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National Cancer
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2018
28-30 JUNE
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*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



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



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%)

Parsons HM, et al. *J Clin Oncol* 2012; 30(19): 2393-2400
Kwak M, et al. *J Clin Oncol* 2013; 31(17): 2160-66



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

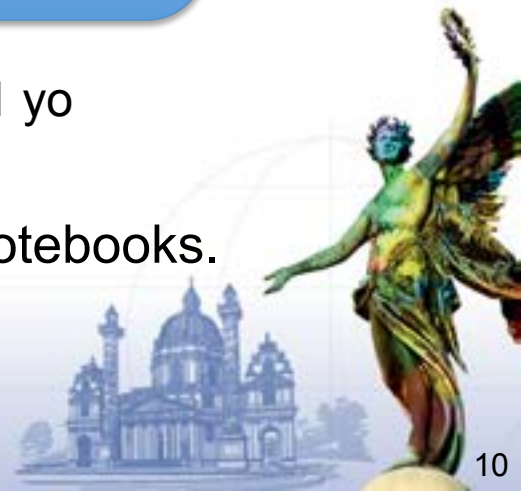
I thought my thinking process was slower than normal, [...] I didn't realize until after I went back to work.

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?



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	Chiaravollti A, et al.	Amidi A, et al.	Miao H, et al.	Tao L, et al.
Type of cancer	Hodgkin's Lymphoma	Testicular Cancer	Breast Cancer	Breast Cancer
Study design	Longitudinal (3 scans)	Longitudinal (2 scans)	Cross-sectional	Cross-sectional
Neuro psychological test		√	√	√
Gray Matter Reductions observed				
Frontal lobe	√	√	√	√
Parietal lobe	X (Increase)	√		√
Temporal lobe			√	√
Occipital lobe			√	
Limbic cortex	√			√

Chiaravalloti A, et al. *Nuclear medicine communications* 2013; 34(1): 57-63

Amidi A, et al. *Brain Imaging and Behavior* 2016; 1-15

Miao H, et al. *European Journal of Radiology* 2016; 85(6): 1053-7

Tao L, et al. *European Journal of Cancer Care* 2016

www.mascc.org/meeting



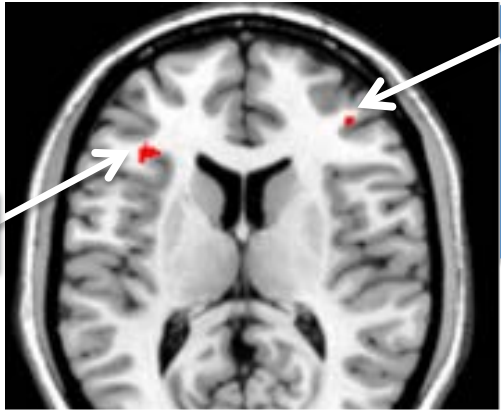
Comparison of Brain Morphologies between AYA Cancer Survivors and Healthy Controls



Right inferior frontal gyrus

Right middle frontal gyrus

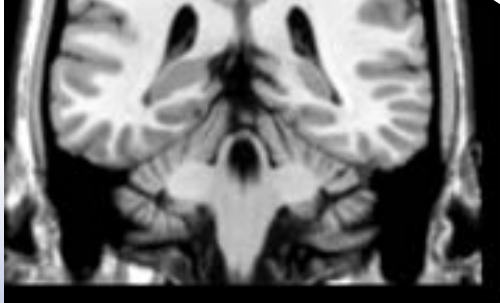
Left insula



Right middle frontal gyrus

Volume of Gray Matter

AYA Cancer Group (mean ± SD), ml	Healthy Control Group (mean ± SD), ml
647.4 ± 69.8 ml	706.0 ± 84.8 ml



Right inferior frontal gyrus



Can we use a rapid screening tool to identify AYA cancer patients with CRCI?



Supportive Care in Cancer
<https://doi.org/10.1007/s00520-018-4189-y>

ORIGINAL ARTICLE



Assessment of psychological distress among Asian adolescents and young adults (AYA) cancer patients using the distress thermometer: a prospective, longitudinal study

Alexandre Chan^{1,2} · Eileen Poon³ · Wei Lin Goh³ · Yanxiang Gan² · Chia Jie Tan^{1,2} · Kelvin Yeo^{1,2} · Annabelle Chua^{1,2} · Magdalene Chee³ · Yi Chye Law³ · Nagavalli Somasundaram³ · Ravindran Kanesvaran³ · Quan Sing Ng³ · Chee Kian Tham³ · Chee Keong Toh³ · Soon Thye Lim³ · Miriam Tao³ · Tiffany Tang³ · Richard Quek³ · Mohamad Farid³

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Distress Thermometer



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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

Second, please indicate if any of the following has been a problem for you in the past week including today. Be sure to check YES or NO for each.

YES NO Practical Problems

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

Family Problems

- Dealing with children
- Dealing with partner
- Ability to have children
- Family health issues

Emotional Problems

- Depression
- Fears
- Nervousness
- Sadness
- Worry
- Loss of interest in usual activities

- Spiritual/religious concerns

Other Problems: _____

YES NO 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



Demographics

- 65 Asian AYA cancer patients were included in this published analysis
 - Mean (\pm 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



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

*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

	At diagnosis	One month after diagnosis	Six months after diagnosis
All patients (n=65)	20.0%	16.9%	16.9%
Patients ≤ 24 years old (n=24)	8.3%	8.3%	12.5%
Patients > 24 years old (n=41)	27.5%	22.0%	19.5%





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‘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

Chan A, Ng T, Chan RJ, Poon E, Farid M, et al. *Expert Opinion of Quality of Life in Cancer* 2016; 1(3): 187-88.





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.





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**Thank
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