Breast cancer in the 'older' pts

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Based on SIOG recommendations:

Lancet Oncol 2007 (8) p 1101

Introduction

- INCIDENCE: >40% occurs > 65y of age
- TUMOR BIOLOGY:
  - more favourable in elderly: ↑ hormone sentivity, ↓ Her2neu overexpression, ↓ grade and proliferative indices.
  - more often advanced stage, more N+
  - For same stage, no major differences in outcome with increasing age
- UNDERTREATMENT frequent ⇒ impact on survival
- UNDERREPRESENTATION of elderly in clinical trials

Case Report

- ♀ 74y
- Nodule left breast 2.5 cm at 2h
- Mammo/echo: spicular lesion 2,1 cm
- Core biopsy: invasive ductal carcinoma gr III, ER pos PR neg
- cT2N0M0

⇒ 1/ is surgery really necessary? Or hormone therapy alone?
2/ if surgery: breast conserving surgery? Mastectomy?
3/axilla: lymph node dissection? SLN?

⇒ **What do you do?**

Geriatric assessment (CGA)!

- CGA improves therapeutic outcome
  - detects **multiple problems**
  - leads to significant reduction in **functional decline**
  - improvement in **quality of life** in terms of mobility, social interaction and morale (Fletcher Lancet 2004)
- Better view on comorbidity, functionality, cognition, depression, nutrition, social problems
- Several screening tools available (PACE, G8, VES-13, GRP, …)

Case Report

- ♀ 74y
- Geriatric assessment: G8 16/17, no further assessment
- Comorbidity: deep venous thrombosis 1998, hypertension
- Medication: bisoprolol, aspirine
- Lives with husband

Early Breast Cancer

Surgery

1 / Surgery or no surgery? ⇒ local control ↑, OS =

study	n pat	therapy	F.U. (Mo)	Overall Survival %	Local Recurrence %
Van dalsen (retrospective)	171	TAM Surg	41	68 72	27 6
Robertson	135	TAM Surg	24	85 74,6	44 24,6
Gazet	200	TAM Surg	72	67 72	56 44
Bates	381	TAM Surg+TAM	34	82,5 84,8	23 7,5
GRETA	474	TAM Surg+TAM	80	38,7 45,6	47,2 11

Surgery

2/ Type of Surgery?

- Breast conserving surgery
  - less used!
  - Outcome similar to mastectomy in elderly (few data >70y)
  - Better QoL, also in >70y
  - Preferred by most older patients
- Mastectomy

Surgery

3/ Axilla?

- Low risk tumors (node negative, small)
  - ALND:
    - concerns of causing comorbidity
    - little influence on adjuvant treatment decisions
    - Studies showing no inferior prognosis in low risk tumors when ALND is omitted.
  - SLN biopsy procedure = solution
- High risk tumors:
  - ALND standard

Surgery

SIOG Recommendation

- Don't deny surgery for ≥ 70y only on the basis of age
- Kind of surgery for older = younger
- Axilla:
  - small clinically node negative tumours:
    - ALND? comorbidity without influencing adjuvant treatment decisions or prognosis.
    - SLN biopsy procedure = solution for tumor < 2-3 cm
  - high risk tumours:
    - ALND standard

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Case Report

- ♀ 74y
- Breast conserving surgery and SLN
- SLN positive, further axillary dissection
- Final pathological report:
  - Invasive ductal carcinoma
  - Lymphovascular invasion
  - 3 cm
  - 11/24 nodes involved
  - ER 8/0, PR 0/0, HER-2 0
- pT2N3M0

⇒ radiotherapy: 1/ breast?
2/ boost?

Early Breast Cancer

Radiotherapy

1/ Breast irradiation after BCS

	BCS	BCS+RT
5-y local recurrence	26%	7%*
15-y mortality	35,9%	30,5%*

	<50y	>70y
5y local recurrence after BCS	33%	13%*
5y local recurrence risk reduction of RT	22%	11%*

- RT should be considered in all pts after BCS irrespective of age.
- If ≥ 70y and low risk (tumours ≤2cm, clear margins, node negative, hormone sensitive)

↓

absolute benefit small

↓

RT discussed individually ~ general condition/patient preference

Radiotherapy

2/ BOOST after BCS

5-y local recurrence	boost	No boost
Whole population (n = 5318)	6,2%	10,2%*
> 60y (n = 1732)	3,8%	7,3%*

- boost decreases the relative risk of local relapse by almost 50% independently of age
- Absolute benefit/survival benefit might be rather small
- Tailored approach ~ tumor and patient related risk factors

Radiotherapy

3/ Postmastectomy radiotherapy

- Benefit of RT independent of age

  local recurrence reductions at 5y ± 18% in all age groups

- ≥ 4 lymph nodes or T3:

  10y OS 10% ↑ (OS benefit only after 5 y).

- 1-3 nodes or high risk N- (grade 3, LVI):

  more controversial

Radiotherapy

SIOG Recommendation

- BCT:
  - RT decreases the risk of local relapse and should be considered irrespective of age.
  - The absolute benefit of RT might be (very) small in low risk tumors.
  - The effect of RT on overall survival (OS) in elderly is not clear and probably much more influenced by comorbidity, aging and distant metastases.
  - A decision on RT in elderly should take into account patient health, functional status, risk of mortality from comorbidity, and risk of local recurrence.
- Boost after BCS:
  - Should be considered in all older pts to decrease risk of local relapse
- Postmastectomy chest wall irradiation:
  - ≥ 4 lymph nodes or T3-4: indicated
    - if life expectancy ≤ 5y, only expected benefit on loco-regional control
  - 1-3 nodes or high risk N- (grade 3, LVI): limited data available to support systematic postmastectomy chest wall irradiation.

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Case Report

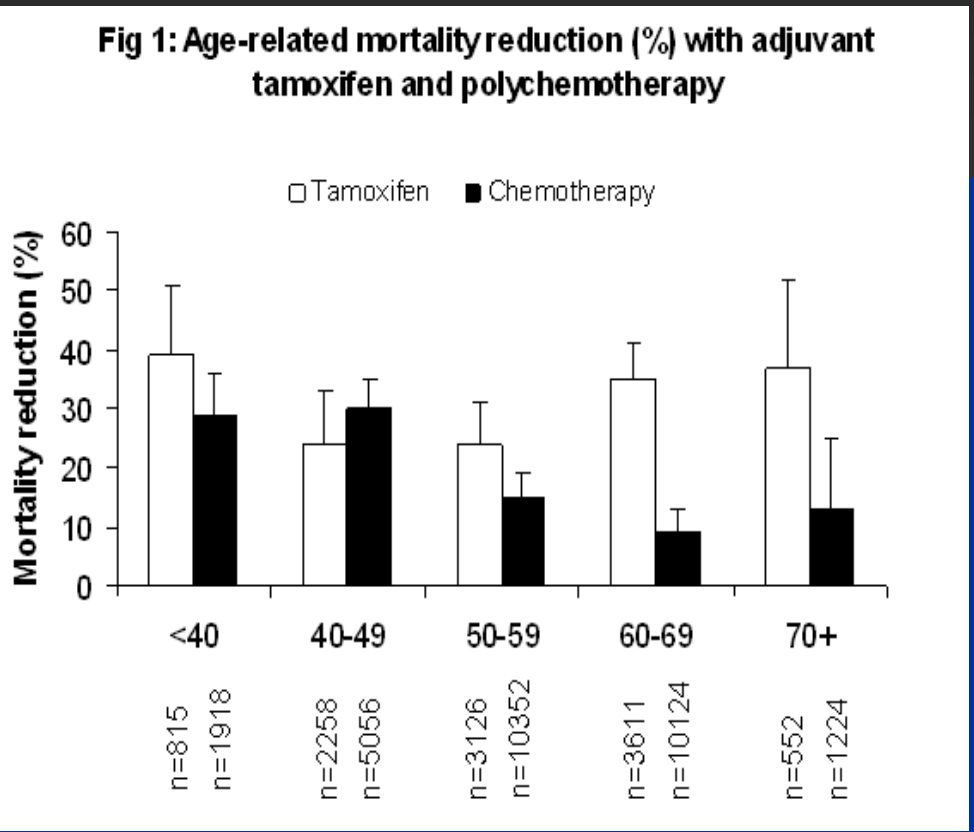
- ♀ 74y
- Tumorectomy + SLN → ALND: pT2N3M0
  - Invasive ductal carcinoma
  - Lymphovascular invasion
  - 3 cm
  - 11/24 nodes involved
  - ER 8/0, PR 0/0, HER-2 0
- Radiotherapy breast + boost + internal mammary node RT

⇒ hormonal therapy:

1/ Tamoxifen?
2/ Aromatase inhibitor?
3/ Switch?

Early Breast Cancer

Hormone therapy



- Benefit of aromatase inhibitors vs tamoxifen largely independent of age
- Higher endoxifen levels in elderly
- Tolerability:
  - TAM: thrombosis, endometrial cancer
  - AI: osteoporosis, arthralgia

Hormone therapy

SIOG Recommendation:

- Benefit of adjuvant HT for older = younger
- No evidence for age related differences in efficacy between tamoxifen and aromatase inhibitors.
- However
  - more vulnerable to some side effects
  - comorbidity can be an important parameter in the choice between tamoxifen and aromatase inhibitors.

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Case Report

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  - ER 8/0, PR 0/0, HER-2 0
- Radiotherapy breast + boost
- Hormonal therapy: aromatase inhibitor 5y

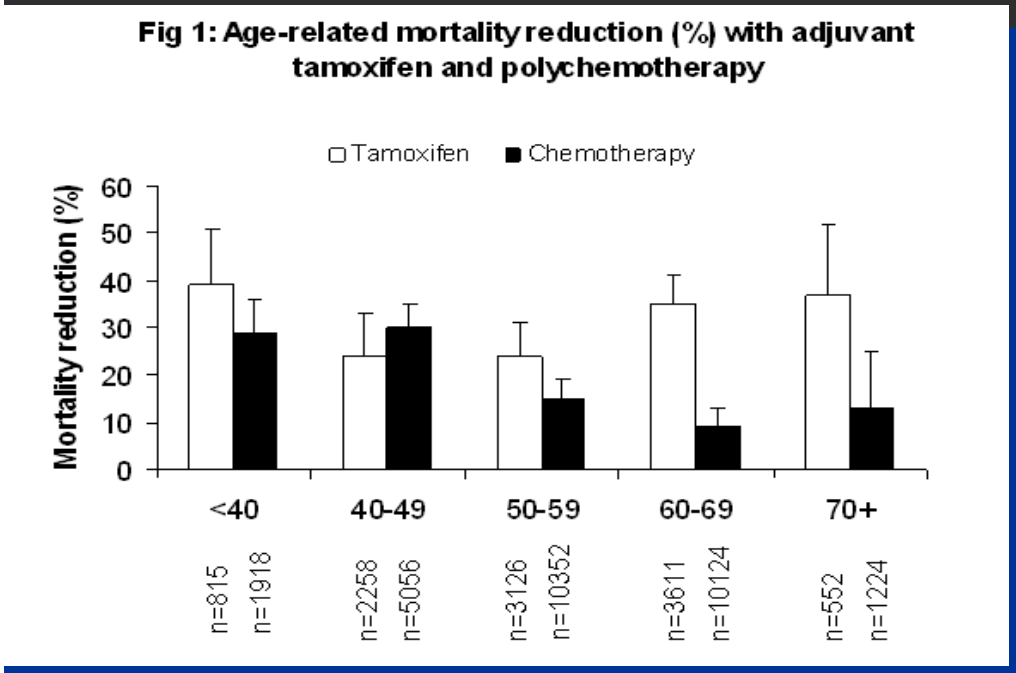
⇒ adjuvant chemotherapy: 1/ yes or no?
2/ if yes: which chemotherapy?

Early Breast Cancer

Chemotherapy

Who Chemotherapy?

- Benefit of CT:



- for younger (<50y) > older
- but in postmenopausal women still substantial benefit
- no clear age trend in groups (50-59, 60-69, >70 y)

Early Breast Cancer

Who Chemotherapy?

Endocrine **non**-responsive

- larger benefit
- Data:

  * SEER database (JCO 18 2750/2757):

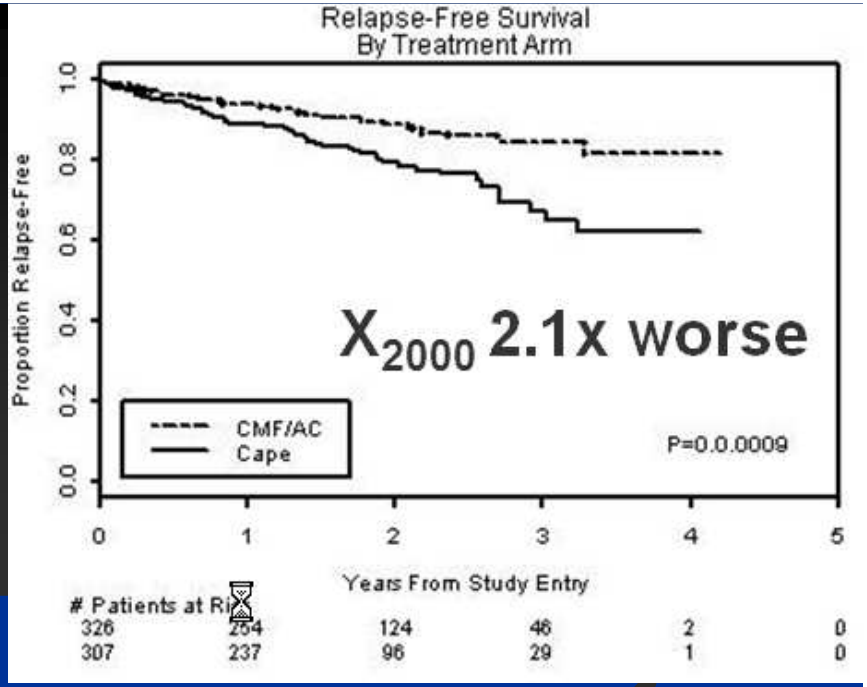
    OS 15%-28% ↑

  * Muss ASCO 2008: AC/CMF > capecitabine!

    34% HR neg

    DFS and OS ↑

    unplanned subanalysis: benefit only in HR neg



- Absolute benefit ~
  - general condition (a.o. comorbidity)
  - tumour parameters (N+, tumor size, HER2 +, tumor grade)

Early Breast Cancer

Chemotherapy

Who Chemotherapy?

Endocrine responsive

- Smaller benefit
- Data:
  - * Anthracycline regimens in postmenopauzal women: OS ↑ (JCO 1990 ; albain SABCS 2004)
    benefit in >70y?
    benefit in highly hormone sensitive tumors?.
  - * Large retrospective review in N+ tumours: similar benefit in older and younger women (JAMA 293 1073)
  - * Ph III trial in 65+: weekly epirubicine plus tamoxifen compared to tamoxifen: DFS ↑, OS = (but tamoxifen concomitant with chemo)
  - * Muss ASCO 2008: AC/CMF > capecitabine! 66% HR+
    DFS and OS ↑ (but in unplanned subanalysis; benefit only in HR neg)
- benefit likely to be higher in tumors that are not clearly endocrine sensitive (e.g. low levels of hormone receptors, absence of ER or PR).

Early Breast Cancer

Chemotherapy

Which Chemotherapy?

- identical regimens compared to non elderly in principle possible;
  but greater toxicity. Treatment related mortality 1,5% if >65y (JAMA 293 1073)
  dose reductions might decrease efficacy

- St-Gallen:
  - endocrine responsive: 4 x AC or 6 x CMF
  - endocrine non responsive/uncertain disease:
    anthracyclines +/- taxanes

panellists acknowledged that special considerations may apply to elderly women

Early Breast Cancer

Chemotherapy

Which Chemotherapy?

- **CMF** in elderly:
  - less tolerated and less effective than in younger (JCO 18 1412; BMC cancer 5 30)
  - 1.28% toxic death if ≥ 65 y (lancet 354 130;)
- **Anthracyclines** in elderly:
  - Anthracyclines superior to CMF: no age trend
  - 10-year cardiac failure rate in women 66-70 y (proc ASCO 2006 521)

    47% if adjuvant anthracyclines ; 33% if CMF ; 28% if no adjuvant CT
- **Taxanes**
  - 4x TC (taxotere – cyclophosphamide) > 4 x AC for DFS and OS
  - well tolerated in >65y (SABCS Jones No 12)

Early Breast Cancer

Chemotherapy

SIOG Recommendations

- WHO chemo?
  - Age by itself ≠ determining factor for adjuvant CT
  - individualized decision ~ estimated absolute benefit, life expectancy, treatment tolerance, and patient preference
- WHICH chemo?
  - 4xAC preferred above 6x CMF
  - AC/CMF > capecitabine
  - 4xTC very attractive alternative without intrinsic cardiotoxicity

Case Report

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  - Invasive ductal carcinoma
  - Lymphovascular invasion
  - 3 cm
  - 11/24 nodes involved
  - ER 8/0, PR 0/0, HER-2 0
- Radiotherapy breast + boost + internal mammary node RT
- Hormonal therapy:
- Chemotherapy:
  - Median life expectancy at 74y: +/- 12 years
  - Adjuvant online: 9% OS benefit with chemo
  - 4 x TC discussed with the patient

Conclusions

- Beware of UNDERTREATMENT!
  - Can lead to inferior outcome
- Beware of OVERTREATMENT!
  - Elderly don't need identical therapy systematically (less absolute gain of chemotherapy, radiotherapy, influence of comorbidity, …)
- Most optimal therapy ~
  - General prognostic tumor related markers
  - Global health status and life expectancy
  - Patient preference
  - NOT chronological age