

Appendix

Predictors for expired CO₂ in neonatal bag-mask ventilation: observational study

Table S1

Linear random intercept models for predictors of expired carbon dioxide (ECO₂) per ventilation sequence in newborns who received more than three ventilation sequences lasting for more than 10 seconds (n=227)

A: First ventilation sequence

Predictors		Univariate model ^a			Multivariate model					
		Coef (95%CI)	P-value	R ² (%)	Coef (95%CI)	P-value	R ² (%)	R ² (%)		
ECO ₂ (unconditional)		2.15 (1.92, 2.38)								
Markers for BMV quality	V_{TE} Per ml/kg increase Per standardized unit	0.41 (0.31, 0.51) 2.65 (2.01, 3.3)	<0.001	27.1	0.40 (0.30, 0.50) 2.60 (1.97, 3.24)	<0.001	23.6 ^b	28.1		
	(V_{TE})² Per unit increase Per standardized unit	-0.0096 (-0.013, -0.006) -1.48 (-2.06, -0.90)	<0.001		-0.0098 (-0.013, -0.0062) -1.51 (-2.06, -0.95)	<0.001				
	Mask leak Per 10 units [%] increase Per standardized unit	-0.28 (-0.35, -0.21) -0.81 (-1.02, -0.60)	<0.001	16.8	-0.024 (-0.086, 0.037) -0.070 (-0.25, 0.11)	0.4 ^b				
	Ventilation frequency Per 10 bpm increase Per standardized unit	-0.11 (-0.19, -0.03) -0.23 (-0.39, -0.065)	0.006	4.2	-0.12 (-0.19, -0.051) -0.25 (-0.40, -0.11)	0.001 ^c	5.2			
	PIP Per 10 mbar increase Per standardized unit	0.062 (-0.34, 0.46) 0.065 (-0.36, 0.49)	0.8	0.3	-0.36 (-0.64, -0.071) -0.38 (-0.68, -0.075)	0.01	-0.4			
	(PIP)² Per unit increase Per standardized unit	-0.019 (-0.055, 0.017) -0.18 (-0.52, 0.16)	0.3		-0.065 (-0.016, -0.071) 0.062 (-0.16, 0.28)	0.6				
	Clinical factors	Birth weight Per kg increase Per standardized unit	0.83 (0.44, 1.23) 0.48 (0.25, 0.70)	<0.001	5.0	0.81 (0.50, 1.12) 0.46 (0.29, 0.64)	<0.001		6.9	11.6
		Initial HR Per 10 bpm increase Per standardized unit	0.20 (0.09, 0.31) 0.42 (0.19, 0.65)	<0.001	3.8	0.15 (0.056, 0.23) 0.30 (0.12, 0.49)	0.001		3.2	
		5 min Apgar Per 1 unit increase Per standardized unit	0.012 (-0.084, 0.11) 0.028 (-0.19, 0.25)	0.802	0.0	0.10 (0.015, 0.19) 0.24 (0.034, 0.44)	0.02		1.9	
	Time Per doubling Per standardized unit	0.23 (0.14, 0.32) 0.36 (0.22, 0.50)	<0.001	3.8	0.13 (0.046, 0.20) 0.19 (0.072, 0.32)	0.002	3.1			
Random effect parameters					Var(_cons) 1.88 (1.50, 2.35)^d Var (Residual) 1.00 (0.80, 1.25) ICC =0.65					

^a ICC in the univariate models varied from 0.64 to 0.68.

^b Mask leak and volume (V_{TE}) were correlated. Excluding V_{TE} from the model, mask leak came out significant with P<0.001, beta -0.28 (-0.35, -0.21) and R² 18.0%.

^c An interaction term for frequency and V_{TE} was significant with P<0.001, beta -0.027(-0.040, -0.013). V_{TE} was still a strong positive predictor for ECO₂, whereas frequency and mask leak lost significance.

^d Explained variance in the total model: 37.3%.

B: Second ventilation sequence

		Univariate model ^a			Multivariate model				
Predictors		Coef (95%CI)	P-value	R ² (%)	Coef (95%CI)	P-value	R ² (%)	R ² (%)	
ECO2 (unconditional)		2.90 (2.65, 3.17)							
Markers for BMV quality	V_{TE}								
	Per ml/kg increase	0.34 (0.27, 0.40)	<0.001	30.1	0.29 (0.21, 0.36)	<0.001	32.0	36.3	
	Per standardized unit	2.19 (1.75, 2.63)			1.88 (1.35, 2.39)				
	(V_{TE})²								
	Per unit increase	-0.0084 (-0.011, 0.006)	<0.001		-0.080 (-0.011, -0.054)	<0.001			
	Per standardized unit	-1.29 (-1.66, -0.91)			-1.22 (-1.62, -0.82)				
	Mask leak			19.0	-0.080 (-0.14, -0.020)	0.009 ^b			
	Per 10 units increase	-0.26 (-0.32, -0.21)	<0.001		-0.23 (-0.40, -0.058)				
	Per standardized unit	-0.76 (-0.90, -0.61)							
	Ventilation frequency			4.5	-0.18 (-0.31, -0.050)	0.006 ^c	7.6		
Per 10 bpm increase	-0.10 (-0.23, 0.024)	0.1		-0.38 (-0.65, -0.11)					
Per standardized unit	-0.22 (-0.49, 0.050)								
PIP			1.6	0.27 (-0.024, 0.57)	0.07	1.4			
Per 10 mbar increase	0.72 (0.33, 1.12)	<0.001			0.29 (-0.027, 0.58)				
Per standardized unit	0.76 (0.35, 1.18)								
(PIP)²				-0.048 (-0.080, -0.015)	0.004				
Per unit increase	-0.78 (-0.12, -0.031)	0.001		-0.46 (-0.77, -0.14)					
Per standardized unit ²	-0.74 (-1.19, -0.29)								
Clinical factors	Birth weight			5.9	0.78 (0.46, 1.09)	<0.001	6.0	10.8	
	Per kg increase	0.99 (0.59, 1.40)	<0.001		0.44 (0.26, 0.63)				
	Per standardized unit	0.57 (0.34, 0.80)							
	Initial HR			1.4	0.12 (0.028, 0.21)	0.01	1.9		
Per 10 bpm increase	0.13 (-0.003, 0.26)	0.05		0.25 (0.058, 0.44)					
Per standardized unit	0.27 (-0.0007, 0.54)								
5 min Apgar			0.3	0.14 (0.040, 0.25)	0.007	3.4			
Per 1 unit increase	0.054 (-0.071, 0.18)	0.4		0.33 (0.092, 0.56)					
Per standardized unit	0.12 (-0.16, 0.41)								
Time			2.6	0.12 (-0.008, 0.26)	0.07	0.3			
Per doubling	0.23 (0.091, 0.36)	0.001		0.19 (-0.012, 0.40)					
Per standardized unit	0.35 (0.14, 0.56)								
Random effects parameters					Var(_cons) 2.03 (1.57, 2.62) ^d				
					Var (Residual) 1.04 (0.64, 1.70)				
					ICC = 0.66				

^a ICC in the univariate models varied from 0.71 to 0.75.

^b Excluding volume (V_{TE}) from the model, mask leak got increasing significance: Beta = -0.25 (-0.32, -0.19), P<0.001, R² 21.0%. Excluding mask leak from the model, R² for V_{TE} alone was 31.5%.

^c Interaction term for frequency and V_{TE} was not significant, beta -0.017(-0.035, 0.014), P<0.07.

^d Explained variance R² in the total model: 43.4%.

C: Third ventilation sequence

		Univariate model ^a			Multivariate model					
Predictors		Coef (95%CI)	P-value	R ² (%)	Coef (95%CI)	P-value	R ² (%)	R ² (%)		
ECO2 (unconditional)		3.14 (2.89, 3.39)								
Markers for BMV quality	V_{TE} Per unit increase Per standardized unit	0.31 (0.22, 0.40) 2.02 (1.42, 2.61)	<0.001	21.4	0.28 (0.19, 0.37) 1.82 (1.25, 2.39)	<0.001	16.2 ^b	25.6		
	(V_{TE})² Per unit increase Per standardized unit	-0.0072 (-0.010, 0.0044) -1.10 (-1.51, -0.68)	<0.001		-0.0067 (-0.009, -0.004) -1.03 (-1.43, -0.63)	<0.001				
	Mask leak Per 10 units increase Per standardized unit	-0.24 (-0.31, -0.18) -0.70 (-0.88, -0.51)	<0.001	10.6	-0.064 (-0.12, -0.005) -0.18 (-0.35, -0.014)	0.03 ^b				
	Ventilation frequency Per 10 bpm increase Per standardized unit	-0.17 (-0.36, 0.015) -0.36 (-0.76, 0.031)	0.07	9.0	-0.16 (-0.30, -0.013) -0.33 (-0.63, -0.026)	0.03 ^c	9.9			
	PIP Per 10 mbar increase Per standardized unit	-0.20 (-1.10, 0.69) -0.21 (-1.16, 0.73)	0.7	-0.9	-0.37 (-0.96, 0.22) -0.39 (-1.01, 0.24)	0.2	-2.6			
	(PIP)² Per unit increase Per standardized unit	0.21 (-0.060, 0.10) 0.20 (-0.57, 0.98)	0.6		-0.011 (-0.039, 0.062) 0.11 (-0.37, 0.59)	0.7				
	Clinical factors	Birth weight Per kg increase Per standardized unit	0.82 (0.38, 1.25) 0.47 (0.22, 0.72)	<0.001	4.7	0.66 (0.31, 1.01) 0.38 (0.18, 0.58)	<0.001		4.5	9.0
		Initial HR Per 10 bpm increase Per standardized unit	0.20 (0.088, 0.32) 0.42 (0.18, 0.66)	0.001	3.8	0.14 (0.040, 0.24) 0.29 (0.082, 0.49)	0.006		2.7	
		5 min Apgar Per 1 unit increase Per standardized unit	0.051 (-0.062, 0.16) 0.12 (-0.14, 0.38)	0.4	0.3	0.11 (0.002, 0.21) 0.25 (0.047, 0.49)	0.05		2.1	
	Time Per doubling Per standardized unit		0.11 (0.029, 0.19) 0.18 (0.047, 0.31)	0.008	1.7	0.028 (-0.047, 0.10) 0.045 (-0.075, 0.17)	0.5		0.7	
Random effects parameters					Var(_cons) 2.32 (1.87, 2.87) ^d Var (Residual) 0.78 (0.63, 0.96) ICC=0.75					

^a ICC in the univariate models varied from 0.71 to 0.75.

^b Excluding volume (V_{TE}) from the model, mask leak got increasing significance: Beta = -0.25 (-0.32, -0.19), P<0.001, R² 8.2%.
Excluding mask leak from the model, R² for V_{TE} alone was 16.7%.

^c Interaction term for frequency and V_{TE} was not significant, beta -0.0067(-0.014, 0.00081), P=0.08.

^d Explained variance R² in the total model: 33.5%.

Table S2

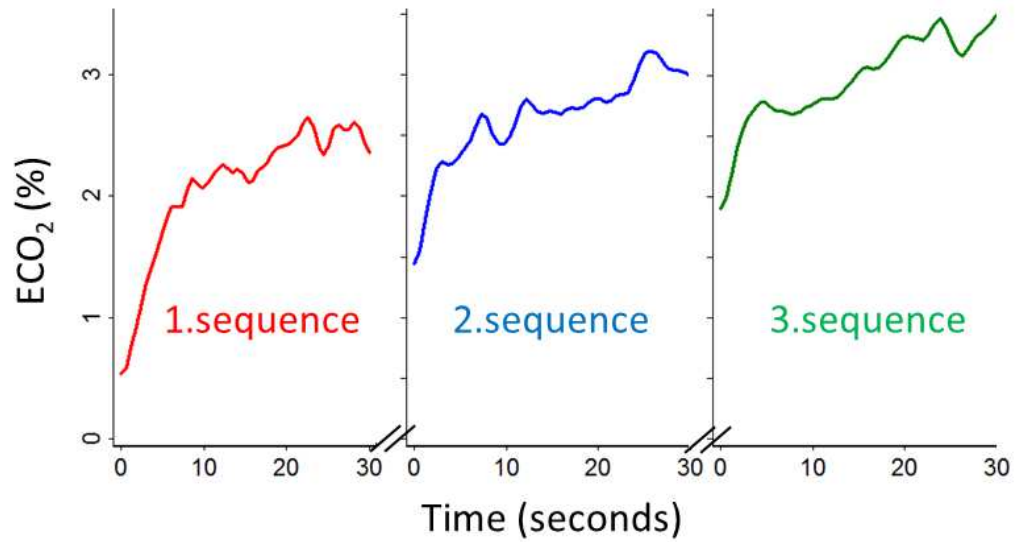
Linear random intercept models for predictors of expired carbon dioxide (ECO₂) in the first 5 minutes substituting volume and frequency with minute volume

		Univariate model			Multivariate model		
Covariates		Coef (95%CI)	P-value	R ² (%)	Coef (95%CI)	P-value	R ² (%)
ECO₂ (unconditional)		2.90 (2.75, 3.05)					
Ventilation factors	Minute volume Per 100 ml/kg min ⁻¹ increase	0.56 (0.48, 0.64)	<0.001	7.5	0.36 (0.27, 0.44)	<0.001	12.4
	(Minute volume)² Per (10 ml/kg min ⁻¹) ² increase	-0.03 (-0.3, -0.2)	<0.001		-0.18 (-0.02, -0.01)	<0.001	
	Mask leak Per 10% increase	-0.30 (-0.33, -0.27)	<0.001	16.1	-0.13 (-0.16, -0.099)	<0.001	
	PIP Per 10 mbar increase	0.41 (0.16, 0.67)	0.001	1.1	0.016 (0.048, 0.36)	0.1	
	PIP² Per 10 mbar ² increase	-0.60 (-0.87, -0.33)	<0.001		-0.34 (-0.53, -0.15)	<0.001	
	Clinical factors	Birth weight Per kg increase	0.78 (0.51, 1.04)	<0.001	4.4	0.80 (0.54, 1.05)	
Initial HR Per 10 bpm increase		0.081 (0.012, 0.15)	0.022	0.6	0.086 (0.019, 0.15)	0.01	
5 min Apgar Per 1 unit increase		0.054 (-0.021, 0.13)	0.16	0.3	0.14 (0.045, 0.20)	0.002	
Log₂ of time in seconds Per unit increase		0.33 (0.28, 0.38)	<0.001	2.0	0.22 (0.17, 0.26)	<0.001	2.1
Random effects parameters					Var (_cons) 2.10 (1.83, 2.42)^a Var (Residual) 1.75 (1.53, 2.01) ICC 0.55		

^a R² for the total model 20.0%

Figure S1

Median expired carbon dioxide (ECO₂) in first three ventilation sequences



The figure displays ECO₂ as smoothed median observed values (per second) for all included newborns in the first 30 seconds per ventilation sequence.