Comparison of the cough reflex test and water swallowing test in healthy participants and neurological patients

I. Battel¹, A. Ceolin¹, I. Koch¹, L. Ventura¹, P. Tonin¹, K. Palmer¹ and F. Meneghello¹

¹IRCCS San Camillo Hospital Foundation, Via Alberoni n° 70, 30126, Venice, Italy; ²Dipartimento di Scienze Statistiche, Università di Padova, Via Cesare Battisti, 241/243, 35121 Padova, Italy

Key-words. Dysphagia; swallowing disorders; cough reflex; silent aspirators; neurologic dysphagia; water swallowing test; aspiration pneumonia

Abstract: Comparison of the cough reflex test and water swallowing test in healthy participants and neurological patients. Background: Silent aspiration is poorly identified by traditional clinical swallowing evaluations. Recently, several studies have proposed the use of a cough reflex test (CRT) for screening patients at risk of aspirations. The first aim of this study is to investigate the CRT thresholds of citric acid concentration for identifying cough responses in healthy participants and neurological patients. The second aim is to compare the results of the CRT with the water swallowing test (WST), a standard screening test for identifying cough responses in neurological patients. Methods: The CRT and then the WST were administered to 100 neurological patients and 100 healthy participants. For the CRT, we administered incremental solutions of citric acid interspersed with placebo doses. We used the results of the CRT in healthy participants to define a citric acid concentration cut-off, which could be used with neurological patients as a screening for aspirations. Results: As all controls coughed at a concentration of 0.1 mol/L, this was used as a cut-off in patients to identify coughing as a screening for aspiration risk. Patients showed cough reflexes at concentrations significantly higher than controls (p=0.001). The WST was not administered to 17 patients, due to cognitive deficits and severe clinical conditions. Thirty-six patients had a cough response above the screening cut-off (> 0.1 mol/L), 25 of which (30.1%) also had a positive cough response during the WST. Conclusion: The CRT correlated significantly with the WST. Unlike the WST, the CRT could be easily administered to severely impaired patients. Our results indicate the use of the CRT as a screening test for silent aspirators.

Introduction

Oropharyngeal dysphagia is a swallowing disorder, which is commonly associated with neurological pathologies.1,2,3 It is widely accepted that the presence of dysphagia is associated with pulmonary complications, increased hospital recovery, dehydration, malnutrition and ultimately, mortality.1,4-6

The VFSS and the FEES are considered the gold standards for assessing dysphagia and aspiration during swallowing.7,8 However, these instrumental investigations are not always available in the screening phase, where an early and reliable assessment is fundamental for implementing appropriate management strategies and decreasing the risk of pneumonia. Consequently, in clinical practice, different dysphagia screening protocols have been proposed to detect the presence of dysphagia. The WST, which is the most commonly used in clinical screening, detects clinical signs of aspiration during water deglutition.9 Nevertheless, it is well known that a high percentage (from 30 to 70%) of dysphagic patients aspirate without observable signs before, during or after swallowing (silent aspiration).10 As silent aspirators are unable to protect airways, their risk of pneumonia is 13-fold higher than patients showing the cough reflex.11 Recently, the CRT, consisting of the inhalation of a nebulized tussigenic agent, has been proposed to identify patients at risk of silent aspiration.12-14 An early study of this application showed a significant relationship between patients who failed the CRT and the presence of aspiration pneumonia.12 Subsequently, high sensitivity and specificity (respectively 0.87 and 0.95) were detected in dysphagic patients who were observed to aspirate silently on the VFSS when the CTR was paired with the WST.15 More recently, results from cough reflex testing in isolation were found
to be significantly associated with the response to aspiration, as observed on both the VFSS (p=.003) and the FEES (p <.001). Even if the use of the CRT is growing, data on administration parameters in healthy persons and neurological patients are still lacking.

The present study investigates the sensitivity of the CRT threshold as a means to differentiate neurologically impaired patients from healthy controls using incremental concentrations of nebulized citric acid. The first aim of this study is to identify the acid citric concentration, which evokes the cough reflex in healthy subjects, and thereafter to use this cut-off as a screening tool in neurological patients for the assessing the risk of silent aspiration. The second aim is to compare the results of the CRT and the WST in neurological patients.

Materials and methods

Participants

This study was conducted in accordance with the Declaration of Helsinki and received the approval of the Ethics Committee of the IRCCS San Camillo Hospital Foundation in Venice, which is a centre specializing in neurorehabilitation. All participants independently provided informed consent; for patients barely responsive or with cognitive deficits, consent was provided by a proxy.

Among a population of 220 consecutive neurologic patients hospitalized at the San Camillo Hospital Foundation from May to September 2014, we recruited the first 100 patients who did not show the following exclusion criteria: absence of vigilance; presence of allergy to citrus; presence of asthma; presence of tracheotomy, which could not be safely occluded for more than one hour; a history of signs of non-neurological pathologies involving the oropharyngeal tract.

The healthy group comprised 100 hospital workers and relatives of inpatients who had no citrus acid allergy or asthma.

All participants firstly underwent the CRT, followed by the WST. All assessments were videorecorded and scored by an expert speech-language pathologist. The latency between the tests ranged from 15 to 20 minutes.

CRT examination:

The CRT was administered in a seated position or elevated in bed in a sitting position. An ultrasonic nebulizer (MO-03 Norditalia Elettromedicali®) was used, with a particle size of 3 µm and a fixed output rate of 0.9 ml/min. The test started with a placebo dose of 0.9% NaCl and continued with inhalations of incremental solutions of citric acid, interspersed with inhalations of placebo (0.9% NaCl), in order to prevent tachyphylaxis. The citric acid was administered in increasing concentrations of 0.01, 0.03, 0.1, 0.4, 0.6 and 0.8 mol/L, according to previous studies. Each citric acid concentration was administered three times before increasing the solutions. Each single administration was presented via a mouthpiece mask with a 15-second delivery period alternating with a 60-second rest period. Patients were instructed to breathe normally through the mouth and cough when they felt the need, if patients found

---

**Figure 1**
Comparison of cough thresholds during the CRT in healthy vs. neurological participants (p-value <0.001)

**Figure 2**
Citric acid concentrations evoking a cough during the CRT in healthy and neurological participants
it difficult to breathe through the mouth, a nose clip was applied. The cough response was considered positive when at least two coughs were elicited. Expiratory airflow without a coughing sound was not counted as a cough. When the subject coughed in two of the three trials, that concentration was considered the threshold and the test was stopped.

**WST**

The WST proposed by Daniels et al.\textsuperscript{16} was adopted. Participants were instructed to swallow water in increasing volumes of 5ml, 10 ml and 20 ml. Each volume was administered twice. When a cough and a wet/hoarse voice appeared, the test was considered positive and stopped. The test was negative if a cough and a wet/hoarse voice was absent after all the trials.

**Data analysis**

The Wilcoxon-Mann-Whitney two-sample test was used to compare whether the citric acid concentration, which evoked a cough, differed according to gender, smoking status and patient group (healthy vs. neurological patients). We determined the citric acid concentration level, which evoked a cough in all healthy patients, as the cut-off for neurological patients.

Within the neurological patient group, we grouped patients into those who did and did not have a cough response during the WST. We then compared the citric concentration, which evoked a cough in the CRT, with the two subgroups of neurological patients using a Wilcoxon-Mann-Whitney two-sample test. The significance level for all statistical analyses was set at $\alpha=0.05$.

**Results**

**Healthy group**

One hundred healthy participants (61 female; 39 male; age: $53.3\pm18.8$ years) underwent the WST and the CRT. None of the healthy participants showed signs of aspiration during the WST. The results of the CRT showed that coughs were elicited at citric acid concentrations ranging from 0.01 to 0.1 mol/L. Males coughed at citric acid concentrations significantly higher than females (Wilcoxon rank sum test $W=5762$, p-value=0.04). Smokers coughed at concentrations significantly higher than non-smoker subjects (Wilcoxon rank sum test $W=2845$, p-value=0.005).

**Neurological patients**

One hundred neurological patients were enrolled (46 female; 54 male; age: $54.12\pm19.2$ years), including patients with stroke (n=24), Parkinson’s disease (n=20), multiple sclerosis (n=18), traumatic brain injury (n=11), amyotrophic lateral sclerosis (n=9), cerebral anoxia (n=6), brain tumour (n=5) and neuropathy (n=7). Five of them had a tracheotomy tube.

It was not possible to administer the WST to 17 patients, due to cognitive deficits and severe clinical conditions. Among the 83 remaining patients, signs of aspiration (a cough or a wet/hoarse voice) appeared in 25 patients (30.1%).

The CRT was administered to all neurological patients, with cough responses occurring at concentrations ranging from 0.03 to 0.8 mol/L. The mean citric acid concentration eliciting a cough was significantly higher in neurological patients (0.22 mol/L) than healthy controls (0.09 mol/L) (Wilcoxon rank sum test $W=3544$, p-value=0.0001) (Figure 1).

In 36 patients (36%), cough responses were evoked at higher concentrations than that eliciting a cough in healthy participants (>0.1 mol/L) (Graph 2). This subgroup of 36 patients consisted of 25 (30.1%) patients who screened positive for coughs on the WST and 11 (18%) patients who did not show signs of aspirations on the WST (Table 1).

**Discussion**

This study assessed the utility of the CRT for the clinical evaluation of airway protection in neurological patients. Previous studies on the CRT reported controversial results. Some authors evidenced high sensitivity and specificity of the test against instrumental evaluation.\textsuperscript{12-14} In contrast, a recent study on stroke patients found low sensitivity and specificity.\textsuperscript{15} The authors concluded that the CRT does not appear to be a useful test for screening silent aspiration. It is likely that the discrepancy lies in the differences between applied methodologies. Although the administration of the CRT is growing, there is a high variability in terms of dosage and methods of assessment, making comparisons
but indicates that they possibly had an increased risk of silent aspiration and needed a more detailed evaluation of swallowing ability.

Comparing the CRT results with those obtained by the WST, we can confirm that all patients who screened positive during the WST showed cough thresholds in the CRT, which were higher than the healthy participants’ cut-offs, in line with a previous study. Conversely, we found that, by using a cut-off based on data from the healthy participants, almost a fifth of patients who screened negative during the WST elicited a cough in the CRT. These results suggest the possibility to detect patients at risk of silent aspirations, as well as whether or not they will appear dysphagic during the WST.

It is well known that dysphagia and silent aspirations are diagnosed only via instrumental examinations. However, in many care settings, it is not feasible to administer the VFS or the FEES. It is therefore essential to identify a screening tool that is reliable when it comes to identifying patients at risk of silent aspirations. The WST is one of the most commonly used screening tools to detect dysphagia in patients, with recent systematic reviews having identified it as a reliable method for dysphagia screening. Nevertheless, our results suggest that the WST is not an accurate method for the detection of silent aspirations. The CRT, instead, appears to detect a significant number of possible silent aspirators. As such, it may be useful to combine the CRT and the WST in a screening phase in order to assess swallowing and the mechanism of airways protection.

To our knowledge, this is the largest study in which the cough reflex has been investigated in healthy subjects and neurological patients. Nevertheless, the major limitation was the lack of any instrumental examination. Further studies

### Table 1

Comparison of participants’ results from the WST and the cut-off from the CRT (0.1 mol/L). WST 0: presence of cough and/or wet voice; WST 1: absence of cough and/or wet voice.

<table>
<thead>
<tr>
<th>WST</th>
<th>CRT 0 Cough &lt; 0.1 mol/L</th>
<th>CRT 1 Cough &gt; 0.1 mol/L</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td>1</td>
<td>47</td>
<td>11</td>
<td>58</td>
</tr>
<tr>
<td>TOTAL</td>
<td>47</td>
<td>36</td>
<td>83</td>
</tr>
</tbody>
</table>
ought to include an instrumental examination in order to assess the specificity and sensibility of the test.

This study has been carried on with a clinical screening approach on a large population of neurological patients hospitalized in a neurorehabilitation unit, but does not provide information on specific subgroups of patients. Further studies should investigate the effect of the CRT on selected populations, as well as assessing the presence of dysphagia with the use of instrumental investigations in order to verify the sensitivity and specificity of the CRT.

**Abbreviations**

CRT: cough reflex test  
WST: water swallowing test  
VFSS: videofluoroscopic swallowing study  
FEES: fibroendoscopic evaluation of swallowing

**Acknowledgements**

We thank the participants for their assistance and Professor Maggie-Lee Huckabee for her contribution to the conception and support for the project.

**References:**


Irene Battel  
IRCCS San Camillo Hospital Foundation,  
Via Alberoni n° 70, 30126  
Venice  
Italy  
Tel.: +39 041/22073700  
Fax: +39 041731330  
E-mail: irene.battel@ospedalesancamillo.net