

Pain Assessment During Less Invasive Surfactant Administration Using Skin Conductance: A prospective Cohort Study

Coralie Dirler¹, Vinzenz Boos¹, Dirk Bassler¹, Stephan Benke-Bruderer², Ulrike Held³, Christoph M. Rüegger¹, Tobias Mühlbacher¹

¹Newborn Research, Department of Neonatology, University Hospital Zurich, University of Zurich, Zurich, Switzerland.

²Clinical Trials Center, University Hospital Zurich, Zurich, Switzerland.

³Epidemiology, Biostatistics and Prevention Institute, University of Zurich, Zurich, Switzerland.

Annual Meeting of the Swiss Society of Neonatology, Aarau, 19.05.2026

Introduction

Less Invasive Surfactant Administration (LISA):

- ↓ Mechanical ventilation, ↓ Bronchopulmonary Dysplasia ¹
- Laryngoscopy → Discomfort^{2,3}
- No consensus regarding routine use of analgesic or sedative medication⁴

¹Abdel-Latif, M. E. et al. Surfactant Therapy Via Thin Catheter in Preterm Infants with or at Risk of Respiratory Distress Syndrome. Cochrane Database Syst Rev 5, CD011672 (2021).

²De Luca, D. et al. Less Invasive Surfactant Administration: A Word of Caution. Lancet Child Adolesc Health 4, 331–340 (2020).

³Pichler, K. et al. Assessment of Comfort During Less Invasive Surfactant Administration in Very Preterm Infants: A Multicenter Study. Neonatology 120, 473–481 (2023).

⁴Tribolet, S. et al. in Neonatology Vol. 119 137-150 (© 2022 S. Karger AG, Basel., 2022).

Pain Assessment

Neonatal Pain, Agitation and Sedation Scale (N-PASS)

- Validated multifactorial scale
- Behavioral and physiological cues
- Evaluator bias

Skin Conductance (SC)

Noxious Stimulus → Sympathetic activation → Sweat Secretion → SC Peak

- SC-Peak 1-2 seconds after stimulus
- Peaks Per Second (PPS)

Population & SC Measurement

Inclusion criteria:

- GA $\geq 27+0$ wks
- PEEP ≥ 6 cmH₂O
- FiO₂ ≥ 0.3

SC-Measurement:

- MedStorm Skin Conductance Monitor
- Ordinal scale 0–10 (0 = 0 PPS, 10 = ≥ 0.4 PPS)
- Video recording for blinded N-PASS assessment



Outcomes

Primary Outcome

Δ SC-PPS from baseline:

- Nasopharyngeal Tube (NPT) Insertion
- Laryngoscopy
- Catheter insertion
- Surfactant administration
- Catheter removal
- 5- and 60-minutes post-procedure

Secondary Outcomes

- Blinded N-PASS Scores
- Cardiorespiratory parameters
- Occurrence of adverse events

Patient characteristics (n = 20)

Demographic data	Median [IQR], n (%)	APGAR	
Gestational age at birth (weeks)	30.00 [28.1, 30.8]	5'	6.5 [5.0, 8.0]
Birth weight (g)	1300 [1058, 1723]	10'	9.0 [9.0, 9.0]
Female sex	8 (40.0%)	Clinical Data	
Mode of delivery		Respiratory support before LISA	
Cesarean section	17 (85.0%)	CPAP	16 (80.0%)
Vaginal delivery	3 (15.0%)	NIPPV	4 (20.0%)
Antenatal corticosteroids		PEEP level	8.0 [8.0, 8.0]
None	1 (5.0%)	Hours of life at LISA procedure (chronological age)	1.65 [0.57, 4.06]
Incomplete (<48h)	9 (45.0%)	Duration of the LISA procedure (minutes) ^a	8.1 [IQR 4.4, 10.8]
Complete	10 (50.0%)	Use of sedative medication	5 (25%)

^atime from baseline-measurement until removal of LISA catheter.

SC & N-PASS

Table 2. Estimated differences from baseline (Δ_{logit} , linear predictor scale) in SC measurements and N-PASS across all steps of the LISA procedure, based on ordinal regression models.

Contrast	Skin Conductance			N-PASS		
	Estimated logit difference	95% CI	p-value	Estimated logit difference	95% CI	p-value
insertion of NPT—Baseline	2.375	0.198 to 4.551	0.025	3.2839	1.3658 to 5.2021	<0.0001
laryngoscopy—Baseline	0.693	−1.503 to 2.889	0.88	3.6020 ^a	1.7749 to 5.4291 ^a	<0.0001
insertion of LISA catheter—Baseline	0.660	−1.555 to 2.875	0.90			
administration of surfactant—Baseline	−0.001	−2.477 to 2.475	1.00	1.8955	−0.0360 to 3.8271	0.057
removal of LISA catheter—Baseline	0.584	−1.715 to 2.883	0.94			
5' after removal of LISA catheter—Baseline	0.025	−2.454 to 2.505	1.00	0.4658	−1.4700 to 2.4017	0.92
60' after removal of LISA catheter—Baseline	−0.131	−2.695 to 2.432	1.00	−1.8470	−4.4210 to 0.7270	0.25

Confidence intervals are asymptotic; *p*-values are adjusted for multiple comparisons. ^avalues of the ordinal regression model after the post-hoc inclusion of N-PASS scores during insertion of the NPT.
Confidence intervals are asymptotic; *p*-values are adjusted for multiple comparisons.
^avalues of the ordinal regression model after the post-hoc inclusion of N-PASS scores during insertion of the NPT.

Primary analysis: no significant correlation between SC-PPS and N-PASS scores (Kendall’s τ_B = 0.10, 95%-CI: -0.07 to 0.27).

Post-hoc: overall positive correlation between SC-PPS and N-PASS scores (Kendall’s τ_B = 0.17, 95%-CI: 0.02 to 0.31).

Why no robust SC response?

- Median age 1.65h → immature skin, elevated baseline-conductivity ^{1,2}
- Inter-individual variability
- SC changes out of predefined windows
- Laryngoscopy does not generate a sufficiently intense autonomic response
- Behavioral responses ≠ true nociception → discrimination of noxious stimuli depends on brain maturation^{3,4}

¹Fowles, D. C. et al. Effects of Epidermal Hydration on Skin Conductance Responses and Levels. Biol Psychol 2, 67–77 (1974).

²Ishiguro, A. et al. Postnatal Changes in Skin Water Content in Preterm Infants. Early Hum Dev 91, 505–509 (2015).

³Green, G. et al. Behavioural Discrimination of Noxious Stimuli in Infants Is Dependent on Brain Maturation. Pain 160, 493–500 (2019).

⁴van der Vaart, M. et al. Premature Infants Display Discriminable Behavioral, Physiological, and Brain Responses to Noxious and Nonnoxious Stimuli. Cereb Cortex 32, 3799–3815 (2022).

Conclusion

- LISA was not associated with elevated SC-PPS, despite increased N-PASS scores during NPT-Insertion and laryngoscopy
- Weak correlation (Kendall's $\tau_B = 0.17$) suggests SC alone may not reliably indicate procedural pain immediately after birth
- Further research is needed → larger samples, controlled post-natal conditions, adapted measurement protocols, to validate SC for neonatal pain assessment.

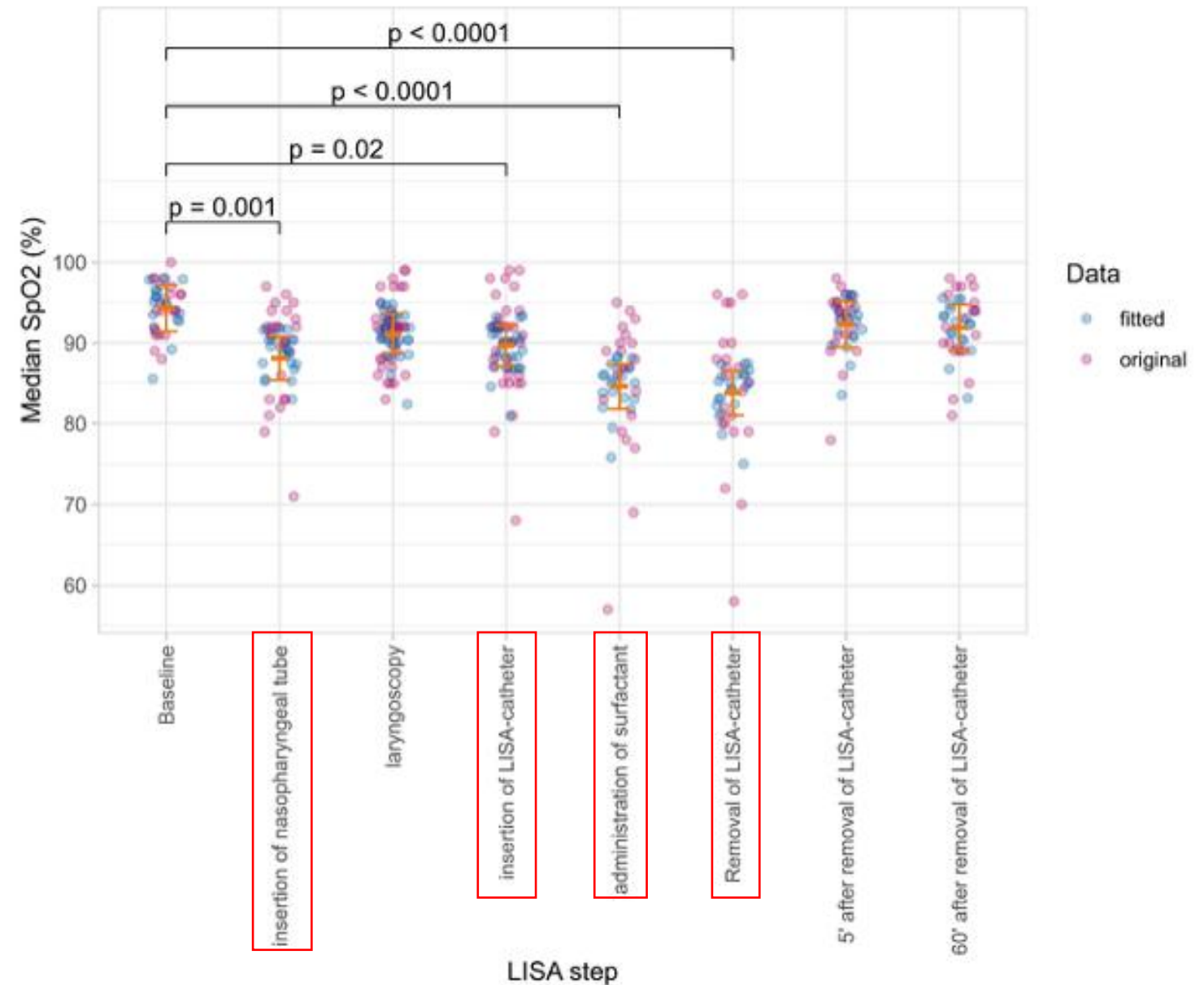
Thank you!

Secondary Outcome: N-PASS

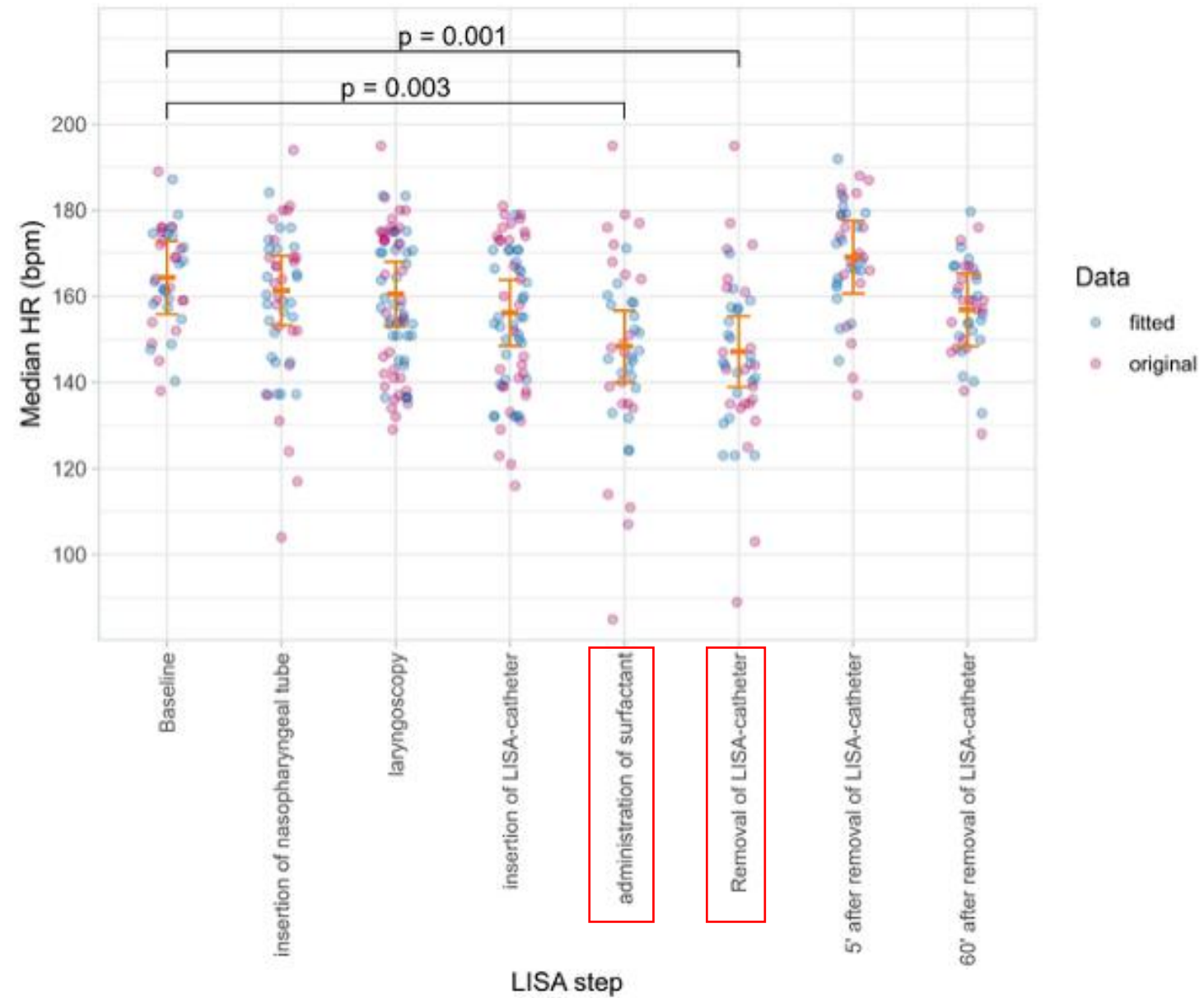
Event	Median baseline subtracted N-PASS [IQR]	Missing values
insertion of nasopharyngeal tube	3.5 [0, 4]	3
laryngoscopy	3 [1, 4]	0
administration of surfactant	0 [0, 3]	1
5' after removal of LISA-catheter	0 [0, 3]	0
60' after removal of LISA-catheter	0 [-0.5, 0]	0

Median baseline subtracted N-PASS scores for the specified events.

Secondary Outcomes: SpO2

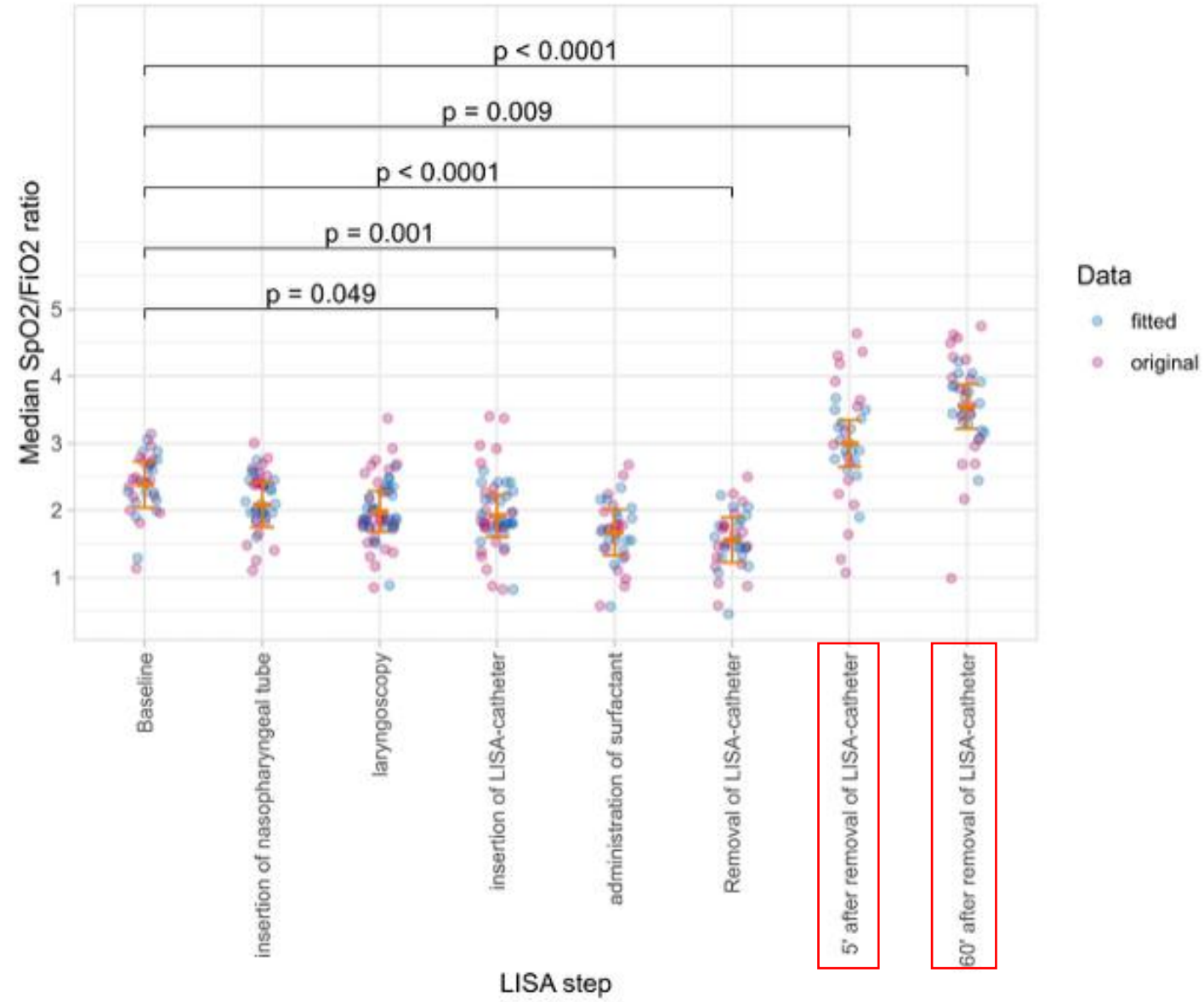


Secondary Outcomes: HR



RESULTS

Secondary Outcomes: SpO2/FiO2 ratio



Secondary Outcomes: Adverse Events

Adverse events:

- Desaturation: 55%
- Bradycardia: 25%
- Apnea: 15%