Managing Challenging Issues in Adolescent and Young Adult (AYA) Cancer Survivors:
Cognitive Impairment in AYA Cancer Survivors

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Disclosure

- Nothing to declare
Overview

• Cancer-related cognitive impairment (CRCI)

• Impact of CRCI on AYA survivorship

• Ongoing Initiatives

• Take Home Messages
Adolescent and Young Adult (AYA) Cancer Patients and Survivors

- No consensus globally; commonly known as 15-39 years old at the time cancer diagnosis

- Most highly prevalent cancers within this age group
  - 15-24: Leukemia, lymphoma, testicular cancer, thyroid cancers
  - 25-39: Breast cancer, melanoma

- Many of these cancers are curable
  - 5-year overall survival can exceed 80%

- Unfortunately, AYA cancer survivors often face survivorship issues

Closing the Gap: Research and Care Imperatives for Adolescents and Young Adults with Cancer Report of the Adolescent and Young Adult Oncology Progress Review Group. National Institute of Health and National Cancer Institute; 2006.
Life after cancer

• When compared with age-matched peers without cancer, fewer AYA cancer survivors report being employed.

• AYA cancer survivors incur a substantially greater loss of productivity than older cancer survivors—Due to greater difficulty in returning to full functionality at school or a work.

Guy GP, Jr., et al. Health Affairs 2014; 33(6): 1024-31
Cancer-related cognitive impairment (CRCI)

- Subtle changes in cognitive function in patients who did not receive brain directed therapies
  - *aka* ‘chemobrain’ or ‘chemofog’ in the literature

- The **International Cognition and Cancer Taskforce (ICCTF)** loosely defined ‘cognitive changes’ as:
  - Any changes on neuropsychological tests in the four main cognitive domains of *attention, memory, processing speed* and *response speed*.
  - Self-perceived cognitive impairment is also important

- Increasingly being recognized that this phenomenon is **not** specifically related to the use of chemotherapy

Is CRCI relevant among cancer AYA?

• AYA Health Outcomes and Patient Experience Study (AYA HOPE)
  – Majority diagnosed with germ cell tumors and lymphomas; >70% with Stage 1-2 disease
  – 40% reported “forgetting” as a problem at 6-14 months after diagnosis
  – 53% reported “forgetting” as a problem at 15-35 months after diagnosis
  – One-third found it difficult to pay attention at work or at school after diagnosis

• Important to note that psychological distress is highly prevalent (up to 41%)

Evidence on CRCI in AYA (I)

- Skaali et al
  - Testicular cancer patients (mean age: 32.5 years), tested pre- and post- chemotherapy
  - No significant change in cognitive test performance
  - Cognitive performance was not associated with distress, fatigue or chemotherapy
  - Cognitive complaints, however, were observed shortly after end of chemotherapy, which returned to baseline levels at 12 months

Evidence on CRCI in AYA (II)

- Wefel JS, et al
  - Non-seminomatous germ cell tumor patients receiving chemotherapy (mean age 31 years)
  - Did not evaluate cognitive complaints
  - Cognitive performance wise, detected a decline in learning and memory
    - Post chemotherapy (28%)
    - 12-months follow up (66.7%)
Focus Group Discussion with Singaporean AYAs

• Almost half of our participants (n=6) complained that their treatment had adversely affected their concentration or memory

  I thought my thinking process was slower than normal, [...] I didn’t realize until after I went back to work.

Pt #3, female, 25 yo

I applied for nursing [...] recently they asked me if I want to withdraw out of nursing because of my condition.

Pt #4, female, 21 yo

• Numerous respondents used memory aids such as notebooks.
### Morphological Changes in AYA Brains after chemotherapy?

<table>
<thead>
<tr>
<th></th>
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<tbody>
<tr>
<td><strong>Type of cancer</strong></td>
<td>Hodgkin’s Lymphoma</td>
<td>Testicular Cancer</td>
<td>Breast Cancer</td>
<td>Breast Cancer</td>
</tr>
<tr>
<td><strong>Study design</strong></td>
<td>Longitudinal (3 scans)</td>
<td>Longitudinal (2 scans)</td>
<td>Cross-sectional</td>
<td>Cross-sectional</td>
</tr>
<tr>
<td><strong>Neuro psychological test</strong></td>
<td>√</td>
<td>√</td>
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#### Gray Matter Reductions observed

<p>| | | | | |</p>
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<th></th>
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<tbody>
<tr>
<td><strong>Frontal lobe</strong></td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>√</td>
</tr>
<tr>
<td><strong>Parietal lobe</strong></td>
<td>X (Increase)</td>
<td>√</td>
<td></td>
<td>√</td>
</tr>
<tr>
<td><strong>Temporal lobe</strong></td>
<td></td>
<td></td>
<td>√</td>
<td></td>
</tr>
<tr>
<td><strong>Occipital lobe</strong></td>
<td></td>
<td></td>
<td></td>
<td>√</td>
</tr>
<tr>
<td><strong>Limbic cortex</strong></td>
<td>√</td>
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</tbody>
</table>

Comparison of Brain Morphologies between AYA Cancer Survivors and Healthy Controls

Volume of Gray Matter

<table>
<thead>
<tr>
<th></th>
<th>AYA Cancer Group (mean ± SD), ml</th>
<th>Healthy Control Group (mean ± SD), ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right inferior frontal gyrus</td>
<td>647.4 ± 69.8 ml</td>
<td>706.0 ± 84.8 ml</td>
</tr>
<tr>
<td>Right middle frontal gyrus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left insula</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Chan A, et al. MASCC 2017

www.mascc.org/meeting
Can we use a rapid screening tool to identify AYA cancer patients with CRCI?
Distress Thermometer

NCCN Distress Thermometer for Patients

SCREENING TOOLS FOR MEASURING DISTRESS

Instructions: First please circle the number (0-10) that best describes how much distress you have been experiencing in the past week including today.

- Extreme distress
- No distress

- Practical Problems
  - Child care
  - Housing
  - Insurance/financial
  - Transportation
  - Work/school
  - Treatment decisions

- Physical Problems
  - Appearance
  - Bathing/dressing
  - Breathing
  - Changes in urination
  - Constipation
  - Diarrhea
  - Eating
  - Fatigue
  - Feeling Swollen
  - Fevers
  - Getting around
  - Indigestion
  - Memory/concentration
  - Mouth sores
  - Nausea
  - Nose dry/congested
  - Pain
  - Sexual
  - Skin dry/itchy
  - Sleep
  - Substance abuse
  - Tingling in hands/feet

Other Problems: ____________________________
Demographics

- 65 Asian AYA cancer patients were included in this published analysis
  - Mean (± SD) age = \(27.8 \pm 6.7\) years
  - Majority Chinese, followed by Malays and Indians
  - >60% had some university level of education
  - >30% were social smokers/ex-smokers; <40% were non-drinkers
  - Majority diagnosed with sarcoma (41.5%), followed by lymphoma (32.3%) and germ cell tumors (15.4%)

## Trajectory of distress levels over time

<table>
<thead>
<tr>
<th></th>
<th>At diagnosis (T1)</th>
<th>One month after diagnosis (T2)</th>
<th>Six months after diagnosis (T3)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Distress score</td>
<td>3.4 ± 2.6</td>
<td>3.3 ± 2.6</td>
<td>2.3 ± 2.7</td>
<td>0.001</td>
</tr>
<tr>
<td>(mean ± SD) [max score =10]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinically significant distress*, n(%)</td>
<td>28 (43.1%)</td>
<td>31 (47.7%)</td>
<td>18 (27.7%)</td>
<td>0.007</td>
</tr>
</tbody>
</table>

*Clinically significant distress is defined as scores of 4 and above on the DT scale
Mean difference between T1 and T2 = -0.1±2.3 (p=0.768)
Mean difference between T1 and T3 = -1.1±2.8 (p=0.002)
Mean difference between T2 and T3 = -1.0±2.9 (p=0.004)
Memory/Concentration issues detected by DT

<table>
<thead>
<tr>
<th></th>
<th>At diagnosis</th>
<th>One month after diagnosis</th>
<th>Six months after diagnosis</th>
</tr>
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<tbody>
<tr>
<td>All patients (n=65)</td>
<td>20.0%</td>
<td>16.9%</td>
<td>16.9%</td>
</tr>
<tr>
<td>Patients ≤ 24 years old (n=24)</td>
<td>8.3%</td>
<td>8.3%</td>
<td>12.5%</td>
</tr>
<tr>
<td>Patients &gt; 24 years old (n=41)</td>
<td>27.5%</td>
<td>22.0%</td>
<td>19.5%</td>
</tr>
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</table>

‘Chemobrain’ in AYA survivors – yay or nay?

- A small handful of studies conducted in AYA, compared to the adult population
- Inconsistent findings among studies – different study population, time points, outcomes
- Postulated Mechanisms and factors driving CRCI in AYA (if any) – relatively unknown
- Direct impact on survivorship is also relatively unknown

Research Development in Singapore

• Adolescent and Young Adult Cancer Patients: Cognitive Toxicity on Survivorship (ACTS)
  – ClinicalTrials.gov Identifier: NCT03476070

• RCT to compare active intervention versus usual care at diagnosis for AYA cancer patients
  – ClinicalTrials.gov Identifier: NCT03515174
Take Home Messages

• Current evidence suggests that AYA cancer survivors are likely to suffer from CRCI.

• The underlying mechanisms that cause CRCI in AYA are still relatively unknown.

• Effective cognitive interventions are urgently needed to facilitate recovery in this group of survivors.
Thank you!

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