Incidence and severity of acute dysphagia in hematopoietic cell recipients

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Introduction

- A potentially underreported and understudied complication in HCT recipients is dysphagia (swallowing disfunction). Swallowing is a complex mechanism occurring in four stages: oral preparatory, oral, pharyngeal, and esophageal.
- The oral phases of swallowing are voluntary, followed by an involuntary reflex, requiring precise coordination between sensory input and motor function in the brain. Six cranial nerves and over 25 muscles are involved and any defect of these structures may affect swallowing.
- In cancer patients, the tumor as well as therapy-related oral complications (e.g., painful oral, oropharyngeal, pharyngeal and esophageal mucositis), pain associated with mucosal infections, xerostomia/hyposalivation and tissue fibrosis) may contribute to dysphagia.
- Disturbed swallowing may contribute to dehydration and digestive problems, reduced food intake and unfavorable dietary changes, that may lead to malnutrition, weight loss and decreased quality of life. In severe cases, dysphagia predisposes to aspiration and potentially life threatening pulmonary complications.
- Acute dysphagia may develop in the first weeks following the conditioning regimen for HCT. However, little is known about the incidence, severity and associated risk factors of dysphagia in HCT recipients.

Aim

The present prospective observational multicenter study aims to determine the incidence and severity of acute dysphagia in HCT recipients, and to study possible associations between dysphagia and HCT-related factors and other clinical parameters during the first weeks after HCT.

Materials and Methods

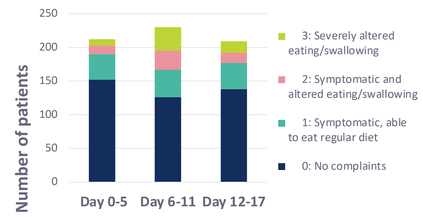
- The Orastem Study is a prospective, international observational multicenter study in HCT recipients. The aims include establishing the nature, incidence and relationships of oral complications related to the conditioning regimen and transplantation. All aims and details of the study protocol are reported elsewhere (Brennan et al, 2018). In this substudy, data on dysphagia are reported.
- Patients were included at six study sides: (1) Sahlgrenska University Hospital, Gothenburg, Sweden; (2) Karolinska University Hospital Huddinge, Stockholm, Sweden; (3) Carolinas Medical Center, Charlotte, NC, USA; (4) BC Cancer, Vancouver, BC, Canada; (5) Amsterdam UMC, location AMC, Amsterdam, The Netherlands; (6) Radboud University Medical Center, Nijmegen
- This study was approved by the Medical Ethical Committees of each center participating in this study.
- Eligible for inclusion were adult patients (>18 years) receiving full intensity conditioning (FIC), reduced intensity conditioning (RIC) or nonmyeloablative conditioning (NMC), followed by hematopoietic cell transplantation (autologous or allogeneic). Inclusion of participants took place between 2011 and 2018.
- Data on general and oral health collected before the start of HCT (phases 1 and 2) and during hospitalization (phase 3, three times a week) from day 0 until hospital discharge.
- Dysphagia was measured using the CTC AE criteria:
  - *-grade 0: no complaints*
  - *-grade 1: Symptomatic, able to eat regular diet*
  - *-grade 2: Symptomatic and altered eating/swallowing*
  - *-grade 3: Severely altered eating/swallowing; tube feeding, TPN or hospitalization indicated*
  - *-grade 4: Life-threatening consequences; urgent intervention indicated*
  - *-grade 5: Death*

  A score of 2 and higher was defined as clinically relevant dysphagia
- Data is restricted to those who answered the dysphagia CTC questionnaire at least once during hospitalization
- Selection criteria for independent variables was based on clinical relevance and then significant association in the crude analysis
- Data were measured using mixed models with random intercept and variable for time, both for crude and multivariate analyses. Data used for these models was limited to the first 17 days after HCT. A p-value of <0.05 was considered statistically significant.

Results

- From the 277 patients that signed informed consent, for 238 patients data on dysphagia were available (56.3% male, 43.7% female). The median age was 56 years (18 – 76).
- 36.1% was treated for acute disease and 63.9% for non-acute disease. 59.7% received allo HCT and 40.3% received auto HCT.
- 53.8% of patients experienced dysphagia during hospitalization.

Figure 1. Incidence and severity of dysphagia



- At the peak of their complaints, patients that suffered from dysphagia rated their throat symptoms (0 (none)-10 (worst)) on average 6.1 ± 2.7, while patients without dysphagia rated their throat symptoms on average 1.7 ± 2.5.
- Patients with a full intensity conditioning regimen, higher oral mucositis scores and more xerostomia during hospitalization had higher odds for dysphagia. The highest odds were for xerostomia.

Table 1. Results of univariate analyses

Independent variables	Odds ratio	95% CI	p-value
Age: 10 year increase	0.8	0.5 - 1.1	0.1767
Gender: Female vs Male	2.8	1.0 – 7.9	0.0576
Type of transplant: Auto vs Allo	2.4	0.8 – 6.9	0.1103
Treatment Intensity: FIC vs RIC/NMA	10.8	3.9 – 29.4	<.0001*
Baseline xerostomia VAS score: >0 vs 0	5.8	2.0 – 17.1	0.0014*
Dry mouth grade 2,3 vs grade 0,1	49.2	22.4 – 108.1	<.0001*
WHO mucositis grades 2,3,4 vs grades 0,1	23.3	11.3 – 47.9	<.0001*
Diarrhea (0=none-10=worst possible): one unit increase	1.1	1.0 - 1.2	0.2744

Table 2. Results of multivariate analyses

Independent variables	Odds Ratio	95% CI	p-value
Treatment Intensity: FIC vs RIC/NMA	3.6	1.2 – 10.4	0.0200*
Baseline xerostomia VAS score: > 0 vs 0	1.3	0.5 – 3.3	0.5743
Dry Mouth CTC: grades 2,3 vs grade 0,1	25.8	11.9 – 56.0	<0.0001*
WHO Mucositis: grades 2,3,4 vs grades 0,1	14.9	7.1 – 31.2	<0.0001*

** p-value < 0.05*

Conclusion

Dysphagia occurs in half of the patients during hospitalization post HCT, with troat symptoms rated on average as 6. Patients with a full intensity conditioning regimen, higher oral mucositis scores and more xerostomia during hospitalization had higher odds for dysphagia.

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