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Efeitos da cânula nasal de alto fluxo comparado com oxigenoterapia convencional após cirurgia cardíaca: uma revisão sistemática com metanálise de ensaios clínicos randomizados

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RESUMO

Introdução: As doenças cardiovasculares são a principal causa de morte em todo o mundo, sendo no Brasil responsável por quase um terço das mortes anuais. Quando necessário o tratamento precisa ser cirúrgico, no qual apresenta risco de desenvolver complicações pulmonares no pós-operatório, como hipoxemia e alterações na mecânica ventilatória, precisando do uso de dispositivos de oxigenoterapia para corrigir essa hipoxemia e evitar complicações maiores. **Objetivo**: Realizar uma revisão sistemática de ensaios clínicos randomizados que avalie os efeitos do cânula nasal de alto fluxo (CNAF) comparado a oxigenoterapia convencional em indivíduos após cirurgia cardíaca na taxa de reintubação, sensação de dispneia, conforto e tolerância da terapia, tempo de permanência na unidade de terapia intensiva e hospitalar, assim como mortalidade. **Métodos**: Trata-se de uma revisão sistemática de ensaios clínicos randomizados com metanálise, nas bases de dados PubMed, EMBASE, The Cochrane Library, e PEDro, com registro na plataforma PROSPERO. **Resultados**: Foram incluídos oito estudos, não sendo observado diferença na taxa de reintubação, sensação de dispneia, mortalidade, conforto e tolerância e no tempo de permanência de internação na unidade de terapia intensiva e hospitalar. **Conclusão**: Não houve superioridade do CNAF frente a oxigenoterapia convencional quando utilizados em indivíduos após cirurgia cardíaca.

Palavras-chave: Cirurgia cardíaca, Oxigenoterapia convencional, Revisão sistemática.

ABSTRACT

Introduction: Cardiovascular diseases are the main cause of death worldwide, being responsible for almost a third of annual deaths in Brazil. When necessary, the treatment needs to be surgical, where there is a risk of developing pulmonary complications in the postoperative period, such as hypoxemia and changes in ventilatory mechanics, requiring the use of oxygen therapy devices to correct this hypoxemia and avoid major complications. **Objective**: To execute a systematic review of randomized clinical trials that evaluates the effects of the High Flow Nasal Cannula (HFNC) compared to conventional oxygen therapy in individuals after cardiac surgery on the reintubation rate, sensation of dyspnea, comfort and tolerance of therapy, length of stay in the intensive care unit and hospital, as well as mortality. **Methods**: This is a systematic review of randomized clinical trials with meta-analysis, in the PubMed, EMBASE, The Cochrane Library, and PEDro databases, registered on the PROSPERO platform. **Results**: Eight studies were included, and no difference was observed in the reintubation rate, sensation of dyspnea, mortality, comfort and tolerance, and length of stay in the intensive care unit and hospital. **Conclusion**: There was no superiority of HFNC compared to conventional oxygen therapy when used in individuals after cardiac surgery.

Key words: Cardiac Surgical Procedures, Oxygen Inhalation Therapy, Systematic review.

LISTA DE ABREVIATURAS E SIGLAS

CEC	Circulação extracorpórea
CNAF	Cânula Nasal de Alto Fluxo
CRM	Cirurgia de revascularização do miocárdio
DCV	Doenças cardiovasculares
DCNT	Doenças Crônicas Não Transmissíveis
FiO_2	Fração inspirada de oxigênio
IRpA	Insuficiência Respiratória Aguda
L/min	Litros por minuto
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
UTI	Unidade de Terapia Intensiva

SUMÁRIO

1 CONTEXTUALIZAÇÃO

1.1 Doenças cardiovasculares

As doenças crônicas não transmissíveis (DCNT) constituem o principal grupo de causa de morte global, sendo responsáveis por perda de qualidade de vida, mortes prematuras, além de impactos econômicos e sociais. Estima-se que 45% de todas as mortes por DCNT no mundo, mais de 17 milhões, são causadas por doenças cardiovasculares (DCV) (OLIVEIRA et al., 2022).

As doenças cardiovasculares são um grupo de doenças do coração e dos vasos sanguíneos, dentre elas temos a doença coronariana, cerebrovascular, doença arterial periférica e cardiopatia congênita. Com o passar dos anos se observa um aumento na incidência de diagnóstico de doenças cardiovasculares, sendo a principal causa de morte em todo o mundo dos últimos anos (MENDIS S, PUSKA P; B, 2011). Mais de três quartos das mortes por doenças cardiovasculares ocorrem em países de baixa e média renda (OPAS/OMS, 2023). No Brasil, é responsável por quase um terço das mortes, afetando principalmente indivíduos com dificuldade no acesso a cuidados de saúde de qualidade (OLIVEIRA et al., 2022).

Os principais fatores de risco do desenvolvimento de um infarto agudo do miocárdio, de um acidente vascular cerebral, de insuficiência cardíaca ou outras complicações são idade avançada, hipertensão arterial, diabetes, hiperlipidemia, sedentarismo, obesidade, uso de álcool e tabagismo. Por isso, políticas de saúde que englobem o combate a alguns hábitos e a prevenção de complicações dessa doença são necessárias, promovendo e motivando a escolha de comportamentos saudáveis.

A abordagem terapêutica das doenças cardiovasculares pode ser clínica ou cirúrgica, tendo sempre como objetivo restabelecer a capacidade funcional do coração de forma a diminuir a sintomatologia e proporcionar ao indivíduo o retorno às suas atividades de vida diária (KOERICH et al., 2017).

Além de hábitos saudáveis, o controle medicamentoso das complicações deve ser realizado como prevenção secundária, fazendo uso de medicamentos como betabloqueadores, anti-hipertensivos, assim como o controle glicêmico e demais medicações necessárias para os sinais e sintomas da doença. Quando necessário a intervenção precisa ser cirúrgica, como a cirurgia de revascularização do miocárdio (CRM), angioplastia, reparação e substituição de válvula cardíaca, ou até o transplante cardíaco, tendo um maior custo para o sistema de saúde (OPAS/OMS, 2023).

1.2 Cirurgia cardiovascular

A maioria das cirurgias cardiovasculares têm a capacidade de alterar a história natural da doença em evolução, revertendo ou melhorando os efeitos que estão colocando em risco a vida do paciente, melhorando assim os sintomas, sua qualidade e a expectativa de vida.

No Brasil de 2008 a 2019, dos 1.280.840 procedimentos cardiovasculares cirúrgicos realizados, 755.411 (58,9%) foram angioplastias coronarianas, seguidas por 265.123 (20,1%) CRM e 151.902 (11,9%) cirurgias valvares. As hospitalizações para procedimentos cirúrgicos por DCV nesse mesmo período aumentaram 64%. Tendo um custo em média de R$7.036 em 2008 e com um aumento de 18% em 2019 (R$8.319) por procedimento. (OLIVEIRA et al., 2022) A taxa de mortalidade hospitalar entre pacientes submetidos a CRM em instituições públicas foi 7,0% (1.566 mortes em 22.537 procedimentos) em 2008 e 6,1% (1.432 em 23.488 admissões) em 2019 (SIM/DATASUS, 2021).

As comorbidades clínicas dos indivíduos no pós-operatório de cirurgia cardíaca são a complexidade da intervenção cirúrgica, a necessidade de internação em unidade de terapia intensiva (UTI), as complicações no pós-operatório, as infecções e as questões sociais que podem prolongar o tempo de internação hospitalar (REIS et al., 2019).

Indivíduos que realizam cirurgia na região do tórax apresentam risco de desenvolver complicações pulmonares no pós operatório (HUANG et al., 2017).

A etiologia dessas complicações é multifatorial. Fatores pré-existentes como tabagismo e presença de outras doenças, somadas com o uso de circulação extracorpórea (CEC), tempo de cirurgia, uso de anestesia, tempo de ventilação mecânica, manipulação na região pleural e na região do nervo frênico, além de dor na região da ferida operatória e nos drenos, corroboram para o desenvolvimento dessas complicações (HUFFMYER; GROVES, 2015; PIECZKOSKI; MARGARITES; SBRUZZI, 2017).

A necessidade e o tempo de uso de CEC durante a cirurgia é um fator importante, pois aumenta o processo inflamatório sistêmico e, também predispõe a complicações respiratórias, a necessidade do uso do balão intra-aórtico e de medicações para manter a estabilidade hemodinâmica. O seu uso também tem relação com a diminuição da complacência pulmonar, hipertensão vascular pulmonar e alterações na permeabilidade alvéolo-capilar devido a essa resposta inflamatória sistêmica (DE ASSIS et al., 2020). O indivíduo durante a cirurgia precisa ser submetido a sedação e a intubação orotraqueal, permanecendo com aparelho de ventilação mecânica até o pós-operatório, sendo extubado quando condições, considerando um nível de sensório capaz de obedecer a comandos e capacidade de ventilar de forma espontânea, o que ocorre normalmente em menos de 24 horas do pós-operatório. (DE ASSIS et al., 2020; LAIZO; DELGADO; ROCHA, 2010).

Uma complicação que pode ocorrer na incisão cirúrgica, na esternotomia realizada, é a contaminação da ferida operatória. A mediastinite é uma infecção dos tecidos profundos podendo estar associada à osteomielite do esterno, podendo acometer também o espaço retroesternal. (LAIZO; DELGADO; ROCHA, 2010). Os drenos de tórax também acarretam alterações da mecânica ventilatória, por atingirem músculos intercostais e a pleura parietal faz com que haja modificações nos volumes pulmonares, podendo alterar a troca gasosa e aumentar o desconforto do indivíduo. (DE ASSIS et al., 2020).

O período pós-operatório pode ter diversos riscos, como a ocorrência de arritmias, instabilidade hemodinâmica inesperada e sangramentos que necessitem de re-intervenção cirúrgica (LIMA et al., 2004). As principais complicações pulmonares são pneumonia, edema pulmonar e insuficiência respiratória aguda (IRpA). Como consequência há um aumento da diferença de pressão de oxigênio alvéolo-arterial e shunt intrapulmonar, além de diminuir a capacidade residual funcional e interferir na mecânica pulmonar, como na redução da complacência pulmonar. Também há um aumento no processo inflamatório e formação de edema pulmonar (NG et al., 2002).

Outra complicação comum entre os indivíduos que passam por cirurgia cardíaca são áreas com atelectasias, podendo levar a piora da hipoxemia, depressão do sistema respiratório e circulatório, aumentando a ocorrência de eventos adversos (HUFFMYER; GROVES, 2015; NG et al., 2002). Então, para evitar possíveis complicações, pode ser necessário oferecer oxigenioterapia para esses indivíduos.

Se após a retirada do ventilador mecânico o indivíduo permanecer estável clinicamente ventilando de forma espontânea por mais de 48 horas é considerado sucesso na extubação (DE ASSIS et al., 2020). Porém após o procedimento cirúrgico e a saída do indivíduo da ventilação mecânica a hipoxemia é uma das maiores causas de falha de extubação (HUANG et al., 2017), que está associada a maior tempo de permanência de internação na UTI e hospitalar, maiores custos e recursos utilizados, e também ao maior risco de morbidade e de mortalidade (DE ASSIS et al., 2020; KOTFIS et al., 2018; WASEEM et al., 2015).

É preciso identificar as possíveis falhas a fim de promover uma melhor assistência, minimizando perdas funcionais, incapacidades e complicações, otimizando a abordagem e o tratamento desse indivíduo e assim, reduzindo custos para o sistema de saúde. Para resolver esse problema é necessário o uso de algum dispositivo de oxigenoterapia de baixo ou alto fluxo, associados ou não com pressões positivas, para manter a via aérea do paciente pérvia e corrigir a hipoxemia, a fim de evitar uma possível reintubação, que poderá provocar mais efeitos deletérios ao indivíduo (DE ASSIS et al., 2020; WASEEM et al., 2015).

1.3 Oxigenoterapia convencional

A exposição repentina a níveis baixos de saturação arterial de oxigênio pode causar comprometimento do funcionamento neurológico. O cérebro é o órgão mais sensível aos efeitos adversos da hipóxia, mas outros órgãos em indivíduos com doença crítica também podem ser vulneráveis ao risco de lesão tecidual por hipóxia. (O'DRISCOLL et al., 2017)

A necessidade de suplementar com oxigênio se dá em indivíduos com hipoxemia aguda, sendo preciso o uso de oxigenoterapia para garantir uma saturação alvo necessária para a funcionamento dos sistemas do corpo humano. O oxigênio deve ser prescrito para atingir normalmente uma saturação alvo de 92 a 98% ou superior a 88% para indivíduos específicos com risco de insuficiência respiratória hipercápnica (O'DRISCOLL et al., 2017). O uso de oxigênio em excesso é prejudicial a saúde, aumentando o risco de mortalidade (O'DRISCOLL et al., 2017; PIRAINO et al., 2022; SIEMIENIUK et al., 2018).

Existem diversos dispositivos para oferta de oxigenoterapia. A escolha pelo óculos nasal ou pelo cateter nasal se dá pela necessidade de baixo fluxo de oxigênio, de 1 a 6L/min, já a máscara facial pode fornecer de 6 a 10 L/min de oxigênio. Quando necessário fluxos maiores de 10 a 15L/min há a opção de uso de máscara não reinalante ou também o uso de máscara de Venturi, que pode oferecer de 24 a 60% de FiO_2, equivalendo de 3L/min a 15L/min (O'DRISCOLL et al., 2017; PIRAINO et al., 2022). Sendo necessário titular o nível de oxigênio e o dispositivo de oferta conforme indicação, sinais como saturação periférica, frequência respiratória, gasometria e a tolerância do indivíduo.

A umidificação não é necessária para o fornecimento de oxigênio de baixo fluxo ou para o uso de oxigênio de alto fluxo por curto prazo. A literatura mostra como indicado usar oxigênio umidificado para indivíduos que necessitam de sistemas de oxigênio de alto fluxo por mais de 24 horas ou que relatam desconforto nas vias aéreas superiores devido ao ressecamento provocado pelo seu uso (O'DRISCOLL et al., 2017).

1.4 Cânula nasal de alto fluxo (CNAF)

Com o objetivo de melhorar a oxigenação, o uso da terapia por cânula nasal de alto fluxo tem crescido cada vez mais e tem sido mostrado benefícios quanto a maior tolerância e conforto para os indivíduos. Ela consiste em aplicação de gás aquecido, com temperatura entre 31-37°C, e umidificado, com fluxo máximo de até 60L/min e concentração de oxigênio (fração inspirada de oxigênio - FiO_2) de 21 a 100%, através de uma pronga nasal (HUANG et al., 2017; ROCA et al., 2016).

Comparado com o uso de métodos de ofertas convencionais de oxigênio, além de gerar uma FiO_2 constante durante o pico de fluxo inspiratório ele apresenta a vantagem de geração de um baixo nível de pressão positiva contínua na via aérea, com aumento do volume pulmonar expiratório final. Pode também aumentar a razão da relação entre pressão arterial parcial de oxigênio e fração inspirada de oxigênio (SPOLETINI et al., 2015), por ser umidificado e aquecido pode promover o movimento mucociliar e melhorar a eliminação de secreções, assim como reduzir a resistência das vias aéreas superiores reduzindo o trabalho respiratório, melhorando a sincronia tóraco-abdominal, podendo diminuir o espaço morto e melhorar a troca gasosa, e também o conforto do indivíduo (HAYAMI, H. et al., 2013; HERNÁNDEZ et al., 2016; RIERA et al., 2013; WANG et al., 2021).

Os efeitos positivos do uso de CNAF têm sido documentados na literatura, com o uso em paciente em insuficiência respiratória aguda, pré e pós intubação, em cirurgia cardíaca, em doenças crônicas como doença pulmonar obstrutiva crônica, e em paciente em cuidados paliativos para maior conforto. Tendo resultados na melhora da oxigenação, na diminuição da dispneia, maior conforto, diminuindo a taxa de intubação, melhorando aspectos hemodinâmicos, diminuindo a falha de extubação e, por consequência, diminuindo o tempo de internação na unidade de terapia intensiva e hospitalar (ROCA et al., 2016).

Por ainda ser uma terapia de alto custo ao hospital e ao paciente, mas cada vez mais utilizada é necessário que haja uma avaliação de profissionais qualificados para indicar e iniciar o uso da terapia no momento correto, também sendo necessário equipes treinadas para manusear e manter o melhor funcionamento do dispositivo. Com cuidados desde a montagem e manutenção do aparelho, assim como do posicionamento adequado da pronga nasal na narina, do posicionamento da traqueia para evitar acúmulo de água no circuito, da troca da água destilada que compõem o circuito e o controle da temperatura para manutenção da umidificação e do aquecimento do gás inalado pelo indivíduo, buscando garantir a efetividade do uso e o conforto do indivíduo.

Por isso, com o risco de falha de extubação após o procedimento de cirurgia cardíaca, faz com que seja preciso analisar evidências que auxiliem a busca de alternativas para melhor tratar esses indivíduos e ter um desfecho positivo, diminuindo o tempo de internação e suas as possíveis complicações. Sendo necessário pesquisar os efeitos da terapia com CNAF nessa população, com o intuito de melhorar a oxigenação.

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2 OBJETIVOS

2.1 Objetivo Geral

Verificar os efeitos da oxigenoterapia com CNAF comparado com oxigenoterapia convencional na taxa de reintubação de indivíduos após cirurgia cardíaca.

2.2 Objetivos Específicos

- Verificar a taxa de mortalidade desses indivíduos, comparando CNAF com oxigenoterapia convencional.

- Comparar o tempo de permanência na UTI e de internação hospitalar entre o grupo CNAF e o que recebeu oxigenoterapia convencional.

- Identificar a taxa de sensação de conforto e tolerância das terapias entre os grupos.

- Avaliar a sensação de dispneia desses indivíduos que realizaram cirurgia cardíaca e usaram CNAF e oxigenoterapia convencional.

3 ARTIGO 1

Effects of high-flow nasal cannula therapy compared to conventional oxygen therapy after cardiac surgery: a systematic review and meta-analysis of randomized controlled trials.

(Formatado conforme normas do periódico Arquivos Brasileiros de Cardiologia – *Qualis B1, Fator de Impacto: 1.679*)

Efeitos da cânula nasal de alto fluxo comparado com oxigenoterapia convencional após cirurgia cardíaca: uma revisão sistemática com metanálise de ensaios clínicos randomizados

Effects of high-flow nasal cannula therapy compared to conventional oxygen therapy after cardiac surgery: a systematic review and meta-analysis of randomized controlled trials

Descritores: Cirurgia cardíaca, Oxigenoterapia, Revisão sistemática.

Keywords: Cardiac Surgical Procedures, Oxygen Inhalation Therapy, Systematic Review.

Número de palavras do manuscrito: 2935

Abstract

Backgroud: Individuals in the postoperative period of cardiac surgery are at greater risk of developing pulmonary complications.

Objective: To systematically review the effects of high-flow nasal cannula (HFNC) oxygen therapy compared to conventional oxygen therapy (COT) on patients after cardiac surgery on reintubation rate, dyspnea score, comfort, tolerance, length of stay in the intensive care unit, hospital length of stay and mortality.

Methods: Searches in PubMed, EMBASE, The Cochrane Library, and PEDro databases until March 2022 included randomized controlled trials that evaluated the effect of HFNC in individuals after cardiac surgery compared with COT. In addition, the risk of bias was assessed using the RoB 2.0 tool.

Results: Eight studies were included, totaling 1086 individuals. Compared with COT, the HFNC showed no difference in reintubation rate, dyspnea score, comfort and tolerance, length of stay in the ICU and hospital, and mortality. The meta-analyses did not show superiority between any of the interventions [MD = 1.17; CI 95%(0.28-4.85), I^2 27%] on reintubation rate, on length of ICU stay [MD= 0.02; CI=95%(-0.14-0.18), I^2 11%], hospital stay [MD= -0.23; CI=95% (-1.14-0.67), I^2 71%] and mortality [MD= 1.34; CI=95% (0.36-5.02), I^2 5%]. Three studies showed some concerns about the risk of bias.

Conclusion: After cardiac surgery, the HFNC has no superiority compared to the use of COT for reintubation rate, dyspnea score, comfort and tolerance, length of stay in the ICU and hospital, and mortality.

Introduction

Individuals in the postoperative period of cardiac surgery are at greater risk of developing pulmonary complications [1]. The etiology of these complications is multifactorial. Pre-existing factors such as smoking and the presence of other diseases added to the use of cardiopulmonary bypass, surgery time, use of anesthesia, mechanical ventilation duration, manipulation in the pleural and in the phrenic nerve region, in addition to pain in the wound surgery and drains, corroborate to the development of these complications [2,3]. The main pulmonary complications are pneumonia, pulmonary edema, and acute respiratory failure (ARF). Hypoxemia is a major cause of extubation failure [1], associated with extended hospital stays and increased mortality risk.

To improve oxygenation, high-flow nasal cannula (HFNC) oxygen therapy has grown increasingly and has shown benefits in terms of greater tolerance and comfort. The device offers the application of heated gas, with a temperature between 31-37°C, and humidified, with a maximum flow of up to 60L/min and oxygen concentration (FiO_2) of 21 to 100%, through a nasal prong. Compared with the use of conventional oxygen therapy (COT) methods, in addition to generating a constant FiO_2 during peak inspiratory flow, it has another advantage, which is the generation of a low level of continuous positive pressure in the airway, leading to an increase in end-expiratory lung volume, a reduction in the work of breathing, decreasing dead space and improving gas exchange and comfort [4–6].

Hernandés et al. [5] in a randomized clinical trial, showed that the use of HFNC compared with COT reduced the risk of reintubation within 72 hours in individuals classified as low risk of reintubation admitted to the ICU, according to criteria such as age, not obese, absence of pulmonary disease and heart failure. Also, Huang et al.[1], in a systematic review with meta-analysis, showed that compared to COT, HFNC might reduce reintubation rates in critically ill individuals with acute respiratory failure under a longer duration of mechanical ventilation but not in postoperative patients.

Considering the lack of evidence of the use of HFNC in individuals after cardiac surgery, this study aimed to answer through a systematic review of randomized clinical trials, the following question: Does the use of high flow nasal cannula compared to conventional oxygen therapy reduces the respiratory failure and need for reintubation in individuals in the postoperative period of cardiac surgery?

Methods

This systematic review of randomized clinical trials (RCTs) with meta-analysis was performed following the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines [7]. In addition, the protocol was registered on PROSPERO (CRD42022308728).

Data sources and search strategy

Two investigators independently performed study searching, screening, and identification. Articles published before March 2022 were searched from PubMed, EMBASE, The Cochrane Library - Cochrane Central Register of Controlled Trials (CENTRAL), Physiotherapy Evidence Database (PEDro). Besides, a manual search was performed in the bibliographic references of already published studies.

The search terms included “Cardiac Surgical Procedures”, “Thoracic Surgery”, “Coronary Artery Bypass”, “Oxygen Inhalation Therapy,” and “High Flow Nasal Cannula.” There were no language or publication date restrictions. The complete search strategy is available in Table 1.

Selection of studies

The RCTs that evaluated the use of HFNC compared to COT in adult subjects in the postoperative period of cardiac surgery were included. Studies with the following characteristics were excluded: pediatric studies, guidelines or conference abstracts, case reports, and inconsistent inclusion criteria.

The primary outcome was therapy failure and, consequently, reintubation. The secondary outcomes included dyspnea score, comfort, tolerance, length of stay in the intensive care unit, hospital length of stay, and mortality.

The reintubation rate was measured according to failure and the patient's need to return to invasive mechanical ventilation. The dyspnea score was evaluated using the modified Borg scale (0 = no dyspnea, 10 = maximal dyspnea) [8] and using categories such as improvement, no improvement, and deterioration of the dyspnea sensation. The comfort and tolerance were assessed in different ways, using the Visual Analogue Scale (VAS) [9], also using a score from not comfortable (zero) to extremely comfortable (ten), and a visual satisfaction scale from very poor (one) to very good (five).

The length of stay in the intensive care unit and the hospital was evaluated by the number of days that the individuals remained in the ICU and the total hospital stay. To assess the mortality rate, deaths were counted during ICU stay and up to 28 days after surgery. All identified publications were inserted into software for managing references, and duplicates were excluded. Initially, studies were selected by titles and abstracts by two independent reviewers (JSP and JBF). Abstracts that did not provide sufficient information for eligibility at this stage were selected for full-text evaluation, which was also performed independently by peers (JSP and JBF). Disagreements between the two phases of study selection were discussed, and if there was no consensus, a third reviewer was consulted (PD).

Data extraction and risk of bias assessment

After selecting the studies, the reviewers (JSP and JBF) extracted the data in a standardized form. Variables such as author and year of publication, population, sample size, gender and age, comparator group, type and protocol of intervention, outcomes of interest, and instruments for measuring outcomes were collected.

We assessed the methodological quality of the study using the "Risk of Bias Toll for Randomized Trials" (RoB 2.0) scale of the Cochrane collaboration for RCTs, in which the following items are considered: "Randomization process"; "Deviations from intended interventions"; "Missing outcome data"; "Measurement of the outcome"; "Selection of the reported result". The quality of each item was categorized into "low risk of bias", "high risk of bias" or "some concerns" and, then, an overall score was given for each outcome assessed [10].

Data synthesis and analysis

Data analysis was performed descriptively. And when possible, data were grouped with the aid of a meta-analytical approach. The data were combined using the random effect meta-analysis model, with the DerSimonian–Laird estimator as variance estimator, and the results were presented as mean difference (MD) and risk ratio (RR) with a 95% confidence interval (95%CI). A value of $p<0.05$ was considered significant. Statistical heterogeneity was assessed in each meta-analysis using the I2 statistics. All analyses were performed by using the R statistical software, version 3.5.2.

Results

Description of studies

Initially, 4,632 studies were found, of which eight met the eligibility criteria and were included. The eight studies were included in the meta-analysis. Figure 1 shows the flowchart of the selection of studies, and Table 2 the characteristics of these studies. It totaled 1,086 individuals, 70% men with a mean age superior of 60 years old. The most common cardiac procedure was coronary artery bypass graft surgery (CABG) (67%), followed by valve replacement, the association of CABG and valve replacement, and other surgeries.

Risk of bias assessment

According to the RoB 2.0 tool, for the randomization process, two studies presented “some concerns” in the outcomes evaluated [11,12]. However, all studies included in this systematic review showed a low risk of bias for the “deviations from intended intervention,” “missing outcome data,” and “measurement of the outcome” categories. For the domain “selection of the reported result,” three studies were considered as “some concerns” [11–13]. The overall showed "some concerns" for these same three studies. The assessment of the risk of bias is fully presented in figure 2.

Effects of the intervention

Reintubation Rate

Eight studies [11–18] reported a reintubation rate with 1086 individuals. The meta-analysis performed with these articles did not show superiority between any of the interventions [MD = 1.17; CI 95%(0.28-4.85), I^2 27%] (Figure 3A). Four studies [12,14,15,18] did not need reintubation in HFNC and COT groups.

Three studies showed a higher rate in the HFNC group, in the report by Parke et al. [16], the number of individuals who needed to be intubated was two for the HFNC group and zero for COT. Theologou et al. [17] had seven individuals in the HFNC groups [Group 1 (G1): HFNC with a gas flow of 60L/min and Group 2 (G2) with 40L/min] and two in the COT. Also, Vourc'h et al. [13] reported three individuals in HFNC and one in the COT group. Meantime, Sahin et al. [11] showed a higher rate in the COT group, being none to HFNC and four for COT.

Dyspnea Score

Two studies [11,15] reported the data of dyspnea scores with a sample size of 255 individuals. The study of Sahin et al. [11] used a classification of improvement, no improvement, or deterioration to classify the dyspnea score. The score was better in the HFNC group on days one and two after surgery (gain of 38% in COT and 62% in HFNC, p < 0. 001 and 54% of COT and 82% of HFNC, p < 0. 001). Corley et al. [15] evaluated the dyspnea score using the Borg scale after 1 and 8 hours post-extubation. They showed a very low score in both groups, being at 8 hours post-extubation 0 (none) to COT and 1 (very slight) to HFNC group (p = 0.008), having statistical significance, but this difference is not clinically relevant.

Comfort and tolerance

Comfort and tolerance were assessed by four studies [11,13,16,17] (678 subjects), which were evaluated using the visual analog scale or quantified numerically by the study researchers. Theologou et al. [17] showed similar scores between the COT and HNFC groups, using a visual analog scale to assess [G1: 7.9 (7.6-8.2), G2: 7.6 (7.3-7.9) and COT 7.5 (7.2-7.7)].

Three studies using different types of scores showed better results for comfort and tolerance with the HFNC group. Parke et al. [16] assessed comfort and tolerance numerically, rating 0 for not comfortable and 10 for highly comfortable. Theirs results showed a lower score in the HFNC group comparing with COT on days 1 and 2 after surgery ($p < 0.001$). In twenty individuals of the HFNC group (11,8%), the lack of tolerability caused early removal, with excess heat being the mean issue.

Sahin et al. [11] used a comfort score (from 1 - very poor to 5 - very good) and showed that individuals with HFNC were better on days one and two postoperative (p=0.002 and p=0.001). Also, Vourc'h et al. [13] used a scale from 1 to 5 at ICU discharge, the occurrence of nasal bleeding, and mucus dryness during oxygen therapy (considered if the patient declared dry mouth, nose, or throat). Their results reported a better score for the HFNC group (p = 0.0002), highlighting the sensation of mucus dryness, 40% in the HFNC versus 71% in the COT (p=0.003).

ICU length of stay (days)

Eight studies [11–18] reported ICU length of stay, with 1086 individuals, all included in the meta-analysis [MD= 0.02; CI=95%(-0.14-0.18), I^2 11%] (Figure 3B).

In the report by Burra et al. [14], the ICU length of stay was shorter in the HFNC group compared to the COT (3.41±1.42 vs. 3.76±1.31; p= 0.67). However, Parke et al. [16] reported a shorter stay in COT than HFNC (1.2±1.0 vs. 1.39±0.95, respectively; p= 0.08). The same was shown by Sahin et al. [11] (2.4 ± 0.5 vs. 2.8 ± 1.7; p= 0.13), Theologou et al. [17] (2.29±1.08 vs. 2.2±1.40 and 2.7±1.14) and by Vourc'h et al. [13] (3.1±1.6 vs. 3.3±2.4; 0.64).

Tatsuishi et al. [12] reported 1±0 for both groups (p= 0.65). As well as Corley et al. [15] (COT 1.61±0.99 vs. HFNC 1.61±1.46, p= 0.99), and Zochios et al. [18] (1±0.74 in both groups; p= 0.94).

Hospital length of stay (days)

Hospital length of stay was reported in five [11,12,16–18] of the included studies, 781 individuals, all included in the meta-analysis [MD= -0.23; CI=95% (-1.14-0.67), I^2 71%], the result was not statistically significant (Figure 3C).

Parke et al. [16] reported that the hospital length of stay was shorter in the COT group compared with the HFNC (11.4±6.7 vs. 11.6±6.6; p= 0.82). The same was seen by Theologou et al. [17] (7.0±2.6 vs. 9.0±3.7 and 8.0±2.9).

Three studies showed better results with the HFNC group compared with COT, Sahin et al. [11] (6.5 ± 0.7 vs. 6.9 ± 1.1; p= 0.03), Tatsuishi et al. [12] (8.0±2.2 vs. 9.0±3.7 p= 0.05) and Zochios et al. [18] (7.0±2.2 vs. 9±6.6 p= 0.01).

Mortality

Mortality was reported in six studies [11,13,14,16–18], with 783 individuals, all included in the meta-analysis [MD= 1.34; CI=95% (0.36-5.02), I^2 5%] (Figure 3D). Two studies had no deaths during the analysis [13,14]. Parke et al. [16] and Zochios et al. [18] reported one death in each group. Sahin et al. [11] showed only two deaths in the COT group. And the mortality rate in the report of Theologou et al. [17] was 9 in the HFNC groups and 1 in the COT group.

Discussion

This systematic review with metanalyses showed that, compared to COT, HFNC did not reduced the reintubation rate in individuals after cardiac surgery. Also, there was no significant difference between in the ICU and hospital length of stay. The same is observed in mortality rates and dyspnea scores.

Extubation failure and the need for reintubation increase the risk of complications during the hospital stay and also increases the risk of mortality [19]. In our analyses, the use of HFNC was not shown to be more effective in reducing the reintubation rate. In previous studies, including a systematic review with metanalyses with only obese individuals after cardiac surgery and others that evaluated postoperative individuals with acute respiratory failure, they found similar data when comparing COT and HFNC [1,20].

In this systematic review, two studies assessed dyspnea. Corley et al. [15] used the Borg scale, measured at one and eight hours post-extubation, and showed no improvements in dyspnea scores. In the meantime, Sahin et al. [11] evaluated the dyspnea by categories such as improvement, no improvement, and deterioration. They showed that the scores were significantly better in the HFNC group after the first and second days of surgery. The same was observed by Rittayamai et al. [21] in a randomized crossover study with individuals who were extubated after using mechanical ventilation. They showed that HFNC significantly improved dyspnea.

Individuals that use HFNC have better adherence due to comfort and tolerance to this therapy [1], with its interface that allows the individual to eat and minimizes the occurrence of skin lesions and symptoms of airways dryness [5,22,23]. In a qualitative analyses, three studies [11,13,16] of this systematic review showed better results in the HFNC groups compared with COT for comfort and tolerance. However, due to the different means used to assess this outcome, further studies with a standardization are necessary for a better comparison between them.

Compared with COT, the use of HFNC did not significantly change the ICU and hospital length of stay, with the same results found in previous studies with the same population [20,24]. The same was observed for mortality. The systematic review with metanalyses by Lu et al. [25] with postoperative individuals also showed that HFNC did not reduce mortality.

We found that most studies included in the present review had a low risk of bias. However, three were classified as having some concerns because of the randomization process and selection of the reported results. Although there are some concerns in the included RCTs and the risk of bias is low, this systematic review summarized the panorama of the use of HFNC and COT for individuals after cardiac surgery, making it possible to guide the application of the techniques. Therefore, this highlights the need for greater clarity in the methodological report.

This systematic review has some limitations; first, the heterogeneity of the studies, with different intervention protocols; second, the small number of included RCTs making it difficult to reach definitive conclusions; third, the data that were not represented by the mean and standard deviation, we used the formula conversion, which may have affected the accuracy of the data. Thus, better-designed RCTs with larger sample sizes are needed to strengthen these findings and demonstrate the best recommendation for each technique.

Conclusion

This systematic review and metanalyses showed that for individuals after cardiac surgery, the HFNC has no superiority compared to the use of COT for reintubation rate, dyspnea score, comfort and tolerance, length of stay in the ICU and hospital, and also mortality. More clinical trials are need to define the best use of the CNAF, in addition to when to start and which population should benefit from this therapy.

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Table 1. Research strategy used on PubMed

#1	"Cardiac Surgical Procedures" [MeSH] OR "Cardiac Surgical Procedures" OR "Procedure, Cardiac Surgical" OR "Procedures, Cardiac Surgical" OR "Surgical Procedure, Cardiac" OR "Surgical Procedures, Cardiac" OR "Surgical Procedures, Heart" OR "Cardiac Surgical Procedure" OR "Heart Surgical Procedures" OR "Procedure, Heart Surgical" OR "Procedures, Heart Surgical" OR "Surgical Procedure, Heart" OR "Heart Surgical Procedure"
#2	"Thoracic Surgery" [MeSH] OR "Thoracic Surgery" OR "Surgery, Thoracic" OR "Surgery, Cardiac" OR "Surgery, Heart" OR "Heart Surgery" OR "Cardiac Surgery"
#3	"Coronary artery bypass" [MeSH] OR "Coronary artery bypass" OR "Artery Bypass, Coronary" OR "Artery Bypasses, Coronary" OR "Bypasses, Coronary Artery" OR "Coronary Artery Bypasses" OR "Coronary Artery Bypass Surgery" OR "Bypass, Coronary Artery" OR "Aortocoronary Bypass" OR "Aortocoronary Bypasses" OR "Bypass, Aortocoronary" OR "Bypasses, Aortocoronary" OR "Bypass Surgery, Coronary Artery" OR "Coronary Artery Bypass Grafting"
#4	#1 OR #2 OR #3
#5	"Oxygen Inhalation Therapy" [MeSH] OR "Oxygen Inhalation Therapy" OR "Inhalation Therapies, Oxygen" OR "Inhalation Therapy, Oxygen" OR "Oxygen Inhalation Therapies" OR "Therapies, Oxygen Inhalation" OR "Therapy, Oxygen Inhalation"
#6	"High Flow Nasal Cannula"
#7	"High Flow Oxygen"
#8	"High Flow; Nasal Cannula"
#9	"High Flow Oxygen Therapy"
#10	"High flow nasal cannula therapy"
#11	#5 OR #6 OR #7 OR #8 OR #9 OR #10
#12	(randomized controlled trial [pt] OR controlled clinical trial [pt] OR randomized controlled trials [mh] OR random allocation [mh] OR double-blind method [mh] OR single-blind method [mh] OR clinical trial [pt] OR clinical trials [mh] OR ("clinical trial"[tw]) OR ((singl*[tw] OR doubl*[tw] OR trebl*[tw] OR tripl*[tw]) AND (mask*[tw] OR blind*[tw])) OR ("latin square"[tw]) OR placebos [mh] OR placebo*[tw] OR random*[tw] OR research design [mh:noexp] OR comparative study [mh] OR evaluation studies [mh] OR follow-up studies [mh] OR prospective studies [mh] OR crossover studies [mh] OR control*[tw] OR prospectiv*[tw] OR volunteer*[tw]) NOT (animal [mh] NOT human [mh])
#13	#4 AND #11 AND #12

Figure 1 – Flowchart of study selection

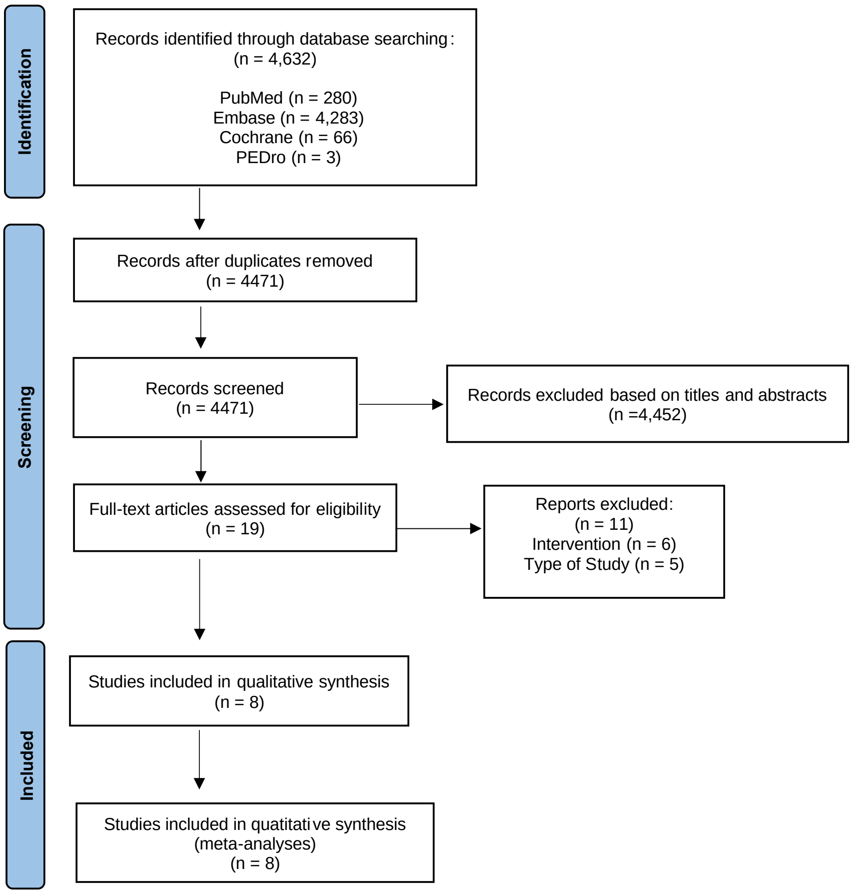


Table 2. Characteristics of included studies

Author, year	Participants (type of surgery)	Intervention	Protocol	Sample	Gender % (M/F)	Age (years) (mean + SD) or median (range)	Primary outcome	Other outcomes(s)
Burra et al., 2021	Elective cardiac surgery - CABG (off pump), MVR, AVR, DVR	HFNC	60 liters/min	30	73.3/26.6	50.6±15.6	Gas exchange (paO2, paCo2) after 1, 2, 4 hours of extubation	Incidence of reintubation, ICU length of stay, ventilation duration, mortality
		COT	Nasal cannula with 4 L/min.	30	70/30	52.5±13.9		
Corley et al., 2015	Scheduled cardiac surgery on cardiopulmonary bypass with BMI ≧ 30 kg/m2	HFNC	Post extubation; Flow commenced at 35 L/min and was titrated to a maximum of 50 L/min, FiO2 to mantain SpO2 ≧ 95%	81	72/28	63 ± 11.4	The degree of atelectasis on chest X-ray	Oxygenation, respiratory rate, dyspnoea score, reintubation rate and ICU length of stay
		COT	Post extubation; 2–4 L/min via nasal cannulae or 6 L/min via simple face mask to mantain SpO2 ≧ 95%	74	76/24	65 ± 11.1		
Parke et al., 2013	Elective cardiac surgery utilizing cardiopulmonary bypass	HFNC	Flow rate of 45 L/min, FiO2 to SpO2 > 93%	169	76.3/23.5	65 (19–88)	The number of patients with a SpO2 /FIO2 ratio of ≥445 on Day 3 after surgery—reflecting a SpO2 on air of > 93%	Atelectasis score of chest X-rays, spirometry, readmission to ICU, ICU and hospital length of stay, mortality and incidence of respiratory complications, use of adjunctive respiratory support therapies, reintubation rate and patient comfort
		COT	2–4 L/min via simple facemask or nasal prongs to maintain a SpO2 of > 93%	171	75.4/24.6	66 (21–87)		
Sahin et al., 2018	CABG with BMI > 30 kg/m2	HFNC	Preliminary flow rate was 25–40 L/min, and the initial FiO2 was 50% to maintain SpO2 > 93%	50	64/36	62.0 ± 6.7	Atelectasis Scoring (radiological atelectasis score system)	Reintubation, length of ICU and hospital stay, respiratory complications, mortality, dyspnea and comfort scores
		COT	Simple face mask with a flow of 2–4 L/min to maintain SpO2 > 93%	50	64/36	61.3 ± 8.5		
Tatsuishi et al., 2020	Offpump CABG	HFNC	45–60 L/min and 21–35% FIO2	72	79.2/20.8	69 ± 7	Percentage of lung volume loss	Total amount of oxygen administered, the duration of oxygen inhalation therapy, reintubation rate, length of ICU and hospital stay and patient comfort
		COT	3–12 L/min and 100% oxygen via a standard oxygen mask with humidification	76	73.7/26.3	69 ± 10		
Theologou et al., 2021	Elective or urgent cardiac surgery	HFNC 1	Initial FiO2 = 0.6 and gas flow = 60 L/min.	33	69.7/30.3	65.7 ± 10.5	The absence of "treatment failure"	Respiratory rate; PaO2/ FiO2; use of accessory respiratory muscles; patient comfort and treatment tolerance, reintunation rate, length of ICU and hospital stay, mortality, adverse events
		HFNC 2	initial FiO2 = 0.6 and gas flow = 40 L/min	33	66.7/33.3	67.0 ± 9.1		
		COT	Venturi mask at 15L/min	33	66.7/33.3	68.6 ± 7.5		
Vourc'h et al., 2020	Scheduled CABG	HFNC	FIO2 of 100% with a gas flow of 45 L/min	47	87/13	65.8 ± 10.1	PaO2/FIO2 at 1 and 24 hours	Effectiveness of oxygen support; reintunation rate; tolerance of the device, patient comfort; radiologic score on chest X-ray; length of ICU stay; mortality
		COT	Hudson RCI non-rebreather mask with a reservoir bag at 15L/min	43	84/16	67.6 ± 9.4		
Zochios et al., 2018	Elective cardiac surgery (CABG, valve surgery or both)	HFNC	FiO2 to SpO2 >95% and starting flow rate was 30 L/min (20–50 L/min)	49	61.2/38.8	67.3 ± 9.3	Hospital length of stay	ICU length stay; ICU re-admission rate; reintubaton rate; mortality rate; pulmonary function tests; patient comfort
		COT	Nasal prongs or a soft facemask and the oxygen flow to SpO2> 95%	45	62.2/37.8	69.1 ± 11.1		

COT: conventional oxygen therapy; HFNC: high flow nasal cannula; CABG: Coronary Artery Bypass Graft Surgery; BMI: body mass index; MVR: mitral valve replacement; AVR: aortic valve replacement; DVR: double valve replacement; paO2: Partial Pressure of Oxygen; paCO2: Partial Pressure of Carbon Dioxide; FiO2: Fraction of inspired oxygen; SpO2: peripheral oxygen saturation; ICU: intensive care unit; L/min: liters per minute, kg/m^2 kilograms per square meter

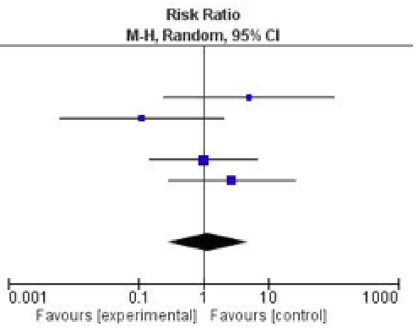
Figure 2: Risk of bias of RCTs included and evaluated through Rob 2.0.

Figure 3 - Comparison between High-flow nasal cannula oxygen therapy (HFNC) versus conventional oxygen therapy (COT) on A) Reintubation rate, B) Intensive Care Unit (ICU) length of stay (days), C) Hospital length of stay (days), D) Mortality. Experimental = HFNC and control= COT

A)

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Burra et al., 2021	0	30	0	30		Not estimable
Corley et al., 2015	0	81	0	74		Not estimable
Parke et al., 2013	2	169	0	171	17.8%	5.06 [0.24, 104.59]
Sahin et al., 2018	0	50	4	50	19.1%	0.11 [0.01, 2.01]
Tatsuishi et al., 2020	0	72	0	76		Not estimable
Theologou et al., 2021	2	33	2	33	34.8%	1.00 [0.15, 6.68]
Vourc'h et al., 2020	3	47	1	43	28.3%	2.74 [0.30, 25.40]
Zochios et al., 2018	0	49	0	47		Not estimable
Total (95% CI)		**531**		**524**	**100.0%**	**1.17 [0.28, 4.85]**
Total events	7		7			

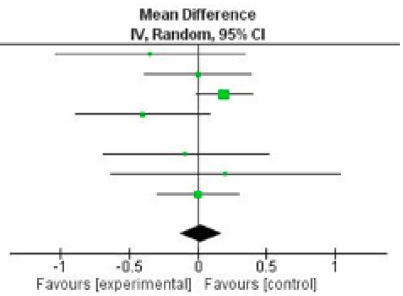
Heterogeneity: Tau² = 0.58; Chi² = 4.12, df = 3 (P = 0.25); I² = 27%
Test for overall effect: Z = 0.21 (P = 0.83)



B)

Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
Burra et al., 2021	3.41	1.42	30	3.76	1.31	30	4.9%	-0.35 [-1.04, 0.34]
Corley et al., 2015	1.61	1.46	81	1.61	0.99	74	14.3%	0.00 [-0.39, 0.39]
Parke et al., 2013	1.39	0.95	169	1.2	1	171	38.9%	0.19 [-0.02, 0.40]
Sahin et al., 2018	2.4	0.5	50	2.8	1.7	50	9.4%	-0.40 [-0.89, 0.09]
Tatsuishi et al., 2020	1	0	72	1	0	76		Not estimable
Theologou et al., 2021	2.2	1.4	33	2.29	1.08	33	6.4%	-0.09 [-0.69, 0.51]
Vourc'h et al., 2020	3.3	2.4	47	3.1	1.6	43	3.4%	0.20 [-0.64, 1.04]
Zochios et al., 2018	1	0.74	49	1	0.74	47	22.8%	0.00 [-0.30, 0.30]
Total (95% CI)			**531**			**524**	**100.0%**	**0.02 [-0.14, 0.18]**

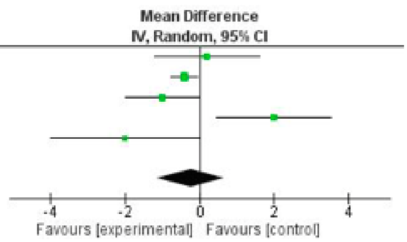
Heterogeneity: Tau² = 0.01; Chi² = 6.75, df = 6 (P = 0.34); I² = 11%
Test for overall effect: Z = 0.25 (P = 0.80)



C)

Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
Parke et al., 2013	11.6	6.6	169	11.4	6.7	171	17.9%	0.20 [-1.21, 1.61]
Sahin et al., 2018	6.5	0.7	50	6.9	1.1	50	30.0%	-0.40 [-0.76, -0.04]
Tatsuishi et al., 2020	8	2.22	72	9	3.7	76	23.1%	-1.00 [-1.98, -0.02]
Theologou et al., 2021	9	3.7	33	7	2.59	33	16.5%	2.00 [0.46, 3.54]
Zochios et al., 2018	7	2.22	49	9	6.66	47	12.4%	-2.00 [-4.00, 0.00]
Total (95% CI)			**373**			**377**	**100.0%**	**-0.23 [-1.14, 0.67]**

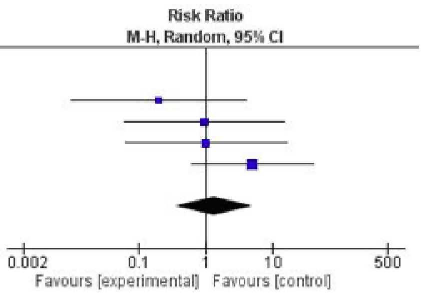
Heterogeneity: Tau² = 0.68; Chi² = 13.88, df = 4 (P = 0.008); I² = 71%
Test for overall effect: Z = 0.50 (P = 0.61)



D)

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Vourc'h et al., 2020	0	47	0	43		Not estimable
Burra et al., 2021	0	30	0	30		Not estimable
Sahin et al., 2018	0	50	2	50	18.6%	0.20 [0.01, 4.06]
Zochios et al., 2018	1	49	1	47	22.3%	0.96 [0.06, 14.90]
Parke et al., 2013	1	169	1	170	22.0%	1.01 [0.06, 15.95]
Theologou et al., 2021	5	33	1	33	37.1%	5.00 [0.62, 40.51]
Total (95% CI)		**378**		**373**	**100.0%**	**1.34 [0.36, 5.02]**
Total events	7		5			

Heterogeneity: Tau² = 0.09; Chi² = 3.15, df = 3 (P = 0.37); I² = 5%
Test for overall effect: Z = 0.43 (P = 0.67)



4 CONCLUSÃO GERAL

Os estudos avaliados não mostraram superioridade da terapia de CNAF frente a oxigenoterapia convencional em indivíduos no pós-operatório de cirurgia cardíaca quando avaliado a taxa de reintubação, sensação de dispneia, mortalidade, conforto e tolerância e no tempo de permanência de internação na unidade de terapia intensiva e hospitalar. Sugere-se que mais estudos com essa população sejam realizados.

A CNAF é um dispositivo relativamente novo que está cada vez mais ganhando espaço nas UTI e emergências dos hospitais brasileiros. Mas ainda são necessárias mais pesquisas e evidências que guiem a tomada de decisão do seu uso, definindo a população e o tempo adequado para o início do uso, evitando a demora da instalação ou o uso indevido para certas patologias e situações clínicas.

5 IMPACTOS DO TRABALHO

Essa dissertação tem um impacto clínico de trazer embasamento científico para guiar os profissionais da área na melhor escolha de terapia para os indivíduos cardiopatas que são atendidos todos os dias nos hospitais, melhorando os desfechos dessa população e otimizando custos para o sistema de saúde. Assim como sugerir que mais pesquisas sobre o tema sejam realizadas.