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A matched analysis of the use of high flow nasal cannula for pediatric severe acute asthma

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Abstract

Rationale: The high-flow nasal cannula (HFNC) device is commonly used to treat pediatric severe acute asthma. However, there is little evidence regarding its effectiveness in real-world practice.

Objectives: We sought to compare the physiologic effects and clinical outcomes for children treated for severe acute asthma with HFNC versus matched controls.

Methods: This was a single-center retrospective matched cohort study at a quaternary care children's hospital. Children ages 2–18 hospitalized for severe acute asthma from 2015 to 2022 were included. Encounters receiving treatment with HFNC within the first 24 h of hospitalization were included as cases. Controls were primarily treated with oxygen facemask. Logistic regression 1:1 propensity score matching was done using demographics, initial vital signs, and medications. The primary outcome was an improvement in clinical asthma symptoms in the first 24 h of hospitalization measured as percent change from initial.

Measurements and Main Results: Of 693 eligible cases, 443 were matched to eligible controls. Propensity scores were closely aligned between the cohorts, with the only significant difference in clinical characteristics being a higher percentage of patients of Black race in the control group (54.3% vs. 46.6%; $p = 0.02$). Compared to the matched controls, the HFNC cohort had smaller improvements in heart rate (−11.5% [−20.9; −0.9] vs. −14.7% [−22.6;-5.7]; $p < 0.01$), respiratory rate (−14.3% [−27.9;5.4] vs. −16.7% [−31.5;0.0]; $p = 0.03$), and pediatric asthma severity score (−14.3% [−28.6;0.0] vs. −20.0% [−33.3;0.0]; $p < 0.01$) after 24 h of hospitalization. The HFNC cohort also had longer pediatric intensive care unit (PICU) length of stay (LOS) (1.5 days [1.1;2.1] vs. 1.2 days [0.9;1.8]; $p < 0.01$) and hospital LOS (2.8 days [2.1;3.8] vs. 2.5 days [1.9;3.4]; $p < 0.01$). When subgrouping to younger patients

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(2–3 years old), or those with the highest severity scores (PASS > 9), those treated with HFNC had no difference in clinical symptom improvements but maintained a longer PICU LOS.

Conclusions: Encounters using HFNC for severe acute pediatric asthma had decreased clinical improvement in 24 h of hospitalization compared to matched controls and increased LOS. Specific subgroups of younger patients and those with the highest severity scores showed no differences in clinical symptom improvement suggesting differential effects in specific patient populations.

KEYWORDS

asthma, clinical research, informatics, pediatrics

1 | INTRODUCTION

Severe acute asthma (SAA), defined as an asthma exacerbation significant enough to require admission to the hospital,[1] carries a high risk of morbidity for affected children.[2,3] Previously entitled status asthmaticus, SAA produces a large economic burden with costs of over $5 billion in the United States in 2017 alone.[4–6] Children hospitalized with SAA are at risk for severe physiologic derangements including hypercarbia, hypoxemia, cardiac dysfunction, and death.[7] Medications and respiratory support devices are used in tandem to treat children with critical asthma in the hospital.[8–11] Among the respiratory support devices available to physicians is the heated, humidified, high-flow nasal cannula (HFNC). While an oxygen facemask only delivers oxygen and nebulized medications, this device can improve patients' work of breathing through washout of nasopharyngeal dead space, minimizing oxygen dilution, conditioning of inspired gases, and reduction of energy expenditure by assisting with inspiratory flow.[12,13] It is also relatively easy to use, and better tolerated by children than higher forms of respiratory support, such as positive pressure ventilation (PPV) devices. While initially used in pediatrics for viral bronchiolitis, its use has expanded over the past decade as its mechanisms of action are likely effective in other respiratory diseases and it is now often used for children admitted to the hospital with asthma.[14–16] However, current evidence regarding its clinical effectiveness in this population is lacking.

Several observational studies suggest that HFNC use in treating SAA in children is safe and effective,[17–19] and one quality improvement study implementing HFNC use into an asthma protocol showed no difference in symptom improvement or length of stay (LOS) between HFNC treatment and aerosol mask treatment. However, concerns have been raised that the HFNC device does not deliver nebulized medications effectively. Several mechanistic studies have shown poor aerosolized medication distribution with HFNC, particularly at high flow rates.[20–23] This is concerning, as one of the primary treatments for SAA is inhaled bronchodilator therapy. A prior study by this group evaluated the hospital LOS for children with SAA using HFNC compared to standard oxygen mask treatment and found that the cohort using HFNC therapy had a longer hospital LOS.[24] However, this study was limited in having a sparsity of clinical variables available for patient matching, and ambiguity regarding the treatment timing and patient population.

The objective of this study was to compare the clinical outcomes of pediatric encounters for SAA treated with the HFNC device compared to matched controls using primarily the oxygen facemask. The primary outcome was improvement in clinical symptoms 24 h after hospitalization. Secondary outcomes included both pediatric intensive care unit (PICU) length of stay (LOS) and hospital LOS.

2 | METHODS

This was a retrospective case-control study at a single, quaternary care, academic pediatric institution. This study was reviewed by the Indiana University Institutional Review Board (IRB #17481) and determined to be Human Subjects Research Exempt). No informed consent was required or obtained. The study population included all encounters for SAA between 1 January 2015 and 31 December 2022 with hospital admission for children ages 2–18 years. The determination of asthma diagnosis was made using a deterministic computational phenotype including an International Classification of Disease 9th or 10th revision diagnostic code for asthma (ICD9: 493, ICD10: J45), the receipt of at least two doses of nebulized albuterol or continuous nebulized albuterol within the first 24 h of admission, and the receipt of an oral or intravenous dose of systemic steroids (prednisone, prednisolone, dexamethasone, or methylprednisolone) in the first 24 h of hospitalization. This phenotype had a positive predictive value of 96% when evaluated with 100 randomly sampled manual chart reviews. Included encounters also required documented Pediatric Asthma Severity Score (PASS) values at admission and at 24 h.

To be an eligible study case, encounters were required to have received HFNC as their first advanced respiratory treatment device, and within the first 24 h of presentation to the hospital. Encounters using PPV devices such as continuous positive airway pressure (CPAP), bi-level positive airway pressure (BiPAP), or invasive mechanical ventilation (IMV) before HFNC use were not

eligible cases. Controls must have presented to the hospital with initial respiratory support of an oxygen facemask. If subjects' initial respiratory device was CPAP, BiPAP, or IMV upon hospital presentation, they were not eligible controls. If subjects began on conventional oxygen masks and then progressed to NIV/IMV, these subjects were eligible controls. Encounters involving an existing tracheostomy, or which included hospital discharge in less than 24 h were excluded.

Our institution's regular practice in the early study period (2015–2017) was to treat SAA with nebulized albuterol via a standard oxygen facemask, and HFNC was typically only used if there were concerns for another, more prominent diagnosis such as pneumonia or acute respiratory distress syndrome. In 2018, there was a transition as we obtained the capability to nebulize continuous albuterol through the HFNC device, and more encounters for SAA began using HFNC therapy. In the latter portion of the study period (2019–2022), our standard practice for SAA encounters was to use HFNC for patients requiring continuous albuterol therapy. Thus, in our matching, we sought to match the most symptomatic SAA encounters in the early study period not treated with HFNC with those in the later study period that were treated with HFNC to create an optimal comparison.

Our institutional policy, with few exceptions during large surge periods, was for any patient receiving HFNC therapy to require admission to the PICU, while patients on albuterol via oxygen facemask may or may not have been admitted to the PICU based on clinical presentation. We chose not to match patients based on PICU admission due to the concern that equally ill SAA patients could fail to be matched based on the institutional policy that patients treated with HFNC must be in the PICU. There were also several weaning protocols implemented in our PICU over the study period that likely affected both groups, including a standard continuous albuterol weaning protocol and an HFNC weaning protocol. We initiated a respiratory therapist-driven HFNC weaning protocol in the PICU in October 2017, and in March 2019 adjusted the protocol to include the weaning of continuous albuterol and HFNC simultaneously. Both protocols were successful in decreasing PICU LOS and remained in place through the end of the study period.[25]

Data for this study were obtained from the Indiana University Health Cerner Enterprise Data Warehouse. The population was determined using the above inclusion criteria. Data obtained for the study included patient demographics, diagnostic data, vital signs obtained longitudinally at hourly intervals, respiratory data including device and flow rate, PASS,[26] medication data, and encounter data. Flow rate was included as a flat rate rather than a weight-based value because prior studies demonstrated increased particle dispersion at flat rates above 6 L/min,[23] and due to the complexity of attempting to use weight-based values for smaller children and flat rates for older children. Vital sign and symptom measurement outcomes were reported as percent change from initial measurements on hospital presentation. Length of stay outcomes were measured in days. The primary study outcome was an improvement in clinical asthma symptoms at 24 h of hospitalization, measured as percent change in heart rate (HR), respiratory rate (RR), and PASS. Outcomes were calculated as the value obtained nearest to 24 h after presentation to the hospital (plus or minus 6 h maximum). Secondary study outcomes included PICU LOS and hospital LOS measured in days. Findings from this study were reported according to the STROBE guidelines.[27]

Propensity score matching was done to control for selection bias. To calculate for propensity to receive treatment with HFNC, a logistic regression model was used which included patient age, initial PASS, initial HR, initial RR, pneumonia diagnosis, and magnesium, ipratropium, and continuous albuterol use in the first 24 h of hospitalization. Encounters were matched 1:1 using the nearest neighbor method, with a caliper of 0.1 standard deviations and a Mahalanobis distance adjustment. Initially, inverse probability weighting was attempted, but this approach was unable to achieve adequate balance in the measured covariates.

Following matching, characteristics and outcomes were compared between the groups using Mann–Whitney U tests for continuous variables and chi-square or Fisher's exact tests for categorical variables. The Holm method was applied to adjust for multiple comparisons. We also conducted three subgroup analyses of the youngest patients (2–3 years old), those with the most severe presenting symptoms (PASS > 9), and those using HFNC flow rates less than 10 L/min. Statistical significance was determined at an alpha level of 0.05. All data processing and statistics were conducted using R version 4.2.3.[28]

3 | RESULTS

In the total population, 693 encounters were eligible cases with 1005 potential controls (Table S1). Following matching, 443 cases were matched to an equal number of controls. The propensity score distribution was similar between the two groups (Figure S1; Table S2). Comparing clinical characteristics between the groups (Table 1), the only significant difference was a higher percentage of encounters with children of Black race in the control group (54.3% vs. 46.6%; $p = 0.02$). No differences in initial vital signs, medication use, or PPV rates were seen. The year of encounter distribution was as expected based on the changes in practice at our institution discussed in the methods section (Figure 1), with most of the control encounters happening in the earlier study period before 2018, and most of the HFNC encounters happening in the later study period after 2018. Subjects in the later study period had higher rates of pneumonia and complex chronic conditions, as well as BiPAP use (Table S3). Of note, 34 (7.5%) of the control group encounters received PPV with either CPAP or BiPAP in the first 24 h of hospitalization, and 4 (0.8%) received IMV. The HFNC flow rate used by the case encounters ranged from 2 L/min to 40 L/min with a median of 10 L/min and an interquartile range of 6–15 L/min.

The primary study outcome was a change in asthma symptoms within the first 24 h of hospitalization. When comparing the HFNC group to the control group, the HFNC group had a smaller

TABLE 1 Matched population characteristics.

Variable	HFNC N = 443	No HFNC N = 443	*P*-Value
Age	6 (3;9)	6 (4;9)	0.34
Sex (% Male)	57.3	58.2	0.84
Race (% Black)	48.3	53.7	0.12
Ethnicity (% Hispanic or Latino)	15.1	12.9	0.38
Pneumonia (%)	20.5	18.7	0.55
Complex chronic condition (%)	4.1	3.4	0.68
Bronchopulmonary dysplasia (%)	3.8	2.0	0.16
Fever (%)	13.8	9.3	*0.046
HR Initial	143 (130;157)	144 (132;155)	0.78
RR Initial	34 (28;40)	32 (28;40)	0.38
PASS Initial	8 (8;10)	8 (7;9)	0.71
Magnesium (%)	74.3	72.9	0.70
Continuous albuterol (%)	82.2	81.3	0.79
Ipratropium (%)	91.6	91.9	1.0
Epinephrine (%)	3.2	2.9	1.0
Aminophylline (%)	0.2	0.7	0.62
PICU admission (%)	93.9	58.0	*<0.01
BiPAP (%)	11.7	8.8	0.18
IMV (%)	1.8	0.7	0.22

Note: Continuous variables presented as median with interquartile range.

Abbreviations: BiPAP, Bi-level positive airway pressure; HFNC, high-flow nasal cannula; HR, heart rate; IMV, invasive mechanical ventilation; PASS, pediatric asthma severity score; RR, respiratory rate.

improvement in HR (−11.5% [−20.9;−0.9] vs. −14.7% [−22.6;−5.7]; $p < 0.01$), RR (−14.3% [−27.9;5.4] vs. −16.7% [−31.5;0.0]; $p = 0.03$), and PASS (−14.3% [−28.6;0.0] vs. −20.0% [−33.3;0.0]; $p < 0.01$) after 24 h of hospitalization (Figure 2). The HFNC cohort also had longer PICU LOS (1.5 days [1.1;2.1] vs. 1.2 days [0.9;1.8]; $p < 0.01$) and hospital LOS (2.8 days [2.1;3.8] vs. 2.5 days [1.9;3.4]; $p < 0.01$) (Figure 3).

On subgroup analysis, we evaluated the same outcomes for those aged 2–3 years, those with presenting PASS values greater than 9, and those using HFNC flow rates less than 10 L/min (Table 2). In the subgroup of the youngest encounters, there were no significant differences noted between those receiving HFNC and controls, except for a longer PICU LOS in the HFNC group (1.9 days [1.3–2.0] vs. 1.3 days [0.7-1.5]; $p = 0.02$). The same findings were observed in the high severity subgroup (PICU LOS of 1.7 days [1.2–2.3] in the HFNC group vs. 1.5 days [0.9-2.1] in the control group; $p = 0.02$). In the low flow rate group, the HFNC cohort had significantly smaller improvements in RR (-12.5 [-25.0;6.7] vs. −16.7 [−31.5;0.0]; $p < 0.01$) and PASS (−12.5 [−25.0;0.0] vs. −20.0 [−33.3;0.0]; $p < 0.01$) compared to the control group, with no significant differences in HR, PICU LOS, or hospital LOS.

4 | DISCUSSION

In this matched cohort study, we compared the use of HFNC in the treatment of SAA in children to an oxygen facemask. We found that, in the full cohort, the use of HFNC was associated with slower improvement in physiologic variables in the first 24 h of hospitalization, including HR, RR, and PASS. We also found that, in the full cohort, the use of HFNC was associated with longer PICU and hospital LOS. However, on subgroup analysis, it was found that some subtypes of encounters had fewer differences in these clinical outcomes, including the youngest patients, those with the most severe symptoms at presentation, and those that used lower HFNC flow rates.

Asthma is characterized by three primary pathologic processes occurring simultaneously in the lungs of affected individuals. These include bronchospasm, airway edema, and increased mucus.[7] Each of these lead to airway obstruction and respiratory distress. This is manifested clinically with increased heart rate, increased respiratory rate, and in increased work of breathing. The first-line treatments for asthma include systemic corticosteroids and inhaled bronchodilator medications.[8] For patients who continue to manifest respiratory

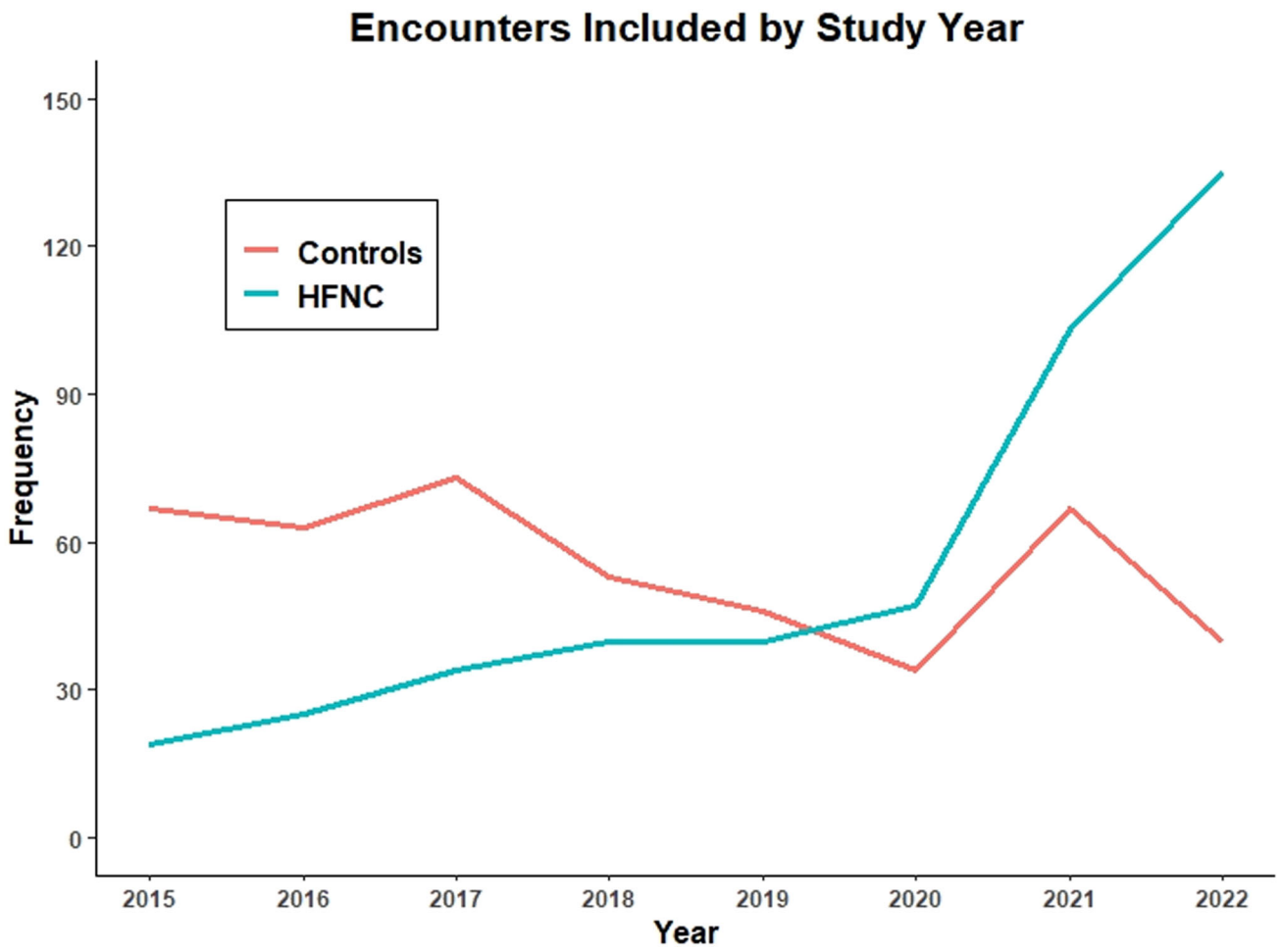

FIGURE 1 Line plot illustrating number of cases and controls for each year of the study.

distress after these treatments, there are a myriad of adjunctive therapies including both medications and respiratory support devices. The use of these adjunctive therapies, including the HFNC device, varies widely between providers and institutions, as the evidence for their use is limited.[11,16] To assess the effectiveness of HFNC, we assessed for changes in the physiologic compensatory mechanisms of airway obstruction. The HFNC device could potentially improve symptoms of airway obstruction through its inherent mechanisms, but it could also impair the delivery of nebulized bronchodilator therapy leading to delayed improvement. In a randomized controlled trial (RCT) by Ballestero et al.,[18] 62 children with SAA were randomized to receive treatment with HFNC versus oxygen mask in the emergency department. They found a greater decrease in clinical symptoms after 2 h in the HFNC group. However, another RCT by Gauto-Benitez[29] ($n = 65$) for SAA in the emergency department found no differences in clinical symptoms at 2 or 6 h of treatment.

In this study, we found that the cohort treated with HFNC had slower improvement in these physiologic mechanisms at 24 h of hospitalization compared to the control group. There are two possible explanations for these findings. The first is that, for most encounters, HFNC impaired delivery of nebulized bronchodilator medications compared to other devices, particularly the oxygen facemask, leading to prolonged symptoms. The second is that, despite propensity score matching, the HFNC cohort had a higher disease burden resulting in more persistent physiologic symptoms. This is unlikely as there were no statistically significant differences in any of the presenting symptoms between the matched cohorts, but it is an important consideration. The discrepancy between our study findings and those of the RCT by Bellestero could be due to that trial being conducted in the emergency department, and the possibility that HFNC provides some initial symptom benefit relative to an oxygen facemask, but it is not sustained at 24 h.

It is interesting to note that there are subjects at both ends of the study period that receive continuous albuterol via the minority device. For example, there are 19 subjects with SAA in 2015 who were treated with HFNC, and there are 40 patients in 2022 who were treated with conventional oxygen mask. The subjects in the first study years who received HFNC treatment were most likely patients who presented with contemporaneous conditions, such as pneumonia and had bronchospasm treated with continuous albuterol.

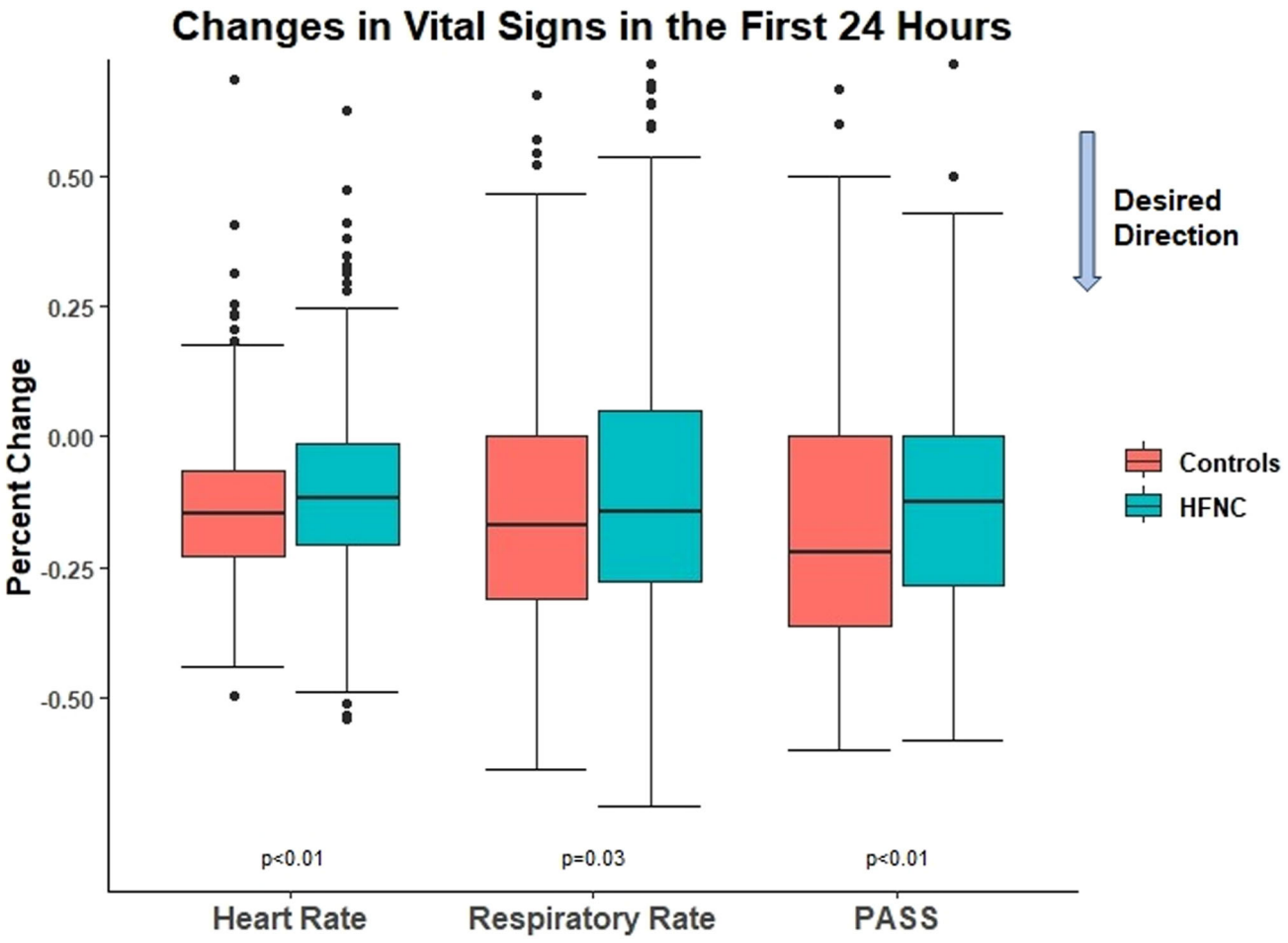

FIGURE 2 Paired boxplots comparing changes in vital signs in the first 24 h of hospitalization for those receiving HFNC versus matched controls. HFNC, high-flow nasal cannula.

This group likely received respiratory support with HFNC, and continuous albuterol via a facemask simultaneously. The second group who did not receive HFNC in the last years of the study period likely represented either patients who quickly progressed to noninvasive devices such as CPAP or BiPAP, or patients who for whatever reason did not tolerate the HFNC device and instead received continuous albuterol via an oxygen facemask.

The use of advanced respiratory support devices, such as HFNC, involves not only the patient and the device but also coordination of care teams and systems to facilitate patient safety and flow. Our institution has several protocols surrounding the use of HFNC that all contribute to important clinical outcomes, particularly time spent in the PICU and the hospital. Patients admitted to our hospital requiring HFNC support are mandatorily admitted to the PICU in most cases. This allows for more prominent nursing and respiratory therapist support to facilitate HFNC use. It is important for pediatric hospitals to determine the optimal distribution of resources to ensure that the highest acuity patients receive the increased support necessary for safe and effective care, but also that patients not requiring these advanced resources are appropriately identified and triaged. Currently, once a patient in our institution with SAA is admitted to the PICU, they are typically treated with both HFNC and continuous albuterol. As a patient improves, each intervention requires its own weaning process before discharge from the PICU. Weaning two interventions often requires a longer process than weaning a single intervention, potentially prolonging PICU and hospital length of stay. Previous research has shown that structured weaning protocols driven by respiratory therapists can safely decrease time spent for these interventions,[30,31] but the concern remains that if the patient does not require both, the process may be unnecessarily prolonged by their receipt.

In this study, we found that the HFNC cohort had longer PICU and hospital length of stay compared to matched controls. This is most likely due to the added time necessary to wean the HFNC device before transfer out of the PICU, which may not benefit the patient's symptoms. It is also possible that, despite matching, the HFNC cohort had a higher level of disease burden resulting in necessarily longer PICU and hospital LOS. This increased LOS was seen despite the implementation of successful respiratory therapist-driven weaning protocols relatively early in the HFNC era.

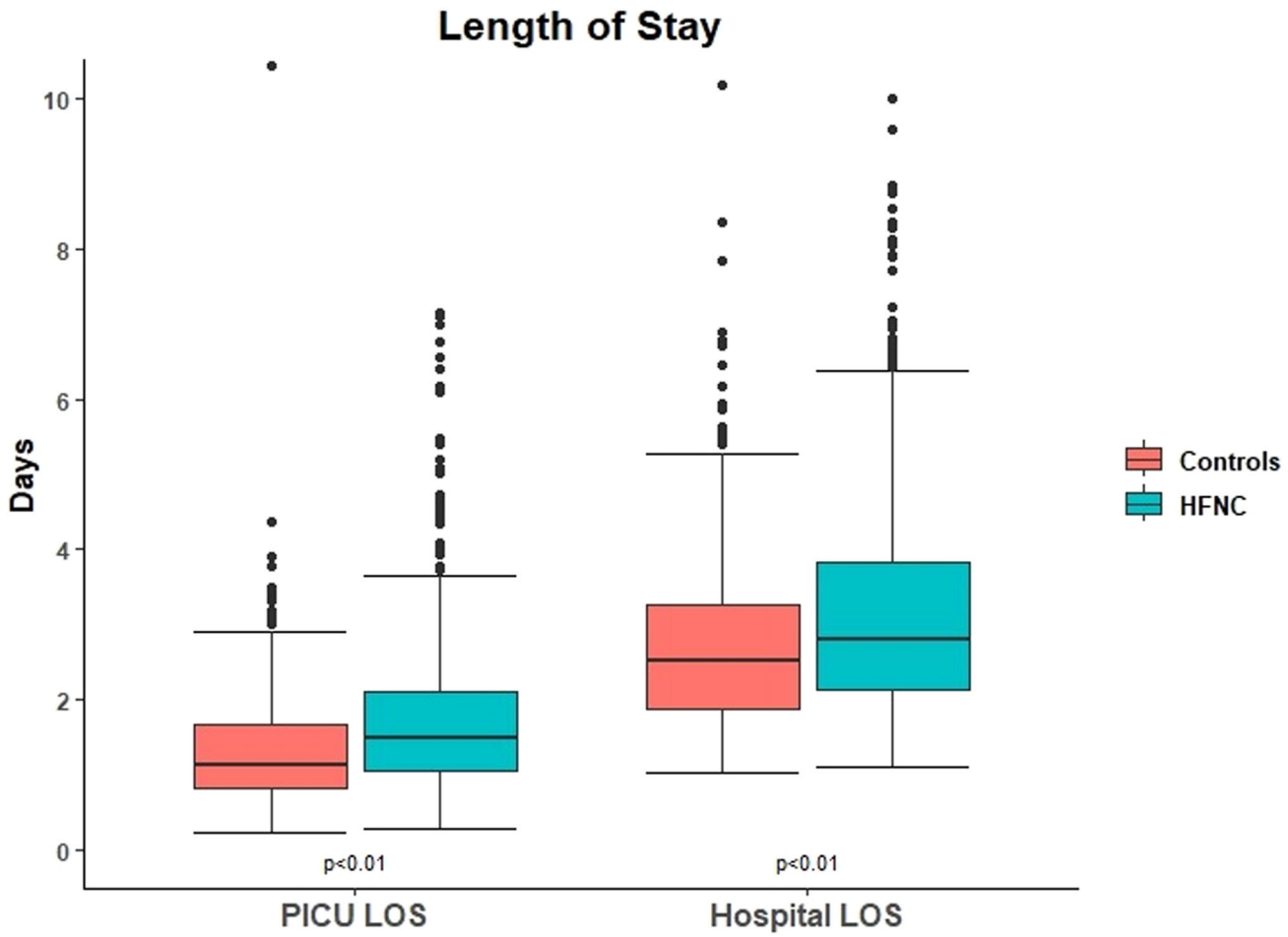

FIGURE 3 Paired boxplots comparing hospital and PICU length of stay for those receiving HFNC versus matched controls with Wilcoxon tests. HFNC, high-flow nasal cannula; PICU, pediatric intensive care unit.

The HFNC device was initially implemented in pediatrics to provide added respiratory support for infants suffering from viral bronchiolitis,[32] and may decrease the need for PPV and IMV.[33] Its mechanisms of action are likely to help with other disease processes, including asthma. The primary debate is whether the benefits of the HFNC device, as seen in treating other disease processes, balance or outweigh the potential detriment of impaired nebulized drug delivery. This study found that, in general, the clinical outcomes of HFNC use in pediatric SAA are inferior to the control group. However, there are likely specific populations experiencing SAA that do benefit from HFNC use relative to other modalities.

We investigated three subgroups of patients with higher likelihood of benefitting from HFNC use and found mixed results. The youngest children can often have a mixed picture of bronchospasm with viral lower respiratory infection and thus may benefit more from HFNC. This group had no significant differences in symptom improvement or hospital LOS between the HFNC cohort and the controls, only a longer PICU LOS in the HFNC cohort. Those with the worst presenting symptoms may benefit more from the added flow rates HFNC can provide. This group had the same findings as the young group, with no significant differences other than a longer PICU LOS compared to the controls. It has been found in previous studies that a flow rate of 6 L/min or less can improve the delivery of nebulized medications. It is not our institutional practice to limit flow rates to these values, and typical rates are 10/min or higher. On subgroup analysis, the HFNC cohort with lower flow rates had delayed improvement in RR and PASS at 24 h compared to the controls, but no other significant differences, including PICU LOS. These subgroup analyses are limited by smaller sample sizes but do provide some evidence that there may be specific subgroups of pediatric SAA patients that could benefit more from HFNC than others. Further research into this is needed before more specific direction can be provided.

This study has several important limitations. It is a retrospective observational study and thus is prone to unmeasured confounding factors. The most important to this study is selection bias, where the HFNC cohort simply may have a higher disease burden leading to worse clinical outcomes compared to the controls. We made substantial efforts to minimize this bias by using propensity score matching methods with several different clinical variables that seek to represent disease burden,

TABLE 2 Clinical outcomes for subgroups.

Variable	Age 2–3 Years HFNC N = 114	Age 2–3 Years No HFNC N = 95	*P*-Value	PASS > 9 HFNC N = 112	PASS > 9 No HFNC N = 111	*P*-Value	HFNC Flow <10 L/min N = 141	No HFNC N = 443	*P*-Value
HR 24-h change (%)	−13.0 (−22.1; −6.4)	−15.1 (−23.1; −6.1)	0.82	−11.6 (−18.3;-2.5)	−13.5 (−22.4; −6.5)	0.07	−13.4 (−20.7;-1.5)	−14.7 (−22.9;-6.4)	0.13
RR 24-h change (%)	−15.8 (−33.3; 5.8)	−15.4 (−33.3; 0.0)	0.60	−17.9 (−33.3; −4.9)	−18.2 (−32.4;-7.2)	0.82	−10.0 (−23.1; 7.1)	−17.1 (−31.3;0.0)	<0.01*
PASS 24-h change (%)	−12.5 (−26.7; 0.0)	−20.0 (−33.3;0.0)	0.04*	−30.0 (−40.0; −18.0)	−30.0 (−50.0; −20.0)	0.09	−11.1 (−25.0; 0.0)	−22.2 (−36.4;0.0)	<0.01*
PICU LOS (days)	1.4 (0.9; 2.0)	1.0 (0.7; 1.4)	<0.01*	1.7 (1.2; 2.3)	1.4 (0.9; 1.9)	<0.01*	1.2 (0.9 1.9)	1.1 (0.8;1.7)	0.33
Hospital LOS (days)	2.6 (1.8; 3.7)	2.5 (1.9; 3.3)	0.32	2.9 (2.2; 3.9)	2.8 (2.2; 3.7)	0.40	2.7 (2.0; 3.7)	2.5 (1.9;3.3)	0.05

Note: Continuous variables presented as median with interquartile range.

Abbreviations: HFNC, high flow nasal cannula; HR, heart rate; LOS, length of stay; PASS, initial PASS on hospital presentation; PICU, pediatric intensive care unit; RR, respiratory rate.

*Statistically significant at an alpha level of 0.05.

and the matches had no significant differences in these variables. We also used medications given within the first 24 h of presentation to the Hospital in our propensity score matching, and these medications could have been given after the initiation of HFNC, potentially adding bias to our matching process. This study was conducted only in a single academic center, and institutional practices influenced both patient selection and clinical outcomes. There were several changes in clinical practices for this population over the study period which both strengthens the study by providing its own comparative controls but also limits it by introducing heterogeneity in treatment effects. There was also a large difference in the frequency of PICU admission between the groups which may add bias to the results, but this may be based more on institutional practice than on patient condition. The data were collected through modern informatics tools applied to electronic health record data, which introduces biases through data missingness and potential inaccuracies, however, the data were thoroughly evaluated before use, and suspect data were removed before inclusion in the analysis.

5 | CONCLUSION

In this study, children with SAA treated with HFNC had slower improvement in clinical symptoms and longer PICU and hospital LOS compared to matched controls. Select subgroups of patients may have differential effects of HFNC relative to the general population. Further research with expanded sample sizes including data from other institutions is needed.

AUTHOR CONTRIBUTIONS

Colin Rogerson: Conceptualization; Investigation; Writing—original draft; Methodology; Validation; Visualization; Writing—review and editing; Formal analysis; Project administration; Data curation. **Samer AbuSultaneh**: Investigation; Methodology; Writing—review and editing; Supervision; Conceptualization. **L Nelson Sanchez-Pinto**: Investigation; Validation; Writing—review and editing; Supervision; Formal analysis. **Benjamin Gaston**: Investigation; Writing—review and editing; Supervision. **Sarah Wiehe**: Investigation; Writing—review and editing; Methodology; Supervision. **Titus Schleyer**: Methodology; Validation; Writing—review and editing; Supervision. **Wanzhu Tu**: Methodology; Validation; Writing—review and editing; Formal analysis; Supervision. **Eneida Mendonca**: Conceptualization; Investigation; Methodology; Validation; Visualization; Writing—review and editing; Formal analysis; Project administration; Data curation; Supervision; Resources.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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