Comparison of Extubation Success between Prophylactic Helmet NIV and Facemask NIV in High Risk Postextubation Patients;A Randomized Controlled Trial

Mr. Napat Jirawat

A Thesis Submitted in Partial Fulfillment of the Requirements
for the Degree of Master of Science in Medicine
Department of Medicine
FACULTY OF MEDICINE
Chulalongkorn University
Academic Year 2022

การศึกษาแบบสุ่มเปรียบเทียบระหว่างการใช้อุปกรณ์แรงดันบวกครอบทั้งศีรษะและอุปกรณ์แรงดันบวกโดยผ่านทางหน้ากากชนิดครอบจมูกและปากต่ออัตราการถอดท่อช่วยหายใจสำเร็จในกลุ่มผู้ป่วยที่มีความเสี่ยงต่อการใส่ท่อช่วยหายใจซ้ำ

นายณภัทร จิรวัฒน์

วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญาวิทยาศาสตรมหาบัณฑิต
สาขาวิชาอายุรศาสตร์ ภาควิชาอายุรศาสตร์
คณะแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย
ปีการศึกษา 2565

Thesis Title	Comparison of Extubation Success between Prophylactic Helmet NIV and Facemask NIV in High Risk Postextubation Patients;A Randomized Controlled Trial
By	Mr. Napat Jirawat
Field of Study	Medicine
Thesis Advisor	Assistant Professor Napplika Kongpolprom, M.D.

Accepted by the FACULTY OF MEDICINE, Chulalongkorn University in Partial Fulfillment of the Requirement for the Master of Science

..... Dean of the FACULTY OF MEDICINE
(Associate Professor CHANCHAI SITTIPUNT, M.D.)

THESIS COMMITTEE

..... Chairman
(Associate Professor Natavudh Townamchai, M.D.)

..... Thesis Advisor
(Assistant Professor Napplika Kongpolprom, M.D.)

..... Examiner
(CHANAT KUMTORNRUT, M.D.)

..... External Examiner
(Assistant Professor Nuttapol Rittayamai, M.D.)

ณภัทร จิรวัฒน์ : การศึกษาแบบสุ่มเปรียบเทียบระหว่างการใช้อุปกรณ์แรงดันบวกครอบทั้งศีรษะและอุปกรณ์แรงดันบวกโดยผ่านทางหน้ากากชนิดครอบจมูกและปากต่ออัตราการถอดท่อช่วยหายใจสำเร็จในกลุ่มผู้ป่วยที่มีความเสี่ยงต่อการใส่ท่อช่วยหายใจซ้ำ. (Comparison of Extubation Success between Prophylactic Helmet NIV and Facemask NIV in High Risk Postextubation Patients;A Randomized Controlled Trial) อ.ที่ปรึกษาหลัก : ผศ. พญ.ณับผลิกา กองพลพรหม

ความเป็นมา: ภาวะการหายใจล้มเหลวซ้ำหลังจากถอดท่อช่วยหายใจเป็นภาวะแทรกซ้อนที่พบบ่อยในหอผู้ป่วยวิกฤตนำมาซึ่งอัตราการเสียชีวิตที่สูงโดยเฉพาะอย่างยิ่งในกลุ่มที่มีความเสี่ยงสูง การช่วยหายใจโดยไม่ต้องใส่ท่อช่วยหายใจมีบทบาทสำคัญในการป้องกันภาวะดังกล่าว โดยอุปกรณ์ที่ใช้เป็นหน้ากากชนิดครอบจมูกและปากเป็นหลัก ส่วนอุปกรณ์ที่เป็นแรงดันบวกแบบครอบทั้งศีรษะยังไม่มีข้อมูลชัดเจน

วัตถุประสงค์: เพื่อประเมินอัตราการถอดท่อช่วยหายใจสำเร็จภายใน 48ชั่วโมงแรกในกลุ่มผู้ป่วยที่มีความเสี่ยงสูงต่อการเกิดภาวะการหายใจล้มเหลวซ้ำหลังการถอดท่อช่วยหายใจ เปรียบเทียบระหว่างอุปกรณ์แรงดันบวกครอบทั้งศีรษะและอุปกรณ์แรงดันบวกผ่านทางหน้ากากชนิดครอบจมูกและปาก

รูปแบบการวิจัย: เป็นการศึกษาแบบสุ่มที่มีกลุ่มควบคุมโดยเปรียบเทียบ ผู้ป่วยทั้งหมด 114คนในกลุ่มผู้ป่วยที่มีความเสี่ยงสูงต่อการเกิดภาวะการหายใจล้มเหลวซ้ำหลังการถอดท่อช่วยหายใจ ช่วง เดือน มิถุนายน 2565 ถึง มิถุนายน 2566 โดยผู้ป่วยได้รับการแบ่งสุ่มเลือกใส่อุปกรณ์หลังจากถอดท่อช่วยหายใจทันทีระหว่างอุปกรณ์แรงดันบวกครอบทั้งศีรษะหรืออุปกรณ์แรงดันบวกผ่านทางหน้ากากชนิดครอบจมูกและปาก ระยะเวลา 24ชั่วโมงแรก โดยผลการศึกษาหลักคืออัตราการถอดท่อช่วยหายใจสำเร็จภายใน 48ชั่วโมงแรก ผลการศึกษารองประกอบด้วยการใส่ท่อช่วยหายใจซ้ำภายใน 7วัน, อัตราต่อการทนอุปกรณ์แรงดันบวกไม่ได้, ภาวะแทรกซ้อนหลังจากใช้อุปกรณ์แรงดันบวกทั้ง 2ชนิด, คะแนนความสบาย, พารามิเตอร์ของสัญญาณชีพและอัตราการแลกเปลี่ยนแก๊สระหว่างการศึกษา

ผลการศึกษา: จากผู้ป่วยการศึกษาทั้งหมด 114คน พบว่าไม่มีความแตกต่างกันระหว่างลักษณะพื้นฐานของ 2กลุ่ม ซึ่งได้แก่ โรคประจำตัว, คะแนนความรุนแรงของโรครวมไปถึงพารามิเตอร์ของสัญญาณชีพและการแลกเปลี่ยนแก๊สตั้งต้น อัตราการถอดท่อช่วยหายใจสำเร็จไม่แตกต่างกันระหว่าง 2กลุ่ม โดย 85.96% ในอุปกรณ์แรงดันบวกครอบทั้งศีรษะและ 87.72% ในอุปกรณ์แรงดันบวกผ่านทางหน้ากากชนิดครอบจมูกและปาก (p = 0.782) โดยในอุปกรณ์แรงดันบวกครอบทั้งศีรษะพบการใช้แรงดันและแรงดันบวกระยะสิ้นสุดหารหายใจออกที่มากกว่าอุปกรณ์แรงดันบวกผ่านทางหน้ากากชนิดครอบจมูกและปากอย่างมีนัยสำคัญทางสถิติ (12.28±2.23 และ 8.58±2.05, p <0.001, 6.14±1.42 และ 5.54±1.18, p = 0.016) โดยหากเปรียบเทียบภาวะลมรั่ว อุปกรณ์แรงดันบวกครอบทั้งศีรษะมีลมรั่วที่น้อยกว่าอุปกรณ์แรงดันบวกผ่านทางหน้ากากชนิดครอบจมูกและปาก (p <0.001) พบอัตราการทนต่ออุปกรณ์แรงดันบวกไม่ได้ในอุปกรณ์แรงดันบวกครอบทั้งศีรษะมากกว่าอุปกรณ์แรงดันบวกผ่านทางหน้ากากชนิดครอบจมูกและปาก (75.44% และ 21.05%, p <0.001) ส่วนอัตราการใส่ท่อช่วยหายใจซ้ำภายใน7วันรวมถึงผลของอัตราการแลกเปลี่ยนแก๊ส ไม่ได้มีความแตกต่างกันระหว่าง 2กลุ่ม ส่วนภาวะแทรกซ้อน พบว่าแผลกดทับและไม่การสัมพันธ์ของเครื่องช่วยหายใจพบน้อยในอุปกรณ์แรงดันบวกไม่ได้ในอุปกรณ์แรงดันบวกครอบทั้งศีรษะ แต่พบภาวะเสียงดังมากกว่า

สรุป: อัตราการถอดท่อช่วยหายใจสำเร็จในกลุ่มที่มีความเสี่ยงสูงต่อการเกิดภาวะการหายใจล้มเหลวซ้ำหลังการถอดท่อช่วยหายใจ ไม่ได้แตกต่างกันระหว่างอุปกรณ์แรงดันบวกครอบทั้งศีรษะและอุปกรณ์แรงดันบวกผ่านทางหน้ากากชนิดครอบจมูกและปาก

สาขาวิชา	อายุรศาสตร์	ลายมือชื่อนิสิต .....
ปีการศึกษา	2565	ลายมือชื่อ อ.ที่ปรึกษาหลัก .....

6470020030 : MAJOR MEDICINE
KEYWORD: helmet NIV facemask NIV high-risk extubation failure extubation success

Napat Jirawat : Comparison of Extubation Success between Prophylactic Helmet NIV and Facemask NIV in High Risk Postextubation Patients;A Randomized Controlled Trial. Advisor: Asst. Prof. Napplika Kongpolprom, M.D.

Background: Post-extubation respiratory failure is a common complication in planned extubated patients, which increases mortality, particularly in high-risk patients. Noninvasive ventilation (NIV) with a facemask effectively prevents post-extubation respiratory failure, but helmet NIV use immediately after extubation is still unproven.

Objective: To compare the success rates of extubation with prophylactic helmet NIV and facemask NIV in the first 48 hours in patients at high risk of developing post-extubation respiratory failure.

Methods: The study was a single-center randomized controlled trial. The data were analyzed for 114 patients at high risk of extubation failure between June 2022 and June 2023. Patients were randomly assigned to either helmet NIV or facemask NIV for 24 hours after extubation. The primary outcome was successful extubation within the first 48 hours. Secondary outcomes included the rate of reintubation within seven days, the rate of NIV intolerance, complications, comfort score, and hemodynamic and gas exchange parameters during the study period.

Results: During the study, 114 patients met the inclusion criteria and were randomly assigned to one of the two groups: facemask NIV or helmet NIV. There were no statistically significant differences in baseline characteristics, including underlying diseases, severity scores, and baseline hemodynamic and gas exchange parameters. The extubation success rate was similar in both groups: 85.96% in the helmet group and 87.72% in the facemask NIV ($p = 0.782$). In helmet NIV, pressure support and PEEP level were higher than in facemask NIV (12.28±2.23 versus 8.58±2.05, $p < 0.001$, 6.14±1.42 versus 5.54±1.18, $p = 0.016$). Compared with facemask NIV, helmet NIV had lower air leakage from baseline to 24 hours after extubation ($p < 0.001$). The helmet group had a significantly higher rate of NIV intolerance than the control group (75.44% versus 21.05%, $p < 0.001$). There were no intergroup differences in the reintubation rate within seven days and gas exchanges, including pH, PaO_2/FiO_2, and $PaCO_2$. Compared with the facemask NIV, the adverse events, namely pressure sore and asynchrony, were lower in the helmet group, but the noise was higher ($p < 0.001$).

Conclusion: The success rates of extubation in mechanically ventilated patients at high risk of extubation failure did not differ between helmet NIV and facemask NIV.

Field of Study:	Medicine	Student's Signature .....
Academic Year:	2022	Advisor's Signature .....

ACKNOWLEDGEMENTS

Thank you to Assistant Professor Dr. Napplika Kongpolprom, who served as the main advisor for this research project, for her kindness and invaluable advice throughout the research process. Thanks also to Associate Professor Dr. Natavudh Townamchai and Dr. Chanat Kumtornrut, for chairman and internal committee member, and Assistant Professor Dr. Nuttapol Rittayamai, the external committee member, for their time and helpful suggestions that contributed to the successful completion of this research.

Finally, I would like to express my gratitude to the physician and nurses at the hospital who provided assistance during the research, as well as all the patients who participated in the study. Thanks to my family and friends for their support and encouragement throughout the research process.

Napat Jirawat

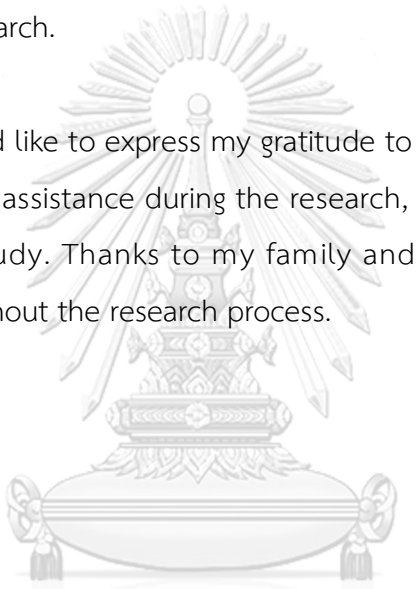

TABLE OF CONTENTS

LIST OF TABLES

Page

LIST OF FIGURES

Page

Chapter One
Introduction

1. Background and rationale

Ten to twenty percent of ICU patients experience post-extubation respiratory failure, requiring reintubation. (1-4) This commonly occurs in the first 48 hours after extubation. Because post-extubation respiratory failure relates to a high mortality rate, there is a strategy for preventing this condition and identifying patients who are at risk as soon as possible. (1, 5) Noninvasive ventilation (NIV) plays an essential role in many situations, including prior to invasive mechanical ventilation in acute respiratory failure patients, weaning facilitation, and reintubation prophylaxis in patients at risk of extubation failure. (6) Recent international guidelines recommend using NIV after extubation in high-risk patients to prevent post-extubation respiratory failure. (7) This trend has been growing up to 10% per year over the last few decades. (8) Even though randomized controlled trials comparing NIV and standard oxygen therapy in patients with high-risk extubation failure have been conducted, few studies have demonstrated efficacy in lowering the reintubation rate. (9-11) However, there is increasing evidence that NIV could help prevent post-extubation respiratory failure. A meta-analysis and systematic review found that reintubation in high-risk patients was reduced. (12)

Patients over the age of 65, those with preexisting cardiac or lung disease, those with an APACHE II score greater than 12, those with a BMI greater than 30 kg/m2, those who have had difficult or prolonged weaning for more than seven days, and those with a Charlson Comorbidity Index greater than two on the day of extubation are considered to be at high risk for post-extubation respiratory failure. (3, 9, 13, 14) NIV with positive end-expiratory pressure (PEEP) can indirectly assist ventilation by

acting as an external pressure for stenting the upper airway and increasing alveolar recruitment. Furthermore, NIV helps in optimizing gas exchange and reducing breathing effort. (6, 15) One of the fundamental processes in NIV use is not only providing the appropriate settings but also selecting the appropriate interface. Most prophylactic NIV interfaces are facemasks, and no studies have been conducted to compare other types of interfaces to determine whether they reduce the reintubation rate. In patients using facemask NIV, which is limited in its efficacy due to air leakage, ineffective demand pressure, and asynchrony may contribute to respiratory failure. (16)

During the COVID-19 pandemic, the helmet is one of the most commonly used NIV interfaces, which plays an important role in preventing hypoxemic respiratory failure. (17) The transparent plastic helmets have a hood with a plastic ring, a padded collar that fastens around the wearer's neck, and two straps that fasten beneath the armpits. (18, 19) According to a meta-analysis, helmet NIV improves oxygenation, decreases carbon dioxide levels, and reduces reintubation rates and in-hospital mortality. (20, 21) However, there have been no studies on the efficacy of helmet NIV in patients at high risk of post-extubation respiratory failure. Only one retrospective research found no statistically significant difference in preventing post-extubation respiratory failure in high-risk patients. (22) Our study aims to compare the success rates of extubation using prophylactic helmet NIV versus facemask NIV in the first 48 hours in patients at high risk of developing post-extubation respiratory failure.

2. Research questions

Primary research question

- Is there a statistically significant difference in the extubation success rate among high-risk postextubation patients during helmet NIV compared to facemask NIV?

Secondary research question

- Is there a statistically significant difference in reintubation rate over 7 days among high-risk postextubation patients during helmet NIV compared to facemask NIV?
- Is there a statistically significant difference in complications and comfort score among high-risk postextubation patients during helmet NIV compared to facemask NIV?
- Is there a statistically significant difference in respiratory rate (RR), mean arterial pressure (MAP), heart rate (HR), PF ratio (PaO_2/FiO_2), SF ratio (SaO_2/FiO_2), and work of breathing score at 30 minutes, 2 hours, 24 hours, and 48 hours after extubation, including arterial blood gas (ABG) at 2 hours, 24 hours, and 48 hours after extubation, among high-risk postextubation patients during helmet NIV compared to facemask NIV?

3. Objectives

Primary objectives

- To compare extubation success rate among high-risk postextubation patients during helmet NIV compared to facemask NIV.

Secondary objectives

- To compare reintubation rate over 7 days, etiologies of reintubation, and time to reintubation among high-risk postextubation patients during helmet NIV compared to facemask NIV.
- To compare complications and comfort scores among high-risk postextubation patients during helmet NIV compared to facemask NIV.
- To compare respiratory rate (RR), mean arterial pressure (MAP), heart rate (HR), PF ratio (PaO_2/FiO_2), SF ratio (SaO_2/FiO_2), and work of breathing score at 30 minutes, 2 hours, 24 hours, and 48 hours after extubation, including arterial blood gas (ABG) at 2 hours, 24 hours, and 48 hours after extubation, among high-risk postextubation patients during helmet NIV compared to facemask NIV.

4. Hypothesis

Efficacy on extubation success rate among high-risk postextubation patients within 48 hours using helmet NIV over facemask NIV at least 21%

5. Conceptual framework

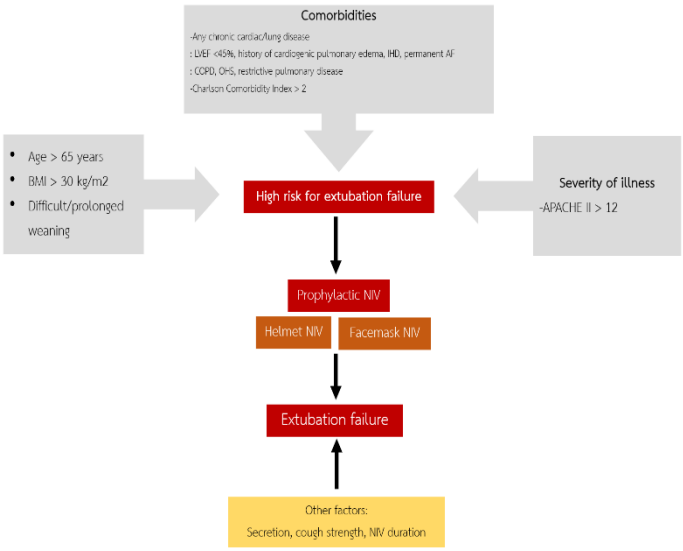

Figure 1: conceptual framework factors associated with extubation success.

6. Assumption

Patients with respiratory failure receive mechanical ventilation via an endotracheal tube (ETT) and require at least 48 hours of intubation, with the possibility of reintubation within 48 hours.

7. Operational definitions

High risk of extubation failure (3, 9, 13, 14)

Patients with high risk of extubation failure were defined as having one of the following conditions after extubation and being at high risk for reintubation within 48 hours: Patients over the age of 65, those with preexisting cardiac disease (echocardiogram-confirmed LVEF ≤45% or history of cardiogenic pulmonary edema or suspected ischemic heart disease or diagnosed with atrial fibrillation) or lung disease (chronic obstructive pulmonary disease or obesity hypoventilation syndrome or

restrictive lung disease), those with an APACHE II score of more than 12, those with a BMI of more than 30 kg/m^2, those with difficult or prolonged breathing for more than 7 days, and those with a Charlson Comorbidity Index greater than 2 on the day of extubation.

Spontaneous breathing trial, SBT

The ventilator is set to PSV mode to determine whether patients can breathe on their own and are ready for extubation by ventilator setting: PSV pressure support 5 cmH_2O and PEPP 5 cmH_2O with adjustable FiO_2 to keep SpO_2 ≥ 90% at least 30 minutes.

Prophylaxis helmet NIV

After extubation, patients in the high-risk group were given prophylactic noninvasive positive pressure ventilation (helmet NIV) for the first 24 hours to prevent post-extubation respiratory failure.

Prophylaxis facemask NIV

After extubation, patients in the high-risk group were given prophylactic noninvasive positive pressure ventilation (facemask NIV) for the first 24 hours to prevent post-extubation respiratory failure.

NIV intolerance

Due to discomfort, the patient cannot tolerate either a helmet or a facemask NIV as the chosen group.

NIV failure

Respiratory failure after applying either a helmet or facemask NIV, which is compatible with post-extubation respiratory failure and needs invasive ventilation.

Extubation success

Within the first 48 hours after extubation, the patient can be free of invasive ventilation and breathe on their own without meeting the criteria for extubation failure.

Postextubation respiratory failure

Respiratory failure after extubation within the first 48 hours that needs immediate intubation and invasive mechanical ventilation and has at least 2 of the following criteria (3, 23)

- Respiratory rate more than 35 breath/min; a duration of at least 2 hours
- Heart rate greater than 140 beats/min or change from baseline, either increasing or decreasing 20%
- Respiratory muscle failure suspected as a result of increased work of breathing
- Respiratory acidosis: pH < 7.30 and pCO_2 > 45 mmHg or increasing from baseline 20%
- FiO_2 > 0.5 is required for oxygen saturation of 90% or PaO_2 of 60 mmHg.

And other criteria for intubation and invasive mechanical ventilation besides post-extubation respiratory failure. (23)

Respiratory failure: with at least two criteria

- Respiratory rate greater than 35 breaths/min or suspected respiratory muscle failure with increased respiratory workload.
- Respiratory acidosis with a pH < 7.30 and pCO_2 > 45 mmHg, or an increase of 20%.
- To achieve greater than 92% oxygen saturation, or PaO_2/FiO_2 greater than 100, a fraction of inspired oxygen (FiO_2) greater than 0.8 is required.

Hemodynamic failure: defined as systolic blood pressure of 90 mmHg or mean arterial pressure of 65 mmHg necessitating vasopressor therapy.

Neurological failure: defined as a Glasgow Coma Scale (GCS) score of less than 13 or unusually high levels of restlessness.

Cardiac or respiratory arrest.

8. Research design

Randomized controlled trial

9. Ethical considerations

Respect for person

All patients and relatives or legal parents of patients participating in the study will have information about the conduct of the research clearly and completely explained by the researcher and in the document explaining the details of the

research project for the patient to thoroughly consider. If you have any questions, the researcher is willing to answer them until a good understanding is reached. Patients can freely decide to agree to participate in the study, so give them time to make independent decisions.

In the event that the patient is unable to make his own decisions, research authors will provide information and explanations. including the documents detailing the research project mentioned above to the patient's relatives or legal representatives.

Beneficence/Non-maleficence

Patients participating in the study must meet the weaning criteria detailed in the inclusion criteria for patient evaluation and be truly prepared to wean themselves from the breathing apparatus. When participating in the study, patients receive standard care, including closely monitoring various adverse events. This is consistent with the standard guidelines after weaning from ventilators and tracheal intubation at Chulalongkorn Hospital (weaning protocol). There is a plan to accommodate patients who are unable to use the equipment as required; for example, in cases where the patient is unable to receive ventilation without intubation (NIV), the patient will be considered for nasal oxygen with a high-flow gas (high-flow nasal oxygen cannula, HFNC) instead, which has comparable efficiency. This is to protect the patient's benefit and safety.

Among the adverse events were extubation failure, for which the investigators established clear criteria for diagnosing this condition in order to be able to provide timely care in which the patient will be intubated and use mechanical ventilation (invasive ventilation), as well as finding the cause of this respiratory failure to correct it. and monitored closely. Patients may not benefit from participating directly in this research. But the results of the study will benefit patients at high risk of reintubation after extubation in the future.

Justice

This research project has clear inclusion and exclusion criteria. All eligible patients will be invited to participate in the trial. and when participating in the research project, there is an equal distribution of risks and benefits. by randomly

entering the study group. All patients, regardless of study group, were equally cared for according to standard guidelines after weaning from ventilators and tracheal extubation at King Chulalongkorn Memorial Hospital (Weaning Protocol).

10. Limitations

Due to the limited data collection period and the relatively large number of patients in each group, the efficacy of the prevention of respiratory failure following endotracheal intubation was not studied in patients at risk for reintubation within 48 hours using a helmet NIV compared to a facemask NIV, which may result in no statistically significant difference. However, this project explores the possibility of comparing the efficacy of a helmet NIV and facemask NIV in patients with a high risk of re-intubation within 48 hours. Therefore, this research is considered useful for further research in the future.

In conjunction with the situation of the 2019 coronavirus outbreak, it may cause normal patients to come to the hospital less than usual. which may not be able to collect the required number of patient groups.

With the care of the patients in this research, it depends mainly on the discretion of the treating physician. Therefore, in terms of protocol compliance, there may be changes in treatment based on established research records by the treating physician.

11. Expected benefits and applications

For the proper and accurate selection of a positive pressure device between a helmet NIV and facemask NIV and to prevent respiratory failure after extubation in patients at risk of re-intubation within 48 hours. Including complications from both groups of devices, the patients in the study themselves may not benefit directly. but from this study, we will be able to use the research results. It can be practical for patients who are at risk of re-intubation in the future.

12. Obstacles and strategy to solve the problems

This study involved patients with respiratory failure receiving endotracheal ventilation, which may not be able to find the required number of patients in time. Together with the limited time, there are still many waves of outbreaks in the current situation of the 2019 coronavirus outbreak. The cause may not receive all of the patients as specified.

During the first 24 hours after removal of the endotracheal tube, some patients may not be able to tolerate prophylactic NIV, possibly due to unfamiliarity with the device. or discomfort from the tightening of the mask on the face. However, the researcher has found a solution by providing equipment such as a respirator mask. suitable for each patient in order to provide treatment that meets the weaning protocol in Chulalongkorn Hospital as much as possible. But if there is still a problem, the high flow nasal cannula can be used instead, which is as effective as the NIV in the following patients: Set the flow rate 50 LPM, Temp 34^{0}c, FiO_2 0.21-0.4 to achieve SpO_2 of 92%. (24)

Chapter Two

Literature review

Several studies have shown that prophylactic noninvasive positive pressure ventilation during the first 24 hours after extubation can prevent respiratory failure after extubation in high-risk patients. But the benefit for low-risk patients may not be clear. (25) Comparing 6 randomized controlled studies, the result was discordant. 2 studies found no efficacy of prophylactic NIPPV to prevent post-extubation respiratory failure in patients at risk. (25, 26) Su et al.(25) conducted the study in critical care unit of 3 Taiwanese hospitals from October 2002 to September 2004 and discovered no statistically significant in reduction of reintubation in high risk patients (P value = 0.37) as well as no reduction in mortality (P value = 0.64) which is consistent with study from Khilnani et al.(26) which found no difference in reintubation rate between prophylactic NIPPV and standard oxygen therapy in 40 planned extubation of chronic obstructive pulmonary disease (COPD) patients.(P value = 0.44) In contrast, there is potential benefit from prophylactic NIV to prevent post-extubation respiratory failure, as shown in several studies. (3, 9-11) Nava et al.(9) conducted a multicenter randomized controlled trial comparing prophylactic NIV and standard oxygen therapy in 97 patients at risk and discovered that the prophylactic NIV group had a lower reintubation rate than the standard oxygen therapy group (P value = 0.027), resulting in a lower mortality rate. Ornico et al.(10) conducted the study in 40 COPD patients, which found a 5% reintubation rate in the prophylactic NIPPV group and a 39% reintubation rate in the standard oxygen therapy group. (P value = 0.016) Ferror et al.(11) conducted a randomized control trial in 162 patients at risk, comparing the reintubation rate, which found 15% in prophylactic NIV and 48% in standard oxygen therapy, which is statistically significant. However, there is no difference in reintubation rate or length of ICU stay at 7 days. The duration of

prophylactic NIV was within the first 24 hours after extubation following standard oxygen therapy in several studies. (3, 10, 11, 23)

Official ERS/ATS Clinical Practice Guidelines: Noninvasive Ventilation for Acute Respiratory Failure stated that prophylactic NIV can prevent post-extubation respiratory failure in high-risk patients, which results in a decrease in reintubation and mortality rates, particularly in well-planned patients, but there is unclear efficacy in unplanned or self-extubated patients, which needs further study. (7) However, the majority of the interface used in prophylactic NIV is a facemask, and no studies have been conducted to compare the other type of interface to see if it reduces the rate of reintubation. During the COVID-19 pandemics, helmet NIV played an important role in the prevention of hypoxemic respiratory failure. (17) Rezoagli et al.(27) conducted a retrospective study between facemask NIV and helmet NIV and found that helmet NIV can decrease the rate of intubation. (P value = 0.016) as well as several studies support the potential benefit of helmet NIV in the prevention of respiratory failure, which is consistent with a meta-analysis from Italy, which found that there are several benefits from helmet NIV, including increasing PaO_2/FiO_2 ratio (weighted mean difference 73.40, 95% confidence interval (95% CI) 43.92-102.87; $p < 0.00001$), reducing $PaCO_2$ (weighted mean difference -1.92, 95% CI -3.21 to -0.63; $p = 0.003$), decreasing intubation rate (relative risk 0.21, 95% CI 0.11-0.40; $p < 0.00001$), and decreasing in-hospital mortality rate. (Relative risk 0.22, 95% CI 0.09-0.50; $p = 0.0004$) (20)

The advantages of helmet NIV over facemask NIV were that patients could eat, converse, better clear their secretions, and tolerate it better than facemask NIV due to the helmet NIV's characteristics of covering the entire head. The other potential benefit over facemask NIV is less leakage. However, there are some potential disadvantages, one of which is CO_2 rebreathing, which we can eradicate by increasing inspiratory gas flow and inspiratory pressure(19, 28); moreover, helmet NIV can aggravate claustrophobia. The potential benefit of helmet NIV and facemask NIV was concluded as shown in table 1.

Although more research is needed to confirm the efficacy of helmet NIV versus facemask NIV, the research on helmet NIV in the prevention of post-extubation respiratory failure is limited due to a lack of study. Park et al.(22) conducted a retrospective study in a Korean hospital between March 2017 and September 2019 and found no statistical significance in the prevention of post-extubation respiratory failure in high-risk patients, so the goal of our study is to evaluate the efficacy of helmet NIV overface mask NIV in extubation success in high-risk extubation failure, and the study is a prospective randomized controlled trial.

Table 1: comparing the potential benefit of helmet NIV and facemask NIV in appropriate condition.

	Facemask NIV	Helmet NIV
Acute setting	Can be used	Can be used
High level of noise	No	Yes
Abnormal facial anatomy	Can't be used	Can be used
Speak and cough	Can be used, but there is still some leakage	Can be used
Cooperating required	Need cooperation	Need cooperation
Air leak	High amount of air leakage	No to small amount of air leakage

Chapter Three

Methods

1. Research design

Randomized controlled trial, unblinded

2. Research methodology

Target population

Every patient with respiratory failure on invasive mechanical ventilation has a high risk of extubation failure within the first 48 hours after extubation.

Study population

Every patient with respiratory failure on invasive mechanical ventilation for at least 48 hours has a high risk of extubation failure within the first 48 hours after extubation.

Inclusion criteria

- Patient are over 18 years of age, have consented to participate in the trial, and must have complete decision-making ability.
- Patients with invasive mechanical ventilation for at least 48 hours in the medicine intensive care unit and medicine general ward, King Chulalongkorn Memorial Hospital.
- Patients with a full assessment of the spontaneous breathing trial who pass the spontaneous breathing trial.

Patients with high risk of reintubation within the first 48 hours after extubation.(3, 9, 13, 14)

- Patients with low or no risk of aspiration.

Exclusion criteria

- Patients with preexisting NIV use
- Patients with contraindications to either helmet NIV or facemask NIV. (29) (cardiac or respiratory arrest, hemodynamic instability; systolic blood pressure < 90 or mean arterial pressure < 65 with vasopressor use, multiple organ failure, severe acidosis; pH < 7.2, neurological failure; Glasgow Coma Score < 8, upper airway obstruction, inability to clear secretion, recent facial surgery or facial trauma, facial deformity, inability to fit a mask, claustrophobia, and intracranial hypertension)
- Patients who are diagnosed with chronic neuromuscular disease.
- Patients with a recent traumatic brain injury
- Patients with accidental or self-extubation.
- Patients with order of do-not-resuscitation after extubation.

3. Sample size

Calculation based on Dichotomous Endpoint, Two Independent Sample Study with 1:1 ratio with the probability of a Type I error (α) = 0.05, The probability of a Type II error (β) = 0.2, power = 0.8

Estimated sample size for two proportions with independent sample by Park et al.(22) which found that facemask NIV has a success rate of extubation success within the first 48 hours of 69%.

$$n = \frac{\{Z_{1-\frac{\alpha}{2}}\sqrt{\bar{p}(1-\bar{p})\left(1-\frac{1}{r}\right)} + Z_{1-\beta}\sqrt{p_1(1-p_1)+\frac{p_2(1-p_2)}{r}}\}^2}{(p_1-p_2)^2}$$

$$\bar{p} = \frac{p_1+p_2}{2}, r = \frac{n_2}{n_1}$$

Beta (β) = 0.2, Alpha (α) = 0.05

formula: Bernard, R. (2000). Fundamentals of Biostatistics (5th ed.) Duxbery: Thomson learning, 384-385.

Fleiss, J. L., Levin, B., &Paik, M.C. (2003) Statistical Methods for Rates and Proportions, (3rd ed.). John Wiley&Sons, 76.

p1: extubation success in high risk extubation patients within the first 48 hours in facemask NIV group (0.69)

P2: extubation success in high risk extubation patients within the first 48 hours in helmet NIV group (0.90) based on the hypothesis Each group has a sample size of 57 patients, which accounts for 80% of the power of study

The total sample size is 114 patients.

4. Research process

- When it was told to the investigator that a patient with respiratory failure had been tested to see if he or she could stop breathing on their own, the ward physician did a spontaneous breathing trial with pressure support ventilation, which the ward physician himself evaluated.

- With the method of evaluating the patient must have the cause of respiratory failure corrected. and symptoms improved, with stable vital signs, of which the details are
    - Systolic blood pressure is between 90 and 160 mmHg without the use of a vasopressor or when a low-dose vasopressor, as the following details indicate. Norepinephrine in a dose not exceeding 0.1 mcg/kg/min; adrenaline in a dose not exceeding 0.1 mcg/kg/min; dopamine in a dose not exceeding 5 mcg/kg/min.
    - The heart rate ranges from 50 to 140 beats per minutes.

- Level of consciousness (Glasgow Coma Scale Score, GCS) from 13 onwards.
- Breathing at a steady level, of which the details are
- Oxygen saturation greater than 90% at a fraction of inspired oxygen (FiO_2) less than equal to 0.4 or arterial oxygen concentration relative to oxygen concentration in mixed gases (PaO_2/FiO_2), more than 150
- The respiratory rate is less than 35 breaths per minutes.
- Noncopious secretion, i.e., less than 2 lines/time of suction secretion and frequency of suction secretion at least 2 hours apart.
- The patient is able to have a strong cough by himself. This is estimated using a cough peak expiratory flow greater than 60 l/min. (30)

- After that, the patient will be assessed to see if he or she has been able to stop ventilation. Using spontaneous breathing trials with pressure support ventilation, the pressure support 5 cmH_2O, and the positive pressure at the end of expiration (PEEP) was determined to be 5 cmH_2O, adjusted by FiO_2 to keep the patient's blood oxygen concentration (SpO_2) ≥ 90% for at least 30 minutes.
- Then the researcher will conduct an initial assessment and consider the criteria for inclusion and exclusion from the research project by introducing yourself and asking for permission from the patient and relatives. before clarifying the research project's objectives and obtaining consent for further participation in the research project.
- History taking and physical examination to collect basic information from clinical data and medical records, such as age, comorbidities, the main causes of respiratory failure, and so on.
- Population sampling for treatment using computerized randomization using the block of four technique. Each experimental group was assigned a ratio of 1:1, including the group receiving the facemask NIV and the helmet NIV.
- After extubation and the application of a positive pressure device according to the preliminary randomization, the NIV mode of ventilation was set by the research team. PEEP was initially set at 5 cmH_2O in both groups, then increased by 2-3 cmH_2O to achieve oxygen saturation (SpO_2) greater than 90% with FiO_2 less than 0.6. Initial pressure support was set at least 4 cmH_2O above PEEP and then increased by 2-3 cmH_2O increments to make the respiratory rate (RR) less than 30 breaths/min in both

the helmet and facemask NIV groups. Avoid food and water for at least 24 hours to prevent aspiration.

- Groups receiving a positive pressure device via facemask NIV or helmet NIV were required to take breaks every 4 hours to do the nursing care, with a break of no more than 30 to 60 minutes per session. And during the break, patients in the group received an oxygen cannula ranging from 1–5 liters per minute to achieve oxygen saturation (SpO_2) greater than 90%, and the rest period was recorded. The duration of wearing the device is at least 18 hours.
- In the NIV intolerance group, the patient was replaced by a high-flow nasal oxygen cannula with an open flow of 50 LPM. FiO_2 is adjusted by the ward physician to make the oxygen saturation (SpO_2) greater than 90%.
- Assessment of respiratory failure after extubation will be done by a doctor and a nurse in the ward by looking at vital signs with indications for tracheal intubation as follows:
    - Respiratory failure with at least two criteria: respiratory rate greater than 35 breaths/min or suspected respiratory muscle failure with increased respiratory workload.
    - Respiratory acidosis with a pH < 7.30 and pCO_2 > 45 mmHg, or an increase of 20%.
    - To achieve greater than 92% oxygen saturation, or PaO_2/FiO_2 greater than 100, a fraction of inspired oxygen (FiO_2) greater than 0.8 is required.
    - Hemodynamic failure was defined as systolic blood pressure of 90 mmHg or mean arterial pressure of 65 mmHg necessitating vasopressor therapy.
    - Neurological failure is defined as a Glasgow Coma Scale (GCS) score of less than 13 or unusually high levels of restlessness.
    - Cardiac or respiratory arrest.
- After the first 24 hours, patients in both treatment groups were switched from helmet NIV and facemask NIV to standard oxygen therapy, in which oxygen cannula from 1 to 5 liters per minute were administered to provide fingertip oxygen concentrations (SpO_2) greater than 90% by wearing a helmet NIV or facemask NIV for no more than 24 hours. (3, 10, 11, 23)

- Assessment of positive pressure device complications and comfort scores between helmet NIV and facemask NIV.
- We assessed the rates of successful extubation in a cohort of patients at risk of re-intubation within 48 hours.
- The researcher is the one who monitors the treatment results observed for 7 days after removal of the endotracheal tube. and record it in the data record according to the specified information.

5. Approach to participants and informed consent process

The investigators explained the information to the patient. or relatives or legal parents including answering questions and distributing information sheets and informed consent forms to patients or their relatives or legal parents to consider before deciding to sign consent to participate in the research project.

- With the following methods of obtaining consent from patients and relatives:
    - The patient will be assessed according to his or her level of consciousness and responding to inquiries for understanding by a team of medical professionals.
    - The care team will assess whether the patient is able to make the decision and sign the informed consent form himself or not.
    - If the care team assesses that the patient can understand the information received and make informed consent decisions on their own, the patient makes the decision and signs the informed consent form himself.
    - If the care team assesses that the patient is unable to understand the information received and is unable to make informed consent decisions on their own, the patient's relatives/legal representatives (next of kin) will receive the information. and to make a decision and sign an informed consent form instead. and can make informed consent decisions on their own. The investigator will personally obtain consent from the patient for the study.
    - Procedures for obtaining consent and providing such information It is performed at the general ward and the intensive care unit at Chulalongkorn Hospital. It is operated by the investigating physician only. The patient's ability

to understand will only be assessed by the attending physician. without regard to obtaining consent.

- All patients and relatives or legal parents of patients participating in the study. Patients will be provided with clear information about the trial, including the purpose of the trial, the potential benefits and risks to the patient, and the trial procedure. From the explanation by the researcher and from the document explaining the details of the research project and if you have any questions, you can ask the researcher freely. The researcher will answer such questions until the patient and their relatives or legal parents have a good understanding. Before signing the consent form, each person who decided to take part in the research project did so on their own.
- The researcher began conducting the research after receiving consent, and collect data from patients' and medical records. Patients seeking informed consent from their legal representatives must obtain their own informed consent again from the investigator when it is possible.

6. Data collection

- The investigator recorded the patient's baseline information in the research record form.
- The investigator recorded the results of the study.
- The data collector is the person who conducts the research. and the data recorder is the investigator.

Observation and measurement

Collect baseline data from clinical data as well as information from medical records.by using data recording forms, including

- Sex
- Age
- Body mass index (BMI)
- Comorbidities
- Smoking history

- Etiologies of respiratory failure prior to study
- Duration of mechanical ventilation prior to study
- Severity score of comorbidities and etiologies of this admission prior to study including Acute Physiology and Chronic Health Evaluation II (APACHE II) Score, Charlson Comorbidity Index, and SOFA score
- Intake/ output (I/O) prior to study
- Arterial blood gas prior to study
- Respiratory rate (RR), mean arterial pressure (MAP), heart rate (HR), PF ratio (PaO_2/FiO_2), SF ratio (SaO_2/FiO_2), work of breathing score, weaning time, rapid shallow breathing index (RSBI), cough peak flow (CPF), and negative inspiratory force (NIF) before randomization

- After randomly allocating the patients according to two types of positive pressure devices and then recording the observational results:

- Respiratory rate (RR), mean arterial pressure (MAP), heart rate (HR), PF ratio (PaO_2/FiO_2), SF ratio (SaO_2/FiO_2), work of breathing score at 30 minutes, 2 hours, 24 hours, and 48 hours after extubation.
- Arterial blood gas at 2 hours, 24 hours, and 48 hours after extubation.
- Pressure support, positive end expiratory pressure (PEEP), FiO_2 after randomization, leakage percentage from each positive pressure devices, and event of NIV intolerance. If such a situation occurs, the patients will receive a high flow nasal cannula oxygen instead.
- Duration of prophylaxis helmet NIV and facemask NIV.
- Rate of extubation success in high risk postextubation patients within 48 hours
- Complications of both helmet NIV and facemask NIV including pressure sores, secretion obstruction, and nasal irritation as well as comfort score after apply positive pressure device.
- Reintubation rate within 7 days, etiologies of reintubation, and time to reintubation.

7. Statistical analysis

- Descriptive statistical analysis which can be divided by type of information as follows:

Quantitative data

As with age and BMI, are presented as medians and interquartile ranges. In the case of non-normal data distribution, display the result in the form of mean and standard deviation (mean +/- SD); in the case of normal data distribution (normal distribution), display the result in the form of mean and standard deviation (mean +/- SD).

Qualitative data

As with gender, comorbidities are displayed as percentages.

- Inferential statistical analysis, including univariate analysis and multivariate analysis, is divided by type of data as follows:

Quantitative data

Analyzed using the Student's T-test for quantitative data with a normal distribution or the Wilcoxon-Mann-Whitney U-test. Test for quantitative data with a non-normal distribution to show differences between study groups. and comparing the study results between groups using a percentage model; a risk difference was defined as a 95% confidence interval where a one-sided p-value less than or equal to 0.05 was considered statistically significant.

Qualitative data

Analyzed by Fisher's exact test to show differences between study groups. and analyzed together with multivariate analysis and logistic regression to analyze the relationship between various factors and the success of weaning from ventilators.

- By statistical analysis, as mentioned above, an intention-to-treat analysis model and a subgroup analysis model were also planned.
- Use the Stata 16 statistics program and the R program.

CHAPTER FOUR

RESULTS

1. Study populations

From June 2022 to June 2023, we enrolled ventilated patients at King Chulalongkorn Memorial Hospital. Initially, 246 patients were considered, but 132 patients were excluded as they did not meet the inclusion criteria. A sample size of 114 patients (57 patients per group) was selected to demonstrate the difference in extubation success rates between the two groups as shown in figure 2

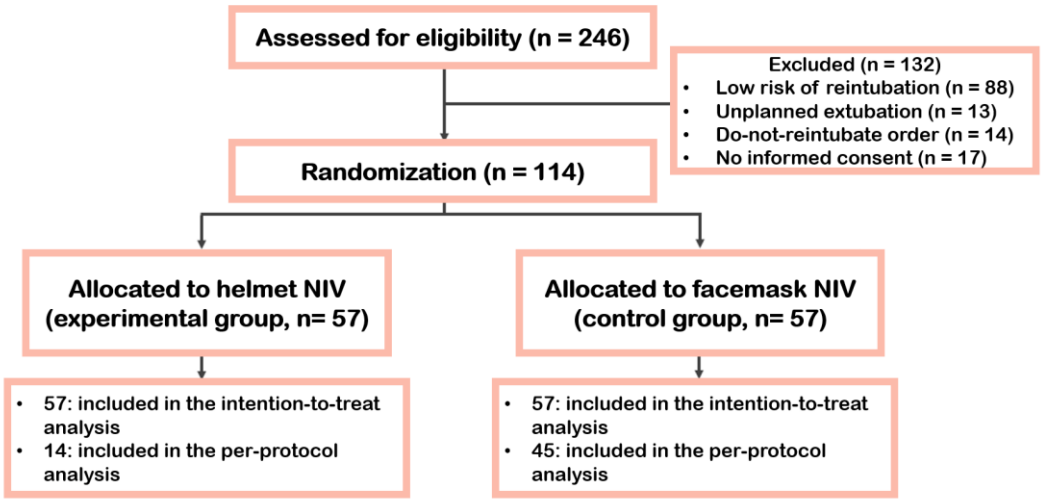

Figure 2: Flow chart of participants in the study

2. Baseline characteristics of study populations

Table 2 showed the demographic data of patients in both groups. There were similarities in age, BMI, underlying diseases and baseline comorbidities, severity scores of current diseases, including APACHE II and SOFA scores, and baseline hemodynamics and gas exchange parameters. The etiologies of respiratory failure and duration of mechanical ventilation were also comparable. The facemask NIV group had more positive net fluid balance than the helmet NIV group (p = 0.012).

The pressure support level (PS), PEEP, inspired (VTi), and expired (VTe) tidal volumes in helmet NIV were greater than facemask NIV (PS 12.28±2.23 versus 8.58±2.05, p <0.001, PEEP 6.14±1.42 versus 5.54±1.18, p = 0.016, VTi 1156.39±172.45 versus 507.19±95.46, p <0.001 and VTe 1040.23±162.42 versus 390.79±78.28, p <0.001). There was significantly less air leakage in the helmet NIV group (10 [8, 12] versus 21 [16, 28], p <0.001). However, NIV intolerance was significantly higher in the helmet NIV group, resulting in a lower median duration of helmet NIV than facemask NIV. FiO_2 settings were comparable across groups.

Table 2: patients' baseline characteristic

Characteristics	**Facemask NIV** (n=57)	**Helmet NIV** (n=57)	**p-value**
Gender Male, n (%)	23(40.35)	26(45.61)	0.570
Age (years), mean ±SD	63.35±18.43	63.49±16.80	0.966
BMI (Kg/m^2), mean ±SD	24.81±6.63	24.27±5.62	0.641
Underlying diseases, n (%)			
Hypertension	40(70.18)	39(68.42)	0.839
Diabetes mellitus	33(57.89)	35(61.4)	0.703
Congestive heart failure	17(29.82)	20(35.09)	0.548
Renal impairment	30(52.63)	33(57.89)	0.572
Conservative treatment	14(24.56)	17(29.82)	0.528
Renal replacement therapy	15(26.32)	17(29.82)	0.677

Cirrhosis	6(10.53)	8(14.04)	0.568
Airway diseases			
COPD	8(14.04)	7(12.28)	0.782
Asthma	0(0)	1(1.75)	>0.05
Small airway disease	0(0)	0(0)	-
Bronchiectasis	2(3.51)	2(3.51)	>0.05
Tracheobronchomalacia	0(0)	1(1.75)	>0.05
Cancer	12(21.05)	13(22.81)	0.821
Former	0(0)	3(5.26)	0.243
Current	12(21.05)	9(15.79)	0.469
Type of malignancy			
Solid organ malignancy			
CNS tumor	0(0)	1(1.75)	>0.05
Head & Neck Cancer	0(0)	0(0)	-
Lung cancer	3(5.26)	2(3.51)	>0.05
Gastrointestinal malignancy	3(5.26)	2(3.57)	>0.05
Gynecologic malignancy	0(0)	2(3.51)	0.496
Breast cancer	0(0)	1(1.75)	>0.05
Hematologic malignancy	6(10.53)	5(8.77)	0.751
Connective tissue disease	4(7.02)	2(3.51)	0.679
The severity of the current disease and pre-existing comorbidities			
Charlson Comorbidity Index, median [Q1, Q3]	6(4,8)	5(3,8)	0.520
APACHE II, mean ±SD	14.65±3.41	14.11±2.89	0.360
SOFA score, median [Q1, Q3]	3(2,5)	3(2,5)	0.823
Vital signs			
RR (rpm), mean ±SD	18.44±3.59	18.89±3.06	0.467
MAP (mmHg), mean ±SD	89.02±11.26	86.00±11.75	0.164

HR (bpm), mean ±SD	87.14±14.32	86.46±14.33	0.799
Gas exchange			
PaO_2/FiO_2, mean ±SD	357.05±89.73	372.87±78.35	0.318
SaO_2/FiO_2, mean ±SD	342.94±71.17	351.88±66.08	0.488
pCO_2 (mmHg), mean ±SD	32.40±7.77	32.59±6.47	0.887
pH, mean ±SD	7.45±0.05	7.45±0.04	0.837
Weaning parameters			
Work of breathing score, median [Q1, Q4]	1(1,2)	1(1,2)	0.603
RSBI, mean ±SD	78.30±13.88	80.18±12.56	0.449
CPF (LPM), mean ±SD	192.89±39.72	190.88±28.90	0.757
NIF (cmH_2O), mean ±SD	-23.82±3.97	-23.36±3.60	0.513
Weaning time (minutes), mean ±SD	47.25±12.40	47.07±13.19	0.939
Volume status			
Net fluid (mL), median [Q1, Q3]	1632(-28,3110)	475(-800,1245)	0.010*
Causes of respiratory failure, n (%)			
Pulmonary causes	38(66.67)	40(70.18)	0.687
Pneumonia	22(38.60)	20(35.09)	0.698
Aspiration	0(0)	1(1.75)	>0.05
ARDS	7(12.28)	5(8.77)	0.542
Secretion obstruction	0(0)	0(0)	-
Bronchospasm	9(15.79)	7(12.28)	0.590
DAH	1(1.75)	1(1.75)	>0.05
Pulmonary edema	18(31.58)	19(33.33)	0.841
Extra-pulmonary causes	28(49.12)	28(49.12)	>0.05
Sepsis	22(38.60)	23(40.35)	0.848
Metabolic acidosis from other causes	10(17.54)	12(21.05)	0.635

Comatose status	9(15.79)	7(12.28)	0.590
Hemorrhagic shock	5(8.77)	5(8.77)	>0.05
Post-extrathoracic operation	0(0)	0(0)	-
Duration of mechanical ventilation before extubation (days), median [Q1, Q3]	4(3,7)	5(3,7)	0.613
NIV settings			
PEEP (cmH_2O), mean ±SD	5.54±1.18	6.14±1.42	0.016*
PS (cmH_2O), mean ±SD	8.58±2.05	12.28±2.23	<0.001*
VTi (mL), mean ±SD	507.19±95.46	1156.39±172.45	<0.001*
VTe (mL), mean ±SD	390.79±78.28	1040.23±162.42	<0.001*
FiO_2, mean ±SD	0.29±0.05	0.29±0.05	0.842
% Leakage at baseline, median [Q1, Q3]	21(16,28)	10(8,12)	<0.001*
NIV duration (hours), median [Q1, Q3]	24(24,24)	7(3,14)	<0.001*

Note: Q1; 25% quartile, Q3; 75% quartile, SD; standard deviation, N; number of patients, No.; number, COPD; chronic obstructive pulmonary disease, CNS; central nervous system, RR; respiratory rate, MAP; mean arterial pressure, HR; heart rate, RSBI; rapid shallow breathing index, CPF; cough peak flow, NIF; negative inspiratory force, ARDS; acute respiratory distress syndrome, DAH; diffuse alveolar hemorrhage, PEEP; positive end expiratory pressure, PS; pressure support, VTi; inspired tidal volume, VTe; expired tidal volume, FiO_2; fraction of inspired oxygen, NIV; non-invasive ventilation

3. The primary outcome

The extubation success rate in the first 48 hours did not differ between helmet NIV and facemask NIV, according to both intention-to-treat and per-protocol analyses (table 3). In the intention-to-treat analysis, the extubation success rate was 85.96% in helmet NIV and 87.72% in facemask NIV, p = 0.782). Similarly, by per-protocol analysis, the extubation success rate was 100% in helmet NIV and 91.11% in facemask NIV, p = 0.564).

Table 3: Primary outcome: successful extubation in the first 48 hours (intention-to-treat and per protocol analysis)

Primary outcome	Facemask NIV	Helmet NIV	p-value
Participants, n	57	57	
Extubation Success (Intention-to-treat analysis)	50 (87.72)	49(85.96)	0.782
Participants, n	45	14	
Extubation Success (Per protocol analysis)	41 (91.11)	14(100.00)	0.564

4. The secondary outcome

The rate of reintubation within seven days and the time to reintubation were similar between helmet NIV and facemask NIV. The reasons for reintubation were also identical in both groups. Facemask NIV had a higher pressure sore score (2 [0, 4] versus 0 [0, 2], p <0.001), nasal irritation (21.05% versus 0%, p <0.001), and asynchrony (24.56% versus 5.26%, p=0.004). The noise was greater in the helmet NIV (70.18% versus 1.75%, p <0.001). When comparing facemask NIV to helmet NIV, there was more leakage detected. The helmet NIV group had lower mean arterial pressure

throughout a 48-hour post-extubation period. Other secondary outcomes were comparable between helmet NIV and facemask NIV (table 4 and table 5).

Table 4: secondary outcomes

Secondary outcomes	**Facemask NIV** (n=57)	**Helmet NIV** (n=57)	**p-value**
Reintubation rate within 7 days, n (%)	12(21.05)	11(19.30)	0.815
Time to reintubation (days), median [Q1, Q3]	0(0,7)	0(0,6)	0.624
NIV intolerance, n (%)	12(21.05)	43(75.44)	<0.001*
Comfort score[#], mean ±SD	4.93±1.82	6.47±2.25	<0.001*
Adverse events			
• Pressure sore score, median [Q1, Q3]	2(0,4)	0(0,2)	<0.001*
• Secretion obstruction, n (%)	1(1.75)	0(0)	>0.05
• Atelectasis, n (%)	0(0)	0(0)	-
• Nasal irritation, n (%)	12(21.05)	0(0)	<0.001*
• Hot air, n (%)	6(10.53)	8(14.04)	0.568
• Noise, n (%)	1(1.75)	40(70.18)	<0.001*
• Asynchrony, n (%)	14(24.56)	3(5.26)	0.004*
• Others, n (%)	0(0)	2(3.51)	0.154
30 minutes after extubation			
RR (rpm), mean ±SD	20.21±3.56	20.44±2.25	0.684
MAP (mmHg), mean ±SD	92.68±12.39	86.14±11.52	0.004*
HR (bpm), mean ±SD	89.89±12.69	87.77±13.59	0.39
SaO_2/FiO_2, mean ±SD	349.56±60.76	354.72±62.44	0.655
% Leakage, median [Q1, Q3]	20(5,51)	10(5,15)	<0.001*
WOB score, median [Q1, Q3]	2(1,4)	2(1,2)	0.302
2 hours after extubation			

RR (rpm), mean ±SD	20.42±3.14	20.51±1.97	0.859
MAP (mmHg), mean ±SD	94.61±12.21	86.84±10.99	0.001*
HR (bpm), mean ±SD	90.40±13.74	87.53±13.30	0.258
SaO_2/FiO_2, mean ±SD	355.63±59.75	364.49±61.86	0.438
PaO_2/FiO_2, mean ±SD	400.93±111.36	403.89±83.62	0.873
pCO_2 (mmHg), mean ±SD	32.20±7.35	32.81±6.40	0.637
pH, mean ±SD	7.45±0.05	7.45±0.03	0.798
% Leakage, median [Q1, Q3]	20(8,50)	9.5(5,15)	<0.001*
WOB score, median [Q1, Q3]	2(1,3)	1(1,2)	0.134
24 hours after extubation			
RR (rpm), mean ±SD	19.60±2.97	19.60±2.17	>0.05
MAP (mmHg), mean ±SD	91.28±11.64	85.12±10.50	0.004*
HR (bpm), mean ±SD	86.60±13.16	86.05±11.93	0.818
SaO_2/FiO_2, mean ±SD	352.76±63.81	365.74±62.02	0.273
PaO_2/FiO_2, mean ±SD	413.07±98.37	408.02±88.24	0.774
pCO_2 (mmHg), mean ±SD	32.21±7.15	32.89±5.79	0.576
pH, mean ±SD	7.45±0.05	7.45±0.04	0.79
% Leakage, median [Q1, Q3]	21.5(0,50)	10(7,24)	0.001*
WOB score, median [Q1, Q3]	1(1,4)	1(1,2)	0.128
48 hours after extubation			
RR (rpm), mean ±SD	19.46±2.32	19.28±1.78	0.651
MAP (mmHg), mean ±SD	90.79±10.34	84.68±9.66	0.001*
HR (bpm), mean ±SD	87.42±10.81	85.07±11.93	0.273
SaO_2/FiO_2, mean ±SD	352.78±60.26	367.29±59.09	0.197
PaO_2/FiO_2, mean ±SD	382.47±80.34	380.95±72.57	0.916
pCO_2 (mmHg), mean ±SD	33.41±6.53	33.22±5.62	0.870
pH, mean ±SD	7.45±0.04	7.45±0.03	0.977
WOB score, median [Q1, Q3]	1(1,3)	1(1,2)	0.497

Note: Q1; 25% quartile, Q3; 75% quartile, SD; standard deviation, N; number of patients, No.; number, RR; respiratory rate, MAP; mean arterial pressure, HR; heart rate, WOB score; work of breathing score, # the higher score, the more discomfort

Table 5: Etiologies of reintubation within seven days

Reasons for reintubation within seven days	**Facemask NIV** (n=57)	**Helmet NIV** (n=57)	**p-value**
Pulmonary cause	**6(10.53)**	**8(14.04)**	**0.568**
Pneumonia	3(5.26)	4(7.02)	>0.05
Aspiration	0(0)	2(3.51)	0.496
ARDS	0(0)	4(7.02)	0.118
Secretion obstruction	2(3.51)	0(0)	0.396
Bronchospasm	1(1.75)	0(0)	>0.05
DAH	0(0)	0(0)	-
Pulmonary edema	1(1.75)	2(3.51)	>0.05
Extrapulmonary cause	**6(10.53)**	**3(5.26)**	**0.490**
Sepsis	4(7.02)	3(5.26)	>0.05
Metabolic acidosis from other causes	2(3.51)	1(1.75)	>0.05
Comatose status	2(3.51)	0(0)	0.496
Hemorrhagic shock	2(3.51)	0(0)	0.496
Post-extrathoracic operation	0(0)	0(0)	-

Note: ARDS; acute respiratory distress syndrome, DAH; diffuse alveolar hemorrhage

5. Parameters of patients with NIV intolerance

Table 6 showed hemodynamic and gas exchange parameters in patients with NIV intolerance. In both helmet NIV and facemask NIV groups, there was a significant increase in respiratory rate when comparing parameters at baseline and at the time of NIV intolerance detection: facemask NIV (16.73±2.83 versus 21.45±2.51, p = 0.001), and helmet NIV (19.16±2.96 versus 20.28±2.18, p = 0.013). The helmet NIV showed a difference in heart rate (83.47±12.29 versus 86.33±12.26, p <0.001). MAP difference was detected in facemask NIV prior to randomization and during intolerance time (84.91±8.40 versus 90.00±8.96, p = 0.014)

Table 6: Hemodynamics and respiratory parameters of patients with NIV intolerance

Parameters Mean ± SD	Facemask NIV (n=12)		p-value	Helmet NIV (n=43)		p-value
Time	at baseline	At NIV intolerance		at baseline	at NIV intolerance	
RR (rpm)	16.73±2.83	21.45±2.51	0.001*	19.16±2.96	20.28±2.18	0.013*
MAP (mmHg)	84.91±8.40	90.00±8.96	0.014*	84.67±11.34	83.21±12.50	0.369
HR (bpm)	86.45±11.89	90.45±10.29	0.082	83.47±12.29	86.33±12.26	<0.001*
PaO_2/FiO_2	355.03±108.97	359.82±44.27	0.894	383.79±84.26	393.28±56.40	0.412
pCO_2 (cmH_2O)	31.12±4.29	31.41±3.32	0.859	32.66±6.94	33.81±5.96	0.094
pH	7.43±0.04	7.44±0.03	0.167	7.45±0.04	7.45±0.03	0.676

Note: SD; standard deviation, N; number of patients, RR; respiratory rate, MAP; mean arterial pressure, HR; heart rate

Chapter five
Discussion Conclusion and Suggestions

1. Discussion

In this single-center randomized controlled trial, prophylactic helmet NIV in patients at high risk for post-extubation respiratory failure appeared to have no difference in extubation success within the first 48 hours, compared with prophylactic facemask NIV.

The benefit of post-extubated facemask NIV prophylaxis has already been demonstrated. (7, 12) According to a recent meta-analysis, the helmet NIV was crucial in the COVID-19 pandemic, which prevented intubation in acute respiratory failure. (17, 21) However, the role of helmet NIV in patients at high risk of reintubation remains unclear. To our knowledge, there is only one retrospective study comparing helmet NIV and facemask NIV among patients with high-risk post-extubation respiratory failure, which found no difference in the reintubation rate. (22) We hypothesized that helmet NIV could have a difference in reintubation rate due to an increase in end-expired lung volume from less air leakage, compared with facemask NIV, which might result in less additional work of breathing from more constant airway pressure. (31, 32) Thus, our study aimed to evaluate the helmet interface's efficacy in post-extubated patients. However, our study demonstrated the extubation success rate was not different between helmet NIV and facemask NIV, even though helmet NIV had less percentage of air leakage with a higher level of pressure support. Moreover, more NIV intolerance was detected, contrasting with the other studies. (32-34) Despite having already adjusted with well-protocolized pressure support and PEEP on NIV mode, our patients with the helmet NIV experienced discomfort with a significant dyspnea score, leading to NIV intolerance after a median of 7 hours. However, when comparing the gas exchange parameters at baseline before randomization and during NIV intolerance, there was no statistically significant difference, indicating that the helmet made patients uncomfortable even if they had no initial claustrophobia, as shown in Table 6. Despite the increased

respiratory and heart rates during NIV intolerance diagnosis, no post-extubation respiratory failure was observed. Furthermore, our patients requested that the device be removed and that, following intolerance, a high-flow nasal cannula with a flow rate of 50 liters per minute and an adjusted FiO_2 be used to achieve oxygenation saturation of at least 92% be used in its place. The high-flow nasal cannula could be a confounding factor in the extubation outcome due to the high rate of intolerance in helmet NIV. Moreover, we found that mean arterial pressure (MAP) was lower in helmet NIV (MAP 92.68±12.39 in facemask NIV versus 86.14±11.52in helmet NIV, p=0.004), which could be due to a difference in transpulmonary pressure transmission between facemask and helmet NIV or to a confounded transpulmonary pressure effect of high flow nasal oxygen. Different populations could explain the difference in helmet NIV intolerance incidence between our study and others. The majority of the studies used helmet NIV in hypoxemic patients before intubation. (21) A pilot study found that low-dose remifentanil could improve patients' helmet and facemask NIV tolerance. (35)

According to the adverse events, helmet NIV significantly lowered pressure sore and nasal irritation rates, but increased noise, consistent with results from other studies. (32, 36) Unlike the face mask, the helmet can expose the entire head to positive pressure, leading to louder noise. This finding may point to using earplugs in certain situations, such as long-term use and when using high airway pressures. Asynchrony, particularly auto-triggering, was found more frequently in the facemask NIV group than in the helmet NIV group. It could be explained by the helmet's significantly longer inspiratory trigger delay and less leakage. (37) In contrast to Racca F et al. study, autocycled breathing was twice as common with helmet ventilation as with face mask ventilation. (38) The elastic properties of the helmet make it susceptible to flow variations that are not tracked by effective inspiratory effort. Thus, the difference was caused by the elasticity of the plastic hood.

2. Conclusion

The helmet NIV did not differ from the facemask NIV in terms of extubation success rate among patients with a high risk of post-extubation respiratory failure who underwent extubation. More research is needed to determine the efficacy of helmet NIV over facemask NIV.

3. Limitations.

- The attending physicians could not be blinded to the study.
- Our study was a single-center study that may need to be more generalizable to other healthcare settings.
- An immensely high rate of NIV intolerance in the helmet group may impact the outcome.
- The challenge of helmet NIV use is determining which patients are good candidates and the medical team's learning curve and education. (39)

REFERENCES

1. Thille AW, Richard JC, Brochard L. The decision to extubate in the intensive care unit. Am J Respir Crit Care Med. 2013;187(12):1294-302.

2. Penuelas O, Frutos-Vivar F, Fernandez C, Anzueto A, Epstein SK, Apezteguia C, et al. Characteristics and outcomes of ventilated patients according to time to liberation from mechanical ventilation. Am J Respir Crit Care Med. 2011;184(4):430-7.

3. Ferrer M, Valencia M, Nicolas JM, Bernadich O, Badia JR, Torres A. Early noninvasive ventilation averts extubation failure in patients at risk: a randomized trial. Am J Respir Crit Care Med. 2006;173(2):164-70.

4. Lin C, Yu H, Fan H, Li Z. The efficacy of noninvasive ventilation in managing postextubation respiratory failure: a meta-analysis. Heart Lung. 2014;43(2):99-104.

5. Frutos-Vivar F, Esteban A, Apezteguia C, Gonzalez M, Arabi Y, Restrepo MI, et al. Outcome of reintubated patients after scheduled extubation. J Crit Care. 2011;26(5):502-9.

6. Munshi L, Mancebo J, Brochard LJ. Noninvasive Respiratory Support for Adults with Acute Respiratory Failure. N Engl J Med. 2022;387(18):1688-98.

7. Rochwerg B, Brochard L, Elliott MW, Hess D, Hill NS, Nava S, et al. Official ERS/ATS clinical practice guidelines: noninvasive ventilation for acute respiratory failure. Eur Respir J. 2017;50(2).

8. Demoule A, Chevret S, Carlucci A, Kouatchet A, Jaber S, Meziani F, et al. Changing use of noninvasive ventilation in critically ill patients: trends over 15 years in francophone countries. Intensive Care Med. 2016;42(1):82-92.

9. Nava S, Gregoretti C, Fanfulla F, Squadrone E, Grassi M, Carlucci A, et al. Noninvasive ventilation to prevent respiratory failure after extubation in high-risk patients. Crit Care Med. 2005;33(11):2465-70.

10. Ornico SR, Lobo SM, Sanches HS, Deberaldini M, Tofoli LT, Vidal AM, et al. Noninvasive ventilation immediately after extubation improves weaning outcome after acute respiratory failure: a randomized controlled trial. Crit Care. 2013;17(2):R39.

11. Ferrer M, Sellares J, Valencia M, Carrillo A, Gonzalez G, Badia JR, et al. Non-

invasive ventilation after extubation in hypercapnic patients with chronic respiratory disorders: randomised controlled trial. Lancet. 2009;374(9695):1082-8.

12. Fernando SM, Tran A, Sadeghirad B, Burns KEA, Fan E, Brodie D, et al. Noninvasive respiratory support following extubation in critically ill adults: a systematic review and network meta-analysis. Intensive Care Med. 2022;48(2):137-47.

13. El-Solh AA, Aquilina A, Pineda L, Dhanvantri V, Grant B, Bouquin P. Noninvasive ventilation for prevention of post-extubation respiratory failure in obese patients. Eur Respir J. 2006;28(3):588-95.

14. Thille AW, Boissier F, Ben-Ghezala H, Razazi K, Mekontso-Dessap A, Brun-Buisson C, et al. Easily identified at-risk patients for extubation failure may benefit from noninvasive ventilation: a prospective before-after study. Crit Care. 2016;20:48.

15. De Jong A, Casey JD, Myatra SN. Focus on noninvasive respiratory support before and after mechanical ventilation in patients with acute respiratory failure. Intensive Care Med. 2020;46(7):1460-3.

16. Carteaux G, Lyazidi A, Cordoba-Izquierdo A, Vignaux L, Jolliet P, Thille AW, et al. Patient-ventilator asynchrony during noninvasive ventilation: a bench and clinical study. Chest. 2012;142(2):367-76.

17. Grieco DL, Menga LS, Cesarano M, Rosa T, Spadaro S, Bitondo MM, et al. Effect of Helmet Noninvasive Ventilation vs High-Flow Nasal Oxygen on Days Free of Respiratory Support in Patients With COVID-19 and Moderate to Severe Hypoxemic Respiratory Failure: The HENIVOT Randomized Clinical Trial. JAMA. 2021;325(17):1731-43.

18. Chiumello D, Pelosi P, Carlesso E, Severgnini P, Aspesi M, Gamberoni C, et al. Noninvasive positive pressure ventilation delivered by helmet vs. standard face mask. Intensive Care Med. 2003;29(10):1671-9.

19. Patroniti N, Foti G, Manfio A, Coppo A, Bellani G, Pesenti A. Head helmet versus face mask for non-invasive continuous positive airway pressure: a physiological study. Intensive Care Med. 2003;29(10):1680-7.

20. Liu Q, Gao Y, Chen R, Cheng Z. Noninvasive ventilation with helmet versus control strategy in patients with acute respiratory failure: a systematic review and meta-analysis of controlled studies. Crit Care. 2016;20(1):265.

21. Chaudhuri D, Jinah R, Burns KEA, Angriman F, Ferreyro BL, Munshi L, et al.

Helmet noninvasive ventilation compared to facemask noninvasive ventilation and high-flow nasal cannula in acute respiratory failure: a systematic review and meta-analysis. Eur Respir J. 2022;59(3).

22. Park M, Kim JS, Kim M, Kim AJ, Lee M-J. Usefulness of non-invasive ventilation delivered by helmet versus oronasal mask among patients at high risk of post-extubation respiratory failure. Eur Respiratory Soc; 2020.

23. Hernandez G, Vaquero C, Colinas L, Cuena R, Gonzalez P, Canabal A, et al. Effect of Postextubation High-Flow Nasal Cannula vs Noninvasive Ventilation on Reintubation and Postextubation Respiratory Failure in High-Risk Patients: A Randomized Clinical Trial. JAMA. 2016;316(15):1565-74.

24. Thille AW, Muller G, Gacouin A, Coudroy R, Decavele M, Sonneville R, et al. Effect of Postextubation High-Flow Nasal Oxygen With Noninvasive Ventilation vs High-Flow Nasal Oxygen Alone on Reintubation Among Patients at High Risk of Extubation Failure: A Randomized Clinical Trial. JAMA. 2019;322(15):1465-75.

25. Su CL, Chiang LL, Yang SH, Lin HI, Cheng KC, Huang YC, et al. Preventive use of noninvasive ventilation after extubation: a prospective, multicenter randomized controlled trial. Respir Care. 2012;57(2):204-10.

26. Khilnani GC, Galle AD, Hadda V, Sharma SK. Non-invasive ventilation after extubation in patients with chronic obstructive airways disease: a randomised controlled trial. Anaesth Intensive Care. 2011;39(2):217-23.

27. Rezoagli E, Villa S, Gatti S, Russotto V, Borgo A, Lucchini A, et al. Helmet and face mask for non-invasive respiratory support in patients with acute hypoxemic respiratory failure: A retrospective study. J Crit Care. 2021;65:56-61.

28. Mojoli F, Iotti GA, Gerletti M, Lucarini C, Braschi A. Carbon dioxide rebreathing during non-invasive ventilation delivered by helmet: a bench study. Intensive Care Med. 2008;34(8):1454-60.

29. Nava S, Hill N. Non-invasive ventilation in acute respiratory failure. Lancet. 2009;374(9685):250-9.

30. Winck JC, LeBlanc C, Soto JL, Plano F. The value of cough peak flow measurements in the assessment of extubation or decannulation readiness. Rev Port Pneumol (2006). 2015;21(2):94-8.

31. Tatham KC, Ko M, Palozzi L, Lapinsky SE, Brochard LJ, Goligher EC. Helmet interface increases lung volumes at equivalent ventilator pressures compared to the face mask interface during non-invasive ventilation. Crit Care. 2020;24(1):504.

32. Coppadoro A, Zago E, Pavan F, Foti G, Bellani G. The use of head helmets to deliver noninvasive ventilatory support: a comprehensive review of technical aspects and clinical findings. Crit Care. 2021;25(1):327.

33. Principi T, Pantanetti S, Catani F, Elisei D, Gabbanelli V, Pelaia P, et al. Noninvasive continuous positive airway pressure delivered by helmet in hematological malignancy patients with hypoxemic acute respiratory failure. Intensive Care Med. 2004;30(1):147-50.

34. Squadrone V, Coha M, Cerutti E, Schellino MM, Biolino P, Occella P, et al. Continuous positive airway pressure for treatment of postoperative hypoxemia: a randomized controlled trial. JAMA. 2005;293(5):589-95.

35. Rocco M, Conti G, Alessandri E, Morelli A, Spadetta G, Laderchi A, et al. Rescue treatment for noninvasive ventilation failure due to interface intolerance with remifentanil analgosedation: a pilot study. Intensive Care Med. 2010;36(12):2060-5.

36. Esquinas Rodriguez AM, Papadakos PJ, Carron M, Cosentini R, Chiumello D. Clinical review: Helmet and non-invasive mechanical ventilation in critically ill patients. Crit Care. 2013;17(2):223.

37. Costa R, Navalesi P, Spinazzola G, Ferrone G, Pellegrini A, Cavaliere F, et al. Influence of ventilator settings on patient-ventilator synchrony during pressure support ventilation with different interfaces. Intensive Care Med. 2010;36(8):1363-70.

38. Racca F, Appendini L, Gregoretti C, Stra E, Patessio A, Donner CF, et al. Effectiveness of mask and helmet interfaces to deliver noninvasive ventilation in a human model of resistive breathing. J Appl Physiol (1985). 2005;99(4):1262-71.

39. Amirfarzan H, Cereda M, Gaulton TG, Leissner KB, Cortegiani A, Schumann R, et al. Use of Helmet CPAP in COVID-19 - A practical review. Pulmonology. 2021;27(5):413-22.

VITA

NAME	Napat Jirawat
DATE OF BIRTH	19 April 1993
PLACE OF BIRTH	Chonburi, Thailand
INSTITUTIONS ATTENDED	King Chulalongkorn Memorial Hospital, The Thai Red Cross Society, Thailand
HOME ADDRESS	10/37 Moo2, Samed, Muang Chonburi, Chonburi, Thailand
PUBLICATION	none
AWARD RECEIVED	none