Clinicians and Patients

TNM System
- T  - Extent of the primary tumor
- N  - The absence or presence and extent of regional lymph node metastasis
- M  - The absence or presence of distant metastasis

Collect both clinical and pathologic TNM, where available
Combine elements (grouping similar prognoses) to obtain stage groups (0-IV)

Value of Clinical Stage

- Develop initial treatment plan
- Review treatment guidelines (based on clinical stage)
- Define initial measures of prognosis
- Facilitate comparison of patient groups
  - Differences in primary therapy (surg vs neoadjuvant therapy) can make comparisons based on pathologic assessment impossible. Some patients get no treatment (ex. lung, advanced GI, head and neck, prostate)
TNM Staging and Importance

**Value of Pathologic Stage**

- Provides best measure of tumor extent
- Most precise estimate of prognosis
- Helps define subsequent therapy after surgery

Both clinical and pathologic stage
- Facilitate exchange and comparison of information among clinicians

**Population-Based Cancer Registries**

Approached staging from a slightly different angle
- Interested in the best measure of prognosis across the population of all cancer patients in the registry
- Developed a system based around collecting data from the medical record using trained personnel
- Using all available information in the medical record, combines the most precise clinical and pathologic documentation of the spread of disease in the cancer patient

**Broad Assessment of Prognosis**

<table>
<thead>
<tr>
<th>Code</th>
<th>Summary Stage</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>In situ</td>
</tr>
<tr>
<td>1</td>
<td>Localized</td>
</tr>
<tr>
<td>2</td>
<td>Regional by direct extension only</td>
</tr>
<tr>
<td>3</td>
<td>Regional lymph node involvement only</td>
</tr>
<tr>
<td>4</td>
<td>Regional by both direct extension and lymph node</td>
</tr>
<tr>
<td>5</td>
<td>Regional, NOS</td>
</tr>
<tr>
<td>7</td>
<td>Distant</td>
</tr>
<tr>
<td>9</td>
<td>Unknown</td>
</tr>
</tbody>
</table>
Elements with Greater Detail

Extent of Disease (EOD)
- Size of the tumor
- Tumor Extension
- Regional Lymph Node Involvement
- Regional Nodes Examined
- Regional Nodes Positive

Collecting elements allowed deriving Summary Stage or TNM-like Stage … but was a combined staging system (merging clinical and pathologic data together)

Value of Combined Stage

- Best measure of outcome available for each patient
- Monitor surveillance trends (early detection efforts)
- Assist with cancer control planning / resource allocation
- Allow for comparison across registries

EOD
- Provide valuable measures for researchers (size, # nodes, etc)
- Facilitate our understanding of disparities in outcomes
- Components help to compare outcomes over time
- Re-evaluate existing TNM stage groups by monitoring survival (explore new prognostic models)

Very Brief History of Staging for Population-Based Cancer Surveillance
1967 Code Manual Introduction

The EBB code in the past contained a crude assessment of prognosis in terms of these "stages"—local, regional, and distant spread of disease. Experience with this seemingly simple classification proved it to be impracticable in practice and pointed to a need for obtaining detailed descriptive data as a basis for a more meaningful summary classification system. Field 0 in the 1967 EBB Code represents, therefore, a change in emphasis since it provides identification of many objectively defined descriptive categories with the necessary resultant expansion of the code number system.

Field 0 has expanded to a three-column field with major emphasis upon a two-digit summary code to be found in columns 34 and 35 with a supplementary code in column 36. For most well-defined sites a separate page will be found which contains a highly specialized code number system.

1967 Code Manual Introduction

After a few years' experience with survival data, it should be possible to combine the descriptive categories of the summary code in columns 34–35 into meaningful prognostic groupings. Presumably, codes with similar survival rates might be grouped together. As such a time, depending upon the results, it is conceivable that the phrase "stage of disease" will again be useful. Moreover, the present Field 0 is not a "stage" code as indicated by the title "Extent of Disease"; it is a site-specific set of descriptive categories.
TNM Staging and Importance

Field O – Extend of Disease (2-digit)

Cancer EOD/Staging: Timeline

The Present – Crossroad

- Transitioning from CS v2 to TNM (effective 2016)
  - Separate Clinical and Pathologic Stage

- Continue Summary Stage 2000 (CDC-NPCR)

- Continue collection of Selected Elements from CS v2
TNM Staging Basics

TNM Staging Resources
www.cancerstaging.org

TNM Staging Resources
www.cancerstaging.org
Reference Dates

<table>
<thead>
<tr>
<th>Edition</th>
<th>Publication</th>
<th>Dates effective for cancer diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>1977</td>
<td>1974-1983</td>
</tr>
<tr>
<td>6</td>
<td>1983</td>
<td>1984-1988</td>
</tr>
<tr>
<td>5</td>
<td>1988</td>
<td>1990-1992</td>
</tr>
<tr>
<td>3</td>
<td>1997</td>
<td>1998-2002</td>
</tr>
<tr>
<td>2</td>
<td>2002</td>
<td>2003-2009</td>
</tr>
<tr>
<td>1</td>
<td>2009</td>
<td></td>
</tr>
</tbody>
</table>

Chapter Outline

TNM Staging Basics
Stage Classifications
Timing Rules
Elements (T, N, M)
Stage Groups
Data Entry
Blanks vs X

Outline – Big Picture
Stage Classifications

Stage can be defined at numerous points in the care of the patient.

Clinical Stage (pretreatment stage) – cTNM
- Evidence acquired before treatment (surg, neoadjuvant, ww)
  - physical examination, symptoms
  - scans, x-rays, other imaging
  - endoscopy and biopsy of primary
  - diagnostic biopsy of In, sentinel node, metastatic site
  - surgical exploration without resection
- Definition varies somewhat by site

Pathologic Stage (postsurgical stage) – pTNM
- Use all Clinical evidence PLUS
  - evidence from operative findings during resection and pathology report findings (can be viewed or palpated without biopsy)
- Definition of what constitutes resection varies by site

Key points
- Clinical information is used to help stage unless disproven by operative or pathologic findings
- Operative findings include surgeon judgement and can overrule pathology if tissue was not submitted

Pathologic staging depends on proven extent of disease

Pathologic staging criteria met without surgical resection of the primary if:
- Microscopic confirmation of highest T and highest N or ……
- Microscopic confirmation of M1
TNM Staging and Importance

Stage Classifications
PostTherapy Stage (neoadjuvant stage) - yTNM
- Documents the extent of disease for patients whose first course therapy includes systemic or radiation therapy prior to surgery or when systemic or radiation treatment is the primary treatment without surgery
- Can be recorded as clinical or pathologic
  - pathologic assessment after neoadjuvant therapy and surgery – yp
- Identifies response to therapy
- Helps define subsequent therapy

Timing of Data Collection
Clinical
- Includes all information obtained before the initiation of definitive treatment (surgery, radiation, systemic therapy, active surveillance) or within 4 months of diagnosis, whichever is shorter. Must be in the absence of disease progression.

Pathologic
- Includes information obtained through the completion of first course definitive surgery or within 4 months of diagnosis, whichever is longer as long as there is no systemic or radiation therapy initiated or disease progression

Defining T
- Primary Tumor (T)
  - T0 - No evidence of primary tumor
  - TIS - Carcinoma in situ
  - T1, T2, T3, T4 - Increasing size and/or local extension of primary tumor
  - TX - Primary tumor cannot be assessed
TNM Staging and Importance

**Defining T**

Clinical classification cT
- Physical exam, imaging, endoscopy, biopsy of primary site, surgical exploration without resection

Pathologic classification pT
- Resection of tumor, may require resection of organ
- Must read each chapter for details
- Biopsy of tumor is adequate (without resection) if highest T

**Defining N**

- Regional Lymph Nodes (N)
  - N0 - No regional lymph node metastasis
  - N1, N2, N3 - Increasing involvement of regional lymph nodes
  - NX - Regional lymph nodes cannot be assessed

**Defining N**

Clinical classification cN
- Physical exam, imaging, diagnostic biopsy/workup

Pathologic classification pN
- Resection of node(s) with surgical resection of primary (pT) – i.e. pT is generally necessary to assign pN
- Any microscopic examination of nodes when pT is available

Exception: excision of nodes is pN when no resection is performed due to unknown primary (T0)
Defining T and N
Pathologic staging depends on proven anatomic extent of disease, whether or not the primary tumor has been completely removed.

When a biopsied tumor cannot be removed or is unreasonable to remove, if the highest T category and the highest N category or the M1 category can be confirmed microscopically, the criteria for pathologic staging have been satisfied.

Example
If diagnostic biopsy proves highest T category
  • Use to assign cT
  • Also use to assign pT if
    • Surgical node dissection or
    • Biopsy of highest N category

Defining M
  • Distant Metastasis (M)
    • M0 - No distant metastasis
    • M1 - Distant metastasis
    • MX – Does not exist (pathologist often don’t have metastatic tissue to assess)
  • Common metastatic sites
    • Lung, Liver, Bone, Brain
    • Distant lymph nodes
TNM Staging and Importance

Defining M

- Classification of cM only required History and Physical
  Infer cM0 status unless known cM1 or pM1
  Extensive imaging is not needed

- The designation MX is not a valid category

- Pathologic (pM0) is not allowed. A case with a negative
  biopsy of a metastatic site is reported as cM0 not pM0

- pM1 classification requires positive biopsy of metastatic
  site

Stage Groups

- Once collected, TNM elements are grouped together
  into anatomic stage/prognostic groups.

- Stage groups range from 0 to IV with increasing
  severity

- Generally a pure clinical and a separate pure pathologic
  stage are recorded. Used for guideline development.

- Nonanatomic factors are incorporated where needed
  (ex. Gleason)

Pure Stage Group

**Rule**

**Clinical Stage Group**
- cT
- cN
- cM or pM
  clinical stage group

**Pathologic Stage Group**
- pT
- pN
- cM or pM
  pathologic stage group
TNM Staging and Importance

**Pure Stage Group - Exceptions**

<table>
<thead>
<tr>
<th>Clinical Stage Group</th>
<th>Pathologic Stage Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>cT cN pM1</td>
<td>cT cN pM1</td>
</tr>
<tr>
<td>clinical stage group IV</td>
<td>pathologic stage group IV</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Pos Biopsy Met Site</th>
<th>Carcinoma In situ</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical Stage Group</td>
<td>Pathologic Stage Group</td>
</tr>
<tr>
<td>pTis cN0 cM0</td>
<td>pTis cN0 cM0</td>
</tr>
<tr>
<td>clinical stage group 0</td>
<td>pathologic stage group 0</td>
</tr>
</tbody>
</table>

**Registry Data Entry**

Data Fields Available in NAACCR layout (FORDS)

<table>
<thead>
<tr>
<th>CLINICAL</th>
<th>T</th>
<th>N</th>
<th>M</th>
<th>Stage Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>PATHOLOGIC</td>
<td>T</td>
<td>N</td>
<td>M</td>
<td>Stage Group</td>
</tr>
</tbody>
</table>

Use appropriate c or p data fields
It is ok, and even expected, for some fields to be left blank
Data fields for assigning stage, not data collection

**Example**

In situ breast cancer with mastectomy and no nodal resection (pTis, cN0, cM0 for clinical and pathologic stage)

<table>
<thead>
<tr>
<th>CLINICAL</th>
<th>T</th>
<th>N</th>
<th>M</th>
<th>Stage Group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>blank</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>PATHOLOGIC</th>
<th>T</th>
<th>N</th>
<th>M</th>
<th>Stage Group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>blank</td>
<td>blank</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>
**TNM Staging and Importance**

---

**Example**

TURB of the bladder with in situ disease. No cystectomy.

<table>
<thead>
<tr>
<th>CLINICAL</th>
<th>T</th>
<th>N</th>
<th>M</th>
<th>Stage Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>blank</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>PATHOLOGIC</th>
<th>T</th>
<th>N</th>
<th>M</th>
<th>Stage Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>blank</td>
<td>blank</td>
<td>blank*</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Cystectomy (radical or partial) req for pathologic staging

---

**Understanding Blanks vs X**

AJCC allows X for T and N categories (TX, NX)

- Used when these variables cannot be assessed (information is unknown to the clinician) and…..
- **Criteria is met** for this specific stage classification (c or p)

Blank is used when:

- **Criteria is not met** for this specific stage classification (c or p) or……
- **Criteria is met** but no information in record if assessment was performed (registrar does not have access to information)
- Blank is also appropriate for stage group

---

**Is Criteria Met for Stage Classification?**

No - **Use blank** not X

X would indicate patient eligible for staging examples: no surgical resection for path stage

no diagnostic workup for clinical stage

Yes - **Use X** if physician did not assess or have info on patient’s T and/or N
example: surgical resection but no nodes examined

**Use blank** if information is not available in the chart
TNM Staging and Importance

Thank you

QUESTIONS?

kward@emory.edu

Extra Slides for Reference

Non-Anatomic Factors

Chapters utilizing additional categories
8. Thyroid - Histology, age
10. Esophagus & Esophageal Junction - Histology, location, grade
13. Appendix - Histology, grade
16. GIET - Metastatic rate
27. Bone - Grade
28. Soft Tissue Sarcoma - Grade
36. Corpus Uteri - Histology
39. Gestational Trophoblastic Tumors - Prognostic scoring index
41. Prostate - PSA, Gleason
42. Testis - Serum Tumor Markers (AFP, hCG, LDH)
57. Primary Cutaneous Lymphomas - Peripheral blood involvement
TNM Staging and Importance

**Overriding Path Report pT**

Clinical information can override pathology report information in certain circumstances.

During operative resection, surgeon observes that cancer extended into the retroperitoneum (no biopsy). This would be T4b. If the path report shows, tumor invaded subserosal fat with the radial margin involved (T3) we can still use the clinical information to assign pT4b.

**Overriding Path Report pN**

Clinical information can override pathology report information in certain circumstances.

Physical exam and imaging show involved ipsilateral supraclavicular nodes (N3c). Pathology resection of axillary nodes only shows mets in 7 nodes (pN2a). Can use clinical information (not disproved by pathology) and assign pN3c.