Geriatric Oncology: An Overview of Considerations in Older Adults Receiving Cancer Treatment

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Learning Objectives
At the end of the presentation, the attendee should be able to:

- Describe the general considerations surrounding the treatment of cancer in geriatric patients
- Describe the patient- and tumour-related factors thought to affect tolerance of chemotherapy in older adults
- Describe the issues surrounding adherence to oral anti-cancer medications in geriatric patients

Disclosures
- Presenter’s Name: Mark Pasetka
- I have had the Relationships with commercial interests:
  - Advisory Board/Speakers Bureau – Amgen, Bohringer Ingelheim, Celgene, Eisai, Eli Lilly, Hoffmann La Roche, Merck, Novartis
  - Funding (Grants/Honoraria): None
  - Research/Clinical Trials: None
  - Speaker/Consulting Fees: Lundbeck
- Speaking Fees for current program:
  - I have received no speaker’s fee for this learning activity

Definitions
Elderly
World Health Organization
- 60 years or older = Elderly
- 80 years or older = Oldest Old
- 100 years or older = Centenarian
- 110 years or older = Super Centenarian
Japan Gerontological Society/Japan Geriatrics Society
- 65-74 = Pre-old age
- 75 years or older = Old age
- More than 90 years = Oldest-old age or Super-old age

Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
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<tbody>
<tr>
<td>CGA</td>
<td>Comprehensive Geriatric Assessment</td>
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<tr>
<td>CRASH</td>
<td>Chemotherapy Risk Assessment Scale for High Age Patients</td>
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<tr>
<td>CARG</td>
<td>Cancer and Aging Research Group</td>
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<tr>
<td>MMS(E)</td>
<td>Mini Mental State (Examination)</td>
</tr>
<tr>
<td>ADL</td>
<td>Activities of Daily Living</td>
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<tr>
<td>IADL</td>
<td>Instrumental Activities of Daily Living</td>
</tr>
<tr>
<td>ECOG PS</td>
<td>Eastern Cooperative Oncology Group Performance Status</td>
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<tr>
<td>MNA</td>
<td>Mini Nutrition Assessment</td>
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<tr>
<td>LDH</td>
<td>Lactate Dehydrogenase</td>
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<tr>
<td>DBP</td>
<td>Diastolic Blood Pressure</td>
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<tr>
<td>GDS</td>
<td>Geriatric Depression Scale</td>
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</table>

Perspective
Definitions & Statistics

http://www.searo.who.int/entity/health_situation_trends/data/chi/elderly-population/en/
http://www.healthyaging.org/resources/research-and-statistics/
WHAT ABOUT AGE?

Chronologic versus Physiologic Age

- **Chronological Age** – The age of a person that is measured from their birth to a particular date.
- **Physiologic Age** – A reflection of the accumulation of effects from medical and psychosocial stressors on the process of ageing which may impact life expectancy.

How are these measured?

- **Chronologic Age** = Current Year – Year of Birth
- **Physiologic Age** – Using measures of functional capacity.

WHY IS THERE CONCERN?

Concerns Regarding Treatment in Older Adults

- **Knowledge of geriatric oncology**
  - Lack of support for the patient
  - In the conscious by the patient
  - Poor nutrition
  - Fatigue
  - Polypharmacy
  - Weight loss

- **Referral and treatment**
  - Lack of evidence in community (e.g., across geriatricians)
  - Lack of time available for assessment
  - Lack of time available for education
  - Lack of knowledge of evidence-based interventions

- **Recruitment to Trials**

| Year | Clinical Trials
<table>
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<tr>
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<tbody>
<tr>
<td>2004</td>
<td>60</td>
</tr>
<tr>
<td>2005</td>
<td>80</td>
</tr>
<tr>
<td>2006</td>
<td>100</td>
</tr>
<tr>
<td>2007</td>
<td>120</td>
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</tbody>
</table>

Clinical Trials

- **2004** years
- **2005** years
- **2006** years
- **2007** years

Lack of evidence in community (e.g., across geriatricians)
- Lack of time available for assessment
- Lack of time available for education
- Lack of knowledge of evidence-based interventions

Concerning treatment with chemotherapy

- **Under/over treatment**
  - Undertreatment
  - Lack of comfort treating older adults with cancer
  - Lack of knowledge and education regarding optimal treatment dosing and toxicity management

- **Overtreatment**
  - Lack of intervention for treating older adults
  - Lack of available evidence-base

Without evidence, one cannot make evidence-informed decisions.

Soto-Perez-de-Celis E et al. Lancet Oncol. 2018; 19: e305

https://www.merriam-webster.com/dictionary/chronological%20age

Rittberg R et al. J Geriatr Oncol. 2018. in press

Doherty J et al. J Geriatr Oncol. 2019. in press


White MN et al. J Geriatr Oncol. 2019; in press

7
8
9
10
11
12
**QUESTION #1**

What is the median age of cancer diagnosis in Canada (2017)?

A. 45-50 years
B. 50-55 years
C. 55-60 years
D. 60-65 years
E. 65-70 years
F. >70 years

**QUESTION #2**

What percentage of all new cancer cases are diagnosed in patients above 60 years old?

A. 45%
B. 55%
C. 65%
D. 75%
E. 85%

**PHYSICAL CHANGES**

Lots to look forward to…

**AGE-RELATED CHANGES**
**Physical Changes**

### Gastrointestinal Tract
- Decreased Gastric Acid Secretion
- Decreased Smaller Bowel Surface Area
- Decreased Splanchnic Blood Flow
- Decreased Gastric Emptying
- Decreased Peristaltic Activity

### Body Composition
- Decreased Muscle Mass
- Increased Body Adipose
  - Increase in \( V_d \) of lipophilic medications → Increased Serum levels
- Decreased Total Body Water
  - Decrease in \( V_d \) of hydrophilic medications → Accumulation

### Liver
- Decreased Volume
- Decreased Circulation
- Decreased First-Pass Metabolism
  - Phase I Reactions (CYP 450)
    - Oxidative
    - Reductive
    - Hydrolytic

### Kidneys
- Decreased Renal Mass
- Decreased Renal Blood Flow
  - Decreases ~10%/decade post 40 years
- Decreased Glomerular Filtration Rate
- Decreased Clearance of Medications
- Hyalinisation of Renal Vasculature

### Cardiovascular System
- Decreased Cardiac Output
- Decreased Heart Rate Modulation
- Decreased Arterial Pliability
- Cardiac Conduction Changes
- Myocardial Hypertrophy
- Impaired Endothelial Function

### Central Nervous System
- Decreased Cortical Volume
- Decreased Synaptic Density
- Decreased Processing Speed
- Decreased Attention, Memory

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Soto-Perez-de-Celis E et al. Lancet Oncol. 2018; 19: e305-16
**PHYSICAL CHANGES**

Respiratory System
- ↓ Lung Volume
- ↓ Elastic Recoil
- ↑ Ventilation-Perfusion Inequality

Skeletal System
- ↓ Bone Mineral Density
- ↑ Risk for Fracture

**Skeletal System**
- ↓ Bone Mineral Density
- ↑ Risk for Fracture

**RESPONSE AND TOLERANCE**

AGAMENON Study
- **Primary Outcome**
  - Overall Survival (OS)
- **Secondary Outcomes**
  - Objective Response Rate (ORR)
  - Progression-Free Survival (PFS)
- **Older Patient**
  - 70 years of age or older

<table>
<thead>
<tr>
<th>Regimen</th>
<th>N (%)</th>
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<tbody>
<tr>
<td>CAPDX</td>
<td>33 (27)%</td>
</tr>
<tr>
<td>COX136M</td>
<td>16 (105)</td>
</tr>
<tr>
<td>Other chemotherapy</td>
<td>4 (31)</td>
</tr>
<tr>
<td>Other chemotherapy, other</td>
<td>5 (40)</td>
</tr>
<tr>
<td>Other chemotherapy, other</td>
<td>4 (31)</td>
</tr>
<tr>
<td>Other chemotherapy, other</td>
<td>4 (31)</td>
</tr>
<tr>
<td>IFN-α</td>
<td>3 (31)</td>
</tr>
<tr>
<td>Other chemotherapy</td>
<td>3 (31)</td>
</tr>
<tr>
<td>Other chemotherapy, other</td>
<td>1 (31)</td>
</tr>
<tr>
<td>Other chemotherapy, other</td>
<td>1 (31)</td>
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<tr>
<td>Other chemotherapy, other</td>
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<tr>
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<td>1 (31)</td>
</tr>
<tr>
<td>Other chemotherapy, other</td>
<td>1 (31)</td>
</tr>
<tr>
<td>Total</td>
<td>98 (100%)</td>
</tr>
</tbody>
</table>

**PHARMACOLOGY**

Additional Considerations in Older Age Patients
- Adults ≥ 65 years
  - ↑ Comorbidities
  - ↑ Geriatric Syndromes (e.g.,
  - ↓ Physiologic Reserves
  - ↓ Functional Capacity
  - ↑ Polypharmacy
  - ↑ Age-Related Physiologic Changes

**RESPONSE AND TOLERANCE**

AGAMENON Study
- **AGAMENON** – A national registry of consecutive cases of advanced gastric cancer (AGC)
- Two populations included
  - Survival and safety-related end points
  - Objective tumour response-related end points
- **Arms**
  - <70 years
  - ≥70 years
- Included
  - Histologically confirmed, untreated or metastatic gastric, gastro-oesophageal, or distal oesophageal adenocarcinoma
  - First-line chemotherapy with two or three chemotherapies in combination
Geriatric Assessment

- Definition: A multi-dimensional, interdisciplinary, diagnostic process focusing on determining an older person’s medical, psychosocial, and functional capabilities in order to develop a coordinated and integrated plan for their treatment and long-term follow-up.
  - Several domains are assessed
  - Tools that are utilized are numerous

domains examined in a comprehensive geriatric assessment

- Demographic and social status
- Comorbidity
- Functional status
- Cognition
- Depression
- Nutrition
- Fatigue
- Polypharmacy
- Geriatric syndromes


Geriatric Syndromes
- Dementia
- Delirium
- Incontinence (faecal and/or urinary)
- Osteoporosis or spontaneous fractures
- Hip fracture
- Failure to thrive
- Self-reported number of falls (within different time frames)
- Constipation
- Polypharmacy
- Pressure ulcers
- Sarcopenia

**Geriatric Assessments**

Chemotherapy Risk Assessment Scale for High-Age Patients (CRASH)
- **Haematologic Toxicity**
  - Diastolic BP ≥ 72 mmHg
  - Impaired IADL
  - LDH > 0.74 x ULN
  - Chemotox (MAX2 score)
- **Non-Haematologic Toxicity**
  - ECOG PS
  - MNA
  - Chemotox (MAX2 score)

**MAX2 Index**
- Data from published clinical trials
- Summary of the overall risk of severe toxicity of a regimen
- Mean of the highest frequency of both Haematologic (Grade 4) and Non-haematologic (Grade 3/4) toxicities

**Additional Resources**

**Geriatric Assessments**

Chemotherapy Risk Assessment Scale for High-Age Patients (CRASH)

**Predictors for experiencing a greater incidence of chemotherapy toxicities:

- Age ≥ 75 years
- GI/GU Cancer
- Standard Chemotherapy Dosing
- Polychemotherapy
- Haemoglobin Level
- Creatinine Clearance
- Hearing Impairment
- > 1 fall in the past six months
- Limited to walking one block
- 2+ social activity because of impaired physical or emotional health
- Needing help with taking medications

**Cancer and Aging Research Group (CARG)**
- Chemotherapy risk model
- Developed in 500 older patients with cancer (mean age: 73 yrs)
- Validated in 250 older patients with cancer (median age: 73 yrs)

**Geriatric Assessments**

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Did someone say drugs?

**POLYPHARMACY & ADHERENCE**

**QUESTION #3**

The definition of ‘Polypharmacy’ is:
- A. Taking more than 10 medications per day for a given amount of time
- B. Taking more than one medication for a particular condition
- C. Taking medications that are noted to have the potential for an interaction
- D. Taking one or more inappropriate medications

**POLYPHARMACY**

A Systematic Review of Definitions
- 138 definitions and associated terms
- Defined by:
  - Number of medications (two or more; 11 or more)
  - Descriptive (minor, moderate, major, hyper-, excessive, severe, persistent, chronic, appropriate, rational, pseudo)
  - Time frame (in combination with number)
  - Combinations thereof
  - Most common definition = 5 or more medications

**POLYPHARMACY**

Polypharmacy – Association with Outcomes
- Prevalence ~ 10-96%
- Risks associated with Polypharmacy:
  - Adverse drug reactions
  - Drug interactions
  - Prolonged hospitalization or increased hospital stay
  - Increase in the cost of health care
- Polypharmacy may contribute to:
  - Worsened patient condition
  - Frailty syndrome
  - Poor physical function
  - Poor survival
  - Greater number of comorbidities

**POLYPHARMACY**

Management of Polypharmacy
1. Appropriate medication history
2. Medication reconciliation and medication review
3. Multidisciplinary approach
4. Patient-centered medication therapy
5. Pharmacovigilance
6. Medication and disease information
7. Polypharmacy education

**DEPREScribing**

1. Reconcile all medications and consider their indications.
2. Consider overall risk of harm when considering the intensity of deprescribing intervention.
3. Assess each drug in terms of current or future benefit in relation to current or future harm.
4. Prioritize drugs for deprescribing, giving preference to those that have the most unfavorable risk/benefit ratio and least likelihood of withdrawal symptoms.
5. Implement a discontinuation plan and monitor for improvement or adverse effects as the result of deprescribing.
ADHERENCE DEFINITIONS

• Adherence
  – The extent to which a person’s behavior – taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a health care provider – World Health Organization. 2003: 1
  – The extent to which a patient takes a medication (or medications) as prescribed by their health care provider (HCP) – Osterberg L et al. N Eng J Med. 2005; 353: 487-97
  – The degree or extent of conformity to the recommendations about day-to-day treatment by the provider with respect to the timing, dosage, and frequency – Cramer JA et al. Value Health. 2008; 1(1): 44-47

PERSISTENCE DEFINITIONS

• Persistence
  – The duration of time from initiation to discontinuation of therapy.
  – The extent to which a patient takes a medication (or medications) as prescribed by their health care provider (HCP)

ADHERENCE

• Categorically
  – Adherent versus Non-adherent

• Continuum
  – Variation from 0 to 100% adherence
    – <80%, <90%, <100%, >100%

• Rate of Adherence
  – Proportion of medication doses actually taken within a specified period of time
SUMMARY

Lies, dam lies, and statistics...

• Cancer is most prevalent in older adults
• Older adults will continue to comprise a significant proportion of the population and this will continue to increase
• Enrollment of less-fit older adults into clinical trials is essential
• Use of geriatric assessment tools to help identify patients at greater risk for treatment-related toxicities is imperative
• Utilize medication management strategies to optimize medication-taking behavior and reduce the risks for negative outcomes

ADHERENCE

SIOG Taskforce Recommendations

ADDITIONAL RESOURCES

• van Alkema DD et al. Patient- and Tumor-Related Predictors of Chemotherapy Intolerance in Older Patients with Cancer: A Systematic Review. J Geriatr Oncol. 2018; 10: 31-41