

1 Article

2 Swallowing Speed as Potential Predictor of 3 Aspiration in Parkinson's Disease Patients

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15

16 **Abstract:** There is still a lack of a clinical test to reliably identify patients with Parkinson's disease
17 (PD) being at risk for aspiration. In this prospective, controlled, cross-sectional study we assessed if
18 swallowing speed for water is a useful clinical test to predict aspiration proven by flexible
19 endoscopic evaluation of swallowing (FEES). Due to this we measured the swallowing speed for 90
20 ml water in 115 consecutive and unselected PD outpatients of all clinical stages and 32 healthy
21 controls. Average swallowing speed was lower in patients compared with controls (6.5 ± 3.9 ml/s vs.
22 8.5 ± 3.2 ml/s; $p < 0.01$). The disease-independent widely used threshold of < 10 ml/s showed
23 insufficient sensitivity of 88% and specificity of 19% with unacceptable false-positive rates of 63% for
24 patients and 69% for controls. Receiver operating characteristic (ROC) analysis was carried out to
25 define a suitable cut-off value for detection of aspiration of water (area under the curve 0.72, $p <$
26 0.001) in PD patients. The optimized cut-off value was 5.5 ml/s with a sensitivity of 69% and a
27 specificity of 64%. Overall, measuring swallowing speed is prone to methodological errors and not
28 suitable as a screening instrument to predict aspiration in PD patients.

29 **Keywords:** dysphagia, FEES, Parkinson's disease, swallowing speed, screening, water test

30

31 1. Introduction

32 Despite its substantial relevance for morbidity and mortality, dysphagia in Parkinson's disease (PD)
33 is still often overlooked. Usually, patients do not complain about dysphagia due to impaired
34 self-perception of swallowing [1-3]. The swallowing act starts with the oral phase, continues with the
35 pharyngeal phase and leads to the esophageal phase. This process is susceptible to impairments as
36 more than 30 nerves and muscles are involved [4]. The impairments are described with the terms
37 "leaking" (i.e. food bolus passes from the oral cavity into the pharynx without a swallowing reflex),
38 "penetration" (i.e. bolus penetrates into the laryngeal inlet without actually reaching the trachea)
39 and "aspiration" (i.e. bolus reaches the trachea). A severe form of aspiration is the silent aspiration,
40 where the bolus in the trachea is not realized by the patient. Food residues play an additional role in
41 the pharynx, due to the danger of later aspiration.

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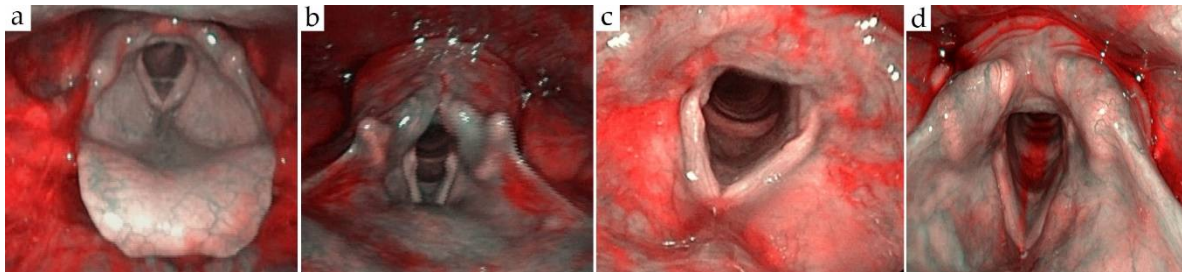


Figure 1. Endoscopic examples. (a) No penetration or aspiration, but residues of thickened water. (b) Bolus penetration above vocal folds. (c) Bolus penetration with contact to vocal folds. (d) Bolus aspiration into the trachea.

It is of great importance to reliably identify PD patients at risk for aspiration requiring further testing and to exclude PD patients without relevant dysphagia from unnecessary interventions. Such a clinical screening tool should be easy and quick to apply in daily clinical practice, cost-effective, non-invasive and safe for the patient. Patients screened at risk for aspiration should then undergo further testing either with flexible endoscopic evaluation of swallowing (FEES) or videofluoroscopic swallowing study (VFSS). The only PD-specific questionnaire-based screening tool for swallowing problems was found to be not sufficient predictive for FEES-proven aspiration [5,6]. Today, the 3-ounce water swallow test is frequently used to screen individuals with different diseases for aspiration risk. The test required to drink approximately 90 ml of water without interruption [7]. Criteria for referral for subsequent investigation are an inability to complete the task, coughing or choking as well as hoarse or wet voice either during or within 1 minute of test completion. However, the test has been found to be prone to over-referral to further testing (e.g. by FEES or VFSS) and unnecessary dietary restrictions due to a high false-positive rate in a large heterogeneous collective of patients [8].

Another predictor used for clinically relevant dysphagia has been swallowing speed. Based on correlation with subjective abnormal swallowing, a threshold of 10 ml/s was proposed [9]. This threshold was adopted by several studies [10-12]. Taking these four studies together, only four percent of all subjects were known to have PD. Thus, it remains unclear if this threshold is reliable for PD patients. Noteworthy, a mean swallowing speed of 7.0 ml/s has been found in 100 PD patients suggesting that a threshold of 10 ml/s might be too high for patients with PD [13]. While it is consensus that average swallowing speed decreases with age in healthy subjects [14-16], data on gender differences in swallowing speed are controversial with the description of slower [10,15,17] or equal [16] speed in women when compared to men.

The main aim of the present study was to evaluate whether swallowing speed of water, i.e. a defined volume of 90 ml water divided by the time needed, is a reliable screening test for FEES-proven aspiration in PD patients and which cut-off value might be adequate for PD. We furthermore assessed a potential impact of age, gender, disease duration, disease severity and cognition on swallowing speed in our PD cohort.

2. Materials and Methods

2.1. Study design and ethical approval

This prospective, controlled, cross-sectional study was approved by the local ethics committee of the Medical Council Hamburg (trial number PV5089) and written informed consent was obtained from all patients.

86 2.2. Subjects

87 Subjects were recruited from the Center for Clinical Neurosciences at the University Medical Center
88 Hamburg-Eppendorf (outpatient clinic) between March 30th and May 13th, 2016. 122 of 146 eligible,
89 consecutive PD patients consented to participate. Three patients had to be excluded (soft palate cancer
90 in one case, early termination of FEES in two cases) and in four patients swallowing times for water
91 could not be measured (premature termination by the examiner because of excessive aspiration of
92 water in two cases, renouncement by the examiner because of preceding aspiration of puree and a
93 teaspoon of water in one case and premature termination by the patient in one case). Thus 115 patients
94 remained for analysis. Control subjects negated a history of diseases of the central nervous system as
95 well as swallowing problems based on a self-developed 6-item screening questionnaire.
96

97 2.3. Assessments

98 All PD patients were examined during medical “on”-state. Non-motor symptoms, including
99 dysphagia in question 3 (NMS-Quest 3), were evaluated by the Non-motor symptoms questionnaire
100 (NMS-Quest). Cognitive function and mood were examined in patients and controls with the Montreal
101 Cognitive Assessment (MOCA) respectively the second edition of the Beck Depression Inventory
102 (BDI-II).
103

104 The FEES protocol was described in detail in a previous publication [3]. The FEES examinations were
105 performed by experienced otorhinolaryngologists with a 2.6-mm-diameter high-definition
106 rhino-laryngo videoscope (ENT-V3, Olympus Medical Systems Corp., Tokyo, Japan). If a teaspoon of
107 green-coloured water could be swallowed inconspicuously, the participants were instructed to drink a
108 standardized volume of 90 ml water at room temperature through a straw as quickly as safely
109 possible. The timer started with the first contact of the water with the lips and stopped with the end of
110 the last swallow as seen during FEES. Swallowing speed was only calculated if the complete volume
111 was applied. Penetration and aspiration of water were assessed according to the eight-step
112 Penetration-Aspiration Scale (PAS) of Rosenbek [18]. Aspiration, i.e. water passes below the vocal
113 folds, is indicated by PAS values of 6 to 8.
114

115 2.4. Statistical analysis

116 Quantitative data was illustrated with means and standard deviation (SD) and differences between
117 groups were analysed using t-test for independent samples. Qualitative data was illustrated with
118 frequencies and analysed using Fisher’s exact test. Correlation coefficients were based on Kendall’s tau
119 and are interpreted according to [19]. We used Clopper-Pearson confidence intervals (CI) for
120 sensitivity and specificity, those for predictive values were calculated according to [20]. All statistical
121 tests were two-tailed and the alpha level was set to 0.05. Statistical analyses were performed with
122 SPSS, version 23 (IBM, USA).
123

124 3. Results

125 3.1. Subject characteristics

126 Demographic and clinical characteristics of patients and controls are presented in Table 1. Although
127 the quantitative scores for cognitive function (MOCA) and mood (BDI-II) were significantly worse in
128 patients, the two groups did not differ substantially if the subjects were allocated to clinically
129 relevant groups (existence of cognitive deficits respectively degree of depression).
130

131 **Table 1.** Subject characteristics of PD patients and controls.

132

	Patients (n = 115) Mean ± SD or N (%)	Controls (n = 32) Mean ± SD or N (%)	P value
Age (years)	68.6 ± 10.2	68.1 ± 10.7	0.78 ^a
Men	76 (66%)	16 (50%)	0.10 ^b
BMI (kg/m ²)	25.5 ± 4.0	24.4 ± 3.6	0.14 ^a
MOCA (score)	22.2 ± 4.4	25.3 ± 3.0	< 0.001 ^a
- Cognitive deficit (i.e. MOCA <26 points)	81 (70%)	17 (53%)	0.09 ^b
BDI-II (score)	10.5 ± 8.9	6.1 ± 7.0	0.01 ^a
- No depression (0-13)	90 (78%)	26 (81%)	0.50 ^b
- Mild depression (14-19)	10 (9%)	4 (13%)	
- Moderate depression (20-28)	7 (6%)	2 (6%)	
- Severe depression (29-63)	8 (7%)	0 (0%)	
Disease duration (years)	9.6 ± 7.1	NA	NA
NMS-Quest 3 ("yes" answers)	9.8 ± 5.0	NA	NA
Hoehn and Yahr			
- Stage 1	5 (4%)	NA	NA
- Stage 2	58 (50%)	NA	NA
- Stage 3	32 (28%)	NA	NA
- Stage 4	17 (15%)	NA	NA
- Stage 5	3 (3%)	NA	NA
MDS-UPDRS			
- Total score (I-IV)	57.0 ± 26.9	NA	NA
- Motor score (III)	30.3 ± 13.3	NA	NA
Deep brain stimulation	27 (23%)	NA	NA
Levodopa equivalency dose (mg)	748 ± 423	NA	NA

133 P values were calculated with ^a T test or ^b Fisher's exact test. *BDI-II* Beck depression inventory
 134 second edition, *BMI* body mass index, *MDS-UPDRS* Movement Disorder Society-sponsored revision
 135 of the unified Parkinson's disease rating scale, *MOCA* Montreal cognitive assessment, *NA* not
 136 applicable, *NMS-Quest 3* Question 3 of the Non-motor symptoms questionnaire. Levodopa
 137 equivalency dose was calculated according to [21].
 138

139 3.2. Results of flexible endoscopic evaluation of swallowing (FEES)

140 The main results are shown in Table 2. Leakage was observed regularly in patients but attained
 141 severe extent in only five cases. In contrast, aspiration of water occurred in nearly every fourth
 142 patient, but in none of the controls.

143

144 **Table 2.** FEES results.

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	Patients (n = 115) N (%)	Controls (n = 32) N (%)
Leakage of water	29 (25%)	1 (3%)
- Base of the tongue or valleculae	18	0
- Lateral channels or tip of the epiglottis	6	0
- Piriform sinus or laryngeal rim (sides or back)	3	1
- Laryngeal vestibule or aspiration before the swallow	2	0
Aspiration of water	26 (23%)	0 (0%)
- PAS 6: material is effectively ejected from airway	2	0
- PAS 7: material is not ejected despite effort	4	0
- PAS 8: silent aspiration	20	0

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147 3.3. Swallowing speed

148 The key findings are illustrated in Table 3. Swallowing speeds differed significantly between
 149 patients and controls. Though, the absolute difference in means was rather small (two seconds). A
 150 relevant gender effect could only be found within patients with men swallowing faster than women.

151

152 **Table 3.** Swallowing speed.

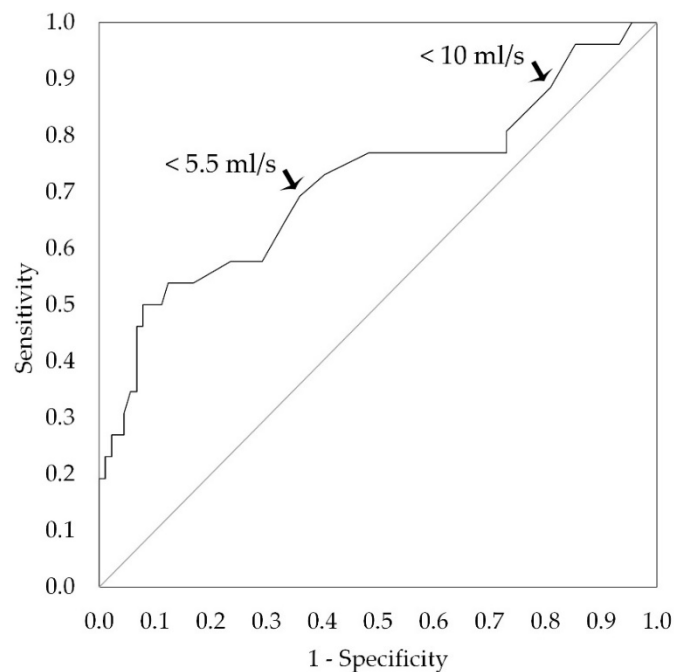
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	PD patients (n = 115)	Controls (n = 32)	P value (T test)
Swallowing speed (ml/s)	6.5 ± 3.9	8.5 ± 3.2	< 0.01
Mean ± SD	male: 7.3 ± 4.2 female: 5.1 ± 2.8	male: 8.6 ± 2.3 female: 8.4 ± 4.0	
	p < 0.01	p = 0.85	

154

155 To determine an appropriate cut-off value for swallowing speed in order to reliably detect aspiration
 156 of water, a receiver operating characteristic (ROC) analysis was carried out as shown in Figure 2. The
 157 points for the formerly proposed cut-off value of < 10 ml/s and the point with the shortest distance to
 158 the upper left corner of the diagram (and therefore the best compromise of sensitivity and
 159 specificity) are tagged. The latter was equivalent to a cut-off value of < 5.5 ml/s.

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162

163 **Figure 2.** Receiver operating characteristic (ROC) curve for swallowing speed for detection of
 164 aspiration of water (PAS 6-8). Area under the curve (AUC) 0.72 [95% CI: 0.59, 0.84], p < 0.001.

165

166 In Table 4 sensitivity, specificity, positive and negative predictive values are listed for a selection of
 167 different cut-off values. Even for the optimized cut-off value of < 5.5 ml/s, sensitivity and specificity
 168 were rather low (69% respectively 64%). This corresponded to a rather low area under the curve
 169 (AUC) of 0.72. The false-positive rate for a threshold of < 10 ml/s was 63% (72/115).

170

171 **Table 4.** Statistical Evaluation of different cut-offs for swallowing speed to detect aspiration of water
 172 (PAS 6-8).

173

Cut-off for swallowing speed	Sensitivity	Specificity	Positive predictive value	Negative predictive value
< 10 ml/s	23/26 = 88% (95% CI 70–98)	17/89 = 19% (95% CI 12–29)	23/95 = 24% (95% CI 21–28)	17/20 = 85% (95% CI 64–95)
< 9 ml/s	21/26 = 81% (95% CI 61–93)	24/89 = 27% (95% CI 18–37)	21/86 = 24% (95% CI 20–29)	24/29 = 83% (95% CI 67–92)
< 8 ml/s	20/26 = 77% (95% CI 56–91)	24/89 = 27% (95% CI 18–37)	20/85 = 24% (95% CI 19–28)	24/30 = 80% (95% CI 65–90)
< 7 ml/s	20/26 = 77% (95% CI 56–91)	31/89 = 35% (95% CI 25–46)	20/78 = 26% (95% CI 21–31)	31/37 = 84% (95% CI 71–92)
< 6 ml/s	19/26 = 73% (95% CI 52–88)	53/89 = 60% (95% CI 48–70)	19/55 = 35% (95% CI 27–43)	53/60 = 88% (95% CI 80–94)
< 5.5 ml/s *	18/26 = 69% (95% CI 48–86)	57/89 = 64% (95% CI 53–74)	18/50 = 36% (95% CI 28–45)	57/65 = 88% (95% CI 80–93)
< 5 ml/s	15/26 = 58% (95% CI 37–77)	63/89 = 71% (95% CI 60–80)	15/41 = 37% (95% CI 27–48)	63/74 = 85% (95% CI 78–90)

174 * Optimized cut-off according to ROC curve (Figure 3). CI confidence interval.

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Applying the cut-off values to our healthy controls led to a high false-positive rate, which attained 69% if a threshold of < 10 ml/s was used (Table 5).

Table 5. False-positive rates in controls for different cut-offs for swallowing speed.

Cut-off for swallowing speed	< 10 ml/s	< 9 ml/s	< 8 ml/s	< 7 ml/s	< 6 ml/s	< 5.5 ml/s	< 5ml/s
False-positive rate	22/32 (69%)	18/32 (56%)	13/32 (41%)	13/32 (41%)	6/32 (19%)	5/32 (16%)	4/32 (13%)

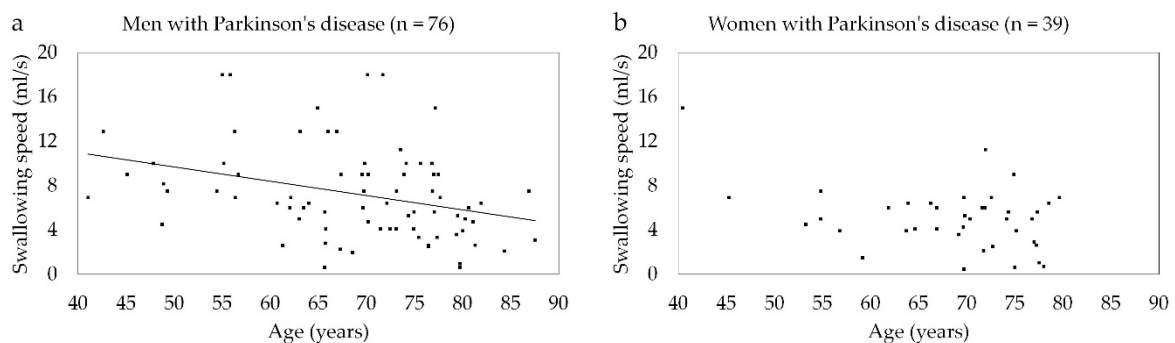
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183 3.4. Influence of patient characteristics on swallowing speed

184 A significant correlation between increasing age and decreasing swallowing speed could only be
185 found for men in the patient cohort and exclusively for women in the control cohort (Figures 3 and
186 4).

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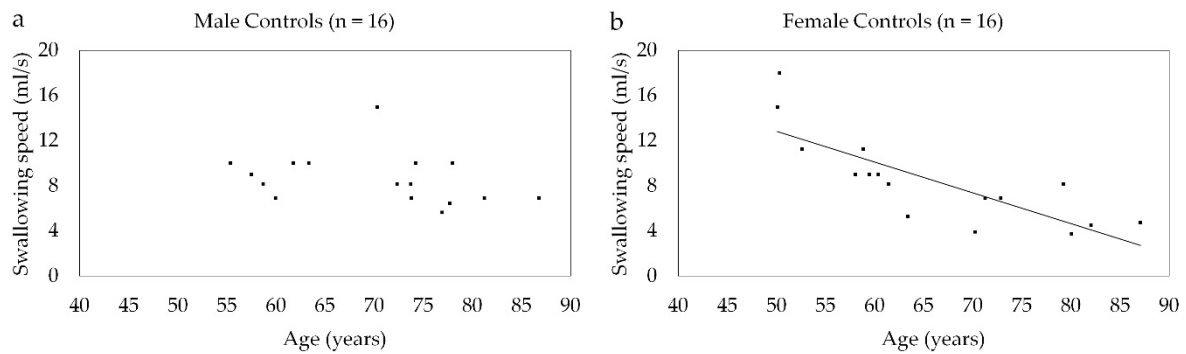
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Figure 3. Relation between age and swallowing speed in patients with Parkinson's disease. (a) There was a weak correlation in men (coefficient -0.25 [95% CI: -0.11, -0.38], $p = 0.001$, R^2 of the regression line 0.11). (b) No significant correlation was found in women.

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Figure 4. Relation between age and swallowing speed in controls. **(a)** No significant correlation was found in men. **(b)** There was a strong correlation in women (coefficient -0.72 [95% CI: -0.42, -0.91], $p < 0.001$, R^2 of the regression line 0.65).

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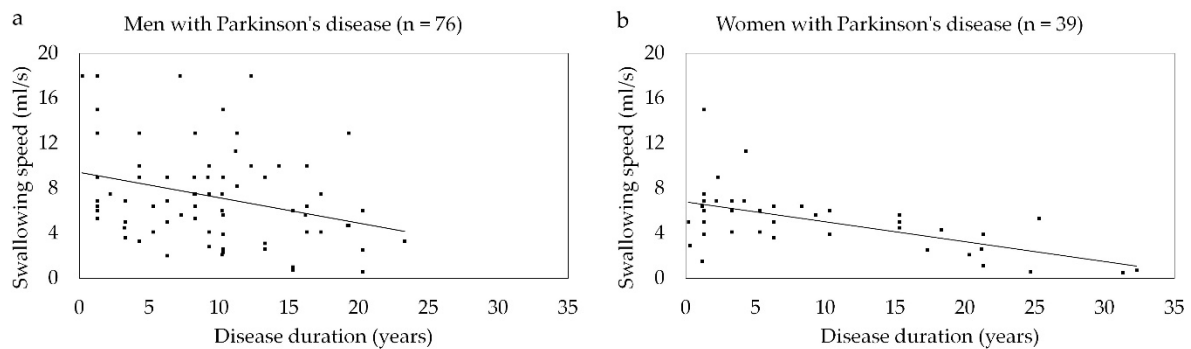
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There was a weak to moderate (male respectively female) correlation of swallowing speed with disease duration (Figure 5).



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Figure 5. Relation between disease duration and swallowing speed in PD patients. **(a)** There was a weak correlation in men (coefficient -0.20 [95% CI: -0.04, -0.34], $p = 0.014$, R^2 of the regression line 0.10). **(b)** There was a moderate correlation in women (coefficient -0.40 [95% CI: -0.17, -0.62], $p < 0.001$, R^2 of the regression line 0.34).

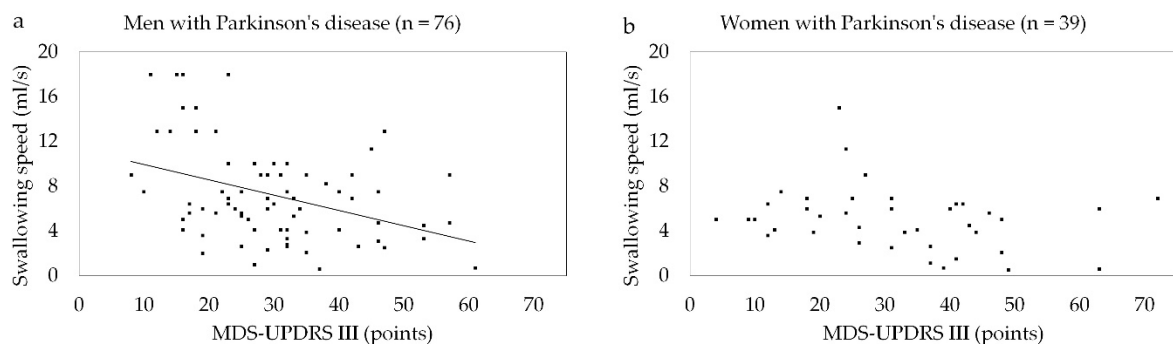
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We found a significant correlation of swallowing speed with disease severity determined as MDS-UPDRS III only for male patients but not in female patients (Figure 6).



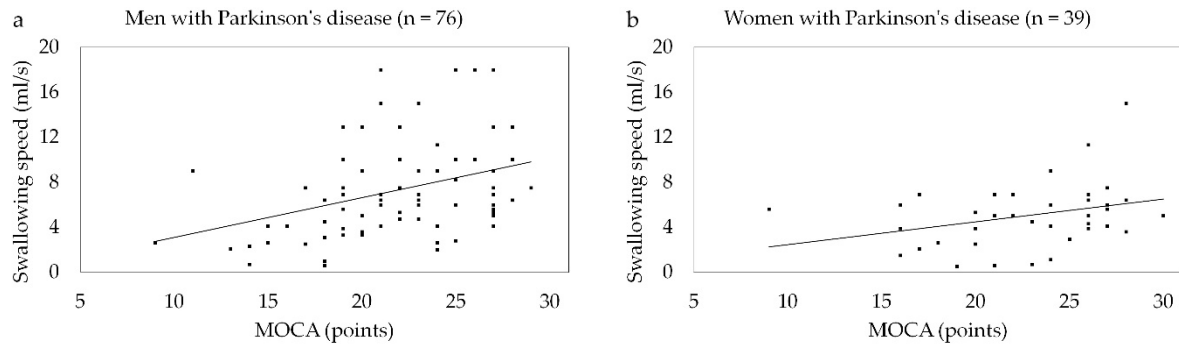
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Figure 6. Relation between disease severity (i.e. MDS-UPDRS III) and swallowing speed in PD patients. **(a)** There was a weak correlation in men (coefficient -0.25 [95% CI: -0.08, -0.40], $p < 0.01$, R^2

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219 of the regression line 0.15). (b) No significant correlation was found in women. *MDS-UPDRS*
 220 Movement Disorder Society-sponsored revision of the unified Parkinson's disease rating scale.

221
 222 There was a weak correlation of swallowing speed with cognition determined as MOCA both in
 223 male and female patients (Figure 7).
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 226
 227 **Figure 7.** Relation between cognition (i.e. MOCA) and swallowing speed in PD patients. (a) There
 228 was a weak correlation in men (coefficient 0.28 [95% CI: 0.12, 0.42], $p < 0.001$, R^2 of the regression line
 229 0.14). (b) There was a weak correlation in women (coefficient 0.25 [95% CI: 0.05, 0.46], $p = 0.03$, R^2 of
 230 the regression line 0.10). MOCA Montreal cognitive assessment.
 231

232 4. Discussion

233 We assessed for the first time swallowing speed of water as a potential predictive parameter for
 234 aspiration in PD patients compared with controls. FEES was applied as the gold standard
 235 examination to prove aspiration.

236 The usual cut-off value of 10ml/s is assumed to indicate dysphagia. We not only found that this
 237 usual cut-off value is too high but also, that even using an optimized and almost two-fold lower
 238 threshold of 5.5 ml/s is not suitable to predict aspiration with reasonable sensitivity and specificity.
 239

240 4.1. Swallowing speed in PD patients

241 Searching the literature revealed that the precedent terminology for swallowing speed is
 242 heterogeneous and includes particularly the terms "swallowing velocity" "swallowing capacity",
 243 "flux of ingestion" or "swallowing flow" as well [13,14,17,22,23]. Considering all these terms, we
 244 found five studies assessing swallowing speed primarily in PD patients but none with an objective
 245 evaluation of aspiration using either FEES or VFSS [11,13,23-25]. Mean swallowing speed in our PD
 246 cohort (6.5 ± 3.9 ml/s) was significantly lower compared with controls (8.5 ± 3.2 ml/s) and in
 247 accordance to findings of Kanna and Bhanu [13] in 100 PD patients (7.0 ± 3.2 ml/s). Studies with
 248 lower numbers of PD patients ($n = 10$ to 75) showed mean swallowing speeds of 4.3 ml/s to 9.5 ml/s
 249 [23-25]. Among the five mentioned studies, cognitive impairment was an exclusion criterion except
 250 for one. Only three studies reported on a clinical examination of swallowing but none correlated
 251 swallowing speed with reliably proven aspiration as it was done in our study.
 252

253 We did not count the number of swallows and therefore could not determine the exact volume per
 254 swallow but prolonged swallowing speed in PD patients might be related to a reduced bolus size as
 255 one mechanism of compensation [26]. Thus, a low swallowing speed may indicate awareness for
 256 dysphagia. This was shown for patients with neurological diseases as the groups with poor
 257 awareness drank water significantly more quickly [9,27]. This appears surprising as intuitively fast
 258 swallowing speeds are interpreted as uncritical. Instead, patients with slow swallowing speed may
 259 need less instruction and guidance regarding compensation maneuvers as they already adapt to

260 dysphagia. However, secure differentiation between adaptation and swallowing problems is,
261 however, only possible by an objective assessment of swallowing, e.g. by FEES. This might also
262 account for the difficulties of finding a screening test suitable for all patient groups equally.

263
264 The speed of swallowing might also be negatively influenced by a prolonged oral phase due to its
265 arbitrary innervation [4]. However, our FEES results suggest that the oral phase is less relevant
266 overall in PD patients as we found severe leakage (as the correlate of an affected oral phase) in only
267 five cases but aspiration in twenty-six cases. Thus, the pharyngeal phase seems to be critical, but it is
268 relatively underrepresented in swallowing times. This is underlined by a videofluorographic study,
269 which found no differences in the duration of the oropharyngeal phase in PD patients with and
270 without aspiration [28]. In addition, 3 of 119 patients (3%) were excluded from the study due to
271 excessive silent aspiration. These patients would have been at relevant risk if a water swallow test
272 with 90 ml had been applied blindly. Silent aspiration (PAS 8) of a lesser degree, which would not
273 have been detected without direct visualization, was encountered frequently (n = 20, 17% of all
274 patients).

276 4.2. Influence of PD patient characteristics on swallowing speed

277 We found men swallowing faster than women (7.3 ± 4.2 ml/s vs. 5.1 ± 2.8 ml/s) which also fits the
278 results of Kanna and Bhanu [13] (7.2 ± 3.4 ml/s in men and 6.6 ± 2.8 ml/s in women). Noteworthy, we
279 detected a statistically significant lower swallowing speed for women exclusively in the patient
280 cohort but not amongst controls. The latter result conforms with a large study which found no
281 significant sex-related differences in healthy subjects [16]. Gender differences may be due to the
282 maximum tolerated oral volume, which was reported to be 71 ml in men respectively 55 ml in
283 women [29]. Higher volumes per swallow may facilitate higher swallowing speed in men.

284
285 Age did not consistently correlate with swallowing speed as a correlation was found only in male
286 PD and female control subjects. The statistically most robust study found an age-related increase in
287 duration of swallowing only in the group of older aged participants, i.e. 66 years of age or older [16].
288 The mean age of our participants was marginally higher than this lower limit. Within the group of
289 PD patients, though not differing with respect to mean age, there were 9 men (12% of all men) but no
290 women at an age of > 80 years. This may account for the weak correlation found in our male patients.
291 Our male control cohort was most likely underpowered (n = 16) to reveal a correlation of swallowing
292 speed with age.

293
294 There was a weak to moderate correlation of disease duration with swallowing speed in men and
295 women. This corresponds to the findings of Kanna and Bhanu [13]. However, disease severity (i.e.
296 MDS-UPDRS III) correlated weakly ($\tau = -0.25$) exclusively in men. Kanna and Bhanu [13] did not
297 differentiate between gender but found a very strong correlation ($r = -0.83$). This discrepancy may be
298 partly due to the usage of Pearson correlation instead of Kendall's Tau, which was used in our study.
299 It is considered more robust but therefore leads to lower correlation coefficients. Furthermore, the
300 versions of UPDRS differed as we used the recent revision, but this should not account for much
301 variance. Our results are supported by a study, which found no correlation of swallowing speed
302 with Hoehn and Yahr disease stage [23]. In analogy to Kanna and Bhanu [13], cognition was weakly
303 correlated with swallowing speed, even though we used the more sensitive MOCA instead of
304 Mini-Mental Status Examination (MMSE).

305 4.3. Swallowing speed in the control cohort

306 Noteworthy, the mean swallowing speed of our healthy controls (8.5 ± 3.2 ml/s) was rather low
307 when compared with similarly aged subjects in the literature (range from 5.7 ml/s to 27.5 ml/s)
308 [13-16], although we carefully ruled out diseases which are accompanied by dysphagia. This led to
309 high false-positive rates in our healthy subjects of 69% if the threshold of < 10 ml/s was applied.

310 Reduction of swallowing speed in controls might be due to the fact that we instructed our
311 participants to use a straw. It is recognized that sipping water through a straw differs significantly
312 compared to the usual practice of drinking water from an open cup [16]. This was the case in the
313 former studies and could have enabled faster swallowing, especially if the participants reclined their
314 heads. However, this maneuver can be dangerous in patients with dysphagia as it promotes
315 aspiration [30]. Hence, using a straw in order to avoid head reclinatio is common practice in FEES.
316 Another reason for slower swallowing speeds in controls may be the verbal instruction. If healthy
317 subjects were instructed to drink in their usual manner, mean swallowing speeds were
318 predominantly below 10 ml/s [31]. The instruction in most former studies was, however “to drink as
319 quickly as *comfortably* possible” respectively “as quickly as possible” [9,11,15], which could have
320 induced them to drink faster than our controls (“to drink as quickly as *safely* possible”). But probably
321 the applied water volume is more relevant. Two of the above-mentioned studies used 150 ml instead
322 of 90 ml [9,15]. Low amounts of water result in lower swallowing speeds. Premotor time (time
323 between stimulus and initiation of the swallow) and pre-swallow time (time between initiation of
324 swallow and beginning to actually swallow) last on average 0.5 s and 0.7 s, according to a former
325 study using electromyography (EMG) [32]. This initiation process is shorter for the swallows
326 following the first during consecutive swallows as shown by a shorter oral-pharyngeal transit time
327 for forced repetitive swallows compared to a single swallow (mean 0.4 s vs. 1.2 s) [23]. Furthermore,
328 the study protocols of several former studies, unlike our protocol, allowed to calculate swallowing
329 speed even if the volume was drunk only partially. Therefore, the swallowing speed calculated there
330 was susceptible to underestimation [9-12]. Additionally, high amounts of water are discussed as
331 critical because of interference with ventilation, which has been proven for a volume of 200 ml [16].
332 Of note, it was shown that flavor and temperature had no systematic effect [9].
333

334 4.4. Limitations of our study

335 It is a limitation of our study that the number of swallows has not been measured. Thus, the volume
336 per swallow, as well as the mean duration of a swallow, could not be calculated. To adjust for
337 divergent volumes of applied water, the average volume per swallow was proposed formerly as an
338 alternative approach [24].
339

340 5. Conclusions

341 This prospective study of unselected and consecutively recruited PD patients shows that the
342 formerly proposed threshold of < 10 ml/s for swallowing speed resulted in a high false-positive rate
343 of 63% and therefore would lead to a high number of unnecessary further instrumental
344 investigations, such as FEES or VFSS, and cause potential medical and social burden. Although 83%
345 of all patients would require further instrumental investigation, 12% of patients with aspiration
346 would still be missed. Even when optimizing the cut-off value according to ROC analysis to < 5.5
347 ml/s, sensitivity (69%) and specificity (64%) remained insufficient. Furthermore, measurement of
348 swallowing speed is prone to methodological errors. Particularly verbal instruction, applied volume,
349 and form of application need to be standardized. Overall, to date swallowing speed cannot be
350 recommended as a simple bedside test to predict aspiration in PD patients. In the case of severe
351 swallowing problems (i.e. silent aspiration), the patients would be in danger of being overloaded
352 with fluid. On the other hand, several unaffected or only mildly affected patients would be
353 examined in vain. Our study group recently proposed an alternative screening approach to detect
354 clinically relevant aspiration in PD. We found a sensitivity of 86% and specificity of 79% by
355 combining age, gender and aspiration signs [2]. These results have to be confirmed in further studies
356 before implementation into clinical routine.

357

358 **Author Contributions:** Conceptualization, Christina Pflug and Carsten Buhmann; Data curation, Moritz Bihler;
359 Formal analysis, Moritz Bihler; Investigation, Christina Pflug, Almut Nießen, Carsten Buhmann and Moritz
360 Bihler; Methodology, Christina Pflug and Carsten Buhmann; Project administration, Christina Pflug and
361 Carsten Buhmann; Software, Moritz Bihler; Supervision, Carsten Buhmann; Validation, Moritz Bihler;
362 Visualization, Moritz Bihler; Writing – original draft, Moritz Bihler; Writing – review & editing, Christina Pflug,
363 Almut Nießen and Carsten Buhmann.

364 **Funding:** There was no funding.

365 **Conflicts of Interest:** The authors declare no conflict of interest.

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