Swallowing Speed as Potential Predictor of Aspiration in Parkinson’s Disease Patients

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

Keywords: dysphagia, FEES, Parkinson’s disease, swallowing speed, screening, water test

1. Introduction

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

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

2.3. Assessments

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

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

2.4. Statistical analysis

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

3. Results

3.1. Subject characteristics

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

Table 1. Subject characteristics of PD patients and controls.
Patients (n = 115) | Controls (n = 32) | P value
--- | --- | ---
**Age (years)** | 68.6 ± 10.2 | 68.1 ± 10.7 | 0.78<sup>a</sup>
Men | 76 (66%) | 16 (50%) | 0.10<sup>b</sup>
BMI (kg/m²) | 25.5 ± 4.0 | 24.4 ± 3.6 | 0.14<sup>a</sup>
MOCA (score) | 22.2 ± 4.4 | 25.3 ± 3.0 | <0.001<sup>a</sup>
- Cognitive deficit (i.e. MOCA <26 points) | 81 (70%) | 17 (53%) | 0.09<sup>b</sup>
**BDI-II (score)** | 10.5 ± 8.9 | 6.1 ± 7.0 | 0.01<sup>a</sup>
- No depression (0-13) | 90 (78%) | 26 (81%) | 0.50<sup>b</sup>
- Mild depression (14-19) | 10 (9%) | 4 (13%) | 0.50<sup>b</sup>
- Moderate depression (20-28) | 7 (6%) | 2 (6%) | 0.50<sup>b</sup>
- Severe depression (29-63) | 8 (7%) | 0 (0%) | 0.50<sup>b</sup>
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

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

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

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

**Table 2. FEES results.**

<table>
<thead>
<tr>
<th>Leakage of water</th>
<th>Patients (n = 115)</th>
<th>Controls (n = 32)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N (%)</td>
<td>N (%)</td>
</tr>
<tr>
<td>Base of the tongue or valleculae</td>
<td>18</td>
<td>0</td>
</tr>
<tr>
<td>Lateral channels or tip of the epiglottis</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Piriiform sinus or laryngeal rim (sides or back)</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Laryngeal vestibule or aspiration before the swallow</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td><strong>Aspiration of water</strong></td>
<td>26 (23%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>PAS 6: material is effectively ejected from airway</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>PAS 7: material is not ejected despite effort</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>PAS 8: silent aspiration</td>
<td>20</td>
<td>0</td>
</tr>
</tbody>
</table>
3.3. Swallowing speed

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

Table 3. Swallowing speed.

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

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

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

Table 4. Statistical Evaluation of different cut-offs for swallowing speed to detect aspiration of water (PAS 6-8).
Table 5. False-positive rates in controls for different cut-offs for swallowing speed.

<table>
<thead>
<tr>
<th>Cut-off for swallowing speed</th>
<th>&lt; 10 ml/s</th>
<th>&lt; 9 ml/s</th>
<th>&lt; 8 ml/s</th>
<th>&lt; 7 ml/s</th>
<th>&lt; 6 ml/s</th>
<th>&lt; 5.5 ml/s</th>
<th>&lt; 5 ml/s</th>
</tr>
</thead>
<tbody>
<tr>
<td>False-positive rate</td>
<td>22/32</td>
<td>18/32</td>
<td>13/32</td>
<td>13/32</td>
<td>6/32</td>
<td>5/32</td>
<td>4/32</td>
</tr>
<tr>
<td>(95% CI)</td>
<td>(69%)</td>
<td>(56%)</td>
<td>(41%)</td>
<td>(41%)</td>
<td>(19%)</td>
<td>(16%)</td>
<td>(13%)</td>
</tr>
</tbody>
</table>

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

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).

3.4. Influence of patient characteristics on swallowing speed

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

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, R² of the regression line 0.11). (b) No significant correlation was found in women.
There was a weak to moderate (male respectively female) correlation of swallowing speed with disease duration (Figure 5).

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

There was a weak correlation of swallowing speed with cognition determined as MOCA both in male and female patients (Figure 7).

![Figure 7](image.png)

**Figure 7.** Relation between cognition (i.e. MOCA) and swallowing speed in PD patients. (a) There was a weak correlation in men (coefficients 0.28 [95% CI: 0.12, 0.42], p < 0.001, R² of the regression line 0.14). (b) There was a weak correlation in women (coefficients 0.25 [95% CI: 0.05, 0.46], p = 0.03, R² of the regression line 0.10). MOCA Montreal cognitive assessment.

### 4. Discussion

We assessed for the first time swallowing speed of water as a potential predictive parameter for aspiration in PD patients compared with controls. FEES was applied as the gold standard examination to prove aspiration. The usual cut-off value of 10ml/s is assumed to indicate dysphagia. We not only found that this usual cut-off value is too high but also, that even using an optimized and almost two-fold lower threshold of 5.5 ml/s is not suitable to predict aspiration with reasonable sensitivity and specificity.

#### 4.1. Swallowing speed in PD patients

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

We did not count the number of swallows and therefore could not determine the exact volume per swallow but prolonged swallowing speed in PD patients might be related to a reduced bolus size as one mechanism of compensation [26]. Thus, a low swallowing speed may indicate awareness for dysphagia. This was shown for patients with neurological diseases as the groups with poor awareness drank water significantly more quickly [9,27]. This appears surprising as intuitively fast swallowing speeds are interpreted as uncritical. Instead, patients with slow swallowing speed may need less instruction and guidance regarding compensation maneuvers as they already adapt to
dysphagia. However, secure differentiation between adaptation and swallowing problems is, however, only possible by an objective assessment of swallowing, e.g. by FEES. This might also allow for the difficulties of finding a screening test suitable for all patient groups equally.

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

4.2. Influence of PD patient characteristics on swallowing speed

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

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

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

4.3. Swallowing speed in the control cohort

Noteworthy, the mean swallowing speed of our healthy controls (8.5 ± 3.2 ml/s) was rather low when compared with similarly aged subjects in the literature (range from 5.7 ml/s to 27.5 ml/s) [13-16], although we carefully ruled out diseases which are accompanied by dysphagia. This led to high false-positive rates in our healthy subjects of 69% if the threshold of < 10 ml/s was applied.
Reduction of swallowing speed in controls might be due to the fact that we instructed our participants to use a straw. It is recognized that sipping water through a straw differs significantly compared to the usual practice of drinking water from an open cup [16]. This was the case in the former studies and could have enabled faster swallowing, especially if the participants reclined their heads. However, this maneuver can be dangerous in patients with dysphagia as it promotes aspiration [30]. Hence, using a straw in order to avoid head repositioning is common practice in FEES. Another reason for slower swallowing speeds in controls may be the verbal instruction. If healthy subjects were instructed to drink in their usual manner, mean swallowing speeds were predominantly below 10 ml/s [31]. The instruction in most former studies was, however, “to drink as quickly as comfortably possible” respectively “as quickly as possible” [9,11,15], which could have induced them to drink faster than our controls (“to drink as quickly as safely possible”). But probably the applied water volume is more relevant. Two of the above-mentioned studies used 150 ml instead of 90 ml [9,15]. Low amounts of water result in lower swallowing speeds. Premotor time (time between stimulus and initiation of the swallow) and pre-swallow time (time between initiation of swallow and beginning to actually swallow) last on average 0.5 s and 0.7 s, according to a former study using electromyography (EMG) [32]. This initiation process is shorter for the swallows following the first during consecutive swallows as shown by a shorter oral-pharyngeal transit time for forced repetitive swallows compared to a single swallow (mean 0.4 s vs. 1.2 s) [23]. Furthermore, the study protocols of several former studies, unlike our protocol, allowed to calculate swallowing speed even if the volume was drunk only partially. Therefore, the swallowing speed calculated there was susceptible to underestimation [9-12]. Additionally, high amounts of water are discussed as critical because of interference with ventilation, which has been proven for a volume of 200 ml [16]. Of note, it was shown that flavor and temperature had no systematic effect [9].

4.4. Limitations of our study

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

5. Conclusions

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