Prospective evaluation of frail preoperative thoracic surgical patients

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Memorial Sloan Kettering Cancer Center
New York, New York

Michigan Society of Thoracic and Cardiovascular Surgery
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Older cancer patients in general are at higher risk for adverse surgical outcomes*. 

90-day mortality in hepatic surgery:
Patients age <75: 2.5%; patients age >75: 4.8%

Older cancer patients in general are at higher risk for adverse surgical outcomes*. 

NB: This is not the same as
‘Frailty’

• Components:
  – Preexisting deficits (e.g. paresis or cognitive dysfunction)
  – Preexisting medical conditions (e.g. CHF)
  – Decreased physiologic and functional reserve

• Not all of the elderly are frail and not all of the frail are old

• Frailty may be reversible with ‘pre-habilitation’
<table>
<thead>
<tr>
<th></th>
<th>Fit (n=33)</th>
<th>Frail (n=24)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colorectal Operations</td>
<td>21%</td>
<td>58%</td>
<td>0.016</td>
</tr>
<tr>
<td></td>
<td>One or more complications</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiac Operations</td>
<td>17%</td>
<td>56%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>One or more complications</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Robinson et al.  
Simple frailty score predicts post-operative complications across surgical specialties  
Prospective evaluation of frail preoperative thoracic surgical patients

- Development of a feasible, efficient, and effective assessment of patient fitness/frailty
- Analysis of prospective data collected to date
- Implications for clinical care of the lung cancer patient
‘eRFA”: Electronic Rapid Fitness Assessment

Web-based patient and care-giver self-reporting

RNs administer Mini-Cog and Timed Up & Go (TUG) and enter the result

Final report
For electronic medical record

WebCore database
Collated with institutional databases

Armin Shahrokn
Final Report

Questionnaire completed by: Patient, with other assistance.

MiniCog test results: Clock drawing: No results entered; Recalled words: No results entered.

Get up and Go test results: <10 seconds.

SOCIO-DEMOGRAPHIC

Marital status: Married.

Highest level of education: College graduate.

Living situation: Living with family or partner.

Smoker status: Never

Tobacco products used other than cigarettes: None.

Alcohol use: 1 drink per day.

PERFORMANCE / FUNCTIONAL STATUS

Functional status: Able to carry on normal activity, minor symptoms.

KPS: 90.

Home care services: No.

Activities limited by health:
Not limited: Bathing; Dressing; Grooming; Feeding; Walking inside the home; Walking outside the home.
Limited a little: Bladder and bowel control.

Total "ADL" Score: 13.

Able to:
Without help: Use the telephone; Go shopping; Prepare meals; Do house work; Handle own medications; Handle money; Visit your doctor.

With some help: Do Laundry.

Total "(ADL)" Score: 15.

Fall(s) in the past year: No.

Devices: Cane.

Vision: Good.

Reading glasses: Yes; Improvement with glasses: A great deal.

Distance vision glasses: Yes; Improvement with glasses: A great deal.

Hearing: Poor.

Hearing aids: No.

SOCIAL SUPPORT

How often do you have someone:

To help with chores when sick: Most of the time.
To turn to with personal problem: Some of the time.
To do something enjoyable with: All the time.
To love and make you feel wanted: All the time.

Total "Social Support" Score: 17.
Visual representation of frailty domains

Fit patient

Frail patient

- ADL
- iADL
- SS
- SA
- GDS
- Distress
- KPS
- Cog
- TUG
- Weight
- Med
- Fall
- Med
Time to complete the eRFA

- $N = 3066$
- Median: 11 minutes
- Mean: 10 minutes
- 90% percentile: 21 minutes

Overall completion rate: 95%
Completion rate without assistance: 80%
<table>
<thead>
<tr>
<th>Instrument</th>
<th>Score Range</th>
<th>Abnormal Score</th>
<th>Prevalence of abnormal score*</th>
</tr>
</thead>
<tbody>
<tr>
<td>KPS</td>
<td>30 to 100</td>
<td>≤80</td>
<td>37%</td>
</tr>
<tr>
<td>ADL</td>
<td>0 to 14</td>
<td>&lt; 14</td>
<td>52%</td>
</tr>
<tr>
<td>iADL</td>
<td>0 to 16</td>
<td>&lt; 16</td>
<td>45%</td>
</tr>
<tr>
<td>Fall in the past year</td>
<td>No fall, one fall, more than one fall</td>
<td>One fall or more</td>
<td>25%</td>
</tr>
<tr>
<td>Timed Up and Go</td>
<td>&lt; 10 seconds, 10-19 seconds, 20 seconds or more</td>
<td>≥ 10 seconds</td>
<td>37%</td>
</tr>
<tr>
<td>Mini-Cog</td>
<td>0 to 5</td>
<td>&lt; 3</td>
<td>16%</td>
</tr>
<tr>
<td>Social Support</td>
<td>4 to 20</td>
<td>≤ 16</td>
<td>43%</td>
</tr>
<tr>
<td>Social Activity Limitation</td>
<td>3 to 15</td>
<td>≥ 8</td>
<td>50%</td>
</tr>
<tr>
<td>Weight change</td>
<td>No change, less than 5 pounds weight loss, 5 to 10 pounds weight loss, 10 to 20 pounds weight loss, more than 20 pounds weight loss</td>
<td>10 pound loss or more</td>
<td>16%</td>
</tr>
<tr>
<td>Distress</td>
<td>0 to 10</td>
<td>≥ 4</td>
<td>55%</td>
</tr>
<tr>
<td>Depression</td>
<td>0 to 4</td>
<td>≥1</td>
<td>55%</td>
</tr>
<tr>
<td>Number of medications</td>
<td>No medication, less than 5 medications, 5 to 10 medications, more than 10 medications.</td>
<td>≥5</td>
<td>45%</td>
</tr>
<tr>
<td>Comorbid conditions</td>
<td>0 to 13</td>
<td>≥4</td>
<td>60%</td>
</tr>
</tbody>
</table>

*Based on preoperative evaluation of 2700 older cancer patients at MSKCC.
Frequency of frailty in surgical patients

Deficits reported by 117 thoracic patients age >75 undergoing in-patient procedures at Memorial Hospital:

- >50% meet definition of geriatric frailty

Deficits reported by 1017 non-thoracic patients age >75 undergoing in-patient procedures at Memorial Hospital:

- >55% meet definition of geriatric frailty
Outcomes after ICU admission: 1100 in-patient non-thoracic surgical patients at MH

Overall rate of ICU admission: 4.5% (57 patients).

ICU admission rate: 6% for frail patients and 2.5% for fit patients.

Hazard rate for overall mortality:
- Fit patients admitted to ICU vs. fit patients who were not: 4.14, p=0.01
- Frail patients admitted to ICU vs. frail patients who were not: 3.30, p<0.001
Hazard ratio for mortality for frail patients (>4 deficits) is 2.2

Survival of 117 thoracic surgery patients age >75 undergoing in-patient procedures at MH (fit–blue, frail–green)

Survival of 1017 non-thoracic surgery patients age >75 undergoing in-patient procedures at MH (fit–blue, frail–green)
Colon surgery (N = 233)

Most common aging-related impairments: Distress, disability, multiple comorbid conditions and limited social support

- Distress level (>4)
- Comorbid conditions (>4)
- Limited social activity (>8)
- Geriatric distress scale (>1)
- Social-support score (≤16)
- Instrumental activities of daily living score (≤5)
- Number of medicines (≤5)
- Karnofsky Performance Status (≤80)
- Timed Up and Go (≥10 seconds)
- Fall during past year (≥1 fall)
- Weight change (≥10 pounds)
- Mini-Cog (≥2)
Six Factors significantly correlated with relative risk of death: KPS, ADL, iADL, weight loss, limited social activity, and slow gait speed.
Frailty significantly correlated with relative risk of death in colorectal patients

P < 0.05
Result: Frailty and colorectal cancer surgery

The overall mortality of FRAIL patients with > 2 (out of 6) impairments was 4.8 x more than FIT patients with 2 or fewer impairments

(HR=4.8, p=0.005)
Outpatient surgery: Correlation between eRFA and 30 day ER visit

30 day UCC visit
30 day ICU admission
30 day mortality
90 day mortality
180 day mortality
One year mortality

P<0.05
Outpatient surgery: UCC visit associated with worse survival after controlling for frailty

HR=1.81, p=0.035

Multivariate analysis adjusting for eRFA variables associated with 30 day UCC visit.
Frail thoracic patients have higher rates of ICU and ER use, and readmission (n = 117)

Total Grade 2 and 3 complications:
Fit: 17%
Frail: 20%
Frail thoracic patients do not have higher rate of complications (n = 117)

Total Grade 2 and 3 complications:
Fit: 17%
Frail: 20%
Lung resections on 122 patients at Memorial Hospital after preoperative frailty assessment

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Count</th>
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<tbody>
<tr>
<td>Pneumonectomy</td>
<td>0</td>
</tr>
<tr>
<td>Lobectomy or bilobectomy</td>
<td>56</td>
</tr>
<tr>
<td>Thoracotomy</td>
<td>12</td>
</tr>
<tr>
<td>VATS</td>
<td>43</td>
</tr>
<tr>
<td>Segmentectomy</td>
<td>9</td>
</tr>
<tr>
<td>Thoracotomy</td>
<td>2</td>
</tr>
<tr>
<td>VATS</td>
<td>7</td>
</tr>
<tr>
<td>Wedge (single or multiple)</td>
<td>57</td>
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<tr>
<td>Thoracotomy</td>
<td>4</td>
</tr>
<tr>
<td>VATS</td>
<td>53</td>
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Demographics of lung resection patients at Memorial Hospital after preoperative frailty assessment

<table>
<thead>
<tr>
<th>Demographic</th>
<th>Value</th>
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</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>122</td>
</tr>
<tr>
<td>Female</td>
<td>69 (57%)</td>
</tr>
<tr>
<td>Age – range (median)</td>
<td>19-93 (77)</td>
</tr>
<tr>
<td>Frail ≥ 4 deficits</td>
<td>62 (51%)</td>
</tr>
<tr>
<td>Fall in past year</td>
<td>16%</td>
</tr>
<tr>
<td>Cognitive dysfunction</td>
<td>9%</td>
</tr>
<tr>
<td>Timed up and go</td>
<td>20%</td>
</tr>
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</table>
Frail lung resection patients do not have higher rates of complications (n = 122)

<table>
<thead>
<tr>
<th>Complication</th>
<th>Fit</th>
<th>Frail</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 1</td>
<td>4%</td>
<td>15%</td>
</tr>
<tr>
<td>Grade 2</td>
<td>11%</td>
<td>13%</td>
</tr>
<tr>
<td>Grade 3</td>
<td>2%</td>
<td>2.6%</td>
</tr>
<tr>
<td>Grade 4</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Grade 5</td>
<td>0%</td>
<td>0%</td>
</tr>
</tbody>
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<table>
<thead>
<tr>
<th>Outcome</th>
<th>Fit</th>
<th>Frail</th>
</tr>
</thead>
<tbody>
<tr>
<td>LOS</td>
<td>4.0</td>
<td>4.9</td>
</tr>
<tr>
<td>30 day UCC</td>
<td>0%</td>
<td>16%</td>
</tr>
<tr>
<td>30 day readmission</td>
<td>0%</td>
<td>11%</td>
</tr>
<tr>
<td>30 day ICU</td>
<td>2%</td>
<td>5%</td>
</tr>
<tr>
<td>Mortality</td>
<td></td>
<td></td>
</tr>
<tr>
<td>30 day</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>90 day</td>
<td>0%</td>
<td>3%</td>
</tr>
<tr>
<td>6 month</td>
<td>0%</td>
<td>6%</td>
</tr>
<tr>
<td>12 month</td>
<td>6%</td>
<td>5%</td>
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Frail lung resection patients have higher rates of ICU/ER use, and readmission (n = 122)

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</tr>
<tr>
<td>Grade 4</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
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<td>0%</td>
<td>0%</td>
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<td>5%</td>
</tr>
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<td></td>
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<td>0%</td>
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</tr>
<tr>
<td>6 month</td>
<td>0%</td>
<td>6%</td>
</tr>
<tr>
<td>12 month</td>
<td>6%</td>
<td>5%</td>
</tr>
</tbody>
</table>
Frailty

‘You cannot say that an event is more likely than another but you can state with confidence that a structure is more fragile than another should a certain event happen.’

Nassim Nicholas Taleb
Author: *The Black Swan*
Total number patients: 174 (5 surgeons; three MH sites)
Men: 77  Women: 97
Operation date (range): 4/15/15 – 3/5/18
Date of birth (range; median): 11/30/22 – 8/25/97; 3/23/40
Race:  Asian: 20
       Black: 7
       White: 135
       Not recorded: 12
Smoking history
       Current 9
       Former 106
       Never 59
Pulmonary function tests
       FEV\(_1\) (N = 155) (range; median): 29-198% predicted; 99%
       DLCO (N = 151) (range; median): 37-177% predicted; 81%
Induction therapy
       Chemotherapy 21
       Radiation therapy 0
Surgical approach
       VATS: 118 (35 with robot)
       VATS converted to thoracotomy: 11
       Thoracotomy: 42
       Median sternotomy/hemiclamshell: 3
Lung resection
       Lobectomy: 66
       Bilobectomy: 2
       Pneumonectomy: 0
       Segmentectomy: 17
       Wedge (single or mult): 88
Location of anatomic lung resection:
       Bilobectomy: RUL/RML 2
       Lobectomy (N = 66):
       LUL: 13
       LLL: 7
       RUL: 22
       RML: 10
       RLL: 14
       Segmentectomy (N = 17):
       LLL: 3
       LUL: 7
       RLL: 4
       RML: 3
Associated major procedures:
       Thymectomy/resection mediastinal mass: 5
Pathology
       Lung:
       Benign 9
       Lung cancer 114
       Pulmonary metastases: 45
       Thymic/mediastinal neoplasm: 5
       Pleural neoplasm (benign fibrous tumor): 1
Univariate analysis of association between components of frailty and outcomes for 182 lung resection patients

Not many adverse events:
- ICU admission 3%
- ER visit 7%
- Readmission 3%
- 90-day mortality 0.7%

<table>
<thead>
<tr>
<th>Component</th>
<th>N = 133</th>
<th>N = 26</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital Length of Stay &lt; 5 days</td>
<td>15.14</td>
<td>14.33</td>
<td>0.04</td>
</tr>
<tr>
<td>Hospital Length of stay &gt; 5 days</td>
<td>7 (5.8%)</td>
<td>7 (14.9%)</td>
<td>0.05</td>
</tr>
<tr>
<td>iADL (mean/SD)</td>
<td>16 (15.4%)</td>
<td>8 (38.1%)</td>
<td>0.01</td>
</tr>
<tr>
<td>Weight loss &gt; 10 pounds in the past 6 months</td>
<td>12 (8.5%)</td>
<td>2 (40.0%)</td>
<td>0.01</td>
</tr>
<tr>
<td>Distress Level (mean/SD)</td>
<td>4.23</td>
<td>6.60</td>
<td>0.03</td>
</tr>
<tr>
<td># of comorbid conditions (mean/SD)</td>
<td>3.31</td>
<td>5.40</td>
<td>0.01</td>
</tr>
<tr>
<td>No ICU admission</td>
<td>153</td>
<td>5</td>
<td>0.03</td>
</tr>
<tr>
<td>ICU admission</td>
<td>13.29</td>
<td>11.80</td>
<td>0.03</td>
</tr>
<tr>
<td>No Emergency room visit (N = 147)</td>
<td>90.75</td>
<td>82.50</td>
<td>0.02</td>
</tr>
<tr>
<td>Emergency room visit (N = 12)</td>
<td>13.32</td>
<td>12.30</td>
<td>0.03</td>
</tr>
<tr>
<td>Impaired TUG</td>
<td>19 (16.4%)</td>
<td>5 (55.5%)</td>
<td>0.004</td>
</tr>
<tr>
<td>Cognitive impairment</td>
<td>12 (10.2%)</td>
<td>3 (33.3%)</td>
<td>0.03</td>
</tr>
<tr>
<td>Limited Social activity score (mean/SD)</td>
<td>7.66</td>
<td>9.00</td>
<td>0.05</td>
</tr>
<tr>
<td>Depression score (mean/SD)</td>
<td>0.78</td>
<td>1.44</td>
<td>0.04</td>
</tr>
<tr>
<td>KPS (mean/SD)</td>
<td>14.96</td>
<td>13.00</td>
<td>0.04</td>
</tr>
<tr>
<td>ADL (mean/SD)</td>
<td>0.78</td>
<td>0.79</td>
<td>0.05</td>
</tr>
<tr>
<td>IADL (mean/SD)</td>
<td>7.66</td>
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<td>0.04</td>
</tr>
<tr>
<td>Depression score (mean/SD)</td>
<td>0.79</td>
<td>1.72</td>
<td>0.04</td>
</tr>
</tbody>
</table>
Results- Those dependent in completing eRFA were more likely to have the eRFA impairment (and be frail).
Patients dependent on completing the eRFA are at higher risk for mortality

HR=1.57 (1.22-2.0)
After adjustment for age, gender, operation time, and ASA PS
Frailty - Conclusions

1. Preoperative assessment of frailty can be performed efficiently for the thoracic surgical patient

2. The frail thoracic patient may not be at increased risk for postoperative complications

3. The frail thoracic patient may have a more difficult time recovering from a complication when it occurs
Frailty – Next steps

A. Create a prognostic nomogram integrating:
   1. cTNM
   2. Frailty index
   3. PET SUV
   4. Pulmonary function

B. Interventions:
   1. Avoidance/treatment of delirium
   2. Medical co-management, including after discharge
   3. ‘Pre-habilitation

C. Prospective trial of surgery vs RT stratified by frailty
Prehabilitation

‘Whilst the evidence for PR prior to thoracic surgery is generally supportive, it has so far been cumulatively of low quality.’

Mahendran K, Naidu B. The key questions in rehabilitation in thoracic surgery
*J Thorac Dis* 2018;10(Suppl 8):S924-S930

Open questions:
1. Characterization of high risk patients for intervention based on overall frailty integrated with pulmonary function
2. Development of focused interventions for components of frailty (e.g. cognitive dysfunction vs poor exercise tolerance)
3. Estimate cost and magnitude of the benefit?
4. Integration with ERAS programs (e.g. increased risk of delirium leads to altered anesthesia and pain management)
Comparing Outcomes of Patients With Early-Stage Non-Small-Cell Lung Cancer Treated With Stereotactic Body Radiotherapy Based on Frailty Status

Govind Raghavan,1 Narek Shaverdian,2 Shawna Chan,3 Fang-I. Chu,2 Percy Lee1

- Retrospective
- Same radiation dose in each group (50-54 Gy)
- Frail group more male (51% vs. 28%; p = .007)
- Frail group older (88% >70 vs 65%; p = .01)
- Local and distant control, recurrence free survival all lower in frail patients
- 18% frail pts and 31% fit patients had no tissue diagnosis of cancer

<table>
<thead>
<tr>
<th>Frailty Status</th>
<th>Total Number</th>
<th># Dead</th>
<th># Alive</th>
<th>Median Survival (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>non-frail</td>
<td>91</td>
<td>21</td>
<td>70</td>
<td>-</td>
</tr>
<tr>
<td>frail</td>
<td>49</td>
<td>22</td>
<td>27</td>
<td>58.7</td>
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Clinical Lung Cancer (in press)
Retrospective
Same radiation dose in fit and frail group
Local and distant control, recurrence free survival (62% vs 34%) all lower in frail patients
18% frail pts and 21% fit patients had no tissue diagnosis of cancer
The eRFA Team

Geriatric RNs: Kathy Romano, Elma Thomas, Carol Koehne.
BMT RNs: Soni Brown, Jennifer Ayala, Ashley Brennan
Dataline data manager: Joseph Schmeltz
Geriatric Physician Office Assistants: Casida Caines, Mannaza Kalsee, Keji Xharo