Prognostic factors in patients with advanced cancer: the use of the Patient-Generated Subjective Global Assessment in survival prediction

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Conceptual model of cancer death trajectory

Fig. 1 – Conceptual model of cancer death trajectory.\textsuperscript{122,123}

Barb Tarbox 1961 - 2003
What constitutes *timely*?

- **Patient view**
  - Vital opportunity to consider planning, priorities and preparation for death
  - Informed choices of treatment options and place of care
  - Establish eligibility for care programs, Palliative benefit plan, EI for family caregiver

- **Health Services view**
  - Recommendation of treatment options and place of care
  - Allocation of scarce resources
The bases of prediction

• Clinical prediction by health care professionals
  – Opinion of specialist physician, hospital or family physician nurse, care aid.

• Statistical estimate based on data
  – Based on empirical data: disease and demographic, performance status, symptoms, quality of life, biological parameters… at least 150 different variables have been used in survival prediction
Notion of *timeliness* is based on *Prognostication* defined as clinical prediction of:

- Disease progression or recurrence
- Disability or discomfort
- Drug toxicity
- Likelihood of completing participation in research
- Use or cost of health care services
- Death
Clinical prediction of survival- how good is it?

Prediction of Patient Survival by Healthcare Professionals in a Specialist Palliative Care Inpatient Unit: A Prospective Study

Feargal Twomey, MB, MRCPI, Norma O’Leary, MB, MRCPI, and Tony O’Brien, MB, FRCPI

Table 2. Accuracy of Survival Prediction by Group

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Weighted Kappa&lt;sup&gt;a&lt;/sup&gt;</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>For all 221 patients</td>
<td>191</td>
<td>0.48</td>
<td>(0.39,0.56)</td>
</tr>
<tr>
<td>Nurse Managers</td>
<td>196</td>
<td>0.48</td>
<td>(0.39,0.56)</td>
</tr>
<tr>
<td>Nurses</td>
<td>180</td>
<td>0.36</td>
<td>(0.27,0.46)</td>
</tr>
<tr>
<td>Care assistants</td>
<td>148</td>
<td>0.41</td>
<td>(0.31,0.51)</td>
</tr>
<tr>
<td>Consultant</td>
<td>200</td>
<td>0.47</td>
<td>(0.39,0.56)</td>
</tr>
<tr>
<td>NCHDs</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Clinical estimation of survival by radiation oncologists

Fig 1. Discrepancy between actual and predicted survival by survival categories. Minus 2 means an underestimation of survival by two categories (i.e., the prognosis was too pessimistic).
Clinical prediction of survival..

• Clinical prediction of survival by all categories of health care providers is inaccurate. (*ie* explains much less than half of the variation in actual survival)

• Most health care providers feel poorly trained to both formulate and communicate a prognosis of death

• Stress and worry connected with inaccurate predictions.

• Coping strategies include avoidance, optimism, vagueness
Statistical estimates of survival:

- Based on empirical data: disease and demographic, performance status, symptoms, quality of life, biological parameters... at least 150 different individual variables have been used in survival prediction

(if you happen to maintain good quality data sets on your patients)
Data considered

- **Oncology**
  - TNM Stage
  - Treatment intervention
  - Performance status
  - Number and location of metastases
  - Blood and laboratory features
  - Nutritional status
  - Prognostic scores

- **Palliative Medicine**
  - Physician – estimated survival
  - Performance status
  - Pain and Symptoms
  - Blood and laboratory work
  - Nutritional status
  - Psychosocial
  - Palliative Prognostic scores
Predicting survival in patients with advanced disease

Paul Glare, Christian Sinclair, Michael Downing, Patrick Stone, Marco Maltoni, Antonio Vigano

<table>
<thead>
<tr>
<th>Variable</th>
<th>Number of positive studies&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Total number of studies evaluating</th>
<th>Strength of association</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poor performance status</td>
<td>14</td>
<td>14</td>
<td>Definite</td>
</tr>
<tr>
<td>Anorexia</td>
<td>8</td>
<td>9</td>
<td>Definite</td>
</tr>
<tr>
<td>Clinical prediction of survival</td>
<td>7</td>
<td>7</td>
<td>Definite</td>
</tr>
<tr>
<td>Cognitive failure</td>
<td>7</td>
<td>8</td>
<td>Definite</td>
</tr>
<tr>
<td>Dyspnoea</td>
<td>7</td>
<td>8</td>
<td>Definite</td>
</tr>
<tr>
<td>Dry mouth</td>
<td>5</td>
<td>6</td>
<td>Definite</td>
</tr>
<tr>
<td>Weight loss</td>
<td>4</td>
<td>5</td>
<td>Definite</td>
</tr>
<tr>
<td>Dysphagia</td>
<td>4</td>
<td>5</td>
<td>Definite</td>
</tr>
<tr>
<td>Primary site</td>
<td>5</td>
<td>10</td>
<td>Possibly yes</td>
</tr>
<tr>
<td>Pain</td>
<td>5</td>
<td>10</td>
<td>Possibly yes</td>
</tr>
<tr>
<td>Serum albumin</td>
<td>3</td>
<td>4</td>
<td>Possibly yes</td>
</tr>
<tr>
<td>Tachycardia</td>
<td>3</td>
<td>4</td>
<td>Possibly yes</td>
</tr>
<tr>
<td>Gender (male)</td>
<td>3</td>
<td>11</td>
<td>Possibly yes</td>
</tr>
<tr>
<td>Marital status</td>
<td>2</td>
<td>5</td>
<td>Probably not</td>
</tr>
<tr>
<td>Nausea</td>
<td>2</td>
<td>5</td>
<td>Probably not</td>
</tr>
<tr>
<td>Age</td>
<td>2</td>
<td>9</td>
<td>Probably not</td>
</tr>
<tr>
<td>Fever</td>
<td>1</td>
<td>4</td>
<td>Probably not</td>
</tr>
<tr>
<td>Anaemia</td>
<td>0</td>
<td>4</td>
<td>Probably not</td>
</tr>
</tbody>
</table>

<sup>a</sup> Positive on either univariate or multivariate analysis.
Palliative Prognostic Score

A prognostic scoring system based on Clinical Prediction, Karnofsky performance, symptoms and blood work.

<table>
<thead>
<tr>
<th>Prognostic Factor</th>
<th>Partial Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dyspnea</td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>0</td>
</tr>
<tr>
<td>Present</td>
<td>1</td>
</tr>
<tr>
<td>Anorexia</td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>0</td>
</tr>
<tr>
<td>Present</td>
<td>1.5</td>
</tr>
<tr>
<td>Karnofsky performance status</td>
<td></td>
</tr>
<tr>
<td>≥ 50</td>
<td>0</td>
</tr>
<tr>
<td>30-40</td>
<td>0</td>
</tr>
<tr>
<td>10-20</td>
<td>2.5</td>
</tr>
<tr>
<td>Clinical prediction of survival</td>
<td></td>
</tr>
<tr>
<td>&gt; 12 weeks</td>
<td>0</td>
</tr>
<tr>
<td>11-12 weeks</td>
<td>2.0</td>
</tr>
<tr>
<td>9-10 weeks</td>
<td>2.5</td>
</tr>
<tr>
<td>7-8 weeks</td>
<td>2.5</td>
</tr>
<tr>
<td>5-6 weeks</td>
<td>4.5</td>
</tr>
<tr>
<td>3-4 weeks</td>
<td>6.0</td>
</tr>
<tr>
<td>1-2 weeks</td>
<td>8.5</td>
</tr>
<tr>
<td>Total WBC count (cell/mm³)</td>
<td></td>
</tr>
<tr>
<td>Normal: 4,800-8,500 cells/µL</td>
<td>0</td>
</tr>
<tr>
<td>High: 8,501-11,000 cells/µL</td>
<td>0.5</td>
</tr>
<tr>
<td>Very high: &gt; 11,000 cells/µL</td>
<td>1.5</td>
</tr>
<tr>
<td>Lymphocyte percentage</td>
<td></td>
</tr>
<tr>
<td>Normal: 20.0%-40.0%</td>
<td>0</td>
</tr>
<tr>
<td>Low: 12.0%-19.9%</td>
<td>1.0</td>
</tr>
<tr>
<td>Very low: 0%-11.9%</td>
<td>2.5</td>
</tr>
</tbody>
</table>

NOTE. The risk groups and total scores were as follows: group A: 30-day survival probability of ≥ 70%, score = 0 to 5.5; group B: 30-day survival probability of 30% to 70%, score = 5.6 to 11.0; and group C: 30-day survival probability of < 30%, score = 11.1 to 17.5.

*Palliative Prognostic Score = dyspnea score + anorexia score + Karnofsky performance status score + clinical prediction of survival score + total WBC count score + lymphocyte percentage score.
**Palliative Performance Scale (PPSv2) version 2** (developed by Victoria Hospice Society)

<table>
<thead>
<tr>
<th>PPS Level</th>
<th>Ambulation</th>
<th>Activity &amp; Evidence of Disease</th>
<th>Self-Care</th>
<th>Intake</th>
<th>Conscious Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>100%</td>
<td>Full</td>
<td>Normal activity &amp; work + No evidence of disease</td>
<td>Full</td>
<td>Normal</td>
<td>Full</td>
</tr>
<tr>
<td>90%</td>
<td>Full</td>
<td>Normal activity &amp; work + Some evidence of disease</td>
<td>Full</td>
<td>Normal</td>
<td>Full</td>
</tr>
<tr>
<td>80%</td>
<td>Full</td>
<td>Normal activity with Effort + Some evidence of disease</td>
<td>Full</td>
<td>Normal or reduced</td>
<td>Full</td>
</tr>
<tr>
<td>70%</td>
<td>Reduced</td>
<td>Unable Normal Job/Work + Significant disease</td>
<td>Full</td>
<td>Normal or reduced</td>
<td>Full</td>
</tr>
<tr>
<td>60%</td>
<td>Reduced</td>
<td>Unable hobby/house work + Significant disease</td>
<td>Occasional assistance necessary</td>
<td>Normal or reduced</td>
<td>Full or Confusion</td>
</tr>
<tr>
<td>50%</td>
<td>Mainly Sit/Lie</td>
<td>Unable to do any work + Extensive disease</td>
<td>Considerable assistance required</td>
<td>Normal or reduced</td>
<td>Full or Confusion</td>
</tr>
<tr>
<td>40%</td>
<td>Mainly in Bed</td>
<td>Unable to do most activity + Extensive disease</td>
<td>Mainly assistance</td>
<td>Normal or reduced</td>
<td>Full or Drowsy +/- Confusion</td>
</tr>
<tr>
<td>30%</td>
<td>Totally Bed Bound</td>
<td>Unable to do any activity + Extensive disease</td>
<td>Total Care</td>
<td>Normal or reduced</td>
<td>Full or Drowsy +/- Confusion</td>
</tr>
<tr>
<td>20%</td>
<td>Totally Bed Bound</td>
<td>Unable to do any activity + Extensive disease</td>
<td>Total Care</td>
<td>Minimal to sips</td>
<td>Full or Drowsy +/- Confusion</td>
</tr>
<tr>
<td>10%</td>
<td>Totally Bed Bound</td>
<td>Unable to do any activity + Extensive disease</td>
<td>Total Care</td>
<td>Mouth care only</td>
<td>Drowsy or Coma +/- Confusion</td>
</tr>
<tr>
<td>0%</td>
<td>Death</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

*Home is defined as the patient’s usual residence (may include long term care facility)*
A salad of prognostic tools……

• Palliative prognostic score (PaP)
• Palliative Performance Index (PPI)
• Palliative performance scale (PPS)
• Cancer prognostic score
• Intrahospital cancer mortality risk model (ICMRM)
• Glasgow Prognostic Score
• Prognostat
Palliative instruments

• Based on different input data
• Data may be specific to one care setting
• Some small convenience samples; few large, population–based data sets of high quality
• Pragmatic clinical information-based
• Based on lab tests, new research measures (ie interleukin-6)
• No common minimum data set
Nutrition and Prognostication

• Many prognostication instruments contain a nutrition–related element on dietary intake
• The nutrition elements are often weak – it has not been established that they are indeed the most prognostic variables and the quantification of “anorexia” is vague
Nutrition elements

• PGSGA Nutrition Instrument
• RD – Oncology recommended tool
  – Weight history, body mass index
  – Food intake score
  – “Nutrition Impact” symptoms YES/NO
  – Functional status score = Eastern Clinical Oncology Group ECOG score
1. **Weight** *(See Worksheet 1)*

In summary of my current and recent weight:

I currently weigh about _______ pounds  
I am about __________ feet __________ tall

One month ago I weighed about _______ pounds  
Six months ago I weighed about _______ pounds

During the past two weeks my weight has:

- [ ] decreased (₁)  
- [ ] not changed (₀)  
- [ ] increased (₀)  

Box 1 [ ]
2. **Food Intake:** As compared to my normal intake, I would rate my food intake during the past month as:

- [ ] unchanged (0)
- [ ] more than usual (0)
- [ ] less than usual (1)

I am now taking:

- [ ] *normal food* but less than normal amount (1)
- [ ] little solid food (2)
- [ ] only liquids (3)
- [ ] only nutritional supplements (3)
- [ ] very little of anything (4)
- [ ] only tube feedings or only nutrition by vein (0)

Box 2
3. **Symptoms:** I have had the following problems that have kept me from eating enough during the past two weeks (check all that apply):

- no problems eating (0)
- no appetite, just did not feel like eating (3)
- nausea (1)
- constipation (1)
- mouth sores (2)
- things taste funny or have no taste (1)
- problems swallowing (2)
- pain; where? (3)
- other** (1)

** Examples: depression, money, or dental problems

Box 3
4. **Activities and Function**: Over the past month, I would generally rate my activity as:

- normal with no limitations
- not my normal self, but able to be up and about with fairly normal activities
- not feeling up to most things, but in bed or chair less than half the day
- able to do little activity and spend most of the day in bed or chair
- pretty much bedridden, rarely out of bed

Box 4
Prognostic Factors in Patients With Advanced Cancer: Use of the Patient-Generated Subjective Global Assessment in Survival Prediction

Lisa Martin, Sharon Watanabe, Robin Fainsinger, Francis Lau, Sunita Ghosh, Hue Quan, Marlis Atkins, Konrad Fassbender, G. Michael Downing, and Vickie Baracos
Regional Palliative Care Program

General admission criteria:
- Patient experiencing a life-threatening illness
- Patient requires active care to alleviate distressing symptoms (physical, psychosocial, spiritual needs)

Training Set

Palliative Home Care
Admission criteria:
- Desire to be cared for at home
- Does not require acute/tertiary care
- Expected length of stay 3-4 months

Assessed for eligibility (n = 1,339)

Tertiary Palliative Care Unit
Admission criteria:
- Intensive, interdisciplinary management of severe symptoms
- Symptoms require ongoing monitoring and assessment
- Average length of stay 3-4 weeks

Assessed for eligibility (n = 158)

Validation Set

Pain and Symptom Control Consult Service
Admission criteria:
- Interdisciplinary management of symptoms and/or establishment of community supports.
- Inpatient or outpatient setting for patients receiving treatment at the Cross Cancer Institute

Assessed for eligibility (n = 468)
Univariate analysis of Body mass index and weight loss, some surprises:

- Mean BMI 24.0±5.3 closer to overweight than underweight
- BMI > 30 (obese) predicts longer survival
- Weight loss relationship U-shaped, short term weight gain a poor prognostic factor
Predicted survival in multivariate analysis

- Cancer site
- ECOG performance (patient – self rated)
- Weight loss or weight gain
- Food intake
  - Little solid food
  - Only liquids
  - Very little of anything
- Dysphagia
Testing the model: concordance statistics

- C-stats were used to test the predictive accuracy of models based on the training and the validation data sets.
- C-stat is the probability that a participant from an event group (i.e., a group with a poor prognostic factor) has a higher risk of an event (i.e., death) than a participant from a non-event group.
- C-stat of 0.50 means that the model predicts the outcome as well as chance; 1.00 is a perfect prediction.
- Structured sort of like a “bet” where each patient’s actual survival is compared with their predicted survival.
Table 3. Discrimination of Overall Survival for a Predictive Model in a Training and Validation Set and for Two Measures of Functional Status

<table>
<thead>
<tr>
<th>Variable</th>
<th>Training Set (n = 1,164)</th>
<th></th>
<th>Validation Set (n = 603)</th>
<th></th>
<th>PG-SGA PS† (n = 1,767)</th>
<th></th>
<th>PPS† (n = 1,283)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Base Model*</td>
<td>Full Model†</td>
<td>Base Model*</td>
<td>Full Model†</td>
<td>0.93</td>
<td>0.93</td>
<td></td>
</tr>
<tr>
<td>C-statistic</td>
<td>0.90</td>
<td>0.88</td>
<td>0.88</td>
<td>0.87</td>
<td>0.93</td>
<td>0.93</td>
<td></td>
</tr>
<tr>
<td>95% CI</td>
<td>0.86 to 0.93</td>
<td>0.83 to 0.91</td>
<td>0.82 to 0.93</td>
<td>0.80 to 0.92</td>
<td>0.90 to 0.96</td>
<td>0.90 to 0.96</td>
<td></td>
</tr>
</tbody>
</table>

NOTE. There are no statistical differences between concordance statistics (c-statistics; P > .05).
Abbreviations: PG-SGA PS, patient-generated Subjective Global Assessment performance status; PPS, Palliative Performance Scale.
*Base model includes cancer diagnosis and functional status.
†Full model includes cancer diagnosis, functional status, percent weight change, dietary intake, and dysphagia.
‡The calculations of c-statistics were performed on PG-SGA PS and PPS only (ie, no other variables were included).
<table>
<thead>
<tr>
<th>Variable</th>
<th>No. of Patients</th>
<th>No. of Events</th>
<th>Median Survival (months)</th>
<th>95% CI</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patient-reported PG-SGA PS (n = 1,767)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-2</td>
<td>442</td>
<td>372</td>
<td>3.7</td>
<td>3.3 to 4.1</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>3</td>
<td>419</td>
<td>377</td>
<td>2.0</td>
<td>1.6 to 2.3</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>51</td>
<td>51</td>
<td>1.0</td>
<td>0.5 to 1.5</td>
<td></td>
</tr>
<tr>
<td><strong>Physician-reported PPS (n = 1,283)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 70%</td>
<td>222</td>
<td>202</td>
<td>3.4</td>
<td>2.9 to 3.8</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>40%-60%</td>
<td>419</td>
<td>386</td>
<td>1.8</td>
<td>1.6 to 2.1</td>
<td></td>
</tr>
<tr>
<td>0%-30%</td>
<td>13</td>
<td>13</td>
<td>0.3</td>
<td>0.2 to 0.5</td>
<td></td>
</tr>
</tbody>
</table>
Conclusions

• Prognostic nutrition information
  – Nutrition information prognostic, in unanticipated ways.
  – Potential dual use of nutrition screening tools: nutrition risk assessment and prognostication

• Populations, data sets
  – Population –based data sampling, appropriate stats

• Patient – generated information of value
  – Think about prognostic tools in terms of cost, time spent, invasiveness – necessary?

• Pretty good, but not perfect predictive models
  – Taking bets? How to refine the predictions that we have?
Future Hope

• Assembly of important data sets
• Reduce the number of assessments
• Prediction with high accuracy
• Timely access to end of life care