

NCCN National Comprehensive Cancer Network*

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Background

- US Census 16.7 million Americans >80, 65% women¹.
- Cancer is 2nd most common cause of death in women >75².
- Risk of breast cancer triples women aged 70-80 to 43/1000²
- Older women underrepresented in clinical trials

1. Werner, CA. The older population: 2010: 2010 census briefs. U.S. Dept. of Commerce, Economics and Statistics Administration, U.S. Census Bureau. Washington, D.C. 2011.

 Kimmick GG, Muss HB. Chapter 95. Breast Disease. In: Halter JB, Ouslander JG, Tinetti ME, Studenski S, High KP, Asthana S. eds. *Hazzard's Geriatric Medicine and Gerontology, 6e*. New York, NY: McGraw-Hill; 2009. Accessed December 10, 2015

Mammography screening guidelines

American College of				
Radiology (ACR), 200 Society of Breast Imaging (SBI)	7 40	Annual mammography and clinical breast exam	When life expectancy is <5 years	Insufficient evidence to recommend BSE
American College of Obstetrics and 200 Gynecology	40-49 50	Mammography every 1-2 years for patients age 40-49. Annual for age 50 and above. Annual CBE		BSE can be recommended
American College of Surgeons (ACS) 200	9 40	Annual screening mammography	None specified	No recommendation
National Comprehensive Cancer Network (NCCN)	9 40	Annual screening mammography	None	Recommend for Clinical Breast Exam
US Preventive Services 200 Task Force	9 50	Biennial mammography	74	Recommend against BSE and insufficient evidence for CBE
American Cancer 201 Society (ACS)	5 45-54 50	Annually Every other year	Life expectancy >10yrs	Recommend against BSE and insufficient evidence for CBE

Breast cancer detection

- Most studies show breast cancers most likely to present with clinically palpable disease ^{1.2.}
- Litvak et al retrospective review 354 pts >70 found in pts > 80 only 38% mammographically detected ^{1.}
- Vetter et al found In older patients, tumors were more often detected by a clinical breast examination (38.9% vs. 17.0%, p < 0.001) and less often by radiologic procedures (10.4% vs. 29.9%, p < 0.001)².

1. Litvak DA, Arora R. Treatment of elderly breast cancer patients in a community hospital setting. *Arch Surg.* 2006;141(10):90; discussion 990.

2. Vetter M, Huang DJ, Bosshard G, Guth U. Breast cancer in women 80 years of age and older: A comprehensive analysis of an underreported entity. *Acta Oncol.* 2013;52(1):57-65







Surgical tx

- Joerger et al population based study of care of elderly patients with breast cancer (BC),
- 4820 pts 2003-2005
- Found >80 less likely to have BCT compared to mastectomy
- · Less likely to have axillary staging
- Higher axillary recurrence 1% vs. 4% p<0.05
- Less likely to have adjuvant tx i.e. radiation with BCT

Joerger M, Thurlimann B, Savidan A, et al. Treatment of breast cancer in the elderly: population-based Swiss study. *J Geriatr Oncol* 2013;4:39-47.





No Surgery Group

- Between 1990 and 2005, 584 patients with resectable breast cancer and not receiving surgery were identified at the five participating centres
- 187 (32%) patient choice no surgery
- No surgery group 92% endocrine tx

Hamaker, M.E, Omission of surgery in elderly patients with early stage breast cancer. *European Journal of Cancer.* 2013; 49 (3): 545–552

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Surgery vs Endocrine

- Cortadellos et al Barcelona Spain
- 465 pts single institution
- 75% std surgery vs 25% endocrine
- · Matched co-morbidities Charleston index
- If life expectancy >2yrs and acceptable risk for anesthesia should have std surgical tx

Cortadellas, T., et al. Surgery improves breast cancer-specific survival in octogenarians with early-stage breas cancer. International Journal of Surgery. 2013;11(7): 554–557.





Cortadellas, T., et al. Surgery improves breast cancer-specific survival in octogenarians with early-stage breast cancer. *International Journal of Surgery*. 2013;11(7): 554–557.

Surgical Comp

- 213 pts tx art MD Anderson >80 1989-2004.
- Overall, 12% complications rate all types of treatment (26/208).
 There were 2 deaths, 1 after surgery and 1 related to chemotherapy.
- Surgery resulted in complications in 6% (11/188) of patients.
- Five percent (5/112) of patients who received radiation suffered adverse effects.
- Chemotherapy-related complications affected 30% (6/18) of treated patients.
- Hormonal agents resulted in complications in 3% (3/112) of patients.
- No correlation between the American Society of Anesthesiologists score and incidence of complication was observed (P = .58).

Rosencrantz et al. The American Journal of Surgery. 2006; 192 (4): 541-544

Surgical Comp Europe

- 140 operations for breast cancer were performed in 129 women 1990–2005
- Complications occurred in 37.1% of the cohort
- 31.4% were minor complications and only 5.7% were major (stroke, heart attack, thromboembolic).
- Intraoperative morbidity was 18.6% i.e. bleeding
- Postoperative morbidity was 20%.
- Late complications occurred in 5% of patients.
- The most common complications were wound infections (50%).
- The perioperative mortality in this group of elderly women was zero.

Chatzidaki, et al. Annals of Surgical Oncology. 2011; 18 (4): 923-931.







%, P<.001 for all covariates.	Total patients (N=502,807)	Age 0-49 (26.46%)	50-79 (64.13%)	80 and older (9.41%)
Race White A-A Hispanic	74 9.44 7.12	65.24 11.93 9.41	75.98 8.88 6.69	85.15 6.26 3.59
Marital Status Single Married Previously	12.88 59.21 27.92	19.47 67.79 12.74	10.96 60.49 28.55	7.26 25.88 66.87
Histology Ductal Lobular	73.12 7.24	76.55 4.96	72.35 7.76	68.71 10.00
Stage 1 2 3 4	44.95 40.88 7.04 3.69	35.62 48.79 8.74 3.22	48.47 37.96 6.14 3.86	47.7 38.2 8.18 3.86
Hormone Status ER/PR negative	20.59	25.62	19.38	14.65

Weiss A. Blair SL. Et al. Hormone receptor-negative breast cancer: undertreatment of patients over 80. Annals Surgical Oncology 2013 Oct;20(10):3274-8

	Breast Cancer	Cardiovascular	Breast Cancer	Cardiovascular
	Survival	Survival	Survival	Survival
Age 0-49				
5 year	.78 [.7879]	.996 [.995997]	.94 [.9394]	.998 [.998999]
10 year	.74 [.7374]	.994 [.992995]	.86 [.8586]	.995 [.994996]
Age 50-79				
5 year	.79 [.798]	.98 [.98983]	.939 [.93794]	.98 [.98981]
10 year	.74 [.7475]	.95 [.95958]	.88 [.87988]	.948 [.94695]
Age 80 and >				
5 year	.67 [.6669]	.85 [.8386]	.88 [.87889]	.85 [.8485]
10 year	.62 [.6063]	.63 [.6066]	.81 [.81 82]	.63 [.6264]













Lumpectomy Plus Tamoxifen With or Without Irradiation in Women Age 70 Years or Older With Early Breast Cancer: Long-Term Follow-Up of CALGB 9343

- July 1994 and February 1999, 636 women (age ≥ 70 years) who had clinical stage I
- (ER) positive breast carcinoma treated by lumpectomy
- randomized to tamoxifen plus radiation therapy (TamRT; 317 women) or tamoxifen alone (Tam; 319 women).
- Primary end points were time to local or regional recurrence, frequency of mastectomy, breast cancer– specific survival, time to distant metastasis, and overall survival (OS).

Hughes KS, Schnaper LA, Bellon JR, et al. J Clin Oncol 2013;31:2382-2387







Mortality rate < std tx

- 1,837 women > 65 + operations + stage I or II breast cancer in SEER.
- Compared with women receiving mastectomy, those receiving BCS without RT were twice as likely to die of breast cancer (adjusted hazards ratio [HR] = 2.19, 95% confidence interval [CI], 1.51 to 3.18).
- In the subset of 886 chemotherapy-naive women treated with tamoxifen, those treated with tamoxifen for less than 1 year had > breast cancer mortality rate than those exposed 5 years or more (adjusted HR = 6.26, 95% CI, 3.10 to 12.64).

Yood M., et al. Mortality Impact of Less-than-Standard Therapy in Older Breast Cancer Patients. *Journal of the* American College of Surgeons. 2008; 206 (1): 66–75.



Conclusion

- Breast ca in the elderly is more likely to present with palpable masses
- Less likely to receive standard surgical tx
- Pts undergoing std surgical tx have better survival than pts having hormonal tx only
- Pts with triple neg disease have worse prognosis and are more likely to die of breast ca than cardiovascular disease
- Surgical tx has relatively low morbidity and mortality even in oldest pts



Conclusion

 Standard breast cancer tx including surgery + radiation should be considered in pts with a life expectancy > 2 years





Strategies for management of early stage breast cancer in older women: systemic therapy

Lee Schwartzberg MD, FACP NCCN Annual Conference 2016







Life Expectancy: Woman						
	Life Expectancy (years)					
Age	Healthy	Average	Sick			
65	20.0	18.5	9.7			
70	15.8	14.8	8.6			
75	12.1	11.5	7.3			
80	8.8	8.4	5.9			
85	6.1	5.9	4.5			
Extermann, et al. JCO 2000						









Dread				
Breast Cancer Subtypes in Older Women				
Tumor Phenotype	Frequency	Natural History	Adjuvant Therapy	
HR+ HER2-	75%	Slower growing, frequent relapses after 5 yrs	Al or Tam for most; Add Chemo for high risk	
TNBC	15%	Almost all relapses <5 yr	Chemo if expected improvement in survival >3 %	
HER2+	15%	Most recurrences w/in 5 yrs: ER+HER2+ have later relapses	Chemo + anti- HER2 therapy for most; endocrine for ER+	
				(













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Adverse Event	CMF (N=132)	Doxorubicin plus Cyclophosphamide (N=183) no. of patients (%)	Capecitabine (N=299)
Death	0	0	2 (1)†
≥1 Event	92 (70)	109 (60)	101 (34)
≥1 Hematologic adverse event	68 (52)‡	99 (54)	7 (2)
Hematologic adverse event			
Anemia	4 (3)	7 (4)	2 (1)
Requirement for transfusions	0	2 (1)	0
Leukopenia	53 (40)	79 (43)	3 (1)
Neutropenia	35 (27)	59 (32)	5 (2)
Thrombocytopenia	5 (4)	7 (4)	1 (<1)
≥1 Nonhematologic adverse event	53 (40)‡	44 (24)	98 (33)
Nonhematologic adverse event			
Fatigue	15 (11)	8 (4)	15 (5)
Mucositis	2 (2)	8 (4)	3 (1)
Nausea	9 (7)	8 (4)	6 (2)
Vomiting	8 (6)	3 (2)	6 (2)
Diarrhea	10 (8)	5 (3)	20 (7)
Hand-foot skin reaction	1 (<1)	0	47 (16)
Febrile neutropenia	11 (8)	16 (9)	2 (1)
Thrombus or embolism	5 (4)	4 (2)	3 (1)











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National Comprehensive Cancer Network* Invasive Breast Ca	Version 1.2016 ancer
DOSING SCHEDULE FOR COMBINATIONS FOI DISEASE: PREFERRED REGIMENS	R HER2-POSITIVE
AC followed by T chemotherapy with trastuzumab • Doxorubicin 60 mg/m² IV day 1 • Cyclophosphamide 600 mg/m² IV day 1 Cycled every 21 days for 4 cycles. Followed by: Paclitaxel 80 mg/m² by 1 h IV weekly for 12 wks With: • Trastuzumab 4 mg/kg IV with first dose of paclitaxel Followed by: • Trastuzumab 2 mg/kg IV weekly to complete 1 y of treatment. As an alternative, trastuzumab 6 mg/ kg IV every 21 days may be used following the completion of paclitaxel, and given to complete 1 y of trastuzumab tratment. Evaluate left ventricular ejection fraction (LVEF) prior to and during treatment.	AC followed by T chemotherapy with trastuzumab + pertuzumab • Doxorubicin 60 mg/m ² IV day 1 • Cyclophosphamide 600 mg/m ² IV day 1 Cycled every 21 days for 4 cycles. Followed by: • Pertuzumab 840 mg IV day 1 followed by 420 mg IV • Trastuzumab 8 mg/kg IV day 1 followed by 6 mg/kg IV • Trastuzumab 8 mg/kg IV day 1, 8, and 15 Cycled every 21 days for 4 cycles • Trastuzumab 6 mg/kg IV day 1 Cycled every 21 days to complete 1 y of trastuzumab therapy Evaluate LVEF prior to and during treatment.
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National Cancer Institute Sponsored Trials



Recommendations for Adjuvant Chemotherapy in Older Breast Cancer Patients HER2-Regimen Evidence in Elderly Recommendations AC->T Subgroup Only fit and high-risk pts; CMF Prospective Feasible w/precautions AC Prospective Feasible w/precautions TC Feasible w GCSF Subgroup Weekly doc Prospective Not recommended Weekly pac Subgroup Feasible HER2+ AC->TH Subgroup Only fit and high-risk pts ТСН No evidence Concern about tox Weekly Pac-H Subgroup Feasible TC-H No evidence Feasible

Systemic Treatment of Breast Cancer in the Older Woman

- Treatment decisions should not be made by age alone
- Fit older patients can and do benefit from systemic chemotherapy
- With proper support standard therapies are tolerable
- Avoid under-treatment when therapy can be curative
- Avoid toxicity in palliative setting, frailty, dependence
- Maintain independence





