

**Identifying Aspiration and Reducing Pneumonia in Stroke Patients using Cough  
Reflex Testing  
District Health Board Research Fund Translational Research Project  
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## **Background Information**

Swallowing impairment (dysphagia) represents a substantial health issue in New Zealand. Of approximately 2,724 new stroke events each year (Ministry of Health, 2004), up to 70% will present with dysphagia and up to 44% of those with dysphagia will have persisting swallowing impairment and aspiration in the post-acute phase (Marik & Kaplan, 2003). Significant health issues and health service costs are associated with post stroke pneumonia related to dysphagia (Garon, Engle, & Armiston, 1996; Katzan, Cebul, Husak, Dawson, & Baker, 2003; Schmidt, Holas, Halvorson, & Reding, 1994). Of particular concern is the phenomenon of silent aspiration, in which a patient aspirates but does not present with clinical indicators. Silent aspiration (aspiration without a cough response) has been linked with increased prevalence of pneumonia and mortality (Aviv, Sacco, Thomson, & Tandon, 1997; Nakagawa et al., 1997) with one study finding a thirteen fold increased risk of pneumonia if a patient silently aspirates on their videofluoroscopic study of swallowing (VFSS) (Pikus et al., 2003).

Clinical swallowing evaluation is not able to effectively identify silent aspiration with research suggesting that up to 70% of patients with severe aspiration are not detected on clinical assessment (Smithard, et al., 1998; Splaingard, Hutchins, Sulton, & Chaudhuri, 1988). The critical flaw in the clinical swallowing assessment lies in the nature of impairment in many neurologically impaired patients. For those patients with neuro-sensory impairment, cough response to aspiration may be absent or impaired. This leaves the clinician with a diagnostic conundrum: Is the patient aspirating but without cough response? Or is the patient not aspirating?

Cough reflex testing consists of challenging sensory integrity of the aerodigestive tract by introduction of a tussive agent, which essentially aids in ruling out the phenomena of 'silent aspiration'. Although used in respiratory medicine for 50+ years, only recently has a derivative been applied to clinical swallowing assessment (Addington, et al., 1999) which provided preliminary evidence of decreased pneumonia rates in a large sample of stroke patients who underwent cough reflex testing compared to a sample who were not evaluated using this technique.

Reduced laryngeal sensitivity/ cough sensitivity has been found to be significantly related to increased pneumonia rates (Nakajoh, et al., 2000) (Addington, Stephens, Widdicombe, & Rekab, 2005; Niimi, et al., 2003; Sekizawa, Ujiie, Itabashi,

Sasaki, & Takishima, 1990) in patients with and without underlying neurological conditions. Patients with lower cough sensitivity and slower swallowing responses were more likely to develop pneumonia (Nakajoh, et al., 2000). Addington and colleagues concluded that if a participant had a brainstem or cerebral stroke and an abnormal cough reflex, they had a significantly higher risk of pneumonia (Addington, et al., 2005). A more recent study by Wakasugi and colleagues evaluated the use of cough reflex testing using citric acid, paired with a water swallow test in comparison to the VFSS results. When evaluating all patients with documented aspiration, sensitivity of the clinical examination for detection of aspiration was 0.67, specificity was 0.97; positive predictive value was 0.98, and negative predictive value was 0.61 (Wakasugi, et al., 2008). The addition of a reliable test of cough reflex sensitivity to a clinical swallowing evaluation may indeed identify those at risk of silently aspirating and therefore has the potential to reduce pneumonia rates after stroke if the results of the test change management (Addington, Stephens, Widdicombe, Anderson, & Rekab, 2003; Addington, Stephens, & Gilliland, 1999; Wakasugi, et al., 2008).

Prior research suggests that cough testing can provide key information to enhance the sensitivity and specificity of the clinical swallowing assessment. However, shortcomings exist in this research that limit clinical translation. Specifically, prior research has failed to control for type and concentration of tussive agent utilised in the test, has incorporated the test without normative values for comparison, and has incorporated methods, which can be difficult for patients with neurologic impairment to execute.

This translational research project sought to carry this technique into clinical practice in New Zealand by controlling for prior research limitations and evaluating the clinical utility of a cough reflex test for reducing pneumonia in acute stroke patients. Specifically, it was proposed that inclusion of cough reflex testing in clinical swallowing assessment would reduce the proportion of patients who were prescribed antibiotics for confirmed chest symptoms, when compared to a control group who did not receive cough testing. Additionally secondary outcomes of length of hospital stay and hospital readmission, referral for instrumental swallowing assessment and diet recommendations were evaluated.

### **Summary of research methods:**

All acute stroke patients referred to speech language therapy for a swallowing evaluation in four urban hospitals (Middlemore, Auckland City, North Shore and Christchurch) between March 2009 and March 2010 were approached for participation in the study. Patients were only excluded if palliative swallowing advice was requested rather than active treatment. The study recruited 311 participants (165 females, 146 males), ranging in age from 22-102 years (mean of 78 years). The majority of the participants were New Zealand European (205), followed by Pacific Island (31), New Zealand Maori (27), Asian (14), European (24), and other (10). All participants presented clinically with an acute stroke and gave informed consent independently, or consent by proxy was provided by their next-of-kin.

Participants were randomly assigned to receive either 1) standard clinical swallowing evaluation (control group) or 2) standard swallowing evaluation with inclusion of cough reflex testing (experimental group). For those in the control group, clinical swallowing evaluation was executed as defined by the clinical protocols of the local speech and language therapy departments. At all sites, this involved a case history, cognitive/ communication screen, cranial nerve examination and observation of oral trials. Management of swallowing impairment followed existing protocols based on recommendations from the clinical swallowing evaluation. For participants in the experimental group, the standard evaluation was completed with the inclusion of cough reflex testing prior to any oral trials. Clinicians were encouraged to incorporate the results of this novel assessment into their clinical decision-making. All clinicians who participated in the trial received formal teaching, equipment demonstrations and the opportunity for reflective practice on a regular basis throughout the recruitment period.

The cough reflex test was administered using a PulmoMate Compressor/Nebuliser with a predetermined flow output of 8 litres per minute. A facemask method, as described in prior research (Wakasugi, et al., 2008) and as utilised in establishing normative data (Monroe, et al., unpublished) was used. Citric acid solutions diluted in 0.9% sodium chloride were prepared by each hospital pharmacy weekly. Two doses were evaluated: 0.8mol/L at which 92.5% of healthy individuals produce a natural cough and 1.2mol/L at which 80% of healthy individuals are no longer able to suppress a cough (Monroe, et al., unpublished). Patients were told that they were participating in a cough test and they were asked to “cough if they feel the need to cough”. Initially a placebo dose (0.9% NaCl) without

citric acid was presented to coach the participant on task completion. Presence or absence of cough during a 15 second period was documented. Cough response was considered positive if two or more coughs were triggered as recommended by the ERS Task Force (Morice, et al., 2007). The test was repeated three times with the low concentration, with a 30 second interval between each inhalation to prevent tachyphylaxis. Clinicians were trained to document a 'full cough' not 'throat clear' as a cough. The clinician then asked the patient to "try to suppress the cough as much as they can" while the same low dose was administered. If they were able to suppress a cough at 0.8mol/L (2 out of 3 trials), the 1.2mol/L concentration was administered. The suppressed cough threshold was reached when participants coughed on at least 2 out of 3 trials of that dose.

The combined results of the clinical swallowing evaluation and the cough reflex test were incorporated into multidisciplinary dysphagia management decisions. The multi-disciplinary team was asked to be cautious in the initiation of oral intake in patients who failed cough reflex testing or presented with a weak cough. Where a patient passed the cough reflex test the multidisciplinary team was advised that patients were likely to show overt signs of aspiration and were at lower risk of developing aspiration pneumonia.

## **Study Execution**

Our predicted recruitment was calculated on the reported incidence of dysphagia following stroke, allowing for a near 40% rate of exclusion. Recruitment rate was slower than predicted. To counteract the slow recruitment rate two additional data collection sites were added in October 2010: North Shore Hospital and Christchurch City Hospital. The addition of these sites allowed for the data collection to be completed as planned. The three-month data collection follow up was delayed at the Christchurch site as a result of the large Earthquake in February 2011. However at the date of this report, all data have been collected and analysed.

## **Results**

### **Patient demographics:**

Although blind randomization was used to assign groups, the control group (46%) had fewer male participants than the experimental group (53%) ( $p=0.05$ ).

### **Primary outcome measure: pneumonia rates based on experimental group**

The primary hypothesis speculated that for patients in the experimental group, the knowledge of cough sensitivity by the multidisciplinary team would result in decreased pneumonia rates. This was not found to be the case with 21% of participants in the control group and 26% of participants in the experimental group developing confirmed pneumonia within the study period ( $p= 0.38$ ).

A further confirmative analysis including all baseline covariates revealed that elder age, male, study sites, cardiac comorbidities and respiratory comorbidities were significantly associated with pneumonia rate. Interaction between randomized groups (experimental vs. control) and respiratory comorbidities was found to be significant ( $p=0.04$ ). This led to a further subgroup analysis. In patients with respiratory comorbidities, there was a non-significant trend that inclusion of cough reflex test was associated with lower pneumonia rates. However, in patients without respiratory comorbidities, inclusion of cough reflex test was associated with higher pneumonia rate.

### **Secondary outcome measures:**

Of the secondary hypotheses, only one was found to be significant. A higher percentage of patients who were assigned to the experimental group (e.g. received cough reflex testing) (18%) were referred for instrumental assessment of swallowing when compared to the control group (7%) ( $p=0.004$ ).

### **Exploratory analyses**

Although our a priori hypotheses were not proven, the study provided very valuable information, not only about the utility of the cough test, but clinical inclusion of the results in practice. Further analyses evaluated only the outcomes of the 148 patients within the experimental group, based on the factor of test result (passed  $N=91$ ; weak  $N = 31$ ; fail  $N= 26$ ).

Several interesting relationships were identified. Patients with respiratory comorbidities were more likely to produce a weak cough response (23%) compared to those with failed cough response (8%) or passed cough response (7%) ( $p = 0.04$ ). Based on results of cough testing, two variables differed between response groups. Patients with pass on cough testing were placed on least restrictive diets, followed by those with weak cough, with most restrictive diet assigned to those with failed cough response, suggesting that clinicians were integrating results into diet

recommendations ( $p < 0.001$ ). Finally, clinician referral for instrumental swallowing assessment varied by response group. Of those who failed cough reflex test, 46% were referred for instrumental assessment, whereas those with weak cough had a 26% referral rate and those with passed cough response had an 8% referral rate ( $p < 0.001$ ).

Although numbers were small and statistical power was reduced, there was a non-significant trend toward increased mortality ( $p = 0.09$ ) and confirmed pneumonia ( $p=0.11$ ) in patients with failed cough test result. These data are presented in the following Figure 1 and suggests that cough test is sensitive to identifying patients at high risk.

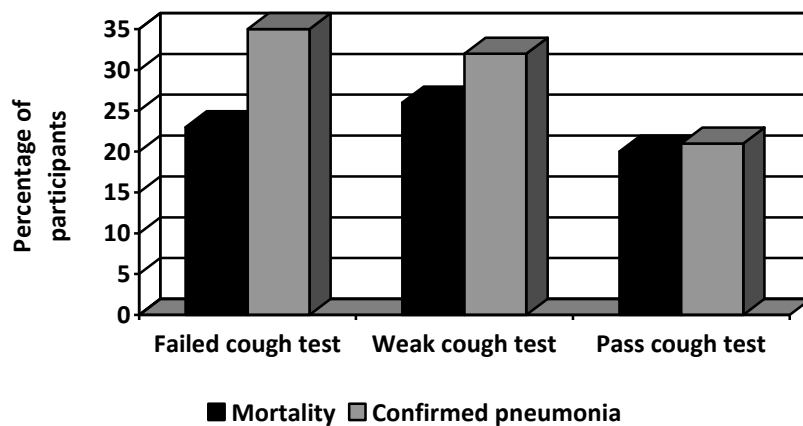


Figure 1. Non-significant trend toward increased mortality and confirmed pneumonia based on cough test result.

Further exploratory analyses were conducted across both experimental groups to identify risk ratios for development of pneumonia. Every 10 years increase in age was associated with 1.4 times higher risk for developing pneumonia (CI 1.1-1.8), with cardiac comorbidities associated with 3.0 times higher risk of pneumonia (CI 1.4-6.5); additionally respiratory comorbidities were associated with 4.3 times higher risk of developing pneumonia (CI 2.0- 9.1). Patients with confirmed pneumonia had significantly higher mortality rates than patients without (35.6% vs. 10.9%,  $p < 0.0001$ ) and significantly prolonged acute ward length of stay (median length of stay is 10 (IQR : 6-17) vs. 6 (IQR: 5-10) ( $p < 0.0001$ ).

## Key Research Outcomes

**1. The Cough Reflex Test did not change the clinical outcome for patients with dysphagia post stroke.** Based on prior research by Addington, et al (2005), we

hypothesized that inclusion of cough reflex testing in a clinical swallowing assessment protocol would provide clinicians with key information that would subsequently alter management plans sufficiently to reduced the end-outcome of pneumonia. Our data suggest that clinicians did integrate information into diet selection and referrals for instrumental assessment; however, incorporation of the test results in multidisciplinary practice was insufficient to change patient health outcomes.

Several reasons may account for this finding. Firstly, and likely most importantly, development of pneumonia is multifactorial; thus a single change in the course of a patient's assessment is not likely to be powerful enough to alter this primary endpoint unless that change strictly controls a host of consequent outcomes. The protocol used by Addington and colleagues (1999) stipulated that management decisions were dictated by a single measure: cough response. The weakness of this study lies in the possibility that some patients may not present cough but also do not aspirate; thus making these patients non-oral appears overly restrictive. In our study, we acknowledged that development of pneumonia is dependent on a number of factors and we chose to allow individual clinicians to integrate this new information from the cough test into their existing decision making construct. It was felt that this would provide more relevant and precise information. However in doing so it allowed for a significantly greater degree of freedom in leading to final outcomes: that of clinician skill

Interestingly, the clinicians involved in the study had a positive approach to the use of cough reflex testing. Ten of the speech-language therapists involved in the study completed a feedback questionnaire. Eighty percent reported they found it a useful addition to the bedside clinical swallowing evaluation and the same proportion stated it was easy to incorporate into bedside testing. Ninety percent indicated they would continue to use it if available at their DHB. However anecdotally, they did not appear to 'trust' the findings of the cough test, with several instances of clinicians identifying a patient with silent aspiration, acknowledging the risk imposed, and electing to continue oral feeding in spite of this.

One of the challenges involved in assimilating this information into clinical practice may also relate to involvement of the Multidisciplinary team (MDT). Only two members of the MDT completed the feedback questionnaire indicating an overall lack of involvement of other professionals. The resultant questionnaires reported being involved with patients in the study but voiced a lack of knowledge regarding the

clinical implications or application of the cough reflex test. Given that MDT management of dysphagia is an essential component of best practice stroke care and secondary complications prevention, the shortcomings of this study may lie in insufficient MDT inclusion of the cough reflex test results in clinical decision making.

**2) The Cough Test does indicate those dysphagics at greatest risk of secondary complications post stroke.** In this study, although knowledge of cough response did not decrease pneumonia rates, there is early evidence that the cough test itself is a sensitive tool for identifying at risk patients. This study found the cough reflex test interventions associated with higher risk of mortality and pneumonia. These two findings did not reach statistical significance but are clinically quite significant. The findings suggest that further research into this clinical tool and, more importantly integration of information into clinical decision-making, is warranted.

**3) Significant information on rates and indicators of pneumonia in New Zealand were acquired.** This research study highlights the significant secondary complications for patients with dysphagia in the acute stages of stroke in New Zealand. Pneumonia rates were 26% in the control group; this increased to 38% of participants in the experimental group who failed the cough test. These rates of pneumonia are unacceptably high and suggest the strong need to address multidisciplinary management practices of patients who are at risk. Increased age, cardiac and respiratory comorbidities are all associated with increased risk of pneumonia. As found internationally, pneumonia was significantly associated with increased length of acute hospital stay and mortality.

**Future research prospects:**

This study suggests that the cough reflex test clinically indicates those at risk of pneumonia and consequent mortality and therefore has potential as an addition to the clinical swallowing evaluation for people following stroke. Considerable shortcomings exist in integrating the information from the additional test toward the development of management practices that inhibit secondary morbidities. Areas for future research include:

*Validation of the Cough Reflex Test*

- Does the cough reflex test result correlate with penetration/ aspiration and laryngeal sensation (through validated instrumental assessment)?

*Integration of Cough Reflex Test results into clinical management paradigms.*

- What factors inhibited clinicians from fully integrating results of cough reflex test into clinical decision making?
- Why did the clinicians' freedom in clinical decision-making in this study result in substantially poorer pneumonia outcomes than the strictly defined protocols in prior research?

*Investigation of other factors affecting the incidence of pneumonia for dysphagic patients after stroke in New Zealand*

- Does the inclusion of an intensive oral care protocol reduce the incidence of pneumonia in patients with dysphagia post stroke?
- Does the presence of a ward-based dental hygienist reduce the incidence of pneumonia in patients with dysphagia post stroke?

*International benchmarking*

- How do pneumonia rates in patients with dysphagia following stroke in New Zealand compare to other countries?
- How do New Zealand referral rates to instrumental assessment in acute stroke compare to other countries?
- What are the attitudes of speech-language therapists and medical practitioners towards instrumental assessment in patients with dysphagia post stroke?

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