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Assessing the Laryngeal Cough Reflex and the Risk of Developing Pneumonia After Stroke: An Interhospital Comparison

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Background and Purpose—We sought to evaluate the efficacy of testing the laryngeal cough reflex in identifying pneumonia risk in acute stroke patients.

Methods—We performed a prospective study of 400 consecutive acute stroke patients examined using the reflex cough test (RCT) compared with 204 consecutive acute stroke patients from a sister facility examined without using the RCT. The binary end point for the study outcome was the development of pneumonia.

Results—Of the 400 patients examined with the RCT, 5 developed pneumonia. Of the 204 patients examined without the RCT, 27 developed pneumonia ($P<0.001$). Three of the 27 patients died in the rehabilitation hospital of respiratory failure secondary to pneumonia. Seven others were transferred to the emergency department with acute respiratory distress. Power analysis for this comparison was 0.99. There were no other significant differences between the 2 groups.

Conclusions—A normal RCT after an acute stroke indicates a neurologically intact laryngeal cough reflex, a protected airway, and a low risk for developing aspiration pneumonia with oral feeding. An abnormal RCT indicates risk of an unprotected airway and an increased incidence of aspiration pneumonia. Alternate feeding strategies and preventive measures are necessary with an abnormal RCT. Clinical treatment algorithm and prescription of food, fluids, and medications are discussed on the basis of RCT results. **(*Stroke*. 1999;30:1203-1207.)**

Key Words: aspiration ■ cough ■ pneumonia ■ stroke ■ videofluoroscopy

After a stroke, one of the most challenging decisions clinicians face is instituting the prescription of fluids, foods, and oral medications safely. The question of whether it is safe to feed the patient has been left mostly to guesswork and to a trial-and-error approach. Physicians have historically deferred this dilemma to speech pathologists or other personnel. It is estimated that up to 38% of stroke victims die within the first month after stroke onset.[1,2] Pneumonia contributes to up to 34% of all stroke deaths and represents the third highest cause of mortality in the first month after stroke. Pneumonia has been estimated to occur in one third of all stroke victims and is the most common respiratory complication.[3]

The Florida Hospital Association reports total charges for dysphagia and food/vomit pneumonitis to be $1.2 billion in 1997 for the state of Florida, increased from $1.1 billion in 1996. In 1996, Florida was ranked the 15th highest nationwide in charges for the following *International Classification of Diseases, Ninth Revision* codes: 787.2 (dysphagia) and 507.0 (food/vomit pneumonitis).[4,5] The effects of pneumonia development have been described in terms of individual cost of care. The development of pneumonia after stroke resulted in an additional financial burden of approximately $10 000 per event and extended hospital length of stay an average of 7 days.[6] Given the incidence of stroke, the prevalence of dysphagia, the risk of aspiration, and the effects of pneumonia in terms of morbidity, mortality, and cost of care, the identification of which patients are at risk for the development of pneumonia is clinically and financially significant.

Testing of the laryngeal cough reflex (LCR) and the prevention of pneumonia secondary to aspiration after stroke is the main focus of our study. We used chemoirritant stimulation with tartaric acid to study the LCR. Chemoirritant receptors in the laryngeal aditus, when stimulated, induce an involuntary reflex cough.[7–9] This reflex cough is critical to airway protection and the prevention of aspiration pneumonia. After a stroke or other neurological event, the LCR may be weakened or absent.[10] This increases aspiration risk for food, fluids, medications, or secretions past the true vocal cords and may lead to the development of pneumonia. The only way to test the status of the airway protection mechanism is to stimulate the reflex.

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A commercial party with a direct financial interest in the reflex cough test may confer a financial benefit on one or more of the authors. The reflex cough test (Pneumoflex) of the laryngeal cough reflex is patented and trademarked by Dysphagia Systems, Inc, Melbourne, Fla. Pneumoflex has not been used commercially in the past or present. Dysphagia Systems, Inc, is pursuing Food and Drug Administration application and approval. Use of this technique in the healthcare system requires Food and Drug Administration approval.

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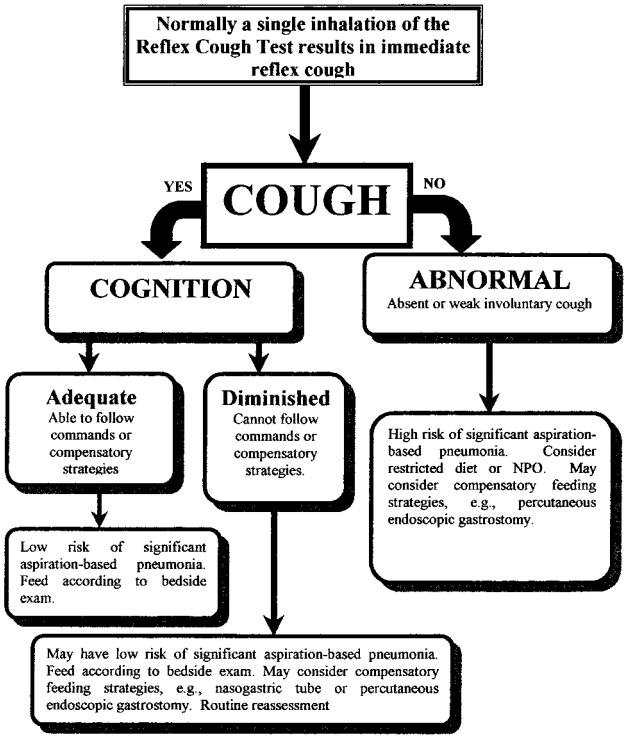
The internal branch of the superior laryngeal nerve, specifically the middle ramus, conveys the afferent information of the LCR to the brain stem.[11,12] The receptors in the laryngeal aditus appear polymodal in nature.[13–20] Chemoirritant stimulation of these receptors elicits an electrophysiological response that has been recorded.[8,9] The internal branch of the superior laryngeal nerve splits into superior, middle, and inferior rami. Branches of the superior ramus distribute to the mucosa of the piriform recess. The middle ramus innervates the mucosa of the vestibule or supraglottic region of the larynx.[11]

The LCR is a primal brain stem survival mechanism. If the LCR does not recover quickly after a neurological event, morbidity and mortality increase. As with other involuntary neurological processes, such as respiratory drive, these tend to recover quickly or a resulting poor outcome occurs. After stroke, the LCR may be impaired up to a month or longer, and in some cases it may remain impaired indefinitely.[21] The purpose of this study is to compare patient outcomes with the use of the RCT and clinical treatment algorithm, as shown in the Figure, with patient outcomes with the use of the standard assessment and treatment approach for the binary end point of pneumonia development.

Subjects and Methods

The reflex cough test (RCT) stimulated cough receptors in the vestibule of the larynx and initiated the LCR.[9,22–25] The test used a 20% solution of prescription-grade *l*-tartaric acid dissolved in 2 mL of sterile normal saline. The solution was placed in a Bennett Twin nebulizer and inhaled as a microaerosol. During the inhalation, the subject's nose was pinched closed. The nebulizer output was 0.2 mL/min.[7,9,10,22,23,25] The test was administered by either a speech pathologist or a respiratory therapist at bedside and required ≈10 minutes to complete.



Clinical algorithm for the RCT. NPO indicates nothing by mouth.

TABLE 1. Results of RCT and Voluntary Cough

	No. of Subjects	Percentage of Total
RCT		
Normal	360	90
Abnormal (weak or absent)	40	10
Voluntary cough		
Normal	319	79.7
Abnormal (weak or absent)	81	20.3

Subjects were tested for a maximum of 3 effective inhalations. The subject was asked to exhale and then to place the mouthpiece and take a sharp, deep inhalation. Leakage around the mouthpiece and "puffing" the nebulizer were not considered effective inhalations. The test ended when either a cough response was elicited or the subject failed to respond after 3 inhalations. The LCR response was judged normal or abnormal (weak or absent). If the subject's response was absent, higher concentrations of tartaric acid were not used. The RCT algorithm was followed for subsequent treatment strategies such as restricted diet, nothing by mouth, or nutritional support by means of percutaneous endoscopic gastrostomy (PEG) (Figure). These treatment strategies were noted for all subjects.

After testing the reflex cough, a speech pathologist performed a bedside swallow evaluation and tested for cognition, preswallow and postswallow voice quality, and cranial nerve function. In this study, the bedside swallowing evaluation comprised a 3-part screen including an evaluation of voluntary cough, a 2-part water test, and a progressive trial of foods and liquid consistencies. The water test assessed the subject's ability to hold 15 mL of water in his or her mouth for 10 seconds. The test was repeated with 30 mL of water. The volume of water returned to the receptacle was recorded. The foods used in this evaluation included pureed, chopped, and cohesive bolus foods. Thin and thick liquids ranged from water to spoon-thick fluids. The standard bedside swallow evaluation was performed at the sister hospital by speech pathologists, and videofluoroscopic examinations were done when believed to be clinically indicated by their staff.

This was a prospective study in which 400 consecutive acute stroke patients were tested with the RCT on admission to an acute rehabilitation hospital. The patients were then treated clinically on the basis of the test result of normal, weak, or absent LCR. A clinical algorithm treatment plan was followed (Figure). A similar group of 204 consecutive acute stroke patients from a nearby sister rehabilitation hospital was used to compare pneumonia incidence between the groups. The chart review of the 204 consecutive acute stroke patients (<30 days after onset) was performed with use of the standard criteria for pneumonia development. Pneumonia was diagnosed if a patient had respiratory symptoms with either temperature >101°F, leukocytosis, or both. Infiltrate was required to have chest x-ray confirmation.

The *t* test compared the 2 groups for age and time from stroke onset until admission to acute rehabilitation. The χ^2 test was performed for sex and as a predictor for pneumonia development. Logistic regression assessed the length of stay in acute rehabilitation for the 2 facilities.

The binary principal end point for this study was the development of pneumonia. Using the odds ratio test, we compared the odds in favor of not developing pneumonia among the patients who were administered the RCT with the odds in favor of not developing pneumonia among the patients who were not administered the RCT.

In unmatched studies, there are standard formulas for determining sample sizes for the comparison of proportions. The level of significance, power of the test, and proportions were evaluated.

Results

Of the 400 subjects in this study, 40 (10%) had a weak or absent LCR when tested with the RCT. When asked to

TABLE 2. χ^2 Test for Development of Pneumonia

	Pneumonia	
	Positive	Negative
RCT		
Yes	a	b
	5	395
No	c	d
	27	177
	($P<0.001$)	

χ^2 test: RCT× pneumonia during rehabilitation cross-tabulation	Pneumonia in Rehabilitation		
	No	Yes	Total
RCT			
No			
Count	177	27	204
Percent	86.8	13.2	100.0
Yes			
Count	395	5	400
Percent	98.8	1.2	100.0
Total			
Count	572	32	604
Percent	94.7	5.3	100.0

produce a voluntary cough, 81 of the 400 subjects (20.3%) had an abnormal (weak or absent) voluntary cough (Table 1). The binary principal end point for the study was the development of pneumonia (Table 2). An appropriate test of the significance for this situation is the χ^2 test, with the null hypothesis that there is no difference between patients who were administered the RCT and patients who were not administered the RCT. A significant difference was found ($P<0.001$). There were no adverse side effects or complications from administering the RCT.

Five of the 400 patients administered the RCT developed pneumonia. They were treated with oral antibiotics and recovered. None of the 5 required transfer from the rehabilitation facility. Of the 400 patients who received the RCT, 20 received percutaneous endoscopic gastrostomy placement. Of these, 7 were removed before discharge. The 204 patients at the sister facility did not receive the RCT, and 27 of these patients developed pneumonia. Three of the 27 patients died of pneumonia in the rehabilitation hospital, and 7 were transferred to the emergency department and intensive care setting.

In addition to a test of significance, it is of interest to determine a 95% CI for p_1-p_2, where p_1 is the proportion of patients who developed pneumonia after the RCT was administered and p_2 is the proportion of patients who developed pneumonia without being administered the RCT. An appropriate CI is the CI for independent samples. The 95% CI for p_1-p_2 is -0.167 to -0.072, with a 95% confidence level.

The odds in favor of not developing pneumonia among the patients who were administered the RCT were compared with the odds in favor of not developing pneumonia among the patients who were not administered the RCT. The odds ratio

TABLE 3. Risk Estimate for Development of Pneumonia

	Value (95% CI)
Odds ratio for RCT (no/yes)	0.083 (0.031–0.219)
For cohort PNE-Rehab=no	0.879 (0.832–0.928)
For cohort PNE-Rehab=yes	10.588 (4.139–27.085)
No. of valid cases	604

PNE=Rehab indicates development of pneumonia in rehabilitation.

test indicated that the odds in favor of not developing pneumonia for those patients who did not receive the RCT were significantly smaller than the odds in favor of not developing pneumonia for those patients who received the RCT. In fact, the ratio of the odds is 0.08, which is significantly <1, and the 95% CI for the odds ratio is 0.031 to 0.219 (Table 3).

In unmatched studies, there are standard formulas for determining sample sizes for the comparison of 2 proportions. The choice of sample sizes depends on the level of significance, the power of the test, and the proportions. The sample sizes for this study were fixed at $n_1=400$ (patients who received the RCT) and $n_2=204$ (patients who did not receive the RCT). A power analysis is crucial to determine the appropriate choice of sample sizes. When the level of significance is fixed at 0.05, the power of the test is 0.99. Thus, there is a 99% chance of finding a significant difference with the use of the sample sizes ($n_1=400$, $n_2=204$). There was no significant difference between the 2 groups for age (Table 4), length of stay in the acute care setting (Table 5), and sex (Table 6).

Discussion

Assessing the neurological integrity of the LCR after a neurological event is essential to determining the appropriate clinical treatment plan for prescription of food, fluids, and medications. The RCT helps to stratify pneumonia risk and improves outcomes through decreased morbidity, mortality, and cost.

The function of the LCR may or may not mirror the degree of dysphagia present in a stroke patient. The term *silent aspiration*, as interpreted clinically, may be used as a negative description of a normal physiological process. Everyone aspirates his or her own secretions to some degree, which necessitates the need for throat clearing, a voluntary clearing cough and the natural pulmonary ciliary cleansing system. An intact LCR involuntarily clears abnormal boluses of food, fluids, secretions, or medications that enter the airway. What these receptors recognize as normal or abnormal is not entirely clear, and there are probably different degrees of reflex response depending on the stimulant.

A chemoirritant such as tartaric acid stimulates an abrupt, forceful, and involuntary LCR in normal patients without

TABLE 4. Comparison of Age by *t* Test

	Mean	SD	SEM
Did not receive RCT (n=204)	74.64706	9.74265	0.68212
Received RCT (n=400)	74.88608	9.20217	0.46301

TABLE 5. Comparison of Length of Stay in Acute Care Unit by *t* Test

	Mean	SD	SEM
Length of stay in acute care unit*			
No (n=204)	10.45771	8.58600	0.60561
Yes (n=400)	9.02500	9.20281	1.45509

*Before admission to rehabilitation hospital.

neurological impairment.[22,25–27] This same response was seen in all of the normal RCT stroke patients regardless of the degree of hemiparesis, dysphagia, dysarthria, or cognitive deficits. Many of the normal LCR patients had wet voice qualities or severe dysphagia but were fed on the basis of experienced speech pathologists' bedside evaluations, using the RCT response as a pivotal factor indicating airway protection. Many were started on modified diets or placed in a supervised dining setting, with diet advancement based on clinical examination and improvement. Videofluoroscopic examination was used only to evaluate structural problems such as fistula, tracheostomy, or tumor and only if the patient had a normal LCR.

If the neurological airway protection mechanism, ie, LCR, functions normally, then patients may be fed on the basis of the bedside physiological findings and diet may be advanced on the basis of improvement with therapeutic swallow exercise treatments. An abnormal LCR (weak or absent) should be viewed as a warning signal. Patients with abnormal LCR require close attention and planning to prevent aspiration pneumonia. In patients with poor caloric intake, lethargy, or significant aphasia, a PEG may be warranted. This would allow no food, fluids, or medications by mouth. In cases of a neurologically unprotected airway, this would help to decrease the production of oral secretions that may be aspirated in volumes that could cause pneumonia. Nasogastric tubes were avoided because of the development of increased secretions and decreased pharyngeal proprioception caused by prolonged use.

Patients with an abnormal LCR were observed clearing their throats less often and did not as readily initiate a voluntary clearing cough as those with a normal LCR.

TABLE 6. Comparison of Sex by χ^2 Test

	RCT		
Sex×RCT Cross-tabulation	No	Yes	Total
Sex			
Female	108	178	286
Male	96	222	318
Total	204	400	604

χ^2 tests	Value	*df*	Asymptomatic Significance (2-Sided)
Continuity correction*	3.530	1	0.060
No. of valid cases	604		

*Computed only for a 2×2 table.

Surprisingly, many patients with severe dysarthria, dysphagia, and dense hemiparesis have a normal cough reflex and are able to take in adequate calories and medications orally, solely on the basis of a bedside examination. Conversely, other stroke patients, who historically would be classified as low risk (because of few physical deficits), have no response to the chemoirritant. These are often persons with stroke locations in the brain stem. These patients were not fed by mouth initially and received PEG placement. While in rehabilitation, these patients had recovered their LCR as determined by RCT, and they were then fed by mouth. The PEG was then safely removed no earlier than 4 weeks after insertion. It is likely that patients in this category previously developed "silent aspiration pneumonia" despite being at a high functional level. Twenty-five patients with abnormal RCTs did not receive PEGs and were eventually retested as normal on the RCT and orally fed. Six PEGs were inserted before admission to the rehabilitation setting. During rehabilitation, 20 PEGs were inserted; 7 of these patients had a normal RCT, and 13 had an abnormal RCT. Seven of the 20 PEGs were removed before the patients were discharged from the rehabilitation setting, and 13 were still in place 3 months after stroke onset.

The neurology of airway protection and the physiology of swallowing are separate processes. The neurological examination of the LCR and airway protection is more important in regard to pneumonia risk than the physiological examination of dysphagia. If the neurological protection of the airway is intact, the physiological deficit of swallowing may be more aggressively treated, and diet may be more readily advanced with a reduced risk of pneumonia development. An abnormal LCR gives rise to further discussion and treatment plan modification.

Routinely, families are included in the decision-making process regarding whether or not the patient should have a PEG or should be fed orally, despite the risk of pneumonia development, on the basis of living wills or healthcare surrogates. Many of these patients receive a PEG for the bulk of their caloric and medication intake and are then fed the safest consistencies orally for quality of life and pleasure. Having informed knowledge of adverse risk helps families and patients to make difficult decisions about feeding, which affects quality of life.

The RCT is a safe, reliable, and cost-effective procedure for testing the LCR. Additionally, other medical conditions may require the need to assess the reflex cough. This procedure is currently under review for approval by the Food and Drug Administration.

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