The Cancer-Focused Comprehensive Geriatric Assessment: Implications, Content, and Utility

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Many slides c/o Tanya M. Wildes, MD, MSCI
Assistant Professor of Medicine
Disclosures

• Consultant for Seattle Genetics
Overview

• Comprehensive Geriatric Assessment (CGA) for older cancer patients
  • How CGA is defined for cancer care
  • Utility of CGA for older patients with cancer
  • Implications of results for decision-making
  • Implications of results for CGA-driven interventions
• Collaboration throughout trajectory
  • Case study
Case Study: Advanced Prostate Cancer

- An 86-year old with metastatic prostate cancer is being seen for the first time. He was previously followed by his urologist.

- He was diagnosed with Gleason 7 prostate cancer approximately 6 years ago
  - He was started on Lupron 3 years ago
  - He was most recently treated with bicalutamide, which was discontinued several months ago due to a rising PSA

- His disease is widespread through the bones and a recent bone scan shows progression with new lesions in multiple areas

- His PSA nadired to 6 on bicalutamide, but is now 20

- His testosterone level is 10
Comprehensive Geriatric Assessment

- Function
  - Activities of Daily Living
  - Instrumental Activities of Daily Living
  - Physical function
  - Falls
- Comorbidities
- Medications
  - Polypharmacy
  - Inappropriate medications
  - START/STOPP criteria
- Psychological status
  - Depression/Anxiety
  - Cognitive impairment
  - Dementia
  - Delirium
- Incontinence
- Social support
- Vision/hearing
- Goals of Care
- Frailty
Utility of Comprehensive Geriatric Assessment in Older Adults with Cancer

Risk Prediction
- Chemotherapy Toxicity
- Survival

Cancer treatment modification
- Modification of treatment/chemotherapy
- Modification of supportive care

Intervention
- General Geriatrics vs. Cancer-focused
- Goals

c/o Tanya Wildes
Chemotherapy Toxicity:
Cancer and Aging Research Group Study

Eligibility criteria
- Age 65 or older
- Diagnosis of cancer
- To start a new chemotherapy regimen

Pre-chemo Assessment → End chemo

Chemotherapy toxicity
NCI CTCAE v3.0 (2 MDs)

Sample size: 500 patients
7 participating institutions (CARG)

Hurria J Clin Oncol 2011
Hurria J Clin Oncol 2016
Toxicity Summary

Incidence

Grade 3-5 | Grade 4 | Grade 3 | Grade 5
---|---|---|---
All types | 53% | 50% | 12% | 12% | 0% | 2% | 43% | 42% | 6% | 2%
<table>
<thead>
<tr>
<th>Risk factor for Grade III-V Toxicity</th>
<th>OR (95% CI)</th>
<th>Score</th>
</tr>
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<td>1.8 (1.2-2.8)</td>
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<td>1</td>
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</table>

Possible score 0-25
CRASH Trial

- Chemotherapy Risk Assessment Scale for High Age Patients
- Location: USF/Moffitt and 6 community centers
- Predictors:
  - Age, sex, BMI, diastolic blood pressure, comorbidity (CIRS-G)
  - CBC, LFTs, CrCl, albumin, LDH
  - Self-reported health, ECOG PS, IADLs, GDS, MMS, MNA
  - cancer stage, marrow invasion, prior chemotherapy, tumor response, toxicity of chemo regimen (MAX2)

Extermann, Cancer 2012
CRASH Trial

• N=518 evaluable
• Median age 76 (range 70-92)
• 54.8% had stage IV cancer

• Toxicity:
  – 31.8% grade IV hematologic toxicity
  – 56% grade III/IV nonhematologic toxicity
  – Combined: 67.8%

Extermann, Cancer 2012
Table 4. The Chemotherapy Risk Assessment Scale for High-Age Patients (CRASH) Score

<table>
<thead>
<tr>
<th>Predictors</th>
<th>0</th>
<th>1</th>
<th>2</th>
</tr>
</thead>
</table>

**Hematologic score**\textsuperscript{a}
- Diastolic BP \(<72\) \(\geq 72\)
- IADL \(26-29\) \(10-25\)
- LDH (if ULN 618 U/L; otherwise, 0.74 \(\text{L}^*\text{ULN}\)) \(<459\) \(\geq 459\)
- Chemotox\textsuperscript{b} \(<0.44\) \(0.45-0.57\) \(>0.57\)

**Nonhematologic score**\textsuperscript{a}
- ECOG PS \(0\) \(1-2\) \(3-4\)
- MMS \(30\) \(<30\)
- MNA \(28-30\) \(<28\)
- Chemotox\textsuperscript{b} \(<0.44\) \(0.45-0.57\) \(>0.57\)

Abbreviations: BP, blood pressure; Chemotox, toxicity of the chemotherapy regimen (for details, see text); ECOG PS, Eastern Cooperative Oncology Group performance status; IADL, Instrumental Activities of Daily Living; LDH, lactate dehydrogenase; MMS, Mini Mental Health Status; MNA, Mini Nutritional Assessment; ULN, upper limit of normal.

\textsuperscript{a}For the combined score, add the points from the hematologic and nonhematologic score, counting Chemotox only once.
CGA in Predicting Early Death

**Table 4. Logistic Regression Model Analysis for Early Deaths (within 6 months) That Occurred for All Patients Who Received First-Line Chemotherapy (n = 339)**

<table>
<thead>
<tr>
<th>Risk Factor*</th>
<th>Odds Ratio</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>1</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>2.40</td>
<td>1.20 to 4.82</td>
<td>.013</td>
</tr>
<tr>
<td>Tumor stage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Localized</td>
<td>1</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>Advanced</td>
<td>3.9</td>
<td>1.59 to 9.73</td>
<td>.003</td>
</tr>
<tr>
<td>Mini Nutritional Assessment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Good nutrition, score &gt; 23.5</td>
<td>1</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>At risk/poor nutrition, score ≤ 23.5</td>
<td>2.77</td>
<td>1.24 to 6.18</td>
<td>.013</td>
</tr>
<tr>
<td>Timed Get Up and Go</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No impairments (≤ 20 seconds)</td>
<td>1</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>Impaired</td>
<td>2.55</td>
<td>1.32 to 4.94</td>
<td>.006</td>
</tr>
</tbody>
</table>

NOTE: Model was adjusted for treatment site (regional and teaching hospitals vs community hospitals).
*Age, tumor site, Activities of Daily Living, Mini-Mental State, platelet count, and performance status were also included in the model but not retained because they were not significant.

Soubeyran *J Clin Oncol* 2012
Case Study: Discussion Points

• Information about the patient’s health status could help make decisions about the next steps

• Consider the following:
  • Symptoms from prostate cancer
  • Patient preferences for treatment
  • Geriatric assessment
Case Study continued

• The patient has several areas of pain that have been bothering him over the last few weeks including in the scapula and right hip
  – His pain is worse in the morning and is better when he takes acetaminophen, which he takes twice a day
  – He has tried oxycodone in the past but stopped because it caused confusion
  – He would be interested in treatment if it helps with symptoms

• Geriatric assessment reveals intact function (instrumental activities of daily living) and cognition
  – He lives in independent living and is the caregiver for his wife with dementia
  – He has a daughter who is very supportive and drives him to his appointments
  – He does not drive himself due to balance issues and uses a cane to walk; one recent fall
  – He is not depressed or anxious
  – He does not have significant nutritional issues

• He is on dialysis for the last 8 years which he is doing well with.

• He is only receiving metoprolol and a baby aspirin.
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*Score is 20*
MD-rated KPS vs. Model

Chi-square test

\[ p = 0.17 \]

Chi-square test

\[ p < 0.0001 \]
Utility of Comprehensive Geriatric Assessment in Older Adults with Cancer

Risk Prediction
- Surgical Complications and Chemotherapy Toxicity
- Survival

Cancer Treatment Modification
- Modification of treatment/chemotherapy
- Modification of supportive care

Intervention
- General Geriatrics vs. Cancer-focused
- Goals
Cancer Treatment Modifications Based on CGA

Oncologist assessment: Initial treatment plan

CGA

Oncologist and geriatrician: Final treatment plan

- French ASRO study
- N=217, mean age 83 years
- 40% treatment recommendation modifications
- On multivariate analysis: ADL dependence and Fried’s frailty markers associated with treatment modifications

Farcet PLOS One 2016
Example from Multiple Myeloma: Clinical trial design and clinical practice

**Fit**

- Age \( \leq 75 \)

**AND**

- All of the following:
  - Dependence in \( \leq 1 \) ADL
  - Dependence in \( \leq 2 \) IADLs
  - Charlson comorbidity index score 0-1

**Intermediate Fit**

- Does not meet criteria for Fit or Frail categories

**Frail**

- Age \( \geq 80 \)

**OR**

- Any 2 of the following:
  - Age 76-80
  - Dependence in \( \geq 2 \) ADLs
  - Dependence in \( \geq 3 \) IADLs
  - Charlson comorbidity index score \( \geq 2 \)

Modified chemotherapy regimens and doses

Palumbo Blood 2015
## Modifying Supportive Care Based on CGA
See NCCN OAO-H for full details at nccn.org
*credit to Dr. Holly Holmes*

<table>
<thead>
<tr>
<th>Therapeutic class (Examples)</th>
<th>Conditions adversely affected</th>
<th>Modification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Corticosteroids</td>
<td>Delirium, Diabetes</td>
<td>Consider dose and duration. Use lowest possible dose.</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>Falls, Cognitive Impairment, Delirium</td>
<td>Avoid for insomnia, agitation, delirium. Consider alternatives.</td>
</tr>
<tr>
<td>First-generation antihistamines</td>
<td>Delirium, Cognitive Impairment, Urinary retention</td>
<td>Use only when convincing benefit exists. Don’t use for sleep!</td>
</tr>
<tr>
<td>Phenothiazine antiemetics (prochlorperazine)</td>
<td>Parkinson Disease</td>
<td>Avoid</td>
</tr>
</tbody>
</table>

c/o Tanya Wildes
Case Study continued: Treatment and Supportive Care Modifications

- Avoid Steroids
- Avoid Chemotherapy
  - Due to Risk
  - Due to premedications
- Pain management
  - Patient did not want increase or change in narcotics
  - Supportive treatments for bone mets contra-indicated due to renal insufficiency
Timing: Delay Chemotherapy

Clinically Localized Disease

Rising PSA

Clinical Metastases; Noncastrate

Rising PSA: Castrate; Denosumab

Clinical Metastases: Castrate
Predocetaxel Sipuleucel-T, Abiraterone, Enzalutamide

Clinical Metastases: Castrate
1st-line Chemotherapy Docetaxel

Bone Metastases; Radium-223

Clinical Metastases: Castrate
Post-Docetaxel Cabazitaxel, Abiraterone, Enzalutamide

Enzalutamide Pre-Chemotherapy (PREVAIL)

- 1,717 pts with CRPC randomized to enzalutamide (160 mg) vs placebo

- **Enzalutamide improved overall survival**
  - HR = 0.71, \( P < .0001 \)

- Median time to chemotherapy was 28 months in the enzalutamide group vs 10.8 mths in the placebo arm

- Fatigue, constipation, joint aches more common in treatment group
  - Grade 3 or higher adverse events were reported in 43%
  - However, symptoms from prostate cancer was delayed and overall quality of life was improved for those getting treatment

Utility of Comprehensive Geriatric Assessment in Older Adults with Cancer

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- General Geriatrics vs. Cancer-focused
- Goals
Delphi Consensus of Geriatric Oncology Experts

- 30 geriatric oncology experts
- 3 rounds of consensus
- Selecting patients for geriatric assessment
  - 93% consensus using criteria “Age ≥ 75 or younger with age-related issues or concerns”
  - 89% consensus using evidence-based screening tools such as VES-13, impaired objective physical performance, CARG and CRASH tools

Mohile et al JNCCN 2015
<table>
<thead>
<tr>
<th>Tool</th>
<th>Components</th>
<th>Data in community dwelling elderly</th>
<th>Data in oncology patients</th>
</tr>
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<tbody>
<tr>
<td>VES-13</td>
<td>Age, self-rated health, functional capacity and physical performance</td>
<td>Score predictive of increased risk of death or functional decline over 2 years</td>
<td>Mixed results for identifying CGA impairment in different populations</td>
</tr>
<tr>
<td>Groningen Frailty Indicator</td>
<td>Mobility/physical fitness, vision/hearing, nutrition, co-morbidity, cognition, psychosocial</td>
<td>Correlation between the GI score and CGA</td>
<td>Predicts mortality in older cancer patients receiving chemotherapy</td>
</tr>
<tr>
<td>G8</td>
<td>Nutrition, mobility, cognitive deficit, polypharmacy, age, self-perceived health status</td>
<td>Derived from MNA</td>
<td>Sensitive for predicting deficits on CGA</td>
</tr>
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### Physical Performance: Interventions and Treatment Decisions

#### Interventions:
--Round 2: Ratings
--Round 3: **Consensus (93%)**

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<tr>
<th>Intervention</th>
<th>Average Rating</th>
<th>IQR</th>
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<tr>
<td>Physical Therapy</td>
<td>9.10</td>
<td>2</td>
</tr>
<tr>
<td>Exercise</td>
<td>8.39</td>
<td>1.75</td>
</tr>
<tr>
<td>Occupational Therapy</td>
<td>8.36</td>
<td>2</td>
</tr>
<tr>
<td>Home Safety Evaluation</td>
<td>8.17</td>
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#### Treatment Decisions:
--Round 2: Ratings
--Round 3: **Consensus (93%)**

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<th>Δ To TX Plan</th>
<th>Average Rating</th>
<th>IQR</th>
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<tr>
<td>Address safety during treatment</td>
<td>8.44</td>
<td>2</td>
</tr>
<tr>
<td>Modify treatment choice</td>
<td>7.96</td>
<td>2.75</td>
</tr>
<tr>
<td>Modify dosage</td>
<td>7.35</td>
<td>3</td>
</tr>
<tr>
<td>Impairment Domain</td>
<td>Assessment Options</td>
<td>Process Options</td>
</tr>
<tr>
<td>----------------------------------------</td>
<td>------------------------------------------------------------------------------------</td>
<td>---------------------------------------------------------------------------------</td>
</tr>
</tbody>
</table>
| Functional status                      | 1. Both ADL/IADL  
2. IADL  
3. Gait speed  
4. ADL | 1. Physical therapy  
2. Occupational therapy  
3. Home safety evaluation  
4. Refer to social work  
5. Evaluate fall risk  
6. Exercise |
| Cognition                              | 1. Mini Mental State Examination  
2. Montreal Cognitive Assessment  
3. Blessed OMC | 1. Involve caregiver  
2. Assess/minimize medications  
3. Delirium prevention  
4. Refer to social work  
5. Assess capacity and ability to consent to treatment  
6. Identify health care proxy  
7. Cognitive testing/neuropsychology referral |
| Social support                         | 1. Caregiver burden/support  
2. Medical Outcomes Study survey  
3. Social support from medical history | 1. Refer to social work  
2. Transportation assistance  
3. Nursing/home health  
4. Caregiver management  
5. Home safety evaluation  
6. Support groups  
7. Refer to psychiatry/psychology  
8. Spiritual care |
| Objective physical performance         | 1. Gait speed  
2. Timed Up and Go  
3. Short Physical Performance Battery | 1. Physical therapy  
2. Exercise  
3. Occupational therapy  
4. Home safety evaluation  
5. Rehabilitation  
6. Nursing/home health |
| Psychological status: anxiety/depression | 1. Geriatric Depression Scale  
2. Hospital Anxiety & Depression Scale  
3. Mental Health Inventory | 1. Refer to social work  
2. Counseling  
3. Refer to psychiatry/psychology  
4. Start medications  
5. Support programs  
6. Spiritual care |
| Nutrition                              | 1. Weight loss/gain  
2. Mini Nutritional Assessment | 1. Nutrition consult  
2. Make specific dietary recommendations  
3. Oral care  
4. Supplements  
5. Refer to social work  
6. Physical/occupational therapy |
## Case Study: Implementing Interventions

<table>
<thead>
<tr>
<th>Domain</th>
<th>Assessment</th>
<th>Selected Examples of GA-driven interventions</th>
</tr>
</thead>
</table>
| Physical Performance | Fall history  
Standardized assessment such as Short Physical Performance Battery  
Assess for neuropathy | -Physical therapy consult for balance/strength training and assist device evaluation  
-Home safety evaluation and modification  
-LifeAlert system  
-Consider chemotherapy with low risk of neuropathy  
-Osteoporosis risk review |
Case Study

- **Oncology** → stage the cancer
  - Make predictions of life expectancy based on cancer
    - 2 year life expectancy with enzalutamide
    - Improved symptoms
  - Expected side effects of cancer therapy
    - Fatigue from enzalutamide

- **Geriatrics** → stage the aging
  - Make predictions of life expectancy
    - 2-5 years
  - Anticipate potential complications
    - Functional or physical performance decline
  - Evaluate whether the benefits of therapy outweigh the risks given underlying health status in light of patient’s preferences
    - Patient would like to try treatment

Geriatrics and Oncology Collaboration

- Train a geriatrics leader who is interested in working with cancer treatment specialists
  - Cancer and Aging meetings at AGS, ASCO, SIOG
  - R25 program for Nurses
- Mail self-report assessments ahead of time
- Have clinic staff help with cognitive and physical performance assessments
- Geriatrics-trained health professionals should partner with oncology teams to provide input and guide care delivery
  - Develop a clinic in the cancer center
  - Engage in tumor boards
  - Call and discuss the patient’s history with cancer treatment specialists
- Partner with local visiting nurse services to deliver interventions
  - Social work, safety evaluations, physical therapy, occupational therapy, medication review
Case Study

- Patient started enzalutamide at 50% dosing for one month
- Discussed with pharmacist: no drug interactions and no recommendations for dose reductions with renal impairment
- Assessed safety in assisted living; instituted physical activity interventions
- He did well with improvement of pain and without progression of disease for 2 years
- Stopped treatment due to progression of disease
- Discussed risks and benefits of chemotherapy and we decided against chemotherapy
- Passed away 2 months later from a complication from fistula repair
Reconciling the goals...

- Cancer focused
- Patient’s Goals
- Geriatric focused
- Palliative care
Resources

• NCCN Older Adult Oncology Guidelines
• International Society of Geriatric Oncology (siog.org)
  – Position papers
  – Geriatric Assessment Tools
• Journal of Geriatric Oncology
• ASCO website:
  https://urldefense.proofpoint.com/v2/url?u=http-3A__university.asco.org_geriatric-2Doncology&d=CwIGaQ&c=4sF48jRmVAe_CH-k9mXYXEGfSnM3bY53YSKuLUQRxhA&r=prXDLmnedlQbvED9cYrIS13t6lFAqKUXckqhTJoplP-EpPV_3sVbzR1O_em4K_yU&m=RgRnqJiCQay_N3Yw3RyOa6uK0UIAypEXTuRxO9TAYFM&s=rUs3OfgCOMzXG9W1qdoaKQnsjz28DBOx3DxTlYASJgY&e=
Medicine of the Highest Order