Comparative Study Between The Efficacy Of Non-Invasive Ventilation At The Pulmonary Infection Control Window, And Spontaneous Breathing Trials As Strategies For Weaning Invasive Ventilation In Patients With Acute Exacerbation Of Chronic Obstructive Pulmonary Disease Caused By Pulmonary Infection

Thesis

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List of Abbreviations

AECOPD	: Acute exacerbation of chronic obstructive pulmonary disease
ATS	: American thoracic society
BAL	: Broncho-alveolar lavage
CB	: Chronic bronchitis
COPD	: Chronic obstructive pulmonary disease
CPAP	: Continuous positive airway pressure
CPIS	: Clinical pulmonary infection score
DHI	: Dynamic hyperinflation
ECOPD	: Exacerbation of chronic obstructive pulmonary disease
FiO2	: Fraction of inspired oxygen
GOLD	: Global initiative for chronic obstructive lung disease
HR	: Heart rate
ICU	: Intensive care unit
IMV	: Invasive mechanical ventilation
iPEEP	: Intrinsic positive end-expiratory pressure
MAP	: Mean arterial pressure
MENA	: Middle East and North Africa
MRN	: Medical record number
MV	: Mechanical ventilation

NIV : Non-invasive ventilation

NPPV : Noninvasive positive pressure ventilation

NTIS : Non-thyroidal illness syndrome

$PaCO_2$: Partial pressure of carbon dioxide

PaO2 : Partial pressure of oxygen

PIC : Pulmonary infection control

PS : Pressure Support

PSB : Protected specimen brush

PSV : Pressure support ventilation

QoL : Quality of life

RR : Respiratory rate

SBP : Systolic blood pressure

SBT : Spontaneous breathing trial

SIMV : Synchronized intermittent mandatory ventilation

SpO_2 : Arterial oxygen saturation

VALI : Ventilator-associated acute lung injury

VAP : Ventilator-associated pneumonia

V_M : Minute volume

V_T : Tidal volume

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Introduction

Chronic obstructive pulmonary disease (COPD) is a major public health problem. In 2020, COPD is projected to rank in the fifth place worldwide in terms of disease burden and third in terms of mortality. Although COPD has received progressively focused attention from the medical community in recent years, its impact is still relatively underestimated or ignored by the community as well as mass-media, public health and government officials **(Jørgen et al., 2013).**

In the Middle East and North Africa (MENA), the prevalence of COPD has been estimated at around 4% of adults aged over 40 years among the general population. This prevalence is expected to expand rapidly, since smoking rates in the region are generally elevated and rising. Moreover, the principal COPD comorbidities are also abundantly existent in this region. For example, the prevalence of diabetes in the MENA region being one of the highest among the world (11%). Furthermore, it was reported in 2000 that six of the ten countries with the highest prevalence of diabetes in the world exist in this

region. In the first decade of this present century, the prevalence of diabetes in Saudi Arabia increased from 10% in 1999 to 30% in 2009, whereas the overall worldwide prevalence was declared to be only 2.8% in 2000 **(Bassam et al., 2016).**

Historically, COPD has been defined in terms of symptoms as chronic bronchitis (CB), anatomically as emphysema, or, most recently, physiological-wise as airway obstruction. The physiological definition has emerged to be the most common, although studies using other definitions are still published. Despite growing consensus on the use of spirometry as a physiological criterion, spirometric cut-off points for establishing airflow obstruction show significant differences. Since lung function declines with age, COPD prevalence estimations are highly dependent upon the age range and distribution of individuals included. Since smoking is the primary risk factor for COPD, prevalence estimates may also vary by underlying smoking habit rates. With the rise in smoking frequencies in females, there are ongoing controversies as to the relative impact of smoking on the development of COPD among both genders. Finally, the

contribution of other aerosolized and inhaled exposures (e.g. occupational smoke, vapors or dust, ambient air pollution, and biomass fuel) to population prevalence rates have yet to be determined and studied for most countries **(Halbert et al., 2016).**

Exacerbations are common events in the natural history of patients suffering from chronic obstructive pulmonary disease (COPD). Moreover, these patients have been shown to encounter a higher rate of hospital admission due to respiratory tract infection, which increases in rate and impact with the severity of the disease. Lower respiratory tract infection (LRTI) is considered one of the most commonly diagnosed causes of decompensation in COPD in hospitalized patients, accounting for 51%–70% of exacerbations. These episodes are difficult to pin-point, and there are no universally agreeable clinical criteria to identify them, although the combination of symptoms described by Anthonisen (namely, increased dyspnea, sputum production and sputum purulence) has been used to identify cases in exacerbations with an infectious etiology **(Ramon et al., 2016).**

Exacerbation of chronic obstructive pulmonary disease (ECOPD) and community-acquired pneumonia are common respiratory disease events that contribute to patients' hospitalization and mortality rates. It is considerably controversial whether the coexistence of these two entities might be posing a contributing factor in increasing mortality. The results of studies published to present date reporting on mortality have been inconsistent, probably due to their considerably heterogeneous structure **(Loke et al., 2013).**

A long-term follow-up study of a cohort of patients diagnosed with COPD found that 50% of patients died within 3.6 years of their initial hospitalization for COPD exacerbation. Following the first severe COPD exacerbation, a period of stable risk was noted till occurrence of the second event. However, each subsequent recurrence of a severe exacerbation that required hospitalization increased the risk of a subsequent event and mortality, with subsequent events being of progressive severity. This highlights the consistent need for improvement in prevention and treatment approaches to severe exacerbations of COPD **(Pavord et al., 2016).**

Aim of the Work

The aim of this work is to examine the efficacy of implementing Pulmonary Infection Control (PIC) window as the optimum switching point to wean invasive mechanical ventilation (IMV) in intubated patients for AECOPD with pulmonary infection, compared to conventional weaning strategies implementing the use of 2-hours Spontaneous Breathing Trials (SBT) either through pressure support ventilation (PSV) or T-tube, based on daily screening of weaning parameters predicting successful extubation.

Chronic Obstructive Pulmonary Disease (COPD)

DEFINITION OF COPD

Several definitions of COPD have been existing among the medical community, and it would be incorrect to say that one is clearly superior to another. Neither of these definitions is particularly precise and can easily include disease entities that are not usually considered as COPD, such as cystic fibrosis, sarcoidosis, and bronchiectasis. Importantly, neither of these definitions declares a clear difference between COPD and chronic asthma with airway remodeling. There are reasons for this; there is a significant overlap, and as acknowledged by the American Thoracic Society (ATS) mentioning airway hyper-reactivity, one of the hallmarks of asthma, some patients with COPD possess features that make separating them from patients with chronic ongoing asthma particularly challenging.

In 2001, the Global Initiative for Chronic Obstructive Lung Diseases (GOLD) was launched; in their seminal document from 2001, they defined COPD as: "… a disease state characterized by airflow limitation that is not fully reversible. The airflow obstruction is usually both progressive and associated with an abnormal response of the lungs to noxious particles or gases."

The GOLD document has been revised twice, in 2006 and 2011. On both occasions, the definition has been altered. According to the GOLD 2011 revision:

"COPD, a common preventable and treatable disease, is characterized by persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways and the lung to noxious particles or gases. Exacerbations and co-morbidities contribute to the overall severity in individual patients **(Vestbo, 2014).**

COPD Exacerbations

IMPACT OF EXACERBATIONS

Exacerbations remarkably contribute to the overall course and severity of COPD, the pulmonary function decline, the impairment of quality of life (QoL) and eventually to morbidity and mortality. Exacerbations also potentiate the risk of cardiovascular disease, of developing further exacerbations, contribute to reduced muscle mass, impair physical activity, precipitates anxiety, depression, work absenteeism, and healthcare costs. Exacerbations may occur regardless of the extent of functional impairment and it has been shown that mild and moderate exacerbations, which often pass unreported and thus untreated, also pose an impact on health status. Therefore, it is imperative to predict and promptly identify exacerbations, and assess their severity and frequency, in order to appropriately manage them, prevent hospitalization, optimize the patient's QoL and effectively control the high costs associated with their treatment **(Guimarães et al., 2016).**

DEFINITION OF EXACERBATION

There is no universally agreed definition for an exacerbation of COPD, since exacerbations have a wide spectrum of causes and severities. It seems reasonable to implement a definition that does not imply etiology or degree of severity **(Burge and Wedzicha, 2003).**

A previous consensus definition stated that COPD exacerbation is:

"A sustained worsening of the patient's condition, from the stable state and beyond normal day-to-day variations, that is acute in onset and necessitates a change in regular medication in a patient with underlying COPD." **(Rodriguez-Roisin, 2000).**

An amendment of the above-mentioned definition is recommended, as follows, to include exacerbations of similar severity where extra treatment was not sought:

"... Sustained worsening of the patient's condition from the stable state and beyond normal day-to-day variations that is acute in onset and may warrant additional treatment in a patient with underlying COPD." **(Burge and Wedzicha, 2003).**