Modification of the G8 screening tool for frailty in elderly patients with cancer: the ELCAPA-07 cohort study

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Geriatric assessment (GA) is recommended in older cancer patients (SIOG 2005)

Multidimensional assessment

to identify health and functional status deficiencies
to help implement directed multidisciplinary interventions

• GA is time- and resource-consuming and actually not necessary in all patients

► Screening tools for identifying patients in need of a complete GA

Ideally brief, simple tools with high sensitivity, negative predictive value and specificity
• Numerous tools developed
  • Mostly after expert opinions using indicators known for their association with mortality or GA domains
    *G8, fTRST, VES-13, ...*
  • Varying but *perfectible diagnostic performance properties*
  • Evidence for *heterogeneous performance across cancer localizations*

• **G8**
  • 8 *categorical items* covering
    1. Food intake; 2. BMI; 3. Weight loss; 4. Mobility;
    5. Neuropsychological problems; 6. # of medications;
    7. Self-rated health status; 8. Age
  • One of the *highest sensitivity* (>80% in 6 studies)
  • With a *lower specificity* (>60% in 4 studies)
To modify the G8 screening tool in older patients with cancer

- By following a detailed step-by-step statistical analysis
- By optimizing current items and adding potentially useful new items
- Targeting high discriminative power, usability and clinical relevance
ELCAPA cohort (Elderly CANcer PATients)

• French multicenter prospective cohort
• 70y and older patients with cancer (solid / hematologic malignancies)
• Patients included since 2007 at first referral to the geriatrician for GA
• Data collected relating to
cancer, cancer treatment and other medications, sociodemographic, clinical (GA) and biological features

► N=729 patients with G8 and GA data entered into the database at the time of analysis
Geriatric assessment (GA) as the reference procedure

≥1 deficiency across the following domains:

<table>
<thead>
<tr>
<th>Domains</th>
<th>Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Functional status</td>
<td>ADL ≤ 5</td>
</tr>
<tr>
<td></td>
<td>IADL ≤ 7</td>
</tr>
<tr>
<td>Mobility</td>
<td>GUG ≥ 20 sec</td>
</tr>
<tr>
<td>Nutritional state</td>
<td>MNA ≤ 23.5</td>
</tr>
<tr>
<td>Cognitive state</td>
<td>MMSE ≤ 23</td>
</tr>
<tr>
<td>Depression</td>
<td>mini-GDS ≥ 1</td>
</tr>
<tr>
<td>Comorbidity</td>
<td>CIRS-G (level 3/4)</td>
</tr>
</tbody>
</table>
Methods (3)

3-steps methodology

1 Candidate items selection

- Initial panel
  - G8 original items
  - G8 modified items
  - New items
  
optimizing thresholds / categorizations
functional, sociodemographic items
selected comorbidities / ECOG-PS

- Selection process
  - Univariate analysis
to assess the individual discriminative power of each item
  - Multiple Correspondence Analysis
  MCA to analyze the underlying structure and possible redundancies across variables
Methods (3)

3-steps methodology

1. Candidate items selection
2. Multivariate regression model

- **Logistic regression model** entering selected candidate items (step 1)
  - Stepwise backwards procedure to determine the independent predictors of an altered GA
  - Scaling and rounding of the coefficients (Cole algorithm)

- **Final model performance**
  - Discrimination: Area under the ROC curve (AUROC)
  - Calibration: Hosmer & Lemeshow

- **Multiple imputation** to account for missing data
Methods (3)

3-steps methodology

1. Candidate items selection
2. Multivariate regression model
3. Internal validation

- To check for evidence of «overoptimism» in the estimates
- To adjust performance indicators (AUROC) for overfitting
- *Boostrapping* techniques
  
  Repeated resampling with reconduction of all previous steps to assess stability
  Measure of optimism (x%)
### Results (1)

#### Main characteristics (N=729)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (M/F)</td>
<td>387 / 342</td>
<td>53.1% / 46.9%</td>
</tr>
<tr>
<td>Median age (Q1-Q3)</td>
<td>80</td>
<td>(76-84)</td>
</tr>
<tr>
<td>Top 5 cancer localization</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breast</td>
<td>137</td>
<td>18.7%</td>
</tr>
<tr>
<td>Colorectal</td>
<td>131</td>
<td>17.9%</td>
</tr>
<tr>
<td>Urinary</td>
<td>118</td>
<td>16.1%</td>
</tr>
<tr>
<td>Digestive</td>
<td>117</td>
<td>16.0%</td>
</tr>
<tr>
<td>Prostate</td>
<td>99</td>
<td>13.5%</td>
</tr>
<tr>
<td>Metastasis</td>
<td>299</td>
<td>41.0%</td>
</tr>
<tr>
<td>Comorbidities level 3/4 (CIRS-G)</td>
<td>414</td>
<td>56.7%</td>
</tr>
</tbody>
</table>

#### G8 diagnostic performance

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value (CI95)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity (CI95)</td>
<td>87.2% (84.3 - 89.7)</td>
</tr>
<tr>
<td>Specificity (CI95)</td>
<td>57.7% (47.3 - 67.7)</td>
</tr>
<tr>
<td>Area under the ROC curve (CI95)</td>
<td>86.5% (83.5 - 89.6)</td>
</tr>
</tbody>
</table>
Step 1  Candidate items selection

22 items as the initial panel
14 items selected for multivariate analysis
after univariate analyses (p<0.1) and MCA

• Age (G8)
• Weight loss (G8)
• Depression / Dementia (G8)
• Self-rated health status (G8)
• # of medications (G8 ≥6)
• ≥1 fall during the last 6 months
• ECOG-PS
• Asthenia
• Incontinence
• Selected comorbidities: heart failure or CAD / diabetes / Renal failure / HBP / Respiratory failure
Results (2)

Step 1  Candidate items selection

22 items as the initial panel
14 items selected for multivariate analysis after univariate analyses (p<0.1) and MCA

- Age (G8)
- **Weight loss** (G8)
- Depression / Dementia (G8)
- Self-rated health status (G8)
- # of medications (G8 ≥6)
- ≥1 fall during the last 6 months
- ECOG-PS
- Asthenia
- Incontinence
- Selected comorbidities: heart failure / CAD / diabetes / Renal failure / HBP / Respiratory failure
Results (2)

Step 1  Candidate items selection

22 items as the initial panel
14 items selected for multivariate analyses (p<0.1) after univariate analyses

- Age (G8)
- **Weight loss (G8)**
- Depression / Dementia (G8)
- Self-rated health status (G8)
- # of medications  (G8 ≥6)
- ≥1 fall during the last 6 months
- ECOG-PS
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![Weight loss vs Food intake diagram](image-url)
22 items as the initial panel
14 items selected for multivariate analysis after univariate analyses (p<0.1) and MCA

- Age (G8)
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- Depression / Dementia (G8)
- Self-rated health status (G8)
- # of medications (G8 ≥6)
- ≥1 fall during the last 6 months
- **ECOG-PS**
- Asthenia
- Incontinence
- Selected comorbidities: heart failure / CAD / diabetes / Renal failure / HBP / Respiratory failure
22 items as the initial panel
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- # of medications (G8 ≥6)
- ≥1 fall during the last 6 months
- ECOG-PS
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- Selected comorbidities: heart failure / diabetes / Renal failure / HBP / Respiratory failure

Step 1: Candidate items selection
Area under the ROC curve

Results (4)

Modified G8  AUC=91.6%

Original G8  AUC=86.5%

p-value = 0.0002
Results (5)

Area under the ROC curve per cancer localization

- Colorectal
- Digestive
- Breast
- Prostate
- Urinary
- Malignant Hemopathy

Modified G8
G8
## Results (6)

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Original G8 /17</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤14 points</td>
<td>87.2%</td>
<td>57.7%</td>
</tr>
<tr>
<td><strong>Modified G8 /35</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥6 points</td>
<td>89.2%</td>
<td>79.0%</td>
</tr>
<tr>
<td>≥7 points</td>
<td>85.8%</td>
<td>88.4%</td>
</tr>
</tbody>
</table>

### Step 3  Internal validation

- Optimism = 0.89% (±0.13%)
- AUC adjusted for overfitting = 91.6 – 0.9 = 90.7%
Discussion

• G8 modified:
  o **High sensitivity** and **high specificity**
  o **Higher homogeneity** across cancer localizations
  o 6 items easy to collect and clinically relevant

• **Interest of statistical methods** *complementary to expert judgment* to check and account for **overfitting** of development models to account for **missing data**

• Limits
  o **External validation needed**
  o Data unavailable at the time of analysis (e.g. detailed items within GA scales)
Validation and optimization is an ongoing and continuous process

Future works will focus on

- Investigating new candidate items
- Studying the impact of varying definitions for “impaired GA”
- The predictive ability of the tool towards different outcome parameters