A prospective evaluation of symptom change over 4 weeks for outpatients with common solid tumors: Results from E2Z02 (the SOAPP study)

A Prospective Evaluation of Symptom Change over 4 weeks for Outpatients with Common Solid Tumors: Results from E2202 (the SOAP Study)


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Abstract

Background

Box: supportive care in oncology should improve the most important symptoms. Proportion of patients who improve or worsen with usual care for symptoms in a 4-week period is unknown.

Methods

Patients with invasive cancer of the breast, prostate, colon/rectum, or lung were cohorted from multiple academic sites (n=38) and community sites (n=32). At baseline and 4 weeks later patients rated their symptoms on a 0-10 numerical rating scale (NRS). A 1-point change was considered clinically significant for improvement or worsening. A multilevel model was used to examine the effects of demographic and clinical factors on symptom change.

Results

3162 patients were analyzable. Fatigue, sleep disturbance, diarrhea, pain, and distress were most prevalent and the most responsive symptoms. There was improvement in 1.1-2.3% of patients for these symptoms and worsening in 0.8-2.6. Among the patients with a least moderate baseline symptom intensity (5/10), 4.5% improved and 6.3% worsened. Patients with poor performance status were more likely to report improved pain (P=0.04 vs. P=0.16), depression (P=0.01), vs. PS 3, P=0.06) and diarrhea (P=0.04 vs. PS 3, P=0.001). Those with advanced disease were more likely to report improved sleep (P=0.001). Patients with prior radiation and those from non-academic-based enrolment sites were more likely to report improved fatigue (P=0.001, P=0.01, respectively).

Conclusions

In this national sample, outpatients with common solid tumors who were more ill and had higher symptoms were more likely to improve over a 4-week period. Further analyses of the symptom change variations will provide insight into the role of standard interventions and other factors.

Key Patient Characteristics

- Median age 64
- 16% age 65 or older
- 35% age 75 or older
- 35% 80+
- Non-Hispanic white
- Performance status: 0-1
- Disease course: 0.57
- Primary site: Breast, Prostate, Lung
- Distress: 0-4
- Social support: 3-2, 6-17, 13%
- Primary sites: Breast 54%, Lung 17%, Prostate 18%

Primary Objective

To describe the patterns of change over a 4-week period regarding the most common physical and psychological symptoms:

- 1a: patients with common solid tumors
- 1b: those with a significant improvement in one or more symptom scores after 4 weeks

Conclusion

Outpatients with common solid tumors who are more ill and symptomatic at baseline are less likely to experience significant improvement on any given symptom.

Multilevel Model Findings

These data were collected cluster-correlated, patients treated as level 1 units with weight at level 2.

- Patients with colorectal cancer were the only group of patients who significantly improved their pain, and this improvement is significantly better than patients with lung cancer after adjusting for other explanatory variables.

- Patients with poor PS (2-4) also significantly improved their pain, and this improvement is significantly better than those with PS 0-1 after controlling for other explanatory variables.

ADJUSTED MEANS ON Pain RESPOSIVENESS

Pre-treatment levels 4-week levels Standard Error P-value (full model) P-value (final model)

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Pre-treatment</th>
<th>4-week</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain</td>
<td>6.2</td>
<td>5.9</td>
<td>0.048</td>
<td>0.001</td>
<td>0.048</td>
</tr>
<tr>
<td>Sleep</td>
<td>6.2</td>
<td>5.3</td>
<td>0.048</td>
<td>0.001</td>
<td>0.048</td>
</tr>
<tr>
<td>Fatigue</td>
<td>6.2</td>
<td>5.9</td>
<td>0.048</td>
<td>0.001</td>
<td>0.048</td>
</tr>
</tbody>
</table>

ADJUSTED MEANS ON Distressful Sleep RESPOSIVENESS

Pre-treatment levels 4-week levels Standard Error P-value (full model) P-value (final model)

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Pre-treatment</th>
<th>4-week</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain</td>
<td>6.2</td>
<td>5.9</td>
<td>0.048</td>
<td>0.001</td>
<td>0.048</td>
</tr>
<tr>
<td>Sleep</td>
<td>6.2</td>
<td>5.3</td>
<td>0.048</td>
<td>0.001</td>
<td>0.048</td>
</tr>
<tr>
<td>Fatigue</td>
<td>6.2</td>
<td>5.9</td>
<td>0.048</td>
<td>0.001</td>
<td>0.048</td>
</tr>
</tbody>
</table>

Conclusion

Outpatients with common solid tumors who are more ill and symptomatic at baseline are less likely to experience significant improvement on any given symptom.

In the overall cohort, patients did not improve in the most prevalent symptoms, except for sleep and nausea.

These data provide richer description of how symptoms respond to current outpatient management. Further analyses of symptom change variations will provide insight into the role of standard interventions and their important factors.
Background

- The NCI State of the Science Conference on Symptom Management in Cancer in 2002 concluded that too many patients with pain, depression, and fatigue receive inadequate treatment for their symptoms, and that
- “research is needed on the definition, occurrence, assessment, and treatment of pain, depression, and fatigue alone and together through adequately funded prospective studies.” [JNCI Monographs 2004 2004(32):9-16]
- Supportive care in outpatient oncology should improve the most prevalent and bothersome physical and psychological symptoms
Primary Objective

- To describe the patterns of change over a 4-week period regarding the most common physical and psychological symptoms
- In patients with common solid tumors
- Followed on an outpatient basis at ECOG-affiliated academic institutions or community practices (CCOPs)
Methods

- Study conducted between March 2006 and May 2008
- 6 academic sites and 32 community practices in the United States
  - CCOP refers to the Community Clinical Oncology Program
  - Minority-based CCOPs are clinics where 40% or more of the patients are from designated minority groups
- Pre-defined sampling algorithms used at each site to reduce selection bias
Methods: Symptom Measurement

- Symptom intensity measured using the M.D. Anderson Symptom Inventory (MDASI-ECOG)
  - 0-10 numerical rating scale where “10” represents worst severity for each symptom item
  - 2 point change (worse or better) is considered clinically significant
    - Response % represents the proportion of patients who experienced ≥ 2 point change between baseline and 4-5 week follow-up
3,123 Enrolled Patients

3,102 Analyzable Patients

- 10 in pilot study
- 7 never started study (1 ineligible, 1 coding error, 1 registry cancellation, 1 pt. refusal, 3 others)
- 4 no primary site information

Academic (N=303)

Community (N=2,799)

CCOP (N=2,212)

MBCCOP (N=587)

- Breast (N=115)
- Colorectal (N=65)
- Prostate (N=63)
- Lung (N=60)

- Breast (N=1,149)
- Colorectal (N=472)
- Prostate (N=194)
- Lung (N=397)

- Breast (N=279)
- Colorectal (N=180)
- Prostate (N=63)
- Lung (N=65)
Key Patient Characteristics

- Median age 61 years
  - 10% under age 45
  - 15% age 75 or older
- Men—30%
- Minority participants —22%
- Performance status
  - 0=57%
  - 1=36%
  - ≥2=7%

- Primary Sites
  - Breast 50%
  - Colorectal 23%
  - Lung 17%
  - Prostate 10%

*See ASCO 2009 abstract #9619 for further description of patient characteristics and study findings*
Overall Cohort: response proportions for the 5 most prevalent symptoms

* A 2-point change on the 0-10 scale is considered significant
* Follow-up for symptom response was at 4 weeks
Response proportions for patients with moderate-to-severe symptoms at baseline

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Better</th>
<th>Worse</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td>43</td>
<td>13</td>
</tr>
<tr>
<td>Sleep</td>
<td>55</td>
<td>9</td>
</tr>
<tr>
<td>Drowniness</td>
<td>55</td>
<td>10</td>
</tr>
<tr>
<td>Pain</td>
<td>52</td>
<td>10</td>
</tr>
<tr>
<td>Distress</td>
<td>56</td>
<td>11</td>
</tr>
</tbody>
</table>
Response proportions for patients with moderate-to-severe GI symptoms at baseline

- Nausea: 65% Better, 7% Worse
- Vomiting: 78% Better, 2% Worse
- Anorexia/Cachexia: 53% Better, 10% Worse
- Diarrhea: 64% Better, 10% Worse
- Constipation: 57% Better, 11% Worse
- Sore Mouth: 69% Better, 6% Worse
- Dry Mouth: 55% Better, 10% Worse
Response proportions for patients with other moderate-severe symptoms at baseline

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Response %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sadness</td>
<td>54%</td>
</tr>
<tr>
<td>Distress</td>
<td>56%</td>
</tr>
<tr>
<td>Cognitive Difficulty</td>
<td>52%</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>53%</td>
</tr>
<tr>
<td>Coughing</td>
<td>59%</td>
</tr>
<tr>
<td>Skin Rash/Pruritis</td>
<td>74%</td>
</tr>
<tr>
<td>Hair Loss</td>
<td>44%</td>
</tr>
</tbody>
</table>

Bars indicate percentage of patients reporting better or worse symptoms compared to baseline.
Clinician Judged Response to Symptom Directed Therapy at 4 weeks

- Complete response: 67%
- Partial response: 18%
- Stable response: 7%
- Progressive Sxs: 8%
Clinician Judged Patient Compliance to Symptom-Directed Treatment

- Perfect: 49%
- Acceptable: 49%
- Poor: 2%
Multilevel Model Findings

• These data were considered cluster-correlated
• Patients treated as level 1 units and clinics as level 2
Patients with colorectal cancer were the only group of patients who significantly improved their pain, and this improvement is significantly better than patients with lung cancer after adjusting for other explanatory variables.

Patients with poor PS (2-4) also significantly improved their pain, and this improvement is significantly better than those with PS 0 and PS 1 after controlling for other explanatory variables.
Multilevel Model: FATIGUE

After adjusting for other explanatory variables, patients with prior radiation therapy significantly improved on fatigue, and this improvement is significantly better than those without prior radiation therapy.

Those registered in minority-based clinics also experienced significantly less fatigue, and this improvement is significantly better than their counterparts in other clinics.
Multilevel Model: SLEEP

- After adjusting for other explanatory variables, patients with advanced disease stage significantly improved their sleep disturbance.
Multilevel Model: DROWSINESS

- Patients with worse PS (2-4) improved more on drowsiness than those with better PS
- Those with PS 2-4 were the only group with a significant improvement on drowsiness
Other model findings…

• **Anorexia/Cachexia**
  – Patients losing more weight (≥5%) (p=0.01) and those registered in the minority-based clinics (p=0.01) improved more on this symptom than their counterparts

• **Distress**
  – Patients registered in academic clinics improved more on this symptom than their counterparts (a marginal significance, p=0.06), although neither group of patients reported significant changes in their distress ratings
...Other model findings

• **Dyspnea**
  – Patients registered in academic clinics significantly improved on dyspnea (p=0.03), and this improvement is significantly better than their counterparts (p=0.04)

• **Diarrhea**
  – Patients with ≥5% weight loss in the previous 6 months experienced significantly less diarrhea at follow-up (p<0.01) compared to baseline
Conclusions

• Outpatients with common solid tumors who are more ill and symptomatic at baseline are more likely to experience significant improvement on any given symptom.
• In the overall cohort, patients did not tend to improve in the most prevalent 5 symptoms over a 4-5 week timeframe.
• These data provide a rich description of how symptoms respond to current outpatient management.
• Further analyses of symptom change variations will provide insight into the role of standard interventions and other important factors influencing the patient experience.