Will you still screen me, will you still treat me, when I’m 64?
What about 84?

(A brief tour of the wonderful world of geriatric oncology)

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Division of Geriatric Medicine, U. of T.
Research Scientist, NCIC

Learning objectives

• To describe the burden of cancer in older adults
• To describe special considerations of cancer in older adults
• To briefly review emerging research themes in the area of geriatric oncology

“If you’re not a paediatric oncologist, you’re a geriatric oncologist.”

Saying in Oncology, source unknown

Outline

• What is geriatric oncology?
• Burden of cancer in older adults
• What’s so special about growing old?
• Emerging research in geriatric oncology
• Summary

What is geriatric oncology?

• No one precise definition of a ‘geriatric’ patient; commonly 65 or 70 used
• Among geriatricians/gerontologists, 65-74 are ‘young old’, 75-84 are ‘medium old’, and 85+ are ‘oldest old’
• Overall it is clear that aging has led to an increased focus on cancer in older adults
Outline

- What is geriatric oncology?
- Burden of cancer in older adults
The Population is Aging

Age ≥ 65: Fastest growing segment in Canada

By 2030:
- Age 65 and older: double
- Age 75 and older: triple
- Age 85 and older: double

Cancer and Aging

Yancik, Int'l Society of Geriatric Oncology 2001

Burden of cancer in older adults

- Older adults are fastest growing age group in Western countries
- About 60% of all cancers occur in age 65+
- 71% of all cancer deaths in age 65+
- Odds of dying from cancer are 16-fold higher in people age 65+ compared to <65

2005 Cancer Incidence
Data: Men

From Canadian Cancer Society Cancer Statistics 2005

2005 Cancer Incidence
Data: Women

From Canadian Cancer Society Cancer Statistics 2005

2005 Cancer Mortality
Data: Men

From Canadian Cancer Society Cancer Statistics 2005
Factors accounting for increased cancer incidence

Factors accounting for increased cancer mortality

Outline

• What is geriatric oncology?
• Burden of cancer in older adults
• What’s so special about growing old?

What’s so special about growing old?

• Decreasing life expectancy
• Increasing comorbidity (competing causes of mortality)
• Increasing cognitive and functional impairment
• Increasing frailty
• Altered pharmacokinetics/dynamics as well as homeostasis
• Limited oncology evidence base
**Projected life expectancy (years)**

<table>
<thead>
<tr>
<th>Age now</th>
<th>Life Expectancy</th>
<th>Age of Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>65</td>
<td>17.7</td>
<td>82.7</td>
</tr>
<tr>
<td>70</td>
<td>14.3</td>
<td>84.3</td>
</tr>
<tr>
<td>75</td>
<td>11.2</td>
<td>86.2</td>
</tr>
<tr>
<td>80</td>
<td>8.5</td>
<td>88.5</td>
</tr>
<tr>
<td>85</td>
<td>6.3</td>
<td>91.3</td>
</tr>
<tr>
<td>90</td>
<td>4.5</td>
<td>94.5</td>
</tr>
<tr>
<td>95</td>
<td>3.3</td>
<td>98.3</td>
</tr>
<tr>
<td>100</td>
<td>2.5</td>
<td>102.5</td>
</tr>
</tbody>
</table>

*National Vital Statistics Report*

**Comorbidity**

*Definition:*
Concurrent, independent health condition which may be a predictor of survival and resource requirements

*Key questions:*
1. Is the patient going to die from cancer or another medical problem?
2. Will another medical problem limit the ability to tolerate treatment?

**Major comorbid conditions in older cancer patients**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>42.9</td>
</tr>
<tr>
<td>Heart disease</td>
<td>39.1</td>
</tr>
<tr>
<td>Arthritis</td>
<td>34.9</td>
</tr>
<tr>
<td>Gastrointestinal problems</td>
<td>31.0</td>
</tr>
<tr>
<td>Anemia</td>
<td>22.6</td>
</tr>
<tr>
<td>Eye Problems</td>
<td>19.0</td>
</tr>
<tr>
<td>Urinary Tract</td>
<td>18.0</td>
</tr>
<tr>
<td>Previous cancer</td>
<td>15.4</td>
</tr>
<tr>
<td>Gallbladder problem</td>
<td>14.9</td>
</tr>
<tr>
<td>COPD</td>
<td>14.5</td>
</tr>
<tr>
<td>Diabetes</td>
<td>12.8</td>
</tr>
</tbody>
</table>

*Yancik Cancer 1997; 80:1273*

**Impact of comorbidity**

- ↑ risk of short-term mortality and complications after surgery/radiation
- ↑ risk of complications after chemotherapy
- ↓ overall survival
- ↑ likelihood of dying from other causes

**30-day mortality after radical prostatectomy**

<table>
<thead>
<tr>
<th>Age</th>
<th>Mortality</th>
<th>Any complication</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;50</td>
<td>0%</td>
<td>20.4%</td>
</tr>
<tr>
<td>50-59</td>
<td>0.21%</td>
<td>17.2%</td>
</tr>
<tr>
<td>60-69</td>
<td>0.58%</td>
<td>20.6%</td>
</tr>
<tr>
<td>70-79</td>
<td>0.66%</td>
<td>26.9%</td>
</tr>
</tbody>
</table>

*unadjusted rates

*Alibhai JNCI 2005; 97:1525*

**Predictors of 30-day mortality**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Multivariable</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (per decade)</td>
<td>2.04 (1.22, 3.39)</td>
</tr>
<tr>
<td>Year of Surgery</td>
<td>0.58 (0.33, 1.01)</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>2.43 (1.12, 5.26)</td>
</tr>
<tr>
<td>Stroke</td>
<td>7.84 (1.84, 39.77)</td>
</tr>
</tbody>
</table>

c-statistic=0.69

*Alibhai JNCI 2005; 97:1525*
Impact of age on complication rates

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Probability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Under 60</td>
<td>0.005</td>
</tr>
<tr>
<td>60-69</td>
<td>0.01</td>
</tr>
<tr>
<td>70-79</td>
<td>0.015</td>
</tr>
</tbody>
</table>

Impact of comorbidity on complication rates

<table>
<thead>
<tr>
<th>Diagnosis Count</th>
<th>Probability</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0.005</td>
</tr>
<tr>
<td>1</td>
<td>0.01</td>
</tr>
<tr>
<td>2</td>
<td>0.015</td>
</tr>
<tr>
<td>3</td>
<td>0.02</td>
</tr>
<tr>
<td>4</td>
<td>0.025</td>
</tr>
</tbody>
</table>

Impact of age and comorbidity on all complications

<table>
<thead>
<tr>
<th>Diagnosis Count</th>
<th>Probability</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0.005</td>
</tr>
<tr>
<td>1</td>
<td>0.01</td>
</tr>
<tr>
<td>2</td>
<td>0.015</td>
</tr>
<tr>
<td>3</td>
<td>0.02</td>
</tr>
<tr>
<td>4</td>
<td>0.025</td>
</tr>
</tbody>
</table>

Relationship Between Severity of Comorbidity and Overall Survival

- Overall
- Comorbidity Level
- Mild
- Moderate
- Severe

Age, comorbidity & life expectancy

- Synergistic interaction between age & comorbidity

<table>
<thead>
<tr>
<th>Age</th>
<th>ICED 0</th>
<th>ICED 1</th>
<th>ICED 2</th>
<th>ICED 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>65</td>
<td>12.5 y</td>
<td>10.7 y</td>
<td>7.1 y</td>
<td>2.3 y</td>
</tr>
<tr>
<td>70</td>
<td>9.8 y</td>
<td>8.3 y</td>
<td>5.4 y</td>
<td>1.6 y</td>
</tr>
<tr>
<td>75</td>
<td>7.5 y</td>
<td>6.3 y</td>
<td>3.9 y</td>
<td>1.1 y</td>
</tr>
</tbody>
</table>

Albertsen JAMA 1995; 274:626
Remaining life expectancy

- Key variables in determining remaining life expectancy:
  - Age
  - Comorbidity
  - Disability

Impact of disability

- Several studies have demonstrated an excess risk of morbidity and premature mortality from dependence in activities of daily living (ADLs)
- Independent of age and comorbidity
- Likely a marker of frailty
- In one high quality study, dependence in 1 or more Instrumental ADLs associated with 50% increased risk of dying over next 5 years (JAMA 1998; 285:2750)

Calculating remaining life expectancy

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age 75, no comorbidity, indep. IADLs</td>
<td>12.33 y</td>
<td>15.18 y</td>
</tr>
<tr>
<td>Age 75, mild comorbidity, indep. IADLs</td>
<td>9.70 y</td>
<td>12.44 y</td>
</tr>
<tr>
<td>Age 75, moderate comorbidity, indep. IADLs</td>
<td>6.12 y</td>
<td>8.45 y</td>
</tr>
<tr>
<td>Age 75, moderate comorbidity, dependent 2+ IADLs</td>
<td>4.49 y</td>
<td>6.53 y</td>
</tr>
</tbody>
</table>

Altered pharmacology

- Numerous age-related changes in host organs/tissues at both pharmacokinetic and pharmacodynamic levels
- Pharmacokinetics
  - Absorption
  - Distribution
  - Metabolism
  - Elimination
- Pharmacodynamics
  - Altered tissue sensitivity

Key pharmacokinetic changes

- ↓ absorption surface
- ↑ body fat
- ↓ body water
- ↓ albumin concentration
- ↓ liver blood flow and size
- ↓ GFR (7-10 mL/min/decade after age 30)

Limited oncology evidence base

- Poor recruitment of older adults into clinical trials
- Limited # of older adults even in many large trials to facilitate subgroup analyses
- Highly selected older adults in clinical trials (limited comorbidity, not disabled/frail, cognitively intact)
Outline

• What is geriatric oncology?
• Burden of cancer in older adults
• What’s so special about growing old?
• Emerging research in geriatric oncology

Emerging research

• Age bias – next steps
• Comprehensive geriatric assessment
• Screening – when do we stop (if ever)?
• Elder-specific clinical trials

Age bias

• Systematic discrimination against people simply on the basis of age
• Often synonymous with inappropriate (under) treatment

Age bias

• Numerous studies in oncology have shown that older people are:
  – Less aggressively screened
  – Less systematically staged
  – Receive less standard surgical therapy
  – Receive less adjuvant radiation/chemotherapy
  – Receive less cosmetic surgical reconstruction consultation
  – Receive less dose-intensive chemotherapy
  – Receive CSF’s less often with chemotherapy
  – Receive strong analgesic and anti-emetic drugs less often

Observed probability of receiving treatment within 6 months by age group (n=5,192)

Alibhai Cancer 2004; 100:72
Age bias

- Lots of studies documenting existence of age bias
- Emerging data on various reasons
- Limited intervention studies looking at ways to minimize age bias
  - Some limited success with geriatric oncology specialty clinics and/or CGA-based approaches

Comprehensive geriatric assessment

“A multidisciplinary diagnostic process intended to determine a frail elderly person’s medical, psychosocial, and functional capabilities and limitations in order to develop an overall plan for treatment and long-term follow-up”

Rubenstein, 1982
Comprehensive geriatric assessment

- Key components of CGA:
  - Comorbidity
  - Polypharmacy
  - Functional status
  - Cognitive function
  - Mood
  - Social support
  - Nutritional status

CGA – Who needs it?

- 7 studies of geriatric oncology population:
  - Ages ranged from 68 to 79
  - 31-86% independent in basic ADL's
  - 26-52% independent in instrumental ADL's
  - 14-40% had significant depressive symptoms
  - 25-51% had cognitive impairment
  - Taking a mean of 6 medications

Extermann J Clin Oncol 2007; 25:1824

CGA – Does it work?

- Number of studies using various forms of CGA in oncology settings
- Improved detection rates of comorbidity, polypharmacy, nutritional issues, need for social support, disability, depression
- Some suggestion of decreased age bias in use of surgery and primary/adjuvant chemotherapy

CGA – Does it work?

- Limitations:
  - No randomized studies
  - Unclear if survival or disease control impacted
  - Unclear which method(s) and population(s) optimal for CGA

(P.S. Canada is way behind US and several European nations)

Cancer screening – when to stop?

- Screening asymptomatic individuals to detect early cancers which may be curable
- Use diagnostic tests with high sensitivity
- Natural history of disease can be changed by intervention
- Benefits outweigh risks
- What about elderly?
  - Diminishing benefits with increasing age
  - Increased risk of harms

Cancer screening guidelines

<table>
<thead>
<tr>
<th>Malignancy</th>
<th>ACS</th>
<th>CTFPHC</th>
<th>USPSTF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast</td>
<td>CBE &amp; Mammogram yearly after age 40</td>
<td>CBE &amp; Mammogram every 1-2 y age 50-69</td>
<td>Mammogram every 1-2 y age 50-69</td>
</tr>
<tr>
<td>Cervical</td>
<td>Pap every 2-3 y until age 70*</td>
<td>Pap every 3 y until age 69*</td>
<td>Pap every 3 y until age 69*</td>
</tr>
</tbody>
</table>

ACS = American Cancer Society; CTFPHC = Canadian Task Force on Preventive Health Care; USPSTF = US Preventive Services Task Force; CBE = Clinical breast exam
* - if 3 prior Pap smears were normal
Cancer screening guidelines

<table>
<thead>
<tr>
<th>Malignancy</th>
<th>ACS</th>
<th>CTCPHC</th>
<th>USPSTF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colorectal</td>
<td>Age 50+ either FOBT yearly OR flex sig every 5 y OR colonoscopy every 10 y OR DCBE every 5 y</td>
<td>Age 50+ FOBT every 1-2 y +/- flex sig (interval not specified)</td>
<td>Age 50+ FOBT yearly +/- flex sig (interval not specified)</td>
</tr>
<tr>
<td>Prostate</td>
<td>Annual PSA + DRE age 50+ if LE&gt;10 y</td>
<td>Not routinely recommended</td>
<td>Not routinely recommended</td>
</tr>
</tbody>
</table>

FOBT = Faecal occult blood test; DCBE = Double contrast barium enema; PSA = Prostate-specific antigen; DRE = digital rectal exam

Cancer screening – when to stop?

- Many guidelines do not include age limits to stop screening
- Primary evidence base very limited because of lack of inclusion of sufficient numbers of older adults
- If age limits exist, these are not rational (i.e. do not take into account factors such as comorbidity and disability that impact remaining life expectancy)

Cancer screening – when to stop?

- Researchers are beginning to tackle this by:
  - Constructing fancy decision-analytic models to quantify risks/benefits
  - Doing observational cohort and nested case-control studies using large population-based registries or longitudinal clinical databases

Elder-specific clinical trials

- Some geriatric oncologists have recommended/conducted elder-specific clinical trials to target recruitment of elders and answer age-relevant oncology questions (e.g. treatment of elderly lymphoma)
- Enhanced recruitment compared to traditional trials with broad age range inclusion criteria
- Somewhat more generalizable older oncology patients in trials

Elder-specific clinical trials

- Has not adversely affected recruitment to general cancer trials to date but experience limited
- BUT risks of using less toxic/less efficacious regimens in non-randomized studies
- May be most appropriate to:
  - Answer questions about safety/efficacy of established drug in specific older populations
  - Determine non-inferiority of less toxic regimens compared to standard practice

“Wind up your presentation — he’s losing bone mass.”
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Summary

• Cancer disproportionately affects older adults in terms of incidence, morbidity, and mortality
• Older patients with cancer have more comorbidity, disability, polypharmacy, and altered pharmacology that impact all aspects of oncology research and practice
• Age bias exists in most areas of oncology
• Evidence base to treat older adults with cancer limited in several ways

Summary

• Complex interactions between age, comorbidity, and disability with respect to short-term and long-term outcomes in older cancer patients
• Lots of emerging research ranging from minimizing age bias to setting rational limits on screening to use of CGA to optimize oncology practice
• Lots of opportunities for more work