Can we improve frailty in older cancer patients?

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(and previously a geriatrician at Guy’s and St Thomas’ NHS Trust)
Declarations

None relevant
Summary

- Frailty in context of health and disease
- Definitions and operationalisations
- Frailty in Cancer: prevalence and significance
- How and when does frailty impact the patient?
- Do we want to change frailty or change outcomes?
- What is potentially amenable to change?
- Can we change these things?
- How do frailty measures reflect the clinical course?
- Take home messages
What do we mean by frailty?

“A long-term condition characterised by lost biological reserves across multiple systems & vulnerability to decompensation after a stressor event”

FIT  MILD  MODERATE  SEVERE

SPECTRUM DISORDER

‘MINOR ILLNESS’

INDEPENDENT

DEPENDENT

Unpredictable recovery
• In the general population

• ~10% of people aged 65
• 25% to 50% of those aged 85 and over
Put frailty in context of the dimensions of health
Genetics and general life exposures

Generalised (diffuse) or single organ age-related changes

Specific risk exposures

Medical conditions eg. cancer

multimorbidity

Impairments (measurable)

Social/Environmental

Frailty

Functional abilities

Social participation

Hr-QOL

Healthcare use

Death
Definitions and Measures of frailty

1. Phenotype (Fried et al)
   - distinct from co-morbidity

2. Deficit accumulation model (Rockwood)
   - risk prediction using disability + impairments + comorbidity +

3. CGA based “impression”
Operative definition of frailty in a general older population – The Cardiovascular Health Study

1. Strength (handgrip) in lowest quintile
2. Gait speed in lowest quintile
3. Unintentional weight loss ≥4.5 kg during last year
4. Increased tendency to exhaustion
5. Usual physical activity in lowest quartile

PHENOTYPE FRAILTY INDEX (PFI)
Frail: ≥3 components
Intermediate (pre-frail): 1 or 2 components
Non frail (robust): 0 components

Is the Frailty Phenotype Distinct?

The relationship of frailty with disability and comorbidity according to the PFI – The Cardiovascular Health Study

- Frailty: 26.6% (n=98)
- Disability: 5.7% (n=21)
- Comorbidity: 46.2% (n=170)
- Total: 21.5% (n=79)

Rockwood Frailty Index
(a deficit accumulation score)

- Based on CGA which includes presence or absence of specific diseases, ADL abilities, physical signs
- Each dichotomised (0/1) or trichotomised (0, 0.33, 0.66, 1.0)
- Add all individual item scores
- Divide by number of items
- Thus the Frailty Index score is between 0 and 1
- Predictive ability improves with more parameters, >30 is enough!
- Good evidence for all outcome prediction

Rockwood et al JAGS 2006; 54:975-979
Deficit approach (eFI) based on primary care data

**Frailty is not good for you**

- Fit
- Mild frailty
- Moderate frailty
- Severe frailty

Reducing proportion alive
Genetics and general life exposures

Generalised (diffuse) or single organ age-related changes

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Chance

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BGS OncoGeriatrics 2019
2305 people 70+ in the clinical examination cohort of the 2nd wave of the Canadian Study of Health and Aging.

From: A Comparison of Two Approaches to Measuring Frailty in Elderly People
Box 1: The CSHA Clinical Frailty Scale

1. Very fit — robust, active, energetic, well motivated and fit; these people commonly exercise regularly and are in the most fit group for their age
2. Well — without active disease, but less fit than people in category 1
3. Well, with treated comorbid disease — disease symptoms are well controlled compared with those in category 4
4. Apparently vulnerable — although not frankly dependent, these people commonly complain of being “slowed up” or have disease symptoms
5. Mildly frail — with limited dependence on others for instrumental activities of daily living
6. Moderately frail — help is needed with both instrumental and non-instrumental activities of daily living
7. Severely frail — completely dependent on others for the activities of daily living, or terminally ill

Note: CSHA = Canadian Study of Health and Aging.
Mortality prediction: Clinical Frailty Scale

![Graph showing survival probability over time for different frailty scores.](image-url)

Rockwood CMAJ 2005
Extension of the CFS-case finding

Clinical Frailty Scale*

1 Very Fit – People who are robust, active, energetic and motivated. These people commonly exercise regularly. They are among the fittest for their age.

2 Well – People who have no active disease symptoms but are less fit than category 1. Often, they exercise or are very active occasionally, e.g. seasonally.

3 Managing Well – People whose medical problems are well controlled, but are not regularly active beyond routine walking.

4 Vulnerable – While not dependent on others for daily help, often symptoms limit activities. A common complaint is being “slowed up”, and/or being tired during the day.

5 Mildly Frail – These people often have more evident slowing, and need help in high order IADLs (finances, transportation, heavy housework, medications). Typically, mild frailty progressively impairs shopping and walking outside alone, meal preparation and housework.

6 Moderately Frail – People need help with all outside activities and with keeping house. Inside, they often have problems with stairs and need help with bathing and might need minimal assistance (cuing, standby) with dressing.

7 Severely Frail – Completely dependent for personal care, from whatever cause (physical or cognitive). Even so, they seem stable and not at high risk of dying (within ~ 6 months).

8 Very Severely Frail – Completely dependent, approaching the end of life. Typically, they could not recover even from a minor illness.

9. Terminally Ill – Approaching the end of life. This category applies to people with a life expectancy <6 months, who are not otherwise evidently frail.

Scoring frailty in people with dementia

The degree of frailty corresponds to the degree of dementia. Common symptoms in mild dementia include forgetting the details of a recent event, though still remembering the event itself, repeating the same question/story and social withdrawal.

In moderate dementia, recent memory is very impaired, even though they seemingly can remember their past life events well. They can do personal care with prompting.

In severe dementia, they cannot do personal care without help.


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Genetics and general life exposures

Generalised (diffuse) or single organ age-related changes

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Death
Hybrid – CGA type approach

### Edmonton Frail Scale

<table>
<thead>
<tr>
<th>Frailty Domain</th>
<th>Item</th>
<th>0 points</th>
<th>1 point</th>
<th>2 points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cognition</td>
<td>Clock drawing</td>
<td>No errors</td>
<td>Minor spacing</td>
<td>Other errors</td>
</tr>
<tr>
<td>General health status</td>
<td>In the past year, how many times have you been admitted to a hospital?</td>
<td>0</td>
<td>1-2</td>
<td>&gt;2</td>
</tr>
<tr>
<td></td>
<td>In general, how would you describe your health?</td>
<td>'Excellent'</td>
<td>'Fair'</td>
<td>'Poor'</td>
</tr>
<tr>
<td></td>
<td>'Very good'</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Functional independence</td>
<td>With how many of the following activities do you require help?</td>
<td>0-1</td>
<td>2-4</td>
<td>5-8</td>
</tr>
<tr>
<td></td>
<td>(meal preparation, shopping, transportation, telephone, housekeeping, laundry, managing money, taking medications)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Social support</td>
<td>When you need help can you count on someone who is willing and able to meet your needs?</td>
<td>Always</td>
<td>Sometimes</td>
<td>Never</td>
</tr>
<tr>
<td>----------------</td>
<td>-------------------------------------------------------------------------------------</td>
<td>--------</td>
<td>-----------</td>
<td>-------</td>
</tr>
<tr>
<td>Medication use</td>
<td>Do you use five or more different prescription medications on a regular basis?</td>
<td>No</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td></td>
<td>At times, do you forget to take your prescription medications?</td>
<td>No</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Nutrition</td>
<td>Have you recently lost weight such that your clothing has become looser?</td>
<td>No</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Mood</td>
<td>Do you often feel sad or depressed?</td>
<td>No</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Continence</td>
<td>Do you have a problem with losing control of urine when you don't want to?</td>
<td>No</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Functional performance</td>
<td>Timed up and go</td>
<td>0-10s</td>
<td>11-20s</td>
<td>&gt;20s Unwilling/ unable</td>
</tr>
</tbody>
</table>
Genetics and general life exposures

Generalised (diffuse) or single organ age-related changes

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Edmonton

Guy’s and St Thomas’ NHS Foundation Trust
So.......... 

Frailty measures are different in focus 

Therefore probably different in who they detect and in amenability to change
Frailty in Cancer
• 22 studies from 20 cohorts evaluating 2912 participants
• 16 used CGA as the reference standard for frailty diagnosis
• 5 used the phenotype model

- median prevalence of frailty: 42% (range 6%–86%)
- and pre-frailty was 43% (range 13%–79%)
- 32% (range 11%–78%) classified as fit.
- CGA based prevalence was much higher than Fried phenotype
Association between baseline frailty (or pre-frailty) and mortality

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>log (Hazard ratio)</th>
<th>SE</th>
<th>Frailty or pre-frailty</th>
<th>Total</th>
<th>Fit Total</th>
<th>Hazard ratio IV, Random, 95% CI</th>
<th>Hazard ratio IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1.1 30 day post-operative mortality (frailty)</td>
<td>0.98207847</td>
<td>0.46351139</td>
<td>75</td>
<td>21</td>
<td>2.67 (1.08, 6.62)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kristjansson 2012</td>
<td>0.84586827</td>
<td>0.33835281</td>
<td>80</td>
<td>21</td>
<td>2.33 (1.20, 4.52)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.1.3 6 month mortality (frailty)</td>
<td>1.50629715</td>
<td>1.1308676</td>
<td>47</td>
<td>38</td>
<td>4.51 (0.49, 41.38)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Puts 2011</td>
<td>1.3506718</td>
<td>1.14175318</td>
<td>27</td>
<td>38</td>
<td>3.86 (0.41, 36.18)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.1.4 6 month mortality (Pre-frailty)</td>
<td>1.3506718</td>
<td>1.14175318</td>
<td>27</td>
<td>38</td>
<td>3.86 (0.41, 36.18)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Puts 2011</td>
<td>0.62593843</td>
<td>0.16235235</td>
<td>146</td>
<td>514</td>
<td>1.87 (1.36, 2.57)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.1.5 5 year mortality (frailty)</td>
<td>0.55388511</td>
<td>0.11513048</td>
<td>146</td>
<td>514</td>
<td>1.74 (1.39, 2.18)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Figure 2.** Forest plot showing the association between frailty, pre-frailty and mortality (adjusted data).
Association between baseline frailty (or pre-frailty) and complications, tolerance or toxicity

Figure 3. Forest plot demonstrating the association between frailty, pre-frailty and treatment complications (adjusted data).
Who should be assessed in detail?
Results: Forty-four studies reporting on the use of 17 different screening tools in older cancer patients were identified. The tools most studied in older cancer patients are G8, Flemish version of the Triage Risk Screening Tool (fTRST) and Vulnerable Elders Survey-13 (VES-13).

G8 had better overall predictive value for the presence of issues apparent when a full GA was performed
• Reduced food intake
• Weight loss
• BMI
• Mobility
• Depression/dementia
• 3+ medications
• Self rated health
• Age (in bands)
Receiver operating curve for the G-8 screening tool against the reference exam consisting of seven comprehensive geriatric assessment questionnaires (> abnormal score vs none)
Accuracy of the G-8 geriatric-oncology screening tool for identifying vulnerable elderly patients with cancer according to tumour site: The ELCAPA-02 study

Fig. 2 – Proportion of abnormal CGA and G-8 according to tumour site and metastatic status (A: without metastases; B: with metastases). Abbreviations: CGA, Comprehensive Geriatric Assessment; GI, Gastro-Intestinal; G-8, Geriatric 8.
What can we learn from all this?

• Frailty is generally common and it matters
• Prevalence varies widely between cancer types
• The G8 screen performs a bit differently across cancers
Could CGA alter frailty and if so, how quickly?
Could CGA alter frailty and if so, how quickly?

Firstly, what does cancer and treatment do to measures of Frailty?
A clinical case

4 months of chemo, then a short extra blast and then autologous BMT

<table>
<thead>
<tr>
<th>Frailty assessment</th>
<th>Baseline</th>
<th>Peak of illness</th>
<th>3 months later</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phenotype (0-5)</td>
<td>0</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>Deficit eFl (0-1)</td>
<td>0</td>
<td>0.20</td>
<td>0.03</td>
</tr>
<tr>
<td>CFS (1-9)</td>
<td>3</td>
<td>7</td>
<td>3</td>
</tr>
<tr>
<td>Edmonton (0-17)</td>
<td>1</td>
<td>11</td>
<td>3</td>
</tr>
</tbody>
</table>
So can we, and **do we need** to reduce frailty or improve outcomes?

Since the key notion of frailty is vulnerability to adverse outcomes, ..... 

then reducing adverse outcomes could be interpreted as improving frailty
Opportunities to intervene

- At a baseline assessment before treatment
  - Therapy to improve fitness etc
- At decisions on treatment
  - Reduce the magnitude of stressor (treatment)
- During treatment
  - Therapies to reduce impairments
  - Earlier detection of deterioration
  - Better responses to deterioration
- After treatment
  - Generic frailty type rehabilitation
Any examples?
# Randomized clinical trial of comprehensive geriatric assessment and optimization in vascular surgery

J. S. L. Partridge, D. Harari, F. C. Martin, J. L. Peacock, R. Bell, A. Mohammed, and J. K. Dhesi

1Proactive Care of Older People undergoing Surgery (POPS), Department of Ageing and Health, and 2Department of Vascular Surgery, Guy’s and St Thomas’ NHS Foundation Trust, and 3Division of Health and Social Care Research, King’s College London, London, UK

## Randomized clinical trial

<table>
<thead>
<tr>
<th>Intervention group n=91</th>
<th>Control group n=85</th>
<th>Significance of difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Length of hospital stay (days)</td>
<td>3.3</td>
<td>5.5</td>
</tr>
<tr>
<td>Post operative delirium</td>
<td>9 (11%)</td>
<td>22 (24%)</td>
</tr>
</tbody>
</table>
Optimisation focused on novel areas eg fatigue

Effects

- More people completed treatment as planned
- Fewer had toxicity
- Fewer days in hospital
- Popular with oncologists and patients!
Take home messages

• Frailty matters and cancer and cancer treatment makes it worse

• There is not likely one frailty measure that suits all purposes

• So best to be familiar with the specific in each case and be clear what is the intention of the assessment