Breast Cancer in the Elderly

Lorna Weir
Radiation Oncology, BCCA
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Breast cancer in the elderly – the problem

• 30-40% of breast cancers occur in women aged 70 or more
• Optimal treatment has been controversial because women of this age are often excluded from, or significantly under-represented in randomized trials

Demographics
Canadian females, in 1000's

<table>
<thead>
<tr>
<th>Age Group</th>
<th>2006</th>
<th>2011</th>
<th>2016</th>
</tr>
</thead>
<tbody>
<tr>
<td>70-74</td>
<td>549</td>
<td>593</td>
<td>724</td>
</tr>
<tr>
<td>75-79</td>
<td>484</td>
<td>487</td>
<td>528</td>
</tr>
<tr>
<td>80-84</td>
<td>388</td>
<td>397</td>
<td>401</td>
</tr>
<tr>
<td>85-89</td>
<td>238</td>
<td>281</td>
<td>290</td>
</tr>
<tr>
<td>90+</td>
<td>163</td>
<td>206</td>
<td>250</td>
</tr>
</tbody>
</table>

• For example in one US study, 49% of patients with breast cancer were ≥ 65 years of age, but only 9% of patients in clinical trials were this age
• Clinicians tend not to offer trials to older women, and trial designs often exclude them
Breast cancer risk for American women by age

- by age
  - 50: one in 50
  - 60: one in 24
  - 70: one in 14
  - 80: one in 10
  - 85: one in 9

Why treat the elderly differently?

- Breast cancer is “less aggressive” in the elderly
- They tolerate treatment less well
- They are more likely to die of other causes

Are these statements true?

Is breast cancer less aggressive in the elderly?

University of Chicago study on natural history of breast cancer

- 2136 patients treated with mastectomy from 1927 – 1987
- This era is prior to screening
- 75% did not receive systemic therapy
- Looked at 3 age groups:
  - ≤ 40
  - 41-70
  - > 70
University of Chicago study on natural history of breast cancer

<table>
<thead>
<tr>
<th>T size</th>
<th>&lt; 40</th>
<th>41-70</th>
<th>&gt;70</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 2 cm</td>
<td>32</td>
<td>32</td>
<td>36</td>
</tr>
<tr>
<td>2-5</td>
<td>49</td>
<td>49</td>
<td>46</td>
</tr>
<tr>
<td>&gt;5</td>
<td>19</td>
<td>19</td>
<td>18</td>
</tr>
<tr>
<td>+ nodes</td>
<td>40</td>
<td>42</td>
<td>44</td>
</tr>
<tr>
<td>1-3</td>
<td>32</td>
<td>28</td>
<td>28</td>
</tr>
<tr>
<td>≥ 4</td>
<td>28</td>
<td>27</td>
<td>17</td>
</tr>
<tr>
<td>X &lt;1</td>
<td>3</td>
<td>17</td>
<td></td>
</tr>
</tbody>
</table>

- Multivariate analysis showed that age was not a significant factor for distant disease free survival

Italian study, 2999 post menopausal women who underwent surgery between 1997 – 2002
- Looked at 3 age groups: 50-64, 65-74, ≥ 75
- No difference seen in the 3 age groups for:
  - proportion of patients with Grade 1,2,3 high Ki 65 ER neg
  - 1-3, 4-9 + nodes

- But women aged ≥ 75 had:
  - fewer p T 1 p N 0
  - more 10+ positive nodes
  - fewer Her 2 + LVI
  - more ER/PR +
Effect of under treatment

- Swiss study looking all women ≥ 80
- 407 patients, diagnosed 1989-99
- 4% detected by screening mammo
- Average tumour size 30 mm

Effect of under treatment

<table>
<thead>
<tr>
<th></th>
<th>%</th>
<th>5 yr</th>
<th>5yr</th>
</tr>
</thead>
<tbody>
<tr>
<td>No treatment</td>
<td>12</td>
<td>12</td>
<td>11</td>
</tr>
<tr>
<td>Tam alone</td>
<td>32</td>
<td>32</td>
<td>18</td>
</tr>
<tr>
<td>Lumpectomy alone</td>
<td>7</td>
<td>7</td>
<td>27</td>
</tr>
<tr>
<td>Lumpectomy and adj Rx</td>
<td>14</td>
<td>14</td>
<td>67</td>
</tr>
<tr>
<td>Mastectomy alone</td>
<td>14</td>
<td>14</td>
<td>52</td>
</tr>
<tr>
<td>Mastectomy and adj Rx</td>
<td>19</td>
<td>19</td>
<td>44</td>
</tr>
</tbody>
</table>

* Adjusted HR for death from breast ca

Effect of under treatment

- Authors acknowledge that there are treatment selection biases even with adjusted models
- Can only get this type of information from observational studies
- But this data strongly suggests that undertreatment worsens prognosis
Omission of Axillary dissection

BCCA study
Truong et al. 2002

Objective:
• To determine the effect of omission of AD on survival in women with T1/T2 breast cancer
• Cohort of 8,130 women aged 50-89 referred to the BCCA from 1989-1998 with T1-T2, M0 breast cancer

Results

<table>
<thead>
<tr>
<th>Age</th>
<th>50-64</th>
<th>65-74</th>
<th>75-89</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>3749</td>
<td>2820</td>
<td>1561</td>
</tr>
<tr>
<td>% AD Omission</td>
<td>4%</td>
<td>9%</td>
<td>22%</td>
</tr>
</tbody>
</table>

Ax dissection- Conclusions

• Axillary dissection is more frequently omitted with advanced age
• Omission of AD is associated with more favorable tumor characteristics (T size, grade, LV-, ER+)
Ax dissection - Conclusions

- Omission of AD is associated with:
  - lower overall survival for the entire cohort analyzed and for women aged >65
  - lower breast cancer specific survival for women aged 65-74

- The lower survival cannot be attributed to tumor characteristics or adjuvant radiotherapy and systemic treatment

Omission of Axillary dissection

- Italian Study, 2003
- women age ≥ 70 with operable and clinically node negative breast cancer
- All patients had conservative breast surgery and received Tamoxifen ***

671 women → 172 AD +
  → 499 AD -

Axillary dissection

- AD – group were older and had larger tumours
- 71% of them did not have breast RT

<table>
<thead>
<tr>
<th></th>
<th>AD -</th>
<th>AD+</th>
</tr>
</thead>
<tbody>
<tr>
<td>Axillary recurrence</td>
<td>5.4</td>
<td>0</td>
</tr>
<tr>
<td>Distant recurrence</td>
<td>7.4</td>
<td>8.7</td>
</tr>
<tr>
<td>Breast cancer deaths</td>
<td>9.2</td>
<td>8.1</td>
</tr>
<tr>
<td>Unrelated deaths</td>
<td>21.2</td>
<td>12.8</td>
</tr>
</tbody>
</table>

Conclusions:

- No significant difference between AD – and AD + for endpoints of breast cancer mortality and distant recurrence
- This was felt to be attributable to the fact that all women were treated with Tamoxifen
Randomized trials of treatment for elderly women

- Italian trial
- 474 women ≥ 70 with operable breast ca
- 1987-92, median age 76
- Median FU 80 months

- Randomized to: Tam alone
  Surgery then Tam
- ER known in only 1/2 of pts in surgery arm

Authors conclude that treatment of elderly women should include minimal surgery and Tamoxifen

Even though survival not improved, it is important to minimize local progression

Randomized trials of treatment for elderly women

<table>
<thead>
<tr>
<th></th>
<th>Tam</th>
<th>Surgery then Tam</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local progr</td>
<td>45.2</td>
<td>11.2</td>
</tr>
<tr>
<td>EFS</td>
<td>20</td>
<td>42</td>
</tr>
<tr>
<td>Br Ca deaths</td>
<td>23.8</td>
<td>23</td>
</tr>
<tr>
<td>Overall deaths</td>
<td>61.3</td>
<td>54.4</td>
</tr>
</tbody>
</table>

Randomized trials of treatment for elderly women

- UK study of 455 women ≥ 70
- 1984-91, med FU 12.7 years

- Randomized to: Tam alone
  surgery + Tam (40 mg)
- ER not known
Randomized trials of treatment for elderly women

<table>
<thead>
<tr>
<th>Progression</th>
<th>Tam (pts)</th>
<th>Surgery (pts) and Tam</th>
</tr>
</thead>
<tbody>
<tr>
<td>local</td>
<td>141</td>
<td>57</td>
</tr>
<tr>
<td>axilla</td>
<td>21</td>
<td>12</td>
</tr>
<tr>
<td>distant</td>
<td>14</td>
<td>20</td>
</tr>
<tr>
<td>5 yr OS %</td>
<td>59.5</td>
<td>67.4 (p = ns)</td>
</tr>
<tr>
<td>10 yr OS %</td>
<td>28.8</td>
<td>37.7 (p = ns)</td>
</tr>
</tbody>
</table>

Breast ca death 68 43

Randomized trials of treatment for elderly women

Authors conclude:

• If fit for surgery they should have it

-------------------------------------------------------------------------

• There are also 4 small randomized studies looking at Tam alone vs surgery alone
• All show similar results, with Tam alone there is much increased loco regional progression

Randomized trials of treatment for elderly women

• NEJM September 2004 - 2 studies:

• Hughes et al
• 636 patients age 70 or older with clinical stage T1N0 invasive cancer
• Following lumpectomy, randomized to:
  - breast RT + Tam
  - Tam alone
• 64% had no axillary node dissection (stratified)
• Med FU 5 yrs

Randomized trials of treatment for elderly women

RT + Tam  Tam

Freedom from LR recurrence
At 5 yrs

99 % 96 %

5 yr OS 86 % 87 %
Randomized trials of treatment for elderly women

- Axillary recurrence rate was 0% for patients receiving RT and Tam

- In patients with no axillary dissection receiving Tam alone, axillary recurrence rate was 1%

- They conclude axillary dissection not necessary in women ≥ 70 with clinical T1N0 breast cancer

Randomized trials of treatment for elderly women

- Fyles et al

- 759 women with pathological T1 or T2 invasive cancer aged ≥ 50

- all were node negative, but if aged 65 or older could be clinically staged node negative (17% of the patients in this category)

- randomized after lumpectomy to either breast RT and Tam, or Tam alone

<table>
<thead>
<tr>
<th></th>
<th>RT + Tam</th>
<th>Tam</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 yr DFS</td>
<td>91%</td>
<td>84%</td>
</tr>
<tr>
<td>5 yr OS</td>
<td>93%</td>
<td>93%</td>
</tr>
<tr>
<td>5 year axillary relapse rate</td>
<td>0.5%</td>
<td>2.5%</td>
</tr>
<tr>
<td>patients ≥ 65 with no axillary node dissection</td>
<td>0.6%</td>
<td>3.3%</td>
</tr>
</tbody>
</table>

Randomized trials of treatment for elderly women

- median FU was 5.6 years

- stratified for node dissection or not

<table>
<thead>
<tr>
<th></th>
<th>RT + Tam</th>
<th>Tam</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 yr DFS</td>
<td>p = 0.049</td>
<td></td>
</tr>
<tr>
<td>5 yr OS</td>
<td>p = 0.049</td>
<td></td>
</tr>
<tr>
<td>5 year axillary relapse rate</td>
<td>p = 0.07</td>
<td></td>
</tr>
</tbody>
</table>

Overall Conclusions

- Breast cancer in elderly women will be an increasing health care issue over the next 2 decades due to demographics and increased use of screening mammography

- Breast cancer in the elderly is NOT a less aggressive disease compared to younger women

- Under treatment will result in poorer breast cancer survival
Overall Conclusions

• Tamoxifen alone is not adequate treatment for elderly women with operable breast cancer

• Minimal surgery plus adjuvant hormonal therapy should be considered for all women who are fit for it

• It would appear that elderly women with clinically early (T1-2, N0) breast cancer do not need a full node dissection

• Breast radiation treatment confers a modest benefit only

Overall Conclusions

• Elderly patients with inoperable breast cancer are treated on an individual basis

• Neoadjuvant treatment with chemotherapy or hormones followed by surgery is possible for many

• Elderly women should be encouraged to discuss treatment options with breast cancer specialists