

**RISK FACTORS OF POST EXTUBATION DYSPHAGIA (PED)
AMONG CRITICALLY ILL PATIENTS IN INTENSIVE CARE UNIT**

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RISK FACTORS OF POST EXTUBATION DYSPHAGIA (PED) AMONG CRITICALLY ILL PATIENTS IN INTENSIVE CARE UNIT

ABSTRACT

Objective: Post-extubation dysphagia (PED) is a common disorder that occurs following extubation. The prevalence of post-extubation dysphagia varies significantly from 3% to 62% to even 84% of adult patients who undergo prolonged mechanical ventilation due to the different diagnostic criteria and also population characteristic. This study will provide information on predictive risk factors in critically ill patient that are contributing to the development of PED.

Methods: A prospective observational study over the period of 4 months from October 2018 to January 2019 were carried out in intensive care unit (ICU) at the University Malaya Medical Centre (UMMC). Fifty seven critically ill patients aged 18 years and above who were mechanically ventilated with endotracheal intubation for any duration were recruited in this study. Patient's demographic and ICU related data were collected daily until maximum 14 days. Within 48hrs post extubation, patients were asked to perform the Repetitive Saliva Swallowing test (RSST) and completed the Sydney Swallowing Questionnaire (SSQ). These evaluations were repeated at day 7 post extubation.

Results: The prevalence of PED in this study was 35.1%. Repeated evaluation at day 7 post extubation showed 94.3% of patients were at low risk of PED. Incremental factors associated with an increased risk for PED include higher SAPS II score ($p=0.026$), ischemic heart disease ($p=0.027$) and chronic obstructive pulmonary disease ($p=0.031$). Age and duration of mechanical ventilation did not increase the risk of PED.

Conclusion: In this prospective study, patients with higher SAPS II score, comorbidities ischemic heart disease and chronic obstructive pulmonary disease were associated with

higher risk of PED. Majority of the patients were able to recover from PED by day 7 post extubation.

Keywords: PED, RSST, SSQ

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TABLE OF CONTENTS

Abstract	Error! Bookmark not defined.
Acknowledgements	v
Table of Contents	vi
List of Tables.....	vError! Bookmark not defined.
List of Symbols and Abbreviations.....	viii
List of Appendices	ix
CHAPTER 1:INTRODUCTION	1
CHAPTER 2: LITERATURE REVIEW	3
CHAPTER 3: METHODOLOGY	7
CHAPTER 4: RESULTS	9
CHAPTER 5:DISCUSSION.....	14
CHAPTER 6: CONCLUSION	17
References.....	18
Appendix.....	20

LIST OF TABLES

TABLE 1..... 9

TABLE 210

TABLE 311

TABLE 4..... 12

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LIST OF SYMBOLS AND ABBREVIATIONS

PED : Post-extubation dysphagia

ICU: Intensive Care Unit

UMMC : University Malaya Medical Centre

EMR : Electronic Medical Record

CIM: Critical Illness Myopathy

CRF: Case Report Form

SOFA: Sequential Organ Failure Assessment

SAPS: Simplified Acute Physiology Score

APACHE: Acute Physiology and Chronic Health Evaluation

NUTRIC: Nutrition Risk in the Critically ill

SGA: Subjective Global Assessment

GCS: Glasgow Coma Scale

MV: Mechanical Ventilation

IHD: Ischemic Heart Disease

COPD: Chronic Obstructive Pulmonary Disease

RSST: Repetitive Saliva Swallowing Test

BSE: Bedside Swallowing Evaluations

VFSS: Videofluoroscopy Swallowing Study

FEES: Fiberoptic Endoscopic Evaluation of Swallowing

LIST OF APPENDICES

APPENDIX A.....	20
APPENDIX B.....	21
APPENDIX C.....	22
APPENDIX D.....	25

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CHAPTER 1: INTRODUCTION

Post-extubation dysphagia (PED) is a common disorder that occurs following extubation. PED is defined as the inability to effectively transfer food and liquid from the mouth into the stomach (Baker et al, 2009). The prevalence of PED varies significantly from 3% to 62% (Skoretz et. al, 2010) to even 84% (Match et.al 2011), among adult patients exposed to prolonged endotracheal intubation in ICU, multiple intubations and also any surgery of head and neck cancer (Macht, White, & Moss, 2014). The incidence varies due to the different diagnostic criteria and also population characteristic.

The etiology of dysphagia after mechanical ventilation (MV) is unknown and considered multifactorial. Endotracheal tubes that are used may cause direct trauma to the anatomy and physiology of the pharynx and larynx and considered a key risk factor for dysphagia. Other identified mechanisms including neurologic disease including neuromuscular weakness, altered consciousness, reduced sensorium and motor response, use of sedative/analgesic drugs, direct oropharyngeal or laryngeal trauma, tracheostomy, increased gastrointestinal reflux, prolonged intubation, dyssynchronous breathing and swallowing may all contributes to development of dysphagia (Patrick et.al 2019).

PED often persists at time of discharge from ICU and commonly associated with poor outcomes (Macht et al., 2011). The consequences of dysphagia include aspiration, pneumonia, malnutrition, placement of feeding tubes, decreased quality of life, increased institutional care and increased mortality. (Medeiros, Sassi, Zambom, & Andrade, 2016). They also added that it may delay the initiation of oral feeding, increase hospital length of stay, reintubation and increased risk of morbidity and mortality.

Considering that post-extubation dysphagia is not routinely screened for in most ICU (Brodsky MB et.al, 2014), possibly due to limited awareness, PED appears a rather poorly recognised health care problem. Therefore, early detection of post-extubation dysphagia is vital to reduce other complications and it is beneficial to develop approaches that cope with the disorder and thus decreasing morbidity among the critically ill patients (M. J. Kim et al., 2015).

The annual incidence of Malaysian patients admitted to intensive care unit (ICU) who require mechanical ventilation is approximately 28,000 (Malaysian Registry of Intensive Care, 2016). However no local study has been done to explore the incidence and risk factors of PED among mechanically ventilated critically ill patients in Malaysia. This study will provide information on predictive risk factors that are contributing to the development of PED in critically ill patient. The identification of risk factors of PED by involvement of multidisciplinary team will reduce its incidence, enable early interventions and minimize the occurrence of its complications.

CHAPTER 2: LITERATURE REVIEW

Post-Extubation Dysphagia (PED) can be defined as the failure of transportation of food from the mouth into the stomach (Baker et al, 2009). Its incidence among the critically ill patients is from 3% to 62% (Skoretz et. al, 2010). In a subsequent retrospective observational cohort study, a dysphagia prevalence of up to 84% was reported (Macht et. al, 2011). It varies significantly due to the different diagnostic criteria and also population characteristics (Scheel, Pisegna, McNally, Noordzij, & Langmore 2016). One of the major consequences of PED is swallowing disorder after extubation which may result in aspiration, multiple intubations, pneumonia and longer hospital stay (Macht et al.,2011). Study by Schefold JC et all (2017) showed that PED persisted until ICU discharge in more than 80% of cases and more than 60% of patients with impaired deglutition on ICU remained dysphagic at hospital discharged. This can lead to delayed oral intake which may lead to the development of malnutrition and dehydration (See et al., 2016).

Several predictors and risk factors contributing to the development of post-extubation dysphagia had been identified in various studies . Many studies are reporting that post-extubation dysphagia is independently associated with prolonged intubation during ICU stay and increased in age. In a review paper by (Skoretz et al., 2010), they cited at least six studies in which 44% to 62% of patients who developed dysphagia had prolonged intubation in the ICU. Prolonged intubation, typically defined as longer than 48 hours in the literature (Ajemian et al 2001) is thought to contribute to swallowing dysfunction via numerous factors. Barker et al, 2009, investigated the incidence of dysphagia after cardiac surgery and found that the number of intubations and the total duration of mechanical ventilation were both associated with postoperative dysphagia. Similarly, a study by Ajemian et al in 2001, had identified about 50% of patients intubated longer than 48 hours has a significant risk factor for postextubation dysphagia.

A study in trauma patients found that the number of ventilator days and an age more than 55 years old were independent risk factors (Bordon A et al. 2011). Each day of intubation increased the risk of PED by 14%, and patients older than 55 years old had a 37% increased risk of dysphagia compared with younger patients. However, in contrast to other findings, El Solh, Okada, Bhat, & Pietrantonio (2003) found that neither age nor duration of intubation is associated with higher incidence of swallowing dysfunction after extubation. They postulated that extensive mucosal inflammation can already be observed after 24 hours of mechanical ventilation. Therefore, the duration of intubation does not relate to the severity of swallowing dysfunction following extubation.

Rassameehiran et al. (2015) in their study listed that other risk factors including preexisting neurological diseases such as stroke and Parkinson's disease, low Glasgow Coma Scale scores of less than 14 were associated with higher post-extubation dysphagia risk. Macht et al. (2013) in their study stated that supine positioning together with increased usage of sedation and paralytics were associated with gastroesophageal reflux which is one of the mechanisms of PED. Patients that undergo tracheostomy are also at risk of developing PED as tracheostomy will interfere with the normal physiological and mechanical swallowing functions by causing muscle atrophy of both larynx and pharynx (Brown et al., 2011). The occurrence of PED also increased in conditions that may irritate the larynx causing inflammation at the laryngeal region. Therefore, it is said that the presence of nasogastric tube is also associated with higher risk of developing dysphagia after extubation (Rassameehiran et al., 2015) especially when larger-bore nasogastric tube was used (Macht et al., 2012).

Two different studies by Macht, Wimbish, Bodine, & Moss (2013) and Brodsky et al. (2014), found that post-extubation swallowing assessment was rarely performed in ICU. Only 41% of hospital routinely performed the screening and only 44% of patients

completed the evaluation. Commonly, evaluation of dysphagia after extubation is performed using several methods which include screenings, bedside swallowing evaluations (BSE) and also instrumental examinations in the form of endoscopy, fluoroscopy and cervical auscultation (Scheel et al., 2016b). An ideal screening tool should be rapid and not invasive. At least three studies cited by G. Medeiros et al. (2014) has agreed that videofluoroscopy swallowing study (VFSS) is the gold standard of swallowing function evaluation. Macht et al. (2012) in their national survey of diagnosis and treatment of post- extubation dysphagia had stated that videofluoroscopic swallow study (VFSS) was the most widely available diagnostic tool followed by fiberoptic endoscopic evaluation of swallowing (FEES) with frequencies of 41% and 60% of them using BSE to assess presence of dysphagia after extubation. BSE is indeed a safe, widely available and non-invasive test. However, it has a variable sensitivity between 42% to 92% and specificity of 59% to 91% (Ramsey, Smithard, & Kalra, 2003).

Most critical care expert usually wait until 48 hours after extubation before performing swallowing evaluation (Scheel et al., 2016b). In this study, Repetitive Saliva Swallowing Test (RSTT) is used as the screening test to determine post- extubation dysphagia among critically ill patients. This test is relatively safe and non-invasive and is used to assess aspiration risk by observing the voluntary ability of patients to swallow (Melorose, Perroy, & Careas, 2015). A group of Japanese researchers (Oguchi et al., 2000) has studied the reliability of RSTT as a screening test, and the result is compared to those of VFSS. In their study, they concluded that RSTT had higher sensitivity and specificity which were 0.98 and 0.66 respectively. They also added that to determine the risk of PED further, it is reasonable to perform RSTT before using another test. When the frequency of swallowing is 2 or lesser within 30 seconds, patient's clinical and

medical history should be examined, and a further test should be performed if necessary.

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CHAPTER 3: METHODOLOGY

A prospective observational study over the period of 4 months from October 2018 to January 2019 was carried out among mechanically ventilated critically ill patients in the intensive care unit (ICU) of University Malaya Medical Centre (UMMC). Ethical approval was obtained from the UMMC ethical committee (MREC ID NO: 201868-6376).

For this study, consecutive sampling was used to recruit subjects. All newly admitted patients into the ICU were screened according to inclusion and exclusion criteria. The inclusion criteria were age more than 18 years old and mechanically ventilated with endotracheal intubation for any duration. The exclusion criteria for this study were head and neck surgery or cancer and unable to feed orally before their critical illness. Consent was obtained from all eligible patients or legal guardian prior to patient recruitment.

Data collection was performed by the investigator (ICU research assistant). Patient's vital signs, ICU related data and laboratory data were continuously collected for 14 days or until the day of discharge from ICU. This data collection was done by referring to the electronic medical records (EMR) and ICU chart before transferring the data into a case report form (CRF). Demographic and medical data needed such as name, age, sex, date of admission, weight, height, daily average vital sign, co-morbidities, severity of illness (based on Sequential Organ Failure Assessment (SOFA) score, Simplified Acute Physiology Score (SAPS) II score, Acute Physiology and Chronic Health Evaluation (APACHE II) score Glasgow Coma Scale (GCS) score and Nutrition Risk in the Critically ill (NUTRIC) score at ICU admission were recorded. Assessment of Subjective Global Assessment (SGA) using a quantitative Subjective Global Assessment was done on day one, two and seven after extubation. RSST was performed on day two and seven post extubation. This non-invasive screening test was

performed by the investigator to determine patient's ability to swallow and assess the risk of aspiration after extubation. In this study, the patient was instructed to sit in a resting position, and asked to sip and swallow a small amount of cold water repetitively each time. The number of swallow achieved was recorded through observation or palpation. Two and less number of laryngeal movement during a 30 second period was considered as having a higher risk of aspiration and development of PED. Three or more number of laryngeal elevations were considered as normal and considered as having a low risk of dysphagia and aspiration.

The Sydney Swallowing Questionnaire (SSQ), a 17-item visual analog scale (range, 0–1,700), were used to quantify patient-perceived dysphagia symptom. Patients were asked to complete this questionnaire on day two and seven post extubation. The individual question score was calculated on a 100-mm visual analogue scale. The total score is calculated by summing the individual responses; a higher score indicates a more severe swallowing impairment.

Data was analyzed using SPSS version 23 (Chicago, IL, USA). The low risk and high risk groups for PED were compared by univariate analysis using the unpaired Student t test for continuous variables and Pearson χ^2 with Yates correction for categorical variables. Those variables with P value < 0.20 were entered into logistic regression analyses to identify independent risk factors for PED. Values were reported as frequencies, percentages, median and interquartile range or adjusted odds ratios with 95% confidence intervals; statistical significance was set at P value < 0.05.

CHAPTER 4: RESULTS

Table 1: Demographic and clinical characteristics of patients

Characteristics	All, n = 57
Gender (%)	
Male	44 (77.2)
Female	13 (22.8)
Age (%)	
<60y/o	41 (71.9)
>60y/o	16 (28.1)
Age, median, yr	54 (40, 63)
BMI (%)	
Underweight (<18.5 kg/m ²)	4 (7)
Normal (18.5-24.9 kg/m ²)	44 (77.2)
Overweight (25-29.9 kg/m ²)	5 (8.8)
Obese (>30 kg/m ²)	4 (7)
Type of admission (%)	
Medical	38 (66.7)
Surgical	12 (21.1)
Trauma	7 (12.3)
Comorbidities (%)	
Diabetes mellitus	26 (45.6)
Chronic kidney disease	8 (14)
Ischemic heart disease	11 (19.3)
COPD	7 (12.3)
ICU factors	
APACHE II score, median	17 (12.5, 26)
SOFA score, median	7 (5.5, 10)
SAPS II score, median	42 (32.5, 52)
ICU length of stay, median, day	5 (3, 8)
Use of vasopressor (%)	34 (59.6)
Length of sedation, median, day	2 (1, 4)
Intubation factor	
Endotracheal tube size (%)	
Size 7.0 mm	5 (8.8)
Size 7.5 mm	21 (36.8)
Size 8.0 mm	31 (54.4)
Reintubation, (%)	7 (12.3)
Prolong Intubation (>48hrs) (%)	37 (64.9)
Intubation duration, median, day	3 (2, 5)

Table 2: Result of RSST assessment at day 2 and day 7 post extubation

Day Post Extubation	N	RSST Screening (%)		p value
		High risk PED	Low Risk PED	
Day 2	57	20 (35.1)	37 (64.9)	0.63
Day 7	35	2 (5.7)	33 (94.3)	

A total number of 57 patients were recruited in this study from October 2018 to January 2019. Table 1 shows the characteristics of the study population. The majority of patients in this study belonged to the middle age group with mean age of 54 (40, 63) years old. Majority of the patients were male, 77.2% and normal BMI categories 77.2%. Most of the type of admission were medical cases 66.7% followed by surgical 21.1% and trauma 12.3%. The median durations of endotracheal intubation and of ICU length of stay were 3 (2, 5) days and 5 (3, 8) days, respectively. Total of 37 patients (64.9%) were intubated more than 48 hours and 7 patients (12.3%) had repeated intubations in this study.

Table 2 shows the result of RSST assessment of the swallowing ability at day 2 and day 7 post extubation. Assessment on day 2 post extubation, showed 20 out of the 57 patients (35.1%) were at higher risk of PED. Total of 35 patient were reevaluated on RSST assessment at day 7 post extubation. Result showed 94.3% of patients were at low risk of PED at day 7 post extubation.

Table 3: Result of characteristic of patient with risk of dysphagia from RSST screening

Characteristic	RSST Screening (%)		p value
	High risk PED	Low risk PED	
Gender			
Male	15 (75.0)	29 (78.4)	0.772
Female	5 (25.0)	8 (21.6)	
Age			
<60y/o	14 (70.0)	27 (73.0)	0.812
>60y/o	6 (30.0)	10 (27.0)	
Age, median, yr	58 (45.0, 65.5)	48 (36, 61)	0.064
BMI			0.319
Underweight (<18.5 kg/m ²)	2 (10.0)	2 (5.4)	
Normal (18.5-24.9 kg/m ²)	16 (80.0)	28 (75.7)	
Overweight (25-29.9 kg/m ²)	0 (0.0)	5 (13.5)	
Obese (>30 kg/m ²)	2 (10.0)	2 (5.4)	
Type of admission			0.906
Medical	14 (70.0 %)	24 (64.9)	
Surgical	4 (20.0%)	8 (21.6)	
Trauma	2 (10.0%)	5 (13.5)	
Comorbidities			
Diabetes mellitus	10 (50.0)	16 (43.2)	0.625
Chronic kidney disease	3 (15.0)	5 (13.5)	0.877
Ischemic heart disease	7 (35.0)	4 (10.8)	0.027
COPD	5 (25.0)	2 (5.4)	0.031
ICU factors			
APACHE II score, median	20.5 (13.3, 27.5)	16 (12, 23.5)	0.251
SOFA score, median	8.5 (6.3, 12)	7 (5, 9)	0.082
SAPS II score, median	49.5 (34.5, 61)	40 (31, 47)	0.026
ICU length of stay, median, day	6 (4, 8.7)	5 (3,8)	0.429
Use of vasopressor (%)	13 (65.0)	21 (56.8)	0.545
Length of sedation, median, day	2 (1, 4)	2 (1,3.5)	0.654
Intubation factor			
Endotracheal tube size			0.574
Size 7.0 mm	2 (10.0)	3 (8.1)	
Size 7.5 mm	9 (45.0)	12 (32.4)	
Size 8.0 mm	9 (45.0)	22 (59.5)	
Reintubation	1 (5.0)	6 (16.2)	0.218
Prolong Intubation (>48hrs)	14 (70.0)	23 (62.2)	0.554
Intubation duration, median, day	3 (2, 4)	3 (2,5)	0.885
Day 2 SSQ score, median	105 (61, 183)	68 (22,170)	0.148

Table 4 Final multivariate logistic regression model associated with the risk of post extubation dysphagia

Variable	OR (95% CI)	p value
Age	1.010 (0.967-1.054)	0.661
Ischemic heart disease	4.134 (0.867-19.715)	0.075
COPD	6.300 (0.862-46.025)	0.070
SAPS II score	1.049 (0.997-1.104)	0.66

Table 3 shows the result of characteristic of patient with risk of dysphagia from RSST screening. The higher risk of PED were patients at median age of 58 (45,65.5) years old and the lower risk patients at median age of 48 (36, 61) years old. Majority of patients with higher risk PED were male, 75%. This could also be due to the fact that most of our patients admitted to ICU were male. Patient with ischemic heart disease (p value: 0.027) and patient with chronic obstructive pulmonary disease (COPD) (p value: 0.031) were noted to be statistically significant of having high risk of PED. For severity of illness, only SAPS II score were statistically significant in having higher risk PED (p value: 0.026). Otherwise risk of PED did not differ statistically with regard to endotracheal tube size, reintubation, length of intubation duration, length of sedation or use of vasopressor. These findings are depicted in table 3.

Table 4 shows final multivariate logistic regression model associated with the risk of dysphagia. The variables potentially associated (at $P < 0.2$) with risk of PED were age, ischemic heart disease (IHD), COPD and SAPS II score. In the multivariable logistic regression analysis, none of the variables were significantly associated with higher risk of PED. Age [odds ratio 1.010; 95% confidence interval (CI) 0.967-1.054; $p=0.661$] was not found to be a predictor of swallowing dysfunction post extubation after correction for comorbidity IHD, COPD and SAPS II score. However, individuals with IHD had a 4.1-fold increased chance and patient with COPD had 6.3 fold increased chance of developing PED.

CHAPTER 5: DISCUSSION

Dysphagia is defined as the difficulty or inability to safely and efficiently transfer food and fluids from the oral cavity to the stomach, and is usually observed in critically ill patients who required endotracheal intubation for mechanical ventilation (Baker et al, 2009). The endotracheal tube can cause laryngeal complications related to duration of intubation, ETT tube size and cuff pressure, that may cause irreversible sequelae to the patient (Mota et al, 2012). Among the possible complications resulting from prolonged endotracheal intubation, post extubation dysphagia is a notable cause.

The incidence of PED obtained in this study was 35.1%. Our findings showed that the overall rate of PED was comparable to previously published data in which the incidence was from 3% to 62% (Skoretz et. al, 2010). In this study 94.3% patients recovered from PED by day 7 post extubation. Study by Schefold JC et al, 2017 showed that PED persisted until ICU discharge in more than 80% of cases and more than 60% of patients with impaired deglutition in ICU remained dysphagic at hospital discharge. The lower incidence of PED in this study could be attributed to the tools used in the diagnosis which were clinical evaluations, as well as related to the characteristics of the study population.

This study revealed that the median age for high risk of PED was 58 years old compared to a much younger age group with median age 48 years old who was at low risk of PED. Some studies have shown an increased risk of PED in patients 55 years of age or older (Bordon A et al., 2011). The patients age appear to significantly affect the resolution of dysphagia, since the return to oral feeding in the elderly tends to be delayed. However, in contrast to other findings, El Solh, Okada, Bhat, & Pietrantonio (2003) found that neither age nor intubation length is associated with higher incidence of swallowing dysfunction after extubation.

In this study, it was observed that the length of intubation duration did not result in the development of PED. In a review paper by (Skoretz et al., 2010), they cited at least six studies in which 44% to 62% of patients who developed dysphagia had prolonged intubation in the ICU. Study by Barker et al 2009, found that the number of intubations and the total duration of mechanical ventilation were both associated with postoperative dysphagia. Prolonged intubation defined as intubation that lasts longer than 48 hours contribute to oropharyngeal muscle inactivation, glottis injury, mucosal inflammation causing tissue alterations and also ulcerations at the vocal cord (G. Medeiros, Sassi, Mangilli, Zilberstein, & Andrade, 2014).

It is known that the instrumental assessment of swallowing, performed by videofluoroscopy or videoendoscopy, is the most reliable method of swallowing assessment (Carnaby et.al 2018). However, it is not always performed in clinical practice due to patients' clinical condition and the inability of patients to cooperate. This technique may not be available in some hospitals due to lack of equipment or expertise. Our institution does not have enough resources to perform instrumental evaluation of swallowing. It is vital that hospitals are equipped with the necessary instrument and trained personnel in order to diagnose PED and in an ideal situation the service should be provided to patients whilst they are still in ICU and subsequently followed up on the wards after ICU discharge.

There are several limitations to our study. First, the sample size was small, which may not reflect the true incidence of PED and its associated risk factors. Likewise, not all potentially important variables associated with post extubation dysphagia were available for evaluation, such as commodities preexisting neurological diseases, Glasgow Coma Scale (GCS), supine position and size of nasogastric tube. Lasty is the type of evaluation used to determine the risk indicators for dysphagia which

was made exclusively through the bedside RSST assessment and not the gold standard via video-fluoroscopy.

Despite such limitations, this study may be used as a pilot study to screen patients at risk of developing PED and identifying the possible predisposing factors. Early recognition of PED would lead to an early referral to Speech Therapists and hopefully through their intervention would result in reduced complications related to dysphagia in extubated patients.

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CHAPTER 6: CONCLUSION

The predictive factors that increased the risk of post extubation dysphagia in this study were higher SAPS II score, and comorbidities ischemic heart disease and chronic obstructive pulmonary disease. Increasing age and length of intubation duration did not increase the risk of PED. Majority of the patients were able to recover from PED by day 7 post extubation.

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