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High Flow Nasal Cannula vs. Non-Invasive Ventilation in Post-Extubation Pediatric Cardiac Surgery Patients: A Randomized Controlled Trial

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RESEARCH PROPOSAL

Research Title

High Flow Nasal Cannula vs. Non-Invasive Ventilation in Post-Extubation Pediatric Cardiac Surgery Patients: A Randomized Controlled Trial

Research Obejctives:

This study aims to compare the extubation success rate between the use of High Flow Nasal Cannula (HFNC) and Non-Invasive Ventilation (NIV) in pediatric patients post-cardiac surgery at the National General Hospital Dr. Cipto Mangunkusumo (RSCM). Additionally, this study seeks to identify factors influencing extubation failure in high-risk patient populations, compare CICU length of stay, sedation usage and COMFORT scale between patients receiving HFNC and those receiving NIV.

Research Methodology:

This study is a randomized controlled clinical trial involving two intervention groups: one receiving High Flow Nasal Cannula (HFNC) therapy using Airvo^{TM}3 Nasal High Flow/HFNC System and the other receiving Non-Invasive Ventilation (NIV). The study population consists of pediatric patients admitted to the Cardiac Intensive Care Unit (CICU) at Dr. Cipto Mangunkusumo National General Hospital (RSCM) following cardiac surgery. A total of 114 subjects will be enrolled, with 57 patients allocated to each group. Patients will be monitored for 24 hours post-extubation to evaluate the incidence of extubation failure and the associated risk factors. Reintubation will be performed in cases of respiratory failure or other complications requiring airway support.

Expected Outcomes:

The use of HFNC is expected to achieve an extubation success rate that is comparable to NIV, while offering a lower risk of complications and enhanced patient comfort. The findings of this study are anticipated to provide significant evidence regarding the differences between these two modalities in preventing extubation failure.

Outcome of Study:

The expected outcomes include a reduction in reintubation rates at 48 - 72 hours, 7 days, and 28 days post-extubation in the HFNC group compared to the NIV group. Additionally, this study aims to decrease mortality rates in the CICU and shorten the length of hospital stay for pediatric patients following cardiac surgery.

CHAPTER 1 Introduction

1.1. Background

Congenital heart disease (CHD) is a significant global health concern, with a prevalence of 0.8–1.2% of total live births. In developed countries, post-cardiac surgery mortality rates among pediatric patients tend to be low. However, data from Indonesia, particularly from Dr. Cipto Mangunkusumo National General Hospital (RSCM), indicate a significant mortality rate. Over the past 3–5 years, the post-cardiac surgery mortality rate among pediatric patients at RSCM has been approximately 13.6%, primarily due to complications such as low cardiac output syndrome (LCOS), arrhythmias, multi-organ dysfunction, and extubation failure.[1] The incidence of extubation failure in pediatric cardiac surgery patients ranges from 9.7% to 17.6%.[2,3] often associated with airway, neurological, cardiac, diaphragmatic, and electrolyte-related factors.[4–6] Patients experiencing repeated extubation failure have a higher risk of mortality compared to those who either do not experience it or fail extubation only once.[7] Therefore, identifying effective solutions to mitigate the risk of extubation failure is of critical importance.

Non-invasive ventilation (NIV) and high-flow nasal cannula (HFNC) are commonly implemented in healthcare centers to reduce the incidence of extubation failure. However, the effectiveness of HFNC in minimizing extubation failure among high-risk pediatric cardiac surgery patients remains uncertain, particularly in Indonesia. At RSCM, the systematic and widespread use of HFNC in managing post-cardiac surgery pediatric patients requires further investigation to establish its efficacy. This study aims to address this gap by comparing extubation success rates between HFNC and NIV at RSCM.

1.2. Relevance to Priority Research Topics

This research aligns with RSCM's priority health topics, specifically the improvement of intensive care and post-operative recovery in pediatric cardiac surgery patients. Investigating respiratory management strategies, such as HFNC versus NIV, directly contributes to enhancing healthcare quality at RSCM. If HFNC proves to be comparable to NIV in preventing extubation failure, its implementation could optimize patient recovery and reduce complication rates.

1.3. Research Problem Statement

Given the high incidence of extubation failure among pediatric post-cardiac surgery patients at RSCM, there is a pressing need to identify a more effective approach to prevent extubation failure. This study aims to answer the following research question: **Is HFNC as effective as NIV in preventing extubation failure in pediatric patients following cardiac surgery?**

1.4. Research Questions

1. How does the extubation failure rate compare between HFNC and NIV in pediatric patients admitted to the CICU following cardiac surgery?
2. What factors influence extubation failure in pediatric patients receiving HFNC compared to those receiving NIV?

1.5. Research Objectives

General Objective: To determine the effectiveness of HFNC compared to NIV in preventing extubation failure among pediatric post-cardiac surgery patients at RSCM.

Specific Objectives:

1. To compare the extubation failure rate between patients receiving HFNC and those receiving NIV.
2. To identify factors influencing extubation success in each intervention group.

Secondary Objectives:

1. To compare CICU length of stay between patients receiving HFNC and those receiving NIV.
2. To compare sedation usage (duration and total dose) between patients receiving HFNC and those receiving NIV
3. To compare COMFORT scale between patients receiving HFNC and those receiving NIV

1.6. Research Significance

This study is expected to provide significant contributions to improving the quality of care for pediatric post-cardiac surgery patients at RSCM. The findings will generate valid data regarding the effectiveness of HFNC in preventing extubation failure, serving as a reference for selecting optimal respiratory therapy for these patients.

For RSCM, this research will facilitate the development of improved clinical care standards for pediatric post-cardiac surgery patients, reduce complication rates, and enhance recovery outcomes.

1.7. Strategic Research Outcomes

1.7.1. Internal Implementation at RSCM

The results of this study are expected to be implemented at RSCM in the form of **Clinical Practice Guidelines (CPG), Standard Operating Procedures (SOPs),** or **Work Instructions (WIs)** for the management of pediatric post-cardiac surgery patients. The integration of HFNC as a routine care modality will be incorporated into RSCM's existing **clinical pathways**, supported by internal policies and regulations.

1.7.2. Eksternal Adaptability outside RSCM

The findings of this study have the potential to be adopted by other institutions outside RSCM, particularly hospitals that manage pediatric cardiac surgery cases. By demonstrating the effectiveness of HFNC, other hospitals may implement similar modalities to enhance the quality of care for pediatric post-cardiac surgery patients

CHAPTER II Literature Review

Pediatric patients undergoing cardiac surgery are at high risk of developing respiratory complications, particularly following extubation. Unsuccessful extubation can lead to respiratory failure, increasing the need for reintubation and further medical interventions. Extubation failure is defined as the necessity for reintubation within 72 hours after planned extubation. Several studies have reported that the incidence of extubation failure in pediatric post-cardiac surgery patients ranges from 9.7% to 17.6%, depending on factors such as cardiopulmonary bypass (CPB) duration, congenital heart disease severity, and high inotropic support requirements.[1] One potential strategy to reduce this rate is the implementation of non-invasive ventilation (NIV) or high-flow nasal cannula (HFNC) as a transitional modality before initiating low-flow oxygen therapy.[8,9] However, the effectiveness of these approaches remains controversial, particularly in high-risk post-cardiac surgery populations. Furthermore, at the RSCM Cardiac ICU, a modified form of NIV is still in use, which may not be ideal due to the potential for inadequate airflow delivery.

High Flow Nasal Cannula (HFNC)

HFNC is one of the method use to support post-extubation patients to reduce the need for invasive intubation. HFNC delivers high-flow oxygen via a nasal cannula, equipped with optimal humidification and heating, thereby increasing patient comfort and reducing respiratory workload. HFNC also helps improve oxygenation and reduce the need for invasive mechanical ventilation.[10] Research conducted by Mayfield et al. showed that the use of HFNC in pediatric patients with bronchiolitis can significantly reduce the need for admission to the pediatric intensive care unit (PICU) by up to fourfold compared with the use of low-flow oxygen therapy.[11] HFNC has also been recognized as a safe modality for use in non-ICU settings, including in pediatric wards.[11] McKiernan et al. emphasized that HFNC can reduce the rate of re-intubation in pediatric patients with bronchiolitis, as well as improve oxygen saturation without the risk of side effects such as pneumothorax or bradycardia.[12]

Non-Invasive Ventilation (NIV)

NIV is a respiratory support technique that utilizes positive pressure ventilation without invasive intubation. It is commonly employed in patients with acute respiratory distress to maintain airway patency and enhance gas exchange. Although NIV has been proven effective in preventing extubation failure in pediatric patients, it has several limitations. The use of masks or nasal interfaces in NIV can cause discomfort, particularly in infants and younger children, and may also increase the risk of air leakage, reducing the efficacy of the therapy.[6] A study by Thille et al. found that factors such as prolonged cardiopulmonary

bypass duration and high inotropic support postoperatively increased the risk of extubation failure in patients receiving NIV.[6] Additionally, research by Miura et al. indicated that neonates experiencing extubation failure due to cardiovascular complications were at a higher risk of repeated extubation failure, which further elevated mortality risk.[3]

Comparison of the Effectiveness of HFNC and NIV

Studies comparing HFNC and NIV in pediatric post-cardiac surgery patients have yielded mixed results. Some research supports HFNC as a more comfortable and easier-to-implement modality, particularly due to its less invasive nasal cannula interface compared to the masks used in NIV. Furthermore, HFNC is considered more user-friendly in non-ICU settings.[13] Conversely, NIV has been utilized for a longer duration in intensive care settings and is known for providing stable positive pressure, which helps prevent alveolar collapse and improves gas exchange in patients with compromised pulmonary function.[8]

A study by Zhou et al. (2024) found that HFNC significantly reduced reintubation risk (RR = 0.36, $P < 0.00001$)14 and shortened ICU stay duration (MD = -4.75, $P = 0.04$). Similarly, research by Elmitwalli et al. (2024) reported that HFNC decreased reintubation rates (RR = 0.45, $P < 0.01$), mortality (RR = 0.31, $P < 0.01$), as well as length of hospital stay (-8.76 days, $P < 0.01$) and ICU stay (-4.63 days, $P = 0.04$).[15] However, compared to conventional oxygen therapy, no significant differences were observed in reintubation rates. A study by Kuitunen (2023) concluded that there was insufficient evidence to establish a definitive difference in reintubation rates and other clinical outcomes between different non-invasive ventilation strategies, due to high bias risk and limited study numbers.[16]

The debate continues regarding which modality is more effective in reducing extubation failure and mortality. HFNC provides benefits for patients with moderate-to-severe respiratory failure risk, whereas NIV may be more suitable for patients with severe pulmonary conditions. Further research is required to determine the optimal post-extubation strategy for pediatric post-cardiac surgery patients.

CHAPTER III Theoretical Framework, Conceptual Framework, and Operational Definitions

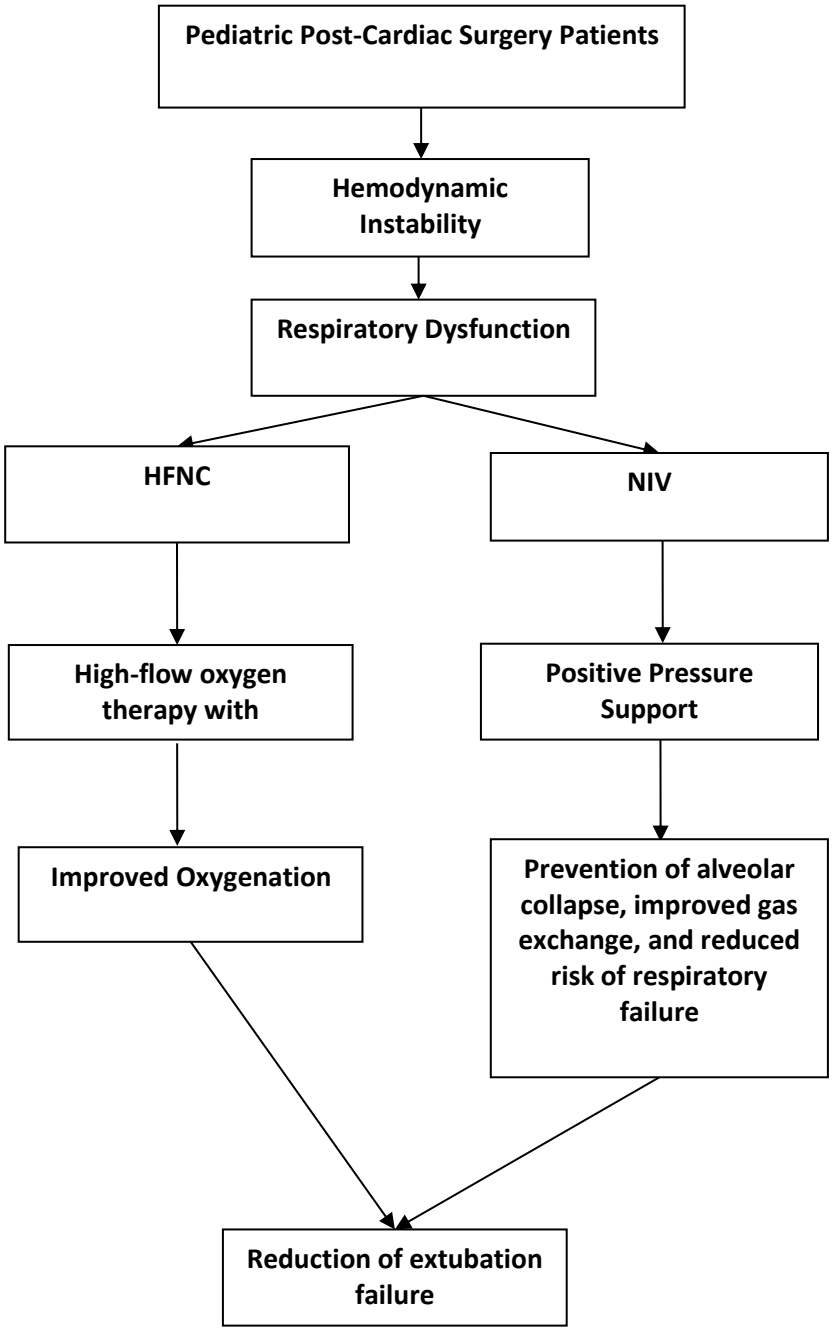

Image 1. Theoretical Framework

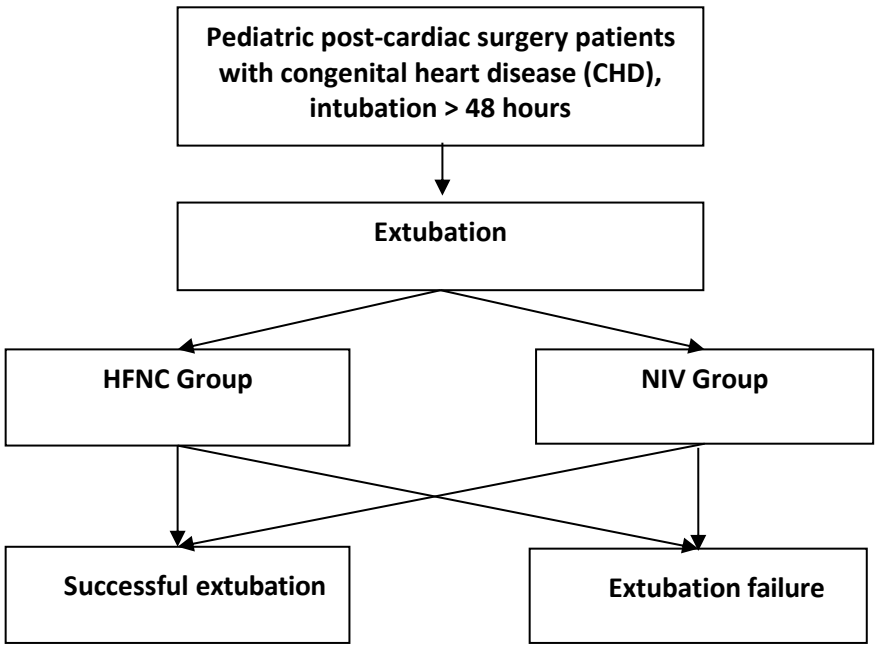

Image 2. Conceptual Framework

Table 1. Operational Definitons

Variable		Definition	Scale	Measurement Criteria
Age	Age <12 months	Patient age categorized as less than 12 months.	Categorical	Medical history, medical records
	Age >12 months	Patient age categorized as more than 12 months.	Categorical	Medical history, medical records
Weight	Weight	Patient weight measured using a scale before intervention.	Numeric	Weight measurement (kg)
RACHS	RACHS	Risk stratification for cardiac surgery.	Categorical Ordinal	Based on RACHS Classification in Medical Records
Operation Type	Off CPB	Surgery without the use of cardiopulmonary bypass.	Categorical	Based on Surgical Records
	CPB	Surgery without the use of cardiopulmonary bypass.	Categorical	Based on Surgical Records
Gender	Male	Male patient.	Categorical	Medical history, medical records
	Female	Female patient.	Categorical	Medical history, medical records
Malnutrition	Yes	Patient diagnosed with malnutrition based on clinical assessment.	Categorical	Clinical Assessment
	No	Patient not diagnosed with malnutrition based on clinical assessment.	Categorical	Clinical Assessment
Respiration Diagnosis at Extubation	Pneumonia	Patient diagnosed with pneumonia at the time of extubation.	Categorical	Based on Clinical Evaluation
	Effusion	Patient diagnosed with pleural effusion at the time of extubation.	Categorical	Based on Clinical Evaluation

Vasoactive-Inotropic Score before Extubation	VIS	Vasoactive-Inotropic Score (VIS) to assess inotropic and vasoconstrictor therapy before extubation.	Numeric	VIS Calculation based on Drug Dosage
ABG 1 hour before extubation	pH	Arterial blood pH measured 1 hour before extubation.	Numeric	Arterial Blood Gas (ABG) Measurement
	PCO2	Partial pressure of carbon dioxide (PaCO2) in blood, measured 1 hour before extubation	Numeric	Arterial Blood Gas (ABG) Measurement
	PaO2	Partial pressure of oxygen (PaO2) in blood, measured 1 hour before extubation	Numeric	Arterial Blood Gas (ABG) Measurement
	BE (Base Excess)	Base excess or deficit in blood, measured 1 hour before extubation	Numeric	Arterial Blood Gas (ABG) Measurement
	HCO3	Bicarbonate concentration in blood, measured 1 hour before extubation	Numeric	Arterial Blood Gas (ABG) Measurement
	PF ratio	Ratio of PaO2 to FiO2, measured 1 hour before extubation	Numeric	Arterial Blood Gas (ABG) Measurement
	OI/OSI	Oxygenation Index (OI) or Oxygen Saturation Index (OSI), measured 1 hour before extubation	Numeric	Arterial Blood Gas (ABG) Measurement
Weaning Method	Pressure Support	Ventilator weaning method with pressure support.	Categorical	Medical Records on the Method Used
	T-piece	Ventilator weaning method using a T-Piece without pressure support.	Categorical	Medical Records on the Method Used
ABG 1 hour after NIV/HFNC	pH	Arterial blood pH measured 1 hour after initiation of NIV or HFNC.	Numeric	Arterial Blood Gas (ABG) Measurement
	PCO2	Partial pressure of carbon dioxide (PaCO2) in blood, measured 1 hour fater initiation of NIV or HFNC	Numeric	Arterial Blood Gas (ABG) Measurement
	PaO2	Partial pressure of oxygen (PaO2) in blood, measured 1 hour fater initiation of NIV or HFNC	Numeric	Arterial Blood Gas (ABG) Measurement
	BE (Base Excess)	Base excess or deficit in blood, measured 1 hour fater initiation of NIV or HFNC	Numeric	Arterial Blood Gas (ABG) Measurement
	HCO3	Bicarbonate concentration in blood, measured 1 hour fater initiation of NIV or HFNC	Numeric	Arterial Blood Gas (ABG) Measurement
	PF ratio	Ratio of PaO2 to FiO2, measured 1 hour fater initiation of NIV or HFNC	Numeric	Arterial Blood Gas (ABG) Measurement
	OI/OSI	Oxygenation Index (OI) or Oxygen Saturation Index (OSI), measured 1 hour fater initiation of NIV or HFNC	Numeric	Arterial Blood Gas (ABG) Measurement
Successful Extubation	No Reintubation in 72 hours	Patient does not require reintubation within 72 hours after extubation	Categorical	Based on Clinical Observation
Extubation Failure	Reintubation within 72 hours	Patient requires reintubation within 72 hours after extubation	Categorical	Based on Clinical Observation
Reintubation	Reintubasi at 72 hours, 7 days and 28 Days	Frequency of patients requiring reintubation at 72 hours, 7 days and 28 days	Categorical	Based on Clinical Observation
Mortality in CICU	Mortality During CICU Stay	Number of patient deaths during CICU hospitalization	Categorical	Based on Mortality Records
Length of CICU Stay	Total Length of CICU Stay (in Days)	Total length of CICU stay measured in days	Numeric	Based on Hospital Records
Length of Hospital Stay	Total Length of Hospital Stay (in Days)	Total length of hospital stay measured in days	Numeric	Based on Hospital Records
Sedation usage	Duration of sedation (in Hours) and total dosage	Total duration of sedation after extubation measured in hours and total dosage	Numeric	Based on Hospital Records
COMFORT scale	Patient's comfort during sedation post extubation	Patient's comfort measured in COMFORT behavioral scale	Categoric	COMFORT behavioural scale assessmen

CHAPTER IV Research Methodology

4.1. 4.1. Study Design

This study employs a Randomized Controlled Trial (RCT) design to compare two intervention groups: patients receiving oxygen therapy using Non-Invasive Ventilation (NIV) and those receiving therapy with High Flow Nasal Cannula (HFNC) using Airvo^{TM}3 Nasal High Flow/HFNC System. Patients will be monitored for the incidence of extubation failure and other clinical parameters throughout their hospitalization.

4.2. Study Setting and Duration

This study will be conducted in the Cardiac Intensive Care Unit (CICU) at Dr. Cipto Mangunkusumo National General Hospital (RSUPN Cipto Mangunkusumo), Jakarta. The study period will run from January 2025 to December 2025.

4.3. Population and Sample

The study population consists of **pediatric patients undergoing post-cardiac surgery** and receiving care in the **CICU at RSUPN Cipto Mangunkusumo, Jakarta**. The study sample will be selected based on predefined **inclusion and exclusion criteria**, with the total sample size determined using an appropriate statistical estimation formula. The sample size estimation will be calculated using the following formula:

$$n1 = n2 = \left(\frac{Z\alpha\sqrt{2PQ}+Z\beta\sqrt{P1Q1+P2Q2}}{P1-P2}\right)^2$$

Description:

n1 = n2 = Sample size

Za = Standard deviation for Type I error = 5% = 1,96

Zb = Standard deviation for Type II error = 20% = 0,84

P1 − P2 = Minimum significant difference in proportion = 0,25

P2 = Extubation failure rate with HFNC based on literature is 17% or equivalent to 0.17.

Q2 = 1 − 0,17 = 0,83

P1 = P2 + 0,25 = 0,17 + 0,25 = 0,42

Q1 = 1 − P1 = 1 − 0,42 = 0,58

P = (P1 + P2)/2 = (0,42 + 0,17)/2 = 0,295

Q = 1 − P = 1 − 0,295 = 0,705

$$n1 = n2 = \left(\frac{1{,}96\sqrt{2x0{,}295x0{,}705} + 0{,}84\sqrt{0{,}42x0{,}58 + 0{,}17x0{,}83}}{0{,}42 - 0{,}17}\right)^2$$

= 51

Meanwhile, when estimating the sample size based on the outcome of reintubation rate reduction, the calculation is as follows

$$n1 = n2 = \left(\frac{Z\alpha\sqrt{2PQ} + Z\beta\sqrt{P1Q1 + P2Q2}}{P1 - P2}\right)^2$$

Description:
P1 (HFNC) = 0.37 (HFNC reintubation rate)
P2 (NIV) = 0.15 (NIV reintubation rate)
P1 - P2 = 0.25 (Difference to be detected)
Q1 = 1 - P1 = 1 - 0.37 = 0.63
Q2 = 1 - P2 = 1 - 0.15 = 0.88
P = (P1 + P2) / 2 = (0.37 + 0.17) / 2 = 0.245
Q = 1 - P = 1 - 0.245 = 0.755

$$n1 = n2 = \left(\frac{1{,}96\sqrt{2x0{,}245x0{,}755} + 0{,}84\sqrt{(0{,}37x0{,}63) + (0{,}12x0{,}88)}}{0{,}25}\right)^2$$

= 45.22 ~ 46 subjects

Similarly, when estimating the sample size based on the outcome of mortality reduction, the calculation is as follows:

$$n1 = n2 = \left(\frac{Z\alpha\sqrt{2PQ} + Z\beta\sqrt{P1Q1 + P2Q2}}{P1 - P2}\right)^2$$

Description:

P1 (HFNC) = 0.1 (Mortality rate with HFNC)
P2 (NIV) = 0.35 (Mortality rate with NIV)
P1 − P2 = 0.25 (The difference to be detected)
Q1 = 1 - P1 = 1 - 0.1 = 0.9

Q2 = 1 - P2 = 1 – 0,35 = 0,65
P = (P1 + P2) / 2 = (0.1 + 0,33) / 2 = 0,225
Q = 1 - P = 1 – 0,225 = 0,77

$$n1 = n2 = \left(\frac{1{,}96\sqrt{2x0{,}225x0{,}775} + 0{,}84\sqrt{(0{,}1x0{,}9) + (0{,}35x0{,}65)}}{0{,}25}\right)^2$$

= 42.54 ~ 43 subjek

Based on these calculations, the required **sample size is 51 subjects per group**, resulting in a total of **102 subjects** for both groups. Considering an **additional 10% to account for loss to follow-up**, the adjusted sample size is calculated as follows:
Additional subjects:
10%×102=10,2

Total subjects after addition:
102+10,2=112,2~113 subjek
57 subjects/group

Thus, this study requires **57 subjects per group**, with a total of **114 subjects.**

4.4. Inclusion and Exclusion Criteria

Inclusion Criteria:

- Patients under 18 years of age.
- Post-cardiac surgery patients in the CICU of RSUPN.
- Patients at high risk of extubation failure (e.g., young age, open sternotomy, mechanical ventilation >48 hours).
- Patients who pass the extubation readiness test and spontaneous breathing trial.

Exclusion Criteria:

- Diaphragmatic paralysis.
- Decreased consciousness.
- Neuromuscular disease.
- Pneumothorax without drainage.
- Airway obstruction.
- Patients with a tracheostomy.
- Unplanned extubation.
- Patient received PEEP >7 prior to extubation

4.5. Sample Size Estimation

The sample size calculation follows the formula for unpaired categorical analytical studies. Based on the literature, the extubation failure rate with HFNC is 17%, and the minimum significant difference in proportion is 25%. The estimated sample size for each group is 57 patients, with a total of 114 patients for both groups.

4.6. Sampling Method

Sampling is conducted consecutively from pediatric post-cardiac surgery patients who meet the inclusion criteria during the study period in the CICU of RSUPN Cipto Mangunkusumo. Subjects meeting the inclusion and exclusion criteria will be randomized into two intervention groups: the High Flow Nasal Cannula (HFNC) group and the Non-Invasive Ventilation (NIV) group, using a simple randomization method. Block randomization was employed to ensure balanced allocation between the intervention and control groups. Subject assignment within each block was conducted randomly using statistical software (e.g., SPSS or Excel), with allocation concealed from investigators involved in data collection to minimize potential bias.

4.7. Data Collection Technique

Data is collected through clinical observation and measurement of patients' respiratory parameters before and after therapy. A blood sample of 0.5–1.0 mL is taken one hour before and after therapy. Monitoring is conducted by a trained medical team, and data on extubation failure, vital parameters, and patients' clinical conditions are continuously recorded during hospitalization.

4.8. Data Analysis

Data will be processed using statistical software and analyzed through univariate and multivariate analyses.

- Univariate analysis will be used to describe subject characteristics.
- Multivariate analysis using binary logistic regression will be performed to identify factors influencing extubation failure.

4.9. The Research Flowchart includes input, process, output, and outcome components based on the achievement indicators.

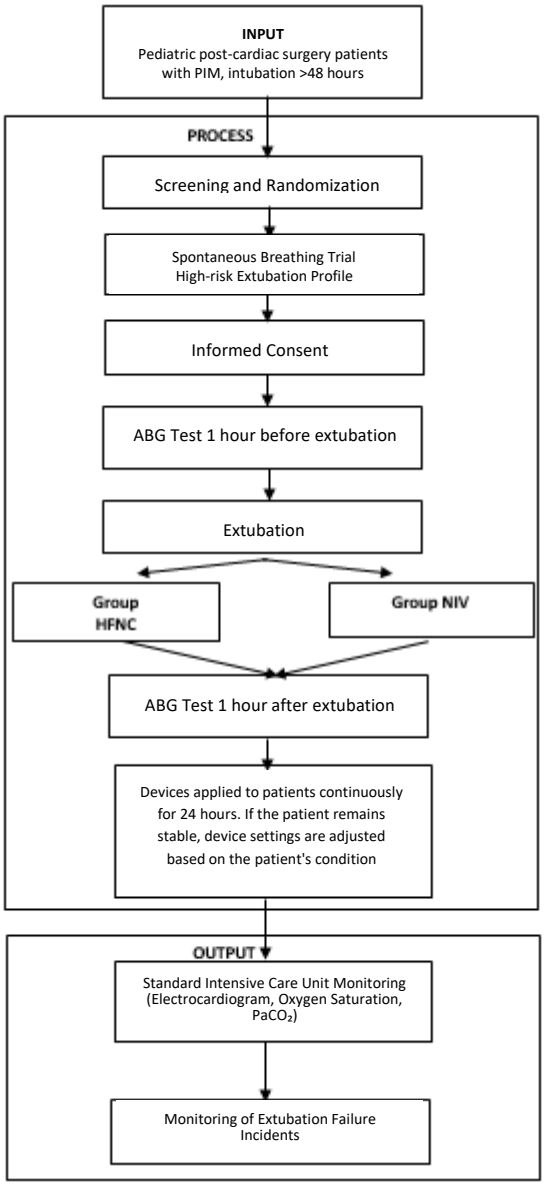

Image 3. Research Flowchart

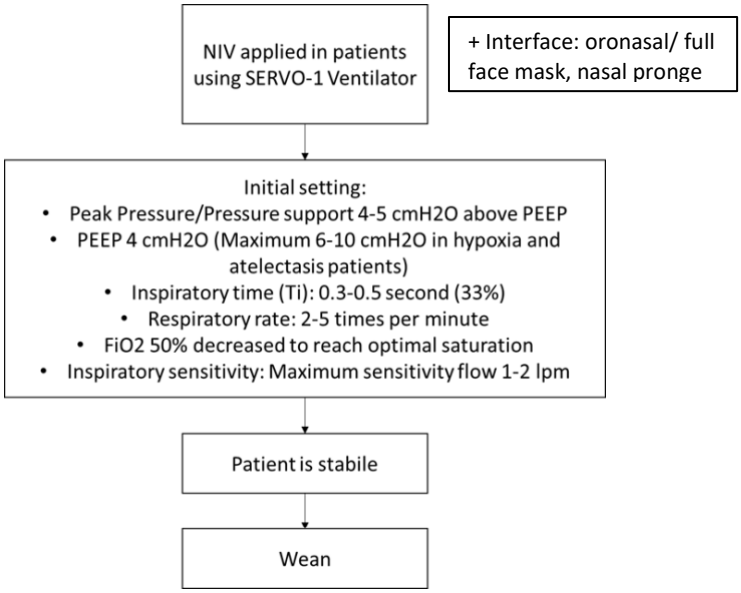

Image 4. NIV Group Procedure

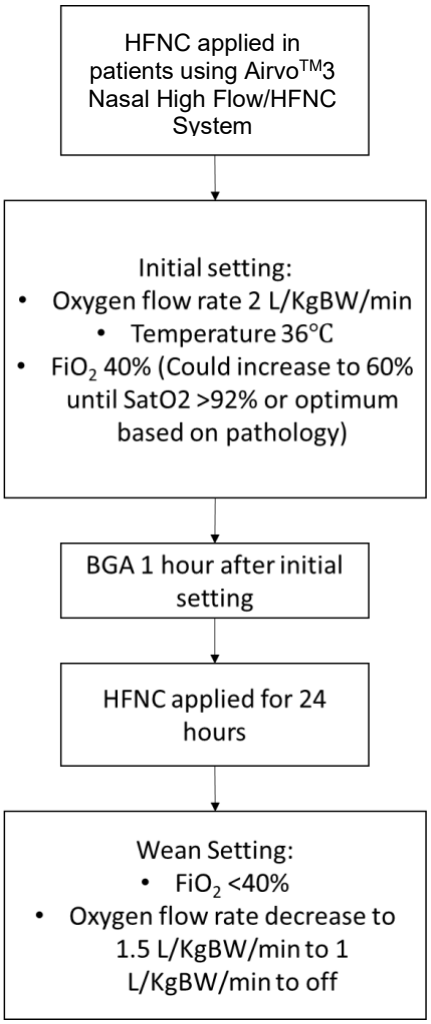

Image 5. HFNC Group Procedure

4.10. **Research Timeline**

No	Action Plan	Month										
		1	2	3	4	5	6	7	8	9	10	11
1.	Preparation and Ethical Approval Submission											
2.	Patient Recruitment and Randomization											
3.	Intervention Implementation (HFNC and NIV)											
4.	Data Collection and Monitoring											
5.	Data Analysis and Report Writing											

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