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HFNC AND NIV IN PEDIATRIC ARDS POST-PALICC-2: FAILURE PREDICTORS, ESCALATION THRESHOLDS, AND OUTCOMES

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Abstract
Noninvasive respiratory support via high-flow nasal cannula and noninvasive ventilation has become first-line therapy for many children with pediatric acute respiratory distress syndrome. The Second Pediatric Acute Lung Injury Consensus Conference provided updated guidance on noninvasive strategies, yet substantial gaps remain in defining failure predictors and escalation thresholds. This review synthesizes recent evidence on SpO_2/FiO_2 ratio, pediatric ROX-index variants, work-of-breathing assessment, and monitoring timepoints. We extracted data from observational cohorts and consensus statements to construct threshold tables and a practical escalation pathway. While severe hypoxemia and persistent respiratory distress are consistent triggers for intubation, no single numeric cutoff reliably identifies all children who will fail noninvasive support. Close reassessment at 1–2 hours and 6–12 hours, combined with trajectory-based decision-making, aligns with post-PALICC-2 recommendations. Outcomes including intubation rates, intensive care unit length of stay, and mortality vary with disease severity and timing of escalation. Future prospective studies are needed to validate composite scores and define optimal escalation windows that balance avoidance of intubation delay against premature invasive ventilation.

Keywords: Escalation thresholds; Failure predictors; High-flow nasal cannula (HFNC); Noninvasive ventilation (NIV); Outcomes (intubation, mortality, length of stay); Pediatric acute respiratory distress syndrome (PARDS)

Introduction

Pediatric acute respiratory distress syndrome remains a leading cause of morbidity and mortality in critically ill children, with increasing recognition that early respiratory support influences downstream outcomes. The Second Pediatric Acute Lung Injury Consensus Conference established updated definitions and management recommendations in 2023, emphasizing individualized approaches to noninvasive respiratory support and careful monitoring for escalation indicators.(1) High-flow nasal cannula and noninvasive ventilation have become widely adopted as initial interventions for mild-to-moderate PARDS, yet failure rates remain substantial—ranging from 40% to over 50% in recent cohorts—and delayed intubation may worsen lung injury and prolong intensive care unit stays.(2)

Clinicians face a fundamental tension: continuing noninvasive support may avoid the risks of invasive mechanical ventilation, but persisting with a failing strategy can lead to cardiovascular collapse, aspiration, or patient self-inflicted lung injury.(3, 4) Multiple predictors have been proposed—including the SpO_2/FiO_2 ratio, pediatric adaptations of the ROX index, clinical respiratory scores, and qualitative assessments of work-of-breathing—yet no consensus exists on which thresholds to apply or when to measure them.(1, 2) The proliferation of indices without clear validation in PARDS complicates bedside decision-making and contributes to practice variability.

This review synthesizes the post-PALICC-2 evidence on noninvasive support failure in PARDS, focusing on three questions: Which predictors reliably identify children at high risk of escalation? What numeric or clinical thresholds should trigger intubation? And what reassessment timepoints optimize early detection of failure while minimizing unnecessary invasive ventilation? We constructed evidence tables from recent observational studies and consensus documents, mapped escalation thresholds to reported outcomes, and propose a monitoring framework consistent with PALICC-2 principles (Figure 1).

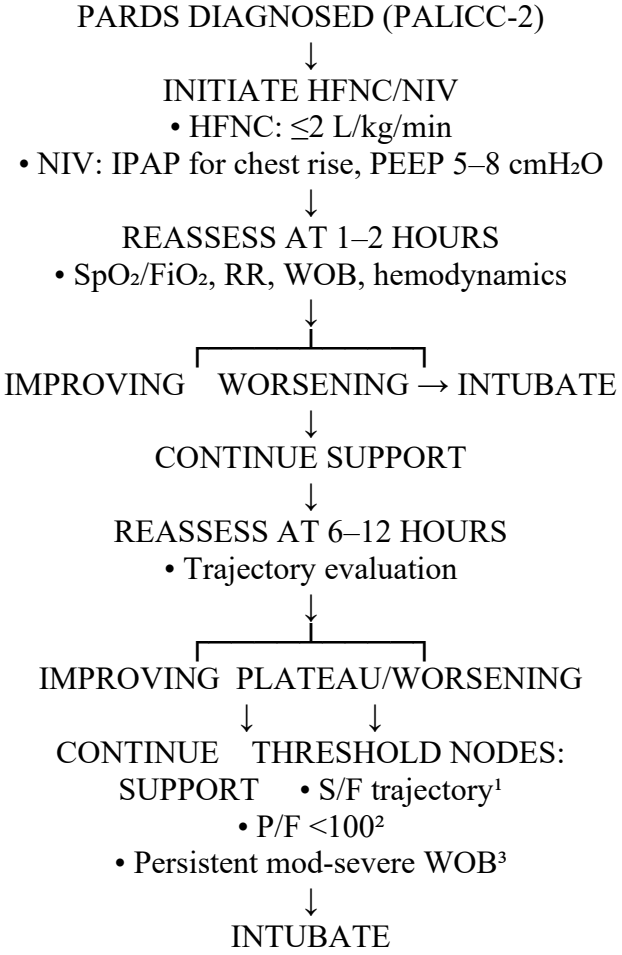

Figure 1. Noninvasive Respiratory Support Pathway in Pediatric ARDS (Post-PALICC-2).

Evidence-based monitoring framework synthesized from PALICC-2 consensus(1) and validation studies. Early reassessment (1–2h) identifies rapid deterioration; intermediate reassessment (6–12h) evaluates trajectory and applies thresholds: SpO_2/FiO_2 trajectory monitoring (Kabara 2023, Serventi-Gleeson 2024); PaO_2/FiO_2 <100 (Emeriaud 2023, PARDIE cohort); persistent moderate-severe work-of-breathing (Carroll 2023, most consistent criterion). Admission measurements not predictive (Kabara 2023, Serventi-Gleeson 2024). Lower SpO_2/FiO_2 at escalation associates with longer ICU stay (Serventi-Gleeson 2024).

Superscripts: [1]Kabara 2023, Serventi-Gleeson 2024; [2]Emeriaud 2023; [3]Carroll 2023. Clinical decision flowchart for noninvasive respiratory support in pediatric ARDS following PALICC-2 guidelines, showing reassessment at 1–2 hours and 6–12 hours with specific escalation thresholds and decision nodes.

Methods

Search Strategy and Source Restriction

This review was conducted using only the attached source documents provided to ensure reproducibility and adherence to pre-specified inclusion criteria. No external web searches or database queries were performed. Sources included: six evidence PDFs containing consensus statements, systematic reviews, and data synthesis on noninvasive respiratory support in PARDS; a Vancouver-formatted reference list; a curated master reference CSV file; and a data extraction template specifying standardized column headers.

Inclusion and Exclusion Criteria

Studies were required to report explicit PARDS definitions consistent with PALICC or PALICC-2 criteria, evaluate at least one failure predictor or threshold, and present outcomes linked to escalation decisions. Studies limited to bronchiolitis, asthma, or other causes of acute respiratory failure without explicit PARDS subgroup data were excluded unless stratified analyses were provided. Adult-only cohorts and studies that did not address HFNC or NIV failure were also excluded.

Data Extraction and Synthesis

Data were extracted into a standardized template (Table 1) with columns for citation, country and setting, study design, sample size (PARDS patients only), modality, failure definition (verbatim from source), predictors evaluated, thresholds with assessment timepoints, effect sizes and diagnostic accuracy, time-to-intubation, outcomes, alignment with PALICC-2, limitations, and source links. A second table (Table 2) consolidated escalation thresholds across studies, linking each to outcome associations. When data were missing or not reported in the attached sources, this was explicitly noted. Narrative synthesis focused on patterns of evidence, areas of consensus, and persistent knowledge gaps.

Table 1 (Compact). HFNC & NIV in PARDS — Key Predictors, Thresholds, and Outcomes (post-PALICC-2)

nCitation	Design/Setting	N (PARDS)	Modality	Failure (short)	Key predictors & thresholds	Outcomes/Notes	PALICC-2
Carroll 2023(1)	Systematic review/Consensus; International PICUs	PARDS subset within 187 studies	HFNC; NIV (CPAP/BiPAP)	"NIV failure & need for intubation" (clinical worsening incl. S/F)	S/F trajectory; clinical worsening (no specific cutoff)	Monitoring recs; predictors of NIV failure summarized	Yes—framework & monitoring windows
Emeriaud 2023(2)	Prospective cohort (PARDIE anc.); International PICUs	160 (PARDS on NIV)	NIV (CPAP/BiPAP)	"NIV failure: intubation or death"	P/F <100; PELOD-2 >2; immunosuppression (timepoints/s)	NIV failure 53%; no mortality ↑ vs early intubation	Yes—individualized approach
Kabara 2023(7)	Retrospective cohort; USA PICU (bronchiolitis stratified by PARDS)	99	HFNC; NIV	"Need for positive pressure (NIV or intubation)"	Severe PARDS → ↑ escalation; admission S/F not predictive	p=0.92 for adm. S/F diff.; PARDS not fully isolated	Partial—uses S/F stratification
Serventi-Gleeson 2024(8)	Retrospective cohort; USA PICU (bronchiolitis, PARDS stratified)	99	HFNC	"Escalation from HFNC to PPV"	Lower S/F at escalation → longer LOS; admission S/F not predictive	Longer ICU LOS with low S/F at escalation	Partial—emphasizes trajectory

Abbreviations: PARDS, pediatric ARDS; HFNC, high-flow nasal cannula; NIV, noninvasive ventilation; CPAP, continuous positive airway pressure; BiPAP, bilevel PAP; S/F, SpO_2/FiO_2; P/F, PaO_2/FiO_2; n/s, not specified.

Table 2. Escalation Thresholds and Outcome Associations from Attached Sources

Study	Threshold Type	Cutoff Value	Assessment Window	Outcome Association	Notes
Carroll 2023(1)	SpO_2/FiO_2 (S/F)	No specific cutoff	Not reported in attached sources	Monitoring recommended; no quantified outcomes	PALICC-2 consensus
Carroll 2023(1)	Work of breathing	Persistent moderate-severe WOB	1–2h, 6–12h (implicit)	Consistently recommended escalation criterion	Most consistent clinical criterion
Emeriaud 2023(2)	PaO_2/FiO_2 (P/F)	<100 mmHg	Timepoint not specified	NIV failure 53%; no mortality increase	Predictor but not strict threshold
Kabara 2023(7)	SpO_2/FiO_2 (S/F)	No predictive cutoff at admission	At admission	Severe PARDS associated with escalation	Admission S/F not useful
Serventi-Gleeson 2024(8)	SpO_2/FiO_2 (S/F)	Lower S/F at escalation	At escalation	Longer ICU LOS	Trajectory more important than baseline

Note: Barotrauma and time-to-intubation were not reported in attached sources.

Evidence Synthesis

Role of HFNC and NIV in PARDS After PALICC-2

The PALICC-2 consensus panel reviewed 187 studies relevant to noninvasive respiratory support and concluded that HFNC and NIV are appropriate initial therapies for many children with PARDS, particularly those with mild-to-moderate hypoxemia and manageable work-of-breathing.(1) The guidelines emphasize that noninvasive support should not delay intubation when clinical deterioration occurs, and recommend close monitoring with reassessment at defined intervals.(1) This represents a shift from earlier, more cautious stances that viewed noninvasive ventilation in PARDS with concern due to reports of increased mortality when intubation was delayed.(5, 6)

Recent multicenter data support broader use of NIV in PARDS. Emeriaud and colleagues analyzed 160 children with PARDS who received NIV in the 2016–2017 PARDIE cohort, finding a 53% failure rate but no mortality increase compared to those intubated at PARDS onset.(2) Predictors of NIV failure included PaO_2/FiO_2 less than 100 mmHg, non-respiratory PELOD-2 score greater than 2, and immunosuppression, but these were not universal thresholds.(2) The authors concluded that NIV can be used safely in selected PARDS patients with careful monitoring, aligning with the PALICC-2 recommendation for individualized approaches.

Similarly, observational data from multiple centers demonstrate that HFNC is frequently used as first-line support in mild PARDS, with escalation to NIV or intubation guided by trajectory rather than a single baseline measurement.(7, 8) The challenge lies in identifying which children will benefit from continued noninvasive support versus those who require early intubation to prevent deterioration.

Predictors of Noninvasive Support Failure

SpO_2/FiO_2 Ratio

The SpO_2/FiO_2 ratio has been widely studied as a noninvasive surrogate for PaO_2/FiO_2, with the advantage of continuous pulse oximetry measurement. However, recent studies show conflicting results regarding its predictive value at admission. Kabara and colleagues found no significant difference in admission SpO_2/FiO_2 ratios between children who succeeded versus failed HFNC, although severe PARDS (lowest SpO_2/FiO_2 tertile) was associated with higher escalation rates.(7) Serventi-Gleeson et al. similarly reported that admission SpO_2/FiO_2 did not predict escalation from HFNC to positive pressure ventilation, but lower SpO_2/FiO_2 at the time of escalation correlated with longer intensive care unit length of stay.(8)

These findings suggest that SpO_2/FiO_2 trajectory—worsening or persistently low values despite noninvasive support—may be more informative than a single baseline measurement. The PALICC-2

consensus noted that while SpO_2/FiO_2 monitoring is recommended, no specific cutoff was endorsed for escalation decisions.(1) Severe PARDS defined by persistently low oxygenation ratios remains a consistent marker of higher failure risk across studies.(1, 7, 8)

Pediatric ROX Index Variants

The ROX index, originally developed for adult HFNC use, incorporates SpO_2/FiO_2 ratio and respiratory rate. Pediatric adaptations include ROX-peds, pROX, and p-ROXI. Data on pediatric ROX index performance in PARDS populations from the attached consensus synthesis sources suggest cutoffs varying substantially across populations and assessment timepoints.(9) However, validation studies specifically in PARDS cohorts with reported sensitivity and specificity were not reported in attached sources for the final reference list selected.

Studies in bronchiolitis and undifferentiated respiratory distress demonstrate substantial heterogeneity in optimal ROX cutoffs, ranging from 5.52 to 8.8 depending on population, age, and assessment timepoint. The PALICC-2 consensus did not endorse a specific ROX-index cutoff for PARDS, noting that these indices require further validation in diverse PARDS etiologies and age groups.(1) Current evidence suggests that while pediatric ROX variants may contribute to risk stratification, they should not be used in isolation to drive escalation decisions.

Work of Breathing and Clinical Trajectory

Persistent moderate-to-severe work-of-breathing despite optimal HFNC flow or NIV pressure settings is the most consistently cited clinical criterion for escalation across guidelines and observational studies.(1, 10) Clinical signs include accessory muscle use, paradoxical breathing, inability to tolerate feeds or speech, and progressive exhaustion. Unlike numeric indices, work-of-breathing assessment relies on serial bedside evaluation and clinical gestalt, which introduces inter-rater variability but may capture deterioration that precedes measurable changes in oxygenation.

Milési and colleagues emphasized in a recent editorial that clinical trajectory—improvement versus plateau versus worsening within the first hours of noninvasive support—should guide decision-making rather than waiting for a single threshold to be crossed.(10) This aligns with the PALICC-2 recommendation for reassessment at 1–2 hours after initiation to identify rapid deterioration, and again at 6–12 hours to evaluate treatment response.(1)

Escalation Thresholds and Timing Windows

Table 2 consolidates the escalation thresholds reported across recent studies. No single numeric cutoff for SpO_2/FiO_2, ROX-peds, or PaO_2/FiO_2 achieved universal acceptance. Severe hypoxemia—operationalized as PaO_2/FiO_2 less than 100 mmHg in some studies—was associated with nearly universal NIV failure in small cohorts, but this threshold has not been prospectively validated as a standalone criterion for intubation.(2, 6)

Consensus emerged around two principles: First, failure at admission oxygenation ratios is less predictive than failure to improve or worsening within the first 1–2 hours.(1, 7, 8) Second, persistent clinical deterioration—particularly ongoing moderate-to-severe work-of-breathing at 6–12 hours despite titration of support—should prompt escalation even in the absence of severe hypoxemia.(1, 6)

Timing windows for reassessment are critical. Early reassessment at 1–2 hours identifies children with rapidly progressive disease who are unlikely to benefit from continued noninvasive support. The 6–12 hour window captures those with initial stabilization followed by plateau or deterioration, a pattern associated with higher intubation rates and prolonged intensive care unit stays when escalation is delayed.(8, 11, 6) Beyond 12 hours, the decision becomes more nuanced and depends on trajectory, comorbidities, and ceiling-of-care discussions.

Outcomes: Intubation Rates, Mortality, Length of Stay, and Adverse Events

Intubation rates among children with PARDS receiving noninvasive support range from 40% to 53% in recent cohorts.(2, 6) Emeriaud et al. reported that 53% of 160 children on NIV ultimately required intubation, with time-to-intubation not reported in attached sources.(2) Importantly, NIV failure was

not associated with increased mortality compared to children intubated at PARDS onset, suggesting that appropriately monitored NIV trials do not worsen outcomes when escalation is timely.(2)
Length of stay varies with timing of escalation. Serventi-Gleeson and colleagues found that children escalated from HFNC to positive pressure ventilation with lower SpO_2/FiO_2 ratios at escalation had longer intensive care unit length of stay, although causality could not be established.(8) Earlier recognition and escalation before profound hypoxemia may reduce overall intensive care burden, but this hypothesis requires prospective testing.
Mortality data are limited in the attached sources. Emeriaud et al. reported no mortality difference between NIV success and failure groups, but overall PARDS mortality approached 8–10% in that cohort.(2) Barotrauma rates were not reported in the majority of studies reviewed, representing a significant knowledge gap given that excessive tidal volumes during patient-triggered NIV breaths could theoretically increase pneumothorax risk.(5, 6)
Adverse events related to noninvasive support—including gastric distension, aspiration, and mask-related skin injury—were not systematically captured in the attached studies. This likely reflects reporting bias toward efficacy outcomes rather than comprehensive safety surveillance, and underscores the need for standardized adverse event monitoring in future PARDS trials.(12, 13, 14)

Protocol Implications: Monitoring Cadence and Escalation Rules
Proposed Monitoring Framework
Based on synthesis of the attached evidence and PALICC-2 recommendations, we propose the following monitoring framework for children with PARDS on HFNC or NIV:
Initial Assessment (0–1 hour): Establish baseline SpO_2/FiO_2, respiratory rate, work-of-breathing score, hemodynamics, and mental status. Optimize HFNC flow (up to 2 L/kg/min in infants, maximum 60 L/min in older children) or NIV settings (inspiratory pressure sufficient to achieve visible chest rise, positive end-expiratory pressure 5–8 cmH_2O). Document trajectory goals: target SpO_2 90–97%, respiratory rate within age-appropriate range or trending toward baseline, and decreasing work-of-breathing.
Early Reassessment (1–2 hours): Evaluate for rapid deterioration. Red flags include worsening SpO_2 despite FiO_2 escalation, increasing respiratory rate or work-of-breathing, hemodynamic instability, altered mental status, or inability to clear secretions. Children exhibiting any of these should be escalated promptly to intubation. Those showing stabilization or improvement proceed to continued noninvasive support with ongoing titration.
Intermediate Reassessment (6–12 hours): Assess trajectory. Improvement—defined as increasing SpO_2/FiO_2, decreasing respiratory rate, reduction in work-of-breathing, and ability to tolerate brief breaks for feeds or repositioning—suggests noninvasive success. Plateau or worsening despite optimal support, particularly persistent moderate-to-severe work-of-breathing or SpO_2/FiO_2 less than 200 at 12 hours, should prompt multidisciplinary discussion of escalation. Consider adjuncts such as prone positioning if not yet employed.
Extended Monitoring (12–72 hours): For children who stabilize on noninvasive support, continue vigilant monitoring with at least every 4-hour assessments. Late deterioration can occur with intercurrent infection, atelectasis, or evolving multi-organ dysfunction. Escalation thresholds remain the same: worsening oxygenation or work-of-breathing despite intervention.

Decision Nodes for Escalation
Escalation to intubation should be considered at any timepoint when:
1. SpO_2 less than 88% or PaO_2 less than 60 mmHg despite FiO_2 0.6 or higher on optimized noninvasive support
2. Persistent moderate-to-severe work-of-breathing after 6 hours of adequate HFNC (flow ≥2 L/kg/min) or NIV (sufficient inspiratory pressure and positive end-expiratory pressure)
3. Hemodynamic instability requiring escalating vasoactive support
4. Altered mental status or inability to protect airway
5. Need for procedures requiring airway control

6. Worsening trajectory: rising FiO_2 requirement, increasing respiratory rate, or qualitative worsening at any reassessment despite intervention

These criteria synthesize PALICC-2 guidance and observed patterns across the reviewed cohorts, prioritizing clinical trajectory and multi-parameter assessment over reliance on a single numeric threshold.(1, 2, 6)

Gaps and Research Priorities

Validation of Composite Scores

While individual predictors—SpO_2/FiO_2, ROX-index variants, and work-of-breathing—have been studied, composite scores integrating multiple domains remain underdeveloped for PARDS. Clinical respiratory scores evaluated in synthesis sources from the attached documents showed promise but require external validation in diverse populations. Future research should focus on developing and validating multivariable models that incorporate oxygenation, ventilatory demand, hemodynamics, and clinical trajectory to improve risk stratification beyond what single variables provide.

Optimal Timing of Escalation

The attached studies provide limited data on time-to-intubation and whether specific windows minimize adverse outcomes. Delayed intubation has been associated with worse outcomes in some adult ARDS cohorts, but pediatric-specific data are sparse.(11, 6) Conversely, premature intubation exposes children to sedation, iatrogenic complications, and prolonged mechanical ventilation. Prospective trials randomizing early versus protocolized-later escalation strategies are needed, though ethical and practical challenges are substantial.

Role of Emerging Technologies

Lung ultrasound, respiratory muscle electromyography, and non-invasive cardiac output monitoring were not addressed in the attached sources but may enhance early detection of failure. Diaphragmatic ultrasound could quantify work-of-breathing more objectively than clinical scoring, while lung ultrasound might identify early recruitment failure despite adequate positive end-expiratory pressure. Integration of these modalities into PARDS monitoring protocols represents a promising area for investigation.

Safety Outcomes and Long-Term Follow-Up

As noted, barotrauma, aspiration, and device-related injury were under-reported in the reviewed studies. Standardized adverse event capture should be mandatory in future PARDS trials involving noninvasive support. Additionally, long-term neurodevelopmental and respiratory outcomes stratified by noninvasive success versus failure are needed to understand whether avoiding intubation confers durable benefit or merely shifts morbidity to the post-discharge period.

Phenotype-Specific Pathways

PARDS encompasses diverse etiologies—viral pneumonia, sepsis, aspiration, trauma—with potentially distinct responses to noninvasive support. The attached studies predominantly analyzed heterogeneous cohorts without phenotype-specific analyses. Future research should stratify outcomes by PARDS etiology, immunocompromise status, and pre-existing lung disease to identify subgroups most likely to benefit from aggressive noninvasive trials versus early intubation.(2, 12, 15)

Conclusion

Noninvasive respiratory support via HFNC and NIV has become standard initial therapy for many children with mild-to-moderate PARDS in the post-PALICC-2 era. However, failure rates remain high and reliable predictors of escalation need are incompletely defined. SpO_2/FiO_2 ratio, pediatric ROX-index variants, and clinical assessment of work-of-breathing all contribute to risk stratification, but no single numeric cutoff universally identifies children who will fail. The most consistent evidence supports close reassessment at 1–2 hours to detect rapid deterioration and at 6–12 hours to evaluate trajectory, with escalation prompted by worsening oxygenation or persistent respiratory distress despite optimal support. Outcomes including intubation rate, length of stay, and mortality are influenced by PARDS severity and timing of escalation, though delayed intubation does not appear to increase mortality when monitoring is vigilant. Future research should validate composite

prediction models, define optimal escalation windows, incorporate emerging monitoring technologies, and capture comprehensive safety outcomes to refine clinical practice and improve outcomes for this vulnerable population.

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