Cancer Survivorship and Aging

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Objectives

1- Attitudinally, appreciate that a definition of aging is difficult

2- Recognize the competing risks problem in older cancer survivors

3- Know that functional status reveals heterogeneity of older cancer survivors
Pop Quiz

• What proportion of US Senators are age 65 years or older on Nov 8, 2017?

• What is the median life expectancy of a 90 year old woman in the US?
Case – M.T.

• 90 yo woman
• 1977 Stg I NSCLC (BAC)
  – Left upper lobectomy
• 2001 small population of monoclonal B cells, IgM kappa light chains; 2013 increased to 10%
  – rituximab x 1 cycle
• 2016 T3N0M0 lobular invasive breast ca, ER/PR pos, Her2neu FISH negative
  – letrozole 2.5 daily (CA 15-3 90->45->12 U/mL)
| **Miller 2003** | A process that converts health adults into frail ones with diminished reserves in most physiologic systems and an *exponentially increasing vulnerability* to most diseases and to death. Uniform, broadly-based, deteriorative changes [are] the concern. |
| **Hayflick 2004** | In biological systems, aging is a stochastic process that occurs systemically after reproductive maturity in animals that reach a fixed size in adulthood. It is caused by the escalating loss of molecular fidelity that ultimately exceeds repair capacity and increases *vulnerability* to pathology or age-associated diseases (1–3). The fundamental cause of this molecular disorder is rooted in the intrinsic thermodynamic instability of most complex biological molecules whose precise three-dimensional folded structures cannot be maintained with accuracy indefinitely. |
| **Butler et al. 2004** | The process that converts physiologically and cognitively fit health adults into less fit individuals with increasing *vulnerability* to injury, illness, and death. We are particularly interested in changes in an organism that adversely affect its vitality and functions over most of the adult life span. Biomarkers of aging were defined by participant Richard Miller as traits that meet three criteria: 1. ...should predict the outcome of a wide range of age-sensitive test...better than chronological age; predict remaining longevity at an age at which 90% of the population is still alive....; should not alter life expectancy. |
| **Nuland 2007** | ...most usefully described as the process by which a health individual of any species gradually deteriorates into one that is frail, one whose bodily capacities and reserves are constantly diminishing at an ever-increasing rate, and one who is therefore becoming more and more *vulnerable* to disease and ultimate death. |
Aging in a Population
1. Schematic representation of aging in a population. (A) Survival curve of a hypothetical aging population. The time scale indicates the percentage of maximum lifespan. (B) Gompertz transformation of the underlying survival curve on a semilogarithmic scale.
Figure 2
Age-band specific mortality among 3,533 internally displaced persons due to the 2004 Indian Ocean tsunami in Ampara district, Sri Lanka.
Early September, 2005

49% of identified Hurricane Katrina victims in LA were 75 years and older

>>Burknard et al Disa Med and PH Prep 2008
Aging in an Individual
NEW DETAILS

BRAND NEW IMAGES OF MARATHON BOMBS

MOMENT OF CRISIS AT FINISH LINE
The Paradox of Aging
“In a series of five annual meetings that I chaired recently in an attempt to define common biogerontology terms, the dozen or more experts who attended could not agree on the definition of almost all of them, including “aging.” The committee was disbanded and the communications dilemma remains…. Not only does the problem result in communication failures, it also produces erroneous interpretations of research results; illogical allocation of research funds; and misdirected scientific, economic, social, and political policy decisions [1–3]. There is no other field of science in which a similarly bleak situation exists.”
The Paradox of Aging

Obvious to a 6-year old,
Undefined and Unmeasured by Scientists
“Let’s explore this feeling that people are trying to cheat you.”
A Classical Competing Risks

Baseline

\[ \lambda_1 \]

Primary Event

\[ \lambda_2 \]

Competing Event

B Semi-Competing Risks

Baseline

\[ \lambda_1 \]

\[ \lambda_{2|1} \]

Primary Event

\[ \lambda_2 \]

Competing Event

FIGURE 1. A schematic illustrating (A) classical and (B) semi-competing risks. In (A) either event occurring first makes the other event impossible, whereas in (B) primary event is not possible if the competing event occurs first, but the competing event can still occur if the primary event occurs first. Note \( \lambda \)s are event rates, for example, number of events per 1000 person-years.
<table>
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<th>N</th>
<th>%</th>
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<tr>
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<td>118</td>
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<td>137</td>
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<tr>
<td>80</td>
<td>10</td>
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<tr>
<td>767</td>
<td>100</td>
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Legend:
- Dark Gray - Lions
- Light Gray - Cheetahs, Bears, Wolves

>>Albertsen, Hanley et al. JAMA 1998
**TABLE 3.** Treatment Effect Estimates for 6-Year Event-Free Survival, Cause-Specific Hazards, and 6-Year Cumulative Incidence for Mortality From Different Causes

<table>
<thead>
<tr>
<th>Coefficient</th>
<th>Event-Free Survival</th>
<th>Cause-Specific Hazard</th>
<th>Cumulative Incidence</th>
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<tbody>
<tr>
<td></td>
<td>Cancer</td>
<td>CVD</td>
<td>Other</td>
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<tr>
<td>Treatment</td>
<td>$-0.20 (0.11)$</td>
<td>$0.19 (0.17)$</td>
<td>$-0.57 (0.28)^*$</td>
</tr>
<tr>
<td></td>
<td>$-0.42 (0.17)^*$</td>
<td></td>
<td>$-0.53 (0.28)^*$</td>
</tr>
</tbody>
</table>

*Individual significance at approximately the 5% level at least. Standard errors are given in parentheses.

**FIGURE 2.** Cumulative incidence curves for prostate cancer, cardiovascular disease, and remaining causes of deaths in the treatment and placebo groups. The $P$ values are for testing difference between the 2 groups using Gray's K-sample test ($K = 2$). The $P$ values for comparing the CIFs of placebo and treatment groups for different causes of death are: $P < 0.01$ for cancer, $P = 0.08$ for cardiovascular disease, and $P = 0.05$ for other causes of death.
“It could be one of those things that crawls into your ear and lay eggs, and the eggs hatch and burrow into your—nope. It looks fine.”
Figure. Upper, Middle, and Lower Quartiles of Life Expectancy for Women and Men at Selected Ages

A  Life Expectancy for Women

B  Life Expectancy for Men

Data from the Life Tables of the United States.9
Figure. Upper, Middle, and Lower Quartiles of Life Expectancy for Women and Men at Selected Ages

Data from the Life Tables of the United States.*

> Walter & Covinsky JAMA 2001
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Data from the Life Tables of the United States.9

>>Walter & Covinsky “Cancer Screening...” JAMA 2001
Figure. Upper, Middle, and Lower Quartiles of Life Expectancy for Women and Men at Selected Ages

A  Life Expectancy for Women

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Data from the Life Tables of the United States.®

>>Walter & Covinsky JAMA 2001
Pop Quiz

• What proportion of US Senators are age 65 years or older on Nov 8, 2017?
  – 43%

• What is the median life expectancy of a 90 year old woman in the US?
  – 3.9 years
Case – M.T.

- 90 yo woman
- 1977 Stg I NSCLC (BAC)
  - Left upper lobectomy
- 2001 small population of monoclonal B cells, IgM kappa light chains; 2013 increased to 10%
  - rituximab x 1 cycle
- 2016 T3N0M0 lobular invasive breast ca, ER/PR pos, Her2neu FISH negative
  - letrozole 2.5 daily (CA 15-3 90->45->12 U/mL)
- Deceased dementia, probably Alzheimer’s type
Summary

• To define aging is difficult

• Failure to recognize the competing risks problem in older cancer survivors can lead to poor decisions

• Functional status reveals heterogeneity of older cancer survivors
THANKS