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 sensitivity,
    ↓ 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?

<table>
<thead>
<tr>
<th>Study</th>
<th>n Pat</th>
<th>Therapy</th>
<th>F.U. (Mo)</th>
<th>Overall Survival %</th>
<th>Local Recurrence %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Van dalsen (retrospective)</td>
<td>171</td>
<td>TAM Surg</td>
<td>41</td>
<td>68/72</td>
<td>27/6</td>
</tr>
<tr>
<td>Robertson</td>
<td>135</td>
<td>TAM Surg</td>
<td>24</td>
<td>85/74.6</td>
<td>44/24.6</td>
</tr>
<tr>
<td>Gazet</td>
<td>200</td>
<td>TAM Surg</td>
<td>72</td>
<td>67/72</td>
<td>56/44</td>
</tr>
<tr>
<td>Bates</td>
<td>381</td>
<td>TAM Surg+TAM</td>
<td>34</td>
<td>82.5/84.8</td>
<td>23/7.5</td>
</tr>
<tr>
<td>GRETA</td>
<td>474</td>
<td>TAM Surg+TAM</td>
<td>80</td>
<td>38.7/45.6</td>
<td>47.2/11</td>
</tr>
</tbody>
</table>

⇒ local control ↑, OS =
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
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**
SIOG Recommendation

- Don’t deny surgery for $\geq 70$y 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
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

<table>
<thead>
<tr>
<th></th>
<th>BCS</th>
<th>BCS+RT</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-y local recurrence</td>
<td>26%</td>
<td>7%*</td>
</tr>
<tr>
<td>15-y mortality</td>
<td>35,9%</td>
<td>30,5%*</td>
</tr>
</tbody>
</table>

- 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)

<table>
<thead>
<tr>
<th></th>
<th>&lt;50y</th>
<th>&gt;70y</th>
</tr>
</thead>
<tbody>
<tr>
<td>5y local recurrence after BCS</td>
<td>33%</td>
<td>13%*</td>
</tr>
<tr>
<td>5y local recurrence risk reduction of RT</td>
<td>22%</td>
<td>11%*</td>
</tr>
</tbody>
</table>

↓ absolute benefit small
↓ RT discussed individually ~ general condition/patient preference
Radiotherapy

2/ BOOST after BCS

<table>
<thead>
<tr>
<th>5-y local recurrence</th>
<th>boost</th>
<th>No boost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whole population (n = 5318)</td>
<td>6.2%</td>
<td>10.2%*</td>
</tr>
<tr>
<td>&gt; 60y (n = 1732)</td>
<td>3.8%</td>
<td>7.3%*</td>
</tr>
</tbody>
</table>

- 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
Early Breast Cancer

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
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.
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
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.
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
- 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 postmenopausal 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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- 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:
- 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