The 25th Annual Meeting of the
Japanese Society of
Dysphagia Rehabilitation

ONSET AND EVOLUTION OF DYSPHAGIA IN HUNTINGTON'S DISEASE

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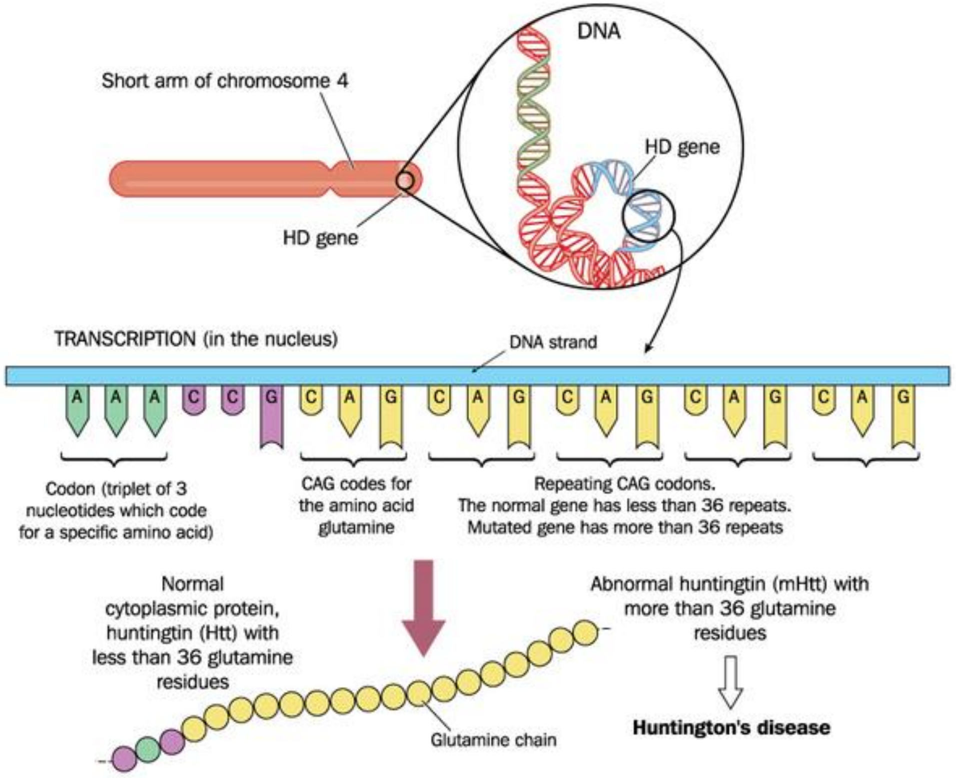
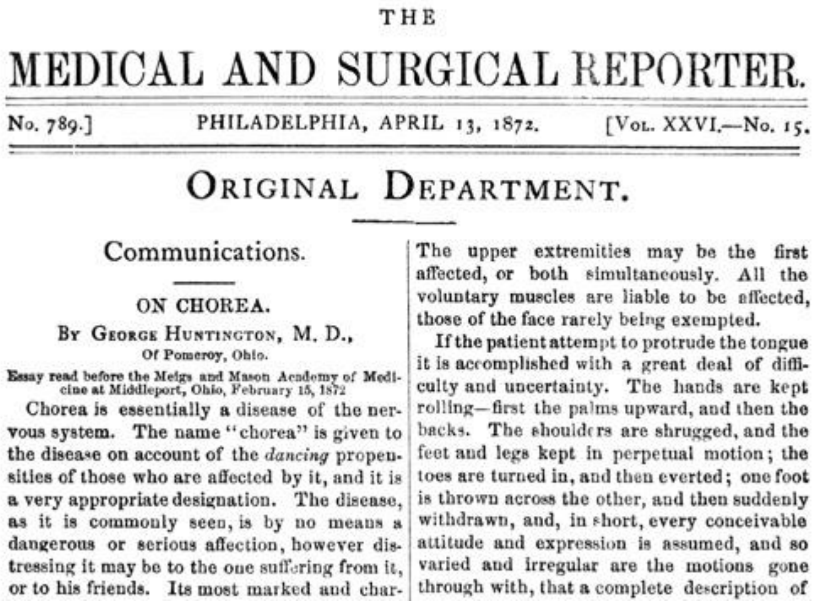
Huntington's disease



Source: https://ghr.nlm.nih.gov



THE

MEDICAL AND SURGICAL REPORTER.

No. 789.] PHILADELPHIA, APRIL 13, 1872. [Vol. XXVI.—No. 15.

ORIGINAL DEPARTMENT.

Communications.

ON CHOREA.

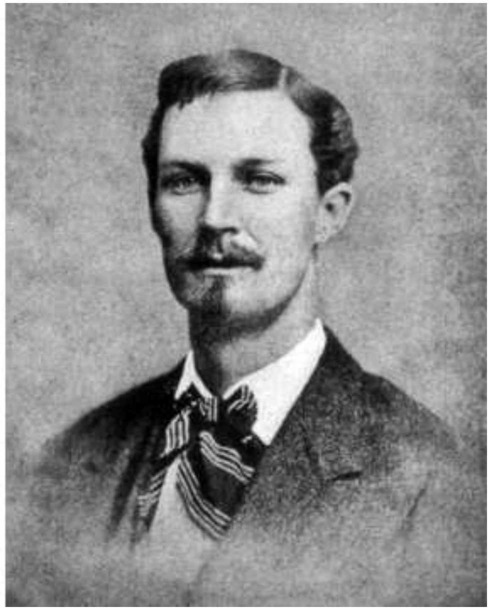
By George Huntington, M. D.,
Of Pomeroy, Ohio.

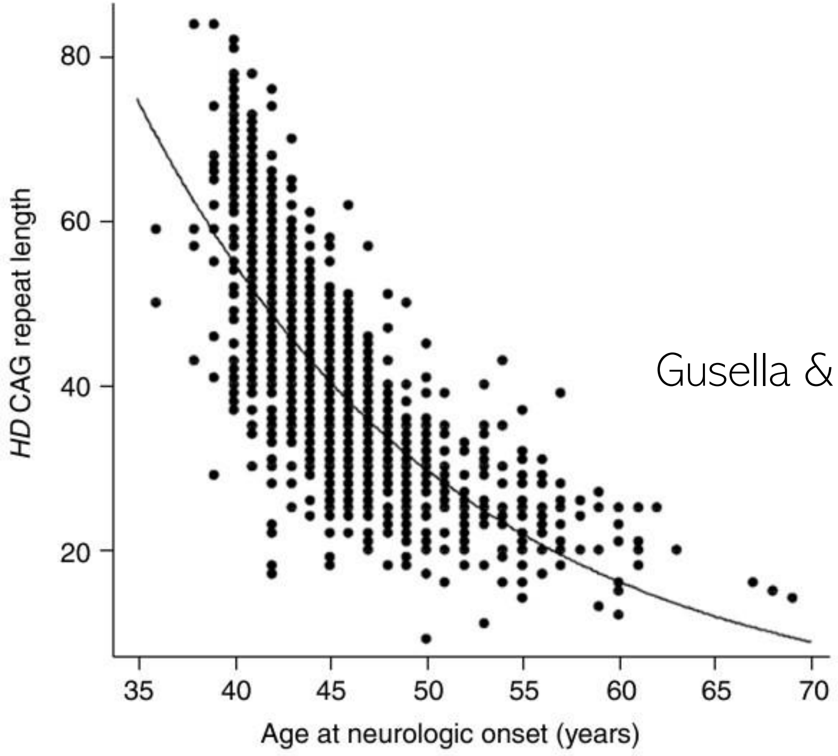
Essay read before the Meigs and Mason Academy of Medicine at Middleport, Ohio, February 15, 1872

Chorea is essentially a disease of the nervous system. The name "chorea" is given to the disease on account of the *dancing* propensities of those who are affected by it, and it is a very appropriate designation. The disease, as it is commonly seen, is by no means a dangerous or serious affection, however distressing it may be to the one suffering from it, or to his friends. Its most marked and char-

The upper extremities may be the first affected, or both simultaneously. All the voluntary muscles are liable to be affected, those of the face rarely being exempted.

If the patient attempt to protrude the tongue it is accomplished with a great deal of difficulty and uncertainty. The hands are kept rolling—first the palms upward, and then the backs. The shoulders are shrugged, and the feet and legs kept in perpetual motion; the toes are turned in, and then everted; one foot is thrown across the other, and then suddenly withdrawn, and, in short, every conceivable attitude and expression is assumed, and so varied and irregular are the motions gone through with, that a complete description of





Gusella & MacDonald, 2009

Clinical manifestation

MOTOR SIGNS

Chorea
Bradykinesia
Incoordination
Myoclonus
Motor impersistence
Incoordination
Impairment of fine motor skills
Gait and postural instability
Dysphagia
Dysarthria
Dystonia

COGNITIVE IMPAIRMENT

Executive functions impairment
Delayed acquisition of new motor skills
Cognitive inflexibility

NEUROENDOCRINE ALTERATIONS

Involuntary weight loss
Muscle wasting
Metabolic dysfunction
Endocrine alterations

BEHAVIOURAL ALTERATIONS

Depression
Dysphoria
Irritability
Obsessive compulsive behaviour
Apathy
Anxiety

Causes of death

TABLE 1 Causes and places of death among patients with manifest Huntington's disease included in the REGISTRY study

Variable	No. of patients (%)
Causes of death	
Pneumonia	104 (19.5)
Other infection	37 (6.9)
Suicide	35 (6.6)
Cancer	18 (3.4)
Stroke	14 (2.6)
Trauma	5 (0.9)
Other	194 (36.4)
Unknown	126 (23.6)
Places of death	
Hospital	152 (29.8)
Home	122 (23.9)
Nursing home	101 (19.8)
Hospice care	17 (3.3)
Unknown	118 (23.1)

REGISTRY of the European Huntington's Disease Network
Rodrigues et al, 2017

Cause of death	N	%
Penumonia	81	55.1
Suffocation	6	4.1
Pulmonary embolism	6	4.1
Cachexia	11	7.5
Cardiac diseases	16	10.9
Other neurological diseases	3	2.0
Shock/sepsis	7	4.8
Suicide	2	1.4
Euthanasia	5	3.4
Other causes	10	6.8

→ 38/81 with autopsy
16 aspiration
17 possible aspiration
5 primary infectious

Heemsker & Ross, 2012

Dysphagia (2011) 26:62–66
DOI 10.1007/s00455-010-9302-4

REVIEW ARTICLE

Dysphagia in Huntington's Disease: A Review

Anne-Wil Heemskerk · Raymond A. C. Roos

Table 2 Overall conclusions of previous studies on dysphagia in HD

Preparatory oral	Oral	Pharyngeal	Esophageal
Postural instability [15, 17]	Impaired voluntary swallowing [13]	Coughing [13–17]	Vomiting [13, 15]
Abrupt postural changes caused flux to the pharynx [15]	Swallow incoordination [15]	Choking [14, 15]	Early satiety [15]
Hyperextension of head and trunk [13, 15]	Short oral transit time (0.23 s) [17]	Aspiration [13–15]	Abnormal esophageal motility [13, 15]
Difficulty controlling rate and amount of food intake [13]	Repetitive swallows [15]	Eructations [15]	Diaphragmatic chorea [15]
Rapidly and impulsively consuming food [13, 17]	Swallow latency [15]	Aerophagia [13, 15]	Reflux [15]
Tachyphagia [15]	Residue after swallowing solid foods [13, 17]	Audible swallows [15]	
Inadequate mastication [13–15, 17]	Intraoral bolus retention [15]	Prolonged laryngeal elevation [15]	
Poor lingual control [14, 17]	Segmented lingual transfer [15]	Difficulty descent larynx [16, 17]	
Tongue protrusion [16]		Phonation during swallow [15]	
Premature liquid transfer [15, 17]		Pharyngeal stasis [13, 15, 17]	
Delayed lingual transfer [15]		Impaired cricopharyngeal function [13]	
Lingual chorea [15]		Inability to stop respiration [15]	
		Wet vocal quality [15]	
		Laryngeal chorea [15, 16]	
		Epiglottis tilt not inferoposterior [17]	

European Journal of Neurology 2010, **17:** 1068–1074 doi:10.1111/j.1468-1331.2010.02973.x

Autonomic symptoms in patients and pre-manifest mutation carriers of Huntington's disease

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Table 2 Autonomic symptoms severity (range 0–100) and frequency (% with an item score ≥ 1) in the study population

	Patients with HD	Pre-manifest	Partners	Controls	*P*-value[a]
Total score (median, IQR)[b]	16 (10–24)[c,d]	14 (7–18)	7 (4–12)	10 (6–14)	<0.001**
Gastrointestinal domain (median, IQR)[b]	14 (5–19)[c,d,e]	5 (2–10)[f]	0 (0–5)	5 (0–10)	<0.001**
Swallowing/choking (%)	71[c,d,e]	48[f,g]	5[h]	16	<0.001**
Sialorrhea (%)	32[c,d,e]	0	0	11	<0.001**
Dysphagia (%)	35[c,d]	14	5	8	<0.001**
Early abdominal fullness (%)	32[c]	24	25	16	0.206
Constipation (%)	11	10	5	9	0.882
Straining for defecation (%)	37[d]	33	10	27	0.134
Fecal incontinence (%)	16[c]	5	0	3	0.021*

Eur Neurol 2015;74:49–53

Dysphagia in Huntington's Disease: Correlation with Clinical Features

Marina de Tommaso Angela Nuzzi Anna Rita Dellomonaco Vittorio Sciruicchio
Claudia Serpino Claudia Cormio Giovanni Franco Marisa Megna

Table 3. Correlations between DOSS scores and main clinical features

	UHDRS-M	Chorea (total)	Chorea (oral)	Bradikinesia	Dystonia	Disarthria	Tongue protrusion	TFC	UHDRS-COG	Age	Illness age
Pearson	−0.542	−0.229	−0.008	−0.315	−0.231	−0.451	−0.477	0.199	0.149	−0.351	0.320
p	**0.0001**	n.s.	n.s.	**0.029**	n.s.	**0.003**	**0.001**	n.s.	n.s.	**0.017**	**0.027**
n	37	37	37	37	37	37	37	37	37	37	37

UHDRS-M = Motor assessment of UHDRS; UHDRS-COG = cognitive assessment of UHDRS.
The significant results were represented in bold character. n.s. = Not significant.

DOSS scores derived from clinical swallow assessment
(Bedside Swallowing Assessment Scale + Water swallow test)

Gap of knowledge and Clinical relevance

No data are available on the prevalence and the characteristics of dysphagia in different stages of HD, as assessed by instrumental evaluation of swallowing

These data may be relevant to define the best timing of swallowing first assessment and re-assessment in this population

Research questions

- Does dysphagia affect patients with HD already at an early disease stage?
- Do signs of dysphagia differ among the disease stages?
- Are there neurological clinical factors that can suggest the presence of dysphagia?

Methods Study design

Cross-sectional study with prospective consecutive recruitment

Approved by the Ethics Committees of the Luigi Sacco Hospital and the IRCCS Istituto Auxologico Italiano

Written informed consent was obtained from participants or their caregivers

Methods Patients

43 genetically confirmed HD patients (CAG≥39)

18M, 25F

Age 57 ± 2 years (27-78)

CAG 43.5 ± 0.6 (39-59)

Onset 49.2 ± 1.9 years (23-71)

Disease duration 7.9 ± 0.7 years (1-19)

Exclusion criteria History of head and neck cancer, other neurological diseases, self-reported or documented dysphagia prior to HD diagnosis

Methods Neurological assessment

Unified Huntington's Disease Rating Scale (UHDRS)

Subscale	Domain
UHDRS I	Motor assessment
UHDRS II	Cognitive assessment
UHDRS III	Behavioural assessment
UHDRS IV	Independence scale
UHDRS V	Functional assessment
UHDRS VI	Total functional capacity

Disease staging based on UHDRS Functional Capacity

score 13-7 Early 20 patients (Shoulson-Fahn stage 1-2)

score 6-4 Moderate 10 patients (Shoulson-Fahn stage 3)

score 3-0 Advanced 13 patients (Shoulson-Fahn stage 4-5)

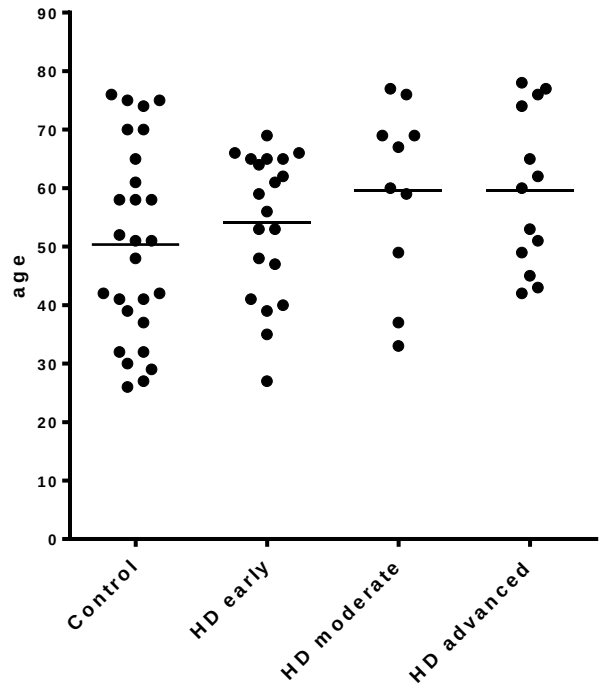
Shoulson & Fahn, 1979; Nóbrega & de Almeida, 2018

Methods Controls

27 age-matched healthy volunteers

14M, 13F

Age 50.4 ± 3.2 years



Inclusion criteria Age>20 years, no medical history of voice, swallowing, gastroenterological, respiratory, neurologic, metabolic, hematologic or neoplastic disorders

Methods Swallowing assessment

Fiberoptic endoscopic examination of swallowing (FEES)

- 5ml, 10ml, 20ml liquid x 3
- 5ml, 10ml, 20ml semisolid x 3
- ½ cracker x 2

Dysphagia severity Dysphagia Outcome and Severity Scale (DOSS)

Swallowing safety Penetration Aspiration Scale (PAS)

Swallowing efficiency Yale Pharyngeal Residue Severity Rating Scale (YPRSRS)

2 independent raters + 3rd rater for disagreements

Rosenbek et al, 1996; O'Neil et al, 1999; Neubauer et al, 2015

Methods Swallowing assessment

Test of Masticating and Swallowing Solids (TOMASS)

Standard ½ cracker (Gran Pavesi™)

Instruction to eat the cracker 'as quickly as is comfortably possible and when you have finished, say your name out loud'

MEASURES

N bites	N masticatory cycles / Bite
N swallows	N swallows / Bite
N masticatory cycles	Time / Bite
Time	Time / Masticatory cycle
	Time / Swallow

Huckabee et al, 2018

Methods Swallowing assessment

Mealtime Assessment Scale (MAS)

Observation of consumption of a full typical meal

SAFETY SCORE

Oral control of the bolus
Residue in the oral cavity
Presence of cough or throat clearing
Voice quality post-swallow

EFFICACY SCORE

Food leakage while chewing
Oral preparation
Ability to complete the meal without exhorations
Fatigue
% Meal eaten
Amount of food eaten

MEAL DURATION

Minutes

Pizzorni et al, 2019

Methods Data analysis

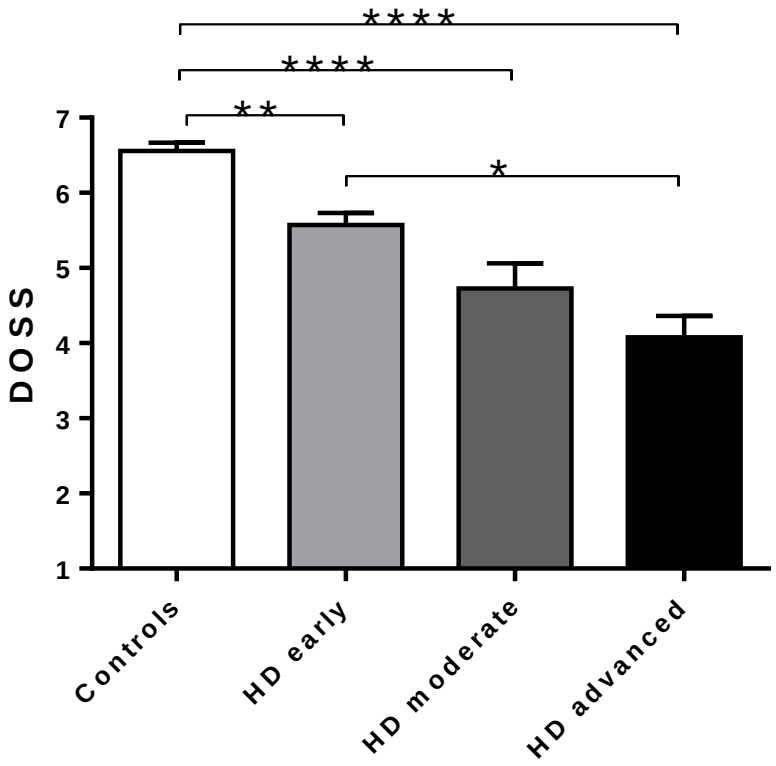
One-way ANOVA or Kruskal-Wallis test + post-hoc multiple comparisons test with Bonferroni correction to compare DOSS, PAS, and YPRSRS, TOMASS, and MAS among controls and patients with different disease stage

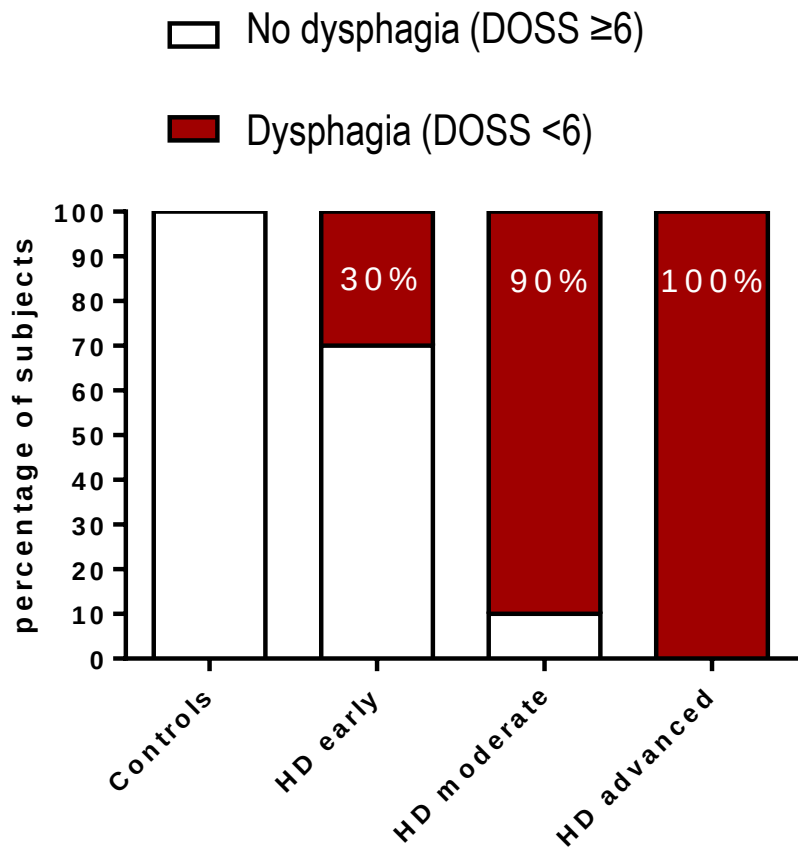
Spearman's correlation test to correlate dysphagia severity (DOSS) and disease severity (UHDRS)

Receiver Operating Characteristic curves with area under the curve (AUC) to test diagnostic accuracy of the UHDRS I (Total Motor scale) to detect presence of dysphagia

Results

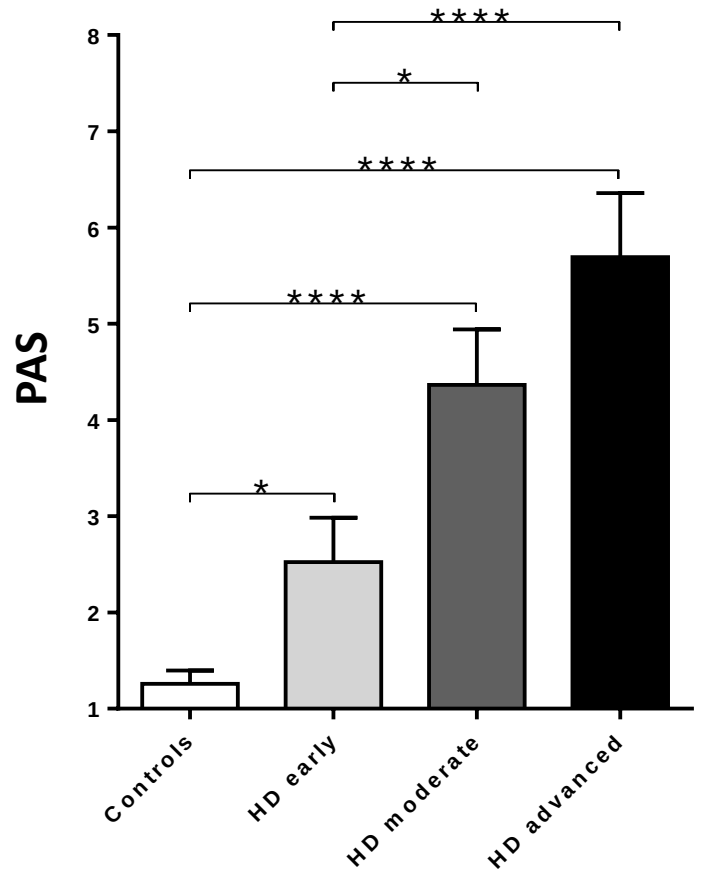
Does dysphagia affect HD patients already at an early disease stage?





Results

Do signs of dysphagia differ among disease stages?



Silent aspiration (PAS =8)

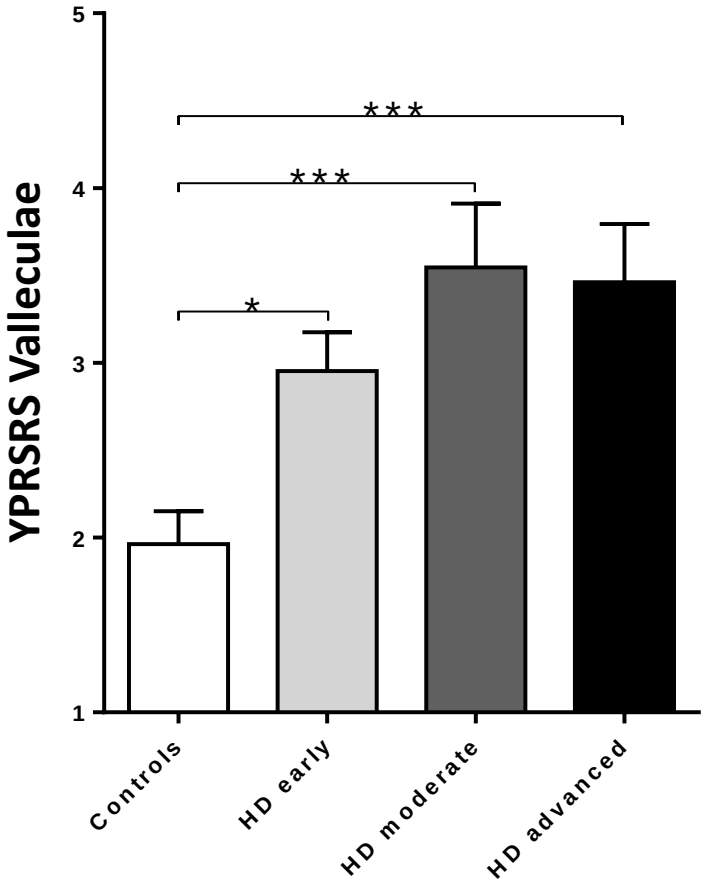
10% Early stage

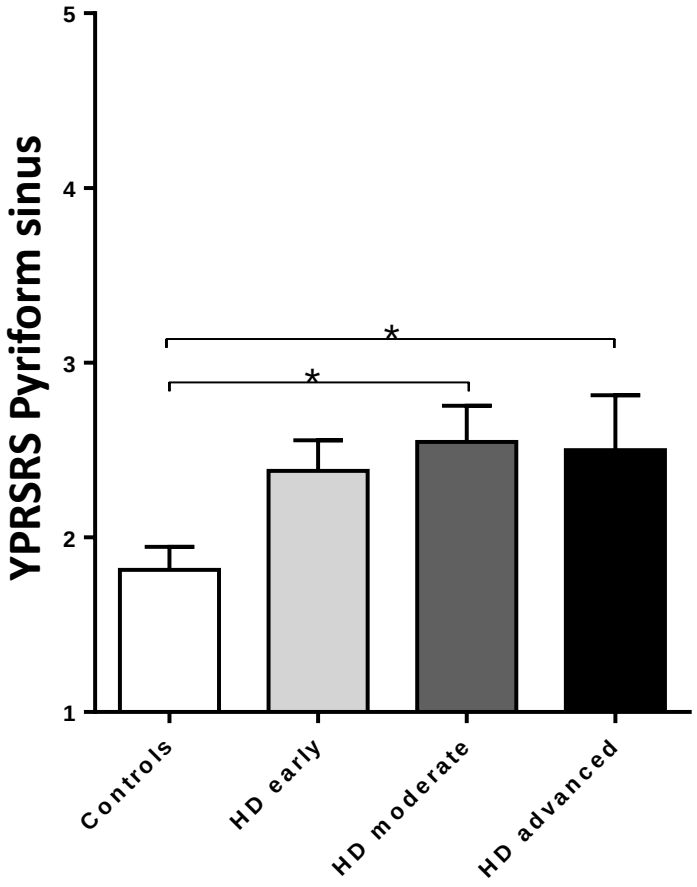
10% Moderate-stage

31% Advanced-stage

Results

Do signs of dysphagia differ among disease stages?

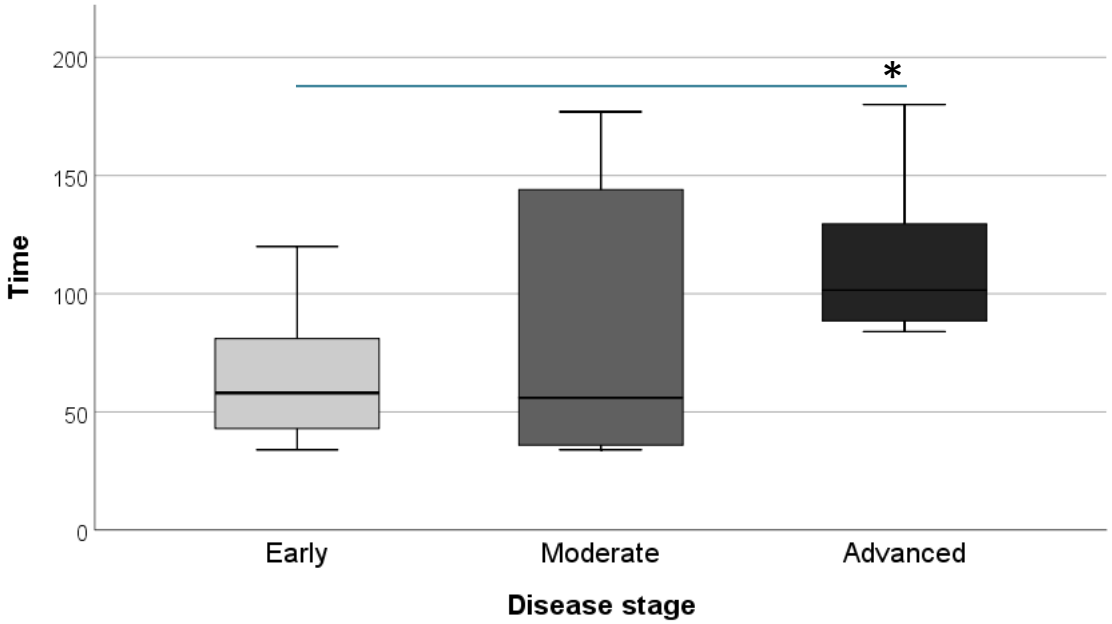




Results

Do signs of dysphagia differ among disease stages?

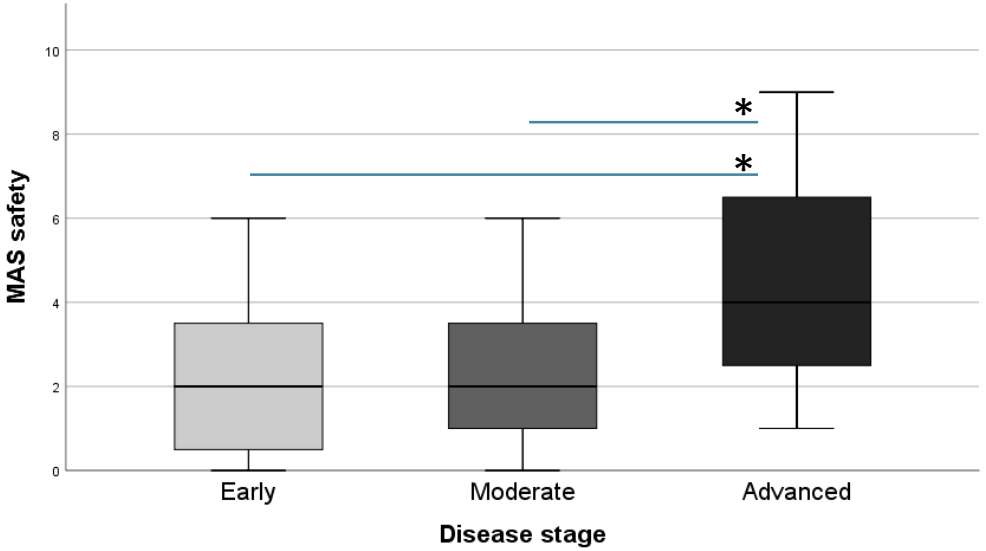
TOMASS was not performed for safety reasons in 2 patients in the early and in the moderate stages and in 5 patients in the advanced stage

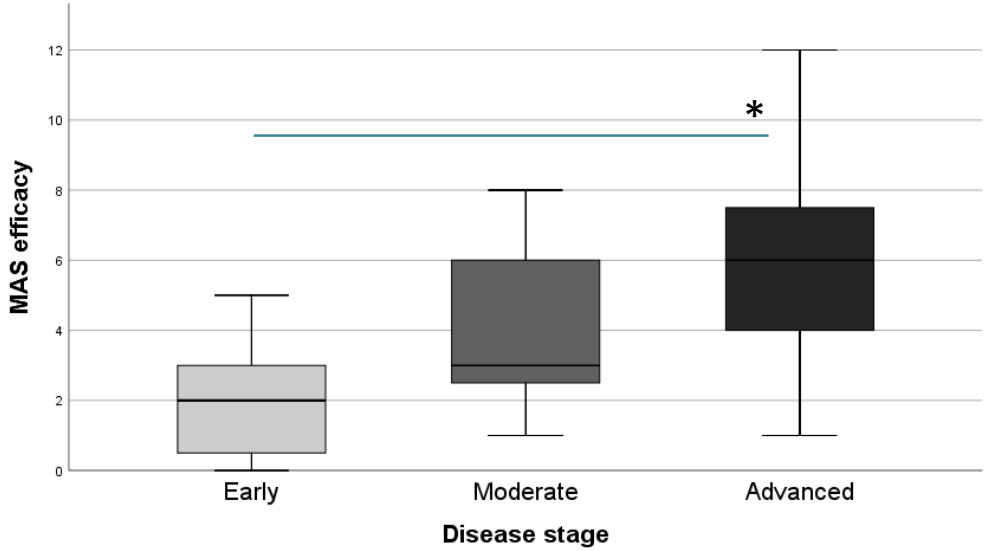


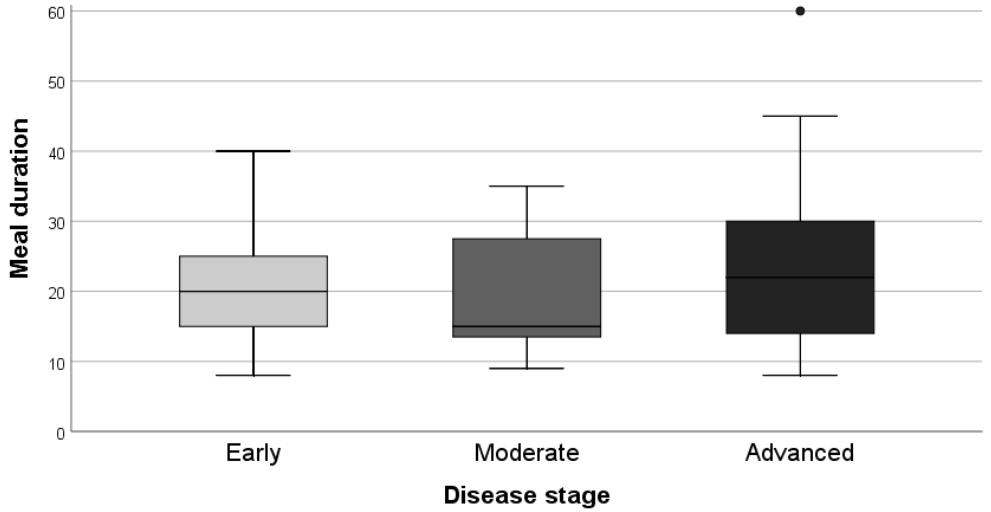
Significant differences in derived measures:

- ✓ Time/Bite Early vs Advanced
- ✓ Time/Masticatory cycle Early vs Advanced + Moderate vs Advanced
- ✓ Time/Swallow Early vs Advanced + Moderate vs Advanced

Results
Do signs of dysphagia differ among disease stages?







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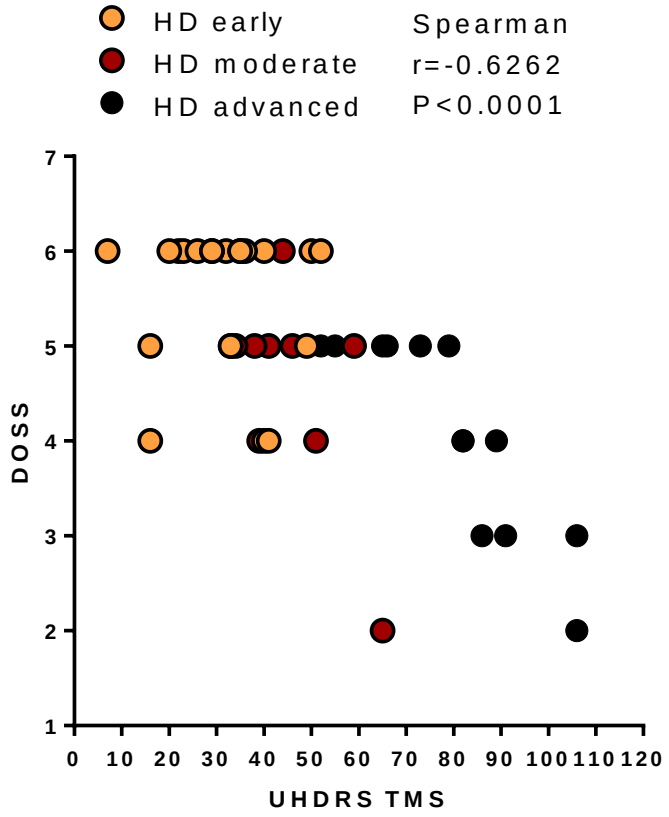
Results

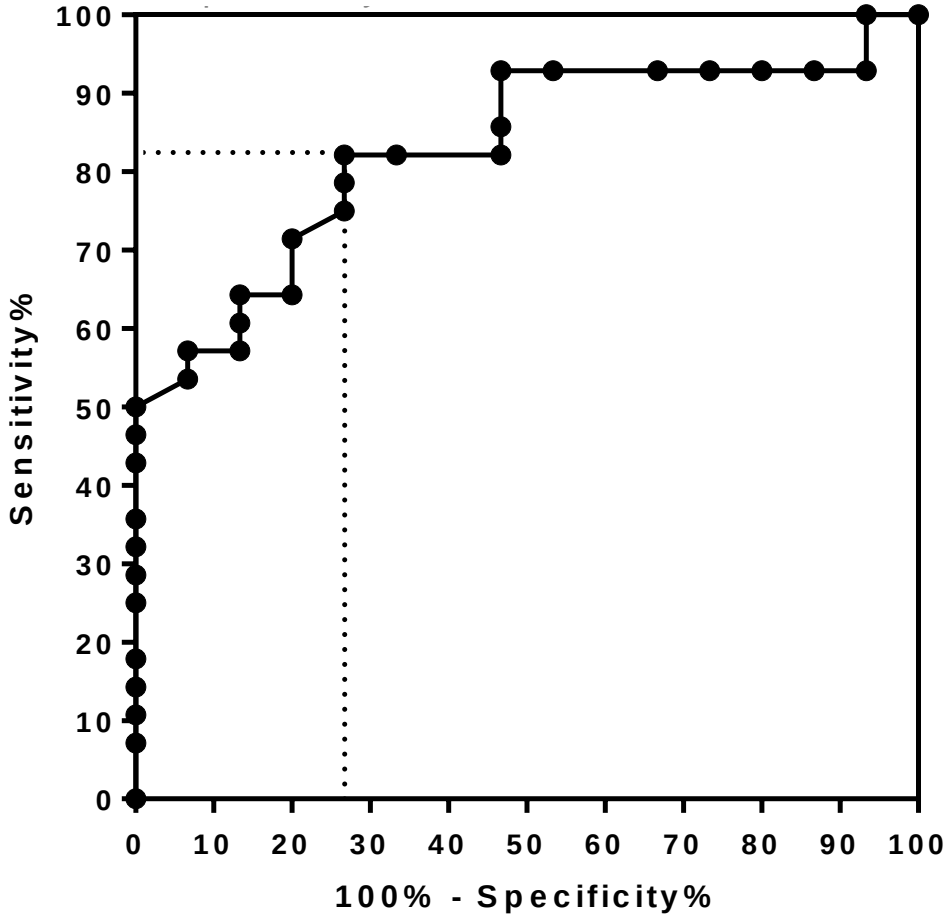
Are there neurological clinical factors that can suggest the presence of dysphagia?



UHDRS I TMS item	Spearman r	p value
Ocular pursuit	-0.4997	**0.0006**
Saccade initiation	-0.5260	**0.0003**
Saccade velocity	-0.5285	**0.0003**
Dysarthria	-0.5435	**0.0002**
Tongue protrusion	-0.4281	**0.0042**
Finger taps	-0.5859	**<0.0001**
Pronate/supinate hands	-0.6051	**<0.0001**
Luria	-0.5276	**0.0003**
Rigidity-arms	-0.4760	**0.0013**
Bradykinesia-body	-0.4250	**0.0045**
Maximal dystonia	-0.4732	**0.0014**
Maximal chorea	-0.2870	0.0620
Gait	-0.4996	**0.0006**
Tandem walking	-0.5227	**0.0003**
Retropulsion pull test	-0.4571	**0.0021**

Results

Are there neurological clinical factors that can suggest the presence of dysphagia?



AUC 0.83 (95%CI 0.71-0.96)

UHDRS I TMS ≥37
Sensitivity 82%
Specificity 73%

Conclusions

- 30% of patients with HD with early-stage disease exhibit dysphagia during FEES and 10% shows silent aspiration. Thus, swallowing assessment is warranted starting already at an early stage of HD.
- Except for penetration and aspiration, swallowing did not significantly changed between the early and the moderate stages. Conversely, both swallowing safety and efficiency significantly worsened in the advanced stage. Thus, both pulmonary and nutritional consequences should be strictly monitored at this stage.
- Multidimensional assessment of swallowing is necessary to record changes in both swallowing safety and efficiency in this population, only partially recorded by FEES.
- Dysphagia severity strongly correlated with the motor function. A UHDRS TMS≥37 can be used as a clinical cut-off for referral to the swallowing team, even in case of no symptoms.

Future perspectives

- Improve sample size within each disease stage
- Longitudinal study on the evolution of dysphagia in HD
- Impact of early dysphagia management on its health and psychosocial consequences
- Treatment possibilities