TUMOR DEPOSITS IN COLORECTAL CANCER

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Overview

- Understanding the definition of Tumor Deposits
- Guidance for pathologists on documenting TD
- Utilizing the new N1c category
- Hindgut Task Force Process for Change

Summary of Changes – 7th Edition

The potential importance of satellites or tumor deposits is now defined by the new site-specific factor Tumor Deposits (TD) that describe their texture and number.

T1-4 tumors that lack regional lymph node metastasis but have tumor deposit(s) will be classified in addition as N1c.
Discrete foci of tumor
- Found in the pericolic or perirectal fat or in adjacent mesentery (mesocolic fat) away from the leading edge of the tumor and
- Showing no evidence of residual lymph node tissue but within the lymph drainage area of the primary carcinoma
- Are considered to be peritumoral deposits or satellite nodules, and
- Their number should be recorded in the site-specific Prognostic Markers on the staging form as Tumor Deposits (TD)

Such tumor deposits may revolve from
- Discontinuous spread
- Venous invasion with extravascular spread
- Totally replaced lymph node(s)

However, if a definitive diagnosis of V1 of N1/2 cannot be made, then the designation of tumor deposit does not apply

If tumor deposits are observed with cancer that would otherwise be classified as T1, T2, T3 or T4
- Then the primary tumor classification (especially T1 or T2) is not changed
- The tumor deposit is recorded as N1c and also as a site specific factor in the TD category
- The number of TD also would be recorded

If tumor deposits are observed with cancer that would otherwise be classified as N1/N2
- The tumor deposits are recorded only as a site specific factor in the TD category
- The number of TD also would be recorded
N1c

- Tumor deposit(s) in the subserosa, mesentery, or nonperitonealized pericolic or perirectal tissues without regional nodal metastasis

Regional Node Involvement

- If regional nodes are positive for tumor
- TD do not affect the T category
- TD do not affect the N category either
- Data will be analyzed to examine relationship between depth of invasion and TD

Prognostic Factors (Site-Specific Factors)
Recommended for Collection - Clinically significant

- Preoperative or pretreatment carcinoembryonic antigen (CEA)
- Tumor deposits (TD)
- Circumferential resection margin (CRM)
- Perineural invasion (PN)
- Microsatellite instability (MSI)
- Tumor regression grade (with neoadjuvant therapy)
- KRAS gene analysis
**Lymph-Vascular Invasion (LVI)**

- Defined in 7th Edition Chapter 1
- Indicates whether microscopic lymph-vascular invasion (LVI) is identified in the pathology report
- This term includes lymphatic invasion, vascular invasion, or lymphovascular invasion (synonymous with “lymph-vascular”)

**Questions**

- Is there a size criterion for TD?
  - No. This was modeled after the N2/3 satellite category of skin melanoma where no size is given.
- How far from the leading tumor edge?
  - There is no consensus yet on how far, but must be discontinuous extension.

**Questions**

- Is there variability between pathologists, so that the data are not consistent?
  - Yes. But this is true in many data items.
- Can this be recorded after neoadjuvant radiation therapy or chemotherapy, where tumor regression and isolated clusters of cells are common?
  - Yes. It is vital to document the neoadjuvant treatment to separate these cases from those receiving surgery without pre-operative neoadjuvant therapy. The pathologic staging after neoadjuvant therapy is delineated with ypTNM to further distinguish these cases.
Pathologist Comments on TD

- What is a Tumor Deposit
- How Best to Document TD
- Lymph-Vascular Invasion (LVI) - Relationship to TD
- When to Utilize N1c

What is a Tumor Deposit

- Some characteristics of TD:
  - Irregular deposits
  - Not associated with organized lymphoid tissue
  - Not surrounded by thick bundles of parallel collagen fibers
- Characteristics of replaced lymph nodes:
  - Rounded deposits with organized lymphoid tissue
  - Thick collagen capsules
- Discretion of the pathologist to make the final decision

How Best to Document TD

- Required
  - Number of TD
- Significant features to document
  - Nodule size
  - Distance from the main tumor
    - ≤1 cm if included in the same block as primary tumor
    - >1 cm if found further away in perivisceral fat
  - Lymphocyte infiltration
Lymph-Vascular Invasion (LVI) – Relationship to TD

- Unclear effect of LVI on prognosis

- TD may represent vascular invasion that has spread through and beyond the vessel wall
Pericolonic adipose tissue with focus of adenocarcinoma, possible origin from lymph-vascular invasion. Code as Tumor Deposit (TD).

Pericolonic adipose tissue with focus of adenocarcinoma, possible origin from lymph-vascular invasion. Code as Tumor Deposit (TD).

**Lymph-Vascular Invasion (LVI) – Relationship to TD**

- Clear cut LVI – L1 and/or V1 – are **not** TD
- TD is that subset **not** associated with any specific pathological entity
- TD **cannot** be unequivocally classified as
  - Nodes (N)
  - Lymphatic invasion (L)
  - Venous invasion (V)
  - Perineural invasion (PN)
Lymph-Vascular Invasion (LVI) – Relationship to TD

- Cancer registrars collect data on
  - Nodes (N)
  - Lymph-Vascular Invasion (LVI which includes L and V)
  - Perineural invasion (PN)
  - Tumor deposits (TD)

When to Utilize N1c

- Tumor deposits have been identified according to the criteria
  and

- There is no involvement of regional nodes

CAP Cancer Protocols and Checklists
Colon & Rectum: Resection Checklist

- Tumor Deposits (discontinuous extramural extension) (Note L)
  - Not identified
  - Present
  - Indeterminate

L. Tumor Deposits (Discontinuous Extramural Extension)

- Irregular discrete tumor deposits in pericolic or perirectal fat away from the leading edge of the tumor and showing no evidence of residual lymph node tissue, but within the lymphatic drainage of the primary carcinoma, are considered peritumoral deposits or satellite nodules and are not counted as lymph nodes replaced by tumor.
- Most examples are due to lymph-vascular or, more rarely, perineural invasion.
- Because these tumor deposits are associated with reduced disease-free and overall survival, their number should be recorded in the surgical pathology report.
- If tumor deposits are observed in lesions that would otherwise be classified as pT1 (tumor confined to submucosa) or pT2 (tumor confined to muscularis propria), then the primary tumor classification is not changed, but the nodule is recorded in a separate N category as N1c.


E. Lymph-Vascular and Perineural Invasion

- Venous invasion has been demonstrated by multivariate analysis to be an independent adverse prognostic factor.
- Invasion of extramural veins, in particular, has been shown to be an independent indicator of unfavorable outcome and increased risk of occurrence of hepatic metastasis.
- The significance of intramural venous invasion is less clear, because data specific to this issue are lacking.
- In several studies, both lymphatic invasion and perineural invasion have been shown by multivariate analysis to be independent indicators of poor prognosis. The prognostic significance, if any, of the anatomic location of these structures is not defined.
- Furthermore, it is not always possible to distinguish lymphatic vessels from postcapillary venules, because both are small, thin-walled structures.
- Thus, the presence or absence of tumor invasion of small, thin-walled vessels should be reported in all cases.
Hindgut Task Force Comments

- Improvements to staging in 6th & 7th Editions
  - 5th Edition did not have substaging for Stages II & III
  - 6th & 7th Edition substaging
    - Based on available outcomes data
    - Accounts for differences in survival

Hindgut Task Force Process for Change

- Population-based validation
  - Depth of invasion and nodal status interact to affect survival

- SEER survival data
  - 35,829 rectal ca pts
  - 109,953 colon ca pts

Hindgut Task Force Process for Change

- T4N0 stratified by T4a and T4b
  - T4a – tumor perforate visceral peritoneum
  - T4b – tumor directly invades other organs or structures

- N1 & N2 stratified by number of involved nodes
  - N1a/N1b – 1 vs 2-3
  - N2a/N2b – 4-6 vs ≥7
Hindgut Task Force Process for Change

5yr observed and relative survival
- T1-2N0 have better survival than T3N0
- T3N0 better than T4N0
- T1-2N2 better than T3-4N2
- T4bN1 similar to T4aN2
- T4a better than T4b by N category
- Number of N+ affects survival for each T category

Hindgut Task Force Process for Change

- SEER population-based analyses supported
  - Subdividing T4 (T4a/T4b)
  - Subdividing N1 (N1a/N1b) and N2 (N2a/N2b)
  - Revised substaging of Stages II/III
    - Shift of T1-2N2 lesions from IIC to IIIA/IIIB
    - Shift of T4bN1 lesions from IIIB to IIIC

Hindgut Task Force Process for Change

- During time frame of pt accrual and data collection
  - SEER definition of extent of disease did not vary for
    - Degree of penetration of primary tumor (T)
    - Number of involved nodes (N)
  - Tumor deposits data when identified
    - Did not affect T
    - Affected N in pts with T1/T2 lesion as TD were classified as involved nodes, as now recommended in 7th Edition
  - Raw data TN categories stratified and published in JCO
  - N1c affects all N0 patients because it moves a Stage group I or II into a IIIA or IIIB
Solution

- Clear definition of Tumor Deposits in 7th Edition Colon and Rectum Chapter sections as follows
  - Pathologic staging
  - Summary of Changes
  - Prognostic Features
  - Definition of TNM

- Tumor Deposits (TD) cannot be ignored
  - Possible negative impact on survival based on retrospective analyses

- Recommend prospective data collection on TD
  - Survival impact by TN category may be appropriately included in subsequent editions of TNM

Conclusion

- Strongly support prospective collection of TD data
- Better determine role TD may play in clinical outcome of patients
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