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Nutrition status in hospitalized patients with COPD on non-invasive ventilation

by

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A THESIS

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Abstract

Nutrition status in hospitalized patients with COPD on non-invasive ventilation

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Background: Nutrition is an important aspect of critically ill hospitalized patient care but the lack of consistent nutritional guidelines for sub-critically ill patients with Chronic Obstructive Pulmonary Disease (COPD) requiring non-invasive positive pressure ventilation (NPPV) may be putting vulnerable patients at risk. Hand grip strength measurements are an emerging metric for nutritional status.

Objective: The objective of this study is to determine if hospitalized patients with COPD on NPPV show a difference in handgrip strength as a marker of nutritional status than those hospitalized patients with COPD not requiring NPPV.

Methods: This was a prospective observational study of 10 hospitalized patients not requiring NPPV (Group 1) and 5 hospitalized patients requiring NPPV (Group 2). 3 measurements of handgrip strength on the patient's dominate hand were averaged every alternating day during hospitalization. Mineral status and physiological parameters were also recorded concurrently with handgrip strength collection.

Results: The two groups were similar overall. Group 2 had a longer length of stay, averaging 5.2 (±0.45) days, with group 1 averaging 3.2 (±0.63) days (p=0.001). Mineral status and physiological parameters between the groups were similar. Group 1 had an average change in handgrip strength of 1.59 (±1.82) kg with group 2 having an average change of -1.08 (±1.22) kg (p=0.016).

Conclusion: Hospitalized patients with COPD on NPPV may be at risk for a decline in nutritional

status compared to those not requiring NPPV as shown by a significant difference in change in

handgrip strength.

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List of Abbreviations

APACHE   Acute Physiology And Chronic Health Evaluation

ASPEN   American Society for Parenteral and Enteral Nutrition

BiPAP   Bi-level Positive Airway Pressure

BMI   Body Mass Index

BUN   Blood Urea Nitrogen

CHF   Congestive heart failure

CHI   Catholic Health Initiative

cm   Centimeters

COPD   Chronic Obstructive Pulmonary Disease

CPAP   Continuous Positive Airway Pressure

dL   Deciliter

FEV_1 Forced Expiratory Volume (1 second)

FVC   Forced Vital Capacity

g   Grams

GOLD   Global initiative for chronic Obstructive Lung Disease

ICU   Intensive Care Unit

ICUAP   ICU-Acquired Paresis

Kcals   Kilocalories

kg   Kilograms

L   Liter

LOS   Length of Stay

mEq   Milliequivalents

mg   Milligrams

NPO   *Nil per os* or Nothing By Mouth

NPPV	Non-invasive Positive Pressure Ventilation
SD	Standard Deviation
SPSS	Statistical Package for the Social Sciences
UNMC	University of Nebraska Medical Center

Chapter 1: Introduction

When patients are admitted to the hospital for medical treatment, their care, including nutrition, is often guided by evidence based guidelines. This is true of patients admitted to the intensive care unit (ICU) for mechanical ventilation; however, this may not always be the case for patients just a step down from being critically ill. Patients on non-invasive, pressure supported ventilation (BIPAP or CPAP) may not be considered critically ill, but are often still very sick. Frequently used to prevent mechanical ventilation, non-invasive measures of ventilation leave more open ended guidelines on how to treat patients. In the case of mechanical ventilation, starting enteral nutrition early, within 24-48 hours of admission to a critical care unit, is a well-accepted standard of practice[1]. When it comes to non-invasive ventilation, the issue of how to provide appropriate nutrition care becomes a gray area. Specialized nutrition care is an important aspect of critical care, but the lack of consistent nutritional guidelines in sub-critically ill patients may be putting vulnerable patients at risk for developing or exacerbating malnutrition. Before best practices can be established, the background on the area of interest needs to be examined. Measuring handgrip strengths is an emerging metric to quickly assess nutritional status.[2, 3, 4] This study seeks to examine the nutritional status of hospitalized patients with Chronic Obstructive Pulmonary Disease (COPD) who required non-invasive means of ventilation, including Bilevel Positive Airway Pressure (BIPAP) and Continuous Positive Airway Pressure (CPAP), by utilizing handgrip strength measurements. It is hypothesized that patients with COPD requiring non-invasive ventilation will show evidence of a greater decline in handgrip strength as a proxy for nutrition status compared to those with COPD who do not require non-invasive ventilation.

Chapter 2: Literature review

Background

The need for assisted ventilation is often a main reason patients are admitted to ICU, but assisted ventilation as we know it today, is a fairly recent development. A full history of mechanical ventilation has been described elsewhere, [5] the highlights are as follows.

Until the 1960, much of the ventilation assistance was provided by negative-pressure ventilation machines, such as the "iron lung." Non-Invasive positive pressure machines in the form of bag and mask, and later bellow and mask, machines were available. Advances in technology, as well as ongoing complication of the "tank" style negative pressure ventilations led to a transition to positive pressure ventilation in the 1960s. Today, these non-invasive ventilation modalities commonly include Bilevel Positive Airway Pressure (BiPAP) or Continuous Positive Airway Pressure (CPAP).

Invasive ventilation began to become available in the 1940-1950s. At first, these machines were quite simple, with much of the monitoring done manually. Over time, they have developed into the more sophisticated machines common in today's ICU.

 Much research has been conducted on the care of patient receiving invasive positive pressure ventilation due to the critical nature of providing this type of care. These patients are monitored closely, with practice guidelines to provide evidence based patient care.

COPD

Chronic Obstructive Pulmonary Disease is a common cause of respiratory distress. As reported by the American Lung Association, COPD is the third leading cause of death in the United States of America.[6] This is especially important in the elderly population, as they are more prone to exacerbations of COPD. In fact, approximately 65% of patients over age 65

discharged from hospitals were admitted with COPD exacerbations.[6] Providing excellent

evidence based care to these patients is important to provide better outcomes, including

reduced re-admission rates and cost of care.[6]

COPD is defined as the presence of airflow limitations and its severity is based on lung

function tests utilizing spirometry. The airflow limitation for a diagnosis of COPD is often defined

as a FEV_1/FVC ratio of <0.70.[7] FEV_1 is the volume that has been exhaled at the end of the first

second of forced expiration and FVC, or Forced Vital Capacity, is the volume of air forcibly

exhaled from the point of maximal inspiration. COPD is often measured in severity by using the

Global Initiative for Chronic Obstructive Lung Disease or GOLD score.[7] This score is calculated in

the presence of an FEV_1/FVC ratio of <0.70 and is based on post-broncholdilator FEV_1. Lung

function tests would be conducted after the administration of an inhaled bronchodilator

medication to reduce variability.[7] For example, a GOLD score of 1 or Mild COPD would have a

FEV_1 that is ≥80% of the predicted value. A GOLD score of 2 or Moderate COPD would have a

measurement of ≥50% but <80% predicted FEV_1. A FEV_1 ≥30% but <50% predicted FEV_1 would

be classified as a GOLD score of 3 or Severe COPD. Lastly, a FEV_1 <30% would be classified as

Very Severe or GOLD 4.[7] Classification of the severity of COPD can help guide the care of the

affected patients.

Treatment for COPD exacerbation is aimed at providing adequate oxygenation,

especially to prevent tissue acidosis associated with poor oxygenation. This includes the use of

medication to promote bronchodilation, corticosteroids, antibiotics, as well as oxygen therapy.

There are various means by which oxygen can be provided to patients. This can range from

simply supplementing extra oxygen, to pressure supported oxygenation, either through a mask

of varying size (non-invasive positive pressure ventilation) to full mechanical ventilation. Due to

the high morbidity and difficulty weaning from ventilation associated with mechanical

ventilation, NPPV has been supported to be an alternative treatment. A Cochrane review of

NPPV supports its use as a primary treatment for exacerbations of COPD.[8] NPPV should be

started early to help promote positive outcomes, including preventing severe acidosis, reducing

mortality, reducing the need for intubation, and decreasing treatment failure.[8] NPPV has been

supported as a way of treating respiratory failure with similar improvement in gas exchange as

conventional ventilation, but with fewer serious complications (66% serious complications in the

mechanical ventilation group versus 38% in the NPPV group). [9]

Nutrition in COPD

Nutrition is an important factor for good health, and this is very much the case for

patients with COPD. Malnutrition has been shown to be very common in patients with COPD.[10]

However it is difficult to quantify the prevalence of malnutrition in COPD as it varies depending

on the population studied and method used to measure malnutrition. Hunter, Carey, and Larsh

found in 1981 that between 19-60% of patient with COPD may be considered malnourished.[11]

The reason for this high prevalence of malnutrition is unclear. Possible etiology for malnutrition

in COPD ranges from increased inflammation[12] to increased work of breathing,[13] to increased

catabolism from high doses of corticosteroids often used for treatment in COPD.[14] Whatever the

cause of malnutrition in COPD, it is definitely an issue that needs to be addressed, especially

during acute exacerbations of COPD that result in hospitalization.

In fact, nutrition status is such an important factor in COPD, that weight loss is

considered a prognostic factor in COPD. Patients with COPD who have a lower body mass index

(BMI) have been shown to have a higher rate of mortality.[15] Conversely, improving nutrition

status and promoting weight gain has been shown to reverse the negative effects of low body

weight in COPD.[15] In fact, multiple studies have shown that nutrition intervention, mostly

through oral nutrition supplements, can improve outcomes in COPD. Schols et al. (1998) demonstrated that nutrition intervention through oral nutrition supplementation improved survivability of COPD by promoting weight gain.[15] Participants who gained >2kg in 8 weeks, when compared to a control with no weight gain, showed on multivariate analysis to be an independent predictor of survival over 48 months of follow up (p=0.01).[15] Another study by Saudny-Unterberger et al. (1997) showed that patients with acute exacerbation of COPD whose diet was supplemented with an oral nutrition supplement demonstrated improved oral intake by an additional 10kcals/kg/day and a trend toward improved general well-being score (+11.96 versus -10.25 for the control, p=0.066). However, even with oral supplementation, patients in this study did not improve measures of muscle strength, and were shown, through nitrogen balance studies, to be in negative nitrogen balance.[14] In order to promote better patient care for patients with chronic and acute COPD, the nutrition status of the patient needs to be taken into consideration, and improved if necessary.

Nutritional requirements in COPD may be difficult to calculate. The "gold standard" of indirect calorimetry is expensive and not always readily available all hospital settings. An energy intake of 27-30kcals/kg, or about 140% basal energy expenditure with a protein intake of 1.2g/kg has been show to maintain energy balance in patients with an acute exacerbation of COPD.[16] However, energy and protein intakes above this level may be necessary to improve nutritional status.[14, 16] This is especially important considering the high prevalence of malnutrition in COPD patients.

Clearly, nutrition is an important part of the care of patients in respiratory distress, but there does not appear to be a consensus on how best to provide nutrition care to these patients. Many studies done on the importance of nutrition support in COPD utilized only oral

nutrition supplements.[12, 14, 15]Another study did note, "As part of standard care, patients with consistently poor intake despite interventions with oral nutrition support were enterally or parenterally fed on 25% of eligible intake days." [17] No distinction was made between patients who received enteral versus parenteral nutrition. Of note, the same study found patients who were only fed orally were less likely to meet nutritional requirements than those who received enteral or parental nutrition.[17] However, in order for patients to obtain oral intake on NPPV, they must be able to tolerate breaks off NPPV.

If a patient is unable to obtain or maintain adequate nutritional intake from an oral diet, the next step is to consider nutrition support. This is especially true of patients that may be unable to tolerate breaks off of NPPV to take oral intake. The axiom, "If the gut works, use it," is very appropriate to consider when determining if a patient should receive enteral or parenteral nutrition support. Barring any other complications, many patients admitted with respiratory distress have working guts. As mentioned previously, early enteral nutrition is part of standard therapy for patients who are invasively ventilated. The American Society for Parenteral and Enteral Nutrition's (ASPEN) Critical Care feeding guidelines supports the use of early enteral nutrition in critically ill patients. In fact, guideline A4 states, "Enteral nutrition should be started early, within 24-48 hours of admission." [1] The difficulty in applying these guidelines is how to define critical illness. Early enteral nutrition is commonly a part of patient care for invasively ventilated patients but not necessarily patients on non-invasive ventilation, who may still be considered critically ill. A poster session by Digby, D'Arsigny, and Parker (2012) detailing their observation of non-invasively ventilated critically ill patients in an Ontario Academic Centre showed significant gaps in the care provided to 32 patients on NPPV.[18] This included gaps in nutrition care, including almost 22% of patient receiving no "enteral nutrition" when on NPPV

for greater than 24 hours. Patients who did receive "enteral nutrition", it was provided orally

(n=18), via feeding tube (n=4), or a combination of both (n=3).[18]

Physicians may be wary of oral or enteral feeding in NPPV. Many patients may be made

NPO (*nil per os,* i.e. nothing by mouth) due to the risk of aspiration. In a study on complications

of non-invasive ventilation, discomfort from the mask was the most common complication,

occurring in 30-50% of patient.[19] Aspiration is a very serious complication of NPPV and is

reported to occur about 5% of the time.[19] Factors thought to reduce the incidence of aspiration

include patient selection and gastric drainage, when appropriate. Of note, over-sedation can

increase risk of aspiration, and care needs to be taken to ensure patients maintain the ability to

protect their airways.[19] Other strategies have been shown to reduce the incidence of aspiration,

including simply maintaining the head of the bed above 30 degrees.[20] If the patient is being

provided with enteral nutrition, routine verification of tube placement, assessment of GI

intolerance such as abdominal distention and excessive residuals, and removing enteral feeding

tubes as soon as possible are other ways to reduce the risk of this complication.[20] However

there is very little research specifically demonstrating the safety of enteral nutrition provision on

NPPV.

Another often cited reason for not providing enteral nutrition to patients on NPPV is

complications with the mask sealing.   One study did note nasogastric tube insertion, along with

the pressure applied to the respiratory system, can lead to worse air leaks from the mask. In

this study, adaptors were used to facilitate the provision of enteral nutrition and improve

patient comfort.[21] Another study done by Antonelli, et al. (1998), also briefly mentions the use

of a seal connector in the dome of non-invasive ventilation mask to reduce air leakage for

patients with nasogastric tubes.[9] However, this study does not delineate if the nasogastric tube

was used for enteral feeding or gastric decompression[9].   Of note, the clinical guidelines

provided by the Royal Children's Hospital in Melbourne, Australia recommend the use of

nasogastric or nasojejunal feeding tube for children on non-invasive ventilation. These

guidelines do note the increased risk of abdominal distention and risk of pressure area

formation and leaks from the mask.[22] Children's nutritional needs vary from those of adults, but

this does serve as a reminder of the importance of adequate nutrition in NPPV and the ability to

provide enteral feeding to those on NPPV. More conclusive research on the safety and best

practices for provided enteral nutrition to patients on NPPV are needed.

Parenteral nutrition is another means of providing nutrition support to patients. Due to

the ease of administration, and perceived decreased risk of complications, cautious physicians

may feel more comfortable providing parenteral nutrition to patients on non-invasive

ventilation.   As noted in APSEN's critical care feeding guideline A3: "Enteral Nutrition is the

preferred route of feeding over Parenteral Nutrition for critical ill patients who require nutrition

support therapy." [1] Therefore, unless a patient has another complication prohibiting using the

patient's GI tract, enteral nutrition should at least be attempted before parenteral nutrition*.*

Overall, ICU patients have better outcomes, including lower infectious complications, when

early enteral nutrition is provided over parenteral nutrition.[23] If a patient is unable to tolerate

enteral feeding, ASPEN's Critical Care feeding guideline B1 supports waiting 7 days in the

previously well-nourished patient before initiating parenteral nutrition.[1] However, guideline B2

supports starting parenteral nutrition sooner in critically ill patients with evidence of protein-

calorie malnutrition .[1] If used correctly, parenteral nutrition can be beneficial in providing

adequate nutrition, but care does need to be taken to ensure the proper use of this therapy.

Hand grip strength dynamometry

Hand grip strength dynamometry is gaining popularity as a means of assessing nutritional status. ASPEN included handgrip strength as one of the six criteria for malnutrition in their consensus statement on *Characteristic Recommendations for the Identification and Documentation of Adult Malnutrition (undernutrition)*.[24] The inclusion of hand grip strength dynamometry as criteria for malnutrition only seeks to highlight its importance in assessing nutritional status. Using handgrip strength as a measure of nutrition status has been increasing in popularity in more recent years but has been considered for longer. Watters, Haffejee, Angorn, and Duffy discussed nutritional assessment utilizing hand grip dynamometry in 1985.[4] Nutritional status is a multifaceted condition and handgrip strength is often utilized as one of many criteria when looking at nutritional status. In ASPEN's consensus statements on malnutrition, two of the six malnutrition criteria must be present to diagnosis malnutrition.[24] As more research emerges on this means of looking at nutritional status, there is data to support hand grip strengths as an independent predictor of nutritional status and change in nutritional status.[2] Muscle function reacts early to nutrition deficiency which makes hand grip strength dynamometer useful in detecting more subtle changes in nutritional status.[3] Due to its ease of execution and benefits in being utilized as a marker of nutritional status and outcome predictor, hand grip strength is being increasingly being used as an outcome variable in nutritional intervention studies.[3] Additional outcomes handgrip strength is associated with include ICU-acquired paresis (ICUAP) or extreme muscle weakness from critical illness and mortality.[25] Utilizing handgrip strength measurements is a simple way to look at nutritional status, functional status, and to predict outcomes in hospitalized patients.

Handgrip strengths can be compared to standard values or as a change from baseline. The JAMAR® brand dynamometer is frequently utilized in research and is often considered the

gold standard.[2,3,26] Baldwin, et al in 2013 showed handgrip dynamometry to have a standard of

error of 2.8kg with a minimal detectable difference with a 95% confidence of 7.8kg in the right

hand for critically ill patients[26]. In the left hand, these numbers were 4.5kg standard of error and

12.5 minimal detectable differences at 95% confidence. In contrast, they showed healthy adults

to have a standard of error of 2.0kg in the right hand, and 2.6kg in the left, with a minimal

detectable difference at 95% confidence of 5.7kg in the right hand and 7.1kg in the left.[26]

However, this is just one study's findings. ASPEN's malnutrition guidelines for hand grip strength

in severe malnutrition states is defined as measurably reduced compared to the manufacturer

guidelines.[24] The JAMAR Hydraulic Hand Dynamometer brand defines measurably reduced as

more than two standard deviations from the mean of their established normal values based on

age, sex, and hand.[27] While comparing a patient's hand grip strength to the normal values can

help to diagnosis malnutrition and be useful when only one measurement is available,

measuring a change from baseline can show changes in nutritional status over time.

Clearly, nutrition is important for patients receiving NPPV for respiratory distress but

how these patients receive nutrition can vary greatly.   Protocols to support feeding patients on

invasive ventilation are widely accepted for their ability to improve outcomes. A consensus on

feeding patients on non-invasive ventilation would likely have similar success. Until this can be

done, further research needs to be done on the safety and best practices for feeding patient's

on non-invasive ventilation. This study seeks to support this by starting to look at the nutritional

status of hospitalized patients with COPD to determine if there is a difference in nutritional

status between those requiring NPPV and those that do not. With the emergence of hand grip

strength as an easy, reliable predictor of nutritional status, this will be utilized as the primary

outcome.

Chapter 3: Methods and Procedures

Approval

Data for this study were collected at CHI Health Saint Elizabeth Hospital, a local,

community based hospital. Institution Review Board (IRB) approval was obtained from the

University of Nebraska Medical Center IRB and the Catholic Health Initiative (CHI) IRB.

Permission for this study was also granted by the research council at CHI Health Saint Elizabeth

Hospital. Following IRB and institutional approval, informed consent was obtained from the

patients.

Criteria

Inclusion criteria were any adult patients ages 19 and over, admitted with COPD

exacerbations. Patients with a history of recent major surgery, trauma, or burns were excluded.

Also, patients with conditions that may alter nutritional status were excluded, including

cirrhosis, uncontrolled diabetes (in ketosis or more than 2 blood sugars >400mg/dL), and chronic

renal failure on dialysis. Patients were also excluded if they had a contraindication that would

prevent peripheral muscle strength testing, including acute or preexisting neurological

condition, or cognitive impairment to follow commands. Additional exclusion criteria included

end of life cares and significant language barrier. Patients who were mechanically intubated on

admission were excluded from the study to help narrow the population of the study. However,

those patients that are admitted on NPPV but later require more aggressive respiratory support

with mechanical ventilation were included.

The participants in this study were classified into 2 groups. Group 1 includes all COPD

patients who did not require non-invasive ventilation. Group 2 includes all COPD patient

enrolled in the study who did require non-invasive ventilation.

Data Collection

Demographic and anthropometric data was obtained from medical record review, including age, self-reported race, sex, height, weight, any change in weight in past 6 months, any change in weight during hospitalization, and BMI. The primary nutritional status endpoint obtained was hand grip strength as measured by a JAMAR® Hydraulic Hand Dynamometer. Following the manufacturer's instructions, measurements of hand grip strength were taken. Three measurements on the patient's dominate hand were recorded. Primary measurements were taken within 24-48 hours of enrolling into the study, with subsequent measurements taken every alternative day, until the patient discharged. Hospital outcomes included length of duration on non-invasive ventilation, and if the patient was mechanically ventilated. Hospital stay and mortality were also collected. Nutrition intervention was also collected including days patient was NPO while on NPPV, or if the patient received enteral or parenteral nutrition. It was also noted if the patient was on steroids, and if they participated in physical therapy.

Additional data was collected on the same day as the handgrip strength measurements. Routine lab values were also collected, as available. These included visceral protein stores of total protein, serum albumin, and pre-albumin. Measurements of mineral status were collected such as serum iron, sodium, and potassium. Physiological parameters including blood urea nitrogen (BUN), creatinine, and fasting (or morning) blood sugar were also recorded. Additionally, average respiratory rate was collected. Average percent of recorded meal intake were also recorded.

Statistical Analysis

Initial goal for recruitment was 30 patients not requiring BiPAP or CPAP (Group 1) and 30 patients requiring BiPAP or CPAP (Group 2). Based on previous literature,[26] this goal was established to achieve 80% power to detect a difference of 2.07 kg between the null hypothesis

that both group mean changes in grip strength are 2.00 kg and the alternative hypothesis that the mean of group 2 (patients requiring BiPAP or CPAP) is 4.07 kg with known group standard deviations of 2.76 for each group and with a significance level (alpha) of 0.05 using a two-sided Mann-Whitney test assuming that the actual distribution is normal.

Normal values were based on the standard of the handgrip dynamometer, which have been described elsewhere. These normal values vary based on age, sex, and hand.[27] Due to this variance, it is not useful to compare the mean handgrips strengths between groups, as each group did have slight differences in age, sex, and dominate hand. Instead, the averages of the 3 measurements for each patient were compared against the standard values. Average measurements were considered to be in the normal range if they fell within 2 standard deviations of the mean for that group.

Statistical analysis was conducted utilizing Statistical Package for the Social Sciences (SPSS) software. Descriptive summaries were presented using means, standard deviations, ranges, frequencies, and percentages. Continuous variables, specifically the change in grip strength over the hospital stay, were compared between the groups using a Mann-Whitney test. Categorical data, such as demographic information, was compared between the groups using Fisher's Exact test.   All comparisons were conducted at the 0.05 level of significance.

Chapter 5: Results

Actual recruitment proved to be more difficult than anticipated. Initial estimates based on expert input anticipated enrolling 30 patients in each group within 3 months. However, patients were enrolled in the study for a 6 month period. 10 participants were enrolled in Group 1 and 5 participants were enrolled in Group 2. Demographics of the groups are shown in Table 1. Unfortunately, anticipate enrollment was not achieved due to a number of factors including

patient not meeting the inclusion criteria. Of the patients screened to be in the study, around 45

did not meet the inclusion criteria. Many of the patients on NPPV in the hospital screened for

and excluded from the study, required it due to exacerbations of Congestive Heart Failure (CHF)

and did not have a diagnosis of COPD. Pneumonia, without any COPD, was also very common in

the screened patients. Many of the patient's screened that did have a diagnosis of COPD were

also unable to participate due to cognitive reasons. COPD primarily affects the elderly and

combined with oxygenation issues, confusion, inability to follow commands, or inability to sign

one's own consent was common in the population. Of those screened, 20 patients met the

exclusion criteria. Additional reasons for exclusion included poorly controlled diabetes (blood

sugar >400 on more than 1 occasion or in diabetic ketoacidosis) and recent, major surgery. A

number of patients also declined to consent to be in the study; 9 of the 24 patients that met

both the inclusion criteria and exclusion criteria declined to participate. This resulted in 63% of

patients able to participate in the study actually consenting to participate in the study. COPD

and being on NPPV can be very tiring, which was an often cited reason for not wanting to

participate in this study. Due to being unable to meet our enrollment goals, this study is unable

to reach 80% power and thus will be considered a feasibility or pilot study for assessing

nutritional status of COPD in hospitalized patient. It may also be a useful feasibility study on

taking measurements of handgrip strength in the hospital as a means of determining nutritional

status.

There were no statistically significant differences in the demographic variables between

the two groups. Group 1 included slightly older participants, with an average of 71.9 (±10.2)

years in the control group and average of 68.6 (±11.1) years in the experimental group (Table 1).

The proportion of males and females were the same in the two groups, with slightly more male

participants in both groups (Table 1). All of the participants listed their ethnicity as white non-

Hispanic in their admission screening. Only 1 participate from group 1 was left handed.

Table 1: Demographic data of COPD patients per group

	Group 1 (N=10)	Group 2 (N=5)	p-value
Age Mean (SD)	 71.9 (10.2)	 68.6 (11.1)	P=.624

Gender
   Male
   Female
	
	6 (60%)
	4 (40%)
		
		3 (60%)
		2 (40%)
			
			P=1.00

Ethnicity White non-Hispanic	 10 (100%)	 5 (100%)	 P=1.00

Dominate hand
   Right
   Left
	
	9 (90%)
	1 (10%)
		
		5 (100%)
		0
			
			P=1.00

Anthropometrics between the two groups were compared. Participants in group 2 were

more likely to be obese with an average BMI of 44.2kg/m^2 (Table 2). The average BMI in group 1

was 25.7kg/m^2 (Table 2). When compared, there was a significant difference in BMI between

the two groups (P=0.005) (Table 2). Out of the 10 participants in group 1, 3 reported significant

weight loss prior to admission as opposed to none of the 5 participants in group 2 reporting any

weight loss (Table 2). Of those that lost weight, the average amount lost with 4.33 (±1.37) kg

with a range of 3.4-5.9kg lost (Table 2).

Table 2: Anthropometrics of COPD patients per group

	Group 1 Mean (SD)	Group 2 Mean (SD)	Significance
Height (cm)	175.5 (9.0)	164.1 (12.3)	
Weight (kg)	80.6 (29.4)	117.88 (18.4)	
BMI (kg/cm^2) **Range**	**25.7 (8.0)** **12.2-37.4**	**44.2 (9.2)** **31.9-55.8**	**P=0.005**
# of patients with weight loss.	3 / 10 participants	0 / 5 Participants	P=0.505
If loss, amount lost? Range	4.33kg (1.37) 3.4-5.9kg	NA	

Additional data about the participants were collected. Steroids and having Physical Therapy could potentially cause differences in handgrip strength, so it was noted what patients utilized these therapies. Overall, there was no difference during the hospitalization in use of steroids or Physical Therapy between the two groups (p=1.00 and p=0.23, respectively) (Table 3). Average days patients were kept NPO were also collected. Only one patient in group 1 and one patient in group 2 were kept NPO for at least a day (Table 3). Overall, there was no difference in average days NPO between the groups (p=0.68) (Table 3). Patients that required mechanical ventilation after failed initial conservative therapies were to be tracked, but no patient in either group required this (Table 3).   A marked difference between the groups was found in the average length of stay. Group 1 averaged 3.2 ±0.63 day and group 2 averaged 5.2 ±0.45 days in the hospital (p=0.001) (Table 3). Mortality was also tracked between the two groups, with no patients in either group succumbing to the disease process (Table 3). Used as a measure of severity of COPD, a GOLD Score was attempted to be tracked, but was unavailable on all the patients in the study.

Table 3: Additional COPD patient factors per group

	Group 1 N=10	Group 2 N=5	p-value
Steroids	9 (90%)	4 (80%)	1.00
Physical Therapy	6 (60%)	5 (100%)	P=0.23
Days NPO Mean (SD)	0.2 (0.63)	0.2 (0.45)	P=0.68
Mechanical Ventilation	0 (0%)	0 (0%)	P=1.00
LOS Mean (SD) Range	**3.2 (0.63) 2-4 days**	**5.2 (0.45) 5-6 days**	**P=0.001**
Mortality	0 (0%)	0 (0%)	P=1.00

Additional lab values were tracked at each time point that handgrip strengths were measured. These lab values include total protein, albumin, pre-albumin, iron, sodium, potassium, blood urea nitrogen (BUN), creatinine, and blood sugar. Data were not available for every patient at each time point. As only 1 patient was available to complete three sets of handgrip strength measurement, mineral status and physiologic data is only available on 1 patient in group 2 for the third measure. No patient had pre-albumin levels drawn at any time point during the study. The only measurement with a difference between the 2 groups was Iron during the 2nd data collection. Group 1 averaged 10.88mg and group 2 averaged 13.57mg (Table 4). All other lab values showed no difference between the two groups at any time point of data collection. Meal intakes, averaged of three meals per day, between the groups showed no difference (Table 4). Respirations per minute showed no difference between the two groups (Table 4).

Table 4: Biochemical, meal intakes, and physiological data of COPD patients per group at each time point

	Group 1 1st Measure	Group 2 1st Measure	P-Value	Group 1 2nd Measure	Group 2 2nd Measure	P-Value	Group 2 3rd Measure *
Total protein (g/dL)	6.8 N=6	6.5 N=4	P=0.394	. N=0	5.6 N=1	.	. N=0
Albumin (g/dL)	3.53 N=6	3.08 N=4	P=0.199	. N=0	3.1 N=1	.	. N=0
Pre-Albumin (mg/dL)	. N=0	. N=0	.	. N=0	. N=0	.	. N=0
Iron (g/dL)	12.00 N=10	12.24 N=5	P=0.902	**10.88 N=6**	**13.57 N=3**	**P=0.039**	13.8 N=1
Sodium (mEq/L)	138.6 N=10	142.6 N=5	P=0.109	140.4 N=7	144.5 N=4	P=0.182	143 N=1
Potassium (mEq/L)	4.1 N=10	4.22 N=5	P=0.951	4.19 N=7	4.12 N=4	P=1.000	4.3 N=1
BUN (mg/dL)	18.5 N=10	24 N=5	P=0.158	23.9 N=7	30.3 N=4	P=0.449	51 N=1
Creatinine (mg/dL)	0.88 N=10	1.04 N=5	P=0.270	0.96 N=7	1.15 N=4	P=0.345	1.43 N=1
Blood Sugars (mg/dL)	161 N=10	199 N=5	P=0.327	165 N=7	183 N=4	P=0.449	131 N=1
Meal Intakes (%)	76 N=9	66 N=5	P=0.280	76 N=9	74 N=4	P=0.751	100 N=1
Respirations (breaths/ min)	19.4 N=9	19.0 N=5	P=0.946	19.0 N=9	21.5 N=4	P=0.825	20 N=1

*No 3rd measurement was available for group 1.

The change in handgrip strength was the primary measurement for this study. The first measure of handgrip strength was taken within 48 hours of admission, after consent was obtained. Subsequent measures were taken every two days after the initial measure. The average change in handgrip strength for group 1 was 1.59 (±1.82)kg, while the average change in handgrip strength of group 2 was -1.08 (±1.22)kg (Table 5). Patients with COPD who require BIPAP (group 2) averaged a negative change in handgrip strength (Table 5). Simple statistical analysis using the Mann-Whitney test to compare the change in handgrip strength did meet the

criteria for significance with a p-value of 0.016 (Table 5). Due to the limited sample size,

attempts to control for confounding variables, such as the difference in length of hospital stay,

by utilizing multiple regression was unable to be completed.

Table 5: Average handgrip strength of COPD patients per group at each time point and overall change

	Group 1 Mean (SD)	Group 2 Mean (SD)	Significance
1st Average Handgrip Strength (kg)	26.00 (9.09) N=10	19.53 (9.05) N=5	P=0.178
2nd Average Handgrip Strength (kg)	26.41 (8.86) N=9	19.92 (8.98) N=4	P=0. 440
3rd Average Handgrip Strength (kg)	- N=0	25.67 (-) N=1	-
Change in handgrip strength (kg)	**1.59 (1.82) N=9**	**-1.08 (1.22) N=4**	**P=0.016**

Handgrip strengths for each time point were compared against normal values for

handgrip strength. As previous described, the normal range is defined as within 2 standard

deviations of the mean for the patient's age, sex, and hand. Overall, most of the measurements

in this study did fall into the normal range (Table 6). Only 1 patient from group 2 fell outside of

the normal range during the second time point of testing (Table 6). Only 1 patient was able to

complete a third set of handgrip strength measurements, and the average did fall within the

normal range. There appears to be no difference between the groups in regard to having

handgrip strengths within the established normal range.

Table 6: Statistical analysis of handgrip strength measurements compared to normal values per group.

	Group 1	Group 2	
1st measurement within 2 SD of normal Mean	100% N=10	100% N=5	P=1.0
2nd measurement within 2 SD of normal Mean	100% N=9	75% N=4	P=0.31
3rd measurement within 2 SD of normal mean	-	100% N=1	-

Chapter 6: Discussion

Demographics

The demographics of the patients in this study are similar to the average patient with

COPD in the region the study was conducted. Average age for both groups was over 65 years

old, as is expected in a disease that typically affects older adults (Table 1). Overall, our patients

tend to be over age 65, with slightly more males then females, which fits the usual

demographics of COPD.[6] All participants identified as Non-Hispanic, Caucasian (Table 1). As the

data collection center location is in Lincoln, Nebraska, it is expected the demographics of

participants to be similar to that of the city. Based on the most recent demographic data,

Lincoln's population is 81% non-Hispanic or Latino White.[28] The rest of the population of Lincoln

is 10% Hispanic or Latino, 5% African-American, about 2% Asian, about 2% identifying as two or

more races, less than 2% American Indian or Alaskan native, and less than 1% as Native

Hawaiian or other Pacific Islander.[28] Overall, the demographics of the patient population were

comparable to the expected population, and there was little difference between the groups.

Anthropometrics

One exception in this study to the expected population of COPD patients was the BMI of

the participants. Being underweight is very common in COPD[10,11,15,23] while these participants on

average were overweight in group 1 with an average BMI of 25.7 ($\pm$8.0)kg/m^2 and obese in

group 2 with an average BMI of 44.2 (±9.2)kg/m^2. The difference in weight may have been related to the participants in group 1 losing more weight prior to admit (Table 2). Weight loss is also very common in COPD[10,11,15,23.].

In contrast, average BMI found by Schols, et al. (1998) was 24.0kg/m^2 in their retrospective study.[15] A similar study on hospitalized patients with COPD by Thorsdottir and Gunnarsdottir (2002) reported BMI of the patient's in the study (n=10) and while the average was not published, it was calculated by this author to average 23.8kg/m^2.[16] In correlation with this study, Reeves, et al. (2013) identified that hospitalized COPD patients with increasing BMI was a risk factor associated with less probability of meeting estimated energy and protein needs.   Average BMI in the Reeves' study was 31.6 (±12.0).[17] This study supports the same trend with group 2 having a higher average BMI and overall decreased in handgrip strength suggesting a decline in nutritional status.

Loss of muscle mass is very common in COPD. Even patients of a normal weight or overweight may have substantial depletion of muscle mass in COPD that is not readily apparent.[23]In another study conducted on hospitalized patients with COPD, mid-upper arm circumference was measured a test of lean body mass. Average mid-upper arm circumference was 21.18 ±2.31cm in males and 21.03±2.57cm in females (normal=27.4-35.5cm), showing significant decrease in all participants.[10] With an average BMI of 19.38±3.1kg/m^2 nearly all subjects in the lean body mass findings had low BMIs.[10]

Additional participant data

Additional data about this patient population was collected. Overall, little difference was noted between the two groups except for longer length of stay in group 2. Patients requiring NPPV tend to be sicker than those who do not require NPPV, so it is logical that group 2 has a

longer average length of stay in the hospital. Our data showed these patients had a longer length of stay by about 2 days (Table 3). Reported length of stay in other studies of acute hospitalized COPD patients is variable. One study gave a median length of stay as 24 days with a range of 2-48 days.[17] Another study gave a range of 5-17 days for the control group and 8-33 days for the treatment group; all patients were admitted to the hospital for COPD exacerbations.[14] The longer length of stay for group 2 participants is significant as this may lead to greater healthcare cost.

Use of steroids and physical therapy may affect handgrip strengths, but no difference was found between the 2 groups in these areas (Table 3). Days NPO can also affect nutritional status by limiting nutritional intake, but no difference in NPO days was found between the groups. In fact, patients in both groups have very few average days NPO with only an average of 0.2 days from both groups (Table 3). No participants in the study required escalation of care to needing mechanical ventilation and there was also no mortality noted during the study (table 3).

As a measure of COPD severity, GOLD status was attempted to be tracked, but was unavailable for every patient in the study. Conducting the lung function tests necessary to determine this GOLD score was likely a limiting factor. To the best of the author's knowledge, this is consistent with the literature, as no reference to a GOLD score for measuring COPD severity was noted in the literature on nutrition status in COPD. Studies did utilize spirometry and other pulmonary functions tests as a measure of COPD exacerbation severity without calculating a GOLD score.[10, 14, 15] One study did however utilize an APACHE (acute physiology and chronic health evaluation) score as a measure of disease severity.[17]

Biochemical and Physiological Data

Data on the mineral status and physiological lab values were recorded, as available, for each patient on the days handgrip strength was collected. Only 1 difference between the groups was found in average Iron status (hemoglobin) during the second set of measurements. Of note, the lower iron average was in group 1 (table 4). Some of the lower average may be due to the lower number of data points available, so 1 low value may affect the overall average more. Not every patient had a second iron level drawn after admit, as evidence by the lower number of data points for both groups (N=6 for group 1 and N=3 for group 2). The study by Gupta, et al. in 2010 had similar collection of physiological and biochemical data that showed most biochemical data to be within normal range but physiological parameters on average were elevated.[10] Average respiratory rate was given as 23.77±2.87 breathes/minute for males and 23.33±2.33 breathes/minute for females with a normal value range of 14-18 breathes/minute.[10] Average respiratory rate found in this study ranged from 19.0-21.5 breathes/minute, which is also elevated compared to the normal values range

Oral intake showed no difference between groups. This is important as oral intake is one of the six ASPEN malnutrition criteria[24] and can play a large part of nutritional status. However, this study only recorded meal intakes as documented in the medical record. This does not take into account what the meal was, or if the intakes meet the patient's estimated nutritional needs. Previous studies have shown that hospitalized COPD patients have elevated nutritional needs, and would need to increase nutritional intake to above 140% basal energy expenditure and protein intake of 1.2 g/kg to promote improved nutritional status. [16] Further research comparing the nutritional intake of hospitalized patient with COPD non-requiring NPPV to those with COPD requiring NPPV may be beneficial.

Handgrip Strength

Handgrip strength was the outcome of most interest in the study. Not every participant

was able to complete more than 1 handgrip strength. Only 1 participant in group 2 was able to

complete 3 handgrip strength measurements. While the limited sample size does not

adequately power the study to support a strong conclusion, the data does suggest that there is a

difference in change in handgrip strength between patients in the hospital with COPD requiring

NPPV, and those in the hospital with COPD but not requiring NPPV(p=0.016) (Table 5).   The

negative change in handgrip strength in patients with COPD who required BIPAP (group 2)

suggests that their nutrition status may have declined over the course of their hospital

admission especially when contrasted against the control group who overall saw an increase in

handgrip strength.

While there does appear to be a difference in change in handgrip strength of the two

groups, the difference is small. Group 1 only showed an average change of 1.59kg while group 2

showed an average change of -1.08kg. Both of these values are within the standard of error for

handgrip strength found by Baldwin, et al. in 2013 for critically ill patients.[26] The change is

handgrip strength of both groups is also lower than the minimal detectable difference of critical

ill patients from the same study.[26]

Both groups did have a relatively short length of stay, with group 1 averaging just over 3

days and group 2 only averaging just over 5 days (Table 3). It is possible that this time frame was

not long enough to demonstrate differences in nutritional status. The ASPEN malnutrition

criteria utilize a time frame of 5-7 days in the criteria for moderate or severe malnutrition in

acute illness.[24] With the exception of one participant in group 2, the rest of the participants did

have average handgrips that were considered to be within the normal range (Table 6). ASPEN's

criterion for severe malnutrition does include measurably reduced handgrip strengths, but that

is not criteria for moderate malnutrition.[18] While the patients in this study may not meet the

conditions for severe malnutrition, group 2 did show an average decrease in handgrip strength

(Table 5).

A study by Flood, et al. compared hand grip strength measurements as a means of

measuring nutritional status to Patient Generated Subjective Global Assessment as a measure of

nutritional assessment.[2] Compared to this study, handgrip strength was measured after 2 weeks

and was found to predict 42% of variability in change in nutrition status over time. [2] Flood, et al.

suggested that handgrip strengths could predict changes in nutritional status earlier than

Patient Generated Subjective Global Assessment and found handgrip strengths to independently

predict nutritional status as well as change in nutritional status,[2] supporting this study's

conclusion that the change in handgrip strength between the two groups demonstrates a

difference in change in nutritional status.

The results of this study suggest that care should be taken not to let these patients'

nutritional status, and thus handgrip strength, decrease further so they do not become severely

malnourished. All in all, there does appear to be a difference between the control group that did

not require NIPPV and the experimental group that did require NIPPV.

Feasibility

With the limited sample size of this study, one of the goals of the study was to

determine the feasibility of utilizing hand grip strength as an outcome of nutritional status in

COPD and patients on BIPAP. This is especially important considering the limited research in the

literature specifically on hospitalized patient's that require BIPAP. Overall, conducting the

handgrip strength measurements was relatively simple. All patients were able to complete the

handgrip dynamometry test once enrolled in the study. The data also appears able to capture

the information needed. Specifically this included if handgrip strength changed overtime and how measures of handgrip strength compared to normal values. The biggest obstacle encountered by this study was in the recruitment phase. A common barrier in research, this will likely still be a factor if additional studies of this type are conducted. However, there are strategies that may be helpful in minimizing this concern. Having a larger pool of participants to draw from, including utilizing a large hospital or having multiple centers may help to mitigate recruitment issues.

Chapter 7: Conclusion

Patient's admitted to the hospital with COPD requiring NPPV may need more aggressive nutrition care than those who do not require NPPV. Handgrip strength is an emerging metric for assessing nutrition status, and the patient's in group 2 that did require NPPV demonstrated a decline in handgrip strength compared to the control in group 1.This data supports the hypothesis that patients with COPD requiring non-invasive ventilation show evidence of a greater decline in handgrip strength as a proxy for nutrition status compared to those with COPD who do not require non-invasive ventilation. This study is limited in its scope, especially in regards to the limited sample size. More research is needed in this area to confirm these findings, as well as determine best practice guidelines for patient's admitted with COPD who require NPPV but not mechanical ventilation.

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