Geriatric screening tools in older patients with cancer

Pr. Elena Paillaud

Henri Mondor hospital, Créteil, France

University Paris-Est Créteil
CONFLICT OF INTEREST DISCLOSURE

I have the following potential conflicts of interest to report

- Sanofi
- Nutricia
- Amgen
- Roche
Introduction

• Age is the most important risk factor for cancer
• 60% of cancers are diagnosed in patients ≥65 years
• Senior adults have been underrepresented in clinical trials, leading to a limited existence of evidence-based guidelines for treatment
• Standard evaluation of older cancer patients may lead to:
  – overtreatment and toxicity
  – undertreatment, loss of efficacy, and poorer outcomes
Therapeutic challenges in older patients with cancer

- Older cancer patients represent therapeutic challenges because they are an heterogeneous population with various combinations of comorbidities, physiological reserves, disabilities and geriatric syndromes.
- The way to approach this heterogeneity is the geriatric assessment.
- Geriatric evaluation gives an opportunity to better:
  - evaluate risks of adverse events
  - appreciate treatment benefits
  - define an adequate treatment strategy

Caillet Ph et al. Clinical Interventions in Aging 2014; 9: 1-16
Why identifying aging-related vulnerabilities?

Comorbidities

Functional status

Social vulnerability

FRAILTY

Cancer

Cancer treatment

Early mortality

Treatment toxicity

Unplanned hospitalizations

Exacerbation of comorbidities

Perioperative complications

Functional decline

Geriatric Assessment (GA)

- GA takes more than one hour
- We are few geriatricians, and less trained to oncology
- GA is not necessary for all elderly cancer patients

A screening strategy appears necessary

<table>
<thead>
<tr>
<th>Domains</th>
<th>Tools</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dependency</td>
<td>Activities of daily living (ADL)</td>
<td>Katz et al, 1963</td>
</tr>
<tr>
<td></td>
<td>Instrumental activities of daily living (IADL)</td>
<td>Lawton et al, 1969</td>
</tr>
<tr>
<td>Mobility</td>
<td>Falls within 6 or 12 last months</td>
<td>Lamb et al, 2005</td>
</tr>
<tr>
<td>Fall risk</td>
<td>Short Physical Performance Battery</td>
<td>Vellas et al, 1997</td>
</tr>
<tr>
<td></td>
<td>Gait speed, [appui monopodal]</td>
<td>Podsialo et al, 1991</td>
</tr>
<tr>
<td>Nutrition</td>
<td>Mini nutritional assessment (MNA)</td>
<td>Guigoz et al, 1997</td>
</tr>
<tr>
<td></td>
<td>Weigh loss within 3 and 6 last months</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Body Mass Index</td>
<td></td>
</tr>
<tr>
<td>Cognition</td>
<td>Mini Mental State Examination (MMSE)</td>
<td>Folstein et al, 1975</td>
</tr>
<tr>
<td></td>
<td>Short Portable Mental Status Questionnaire</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Clock Drawing Test, Trail-making Test a/b</td>
<td></td>
</tr>
<tr>
<td>Mood</td>
<td>Geriatric Depression Scale (GDS)</td>
<td>Yesavage et al, 1983</td>
</tr>
<tr>
<td>Comorbidities</td>
<td>Cumulative Illness Rating Scale – Geriatrics</td>
<td></td>
</tr>
<tr>
<td>Medication</td>
<td>Number of medications a day</td>
<td>Linn et al, 1968</td>
</tr>
</tbody>
</table>
A set of screening tools has been developed to guide the therapeutic decision and to respond at the following questions:

- How to identify older cancer patients who may benefit from a CGA?
- How to identify older cancer patients who are at risk of chemotoxicity?
- How to identify older cancer patients who are at risk of early death?

How to identify older cancer patients who may benefit from a GA?

17 screening tools have been reported to identify frail patients who need a GA (Decoster et al* in a recent review)

- a-CGA (abbreviated CGA)
- ECOG-PS (Eastern Cooperative Oncology Group - Performance Status)
- Fried frailty phenotype
- GFI (Groningen Frailty Indicator),
- F-TRST (Flemish version of Triage Risk Screening Tool),
- G8 (Geriatric 8)
- VES-13 (Vulnerable Elders Survey-13)

In daily geriatric oncology practice, frailty has been defined as an impairment of one or more domains of the GA

Only two screening tests have been specifically developed in older cancer patients: aCGA and G8

The most studied tools in older cancer patients are G8 and VES-13

* Decoster L et al. Annals of Oncology 2015; 26: 288–300
Screening for vulnerability in older cancer patients: Vulnerable Elders Survey-13 screening tool

- A **13-item self-administered tool** that asks to report:
  - age
  - physical status
  - functional capacity
  - self-reported health

- **Time to perform:** 5 to 10 min

- **Abnormal if ≥3 → CGA**

- **Se ranged from 39% to 88%**
  - **Sp ranged from 62% to 100%**


**Decoster L et al. Annals of Oncology 2015; 26: 288–300
Screening for vulnerability in older cancer patients: G8 screening tool*

- 8 questions, by a trained nurse:
  - appetite, weight loss, BMI
  - mobility
  - mood and cognition
  - number medications
  - patient self-reported health
  - age categories

- Time to perform: **4.4 ± 2.9 min**

- Abnormal if ≤14/17 ➔ CGA

- Se from 65% to 92%***
- Sp from 3% to 75%***

*** Decoster L et al Annals of Oncology 2015; 26: 288–300
Modified-G8 screening tool

- G8 lacks sensitivity and specificity.
- We have developed and validated an optimized version of G8

- **6 questions, by a trained nurse:**
  - weight loss
  - cognition and mood
  - performance status
  - self-reported health status
  - polypharmacy
  - history of heart failure/coronary disease

- Time to perform: **3.8 ± 1.5 min**

- Abnormal if ≥6/35 ➔ **CGA**

- Se: 89% (86.5-91.5) vs. 87.2% (84.3-89.7)
  - Sp: 79% (69.4-86.6) vs. 57.7% (47.3-67.7)

---

Martinez-Tapia C et al. The Oncologist 2016; 21(2): 188-95
A screening strategy

1st step
Identify frail patients who need a GA before treatment by a Nurse or an Oncologist

Positive Screening tool

2nd Step
Comprehensive Geriatric Assessment
Comorbidities – social, functional, nutritional, cognitive and thymic status by a Geriatrician

“frail patients”
Vulnerable patients = target population
Moderate dependency or risk for dependency: usual aging

Reduced standard cancer treatment

“Fit patients”
Standard cancer treatment

Negative Screening tool

“Patients too sick”
Pathological aging
Geriatric syndromes and/or advanced comorbidities

Non suitable for standard treatment
A patient-tailored approach will be proposed
How to identify older cancer patients who are at risk of chemotoxicity?

- Older adults are vulnerable to chemotherapy toxicity
- There are limited data to identify patients at risk
- Two screening tools have been developed to identify vulnerable older patients at risk for chemotherapy toxicity
Predicting chemotherapy toxicity in older adults with cancer: a prospective multicenter study

The Cancer and Aging Research Group (CARG) toxicity tool

• 500 out-patients 73 ± 6.2 y. (65-91)
  - 65-69 175 (35%)
  - 70-74 127 (25%)
  - 75-79 105 (21%)
  - 80-84 73 (15%)
  - 85-91 20 (4%) 60%

• 281 females (56%)

• 106 (21%) live alone

• Cancers
  - lung 143 (29%)
  - GI 135 (27%)
  - GYN 87 (17%)
  - breast 57 (11%)
  - GU 50 (10%)
  - others 28 (6%)
The Cancer and Aging Research Group (CARG) toxicity tool

### Table 5. Predictive Model

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>No.</th>
<th>%</th>
<th>No.</th>
<th>%</th>
<th>OR</th>
<th>95% CI</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ≥ 72 years</td>
<td>270</td>
<td>54</td>
<td>163</td>
<td>60</td>
<td>1.85</td>
<td>1.22 to 2.82</td>
<td>2</td>
</tr>
<tr>
<td>Cancer type GI or GU</td>
<td>185</td>
<td>37</td>
<td>120</td>
<td>65</td>
<td>2.13</td>
<td>1.39 to 3.24</td>
<td>2</td>
</tr>
<tr>
<td>Chemotherapy dosing, standard dose</td>
<td>380</td>
<td>76</td>
<td>204</td>
<td>54</td>
<td>2.13</td>
<td>1.29 to 3.52</td>
<td>2</td>
</tr>
<tr>
<td>No. of chemotherapy drugs, polychemotherapy</td>
<td>351</td>
<td>70</td>
<td>192</td>
<td>55</td>
<td>1.69</td>
<td>1.08 to 2.65</td>
<td>2</td>
</tr>
<tr>
<td>Hemoglobin &lt; 11 g/dL (male), &lt; 10 g/dL (female)</td>
<td>62</td>
<td>12</td>
<td>46</td>
<td>74</td>
<td>2.31</td>
<td>1.15 to 4.64</td>
<td>3</td>
</tr>
<tr>
<td>Creatinine clearance, Jelliffe, ideal weight</td>
<td>44</td>
<td>9</td>
<td>34</td>
<td>77</td>
<td>2.46</td>
<td>1.11 to 5.44</td>
<td>3</td>
</tr>
<tr>
<td>Hearing, fair or worse</td>
<td>123</td>
<td>25</td>
<td>76</td>
<td>62</td>
<td>1.67</td>
<td>1.04 to 2.69</td>
<td>2</td>
</tr>
<tr>
<td>No. of falls in last 6 months, 1 or more</td>
<td>91</td>
<td>18</td>
<td>61</td>
<td>67</td>
<td>2.47</td>
<td>1.43 to 4.27</td>
<td>3</td>
</tr>
<tr>
<td>IADL: Taking medications, with some help/unable</td>
<td>39</td>
<td>8</td>
<td>28</td>
<td>72</td>
<td>1.50</td>
<td>0.66 to 3.38</td>
<td>1</td>
</tr>
<tr>
<td>MOS: Walking 1 block, somewhat limited/limited a lot</td>
<td>109</td>
<td>22</td>
<td>69</td>
<td>63</td>
<td>1.71</td>
<td>1.02 to 2.86</td>
<td>2</td>
</tr>
<tr>
<td>MOS: Decreased social activity because of physical/emotional health, limited at least sometimes</td>
<td>218</td>
<td>44</td>
<td>126</td>
<td>58</td>
<td>1.36</td>
<td>0.90 to 2.06</td>
<td>1</td>
</tr>
</tbody>
</table>

Abbreviations: GU, genitourinary; IADL, instrumental activities of daily living; MOS, Medical Outcomes Study; OR, odds ratio.

**Ability of risk score to predict grade 3 to 5 chemotherapy toxicity**

**Ability of Karnofsky Index to predict grade 3 to 5 chemotherapy toxicity**

Predicting the risk of chemotherapy toxicity in older patients:
The Chemotherapy Risk Assessment Scale for High-age patients
score: CRASH Score

- 331 out-patients 76 y. (70-92)
- 166 females (50%)
- No. of medications 6/d (0-20)

- Cancers:
  - lung 71 (21.5%)
  - GI 41 (12.4%)
  - NHL 47 (14.2%)
  - breast 71 (21.5%)
  - bladder 23 (6.9%)
  - other 93 (24.4%)

Stages

- Stage I: 56%
- Stage II: 24%
- Stage III: 14%
- Stage IV: 6%
## Risk Assessment Scale for High-age patients

**score: CRASH Score**

<table>
<thead>
<tr>
<th>Predictors</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hematologic score</strong>&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Diastolic BP</td>
<td>0</td>
</tr>
<tr>
<td>IADL</td>
<td>≤72</td>
</tr>
<tr>
<td>LDH (if ULN 618 U/L; otherwise, 0.74/L*ULN)</td>
<td>0-459</td>
</tr>
<tr>
<td>Chemotox&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0-0.44</td>
</tr>
<tr>
<td><strong>Nonhematologic score</strong>&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>ECOG PS</td>
<td>0</td>
</tr>
<tr>
<td>MMS</td>
<td>30</td>
</tr>
<tr>
<td>MNA</td>
<td>28-30</td>
</tr>
<tr>
<td>Chemotox&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0-0.44</td>
</tr>
</tbody>
</table>

### CRASH Points<sup>b</sup>

<table>
<thead>
<tr>
<th>CRASH Points</th>
<th>Drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Capectabine 2g</td>
</tr>
<tr>
<td>1</td>
<td>Capectabine 2.5 g</td>
</tr>
<tr>
<td>2</td>
<td>Capectabine 4-6/1 g d1,d8</td>
</tr>
</tbody>
</table>

### Toxicity Risk (%)

- **Nonhematologic Toxicity**
  - 0-2: 33% |
  - 3-4: 46% |
  - 5-6: 67% |
  - 7-8: 93% |

- **Hematologic Toxicity**
  - 0-1: 7% |
  - 2-3: 23% |
  - 4-5: 45% |
  - 6-8: 100% |
How to identify older cancer patients who are at risk of death?

• Failure to consider prognosis in the context of clinical decision-making can lead to poor care

• Some studies have reported the ability of GA domains to predict mortality*

• Prognostic models based on GA parameters have been developed in the general geriatric population (e-prognosis Website)

• But they have not yet been studied specifically within the oncology population

• Prognostic tools specifically focusing on older patients with cancer are needed

How to identify older cancer patients who are at risk of death?

• 5 indices that estimate mortality risk for community-dwelling older adults have been developed:
  - Gagne (2011): mortality risk score to predict 1-year mortality
  - Mazzaglia (2007): 7-items questionnaire for primary care to predict 15-month mortality
  - Carey (2004): 2-year mortality index for community-dwelling elders

• 8 indices estimate mortality risk for hospitalized older adults:
  - Inouye (2003): Burden of Illness Score for Elderly Persons to estimate 1-year mortality
  - Teno (2000): 1 and 2-year mortality based on medicine and ICU patients >80 y.
  - Levine (2007): 1-year prognostic model for hospitalized elders following discharge
  - Walter (2001): 1-year mortality index for elders following hospital discharge
  - Drame (2008): 2-year mortality index in hospitalized adults age >75 y. (emergency)

The oncological-multidimensional prognostic index (Onco-MPI)

- One of these tools, the MPI*, has been recently adapted to elderly cancer patients**

- Onco-MPI risk score defined three categories: low risk, medium risk and high risk

- Kaplan-Meier survival curves, within 1 year of follow-up


** Brunello A et al. Cancer Res Clin Oncol 2016; 142: 1069-77
Multidimensional Frailty Score in surgery

• Kim SW et al. has developed a scoring model to predict unfavorable outcomes after surgery in older patients

• High-risk patients (multidimensional frailty score >5) showed an increasing 1-year postoperative mortality risk (HR=9.01; 95%CI(2.15-37.78); *p*=.003)

---

**Table 2. Composition of Multidimensional Frailty Score**

<table>
<thead>
<tr>
<th>Item</th>
<th>0</th>
<th>1</th>
<th>2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malignant disease</td>
<td>Benign</td>
<td>Malignant disease</td>
<td>NA</td>
</tr>
<tr>
<td>Charlson Comorbidity Index</td>
<td>0</td>
<td>1-2</td>
<td>&gt;2</td>
</tr>
<tr>
<td>Albumin, g/dL</td>
<td>&gt;3.9</td>
<td>3.5-3.9</td>
<td>&lt;3.5</td>
</tr>
<tr>
<td>ADLs (modified Barthel Index)</td>
<td>Independent</td>
<td>Partially dependent</td>
<td>Fully dependent</td>
</tr>
<tr>
<td>IADLs (Lawton and Brody Index)</td>
<td>Independent</td>
<td>Dependent</td>
<td>NA</td>
</tr>
<tr>
<td>Dementia (MMSE-KC)</td>
<td>Normal</td>
<td>Mild cognitive impairment</td>
<td>Dementia</td>
</tr>
<tr>
<td>Risk of delirium (Nu-DESC)</td>
<td>0-1</td>
<td>≥2</td>
<td>NA</td>
</tr>
<tr>
<td>MNA</td>
<td>Normal</td>
<td>Risk of malnutrition</td>
<td>Malnutrition</td>
</tr>
<tr>
<td>Midarm circumference, cm</td>
<td>&gt;27.0</td>
<td>24.6-27.0</td>
<td>&lt;24.6</td>
</tr>
</tbody>
</table>

---

*Kim SW et al. Multidimensional frailty score for the prediction of postoperative mortality risk. JAMA Surg. 2014; 149(7): 633-40*
NCAS – Nice Cancer Aging Survival score

Presented at ASCO 2016, this predictive tool has been developed to predict early mortality specifically in geriatric population with cancer

Boulahssass et al. A clinical score to predict the early death at 100 days in older metastatic cancers (in press)

• 312 patients, median age 82 y.
• The independent predictors of death at 100 days were:
  - age >85y. OR = 2.1; p=.03
  - 2 metastatic localizations (ML) >2 ML OR=2.4; p=.004
  - MNA <17 ≤23.5 and ≥17 OR=8.7 p<.0001 OR=5.4; p=.002
  - home confinement OR=1.8; p=.047
  - ADL <5.5 OR=2.1; p=.017
  - cancers with global risk of death at 100 days >30% OR=2.05; p=.016

Boulahssass R et al. A clinical score to predict the early death at 100 days after a comprehensive geriatric assessment (CGA) in elderly metastatic cancers, analysis from a prospective cohort study with 1048 patients. JCO 2016: e21532-e21532
Frailty classifications and mortality


These four frailty classifications have good prognostic performance for predicting 1-year mortality in older patients with various cancers

Take home messages

• Several screening tools exist to identify patients who may benefit from a CGA, but **G8, modified-G8** and **VES-13** are the most studied and used tools in geriatric oncology.

• Two scores have specifically been developed to assess the risk of chemotoxicity: **CARG** and **CRASH** scores.

• Even if many mortality scores have been developed in geriatric setting, only few have been now studied in geriatric oncology setting: **oncology-MPI, multidimensional frailty score**, and **Nice Cancer Aging Survival score for older patients**.
Thank you very much for your attention