Update in Geriatrics

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What’s new about frailty?

- The frailty phenotype and the frailty index: different instruments for different purposes Matteo Cesari 2014; Age & Ageing 43:10-12
Two different concepts of frailty

• The frail phenotype (L. Fried)
  – 5 criteria (weight loss, gait speed, weakness, exhaustion, muscular strength)
  – Depicts an age-related condition in the absence of nosographically specified conditions

• The deficit accumulation: frailty index (Rockwood)
  – 70 items: physical, psychological and social status
  – After clinical extensive assessment
  – Describing nosographically specified conditions
Different instruments for different purposes in different populations

• Frail phenotype
  – In elderly people living at home
  – With no disability
  – After screening (auto-questionnaires)

• Frailty index
  – In more specific populations with chronic diseases
  – After CGA
  – Useful for follow-up (health status trajectories, effectiveness of interventions)
Frailty Consensus: A Call to Action

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• IAGG
• Society on Sarcopenia, Cachexia and Wasting Diseases
• International Academy of Nutrition and Aging
• European Union Geriatric Medicine Society
• American Medical Directors Association
• American Federation for Aging Research
• 7 other experts in the area of frailty

• Writing of a document
• Using a modified Delphi process
Recommandations

1. Physical frailty is an important medical syndrome with multiple causes and contributors to seek for. Associating
   - diminished strength and endurance
   - reduced physiologic function
   - increasing vulnerability
   - developing increased dependency and/or death
In addition

- The target in case finding is the predisabled and not the dependent person (≥ 1 ADL)
- Sarcopenia is only a component of frailty which is more multifaceted than sarcopenia alone
- A number of well-validated models of frailty exist and the diagnosis should be done by a geriatrician using the basic criteria of these models which predict increased vulnerability to adverse health outcomes and mortality
2. Simple rapid screening tests have been developed and validated
   - FRAIL Questionnaire Screening Tool
   - Cardiovascular Health Study Frailty Screening Tool
   - Gerontopôle Frailty Screening Tool

   to allow physicians to objectively recognize frail persons with a Comprehensive Geriatric Assessment
3. **Physical** frailty can potentially be prevented or treated with specific modalities such as:
   - Exercise
   - Protein-calorie supplementation
   - Vitamine D
   - Reduction of polypharmacy

4. All persons older than 70 years and all individuals with weight loss ≥ 5% due to chronic diseases should be screened for frailty
CLINICAL RESEARCH STUDY


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Stroke

- Leading cause of mortality in the world
- 4th leading cause of mortality in USA
- 795,000 new cases per year
- The study analyses variations of strokes incidence and mortality during period 1998-2008
  - from a 20% sample of hospitalized Medicare beneficiaries
  - With a principal diagnosis of stroke at discharge
Incidence of stroke

Fang et al. Twenty-year Trends in Stroke Rates and Outcomes in the United States

- 40%

Figure 1  Age-adjusted incidence of ischemic and hemorrhagic stroke in the US Medicare population from 1988 to 2008.
Figure 2  Risk-adjusted 30-day mortality rates after hospitalization for ischemic or hemorrhagic stroke from 1988 to 2008 in a 20% sample of Medicare patients, adjusted for age, region, race, acute/prior myocardial infarction, congestive heart failure, vascular disease, pulmonary disease, dementia, paralysis, diabetes, renal disease, liver disease, ulcer disease, rheumatologic disease, and cancer.
Medications used for prevention

Figure 3  Prevalence of medications used to prevent stroke among 138,821 participants aged ≥65 years in the MCBS (1992-2008).
Clinical significance

• The rate of stroke in USA has declined by 40% from 1998 to 2008

• 30-day mortality decreased over time for both ischemic and hemorrhagic strokes

• The decline in stroke rates paralleled increasing use of antihypertensive and statin medications and might explain the reduction in stroke rate

• This may illustrate how medical interventions have resulted in significant improvement in health on a population level
Delirium

• Delirium affects 11-30% of hospitalized old patients

• Independently associated with
  – Increased length of stay
  – Long-term cognitive and functional decline
  – Higher mortality
  – Patients and carers distress
  – Elevated costs

• Undetected or misdiagnosed in 50-75%

• Recognition can improve outcomes
Validation of the 4AT, a new instrument for rapid delirium screening: a study in 234 hospitalised older people

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\textsuperscript{7}Department of Medicine, University of Roma Tor Vergata, Roma, Italy
The 4A Test: screening instrument for cognitive impairment and delirium

Patient name: 
Date of birth: 
Patient number: 
Date: 
Time: 
Tester: 

[1] ALERTNESS
This includes patients who may be markedly drowsy (eg. difficult to rouse and/or obviously sleepy during assessment) or agitated/hyperactive. Observe the patient. If asleep, attempt to wake with speech or gentle touch on shoulder. Ask the patient to state their name and address to assist rating.

Normal (fully alert, but not agitated, throughout assessment) 0
Mild sleepiness for <10 seconds after waking, then normal 0
Clearly abnormal 4

[2] AMT4
Age, date of birth, place (name of the hospital or building), current year.

No mistakes 0
1 mistake 1
2 or more mistakes/untestable 2

[3] ATTENTION
Ask the patient: “Please tell me the months of the year in backwards order, starting at December.” To assist initial understanding one prompt of “what is the month before December?” is permitted.

Months of the year backwards
Achieves 7 months or more correctly 0
Starts but scores < 7 months / refuses to start 1
Untestable (cannot start because unwell, drowsy, inattentive) 2

[4] ACUTE CHANGE OR FLUCTUATING COURSE
Evidence of significant change or fluctuation in: alertness, cognition, other mental function (eg. paranoia, hallucinations) arising over the last 2 weeks and still evident in last 24hrs

No 0
Yes 4

4 or above: possible delirium +/- cognitive impairment
1-3: possible cognitive impairment
0: delirium or cognitive impairment unlikely (but delirium still possible if [4] information incomplete)

4AT SCORE

GUIDANCE NOTES
The 4AT is a screening instrument designed for rapid and sensitive initial assessment of cognitive impairment and delirium. A score of 4 or more suggests delirium but is not diagnostic: more detailed assessment of mental status may be required to reach a diagnosis. A score of 1-3 suggests cognitive impairment and more detailed cognitive testing and informant history-taking are required. Items 1-3 are rated solely on observation of the patient at the time of assessment. Item 4 requires information from one or more source(s), eg. your own knowledge of the patient, other staff who know the patient (eg. ward nurses), GP letter, case notes, carers. The tester should take account of communication difficulties (hearing impairment, dysphasia, lack of common language) when carrying out the test and interpreting the score.

Alertness: Altered level of alertness is very likely to be delirium in general hospital settings. If the patient shows significant altered alertness during the bedside assessment, score 4 for this item. AMT4 (Abbreviated Mental Test - 4): This score can be extracted from items in the full AMT if done immediately before. Acute Change or Fluctuating Course: Fluctuation can occur without delirium in some cases of dementia, but marked fluctuation usually indicates delirium. To help elicit any hallucinations and/or paranoid thoughts ask the patient questions such as, “Are you concerned about anything going on here?” “Do you feel frightened by anything or anyone?” “Have you been seeing or hearing anything unusual?” In general hospital settings psychiatric symptoms most often reflect delirium rather than functional psychosis (such as schizophrenia).
Methods

Tested in a cross-sectional observational study

- 234 Consecutive patients ≥70yrs (mean 84 yrs)
- Admitted in 3 geriatrics wards
- Various reasons for admission as in real life
- Gold standard: DSMIV-R by expert
- and CAM-IU by clinicians
Methods

• On admission
  – 4AT
  – Delirium diagnosis: DSM-IV-TR by expert
  – Confusion Assessment Method-Intensive Unit (CAM-IU)

• Within 48 h: multi-dimensional assessment
  – Alzheimer’s questionnaire
  – Clinical Dementia Rate
  – Comprehensive Geriatric Assessment
  – Charlson index

• Outcomes measures
  – 4AT accuracy in delirium diagnosis
  – 4AT accuracy in demented/non demented patients
  – Performance of each item in relation to delirium diagnosis
Results

• Study sample: 234 patients
• Mean age: 83.9 +/- 6.1 yrs
• Women 64%
• Delirium: 29 (12%)
• Delirium and dementia: 17 (23%)
## Results

<table>
<thead>
<tr>
<th>Cut-off ≥ 4</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>LR+</th>
<th>LR-</th>
<th>AUROC</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>89.7%</td>
<td>84.1%</td>
<td>5.624</td>
<td>0.123</td>
<td>0.927</td>
</tr>
<tr>
<td>No dementia</td>
<td>83.3%</td>
<td>91.3%</td>
<td>9.615</td>
<td>0.183</td>
<td>0.921</td>
</tr>
<tr>
<td>Dementia</td>
<td>94.1%</td>
<td>64.9%</td>
<td>2.682</td>
<td>0.091</td>
<td>0.891</td>
</tr>
</tbody>
</table>

LR+ et LR- denotes positive and negative likelihood ratio respectively. AUROC denotes the Area Under the Curve.
Take home message

• Delirium is often undetected in acute hospitals
• Th 4A Test is a brief screening tool,
  – Requiring no special training
  – Able to screen patients for delirium
Preventive Effects of Ramelteon on Delirium
A Randomized Placebo-Controlled Trial

Kotaro Hatta, MD, PhD; Yasuhiro Kishi, MD, PhD; Ken Wada, MD, PhD; Takashi Takeuchi, MD, PhD;
Toshinari Odawara, MD, PhD; Chie Usui, MD, PhD; Hiroyuki Nakamura, MD, PhD; for the DELIRIA-J Group
Background

- No medication against delirium have been approved.
- One RCT using CGA may reduce incidence and severity of patients undergoing surgery for hip fracture.
- Haloperidol, risperidone, olanzapine may be efficient but have many adverse effects.
Randomized clinical trial

• Inclusion criteria
  – Patients 65 to 89 yrs old
  – Admitted for serious medical problems via emergency department to intensive care units or regular acute wards
  – Able to take oral medication
  – Able to stay or alive within 48 hours

• Exclusion criteria:
  – Liver dysfunction
  – Lewy Body disease
  – Psychotic or bipolar disorders

• Observation period: 1 week
RCT

• Randomisation by sealed envelopes in two groups
• Intervention: administration of Ramelteon 8mg at 9PM (1 week)
• Patients with insomnia: hydroxyzine 25mg
• Measures: APACHE II score, Charlson, DCR, DRS-R98 every morning
• Reference diagnosis: DSM IV-R
• Number of subjects needed (α:5% - 1-β: 80%)
  32 per group
## Results

<table>
<thead>
<tr>
<th>Clinical outcomes</th>
<th>Placebo group N=34</th>
<th>Ramelteon N=33</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>78.3 +/-6.8</td>
<td>78.2 +/-6.6</td>
<td>.92</td>
</tr>
<tr>
<td>Previous delirium</td>
<td>1</td>
<td>4</td>
<td>2.2</td>
</tr>
<tr>
<td>Stroke</td>
<td>9</td>
<td>12</td>
<td>.44</td>
</tr>
<tr>
<td>Infection</td>
<td>8</td>
<td>4</td>
<td>.34</td>
</tr>
<tr>
<td>Fracture</td>
<td>8</td>
<td>6</td>
<td>.77</td>
</tr>
<tr>
<td>Heart failure/MI</td>
<td>5</td>
<td>3</td>
<td>.71</td>
</tr>
<tr>
<td>Others</td>
<td>4</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Charlson index</td>
<td>2.6 +/-2.2</td>
<td>3.2 +/-2.4</td>
<td>.29</td>
</tr>
<tr>
<td>PS</td>
<td>3.4 +/-0.8</td>
<td>3.2 +/-2.4</td>
<td>.31</td>
</tr>
<tr>
<td>Delirium</td>
<td>11</td>
<td>1</td>
<td>0.003</td>
</tr>
<tr>
<td>Hydroxyzine</td>
<td>3</td>
<td>6</td>
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</table>
## Results
### Sleep parameters

<table>
<thead>
<tr>
<th></th>
<th>Placebo group N=34</th>
<th>Ramelteon N=33</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Difficulty falling asleep</td>
<td>14 (41)</td>
<td>10 (30)</td>
<td>.45</td>
</tr>
<tr>
<td>Difficulty staying asleep</td>
<td>14 (41)</td>
<td>14 (42)</td>
<td>&gt; .99</td>
</tr>
<tr>
<td>Waking too early</td>
<td>5 (15)</td>
<td>7 (21)</td>
<td>.54</td>
</tr>
<tr>
<td>Poor sleep quality</td>
<td>19 (56)</td>
<td>21 (64)</td>
<td>.62</td>
</tr>
<tr>
<td>Disturbance of natural sleep-wake rythm</td>
<td>3 (9)</td>
<td>7 (21)</td>
<td>.19</td>
</tr>
<tr>
<td>Aweakness per night</td>
<td>1.6 (1.2)</td>
<td>1.3 (1.6)</td>
<td>.28</td>
</tr>
<tr>
<td>Sleep duration</td>
<td>6.3 (1.6)</td>
<td>6.3 (1.6)</td>
<td>.67</td>
</tr>
</tbody>
</table>
Results

Figure 2. Scattergrams of Each Patient’s Highest Total Score on the Delirium Rating Scale–Revised-98 (DRS-R98)

Figure 3. Time to Development of Delirium

Each patient was assessed until the development of delirium or up to 7 days. The cutoff score was 14.5. However, 2 patients with dementia in the placebo group had scores of 17 and 19 but did not have a delirium diagnosis according to criteria in the Diagnostic and Statistical Manual of Mental Disorders (Fourth Edition).
Conclusion

• Association with a lower risk of delirium even after controlling for risk factors
• Possible pathogenic role of melatonin in delirium
• More studies required in real life
• No assessment of side effects (anti prolactin linked)
Place and Cause of Death in Centenarians: A Population-Based Observational Study in England, 2001 to 2010

Catherine J. Evans¹,²*, Yuen Ho¹, Barbara A. Daveson¹, Sue Hall¹, Irene J. Higginson¹, Wei Gao¹, on behalf of the GUIDE_Care project

¹ Department of Palliative Care, Policy and Rehabilitation, Cicely Saunders Institute, King’s College London, United Kingdom, ² Sussex Community NHS Trust, Brighton and Hove, United Kingdom
Figure 1. Centenarian deaths by place of death 2001–2010 (n, %). Bar number = % proportion.
doi:10.1371/journal.pmed.1001653.g001
# Centenarians

## All causes of deaths by age group

<table>
<thead>
<tr>
<th>Cause</th>
<th>80-84 848,674</th>
<th>90-94 533,216</th>
<th>100+ 35,867</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>%</td>
<td>95% CI</td>
<td>%</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>6</td>
<td>5.9-6</td>
<td>11.5</td>
</tr>
<tr>
<td>Cerebro-vascular</td>
<td>12.1</td>
<td>12-12.1</td>
<td>14.5</td>
</tr>
<tr>
<td>Ischaemic heart disease</td>
<td>19</td>
<td>18.9-19</td>
<td>12.8</td>
</tr>
<tr>
<td>Dementia</td>
<td>9.4</td>
<td>9.3-9.5</td>
<td>6.7</td>
</tr>
<tr>
<td>Cancer</td>
<td>24.5</td>
<td>24.6-25.4</td>
<td>7.8</td>
</tr>
<tr>
<td>Old age</td>
<td>0.9</td>
<td>0.9-0.9</td>
<td>12.5</td>
</tr>
<tr>
<td>others</td>
<td>13.8</td>
<td>13.9-14</td>
<td>12.9</td>
</tr>
</tbody>
</table>
Thanks for attention

Frailty in Mexico City