Disclosures

• None
Outline of Talk

• Introduction
  – Defining the “elderly”
  – Chronological v Biological age
  – Demographics & Epidemiology of Cancer in the Elderly
• Approach to decision making
• Tools in treatment planning
• Treatment of specific cancers
  – Breast
  – Colorectal
  – Lung
• Case studies
Defining the Elderly
Chronological Age v Biological Age
The problem

• Cancer more difficult to diagnose in elderly
  – Atypical presentation
  – General symptoms
  – Co morbidities

• Older patients less likely to get effective cancer treatment
  – Under / Late diagnosis
  – Despite evidence they can tolerate and benefit
    • Ageism
    • Paternalistic assumptions
    • Reduce access to care
  – Treatment decisions are difficult

• Under-representation in clinical trials, less data

ESMO Handbook of Cancer in the Senior Patient, 2010
Browner, Applications in Geriatric Oncology. Retrieved from: http://www.hopkinsmedicine.org
Case 1

81y, Chinese, Male, Ex smoker

PMHx: BPH, gastric ulcer, hypertension, hyperlipidaemia, impaired glucose tolerance

R scapular pain x 2/12
For the last 1-2/52:
decline in performance status,
increase in R sided weakness,
numbness and pain,
declining appetite
Now bedbound, fully dependent on ADL (previously ADL independent)
Case 2

74y, Chinese, Female

ECOG 1

PMHx: HTN

Presents with L breast lump and itch x 1-2/12

Treated with antibiotics for cellulitis

Trucut biopsy: invasive ductal carcinoma, ER – PR – HER2 –
Case 3

78y Chinese Female
ECOG 0

PMHx: Nil

Known case of liver limited metastatic sigmoid colon dx Feb’08 (dx age 75)
Apr ‘08 L hemicolecotomy (Histo: pT3N0)
**Declined chemotherapy**
Aug’08 Open resection of liver segment VII & VIII
(Histo: met adenoCa, margins +)
On surveillance since with colorectal surgeons
Repeatedly declines scans / med onc TCU
- Last CT on system 2010: RLL lung mass 2 x 0.9cm
It’s now 2013, she shows up to clinic because after 5 years, her surgeon finally manages to convince her to come (albeit grudgingly!)
What would you do?

? Further cross sectional imaging

? Obtain histological correlation

? Surgery

? Radiotherapy

? Offer systemic treatment

? Best supportive care, no further escalation of care in view of advanced age & co morbidities
Introduction

• Aging population
  – Average life expectancy
  – Population demographics

• Incidence of cancer in the elderly
  – >50% of cancers diagnosed in >65yo
  – >70% of cancer related deaths occur in 65yo
  – Elderly are more prone to develop cancer

• Common cancers
Life Expectancy at Birth

% of citizens aged 65 years and above

2004  | 2009  | 2013  | 2014
---|---|---|---
8.4 | 9.9 | 11.7 | 12.4

*Data from 1980 onwards refer to the resident population. Data for 2014 are preliminary.

Introduction

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  – >70% of cancer related deaths occur in 65yo
  – Elderly are more prone to develop cancer

• Common cancers
## Comparative Major Causes of Death Between 2013 and 2014

<table>
<thead>
<tr>
<th>Cause of Death</th>
<th>2013</th>
<th>2014</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number</td>
<td>Percent</td>
</tr>
<tr>
<td><strong>Natural Causes</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malignant Neoplasms</td>
<td>5,775</td>
<td>30.5</td>
</tr>
<tr>
<td>Heart &amp; Hypertensive Diseases</td>
<td>3,914</td>
<td>20.7</td>
</tr>
<tr>
<td>Lung &amp; Respiratory System Diseases</td>
<td>4,061</td>
<td>21.4</td>
</tr>
<tr>
<td>Cerebrovascular Disease</td>
<td>1,680</td>
<td>8.9</td>
</tr>
<tr>
<td>Kidney &amp; Disorders of Urinary System</td>
<td>963</td>
<td>5.1</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>247</td>
<td>1.3</td>
</tr>
<tr>
<td>Infectious &amp; Parasitic Diseases (Tuberculosis, Septicaemia, etc)</td>
<td>211</td>
<td>1.1</td>
</tr>
<tr>
<td>Other Natural Causes</td>
<td>1,154</td>
<td>6.1</td>
</tr>
<tr>
<td><strong>Accidents and Violence (All Forms)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Accidents</td>
<td>424</td>
<td>2.2</td>
</tr>
<tr>
<td>Suicides</td>
<td>422</td>
<td>2.2</td>
</tr>
<tr>
<td>Other External Causes</td>
<td>87</td>
<td>0.5</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>18,938</td>
<td>100.0</td>
</tr>
</tbody>
</table>

---


Introduction

• Aging population
  – Average life expectancy
  – Population demographics

• Incidence of cancer in the elderly
  – >50% of cancers diagnosed in >65yo
  – >70% of cancer related deaths occur in 65yo
  – Elderly are more prone to develop cancer

• Common cancers
Table 5.3.1: Ten Most Frequent Cancers in Males, 2010-2014

<table>
<thead>
<tr>
<th>Rank</th>
<th>Site</th>
<th>Number</th>
<th>%</th>
<th>CR (95% CI)</th>
<th>ASR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Colo-rectum</td>
<td>5,103</td>
<td>17.2</td>
<td>54.3 (52.8-55.8)</td>
<td>38.2 (37.2-39.3)</td>
</tr>
<tr>
<td>2</td>
<td>Lung</td>
<td>4,454</td>
<td>15.0</td>
<td>47.4 (46.0-48.8)</td>
<td>33.5 (32.5-34.5)</td>
</tr>
</tbody>
</table>

Table 5.3.2: Ten Most Frequent Cancers in Females, 2010-2014

<table>
<thead>
<tr>
<th>Rank</th>
<th>Site</th>
<th>Number</th>
<th>%</th>
<th>CR (95% CI)</th>
<th>ASR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Breast</td>
<td>9,284</td>
<td>29.2</td>
<td>95.8 (93.8-97.7)</td>
<td>64.7 (63.4-66.0)</td>
</tr>
<tr>
<td>2</td>
<td>Colo-rectum</td>
<td>4,221</td>
<td>13.3</td>
<td>43.6 (42.2-44.9)</td>
<td>26.7 (25.9-27.6)</td>
</tr>
<tr>
<td>3</td>
<td>Lung</td>
<td>2,399</td>
<td>7.6</td>
<td>24.8 (23.8-25.7)</td>
<td>15.0 (14.4-15.7)</td>
</tr>
<tr>
<td>4</td>
<td>Corpus uteri</td>
<td>2,089</td>
<td>6.6</td>
<td>21.6 (20.6-22.5)</td>
<td>14.6 (14.0-15.2)</td>
</tr>
<tr>
<td>5</td>
<td>Ovary, etc.</td>
<td>1,719</td>
<td>5.4</td>
<td>17.7 (16.9-18.6)</td>
<td>12.7 (12.1-13.3)</td>
</tr>
<tr>
<td>6</td>
<td>Lymphoid neoplasms</td>
<td>1,410</td>
<td>4.4</td>
<td>14.5 (13.8-15.3)</td>
<td>11.2 (10.5-11.8)</td>
</tr>
<tr>
<td>7</td>
<td>Skin, including melanoma</td>
<td>1,381</td>
<td>4.3</td>
<td>14.2 (13.5-15.0)</td>
<td>8.4 (7.9-8.9)</td>
</tr>
<tr>
<td>8</td>
<td>Thyroid</td>
<td>1,184</td>
<td>3.7</td>
<td>12.2 (11.5-12.9)</td>
<td>9.0 (8.5-9.5)</td>
</tr>
<tr>
<td>9</td>
<td>Stomach</td>
<td>1,115</td>
<td>3.5</td>
<td>11.5 (10.8-12.2)</td>
<td>6.8 (6.4-7.2)</td>
</tr>
<tr>
<td>10</td>
<td>Cervix uteri</td>
<td>1,005</td>
<td>3.2</td>
<td>10.4 (9.7-11.0)</td>
<td>7.1 (6.6-7.5)</td>
</tr>
<tr>
<td></td>
<td>Others</td>
<td>5,962</td>
<td>18.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>All</td>
<td>31,769</td>
<td>100.0</td>
<td>327.8 (324.2-331.4)</td>
<td>217.6 (215.1-220.1)</td>
</tr>
</tbody>
</table>

Aim of Treatment

✓ Improve quality of life
✓ Extend meaningful survival
Approach to decision making

• Estimate life expectancy
  – Actuarial tables
  – Life expectancy calculators e.g. www.eprognosis.com

• Consider prognosis of cancer
  – Tumour biology
  – Stage of cancer

IS THE PATIENT AT RISK OF DYING OR SUFFERING FROM THE CANCER CONSIDERING THE OVERALL LIFE EXPECTANCY
Approach to decision making

• Assessment of general health
  – CGA\textsuperscript{1-4}
    • Detects problems & identify modifiable risk factors
      – Leads to reduction in functional decline
      – Improves QOL (social interaction, mobility, morale)
    • Predict for risk of adverse outcomes
      – Chemo tox, post op M&M
    • Improves therapeutic outcome
    • Prognostic

• Patient factors
  – Assess decision making capacity
  – Assess goals and values $\Rightarrow$ is this consistent with wanting anti-cancer therapy?
  – Social support structure

\textsuperscript{1}Extermann et al JCO 2007
\textsuperscript{2}Pal et al CA Cancer J Clin 2010
\textsuperscript{3}Rodin et al JCO 2007
\textsuperscript{4}Hurria et al Cancer 2005
Comprehensive Geriatric Assessment

- Functional status
  - ECOG¹
  - Get up and go test²
  - BADLs & IADLs
    - Katz index³
    - Lawton scale⁴

- Affective status
  - ECOG¹
  - Geriatric depression scale⁷

- Cognitive status
  - MMSE⁵
  - Clock drawing test⁶

- Co morbidity
  - Charlson Comorbidity Index⁸

- Co morbidity
  - Geriatric syndromes
    - Falls risk
    - Dementia
    - Delirium

- Geriatric syndromes
  - Falls risk
  - Dementia
  - Delirium

- Nutritional status
  - BMI
  - Nutritional screen
    - MNA⁹
    - DETERMINE Index¹⁰

- Poly pharmacy
  - Medication review and reconciliation
  - Evaluate adherence

¹Oken et al Am J Clin Oncol 1982
³Katz et al JAMA 1963
⁴Lawton et al Gerontologist 1969
⁵Folstein et al J Psychiatr Res 1975
⁶Shulman et al Int J Geriatr Psychiatry 2000
⁷van Marwijk et al Br J Gen Pract 1995
⁸Charlson et al J Chronic Dis 1987
⁹Rubenstein et al J Geront 2001
CGA Predicts Chemo-Related Toxicities

Geriatric Factors Predict Chemotherapy Feasibility: Ancillary Results of FFCD 2001-02 Phase III Study in First-Line Chemotherapy for Metastatic Colorectal Cancer in Elderly Patients

Table 3.
Multivariate Analysis for Grade 3 to 4 Toxicity

<table>
<thead>
<tr>
<th>Predictive Factor</th>
<th>OR</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>1.53</td>
<td>0.50 to 4.71</td>
<td>.454</td>
</tr>
<tr>
<td>Primary tumor not resected</td>
<td>1.20</td>
<td>0.34 to 4.21</td>
<td>.779</td>
</tr>
<tr>
<td>No previous adjuvant chemotherapy</td>
<td>3.85</td>
<td>0.67 to 22.03</td>
<td>.130</td>
</tr>
<tr>
<td>Irinotecan arm</td>
<td>5.03</td>
<td>1.61 to 15.77</td>
<td>.006</td>
</tr>
<tr>
<td>Impaired cognitive function (MMSE ≤ 27/30)</td>
<td>3.84</td>
<td>1.24 to 11.84</td>
<td>.019</td>
</tr>
<tr>
<td>Impaired autonomy (IADL)</td>
<td>4.67</td>
<td>1.42 to 15.32</td>
<td>.011</td>
</tr>
<tr>
<td>Better mood</td>
<td>0.41</td>
<td>0.12 to 1.36</td>
<td>.145</td>
</tr>
</tbody>
</table>

Table 4.
Logistic Regression Model Analysis for Early Deaths (within 6 months) That Occurred for All Patients Who Received First-Line Chemotherapy (n = 339)

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Odds Ratio</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>1</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>2.40</td>
<td>1.20 to 4.82</td>
<td>.013</td>
</tr>
<tr>
<td>Tumor stage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Localized</td>
<td>1</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>Advanced</td>
<td>3.9</td>
<td>1.59 to 9.73</td>
<td>.003</td>
</tr>
<tr>
<td>Mini Nutritional Assessment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Good nutrition, score &gt; 23.5</td>
<td>1</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>At risk/poor nutrition, score ≤ 23.5</td>
<td>2.77</td>
<td>1.24 to 6.18</td>
<td>.013</td>
</tr>
<tr>
<td>Timed Get Up and Go</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No impairments (≤ 20 seconds)</td>
<td>1</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>Impaired</td>
<td>2.55</td>
<td>1.32 to 4.94</td>
<td>.006</td>
</tr>
</tbody>
</table>
Nomogram for overall survival of elderly Asian patients with cancer.

Ravindran Kanesvaran et al. JCO 2011;29:3620-3627
Ability of (A) risk score versus (B) physician-rated Karnofsky performance status (KPS) to predict chemotherapy toxicity.

Arti Hurria et al. JCO 2011;29:3457-3465
Limitation of Comprehensive Geriatric Assessment

• Full CGA is time consuming

• Instruments often applied in setting of a clinical study as opposed to real life

• Ongoing research in identifying screening tools as time saving approach
Surgery

• Intent? Curative v Palliative
• Surgical Task Force report from SIOG\textsuperscript{1}
  – Surgical outcomes similar to younger patients
• Pre op assessment – PACE\textsuperscript{2}
  – CGA + fatigue inventory + ASA grade + PS
• Avoid emergent surgery - \textarrow{up} risk of morbidity & mortality
• Post op OT/PT to expedite return to preop function

\textsuperscript{1}Audisio et al EJC 2004
\textsuperscript{2}Audisio et al Oncologist 2005
Radiotherapy

- Intent? Curative v Palliative
- Highly effective and well tolerated
- Caution with chemoRT
- Advanced RT techniques to facilitate normal tissue sparing
- Hypofractionated RT improves tolerability\(^1\)
- Interrupted / incomplete courses of RT compromises efficacy

\(^1\)Donato et al Crit Rev Oncol Hematol 2003
Chemotherapy

- Age alone does not contraindicate chemotherapy
- Increased toxicity due to pharmacokinetics and pharmacodynamic changes a/w aging
- Tools to predict toxicity e.g CRASH score
- Anticipate side effects e.g
  - Cardiac monitoring on anthracycline / trastuzumab
  - Dose adjust for end organ function
  - Prophylactic gCSF as indicated
Tools to Predict Chemotox

### Table 1: Predictors of Chemotherapy Toxicity, and Scoring Algorithm

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age: ≥ 72</td>
<td>2</td>
</tr>
<tr>
<td>Cancer type: gastrointestinal or genitourinary</td>
<td>2</td>
</tr>
<tr>
<td>Chemotherapy dosing: standard dose</td>
<td>2</td>
</tr>
<tr>
<td>Number of chemotherapy drugs: polychemotherapy</td>
<td>2</td>
</tr>
<tr>
<td>Hemoglobin: &lt; 11 g/dL (male), &lt; 10 g/dL (female)</td>
<td>3</td>
</tr>
<tr>
<td>Creatinine clearance (Jelliffe formula – ideal weight): &lt; 34 mL/min</td>
<td>3</td>
</tr>
<tr>
<td>Hearing: described as fair or worse</td>
<td>2</td>
</tr>
<tr>
<td>Number of falls in last 6 months: 1 or more</td>
<td>3</td>
</tr>
<tr>
<td>Needs assistance with taking medications</td>
<td>1</td>
</tr>
<tr>
<td>Limited in walking one block</td>
<td>2</td>
</tr>
<tr>
<td>Decreased social activity because of physical or emotional health</td>
<td>1</td>
</tr>
</tbody>
</table>

**Predictors**

<table>
<thead>
<tr>
<th>Predictors</th>
<th>0</th>
<th>1-2</th>
<th>3-4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hematologic score&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diastolic BP</td>
<td>≤72</td>
<td>&gt;72</td>
<td></td>
</tr>
<tr>
<td>IADL</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LDH (if ULN 618 U/L; otherwise, 0.74/L*ULN)</td>
<td>26-29</td>
<td>10-25</td>
<td>&gt;459</td>
</tr>
<tr>
<td>Chemotox&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0-0.44</td>
<td>0.45-0.57</td>
<td>&gt;0.57</td>
</tr>
<tr>
<td>Nonhematologic score&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ECOG PS</td>
<td>0</td>
<td>1-2</td>
<td>3-4</td>
</tr>
<tr>
<td>MMS</td>
<td>30</td>
<td>&lt;30</td>
<td></td>
</tr>
<tr>
<td>MNA</td>
<td>28-30</td>
<td>&lt;28</td>
<td></td>
</tr>
<tr>
<td>Chemotox&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0-0.44</td>
<td>0.45-0.57</td>
<td>&gt;0.57</td>
</tr>
</tbody>
</table>

**Abbreviations:**
- BP: blood pressure
- Chemotox, toxicity of the chemotherapy regimen (for details, see text)
- ECOG PS, Eastern Cooperative Oncology Group performance status
- IADL, Instrumental Activities of Daily Living
- LDH, lactate dehydrogenase
- MMS, Mini Mental Health Status
- MNA, Mini Nutritional Assessment
- ULN, upper limit of normal

**Footnotes:**
- For the combined score, add the points from the hematologic and nonhematologic score, counting Chemotox only once.
- For examples of Chemotox values for specific regimens, see Table 6.

Extermann et al Cancer 2012
Hurria et al JCO 2011
BREAST CANCER TREATMENT
Early Breast Cancer

• Surgery
  – Mastectomy = BCS + RT
  – SLN v AxLND
• Radiotherapy
• Primary endocrine therapy
  – Consider in frail patients with HR+ breast Ca
  – Inferior to surgery in fit women
• Adjuvant endocrine therapy
• Adjuvant chemotherapy
  – Endocrine sensitive = less responsive to chemo
  – Higher risk disease (LN+) = more benefit from chemo
  – Polychemotherapy superior to single agent (AC > Capecitabine)
  – TC > AC
• Adjuvant Trastuzumab
Advanced Breast Cancer

• Endocrine therapy
  – SERM (Tamoxifen) ; AI (Letrozole, Exemestane, Anastrazole) ; (Fulvestrant) ; Progestins (Megace)
  – Non cross resistant line at PD

• Chemo
  – Rapidly proliferating disease, HR-
  – Single agent preferred
    • Polychemo at expense of tox with no survival benefit
  – Choose chemo with favorable safety profiles
    • Weekly paclitaxel, capecitabine, vinorelbine, gemcitabine

• Biologic agents
  – Trastuzumab in absence of cardiac contraindications
  – Concurrent with chemo / AI

• Bone modifying agents
  – Zolendronic acide ; Denosumab
  – Reduces SRE irrespective of age

• Palliative RT
• Palliative / prophylactic surgery e.g IM nailing
LUNG CANCER TREATMENT
Early NSCLC

- **Surgery**
  - Predictor of negative outcome: poor PS, FEV1 < 60%, FEV1 <1L, ABG parameters
  - After adequate selection, lung cancer surgery is possible but a slight increase in mortality should be anticipated

- **Radiotherapy**
  - Stereotactic radiotherapy as an alternative to surgery
  - Concurrent or sequential with chemo
  - Limited elderly specific prospective data

- **Adjuvant Chemo**
  - Overall 5% improvement of 5y OS
  - Trials are not elderly specific
Advanced NSCLC

• Chemotherapy
  – Single agent vinorelbine, gemcitabine, taxanes improves QoL and survival
    • Supported by elderly specific clinical data
  – Combi chemo
    • Platinum doublet is standard treatment

• Targeted therapy
  – EGFR TKI
    • ORR 70%, PFS 9-10m, OS up to 30+m (overall population)
    • Use only in presence of sensitising EGFR mutation (Exon 19 & 21)
    • Generally well tolerated
    • AE: rash, diarrhoea, abnormal LFT
  – ALK TKI

• Palliative RT
COLON CANCER
Stage 1-3 disease

• Adjuvant chemotherapy
  – Stage 1 observe
  – Stage 2 small benefit
  – Stage 3 improvement in DFS & OS
Metastatic Colon Cancer

• Chemotherapy
  – Infusion 5FU > bolus 5FU with better tox profile
  – Oxaliplatin / Irinotecan
Case 1 Con’t

Staging CT Brain/TAP 4/6/15:
1cm enhancing nodule L cerebellar hemisphere
Large 8.6 x 8.2cm R lung mass
Invasion of chest wall, mediastinum, destruction of R 1\textsuperscript{st}, 2\textsuperscript{nd}, 3\textsuperscript{rd} ribs & T1,T2 vertebrae
Several small nodules in R lung

Underwent CT guided biopsy 23/6/15:
Histo: NSCLC EGFR Exon 19 del+, ALK-

Started on Gefitinib
Case 1 Con’t

8/7/2015

4/9/2015
Case 2 Con’t

CT TAP 19/6/15
4.7 x 4.2cm L breast mass
Prominent but subcentimetre L axillary LN

Bone scan – negative for mets
End organ function normal, 2DE EF 67%

Started on neoadjuvant chemotherapy
Completed 4 cycles of doxorubicin / cyclophosphamide with primary prophylaxis with gCSF

L breast mass 7 x 5.5 cm → 1 x 1.5 cm

Ongoing treatment with curative intent, aim for surgery after 6 months of chemotherapy, patient declines breast conserving surgery
Case 3

Evaluation scans ordered
Case 3

Long discussion on understanding & goals of treatment
Disease slow growing, asymptomatic
Does not desire systemic therapy, AEs nor visits to hospital
Elected to observe
Currently enjoys regular mahjong session & watching getai performances

Nov’14

May’15
Take home message

• Majority of cancer diagnosis & mortalities occur in elderly patients
• Biological age more important than chronological
• Assessing “fitness” is more than gestalt (eye balling)
• CGA is a powerful tool - allows early intervention & prevention
• Avoid under-diagnosis & under treatment
• Elderly adults can tolerate cancer therapies
• Vulnerable & frail benefit from disease & function specific interventions
Questions?

THANK YOU!