Association of polypharmacy and inappropriate medications with physical function in older patients with cancer

Secondary analysis from: URCC 13059 (PI: Mohile)

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Conflict of Interest Disclosure

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Has no real or apparent conflicts of interest to report.
Background

- Polypharmacy (means concurrent use of multiple medications) is a significant health problem in the geriatric population.
- Older adults with cancer are at a higher risk of polypharmacy (PP) due to multiple comorbidities and complexity of treatment regimens.
- Previous data showed a prevalence of PP as high as 92% in this population.

Background

• No consensus on the optimal cut-off number of medications to define PP in older adults
  - Common definition : $\geq 5$ medications

• Potentially inappropriate medications (PIM): drugs that have high risk to benefit ratio
Background

- Functional and physical impairments are predictive of chemotherapy toxicities and lower survival \(^1,2\)
- Therefore, maintenance of a good physical and functional status is important for older patients with cancer
- The relationship of PP/PIM with physical function is understudied in this population

\(^1\) Extermann et al: *Cancer*; 118(13):3377-86, 2012; \(^2\) Maione et al; *JCO*; 23(28):6865-72, 2012
Objectives

- To determine the optimal cut-off value of number of medications in relation to validated physical functional measures
- To examine the association of PP and PIM with physical function impairments in older adults with advanced cancer

**Hypothesis:** PP and PIM are associated with physical function impairment in older adults with advanced cancer
Methods: Study Design

- Cross-sectional analysis of baseline data from a national geriatric assessment study (Geriatric Assessment for Patients (GAP) study; URCC13059, University of Rochester NCI Community Oncology Research Program (NCORP), PI: Dr. Mohile)
Methods: Study Participants

- Aged ≥70 years
- Had a diagnosis of incurable stage III/IV solid tumor or lymphoma
- Had ≥1 impaired domain on geriatric assessment
- Were planning to start a new cancer treatment regimen (chemotherapy or other agents with similar prevalence of toxicity) within four weeks from the time of enrollment
Methods: Medication Screening

- Polypharmacy log including all **regular** medications (both prescription and over the counter (OTC) medications) received within two weeks of study enrollment.
- Antineoplastic and supportive care medications were excluded from the medication count

PIM were captured using the most updated version of **2015 AGS Beers criteria**
2015 AGS Beers criteria

- A list of medications that may be potentially harmful for older adults
- Potential drug-disease interactions
- Combinations of medications known to cause harmful drug-drug interactions
- A list of potentially problematic medications to avoid or adjusted depending on an older person’s kidney function
Methods: Analysis plan

Step 1
• The optimal cut-off value for number of medications was determined using the Youden Index.

\[ \text{The value that is most associated with impairment among the examined physical function measures} \]

Step 2
Separate multivariate stepwise logistic regression models to examine the associations each of the medication variables with physical function outcomes.
Methods: Independent Variables

- PP (≥ 5 medications)
  the commonly used cut-off
- PP- optimal
  the cut-off value resulted from Youden Index
- PIM
  ≥ 1 medications according to Beers criteria
Methods: Outcome Variables (binary)

Activity of daily living (ADL)
- Six items scale assess difficulty basic daily activities as bathing, dressing, and eating
- Impairment: unable to perform one or more activities

Instrumental activity of daily living (IADL)
- Seven items scale assesses instrumental activities such as difficulty using telephone, shopping, and preparing a meal
- Impairment: unable to perform one or more activities

OARS Physical Health (PH)
- Survey assesses difficulty in 10 items including physical activity, climbing stairs, and walking for long distances
- Impairment: one or more responses for “my health limits me a lot”
Methods: Covariates

Demographics
- Age
- Gender
- Race
- Education
- Income
- Retirement

Baseline Clinical
- Cancer type
- Cancer stage
- Performance status (KPS)
- Comorbidities
- Nutritional status
Results: Sample Characteristics (N=439)

<table>
<thead>
<tr>
<th>Variables</th>
<th>All patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD)</td>
<td>76.9(5.4)</td>
</tr>
<tr>
<td>Gender</td>
<td>Female 195 (44.6)</td>
</tr>
<tr>
<td>Race</td>
<td>White 375 (86.0)</td>
</tr>
<tr>
<td>Education</td>
<td>Some college or above 272 (51.9)</td>
</tr>
<tr>
<td>Income</td>
<td>≤$50,000 257 (49.2)</td>
</tr>
<tr>
<td>Cancer type</td>
<td>Gastrointestinal 147 (34.4)</td>
</tr>
<tr>
<td></td>
<td>Lung 125 (29.1)</td>
</tr>
<tr>
<td></td>
<td>Others 157 (36.6)</td>
</tr>
<tr>
<td>Comorbidities</td>
<td>Impaired 295 (67.7)</td>
</tr>
</tbody>
</table>
Results: Physical Function Impairments

- ADL: 70
- IADL: 55
- OARS PH: 78
Results: Prevalence of Polypharmacy

- 71% of patients take >5 medications
- 43% take >8 medications
- 24% take >10 medications

Mean: 7.1 (1-23)
## Results: Prevalence of PIM

### Most commonly used Beers criteria medications (N=273)

<table>
<thead>
<tr>
<th>Medication Class</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proton Pump Inhibitors</td>
<td>36%</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>24%</td>
</tr>
<tr>
<td>NSAIDs</td>
<td>18%</td>
</tr>
<tr>
<td>1st generation Antihistamines</td>
<td>15%</td>
</tr>
</tbody>
</table>

- **No PIM**: 62%
- **≥1 PIM**: 38%
# Results: Optimal cut-off value for PP

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Cut-off for PP</th>
<th>AUC</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADL</td>
<td>8</td>
<td>0.590</td>
<td>0.523</td>
<td>0.626</td>
</tr>
<tr>
<td>IADL</td>
<td>8</td>
<td>0.582</td>
<td>0.479</td>
<td>0.654</td>
</tr>
<tr>
<td>PH</td>
<td>8</td>
<td>0.591</td>
<td>0.459</td>
<td>0.723</td>
</tr>
</tbody>
</table>
### Results: Multivariate Analysis

<table>
<thead>
<tr>
<th>Variable</th>
<th>ADL AOR (95% CI)</th>
<th>IADL AOR (95% CI)</th>
<th>OARS PH AOR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PP- 5 (ref. &lt;5 meds)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PP- 5 (ref. &lt;5 meds)</td>
<td>1.05 (0.99-1.12)</td>
<td>1.15 (0.68-1.77)</td>
<td>1.23 (0.71-2.12)</td>
</tr>
<tr>
<td><strong>PP- optimal (ref. &lt;8 meds)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PP- optimal (ref. &lt;8 meds)</td>
<td>1.61 (1.01-2.58)*</td>
<td>1.26 (0.81-1.97)</td>
<td>1.73 (1.01-2.98)*</td>
</tr>
<tr>
<td><strong>PIM (ref. No)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PIM (ref. No)</td>
<td>1.42 (0.87-2.32)</td>
<td>1.72 (1.09-2.73)*</td>
<td>1.97 (1.15-3.37)*</td>
</tr>
</tbody>
</table>

*All models included age, gender, race, and cancer type as covariates. In addition, we implemented stepwise procedure to select additional covariates with P < 0.157.*
Strengths

- A large sample of older adults with cancer receiving cancer treatment in the community oncology practices
- To our knowledge, this is the first study demonstrating that PIM is associated with physical functional impairment in older adults with cancer
Limitations

- Medications were only captured at one time point.
- We were unable to demonstrate causality.
- Medications were captured from the medication logs which do not take account into medication adherence.
Conclusion

- Receiving $\geq 8$ medications was a better cut-off than $\geq 5$ medications to identify physical functional impairments.
- PP ($\geq 8$) and PIM were independently associated with physical function impairment among older adults with advanced cancer.
- Optimizing medication use may reduce the risk of functional decline, thereby improving quality of life and survival.
- Future studies should evaluate the effect of PP and PIM on the risk of physical and functional decline in older adults with cancer in a longitudinal fashion.
Acknowledgements

- Participants

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- Co-authors

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