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Changes detected in swallowing function in Friedreich ataxia over 12 months

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Abstract

Friedreich ataxia (FRDA) is a multisystem neurodegenerative disorder and the most common hereditary ataxia. Dysphagia (swallowing impairment) is present in 98% of individuals with FRDA and is characterized by lingual and pharyngeal dysfunction (manifesting in impaired bolus preparation and transfer, and post-swallow residue in the mouth and pharynx), delayed swallow initiation, and entry of material into the airway (penetration/aspiration). Dysphagia severity correlates with disease severity and duration however no longitudinal studies describe changes in function in FRDA. The aim of this study was to investigate the progression of dysphagia in FRDA over one year. Fifty-nine individuals with FRDA and confirmed dysphagia were recruited and 23 of them underwent a second assessment 12 months later. Assessments of swallowing related quality of life, oral motor function (Frenchay Dysarthria Assessment 2nd Ed [FDA-2]) and functional swallowing via videofluoroscopy were conducted. Trials of thin liquid, puree and biscuit were interpreted using the Bethlehem Assessment Scale and the Penetration-Aspiration Scale by two blinded raters. Data from the videofluoroscopy revealed a decline in tongue function, pharyngeal clearance and cricopharyngeal function on solid food. However, severity of penetration/aspiration did not increase. Swallowing-related quality of life and oral-motor function remained stable. A decline in function was observed at three anatomical sites considered important for safe and effective swallowing (tongue, pharyngeal, and cricopharyngeal). However, these deficits did not translate into any meaningful functional decline in swallowing related health over 12 months for individuals with FRDA.

Keywords: Dysphagia; Swallowing; Deglutition disorders; Ataxia.

1. Introduction

Friedreich ataxia (FRDA) is an autosomal recessive neurodegenerative condition resulting from deficiency of frataxin. In 96% of affected individuals, it is caused by homozygosity for a GAA trinucleotide repeat expansion in intron 1 of FXN [1], with the size of the smaller allele (GAA1) inversely correlated with symptom onset and severity [2]. FRDA is the most common of the hereditary ataxias, affecting approximately 1 in 29,000 individuals in European populations [3]. Symptoms often present in the teenage years (but can appear earlier or later [4,5]) and include progressive gait and limb ataxia, auditory [6] and optic neuropathy [7], cardiomyopathy, scoliosis, dysarthria [8] and dysphagia [9,10]. These symptoms impose significant morbidity and negatively impact on quality of life (QOL) [9–11].

Dysphagia is present in almost all individuals with FRDA [9]. Delayed pharyngeal swallowing initiation is common, as

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are lingual dysfunction and reduced clearance of solid foods from the pharyngeal structures [9,10], reflecting underlying motor and sensory impairment. Approximately one-third of individuals with FRDA aspirate barium on videofluoroscopy (VFSS) with fluids and/or solids, and many of those do so silently [9]. A relationship is known to exist between aspiration and penetration of the airway and oromotor function relating to coughing, swallowing, and saliva control ($X2(1, N=30)=5.98$, $p=0.01$) [9]. Aspiration can occur at any stage of disease progression [9], necessitating the need for monitoring of swallowing function in affected individuals.

Dysphagia is known to present significant challenges for individuals with FRDA, including reduced ability to participate in social gatherings and overall QOL [9,10]. Significant positive correlations have been reported between swallowing-related QOL and dysphagia (as determined via VFSS), disease severity and duration [9], suggesting swallowing function progressively declines in this population. The rate at which swallowing function changes is unknown. Longitudinal data on swallowing function in FRDA may provide valuable prognostic information on the clinical course of the disease and further inform our understanding of the underlying disease mechanisms in FRDA.

Here we describe the rate of dysphagia progression over one year using scales deemed best clinical practice. An understanding of the relationship between disease and dysphagia progression is important to guide management and intervention [12–14], given dysphagia treatment has been shown to be less effective in the later stages of other neurodegenerative diseases [12]. Longitudinal data on swallowing function in FRDA will also provide valuable information on the clinical course of the disease, enhancing our understanding of the progression of this area of morbidity.

2. Methods

2.1. Participants

Twenty-three of 59 individuals from a previous study [9] participated in swallowing assessment at two timepoints (timepoint 1; TP1, and timepoint 2; TP2). Participants were recruited through the Friedreich Ataxia Clinic in Melbourne, Australia, and all had a genetically confirmed diagnosis of FRDA (homozygous for FXN intron 1 GAA expansions) (Table 1). Participants were excluded if they presented with a neurological disorder other than FRDA, or a speech and/or swallowing impairment prior to the onset of FRDA, or compound heterozygosity for a GAA expansion and a point mutation/deletion in *FXN*. Disease severity was determined via the Friedreich Ataxia Rating Scale (FARS [15]) administered by a physician.

Swallowing was assessed using three outcome measures: a swallowing-related quality of life (QOL) questionnaire (the Swal-QOL) [16]; the Frenchay Dysarthria Assessment (second edition; FDA-2) [17]; and VFSS. All experimental procedures were approved by the Human Research Ethics Committees of Monash Health and The University of Melbourne. All participants gave informed consent prior to inclusion in the study in accordance with the Declaration of Helsinki.

2.2. Assessments

2.2.1. Swallowing related quality of life and oral motor function

The Swal-QOL [16] was used to assess the impact of dysphagia on QOL. It is a validated self-report questionnaire with 44 items covering 10 quality of life domains relating to dysphagia (Burden, Eating Duration, Eating Desire, Food Selection, Communication, Fear, Mental Health, Social, Fatigue, and Sleep) and a symptom frequency scale. A systematic review of self-reported swallowing tools in neurodegeneration reported the Swal-QOL as the preferred subjective swallowing assessment considering psychometric properties and activity and participation limitations [18].

2.2.2. Oral motor function

Oral motor function was assessed using the Frenchay Dysarthria Assessment (2nd edition) (FDA-2) which includes 26 items across seven categories, including 'Reflexes', 'Respiration', 'Lips', 'Palate', 'Laryngeal function', 'Tongue', and 'Intelligibility' [17].

2.2.3. Swallowing function

Swallowing physiology was assessed via VFSS. Three consistencies were trialed, including unmodified/regular fluids (5 ml single bolus and consecutive sips), puree (up to five teaspoons of Foster Clark's Custard®), and biscuit (Arnott's Savoy® Biscuits with a thin spreading of jam mixed with barium powder). The barium powder was MCI Forrest X-OPAQUE-HD barium sulfate suspension formulation. A consistent recipe was used for each VFSS procedure and substances were presented in a random order to control for fatigue, and other possible effects related to bolus presentation. Participants were encouraged to self-feed during the procedure to replicate everyday feeding practice.

VFSS interpretation: VFSS was interpreted using the Bethlehem Assessment Scale (BAS) [19] and the Penetration–Aspiration Scale (PAS) [20]. The BAS is broken down into 10 anatomical domains, including lip function, tongue function, jaw function, soft palate function, reflex initiation, aspiration, residue in the valleculae, residue in the pyriform sinuses, pharyngeal function, and cricopharyngeal function. Each of these parameters was rated using a four-point scale, where 1 equates to no impairment and 4 to severe impairment. The PAS is an 8-point scale describing penetration and aspiration events where higher values indicate more severe penetration and aspiration. In a study of 95 healthy subjects, no PAS score higher than 3 was recorded [21].

2.3. Statistical analysis

Descriptive statistics were used to define the observed swallowing deficits, and report frequency of penetration and

Table 1
Participant information ($n=23$).

ID	GAA1	GAA2	Age at disease onset	Disease duration (at time of VFSS)		FARS	
				TP1	TP2	TP1	TP2
FA001	706	811	13	30.28	31.24	106.5	110
FA002	1099	1099	5	–	–	–	–
FA005	720	720	14	15.66	16.66	66	74
FA006	720	720	15	–	–	68	73.5
FA007	645	771	3	–	–	127.5	123
FA012	650	900	14	–	–	129	120.5
FA013	447	967	18	–	–	102	103.5
FA015	642	1132	8	31.37	32.62	136	136.5
FA016	606	986	28	26.05	26.97	102.5	101
FA021	780	980	7	43.71	45.11	138.5	134
FA029	833	835	14	17.74	18.74	95.5	97
FA032	569	884	14	9.84	10.94	77	95.5
FA034	462	462	21	–	–	84.5	–
FA037	800	800	3	18.5	19.39	109.5	111
FA039	733	943	8	25.97	26.66	117.5	–
FA041	593	957	10	–	–	48.5	–
FA046	489	1207	18	46.31	46.83	140	143
FA047	589	589	17	–	–	–	–
FA048	853	853	14	27.04	27.96	–	–
FA050	998	998	7	–	–	96.5	99
FA051	556	733	4	–	–	66	76
FA052	690	690	16	–	–	109.67	113.5
FA054	674	803	32	16.58	17.96	84	86
Mean	627.53	863.73	15.37	21.76	26.75	91.14	99.68
Standard deviation	193.14	196.97	7.69	10.28	11.05	36.46	23.01
Range	126–1099	320–1345	3–34	4.74–46.31	10.94–46.31	37.50–140	56–143

Note: – indicates participants did not undergo an assessment.

aspiration observed on VFSS. Data from each time point were compared using Wilcoxon Signed Rank Tests. Effect size (r) was calculated using the formula $r=z/\sqrt{N}$ [22]. Values were interpreted as 0.1 to 0.3 = small effect, 0.3 to 0.5 = medium effect, and >0.5 = large effect [23]. Interrater reliability was determined using Gwet's Agreement Coefficient [24], and interpreted as < 0 – *less than chance agreement*; 0.01 to 0.20 – *slight agreement*; 0.21 to 0.40 – *fair agreement*; 0.41 to 0.60 – *moderate agreement*; 0.61 to 0.80 – *substantial agreement*; 0.81 to 0.99 – *almost perfect agreement* [25].

Each VFSS was conducted jointly by a qualified Speech Pathologist trained in VFSS administration and interpretation (first author), and a radiographer. Each VFSS was rated by MK and JD; both qualified Speech Pathologists with over five years of experience in evaluating VFSS. Raters were blinded to the time point of the VFSS. Statistical analysis was performed using SPSS Statistical Software Version 22.0 (SPSS®IBM Corporation, Armonk, New York, USA), and AgreeStat [24].

The relationships between disease severity and entry of matter into the airway during swallowing (penetration and aspiration) were considered in two ways. Firstly, TP2 data (FARS and PAS scores for all consistencies trialed on VFSS) were correlated using Spearman's Rank correlation to determine if any relationships existed between these data. We then considered TP1 and TP2 data together by merging these statistics with the aim of creating a larger sample size in which to investigate relationships between variables. Spearman's Rank correlations were used to examine merged data (FARS $n=73$, PAS fluid $n=43$, PAS Puree $n=41$, PAS biscuit $n=43$).

The relationships between dysarthria (FDA-2 domain scores) and penetration and aspiration were determined using logistic regression analysis. Each scale on the FDA-2 was considered individually. The dependent variable was determined by dichotomizing the sample into two groups: (1) those who maintained airway closure during the swallow, and (2) those who demonstrated penetration and/or aspiration on any consistency.

3. Results

3.1. Participant characteristics

Twenty-three of the original 59 (40%) participants completed the second assessment (Fig. 1). Seventeen participants repeated the Swal-QOL (mean age 37.48 years, standard deviation 13.71 years), 9 participated in repeat FDA-2 assessment, and 12 underwent VFSS (Table 1). Repeated assessments were completed as close to 12 months apart as possible which coincided with the participants' yearly visit to the FRDA clinic. On average, Swal-QOL assessment was

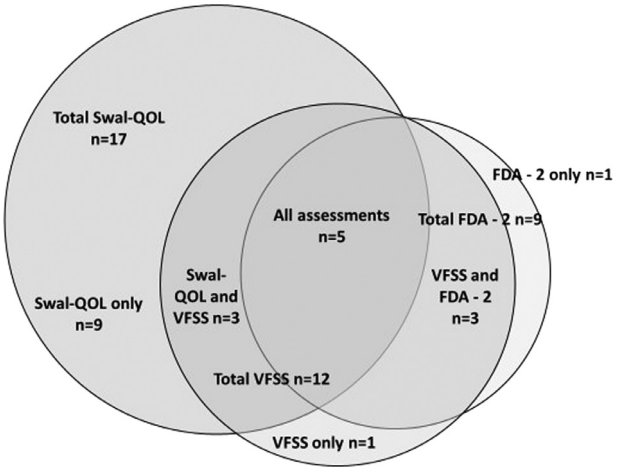

Fig. 1. Participation across assessments.

conducted 332.4 days apart (range 194–423 days), FDA-2 416.1 days (range 306–540 days), and VFSS 365 days (range 190–456 days). FARS scores did not significantly differ between the two timepoints in this study ($Z = -2.3$, $p = 0.02$, $r = -0.47$), however 15 participants were noted to have a higher score (indicating more severe disability) at TP2 (Table 1). The difference in FARS score from TP1 to TP2 ranged from −8.5 points to 18.5 points.

3.2. Swallowing-related QoL

Overall Swal-QOL scores did not significantly differ between time points (TP1: mean 74.82 ± 19.58, TP2: mean 76.82 ± 19.81; $Z = -0.98$, $p = 0.33$, $r = 0.24$). Significant changes in impairment were observed for items related to *Symptom Frequency* (TP1: mean 74.05 ± 18.77, TP2: mean 69.12 ± 22.22; $Z = -2.18$, $p = 0.03$, $r = -0.52$) and *Sleep* (TP1: mean 59.56 ± 33.23, TP2: mean 75.00 ± 26.52, $Z = -2.06$, $p = 0.04$, $r = 0.35$). A significant improvement in function was noted in the *Food Selection* domain (TP1: mean 80.88 ± 23.43, TP2: mean 88.97 ± 21.14; $Z = -2.21$, $p = 0.03$, $r = -0.54$) (Table 2).

3.3. Oromotor function

Overall FDA-2 scores did not significantly differ between TP1 and TP2 however a significant reduction in respiratory function was observed (TP1: mean 2.83 ± 0.79, TP2: mean 3.15 ± 0.64; $Z = -2.83$, $p = 0.01$, $r = 0.67$) (Table 2).

3.4. Swallowing function

Significant change was detected in tongue function, manifesting in difficulty shifting solid food (biscuit) from the oral cavity and oral residue (TP1: mean 2.75 ± 0.75, TP2: mean 3.08 ± 0.67; $Z = -2.12$, $p = 0.03$, $r = 0.43$). Reduced ability to clear residue (puree) from the valleculae (TP1: mean 2.36 ± 0.92, TP2: mean 2.67 ± 0.72; $Z = -2.00$, $p = 0.05$, $r = 0.41$) and above the cricoesophageal sphincter (biscuit) (TP1: mean 2.25 ± 1.06, TP2: mean 2.67 ± 0.98; $Z = -2.33$, $p = 0.02$, $r = 0.48$) was also significantly more commonly seen on the second assessment, indicating worsening of function (Table 2).

3.4.1. Penetration and aspiration

Three participants of 12 (25%) demonstrated aspiration (PAS ≥ 6) on at least one consistency at TP2, and 2/12 demonstrated penetration (PAS ≥ 2). Whilst penetration and aspiration were observed at the second timepoint, no significant differences were evident (Table 2).

3.5. Relationships between disease severity and airway compromise during swallowing

Correlations between timepoint 2 data (FARS and PAS scores with all consistencies) did not yield any significant results (Fluid [$\rho = 0.51$, $p = 0.13$]; Puree [$\rho = 0.02$, $p = 0.96$]; Biscuit [$\rho = 0.61$, $p = 0.6$]).

No significant relationships were revealed between disease severity (FARS) and PAS scores when TP1 and TP2 data were considered together (Fluid [$\rho = 0.12$, $p = 0.49$]; Puree [$\rho = 0.03$, $p = 0.88$]; Biscuit [$\rho = 0.30$, $p = 0.48$]).

4. Discussion

Small but measurable changes in swallowing function were observed in individuals with FRDA over a one-year period. Changes in swallowing function were observed between timepoints on self-report measures of dysphagia symptoms, oromotor performance on respiration tasks and oral and pharyngeal clearance of solid textures of food as determined via VFSS. These changes were observed in the absence of significant change to disease severity. Whilst this study is small in scale, it is the largest study of FRDA-related dysphagia progression to date, and results warrant further investigation into the use of swallowing measures as a marker of FRDA progression.

4.1. Progression of dysphagia-related QoL

Overall swallowing-related QOL (as measured by the total Swal-QOL score) did not change over the course of this study, however participants reported experiencing symptoms of dysphagia more frequently at the second assessment. Increased difficulty selecting appropriate foods to cater for swallowing problems was also reported on follow-up assessment. The limited change in swallowing-related QOL factors exists despite physiological changes observed in swallowing on VFSS, suggesting perceived dysphagia symptoms do not correlate with underling pathology. Further investigation of a larger sample size is needed to explore this relationship. Individuals' awareness and perception of dysphagia may have influenced outcomes at TP2. After the initial assessment (TP1), all participants in this study were provided with education regarding normal swallowing, dysphagia, aspiration, and clinical implications of aspiration (including aspiration-related pneumonia) as per standard

Table 2
Comparisons of swallowing-related QOL, oromotor function, and swallowing function between TP1 and TP2.

Assessment	Domain		TP1		TP2		Wilcoxon signed ranks test and effect size (r)
			Range	Mean ± SD	Range	Mean ± SD	
Swal-QOL	Burden		25–100	84.56 ± 26.34	25–100	82.35 ± 24.63	$Z=-0.43$, $p=0.67$, $r=-0.10$
	Eating desire		17–100	83.82 ± 23.10	8–100	87.25 ± 23.78	$Z=-0.85$, $p=0.40$, $r=0.15$
	Eating duration		0–100	65.44 ± 30.47	0–100	54.41 ± 36.16	$Z=-1.85$, $p=0.07$, $r=-0.44$
	Symptom frequency		29–100	74.05 ± 18.77	9–100	69.12 ± 22.22	$Z=-2.18$, $p=0.03$*, $r=-0.52$
	Food selection		38–100	80.88 ± 23.43	25–100	88.97 ± 21.14	$Z=-2.21$, $p=0.03$*, $r=-0.54$
	Communication		50–100	77.21 ± 20.37	25–100	67.65 ± 21.68	$Z=-1.60$, $p=0.11$, $r=0.27$
	Fear		13–100	72.43 ± 25.01	6–100	76.10 ± 23.72	$Z=-0.92$, $p=0.36$, $r=0.16$
	Mental health		45–100	82.06 ± 23.92	15–100	85.00 ± 22.36	$Z=-1.00$, $p=0.31$, $r=0.17$
	Social		40–100	89.12 ± 19.54	20–100	92.94 ± 20.00	$Z=-1.08$, $p=0.28$, $r=0.19$
	Fatigue		0–100	53.92 ± 30.49	0–100	66.18 ± 29.82	$Z=-1.34$, $p=0.18$, $r=0.23$
	Sleep		0–100	59.56 ± 33.23	0–100	75.00 ± 26.52	$Z=-2.06$, $p=0.04$*, $r=0.35$
	Total		21–100	74.82 ± 19.58	14.41–100	76.82 ± 19.81	$Z=-0.98$, $p=0.33$, $r=0.24$
FDA-2	Reflexes		1–5.67	2.78 ± 0.88	1–5	3.13 ± 0.99	$Z=-1.02$, $p=-0.31$, $r=0.24$
	Respiration		1–7	2.83 ± 0.79	1–5	3.15 ± 0.64	$Z=-2.83$, $p=0.01$*, $r=0.67$
	Lips		1–3.80	2.36 ± 0.37	1–3	2.48 ± 1.28	$Z=-0.56$, $p=0.58$, $r=0.13$
	Palate		1–3.67	2.11 ± 0.75	1–4.3	2.37 ± 1.70	$Z=-1.89$, $p=0.06$, $r=0.45$
	Laryngeal		1–7	4.17 ± 1.35	1.75–6.50	4.33 ± 1.38	$Z=-1.26$, $p=0.21$, $r=0.30$
	Tongue		1–5.33	3.07 ± 0.80	2–4.67	3.02 ± 1.16	$Z=-0.14$, $p=0.89$, $r=0.03$
	Intelligibility		1–6.33	2.19 ± 1.04	1–3.67	2.67 ± 0.12	$Z=-1.79$, $p=0.07$, $r=0.42$
	Total FDA2 score		54–118	76.00 ± 21.77	39–118	78.60 ± 23.22	$Z=-1.40$, $p=0.31$, $r=0.33$
VFSS	Lip function	Fluid	1–2	1.17 ± 0.39	1–2	1.08 ± 0.29	$Z=-1.00$, $p=0.32$, $r=0.20$
		Puree	1–3	1.27 ± 0.47	1–2	1.33 ± 0.29	$Z=-1.73$, $p=0.08$, $r=0.35$
		Biscuit	1–3	1.33 ± 0.49	1–2	1.17 ± 0.29	$Z=-1.41$, $p=0.16$, $r=0.29$
	Tongue function	Fluid	1–3	1.50 ± 0.67	1–2	1.42 ± 0.49	$Z=0.00$, $p=1.00$, $r=0.00$
		Puree	1–3	1.91 ± 0.83	2–4	2.33 ± 0.65	$Z=-1.41$, $p=0.16$, $r=0.29$
		Biscuit	1–3	2.75 ± 0.75	2–4	3.08 ± 0.67	$Z=-2.12$, $p=0.03$*, $r=0.43$
	Jaw function	Fluid	1–2	1.08 ± 0.29	1–1	1.00 ± 0.00	$Z=0.00$, $p=1.00$, $r=0.00$
		Puree	1–1	1.00 ± 0.00	1–2	1.08 ± 0.29	$Z=-1.00$, $p=0.32$, $r=0.20$
		Biscuit	1–2	1.08 ± 0.29	1–2	1.08 ± 0.29	$Z=-1.00$, $p=0.32$, $r=0.20$
	Soft palate function	Fluid	1–4	1.75 ± 0.97	1–2	1.33 ± 0.83	$Z=-0.41$, $p=0.16$, $r=0.29$
		Puree	1–4	1.82 ± 1.17	1–3	1.33 ± 0.83	$Z=-0.41$, $p=0.16$, $r=0.29$
		Biscuit	1–4	1.92 ± 1.16	1–2	1.33 ± 0.83	$Z=-1.00$, $p=0.32$, $r=0.20$
	Reflex initiation	Fluid	2–4	2.92 ± 0.67	1–4	2.33 ± 0.65	$Z=-1.73$, $p=0.08$, $r=0.35$
		Puree	2–4	3.00 ± 0.45	1–4	2.25 ± 0.58	$Z=-0.41$, $p=0.16$, 0.08
		Biscuit	2–4	3.08 ± 0.51	1–4	2.50 ± 0.51	$Z=-0.41$, $p=0.16$, $r=0.08$
	Aspiration	Fluid	1–3	1.67 ± 0.78	1–4	1.75 ± 0.89	$Z=-0.41$, $p=0.16$, $r=0.08$
		Puree	1–3	1.82 ± 0.75	1–2	1.25 ± 0.94	$Z=-0.58$, $p=0.56$, $r=0.12$
		Biscuit	1–2	1.25 ± 0.45	1–3	1.17 ± 0.78	$Z=-1.00$, $p=0.32$, $r=0.20$
	Residue in valleculae	Fluid	1–3	1.50 ± 0.80	1–2	1.58 ± 0.65	$Z=-0.58$, $p=0.56$, $r=0.12$
		Puree	1–4	2.36 ± 0.92	1–4	2.67 ± 0.72	$Z=-2.00$, $p=0.05$*, $r=0.41$
		Biscuit	1–4	3.00 ± 0.95	1–4	2.83 ± 0.79	$Z=-1.00$, $p=0.32$, $r=0.20$
	Residue in pyriform sinuses	Fluid	1–3	1.25 ± 0.62	1−3	1.42 ± 0.67	$Z=0.00$, $p=1.00$, $r=0.0$
		Puree	1–3	1.91 ± 0.83	1–3	1.83 ± 0.51	$Z=-0.41$, $p=0.16$, $r=0.08$
		Biscuit	1–3	1.83 ± 0.72	1–4	1.92 ± 0.75	$Z=-0.71$, $p=0.48$, $r=0.14$
	Pharyngeal function	Fluid	1–3	1.25 ± 0.62	1–3	1.42 ± 0.67	$Z=0.00$, $p=1.00$, $r=0.00$
		Puree	1–3	2.00 ± 0.89	1–4	2.50 ± 0.80	$Z=-2.65$, $p=0.01$*, $r=0.54$
		Biscuit	1–3	2.17 ± 0.83	1–4	2.33 ± 0.89	$Z=-0.41$, $p=0.16$, $r=0.08$
	Cricopharyngeal function	Fluid	1–3	1.33 ± 0.65	1–2	1.25 ± 0.67	$Z=-1.00$, $p=0.32$, $r=0.20$
		Puree	1–3	2.09 ± 0.94	1–4	1.67 ± 0.79	$Z=-0.41$, $p=0.16$, $r=0.08$
		Biscuit	1–4	2.25 ± 1.06	1–4	2.67 ± 0.98	$Z=-2.33$, $p=0.02$*, $r=0.48$
	PAS score	Fluid	1–8	2.83 ± 2.66	1–2	2.25 ± 2.49	$Z=-0.00$, $p=1.00$, $r=0.00$
		Puree	1–8	2.91 ± 2.66	1–2	1.67 ± 2.01	$Z=-1.00$, $p=0.32$, $r=0.20$
		Biscuit	1–8	2.08 ± 2.19	1–2	1.17 ± 0.39	$Z=-1.00$, $p=0.32$, $r=0.20$

SD – Standard deviation.

* Significant at $p < 0.05$.

Swal-QOL – Each item is scored on a scale from one to five, where 5 = optimal, and 1 = maximal impairment. Scores for each Swal-QOL domain are expressed as a percentage of the maximum possible domain score. A total Swal-QOL score is derived by summing each domain score and dividing by 11 giving a total Swal-QOL score that ranges between 0 and 100 (worst–best).

FDA-2 – Items are scored on a 9-point scale, where a score of 1 corresponds to normal oromotor function and a score of 9 indicates absence of function (2–4 = mild, 5–6 = moderate, 7–8 = severe, 9 = profound impairment).

clinical care. Therefore, participants may have developed a greater understanding of swallowing physiology, dysfunction, and effective management at TP2, and potentially felt more equipped to manage their symptoms. Symptom perception is known to influence many aspects of disease management, including health maintenance, accuracy of symptom reporting, and adherence to medical regimes [26]. Further, dysphagia is known to affect the mental state of those afflicted [27,28]. Previous research shows that explanation and education of the normal swallowing mechanism improves dysphagia-related depression and anxiety in individuals with Multiple Sclerosis [27].

4.2. Progression of FRDA-related oromotor function and dysphagia

Oromotor function was relatively preserved except for respiratory function as assessed by tests of lip, palate, laryngeal and tongue function on the FDA-2. It is known that speech changes over the course of the disease, providing additional evidence that observable changes in oromotor performance are a feature of FRDA [29,30].

Site specific changes in swallowing function were observed over the course of the current study, with clearance of solid textures of food from the pharynx worsening at the second time point. Tongue function also declined. Reduced tongue coordination and timing can lead to difficulty forming a cohesive bolus and reduced capacity to shift material from the oral cavity to the pharynx. It can also impact the efficiency of the pharyngeal phase of swallowing [31]. Entry of barium into the airway (penetration and aspiration) did not appear to vary between time points, however three of the participants demonstrated reflexive airway protection mechanisms at the second time point (all with fluid), which was not observed on initial assessment [9]. One third of the participants (4/12) presented new signs of significant airway penetration and/or aspiration (determined at PAS $\geq$ 3) at TP2, and all with fluid, that were not present at baseline. No change in airway entry was noted with puree or biscuit. The use of airway protective behaviors (coughing in response to penetration/aspiration of the airway) in this study has not previously been reported in FRDA [9]. At the second assessment, three participants (25%) recorded a PAS of 7 and only one of these three participants recorded a PAS score greater than 3 on the initial VFSS. These observations suggest airway protective responses may be diminished in FRDA rather than absent. It is possible participants aspirated a greater amount of barium at TP2 compared to TP1, resulting in a reflexive cough which was not apparent at TP1 (given silent aspiration is known to be volume dependent [32]), however this was not measured in the study. Regardless, further investigation of laryngeal sensitivity in FRDA is warranted.

4.3. Limitations of the present study

It is possible the inter-assessment interval was not long enough to capture change in swallowing function. In a study of dysarthria in individuals with FRDA, significant change in speech function was noted across a two-year duration [29]; double the timeframe of the present study. Further, the small sample did not provide adequate statistical power to uncover patterns of change. It is also possible that the tools used to assess function lack the sensitivity and reliability required to track change in this protocol. VFSS only provides a snapshot of swallowing ability and is not a true reflection of swallowing function over a whole meal. A tool that simultaneously quantifies mealtime behaviors, consumption of different consistencies and textures and clinical history may better serve this purpose, such as the Clinical Assessment of Dysphagia in Neurodegeneration [33].

A significant consideration of this study is the small sample size, with only 23 participants being assessed at the second-time point. The small sample size may have hindered the possibility of detecting changes in swallowing function between the timepoints. In this study, FRDA was considered broadly and due to the small size, the sample could not be stratified further to isolate individuals with typical versus atypical FRDA, including late onset FRDA which is typically associated with less severe symptoms. Heterogeneity in the sample will have affected the results.

The present study profiles the oral and pharyngeal stages of the swallow only and does not consider possible oesophageal causes of dysphagia. Atypical oesophageal function during swallowing is reported in other neurogenerative conditions, such as oculopharyngeal muscular dystrophy [34,35]. This dysfunction may be characterized by upper oesophageal constriction resulting in food blockage at the sphincter requiring myotomy [36] or smooth muscle impairment [34]. Given oesophageal dysphagia is present in other neurodegenerative conditions, further investigation is warranted in FRDA.

4.4. Clinical implications and future directions

The longitudinal data gathered in this body of research provide the first step towards improving our understanding of dysphagia progression in FRDA. Regular monitoring of dysphagia should be considered an important component of disease management, and further research is needed to evaluate whether early intervention would modify the swallowing progression seen in individuals with FRDA. The management of FRDA-related dysphagia should be guided and informed via collaboration between the Speech Pathologist, Neurologist, the wider treating team, and the person with FRDA, to address the physical and psychosocial impacts of swallowing impairment. Current data point toward management that includes diet and postural modification, alongside the prescription of specialized feeding equipment such as controlled-flow containers [37]. Drastic textural modifications to food and thickening fluids is not recommended given the impact dysphagia and these modifications have on the QOL of individuals with FRDA. Behavioral treatments targeting speech have been shown to improve swallowing function in Parkinson's disease [38] and

thus may be beneficial in FRDA (using intervention specific to the condition). There is no strong evidence supporting the use of non-systemic behavioral therapy (such as oral motor exercises) in FRDA [39]. Biofeedback via video feedback has also been shown to improve swallowing perception in PD [40], and therefore should also be considered in FRDA.

Given lingual dysfunction has been identified as a key characteristic of FRDA-related dysphagia (manifesting in reduced oral and pharyngeal clearance of ingested material), future studies and interventions may also focus on objective measurement of lingual force which may influence swallowing function. A tool such as the Iowa Oral Performance Instrument (IOPI) would provide these objective data. Judgments of lingual force and strength in the present study were done via VFSS (whereby lingual dysfunction was evident in the presence of oral residue) and on the FDA-2 which includes five measures of tongue function (at rest, protrusion, elevation, lateral, alternate, and in speech). Measures are rated via observation by the assessor, and therefore cannot be considered as robust measures of tongue force or wastage. However, it is noted that 6/10 (60%) participants presented with normal tongue function *at rest* (no involuntary movements or evident asymmetry) on the FDA.2. The remaining four participants presented with mild impairment of the tongue *at rest*. Therefore, it is not expected that tongue wastage was an influencing factor in this population group. Further, investigation must be undertaken into the relationship between truncal muscle disturbance (known to exist in FRDA) [41] and dysphagia in this population group. *Respiration* was the only domain of the FDA-2 in which scores were significant worse at TP2 in this study ($p = 0.01$). In these subtests the participant's respiratory function is rated at rest, during controlled exhalation and in speech. All of these tasks require adequate postural and truncal support, thus evidencing the need for this as a future area of study in this population.

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