

# The Role of Biomarkers in Predicting the Chances of Aspiration in Patients with Difficulty in Swallowing

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## Abstract

**Background:** Aspiration in patients with dysphagia is a major clinical concern due to its association with severe complications such as aspiration pneumonia. Traditional methods for assessing aspiration risk are often invasive and not always predictive.

**Objective:** To evaluate the predictive value of systemic biomarkers C-reactive protein (CRP), procalcitonin, and neutrophil-to-lymphocyte ratio (NLR) for aspiration in patients with dysphagia.

**Methods:** This prospective study included 200 patients with clinically diagnosed dysphagia at a tertiary hospital. Biomarkers were measured at baseline and correlated with the incidence of aspiration determined by video fluoroscopic swallow studies (VFSS) and fiberoptic endoscopic evaluation of swallowing (FEES) over a two-month period.

**Results:** Elevated levels of CRP and procalcitonin were significantly associated with the occurrence of aspiration ( $p < 0.05$ ). CRP demonstrated the highest predictive accuracy with an area under the curve (AUC) of 0.85, followed by procalcitonin with an AUC of 0.78, and NLR with an AUC of 0.72.

**Conclusions:** The findings suggest that CRP and procalcitonin are effective biomarkers for identifying patients at increased risk of aspiration. These biomarkers could potentially be integrated into clinical practice to enhance early identification and management of high-risk patients.

**Keywords:** Dysphagia, Aspiration, Biomarkers, C-reactive protein, Procalcitonin, Neutrophil-to-lymphocyte ratio, Predictive value.

## Introduction

Dysphagia, or swallowing difficulties, is common among patients with neural deficits, head and neck cancer, and the elderly, resulting in considerable morbidity and mortality mainly due to the development of aspiration pneumonia. It is estimated that about 8% of the world population suffers from dysphagia, with the aged and persons with chronic neurologic diseases suffering more (Martino et al, 2005).

The traditional method for assessing the risk of aspirating relies greatly on clinical examination of swallowing, video fluoroscopic swallow studies (VFSS) and fiberoptic endoscopic evaluation of swallowing (FEES). Despite the advantages of these techniques, they also have disadvantages, most notably in terms of availability, expenses, and need for appropriate devices and hired skill (Alagiakrishnan et al., 2013).

In recent years studies have brought to light the possibilities of biomarkers for prediction of health outcomes in a more convenient manner. Markers of inflammation and infection in particular have been employed in various specialties in order to foresee disease progress and therapeutic effects (Sulmasy, 2002). Certain biomarkers should in theory indicate the severity of dysphagic patients who are struggling with swallowing disorders and their possibility of aspiration based on these being a direct indicator of inflammation and muscle wasting (Belafsky et al, 2002).

Finding biomarkers that determine aspiration risk may change the management of dysphagia patients by helping identify patients at risk or targeting therapy more appropriately, thus preventing aspiration pneumonia. The focus of this research is to determine the relationship between chosen markers and dysphagic patients' risk of aspiration, and in doing so, further the active management of such patients.

## Literature Review

### Dysphagia and aspiration risk

Dysphagia, the medical term used where patients have difficulties in swallowing, causes serious health complications like dehydration, malnutrition and aspiration pneumonia which is among the most common causes of mortality among patients with swallowing dysfunction (Marik, 2001). Aspiration which is described as the entry of oropharyngeal or gastric contents into the larynx and lower respiratory tract may occur without any clinical signs and therefore is challenging because of the challenges in identifying and treating it early (Smith et al., 2000). The clinical evaluation as well as the clinical imaging, which are variability the video fluoroscopy swallow studies (VFSS) and fiberoptic endoscopic evaluation of swallowing (FEES), these are the reliable two in diagnosing the disorder of swallowing (Dysphagia) and the assessment of the risk of aspiration (Logemann, 1994). Still, only these techniques that are helpful have been interference by the availability, or economic factors, or the need for repeated the assessments that was done in order to follow how the changes over a period of time.

### Biomarkers in Clinical Practice

The biomarkers have become ancillary managers in medicine as their good benefit is consistent in most diseases as emphasizing on diagnosis accuracy and prognosis determinants. In the instance, however, of a respiratory condition, C-reactive protein and procalcitonin and treat such conditions were effectively used to improve the prognosis of patients with pneumonia (Christ-Crain & Mueller, 2007). Stroke is another condition that some of the biomarkers have been effective in for example neuron-specific enolase and S100 Ca-binding protein B were used effectively to monitor the degree of injury and recovery (Zetterberg et al., 2013).

### Biomarkers and Swallowing Disorders

This review attempted to focus on the current status of the biological markers literature related to swallowing disorders. A few of them have been related to the risk of aspiration and focus on inflammatory mediators such as CRP and some cytokines. These mediators are raised due to inflammation resulting from aspiration events and may have potential for dealing with aspiration risk through early diagnostic means (Belafsky et al., 2002). Additionally, novel markers dependent upon muscle cellular deterioration, creatine

kinase, myoglobin, may reflect swallowing muscle upstructures and function indirectly and give lead about the risk of dysphagia and consequently aspiration (Shaker et al., 2002).

#### Gaps in Current Research

This is not reality as a large number of attempts claim the role of these markers for risk of aspiration and even assessment of dysphagia itself, albeit with a low level of success. So far, only small sample or unlinked studies have focused on clinical episodes of aspiration. Additionally, a lack of such skills limits the availability of longitudinal studies to establish whether or not the said markers have predictive abilities with respect to other indications across populations.

### Methodology

#### Research Type

This research was a prospective in nature and was carried out at a tertiary hospital, to find out the usefulness of some biomarkers in predicting patients with aspiration related dysphagia. The study period was conducted over a year.

#### Participants 'Characteristics

A total of two hundred patients of age eighteen years and older were recruited as study participants and were diagnosed with dysphagia on the basis of clinical history and either a video fluoroscopic swallow study or fiberoptic endoscopic evaluation of swallowing. Subjects were approached from neurology, oncology and geriatric departments within the hospital. Recruitment criteria developed eliminated patients within two weeks of active throat or esophagus surgery, patients with active infection at the time of assessment, and patients unable to give informed consent.

#### Selection and Measurement of Biomarkers

This particular study ran on three major biomarkers targets that they postulated as suitable for predicting the risk of aspirating:

1. C-reactive protein (CRP): As to quantify the systemic inflammation that might be aggravated by the aspiration events.
2. Procalcitonin: This to act as a surrogate for bacterial infection and thus suggest patients at risk for aspiration pneumonia.
3. Neutrophile-lymphocyte ratio (NLR): To evaluate the inflammatory status focusing on stress related inflammation, and infection.

Specimen were taken once on diagnosis and subsequently every two weeks for two months. Measurement of the biomarker levels was made using standard immunoassays in the clinical laboratory of the hospital.

#### Evaluation of Aspiration Status

Aspiration status was established during the evaluation through the video fluoroscopic swallowing study (VFSS) and fiberoptic endoscopic evaluation of swallowing (FEES) done on admission and again on the last day of the study or when there was clinical evidence of aspiration pneumonia. The absence of contrast material above the vocal folds or the signs of penetration were documented.

#### Data Gathering

These included demographic data (age, gender), clinical data (co morbidities, dysphagia severity) and outcomes (yes or no, detected aspiration and its incidence, the period of stay at a hospital and events of aspiration pneumonia) obtained from the patients' medical records.

### Data Processing and Analysis

Descriptive analysis was done to summarize the demographic and clinical data pertaining to the participants. Logistic regression models were utilized to determine the association between aspiration events and levels of the biomarkers with adjustment for covariates including age, sex and general health status. Biomarkers prediction models for aspiration risk were developed using receiver operating characteristic curves (ROC).

### Ethical Considerations

The Ethical guidelines are upheld by this research which had an approval from the Ethics committee. Written informed consent was received from each participant or from a legal representative of the subject. Polygraph examinations were done ethically according to the principles expressed in the Declaration of Helsinki.

## Findings

### Participant Characteristics

A total of 200 patients suffering from dysphagia were recruited. Their mean age was 65 years (SD = 15), with the females constituting 52 percent (104). Most of them had functional disorders due to neurology (60%), then had onco- (25%) and geriatric (15%) conditions. Socio-demographic characteristics and clinical background of the participants are shown in Table 1.

**Table 1: Demographic and clinical characteristics of participants in the study**

Variable	Total (N=200)	Neurological (n=120)	Oncological (n=50)	Geriatric (n=30)
Age in years, mean $\pm$ SD	65 $\pm$ 15	62 $\pm$ 16	68 $\pm$ 14	70 $\pm$ 12
Gender, % (Female)	52	50	56	53
Body mass index (BMI), mean $\pm$ SD	28.3 $\pm$ 5.2	27.8 $\pm$ 5.1	29.0 $\pm$ 5.4	28.5 $\pm$ 4.9

### Levels of Biomarker and Incidence of Aspiration Events

Also presented in Table 2 are the baseline levels of CRP, procalcitonin and NLR as well as their relationship with subsequent aspiration events. We identified statistically significant associations between higher baseline levels of CRP and procalcitonin with aspiration incidents occurring during study period ( $p < 0.05$ ).

**Table 2: Baseline levels of analyzed biomarkers and their association with aspiration.**

Biomarker	Baseline Level (mean $\pm$ SD)	Aspiration Positive (n=80)	Aspiration Negative (n=120)	P-value

CRP (mg/L)	5.2 ±2.4	7.5 ±1.8	3.9 ±1.2	0.001
Procalcitonin (ng/mL)	0.25 ±0.1	0.45 ±0.15	0.15 ±0.08	0.002
NLR	3.1 ±1.0	4.2 ±1.2	2.5 ±0.9	0.010

#### Predictive Accuracy of Biomarkers

The ROC curve analysis revealed that the highest AUC was found with CRP (0.85) then procalcitonin (0.78) and lastly NLR (0.72). This further specifies that these three markers have a good predictive ability to the aspiration risk. Results of ROC curves are provided in Table 3.

**Table 3: ROC curve analysis showing ability of different biomarkers to predict aspiration.**

Biomarker	AUC	95% CI	Sensitivity	Specificity
CRP	0.85	0.79 - 0.91	82 %	79 %
Procalcitonin	0.78	0.71 - 0.85	75 %	73 %
NLR	0.72	0.65 - 0.79	68%	67%

#### Discussion

In this study, we focused on the ability of certain biological markers (CRP, procalcitonin and NLR) to assess the risk of aspiration in patients suffering from dysphagia, which is a critical condition due to a considerable risk of aspiration pneumonia. In this case, findings nonetheless still indicate that heightened levels of CRP and procalcitonin may be more relevant in the notice of patients at higher risk of aspirating. These results support existing literature concerning the existence of systemic inflammation or infection which further complicate the lungs of dysphagic patients.

#### Interpretation of Main Findings

**CRP and Procalcitonin:** The findings regarding high levels of CRP and procalcitonin and the probability of aspirations also confirmed the position that inflammation must be highly regarded among the main risk factors for complications associated with the aspiration. It is also frequent even among healthy individuals because procalcitonin is not measured unless there is some infectious and therefore inflammatory stimuli, which in normal individuals can trigger an increase in the CRP production by the liver. These findings are consistent with previous studies in which the rise of inflammation has been considered one of the mechanisms implicated in the disease process of aspiration (Marik, 2001; Belafsky et al., 2002).

**Neutrophil-to-Lymphocyte Ratio (NLR):** Although NLR did not show a strong association with aspiration events as it was the case with CRP and procalcitonin, it still displayed a degree of statistical significance. NLR has been suggested to reflect systemic inflammation and stress responses and may thus be inversely related to the severity of dysphagia and general wellbeing of the patient, and as such the chances of aspiration.

#### Clinical Implications

The predictive ability of the biomarkers may be employed in clinical settings so as to identify patients at high risks of aspiration at an early stage thereby helping with preventive measures and appropriate treatment options. For instance, elevated biomarkers can prompt swallowing therapy, or diet changes and prophylaxis to avoid the risk of aspiration pneumonia.

### Limitations

There are however limitations to our study. The implications of the findings may be limited by utilizing the data from one tertiary care center. In addition, as this was a cross-sectional type of study, we were unable to establish the causal relationship between high levels of biomarkers and occurrence of aspiration events. More larger populations are warranted in future disease-based investigations incorporating multicenter designs to improve external validity.

### Future Research

It would be interesting for future studies to identify how any change in biomarker levels precedes any improvement in the clinical status of dysphagic patients. If significant changes are achieved in biomarker levels, it would be useful to carry out longitudinal studies to determine if the risk of aspiration and its ramifications can be reduced. Moreover, exploring other potential biomarkers such as the measures of the integrity of the esophageal mucosa or even the strength of esophageal muscles would enhance the understanding of the causes of aspiration in dysphagic patients.

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