Physician to Physician
AJCC 8th Edition

Breast

Gabriel N. Hortobagyi, MD, MACP, FASCO

AJCC

American Joint Committee on Cancer

Validating science. Improving patient care.

Outline

- Established prognostic factors in primary breast cancer
- Effect of prognostic factors on TNM staging
- Changes to the TNM Staging System in the 8th Edition
- Inclusion of Genomic Profiles
- Clinical implications

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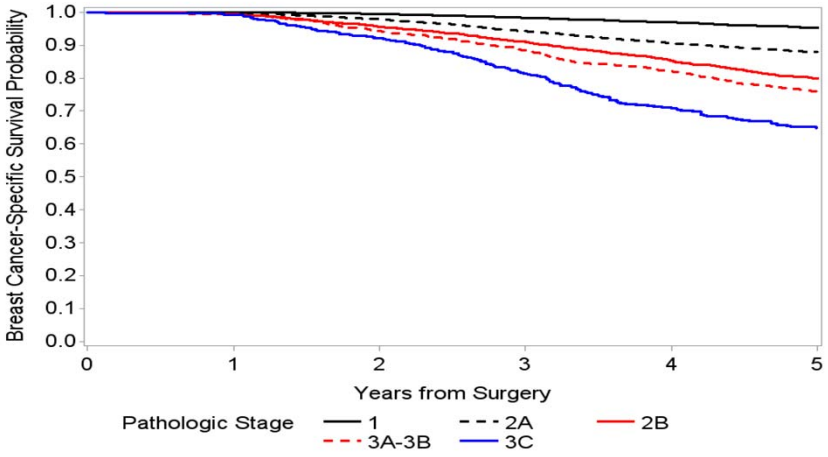
Kaplan-Meier 5-year breast cancer specific survival estimates by pathologic stage

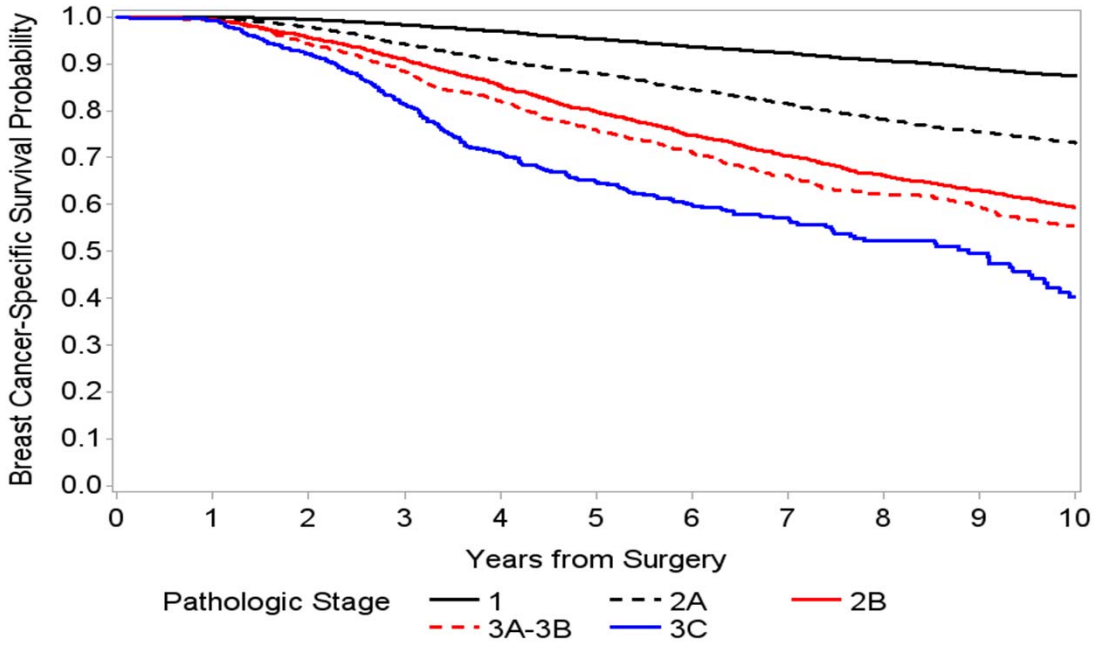


Numbers at risk	0	1	2	3	4	5 years
1	10573	9785	8930	8009	7079	6345
2A	5509	5129	4652	4132	3672	3302
2B	2853	3663	2395	2091	1815	1577
3A-3B	1464	1358	1184	1016	865	713
3C	529	500	433	340	265	216

5-year breast cancer specific survival Kaplan-Meir estimates by pathologic stage

Stage	N N= 20,928	5Y BCSS K-M	5Y BCSS Cox
I	10573	95.3%	94.5%
IIA	5509	87.9%	87.6%
IIB	2853	79.8%	80.7%
IIIAB	1464	75.9%	78.5%
IIIC	529	64.8%	68.0%
Abbreviations ---n: number of patients; BCSS: breast cancer specific survival; 5Y: 5-year			

Kaplan-Meier 10-year breast cancer specific survival estimates by pathologic stage

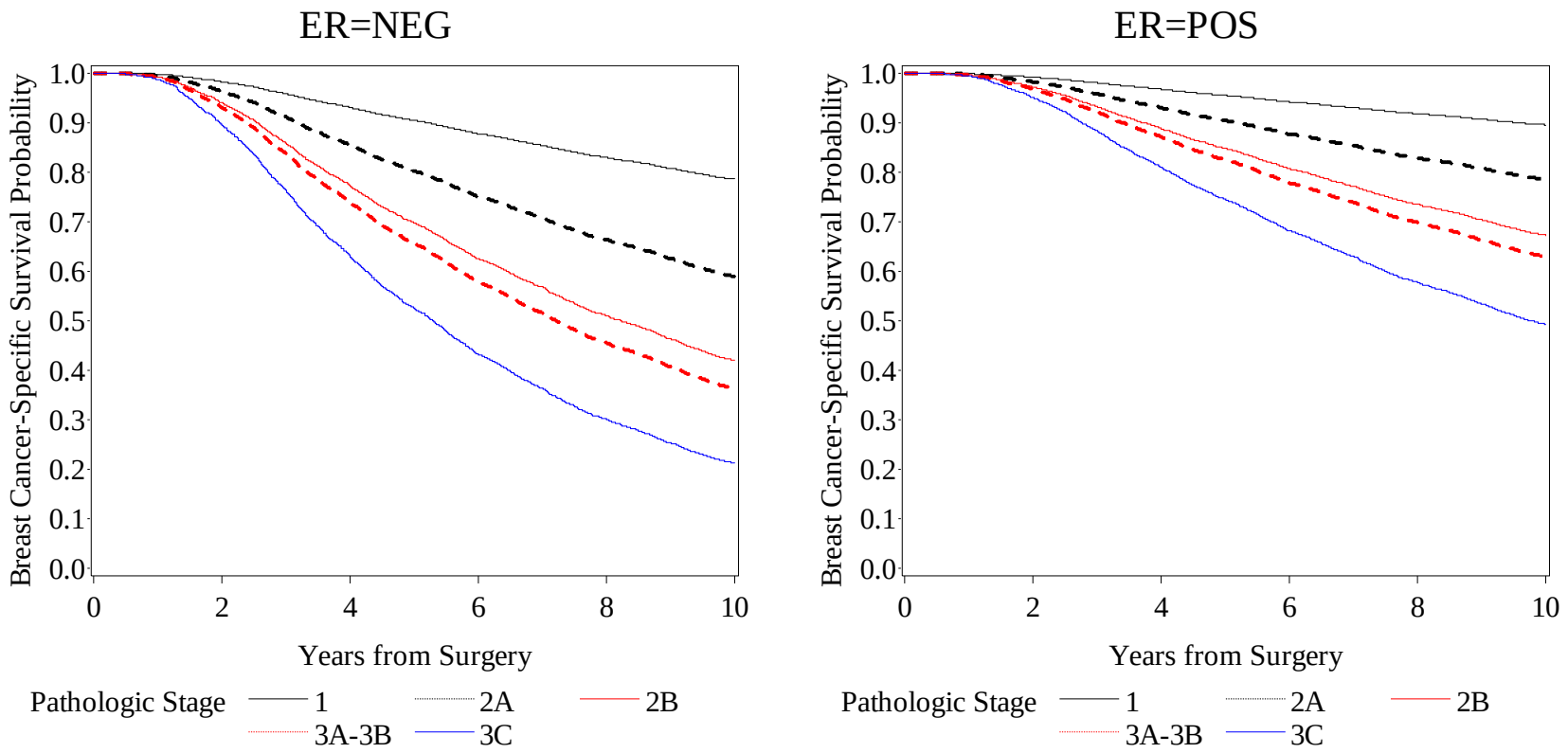


Numbers at Risk	Year 0	Year 1	Year 3	Year 5	Year 7	Year 10
1	10573	9785	8009	6345	4849	2912
2A	5509	5129	4132	3302	2554	1631
2B	2853	3663	2091	1577	1170	723
3A-3B	1464	1358	1016	713	501	252
3C	529	500	340	216	130	38

Cox regression 5-year breast cancer specific survival estimates by pathologic stage and age

Stage	Age < 40		Age: 40-69		Age ≥ 70	
N=20928	N	BCSS	N	BCSS	N	BCSS
I	964	92.5%	8178	94.7%	1431	95.3%
IIA	813	83.6%	4139	88.2%	557	89.5%
IIB	554	75.3%	2062	81.9%	237	83.9%
IIIAB	243	72.2%	1110	79.5%	111	81.7%
IIIC	81	59.8%	409	69.6%	39	72.8%

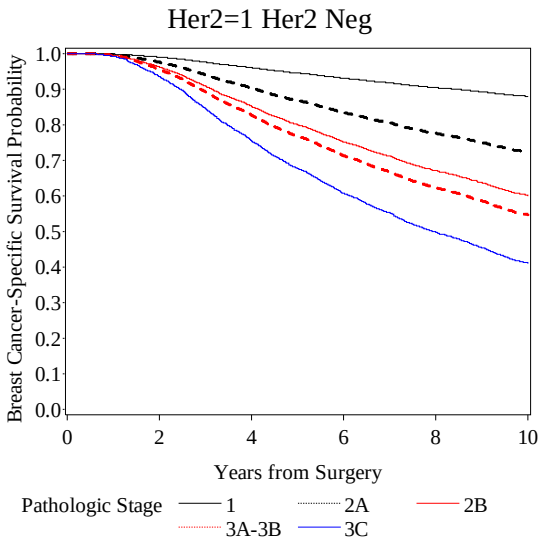
Cox regression 10-year breast cancer specific survival estimates by pathologic stage and ER status

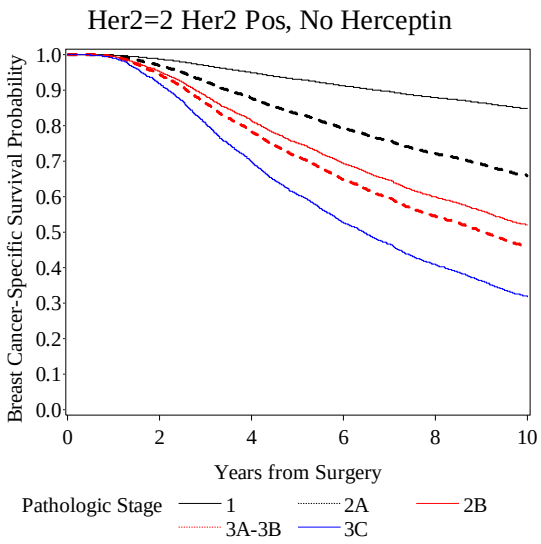


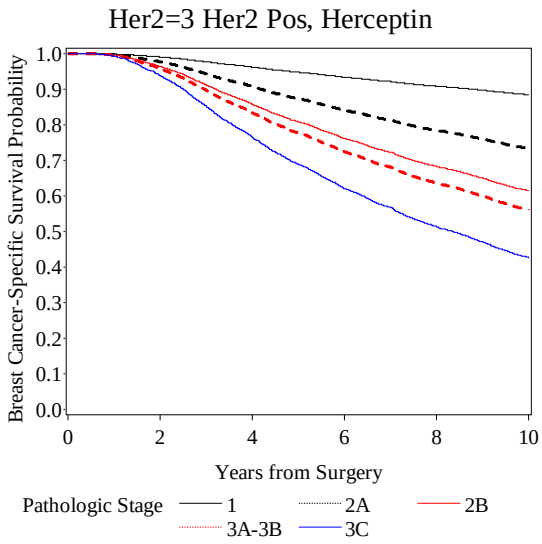
Cox regression 5-year breast cancer specific survival estimates by pathologic stage and ER status

Stage N=19,718	ER positive		ER negative	
	N	BCSS	N	BCSS
I	8071	95.5%	1926	90.5%
IIA	3720	90.5%	1432	80.3%
IIB	1889	84.8%	778	69.7%
IIIAB	1030	82.5%	353	65.6%
IIIC	362	74.5%	157	52.5%

Cox regression 10-year breast cancer specific survival estimates by pathologic stage and HER2 Status







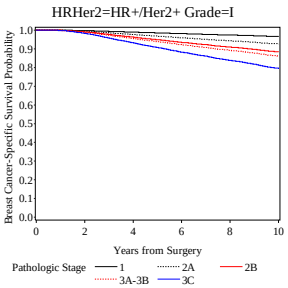
Kaplan Meier 5-year breast cancer specific survival estimates by pathologic stage and HER2 status

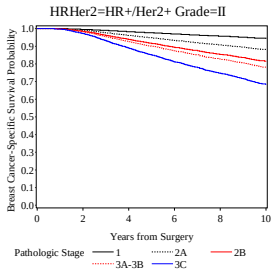
Stage N=16,418	HER2+ (T)		HER2+ (no T)		HER2-	
	N	BCSS	N	BCSS	N	BCSS
I	540	94.8%	424	93.1%	7370	94.6%
IIA	306	87.3%	335	83.3%	3575	86.8%
IIB	146	80.8%	217	75.1%	1802	80.0%
IIIAB	142	77.7%	66	71.2%	1001	76.8%
IIIC	93	68.9%	12	60.6%	389	67.7%

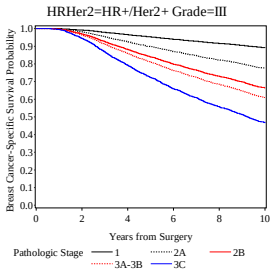
Cox 5-year breast cancer specific survival estimates by pathologic stage, HR status, and HER2 status

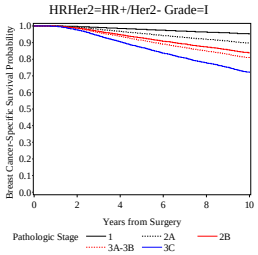
Stage N=15,320	TNBC		HR+/HER2+ (T)		HR-/HER2+ (T)		HR+/HER2-	
	N	BCSS	N	BCS.	N	BCSS	N	BCSS
I	1033	89.0%	350	95.9%	188	93.5%	6326	95.8%
IIA	838	75.9%	183	90.5%	122	85.3%	2724	90.4%
IIB	423	63.2%	89	84.7%	57	76.8%	1374	84.6%
IIIAB	180	57.4%	71	81.7%	69	72.6%	815	81.6%
IIIC	83	42.3%	46	73.1%	46	60.9%	303	73.0%%

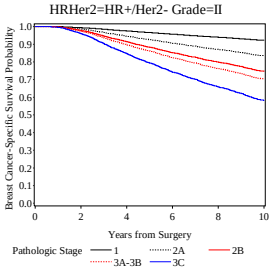
Cox regression 10-year breast cancer specific survival estimates by pathologic stage, HR status, HER2 Status, and nuclear grade

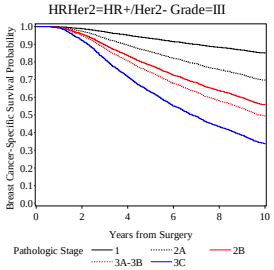


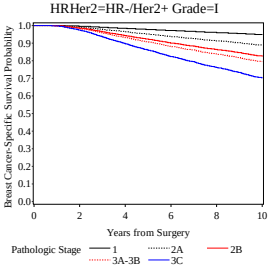


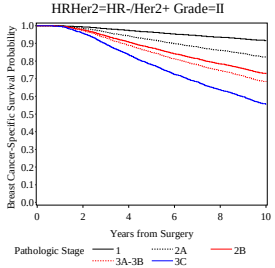


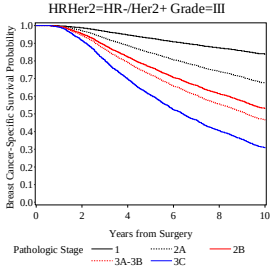


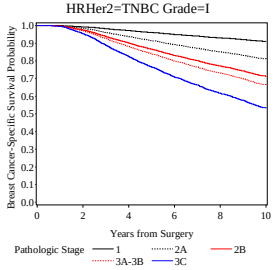


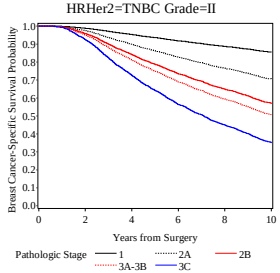


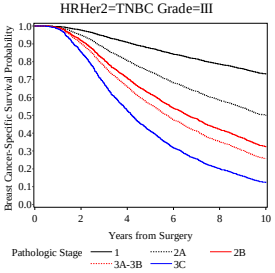












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5-year breast cancer specific survival estimates by pathologic stage, HR status, HER2 status, and nuclear grade

Stage N=14,675	TNBC, Grade 2		TNBC, Grade 3		HR+/HER2+ (T), Grade 2		HR+/HER2+(T), Grade 3		HR-/HER2+(T), Grade 2		HR-/HER2+(T), Grade 3		HR+/HER2-, Grade 1		HR+/HER2-, Grade 2		HR+/HER2-, Grade 3	
	N	BCSS 95% CI	N	BCSS 95% CI	N	BCSS 95% CI	N	BCSS 95% CI	N	BCSS 95% CI	N	BCSS 95% CI	N	BCSS 95% CI	N	BCSS 95% CI	N	BCSS 95% CI
I	117	**93.6** 92.7-94.5	851	**87.6** 86.3-88.9	109	**97.6** 97.0-98.2	232	**95.3** 94.1-96.5	20	**96.3** 95.5-97.2	162	**92.8** 91.2-94.4	1067	**97.9** 97.4-98.5	3628	**96.6** 96.2-97.0	1431	**93.3** 92.6-94.1
IIA	61	**86.3** 84.5-88.1	710	**74.4** 72.2-76.6	52	**94.8** 93.4-96.1	116	**89.8** 87.4-92.2	7	**92.0** 90.1-94.0	109	**84.7** 81.5-87.9	254	**95.5** 94.3-96.6	1406	**92.6** 91.8-93.4	943	**85.7** 84.3-87.1
IIB	27	**78.8** 76.0-81.7	374	**62.0** 58.8-65.3	14	**91.7** 89.6-93.8	70	**84.0** 80.4-87.8	1	**87.4** 84.5-90.5	51	**76.4** 71.8-81.3	72	**92.8** 91.0-94.6	699	**88.3** 87.0-89.6	543	**78.0** 75.9-80.1
IIIAB	9	**75.0** 71.4-78.7	161	**56.1** 52.0-60.6	12	**90.0** 87.5-92.7	53	**81.0** 76.8-85.6	5	**85.0** 81.6-88.6	61	**72.2** 66.9-78.0	46	**91.4** 89.1-93.6	407	**86.1** 84.3-87.9	318	**74.0** 71.2-77.0
IIIC	6	**64.2** 58.8-70.1	72	**41.1** 35.4-47.8	10	**85.1** 81.3-89.1	35	**72.4** 66.3-79.0	2	**77.9** 72.9-83.3	40	**60.7** 53.6-68.7	18	**87.0** 83.6-90.6	139	**79.4** 76.3-82.6	129	**63.0** 58.3-68.0

Multivariate Cox Regression Model (Model 3) (N=14,675)[1]

Covariate	Level	HzR	95% CI	p
Age at Diagnosis	< 40	1.55	1.39-1.72	**<.0001**
	40-69	**REF**		
	≥ 70	1.05	0.90-1.23	0.55
Pathologic Stage	I	**REF**		
	IIA	2.21	1.98-2.48	**<.0001**
	IIB	3.47	3.07-3.91	**<.0001**
	IIIAB	4.27	3.71-4.91	**<.0001**
	IIIC	6.55	5.49-7.81	**<.0001**
Biologic Subtype	TNBC	1.92	1.74-2.12	**<.0001**
	HR+/HER2+ (T)	0.68	0.53-0.87	**0.002**
	HR-/HER2+ (T)	1.07	0.85-1.34	0.58
	HR+/HER2-	**REF**		
Nuclear Grade	1	**REF**		
	2	1.63	1.26-2.11	**0.0002**
	3	3.19	2.47-4.13	**<.0001**

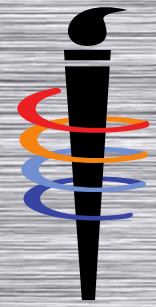
Abbreviations - HzR: hazard ratio, CI: confidence interval, Ref: reference group (1.00)
HzR refers to the hazard ratio of death with breast cancer.

[1] Patients with complete data including age, stage, HR status[2,3], HER2 status, and grade were included
[2] HR+: ER+ or PR+
[3] HR-: ER- and PR-

Summary of Changes

- Two stage group options:
  - Anatomic – For use where biomarker (grade, ER, PR, HER2) not available
  - Prognostic – For use on all U.S.A. patients
- T, N, M changes
- Clarifications for post neoadjuvant therapy classification
- Inclusion of grade, HER2, ER, PR
- Inclusion of multigene panels

Selecting Stage Group



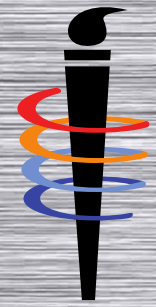
Selecting Appropriate Stage Group Table

- Anatomic Stage Groups
  - Based solely on anatomic extent of cancer
  - Defined only by T, N, and M categories
- Appropriate for regions of world where biomarkers cannot be routinely obtained
- Not appropriate where biomarkers are used for patient care

Selecting Appropriate Stage Group Table

- Prognostic Stage Groups
  - Based on populations of breast cancer patients offered and mostly treated with endocrine and/or chemotherapy and/or anti-HER2 therapy
  - Includes T, N, M, tumor grade, HER2, ER, PR
  - Includes multi-gene panels
  - Can be based on clinical or pathological findings
- Preferred for patient care
- Must be used for reporting of all cancer patients in U.S.

T, N, M Categories



T Category

- Lobular carcinoma in situ removed from Tis category
- Rounding tumor size
  - Exception for tumors between 1.0 - 1.5 mm
  - Do not round down, do not classify as microinvasive T1mi
- Multiple tumors (m) uses dimension of largest tumor
- T4b satellite tumor nodules
  - Must be separate from primary tumor
  - Must be macroscopically identified
  - Those identified on microscopic exam only do not qualify for T4b

N Category

- cN0 assigned when
  - Evaluation of nodes is possible
  - Physical exam or imaging is negative for nodal involvement
- cNX only valid if nodal basin removed
  - Cannot be examined by imaging or physical exam
- Criteria for microscopic measurement of node metastases
  - Largest contiguous tumor deposit used for pN
  - Do not use dimension of area containing several or multiple tumor deposits

M Category

- pM0 is not a valid category

- Valid M categories for clinical and pathological staging
  - cM0 – no signs or symptoms of distant mets
  - cM1 – signs, symptoms, or imaging evidence of distant mets
  - pM1 – microscopic confirmation of distant mets

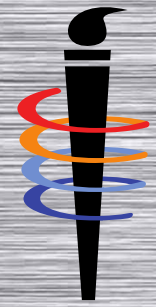
Anatomic Staging Groupings

When T is…	And N is…	And M is…	The Stage Group is…
Tis	N0	M0	0
T1	N0	M0	IA
T0	N1mi	M0	IB
T1	N1mi	M0	IB
T0	N1	M0	IIA
T1	N1	M0	IIA
T2	N0	M0	IIA
T2	N1	M0	IIB
T3	N0	M0	IIB

Anatomic Staging Groupings - 2

When T is…	And N is…	And M is…	The Stage Group is…
T0	N2	M0	IIIA
T1	N2	M0	IIIA
T2	N2	M0	IIIA
T3	N1	M0	IIIA
T3	N2	M0	IIIA
T4	N0	M0	IIIB
T4	N1	M0	IIIB
T4	N2	M0	IIIB
Any T	N3	M0	IIIC
Any T	Any N	M1	IV

Post Neoadjuvant Therapy Classification



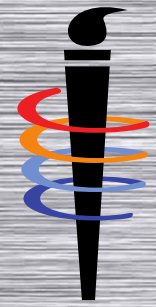
Post Neoadjuvant Therapy Staging

- Assigned after neoadjuvant therapy and surgical resection
- ypT category
  - Largest focus of residual tumor
  - Treatment-related fibrosis near invasive tumor NOT used
  - Multiple foci of residual tumor, use (m)
- ypN category
  - Largest focus of residual tumor in nodes
  - Treatment-related fibrosis near nodal tumor deposits NOT used
- M category
  - If M1 prior to therapy, remains M1 following neoadjuvant therapy
  - Regardless of observed response to therapy
- Pathological complete response (pCR), no residual tumor
  - ypT0 ypN0 cM0 no stage group assigned

Post-neoadjuvant Prognostic Stage Groups

- This part of the AJCC Staging System is under preparation.
- It will include Anatomic TNM, Grade, ER, PR and HER2

Grade, HER2, ER, PR Categories



Biomarkers

- All invasive carcinomas should have the following determined by appropriate assays whenever possible
  - Estrogen receptor (ER) status
  - Progesterone receptor (PR) status
  - Human epidermal growth factor receptor 2 (HER2) status – best scored by 2013 ASCO/CAP standards
- Modified Nottingham (Bloom Scarf Richardson) tumor grade should be documented
- Marker of proliferation is also recommended
  - Ki-67
  - Mitotic count

Grade

- All invasive breast ca should be assigned histologic grade
  - Nottingham modification of SBR grading system recommended
- Nottingham grade determined by totaling scores for
  - Tubule formation
  - Nuclear pleomorphism
  - Mitotic count
- Grade table to equate SBR score of points to G1-G3

G	G Definition
GX	Grade cannot be assessed
G1	Low combined histologic grade (favorable), SBR score of 3–5 points
G2	Intermediate combined histologic grade (moderately favorable); SBR score of 6–7 points
G3	High combined histologic grade (unfavorable); BSR score of 8–9 points

ER and PR

- ER & PR expression measured primarily by IHC
- ≥1% of cells stained considered positive for ER & PR
- Multiple results always use positive results
  - If biopsy and resection specimens are tested, and
  - One is positive, while the other is negative, then
  - Use the positive results to assign the stage group

HER2

- HER2 measurement by IHC or ISH
- 2013 ASCO/CAP Guidelines provide standards
  - Sequential performance of tests to determine HER2 status
- Summary of standards
  - IHC
    - Negative: 0 or 1+ staining
    - Equivocal: 2+ staining
    - Positive: 3+ staining
  - ISH, dual probe (Fluorescent – FISH or Chromogen – CISH)
    - Possible negative:
      - HER2/CEP17 ratio < 2.0 and HER2 copy number < 4
    - Possible equivocal:
      - HER2/CEP17 ratio < 2.0 andHER2 copy number ≥ 4 but < 6
    - Possible positive:
      - HER2/CEP17 ratio ≥ to 2.0 by ISH, or
      - HER2 copy number ≥ to 6 regardless of ratio by ISH

HER2 Equivocal

- HER2 determined to be “equivocal”
  - By ISH (FISH or CISH) testing
  - Under the 2013 ASCO/CAP HER2 testing guidelines

- Categorize HER2 “equivocal” by ISH as HER2 “negative”
  - For assigning stage in Prognostic Stage Group Table

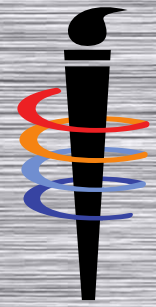
Multigene Panels

- Patients with
  - ER/PR-positive, HER2-negative, node-negative tumors
  - Size less than or equal to 5 cm

  - Combined with any of the following multigene panels
    - Oncotype Dx® recurrence score <11
    - Mammaprint ® low-risk score
    - EndoPredict® low-risk score
    - PAM50® risk of recurrence score in low range
    - Breast Cancer Index in low-risk range

  - Stage IA: Are in same prognostic category as T1a-T1b N0 M0 with ER Positive, HER2 negative

Prognostic Stage Groups



Notes for Prognostic Stage Group Table

- Prognostic value of these Prognostic Stage Groups
  - Based on populations of patients with breast cancer that have been offered and mostly treated with appropriate endocrine and/or systemic chemotherapy

- Stage groups marked by asterisks ***
  - Changed by more than one stage group from 7th Edition
  - Due to use of grade and prognostic factors
  - Comparing 7th edition anatomic stage to 8th prognostic stage
  - Example of patient staged by 7th and 8th editions
    - Anatomic Stage Group IIB in 7th edition
    - Prognostic Stage Group IB in 8th edition

Oncotype Dx® in Prognostic Stage Groups

- Oncotype Dx® applicable only for assigning prognostic stage group to patients with
  - T1–2 N0 M0
  - ER-positive
  - HER2-negative
- Prospective Level I data supports use for patients with score <11
- OncotypeDx® not performed, not available, or score ≥11
  - Group assigned based on anatomic and biomarker categories
- Future updates may include other multigene panels
  - When high level data available to support these assignments

Clinical Prognostic Stage Groups

- Based on history, physical exam, imaging, biopsies and biomarkers (Grade, ER, PR and HER2)
- Relevant to all patients, including those who will receive pre-operative systemic or radiation treatments)
- Determined prior to any treatment
- Allows determination of changes between baseline and pre-operative treatments.
- Allows comparison between groups treated with surgery first or other treatment modalities

Clinical Prognostic Staging Groupings

When TNM is…	And Grade is…	And HER2 Status is…	And ER Status is	And PR Status is	The Clinical Prognostic Stage Group is…
Tis N0 M0	Any	Any	Any	Any	0
T1* N0 MO T0 N1mi M0 T1* N1mi M0	1	Positive	Positive	Positive	IA
				Negative	IA
			Negative	Positive	IA
				Negative	IA
		Negative	Positive	Positive	IA
				Negative	IA
			Negative	Positive	IA
				Negative	IB
	2	Positive	Positive	Positive	IA
				Negative	IA
			Negative	Positive	IA
				Negative	IA
		Negative	Positive	Positive	IA
				Negative	IA
			Negative	Positive	IA
				Negative	IB
	3	Positive	Positive	Positive	IA
				Negative	IA
			Negative	Positive	IA
				Negative	IA
		Negative	Positive	Positive	IA
				Negative	IB
			Negative	Positive	IB
				Negative	IB

*Includes T1mi

Clinical Prognostic Staging Groupings - 2

When TNM is…	And Grade is…	And HER2 Status is…	And ER Status is	And PR Status is	The Clinical Prognostic Stage Group is…
T0 N1** MO T1 N1** M0 T2 N0 M0	1	Positive	Positive	Positive	IB
				Negative	IIA
			Negative	Positive	IIA
				Negative	IIA
		Negative	Positive	Positive	IB
				Negative	IIA
			Negative	Positive	IIA
				Negative	IIA
	2	Positive	Positive	Positive	IB
				Negative	IIA
			Negative	Positive	IIA
				Negative	IIA
		Negative	Positive	Positive	IB
				Negative	IIA
			Negative	Positive	IIA
				Negative	IIB
	3	Positive	Positive	Positive	IB
				Negative	IIA
			Negative	Positive	IIA
				Negative	IIA
		Negative	Positive	Positive	IIA
				Negative	IIB
			Negative	Positive	IIB
				Negative	IIB

**Does not include N1mi

Clinical Prognostic Staging Groupings - 3

When TNM is…	And Grade is…	And HER2 Status is…	And ER Status is	And PR Status is	The Clinical Prognostic Stage Group is…
T2 N1 MO T3 N0 M0	1	Positive	Positive	Positive	IB
				Negative	IIA
			Negative	Positive	IIA
				Negative	IIB
		Negative	Positive	Positive	IIA
				Negative	IIB
			Negative	Positive	IIB
				Negative	IIB
	2	Positive	Positive	Positive	IB
				Negative	IIA
			Negative	Positive	IIA
				Negative	IIB
		Negative	Positive	Positive	IIA
				Negative	IIB
			Negative	Positive	IIB
				Negative	IIIB
	3	Positive	Positive	Positive	IB
				Negative	IIB
			Negative	Positive	IIB
				Negative	IIB
		Negative	Positive	Positive	IIB
				Negative	IIIA
			Negative	Positive	IIIA
				Negative	IIIB

Clinical Prognostic Staging Groupings - 4

When TNM is…	And Grade is…	And HER2 Status is…	And ER Status is	And PR Status is	The Clinical Prognostic Stage Group is…
T0 N2 M0 T1 N2 M0 T2 N2 M0 T3 N1 M0 T3 N2 M0	1	Positive	Positive	Positive	IIA
				Negative	IIIA
			Negative	Positive	IIIA
				Negative	IIIA
		Negative	Positive	Positive	IIA
				Negative	IIIA
			Negative	Positive	IIIA
				Negative	IIIB
	2	Positive	Positive	Positive	IIA
				Negative	IIIA
			Negative	Positive	IIIA
				Negative	IIIA
		Negative	Positive	Positive	IIA
				Negative	IIIA
			Negative	Positive	IIIA
				Negative	IIIB
	3	Positive	Positive	Positive	IIB
				Negative	IIIA
			Negative	Positive	IIIA
				Negative	IIIA
		Negative	Positive	Positive	IIIA
				Negative	IIIB
			Negative	Positive	IIIB
				Negative	IIIC

Clinical Prognostic Staging Groupings - 5

When TNM is…	And Grade is…	And HER2 Status is…	And ER Status is	And PR Status is	The Clinical Prognostic Stage Group is…
T4 N0 M0 T4 N1 M0 T4 N2 M0 Any T N3 M0	1	Positive	Positive	Positive	IIIA
				Negative	IIIB
			Negative	Positive	IIIB
				Negative	IIIB
		Negative	Positive	Positive	IIIB
				Negative	IIIB
			Negative	Positive	IIIB
				Negative	IIIC
	2	Positive	Positive	Positive	IIIA
				Negative	IIIB
			Negative	Positive	IIIB
				Negative	IIIB
		Negative	Positive	Positive	IIIB
				Negative	IIIB
			Negative	Positive	IIIB
				Negative	IIIC
	3	Positive	Positive	Positive	IIIB
				Negative	IIIB
			Negative	Positive	IIIB
				Negative	IIIB
		Negative	Positive	Positive	IIIB
				Negative	IIIC
			Negative	Positive	IIIC
				Negative	IIIC
Any T Any N M1	Any	Any	Any	Any	IV

Pathologic Prognostic Groups

- Based on pathologic findings at definitive surgery and biomarkers (Grade, ER, PR and HER2, as well as multigene prognostic panels)
- Relevant to all patients treated with definitive surgery as initial treatment
- Not appropriate for patients receiving neoadjuvant systemic or radiation treatment
- It is the recommended staging system for use in the USA by all tumor registries

Pathologic Prognostic Staging Groupings

When TNM is…	And Grade is…	And HER2 Status is…	And ER Status is	And PR Status is	The Pathologic Prognostic Stage Group is…
Tis N0 M0	Any	Any	Any	Any	0
T1* N0 MO T0 N1mi M0 T1* N1mi M0	1	Positive	Positive	Positive	IA
				Negative	IA
			Negative	Positive	IA
				Negative	IA
		Negative	Positive	Positive	IA
				Negative	IA
			Negative	Positive	IA
				Negative	IA
	2	Positive	Positive	Positive	IA
				Negative	IA
			Negative	Positive	IA
				Negative	IA
		Negative	Positive	Positive	IA
				Negative	IA
			Negative	Positive	IA
				Negative	IB
	3	Positive	Positive	Positive	IA
				Negative	IA
			Negative	Positive	IA
				Negative	IA
		Negative	Positive	Positive	IA
				Negative	IA
			Negative	Positive	IA
				Negative	IB

*Includes T1mi

Pathologic Prognostic Staging Groupings - 2

When TNM is…	And Grade is…	And HER2 Status is…	And ER Status is	And PR Status is	The Pathologic Prognostic Stage Group is…
T0 N1** MO T1 N1** M0 T2 N0 M0	1	Positive	Positive	Positive	IA
				Negative	IB
			Negative	Positive	IB
				Negative	IIA
		Negative	Positive	Positive	IA
				Negative	IB
			Negative	Positive	IB
				Negative	IIA
	2	Positive	Positive	Positive	IA
				Negative	IB
			Negative	Positive	IB
				Negative	IIA
		Negative	Positive	Positive	IA
				Negative	IIA
			Negative	Positive	IIA
				Negative	IIA
	3	Positive	Positive	Positive	IA
				Negative	IIA
			Negative	Positive	IIA
				Negative	IIA
		Negative	Positive	Positive	IB
				Negative	IIA
			Negative	Positive	IIA
				Negative	IIA

**Does not include N1mi

Pathologic Prognostic Staging Groupings - 3

When TNM is…	And Grade is…	And HER2 Status is…	And ER Status is	And PR Status is	The Pathologic Prognostic Stage Group is…
T2 N1 MO T3 N0 M0	1	Positive	Positive	Positive	IA
				Negative	IIB
			Negative	Positive	IIB
				Negative	IIB
		Negative	Positive	Positive	IA
				Negative	IIB
			Negative	Positive	IIB
				Negative	IIB
	2	Positive	Positive	Positive	IB
				Negative	IIB
			Negative	Positive	IIB
				Negative	IIB
		Negative	Positive	Positive	IB
				Negative	IIB
			Negative	Positive	IIB
				Negative	IIB
	3	Positive	Positive	Positive	IB
				Negative	IIB
			Negative	Positive	IIB
				Negative	IIB
		Negative	Positive	Positive	IIA
				Negative	IIB
			Negative	Positive	IIB
				Negative	IIIA

Pathologic Prognostic Staging Groupings - 4

When TNM is…	And Grade is…	And HER2 Status is…	And ER Status is	And PR Status is	The Pathologic Prognostic Stage Group is…
T0 N2 M0 T1 N2 M0 T2 N2 M0 T3 N1 M0 T3 N2 M0	1	Positive	Positive	Positive	IB
				Negative	IIIA
			Negative	Positive	IIIA
				Negative	IIIA
		Negative	Positive	Positive	IB
				Negative	IIIA
			Negative	Positive	IIIA
				Negative	IIIA
	2	Positive	Positive	Positive	IB
				Negative	IIIA
			Negative	Positive	IIIA
				Negative	IIIA
		Negative	Positive	Positive	IB
				Negative	IIIA
			Negative	Positive	IIIA
				Negative	IIIB
	3	Positive	Positive	Positive	IIA
				Negative	IIIA
			Negative	Positive	IIIA
				Negative	IIIA
		Negative	Positive	Positive	IIB
				Negative	IIIA
			Negative	Positive	IIIA
				Negative	IIIC

Pathologic Prognostic Staging Groupings - 5

When TNM is…	And Grade is…	And HER2 Status is…	And ER Status is	And PR Status is	The Pathologic Prognostic Stage Group is…
T4 N0 M0 T4 N1 M0 T4 N2 M0 Any T N3 M0	1	Positive	Positive	Positive	IIIA
				Negative	IIIB
			Negative	Positive	IIIB
				Negative	IIIB
		Negative	Positive	Positive	IIIA
				Negative	IIIB
			Negative	Positive	IIIB
				Negative	IIIB
	2	Positive	Positive	Positive	IIIA
				Negative	IIIB
			Negative	Positive	IIIB
				Negative	IIIB
		Negative	Positive	Positive	IIIA
				Negative	IIIB
			Negative	Positive	IIIB
				Negative	IIIC
	3	Positive	Positive	Positive	IIIB
				Negative	IIIB
			Negative	Positive	IIIB
				Negative	IIIB
		Negative	Positive	Positive	IIIB
				Negative	IIIC
			Negative	Positive	IIIC
				Negative	IIIC
Any T Any N M1	Any	Any	Any	Any	IV

Clinical Implications of the New Staging System

TNM Groups	Anatomic Staging Groups	Pathologic Prognostic Staging Groups
T1 N0 M0	IA	IA IB
T1 N1 M0	IIA	IA IB 2A
T3 N0 M0	IIB	IA IB IIA IIB IIIA
T3 N2 M0	IIIA	IA IB IIA IIB IIIA

Genomic Profile for Pathologic Prognostic Staging

- Level 1 evidence generated with the 21-gene assay suggests that:
  - When the Recurrence Score is less than 11, and
  - The Tumor is a T1-2 N0 M0
    - Any Grade
    - HER2-negative
    - ER-positive
    - Any PR
  - Then the Pathologic Prognostic Stage is: IA

- Other Genomic Profiles (MammaPrint, ProSigna, Breast Cancer Index, EndoPredict, IHC4, etc.) provide similar prognostic information, although appropriately formatted data are as yet unavailable.

Selection of Genomic Profile for Prognostication

The AJCC Manual is NOT a practice guideline and the Expert Panel is NOT a guideline developer. Physicians are to use the best information available at the time to plan treatment, including the determination to use (one or several) genomic panels, and which genomic panel to select.

Example

- 58 y/o schoolteacher develops a lump in the right breast. By physical exam, it measures 3.5 x 4.0 cm. By imaging, the lesion measures 3.2 x 3.6 cm. There is no palpable axillary node. Biopsy shows a Grade 2, invasive ductal carcinoma, ER+, PR-, HER2-.
- Breast conserving surgery confirms an IDC, measuring 3.0 x 3.5 cm. Sentinel Lymph node biopsy was negative. Oncotype DX Recurrence Score: 9
- Anatomic Stage: pT2 N0 M0 (IIA)
- Clinical Prognostic Stage: IIA
- Pathologic Prognostic Stage: IIA
- With Genomic Modifier: IA

Example

- 63 y/o homemaker develops a lump in the left breast. By physical exam, it measures 7.5 x 6.0 cm. By imaging, the lesion measures 8.2 x 6.6 cm. There is one palpable axillary node measuring 1.5 x 1.5 cm. Biopsy shows a Grade 1, invasive ductal carcinoma, ER+, PR+, HER2+.
- Breast conserving surgery confirms an IDC, measuring 8.0 x 6.5 cm. Sentinel Lymph node biopsy was positive.
- Anatomic Stage: pT3 N1 M0 (IIIA)
- Clinical Prognostic Stage: IIA
- Pathologic Prognostic Stage: IB
- With Genomic Modifier: N/A

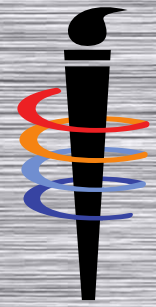
Example

- 72 y/o executive is found to have a mammographic abnormality in the right breast. The lesion is not detectable by physical exam. By imaging, the lesion measures 1.1 x 0.8 cm. There is no palpable axillary node. Biopsy shows a Grade 3, invasive ductal carcinoma, ER-, PR-, HER2-.
- Breast conserving surgery confirms an IDC, measuring 1.0 x 0.7 cm. Sentinel Lymph node biopsy was positive (0.4 cm). ALND not performed. Oncotype DX Recurrence Score: not performed.
- Anatomic Stage: pT1 N1 M0 (IIA)
- Clinical Prognostic Stage: IB
- Pathologic Prognostic Stage: IIA
- With Genomic Modifier: N/A

Example

- 72 y/o executive is found to have a mammographic abnormality in the right breast. The lesion is not detectable by physical exam. By imaging, the lesion measures 1.1 x 0.8 cm. There is no palpable axillary node. Biopsy shows a Grade 1, invasive ductal carcinoma, ER+, PR+, HER2+.
- Breast conserving surgery confirms an IDC, measuring 1.0 x 0.7 cm. Sentinel Lymph node biopsy was positive (0.4 cm). ALND not performed. Oncotype DX Recurrence Score: not performed.
- Anatomic Stage: pT1 N1 M0 (IIA)
- Clinical Prognostic Stage: IA
- Pathologic Prognostic Stage: IA
- With Genomic Modifier: N/A

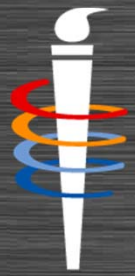
Summary



Summary

- Most significant change is the addition of Prognostic Stage Groups
  - Addition of grade, HER2, ER and PR
  - Use of multigene panels in specific situations
- Chapter text provides important information
  - Clinical, pathological, and post neoadjuvant therapy staging
  - Determining tumor size and nodal involvement size
  - General information and guidance for staging
  - Additional factors recommended for clinical care

Thank you



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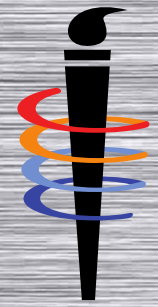

633 N. Saint Clair, Chicago, IL 60611-3211

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