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” (ie, food bolus passes from the oral cavity into the pharynx without a swallowing reflex), “penetration” (ie, bolus penetrates into the laryngeal inlet without actually
reaching the trachea), and “aspiration” (ie, bolus reaches the trachea). A severe form of aspiration is the silent aspiration, where the patient does not realize the bolus in the trachea. 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 applicate 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 sufficiently 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 from a cup 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 is to be prone to over-referral to further examination (eg, 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 by using a cup was proposed.9 This threshold was adopted by several studies.10-12 However, a wide range of test volumes (90-150 mL) was applied, which may have significantly affected the resulting swallowing speeds. Furthermore, the study populations were heterogeneous regarding the underlying diseases and inclusion criteria (subjective complaint of abnormal swallowing, clinically suspected swallowing disorder, or unselected cross section design). When considering these four studies together, only four percent of all subjects were known to have PD.13 While it is consensus that average swallowing speed in our PD cohort.

### Key Points
- There is no well-established cutoff value for swallowing speed in Parkinson’s disease patients when it comes to detecting aspiration. This study aimed to fill this gap.
- A wide range of potential cutoff values was prone to misallocation of patients and healthy controls.
- Swallowing speed is no useful screening instrument to predict aspiration in Parkinson’s disease patients.

## 2 | MATERIALS AND METHODS

### 2.1 Study design and ethical approval

The local ethics committee of the Medical Council Hamburg (trial number PV5089) approved this prospective, controlled, cross-sectional study, and all patients gave written informed consent.

### 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. Exclusion criteria were atypical or secondary Parkinson syndromes and other diseases accompanied with dysphagia, for example, head and neck cancer. 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 instances). 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, renunciation by the examiner because of preceding aspiration of puree and a teaspoon of water in one instance 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 Experienced orotrinolaryngologists performed the FEES examinations in PD patients and control subjects with a 2.6-mm-diameter high-definition rhino-laryngo videoscope (ENT-V3, Olympus Medical Systems Corp). If the proband could swallow a
teaspoon of green-colored water inconspicuously, he or she was instructed to drink a standardized volume of 90 mL water at room temperature through a straw as quickly as safely possible. We chose a straw instead of a cup as a delivery method because it interferes less with endoscopy. The timer started with the first contact of the water with the lips (by eyesight) and stopped with the end of the last swallow (timed water test) with the lowering of the larynx (as observed 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 which is also validated for FEES.19 Aspiration, that is, water passes below the vocal folds, is indicated by PAS values of 6-8.

2.4 | Statistical analysis

Quantitative data were illustrated with means and standard deviation (SD), and differences between groups were analyzed using t test for independent samples. Qualitative data were illustrated with frequencies and analyzed using Fisher's exact test. Correlation coefficients were based on Kendall's tau and are interpreted according to Evans20.0-0.19 indicating a very weak, 0.20-0.39 a weak, 0.40-0.59 a moderate, 0.60-0.79 a strong, and 0.80-1 a very strong correlation. We used Clopper-Pearson confidence intervals (CI) for sensitivity and specificity; those for predictive values were calculated according to Mercaldo et al.21 There are no widely consented cutoff values for sensitivity and specificity to assess a screening test for aspiration. In our opinion, a pair of 80% sensitivity and 70% specificity could be deemed as acceptable and a pair of 90% sensitivity and 80% specificity as good. All statistical tests were two-tailed, and the alpha level was set to .05. Statistical analyses were performed with SPSS, version 23 (IBM).

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 patients and controls were each categorized into the following clinically relevant groups: cognitive impairment (ie, MOCA score below 26) and degree of depression (ie dependent on BDI-II score no, mild, moderate, or severe depression).

3.2 | Results of flexible endoscopic evaluation of swallowing

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 (Figure 1) occurred in nearly every fourth patient, but in none of the controls.

### Table 1 | Subject characteristics of PD patients and controls

|                        | Patients (n = 115) | Controls (n = 32) | P value |
|------------------------|------------------|------------------|---------|
| Age (y)                | 68.6 ± 10.2      | 68.1 ± 10.7      | .78a    |
| Men                    | 76 (66%)         | 16 (50%)         | .10b    |
| BMI (kg/m²)            | 25.5 ± 4.0       | 24.4 ± 3.6       | .14a    |
| MOCA (score)           | 22.2 ± 4.4       | 25.3 ± 3.0       | <.001a  |
| Cognitive deficit (<26)| 81 (70%)         | 17 (53%)         | .09b    |
| BDI-II (score)         | 10.5 ± 8.9       | 6.1 ± 7.0        | .01a    |
| No depression (0-13)   | 90 (78%)         | 26 (81%)         | .50b    |
| 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 (y)   | 57.0 ± 26.9      | NA               | NA      |
| NMS-Quest 3 (“yes” answers) | 9.8 ± 5.0     | NA               | NA      |
| Hoehn and Yahr Stage 1| 5 (4%)           | NA               | NA      |
| Hoehn and Yahr Stage 2| 58 (50%)         | NA               | NA      |
| Hoehn and Yahr Stage 3| 32 (28%)         | NA               | NA      |
| Hoehn and Yahr Stage 4| 17 (15%)         | NA               | NA      |
| Hoehn and Yahr 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      |

Note: Levodopa equivalency dose was calculated according to Tomlinson et al.22
Abbreviations: 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.

*bT test.
*bFisher’s exact test.

3.3 | Swallowing speed

Table 3 illustrates the key findings. Swallowing speeds differed significantly between patients and controls. Though, the absolute difference in means was rather small (2 seconds). A relevant gender effect could only be found within patients with men swallowing faster than women.

A receiver operating characteristic (ROC) analysis was carried out to determine an appropriate cutoff value for swallowing speed to detect aspiration of water reliably (see Figure 2). The points for the formerly proposed cutoff 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 cutoff value of <5.5 mL/s.

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

Applying the cutoff 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 S5).

### TABLE 2 Flexible endoscopic evaluation of swallowing results

|                  | 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                  |                          |
| Piniform 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                 |                          |

### TABLE 3 Swallowing speed

|                              | PD patients (n = 115) | Controls (n = 32) | P value (T test) |
|------------------------------|-----------------------|-------------------|------------------|
| Swallowing speed (mL/s)      | 6.5 ± 3.9             | 8.5 ± 3.2         | <.01             |
| Mean ± SD Male: 7.3 ± 4.2    | 8.6 ± 2.3             | Male: 8.4 ± 4.0   | Female: 5.1 ± 2.8| Female: 8.4 ± 4.0| P < .01| P = .85|

### FIGURE 1

Endoscopic examples for typical swallowing pathologies. 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.

### 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 < .001

### 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 (coefficients of −0.25 and −0.72, respectively Figure 3 and Figure S5). There was a weak to moderate correlation of swallowing speed with disease duration (coefficients of −0.20 for men and of −0.40 for women, Figure S6). We found a significant correlation of swallowing speed with disease severity determined as MDS-UPDRS III only for male patients (coefficient of −0.25) but not in female patients (Figure 4). There was a weak correlation of swallowing speed with cognition determined as MOCA both in male and female patients (coefficients of 0.28 for men and of 0.25 for women, Figure S7).
**TABLE 4** Statistical evaluation of different cut-offs for swallowing speed to detect aspiration of water (PAS 6-8)

| Cutoff 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<sup>a</sup>       | 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) |

Abbreviation: CI, confidence interval.

<sup>a</sup>Optimized cutoff according to ROC curve (Figure 2).

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 cutoff value of 10 mL/s is assumed to indicate dysphagia. We not only found that this usual cutoff value is too high but also that even using an optimized, and almost twofold 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. 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. 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 in 100 PD patients (7.0 ± 3.2 mL/s). Studies with lower numbers of PD patients (n = 10-75) showed mean swallowing speeds of 4.3 mL/s to 9.5 mL/s. 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. 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

![Figure 3](image-url) **FIGURE 3** The relation between age and swallowing speed in patients with Parkinson's disease is shown. A, There was a weak correlation in men (coefficient −0.25 [95% CI: −0.11, −0.38], P = .001, R² of the regression line 0.11). B, No significant correlation was found in women.
Movement Disorder Society-sponsored revision of the unified Parkinson’s disease rating scale (MDS-UPDRS)

The statistically most robust study found an age-related increase in the duration of swallowing only in the group of older aged participants, that is, 66 years of age or older. Instead of a continuous decrease, these data might suggest a rather exponential decrease of swallowing speed as soon as a cutoff age is reached. Though male and female PD patients did not differ for mean age, subjects with an age of 80 years or older were exclusively found in the male group (n = 9, 12%). This may explain why we found no correlation in female PD 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. However, disease severity (ie, MDS-UPDRS III) correlated weakly (coefficient of −0.25) exclusively in men. Kanna and Bhanu found a very strong correlation (coefficient of −0.83). This discrepancy may be partly due to the usage of Pearson correlation instead of Kendall’s Tau, 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 MDS 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. In analogy to Kanna and Bhanu, cognition correlated only weakly with swallowing speed, even though we used the more sensitive MOCA instead of Mini-Mental Status Examination (MMSE).

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 (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 among controls. The latter result conforms with a large study which found no significant sex-related differences in healthy subjects.

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 the duration of swallowing only in the group of older aged participants, that is, 66 years of age or older. Instead of a continuous decrease, these data might suggest a rather exponential decrease of swallowing speed as soon as a cutoff age is reached. Though male and female PD patients did not differ for mean age, subjects with an age of 80 years or older were exclusively found in the male group (n = 9, 12%). This may explain why we found no correlation in female PD patients. Our male control cohort was most likely underpowered (n = 16) to reveal a correlation of swallowing speed with age.

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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-27.5 mL/s). 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.

It is recognized that sipping water through a straw (as our participants were instructed) differs significantly compared to the usual
practice of drinking water from an open cup.16 Drinking from a cup resulted in higher swallowing speeds,29 which might be promoted by a head reclusion. However, this maneuver can be dangerous in patients with dysphagia as it promotes aspiration.30 Hence, using a straw to avoid head reclusion 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 prior 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”).

Several former studies applied higher volumes of up to 150 mL9,10,15 instead of 90 mL. High amounts of water result in higher swallowing speeds. A study showed that the mean oral-pharyngeal transit time is significantly shorter for forced repetitive swallows compared to a single swallow,23 that is, that the initiation process accounts for much of the swallowing time. The protocols of several prior studies, unlike our protocol, allowed to calculate swallowing speed even if the volume was drunk only partially.9,12 This led, on the other hand, to an underestimation of swallowing speed. Of note, high amounts of water are discussed as critical because of interference with ventilation, which has been proven for a volume of 200 mL.16

4.4 Limitations of our study

The average volume per swallow was proposed as a more meaningful indicator as, in contrast to swallowing speed, it is discussed to be less prone to the applied volume of water.24 It is a limitation of our study that we did not measure the number of swallows. Thus, the average volume per swallow, as well as the mean duration of a swallow, could not be calculated. However, reliable measurement of number of swallows needs a second examiner to assess it “hands-on,” and to insist on submental EMG might impede the widespread application of this screening tool. Furthermore, we did not perform a reliability check regarding time measurement (eg, by a second examiner).

5 CONCLUSIONS

In conclusion, swallowing speed cannot be recommended as a simple bedside test to predict aspiration in PD patients. The widely used threshold of <10 mL/s showed insufficient sensitivity and specificity and resulted in a high number of unnecessary further instrumental investigations. Even an optimized cutoff value of 5.5 mL/s with acceptable sensitivity and specificity is not reliable in terms of aspiration.

Overall, measuring swallowing speed is prone to methodological errors and not suitable as a screening instrument to predict aspiration in PD patients.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTIONS

CB and CP were responsible for conceptualization, methodology, and project administration; MB performed data collection, formal analysis, and visualization; AN, CB, CP, and MB carried out the investigations; The study was supervised by CB; MB wrote the original draft, which was reviewed and edited by AN, CB, and CP.

ORCID

Moritz Bihler https://orcid.org/0000-0003-0858-8876

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**SUPPORTING INFORMATION**

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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