Predictive tools

- 2002-2005
- Prospective cohort multicentre study
- Cancer patients 70+
  - Including NHL, excluding breast cancer
  - aCGA
    - MMSE, get up and go (GUG), ADL, IADL, MNA, GDS15, CIRS-G
    - By geriatrician and trained nurse
- Scheduled for 1st line chemotherapy
  - Chosen by clinician (blinded to aCGA results)
- 6-month death

6-month death risk with chemotherapy

- 348 patients
  - Median age 77.45 (70-99.4)
  - M/F: 1.47
  - 37% CRC and gastric cancer, 36% NHL
  - 65% advanced stage
- 12 centres SW France
  - 2 cancer centres, 10 community hospitals
- Chemotherapy
  - Standard regimen and doses: only 45%!
- 6-month death: 56 patients (16.1%)
  - 73% cancer
  - 14% treatment complications
  - 13% intercurrent conditions

Soubeyran, J Clin Oncol 2012

MV analysis

<table>
<thead>
<tr>
<th>MV analysis</th>
<th>OR</th>
<th>95%CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>2.4</td>
<td>[1.2-4.82]</td>
<td>.013</td>
</tr>
<tr>
<td>Advanced</td>
<td>3.9</td>
<td>[1.58-9.73]</td>
<td>.003</td>
</tr>
<tr>
<td>Poor MNA (≤23.5)</td>
<td>2.77</td>
<td>[1.24-6.18]</td>
<td>.013</td>
</tr>
<tr>
<td>Long GUG (≥20 sec)</td>
<td>2.55</td>
<td>[1.32-4.94]</td>
<td>.006</td>
</tr>
</tbody>
</table>

Mv→ no role for
- Age strata, PS, WBC and platelets, LVEF
- Tumour site, treatment schedule, treatment site

Conclusions

- Limitations
  - Main causes of death are cancer (73%) and toxicity (14%)
  - MNA and GUG impairments overlap
    - Increase with advanced stage
    - Increase risk toxicity
- MNA and GUG
  - Other tools? (CRASH, CARG)
  - Routine pretreatment workup?
  - MNA 10’ full version or 3’ stand-alone short version
- Research
  - Rationale for RCT INOGAD: chemo + nutritional support vs chemo + standard support
Screening for disabilities

- Prospective cohort multicentre study
- Cancer patients 70+
- 2 independent physicians
  - C G A
  - MMSE, ADL, IADL, MNA, CIRS-G
  - SOF (Study of Osteoporotic Fractures) index
- Weight loss ≥ 5%, rise from a chair x 5, “do you feel full of energy”
- SOF index vs CGA (reference) in predicting the disability
  - SOF diagnostic accuracy < 80% not acceptable

Luciani, Annals Oncol 2012

SOF vs CGA

- 400 patients
  - Median age 77.2 (range 70–97)
  - 35.2% lung, 19.2% colon, 7% gastric
  - 94.5% ≥ 1 comorbidity (CV 61%, GU and respiratory 23%)
  - CGA classification: 31.8% unfit and 68.2% fit

<table>
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<tr>
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<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Accuracy (%)</th>
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<tr>
<td>CIRS-G (&gt; 3)</td>
<td>71.4 (66.7-76.7)</td>
<td>43.3 (24.5-52.4)</td>
<td>62.5 (57.6-67.3)</td>
</tr>
<tr>
<td>ADL (≤ 5)</td>
<td>28.2 (22.9-33.9)</td>
<td>100.0 (97.1-100)</td>
<td>51.0 (46.0-56.0)</td>
</tr>
<tr>
<td>MNA</td>
<td>56.0 (49.9-62.0)</td>
<td>81.1 (73.2-87.5)</td>
<td>64.0 (59.1-68.7)</td>
</tr>
<tr>
<td>MMSE (≤ 28)</td>
<td>65.9 (60.7-71.5)</td>
<td>87.7 (83.8-75.7)</td>
<td>66.5 (61.6-71.1)</td>
</tr>
<tr>
<td>SOF (&gt; 2)</td>
<td>89.0 (84.7-92.5)</td>
<td>81.1 (73.2-87.5)</td>
<td>86.5 (82.8-89.7)</td>
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<tr>
<td>IADL (≤ 6)</td>
<td>59.3 (53.3-65.2)</td>
<td>97.6 (93.3-99.5)</td>
<td>71.5 (66.8-75.9)</td>
</tr>
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*NPV 77.4% (69.4-84.2), no difference of sensitivity and NPV according to disease stage

Luciani, Annals Oncol 2012

Geriatric assessment in oncology

- Large review of all GA instruments used in the oncology setting (Medline, Embase, Psychinfo, Cinahl, Cochrane Library Jan 1996-Nov 2010)
  - Feasibility and psychometric properties of instruments
  - Effectiveness in predicting/modifying outcomes (treatment decision making, toxicity, mortality)
  - Cross-sectional, longitudinal, interventional, or observational studies


Geriatric assessment in oncology

- 83 articles reporting on 73 studies
  - Quality of most studies poor to moderate
  - 11 studies
    - Psychometric properties/diagnostic accuracy of GA instruments
      - 10-45 min, most often to describe health and functional status
  - Association of GA instruments w/ treatment toxicity: 8/3 studies
    - Mortality: 8/16 studies
    - Cancer treatment decision: 2/4 studies
    - 40-50% of decisions affected

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Conclusions

- Limited to another tool?
- SOF
  - Easy-to-use instrument to promptly recognize and act
- Research
  - Predictive value on outcome (EXPLORE SOF)
- Review on frailty screening methods
  - Even with high sensitivity, NPV ≤ 60%

Geriatric assessment in oncology

- 83 articles reporting on 73 studies
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Conclusions

- Feasible + some prediction
- Practical applications remain limited / deserve further research

Puts, J Natl Cancer Inst 2012

Tough to treat tumours: glioblastoma

- Nordic Clinical Brain Tumour Study Group
- Phase III
- 2000-2009 (in 2004, change of age eligibility to 65+ w/ chemo+XRT <65)
  - 1/ OS 2/ QoL & safety

Malmström, Lancet Oncol 2012
Tough to treat tumours: glioblastoma

- 342 patients (42% 70+)

Malmström, Lancet Oncol 2012

Conclusions

- Limitations
  - Standard XRT
  - Delay to start (46 days = 2 times temozolomide)
  - Less complete vs hypofractionated (72% vs 95%)
  - High cross-over rates
  - Limited data on QoL
  - Duration of study (10 years), low power (recruitment stop)

- Similar results as NOA-08 (Neuro-oncology Working Group of the German Cancer Society)
  - Temozolomide and hypofractionated XRT: standard options for 70+
  - Promoter methylation of O6-methylguanine-DNA methyltransferase gene → better OS w/ temozolomide

- Research
  - EORTC/NCIC: hypofractionated XRT + temozolomide in 65+

Malmström, Lancet Oncol 2012

Bevacizumab and lung cancer

- ECOG 4599
  - OS HR 0.79 (0.67-0.92) favouring bevacizumab + chemotherapy (paclitaxel + carboplatin) (but NS in 65+ subgroup)

- Retrospective cohort study of 4,168 Medicare beneficiaries 65+ w/ stage IIIB-IV non squamous cell NSCLC 2002-2007 (SEER)
  - 2002-2005 (2,666) chemotherapy
  - 2006-2007 (1,502) chemotherapy (79% chemotherapy + bevacizumab (21%)

- Impact on OS (Cox proportional hazards models and propensity score analyses)

JAMA The Journal of the American Medical Association

Zhu, JAMA 2012

Conclusions

- Limitations
  - Observational, lack of essential clinical details in SEER, sample size for bevacizumab group
  - Medicare-fee-for-service beneficiaries

- Addition of bevacizumab to chemotherapy is not associated w/ improvement in OS
  - Only 20% of bevacizumab prescription > 2006: medical oncologists remain circumspect and judicious in their use of new agents with uncertain benefit
  - Magnitude of benefit in cohort lower than in trial (9.7 vs 12.3 mth)

- Research
  - Prospective clinical trials with less narrow selection key (usually only 10% of “true” population included)?

Zhu, JAMA 2012

Management of elderly patients with breast cancer: updated recommendations of the International Society of Geriatric Oncology (SIGOG) and European Society of Breast Cancer Specialists (EUSOMA)

Biganzoli, Lancet Oncol 2012
*General conclusions*

- **Geriatric assessment and screening tool for oncologist**
  - Proven prognostic/predictive value of CGA domains (nutritional, mobility)
  - Some easy-to-use tools
  - Screening tool: 1 for all or all for 1? (G8, SOF, VES-13, etc.)
- **More research**
  - Specific trials (targeted treatments)
  - Less selective eligibility keys to faithfully represent general population
  - First challenge is to prove usefulness of GA on cancer outcome and cost (cost-effectiveness, QALY)
    - Oxaliplatin and colorectal cancer in elderly (Mullins, Cancer 2012)
    - Primary prophylaxis w/ G-CSF with diffuse aggressive NHL in elderly (Chan, J Clin Oncol 2012)
    - Rituximab and diffuse large B-cell NHL in elderly (Griffiths, Cancer 2012)