Moderate Alcohol Intake Might be Protective for Swallowing Function among HNC Patients – an Example from Causal Inference Analysis in Observational Study

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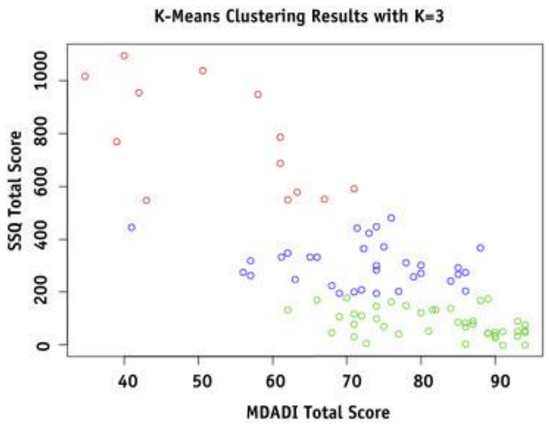
Purpose/Objectives

- Head and neck cancer treatment-related dysphagia (HNCTD) is one of the most important complications among HNC patients, which has been the focus of recent therapeutic efforts to evaluate the oncologic safety of various treatment de-intensification strategies.
- Three cohorts of irradiated head and neck cancer (HNC) patients were identified using an unsupervised cluster analysis of the total scores for Sydney Swallow Questionnaire (SSQ) and the MD Anderson Dysphagia Inventory (MDADI) [1], in a pilot study using 89 patients.



Scatterplot demonstrating the 3 clusters identified in an unsupervised cluster analysis of the MDADI and SSQ in 89 HNC patients (Quon et.al 2017).

- In a subsequent validation study, alcohol intake was significant different across three groups, measured by Functional Assessment of Cancer Therapy-Head and Neck (FACT-HN) scale, before radiation therapy (RT) among 269 HNC patients (Table 1).
- We hypothesized that baseline alcohol intake has causal relationship with swallowing function among HNC patients after RT. Moderate drinking may improve swallowing function.

Materials/Methods

- Study population: HNC patients treated in 12/2015 – 01/2017 with definitive radiation therapy.
- Cluster idenficiation: Unsupervised cluster analysis (k-mean) using the elbow criterion and CLUSPLOT analysis was performed to identify unique patient cohorts in this validation study.
- Characteristics comparision: baseline patients characteristics were compared across three clusters using ANOVA test (continuous variable) or Chi2 test (categorical variable).
- Causal inference analysis:

➢ Potential outcomes and Average Causal Effect (ACE):

❖ For each particular individual, one can generally observe only one, but not both, of the two potential outcomes. The unobserved outcome is called the "counterfactual" outcome.

❖ Assume that the people in the treatment group on average are identical to the people in the control group with respect to their potential outcomes.

❖ Average causal effect (ACE) as the population average of the individual level causal effects

$$ACE = E[\delta] = E[Y_1] - E[Y_0].$$

❖ Assume no unmeasured confounders.

➢ Causal assumption visualization: Causal Directed acyclic graphs (DAG): visual representations of causal assumptions for baseline alcohol intake, baseline confounders and swallowing function outcomes.

Fig 1. Causal assuptions represented by DAG. "C" denotes the baseline confounders (age, race, gender, TNM stage, chemotherapy, HPV status, KPS at consult). "A" denotes the baseline alcohol intake measured by FACT-HN. "S" denotes the swallowing function measured after RT.

➢ Estimate ACE:

❖ Parametric g-formula:
❖ Inverse Probability Weight (IPW):
❖ Augmented Inverse Probability Weight (AIPW):
❖ 95% CI of the ACE estimation was extracted by a bootstrap process from their empirical distributions.

Results

Fig 2. Scatterplot demonstrating the 3 clusters identified in an unsupervised cluster analysis of the MDADI and SSQ in 269 HNC patients (validation cohort).

Results (Cont'd)

Table 1. Patient Reported Alcohol Intake at Baseline, by Three Clusters

	Cluster 1 (red)	Cluster 2 (blue)	Cluster 3 (green)	P
				0.003
Not at all*	17 (47.2)**	15 (20.8)	33 (20.5)	
A little bit	12 (33.3)	38 (52.8)	57 (35.4)	
Somewhat	4 (11.1)	17 (23.6)	53 (32.9)	
Quite a bit	3 (8.3)	2 (2.8)	17 (10.6)	
Very much	0 (0.0)	0 (0.0)	1 (0.6)	

*Five levels of alcohol intake were captured in FACT-HN Q9: "no alcohol intake", "a little bit", "somewhat", "quite a bit" and "very much".
**All the numbers were displayed by count (%).

Table 2. Summary SSQ and MDADI Scores Characterizing Each Dysphagia Group

Group	N	SSQ (min, max)		MDADI (min, max)	
Red	36	711	1443.5	24	81
Blue	72	257.5	646.5	22	91
Green	161	0	251.5	38	93

Table 3. Average Causal Effect (ACE) Calculation Based on SSQ Using Different Causal Inference Modeling, Comparing Somewhat Intake to not at all*

	ACE	95% CI
g-formula	-7.71	-26.57, -0.05
IPW	-168.72	-269.11, -70.29
AIPW	-41.89	-41.89, -8.74

*There was no causal effect of "a little bit" alcohol intake on improving swallowing function, compared to "no alcohol intake". There was no causal effect of alcohol intake on swallowing function assessed by MDADI.

Conclusions

- Analysis of this mature cohort validates that HNCTD can be classified into three unique and reproducible groups consistent with our pilot analysis.
- Qualitative-reported moderate alcohol intake is moderately protective for patient-reported swallow function after RT.
- More established quantity-frequency approaches to measuring alcohol should be considered to improve our understanding of the potential relationship between alcohol and swallow function.

References

1. Quon H, Hui X, Cheng Z, et al. Quantitative Evaluation of Head and Neck Cancer Treatment–Related Dysphagia in the Development of a Personalized Treatment Deintensification Paradigm. Int. J. Radiat. Oncol. 2017;99:1271–1278.