Geriatric Oncology: Current perspectives

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“If you are not a pediatric oncologist, you are a geriatric oncologist”
Learning objectives

- Understand the need for geriatric knowledge in cancer care
- Identify current practice models and assessment tools
- Identify opportunities for research including how geriatric assessment may impact patient outcomes

Personalizing medicine

- Why is this important?
  - Cancer is a big deal
  - Cancer treatment can be toxic
    - Surgery
    - Chemotherapy
    - Targeted treatments with chronic side effects

Cancer is a disease of the aging

- By 2030 number of persons over 65 will double
- Older patients
  - 11 fold increase in cancer incidence
  - 16 fold increase in cancer mortality

Unique population

- Decreased functional reserve
- Decreased renal and hepatic functions
- Decreased hematopoietic reserve
- Decreased life expectancy
- Increased comorbidities
Comorbidities

• Prostate cancer patients’ risk of death differs by age at diagnosis and grade of tumor

A unique patient population

• Goals
• Cost
  – difficult to accurately prognosticate for patients if data are unclear for them
• Transport and support
• Cognitive
Brief history of geriatric oncology

- Venice statement "Cancer in the elderly"¹
- BJ Kennedy ASCO Presidential Address
- Comprehensive Geriatric Oncology – 1st edition
- 1st oncogeriatric guidelines – gCSF in elderly²
- 2000 SIOG Formed
- CGA guidelines published³
- NCCN guidelines for senior adult oncology

¹ Fentman et al Lancet 1990 1020-1022
² Bokemeyer C Onkologie 2002
³ SIOG Extermann Crit Rev Oncol Hematol 2005

"I was diagnosed with cancer a couple of years ago. I’m 82 next year and not afraid to say it! I find it surprising that some people will still make judgements on a person because of their age. We’re all different." — Joyce, 81
Can we learn from trial data?

Real world data

- Compared SEER survival to clinical trial enrollees
  - Advanced pancreatic or lung cancer
  - Received a guideline-recommended 1st line chemotherapy regimen

- Results
  - Trial patients 9.5 years younger
  - Medicare patients tended to live in areas of greater educational attainment
  - <75 years old, similar survival between populations
    - Patients >75 had a shorter survival than the trials
Underrepresented…but interested

- Inclusion/exclusion criteria
  - Organ function
  - Comorbidities
- Complicated trial design
- Travel to an academic center
- Physician censoring/age bias
  - Survey of US oncologists indicated that 51% excluded patients from clinical trials on the basis of age alone

Age bias

- Average life expectancy for 75 year old US man → 11 year in a 75 yo 10-year cause-specific mortality of high risk Pca (conservative rx) → 26%
- In this SEER data 49% of men >65 were ADT alone; 61% of men >75
  - Concurrent rx favored dual rx with HR of 0.63 for OS or 0.51 for disease specific mortality in men >75yo
Do we treat these two men the same?

Understanding our older patients

Mohile et al. Nat Rev Clin Oncol 2012; Mohile JCO 2011; Covinsky, JAMA 2001
Are oncologists trained to make these decisions?

- Do we need to increase
  - Dual training opportunities
  - Geriatricians
  - Education of oncologists

- Current efforts
  - ASCO modules
  - Geri Onc GME Competencies
  - Effort to reduce age bias

Survey of geriatric oncology issues of importance

- Patient care
  - Functional status
- Research
  - Improve tox understanding
- Education
  - Knowledge integration

Moy JOP 2014
How to figure this out?

- Who is the patient
- What is the risk for toxicity
  - Are these risk factors modifiable?

Perform a geriatric assessment
Comprehensive Geriatric Assessment

- Functional status
- Medical
  - Comorbidities
  - Nutritional status
- Psychological state
- Cognition
- Social support
- Environment

Impact of the CGA

- Recommended by:
  - International Society of Geriatric Oncology
  - ASCO
  - NCCN
  - Cancer and Aging Research Group
  - American Geriatrics Society
Barriers

- Time
- Reliance on Eastern Cooperative Oncology Group or Karnofsky Performance Status measures

<table>
<thead>
<tr>
<th>Assessments</th>
<th>Oncogeriatric Outpatient US*4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>75 (median)</td>
</tr>
<tr>
<td>ECOG 0-1</td>
<td>83</td>
</tr>
<tr>
<td>ADL independent, %</td>
<td>79</td>
</tr>
<tr>
<td>IADL independent, %</td>
<td>44</td>
</tr>
<tr>
<td>Depression, %†</td>
<td>26 (GDS)</td>
</tr>
<tr>
<td>Cognitive impairment, %</td>
<td>25 (MMSE &lt; 26)</td>
</tr>
<tr>
<td>Comorbidity, %</td>
<td>36 (CCI); 94 (CIRS)</td>
</tr>
</tbody>
</table>

Hurria JCO 2011; Extermann JCO 2007; Repetto JCO 2002; Extermann Cancer Control 2003

Case

- 84yoF with a past medical history of chronic constipation and tachycardia presents with intermittent hematuria
- Workup reveals a muscle invasive bladder cancer without any nodal or distant spread
- Tumor board discussion of neoadjuvant chemotherapy vs concurrent chemo radiation
Impact of the CGA

- Reduction in:
  - Adverse events
  - Hospitalizations
  - Patient stress
  - Mortality

May reduce relative risk of death by 15.3% (in breast cancer adjuvant therapy)

Impact of CGA

- ADLs
  - Functional dependence associated with ↓ survival
- Assistance with IADLs
  - Important for treatment planning
- Functional status
  - Need for assistance predicts for institutionalization and mortality
- Cognitive function
  - Treatment planning
  - Ability to seek help
Assistance with IADLs $\rightarrow$ Worse Survival in Patients with Lung Cancer

Maione et al, J Clin Oncol, 2005

Screening tools

- Ideally have high sensitivity and negative predictive value
- No agreed upon tool
  - G8 recommended by SIOG
G8

- 8 items in 5 minutes
- Developed for the cancer population
- Compared with CGA in 8 studies
  - Sensitivity 65-92%; specificity 3-75%
    (>60 in 4 studies)
  - high sensitivity for functional decline
  - predictive of chemo toxicity in some

- Food intake
- Weight loss
- Mobility
- Neuropsych
- BMI
- Medications
- Self report of health status
- Age

Vulnerable Elders Survey 13

- Age
- Self estimated health
- Limitations in physical function
- Functional disabilities
Case

- Lives alone
- Independent in all ADLs, IADLs
- Uses walker to get around, uses stair lift, has fallen when trying to get to something in the house
- Children live in the area

Loss of Physical Function Predicts Distress in Older Adults with Cancer

Greatest predictor of distress is impaired physical function

P value = 0.015

Hurnia et al, JCO 2009
Case

- Physical therapy consult is offered and she declines
- She undergoes chemo teaching with the primary oncologist as well as 2 hours with a clinical pharmacist
- When contacted to set up her chemotherapy infusion, she asks, “I can’t just pick up the taxol from the pharmacy?”

Current models of geriatric care

- Inpatient assessment and consultation
- Screening in oncology clinic with referral to geriatric provider
- Geri-onc clinic
- Multidisciplinary tumor boards
Case revisited

• Our patient is getting ready for chemotherapy and radiation given concurrently

• Her risk of chemo toxicity is …

• How to dose her treatment - Low and slow?
  – Does this apply when the intent is curative?
  – Does this apply to oral agents?

Emerging research and future directions

• Incorporation of GA
• Elder specific clinical trials
• Improved therapeutic trials
Should we give older patient chemotherapy?

- Risk of chemo toxicity increases with age\(^1,2\)
- Older adults benefit as much from chemo as younger\(^3,4\)
- Less likely to be offered chemo based on concerns of tolerability\(^5,6\)
  - Or offered dose reduced\(^7,8\)

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Chemo and capecitabine

- Primary endpoint: PFS
- Results:
  - 2 toxic deaths with capecitabine
  - Improvement in disease free survival and OS with CMF/AC

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1. Hurria Drugs and Aging 2005
2. Repetto J Support Oncol 2003
3. Langer JNCI 2002
5. Kwak JCO 1990
7. Shayne Breast Cancer Res Treat 2006
8. Muss JAMA 2009

Muss NEJM 2009
Primary dose reduction

- Age
- Lung cancer
- Renal/ hepatic dysfunction
- Cognitive dysfunction

<table>
<thead>
<tr>
<th>Adverse events</th>
<th>Primary dose reduction</th>
<th>Standard dose</th>
<th>P value</th>
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<tbody>
<tr>
<td></td>
<td>No. (%)</td>
<td>No. (%)</td>
<td></td>
</tr>
<tr>
<td>Grades 3-5 toxicity *</td>
<td>54 (50.5)</td>
<td>212 (53.9)</td>
<td>0.52</td>
</tr>
<tr>
<td>Grade 3 toxicity</td>
<td>52 (48.6)</td>
<td>199 (50.6)</td>
<td>0.71</td>
</tr>
<tr>
<td>Grade 4 toxicity</td>
<td>8 (7.3)</td>
<td>51 (13.0)</td>
<td>0.10</td>
</tr>
<tr>
<td>Grade 5 toxicity</td>
<td>2 (1.9)</td>
<td>7 (1.8)</td>
<td>0.95</td>
</tr>
<tr>
<td>Hematotoxicity</td>
<td>29 (27.1)</td>
<td>102 (26.0)</td>
<td>0.81</td>
</tr>
<tr>
<td>Non-hematotoxicity</td>
<td>43 (40.2)</td>
<td>174 (44.3)</td>
<td>0.45</td>
</tr>
<tr>
<td>Hospitalization</td>
<td>29 (27.1)</td>
<td>86 (21.9)</td>
<td>0.26</td>
</tr>
<tr>
<td>Dose reduction</td>
<td>28 (26.7)</td>
<td>125 (31.8)</td>
<td>0.26</td>
</tr>
<tr>
<td>Dose delay</td>
<td>31 (29.0)</td>
<td>124 (31.6)</td>
<td>0.61</td>
</tr>
<tr>
<td>Discontinuation of chemo</td>
<td>23 (21.3)</td>
<td>83 (21.1)</td>
<td>0.93</td>
</tr>
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Age 65 or older
- Diagnosis of cancer
- To start a new chemotherapy regimen
- N=500

Can Geriatric Assessment Predict Chemo Toxicity?

- Timepoint 1: Pre-chemo Geriatric Assessment
- Timepoint 2: Post-chemo Geriatric Assessment
- Chemotherapy: toxicity grading at each visit
## CARG Chemo toxicity tool

<table>
<thead>
<tr>
<th>Domain</th>
<th>Measure</th>
<th>Items</th>
<th>Description</th>
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<tbody>
<tr>
<td>FUNCTIONAL</td>
<td>ADL (subscale of MOS)</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td></td>
<td>IADL (subscale of OARS)</td>
<td>7</td>
<td>Meal prep, shop, wide range of physical function (dressing to running), phone calls etc</td>
</tr>
<tr>
<td></td>
<td>KPS</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Falls in 6 mos</td>
<td></td>
<td></td>
</tr>
<tr>
<td>COMORBIDITY</td>
<td>Subscale of OARS</td>
<td>13</td>
<td>Measure of 13 comorbid illness</td>
</tr>
<tr>
<td>PSYCH</td>
<td>HADS</td>
<td>14</td>
<td>Depression/anxiety in last week</td>
</tr>
<tr>
<td>SOCIAL ACTIVITY</td>
<td>MOS</td>
<td>4</td>
<td>Degree problems interfered with level of social activity</td>
</tr>
<tr>
<td>SOCIAL SUPPORT</td>
<td>MOS</td>
<td>12</td>
<td>Perceived availability of social support</td>
</tr>
<tr>
<td>NUTRITION</td>
<td>BMI</td>
<td>1</td>
<td>Weight kg/height in m2</td>
</tr>
<tr>
<td></td>
<td>% Wt loss (6 mos)</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

### Risk factors for grade 3-5 toxicity

- Age ≥ 72 years
- GI or GU Cancer
- Standard Dose
- Poly-chemotherapy
- Hemoglobin (male: <11, female: <10)
- Creatinine Clearance (Jelliffe-ideal wt <34)
- Fall(s) in last 6 months
- Hearing impairment (fair or worse)
- Limited in walking 1 block (MOS)
- Assistance required in medication intake (IADL)
- Decreased social activity (MOS)
Chemotherapy toxicity tool

- Association between tool and KPS greater ability to discriminate risk

Risk of Grade 3-5 Toxicity

Case revisited

- Our patient’s risk is calculated at:
Future directions

How to put it together

- Prospective cohort study evaluating CGA in patients with Stage III, IV CRC on chemo
**Unique trial design**

- Focused population
  - CALGB 49907 - Standard adjuvant poly chemo v monochemo in >65yo women with breast cancer
- Stratify into age groups representative of the population
- Prospective cohort study
  - CALGB 369901 – Breast Ca population to focus on decision making
- Embedded study
  - CALGB 361006 – CGA is embedded in an AML study
- Single arm study
  - CALGB 9762 – Prospective trial of paclitaxel pharmacology

**Future directions**

- Improve evidence base
  - Increase representation in trials
  - Amend patent law to allow for a 6 month extension for trials in older patients or patients with multiple comorbidities
    - *such as those in the pediatric realm*
- Expand depth of data for assessing interventions
  - Common set of data elements such as a geriatric assessment

Talarico JCO 2004; Scher JCO 2012
Future directions

• Future study should focus on ability of screening tools to build pathways that predict outcomes