Supplementary figures and tables

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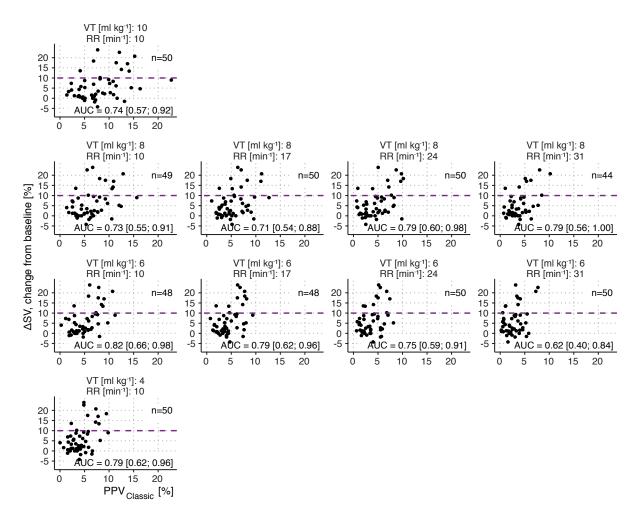


Figure S1: Scatter plots of the relation between PPV calculated with the classic algorithm (PPV_{Classic}) and the stroke volume response (Δ SV) to a 250 ml fluid challenge. Panels are arranged with tidal volumes (VT) in rows and respiratory rates (RR) in columns . One fluid challenge was evaluated for each subject (n = 50), while PPV_{Classic} was calculated for each of the 10 ventilator settings.

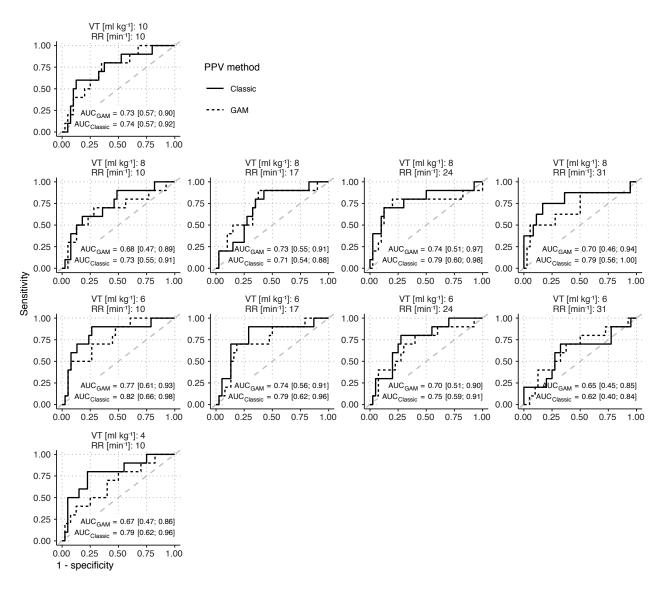


Figure S2: Receiver operating characteristic (ROC) curves for capacity of pulse pressure variation (PPV) to classify fluid responsiveness (stroke volume change > 10%). Panels are arranged with tidal volumes (VT) in rows and respiratory rates (RR) in columns. One fluid challenge was evaluated for each subject (n = 50), while PPV_{GAM} and PPV_{Classic} was calculated for each of the 10 ventilator settings.

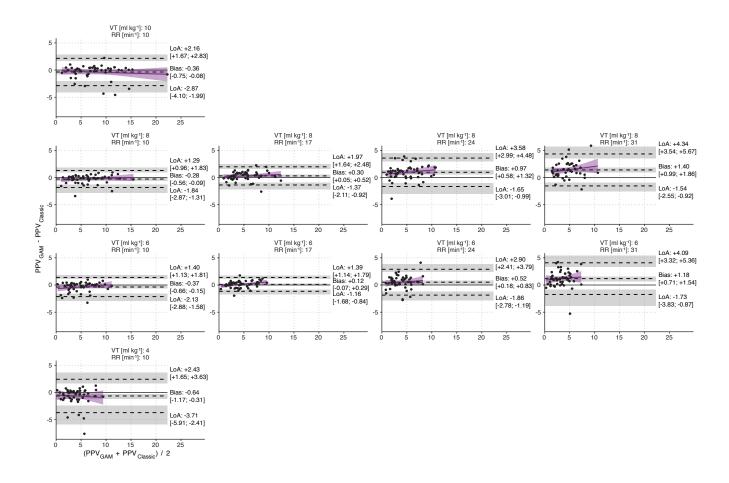


Figure S3: Bland-Altman plots showing the relation between PPV_{GAM} and $PPV_{Classic}$. The outer dashed lines represent 95% limits of agreement (LoA). Grey areas are 95% confidence intervals for bias and LoA. The purple lines and areas are linear regression fits with 95% confidence intervals. Panels are arranged with tidal volumes (VT) in rows and respiratory rates (RR) in columns.

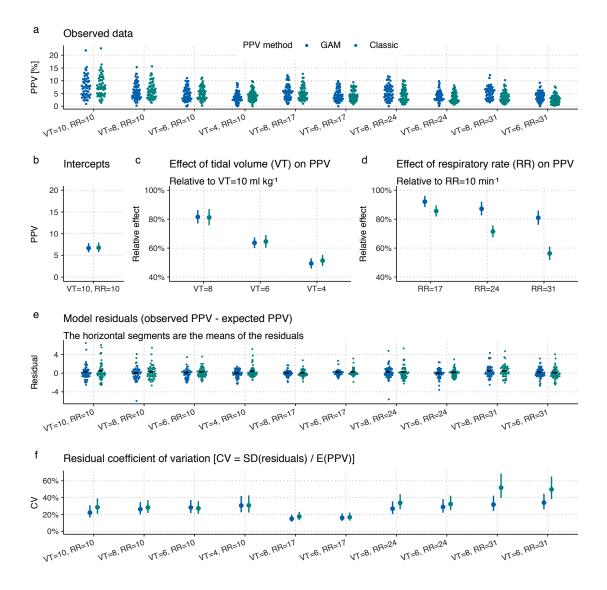


Figure S4: (Extended version of the paper's Fig. 5): Parameter estimates for a Bayesian mixed-effects model, describing the effect of tidal volume (VT) and respiratory rate (RR) on pulse pressure variation (PPV). Parameters are estimated for both PPV derived using a generalized additive model (GAM) and using a classic approach (Classic). Panel **a** presents the observed PPV values (outcomes) using each method (n=507 for both GAM and Classic). Vertical bars are 95% compatibility intervals. Panel **b**, **c** and **d** present parameter estimates. Vertical bars are 95% compatibility intervals. Panel **e** shows model residuals, and panel **f** shows the residual variation relative to the estimated value of PPV.

Table S1

Receiver operating characteristic analysis of fluid-responsiveness prediction using pulse pressure variation (PPV). A positive fluid response was a >10% increase in stroke volume from a 250 ml fluid bolus. PPV was calculated using a classic method and derived from a generalized additive model (GAM). Results are presented as estimate [95% confidence interval].

	GAM PPV				Classic PPV			
		Sensitivity	Specificity	AUC	Optimal threshold ¹	Sensitivity	Specificity	AUC
10	7.9%	0.80 [0.50;1.00]	0.65 [0.50;0.80]	0.73 [0.57;0.90]	11.4%	0.60 [0.30;0.90]	0.88 [0.78;0.97]	0.74 [0.57;0.92
10	6.9%	0.70 [0.40;1.00]	0.72 [0.56;0.85]	0.68 [0.47;0.89]	8.1%	0.60 [0.30;0.90]	0.82 [0.69;0.92]	0.73 [0.55;0.91]
10	5.9%	0.70 [0.40;1.00]	0.74 [0.61;0.87]	0.77 [0.61;0.93]	5.8%	0.90 [0.70;1.00]	0.74 [0.61;0.87]	0.82
10	3.1%	0.80 [0.50;1.00]	0.50 [0.35;0.68]	0.67 [0.47;0.86]	4.9%	0.80 [0.50;1.00]	0.78 [0.62;0.90]	0.79 [0.62;0.96]
17	5.7%	0.90 [0.70;1.00]	0.62 [0.47;0.78]	0.73 [0.55;0.91]	4.9%	0.90 [0.70;1.00]	0.57 [0.42;0.72]	0.71 [0.54;0.88]
17	5.7%	0.70 [0.40;1.00]	0.82 [0.68;0.92]	0.74 [0.56;0.91]	4.4%	0.90 [0.70;1.00]	0.71 [0.58;0.84]	0.79 [0.62;0.96]
24	7.2%	0.80 [0.50;1.00]	0.80 [0.68;0.93]	0.74 [0.51;0.97]	6.7%	0.70 [0.40;1.00]	0.88 [0.78;0.97]	0.79 [0.60;0.98]
24	4.6%	0.70 [0.40;1.00]	0.70 [0.55;0.85]	0.70 [0.51;0.90]	4.1%	0.80 [0.50;1.00]	0.72 [0.57;0.85]	0.75 [0.59;0.91]
31	7.7%	0.50 [0.12;0.88]	0.94 [0.86;1.00]	0.70 [0.46;0.94]	5.0%	0.75 [0.38;1.00]	0.83 [0.69;0.94]	0.79
31	4.3%	0.70 [0.40;1.00]	0.62 [0.47;0.78]	0.65 [0.45;0.85]	3.1%	0.70 [0.40;1.00]	0.68 [0.53;0.82]	0.62
	rate [min-i] 10 10 10 10 17 17 24 24 31	10 7.9% 10 6.9% 10 5.9% 10 3.1% 17 5.7% 17 5.7% 24 7.2% 24 4.6% 31 7.7%	Respiratory rate [min¹¹] Optimal threshold¹ Sensitivity 10 7.9% 0.80 [0.50;1.00] 10 6.9% 0.70 [0.40;1.00] 10 5.9% 0.70 [0.40;1.00] 10 3.1% 0.80 [0.50;1.00] 17 5.7% 0.90 [0.70;1.00] 17 5.7% 0.70 [0.40;1.00] 24 7.2% 0.80 [0.50;1.00] 24 4.6% 0.70 [0.40;1.00] 31 7.7% 0.50 [0.12;0.88]	Respiratory rate [min-1] Optimal threshold 7 Sensitivity Specificity 10 7.9% 0.80 [0.50;1.00] 0.65 [0.50;0.80] 10 6.9% 0.70 [0.40;1.00] 0.72 [0.56;0.85] 10 5.9% 0.70 [0.40;1.00] 0.74 [0.61;0.87] 10 3.1% 0.80 [0.50;1.00] 0.50 [0.35;0.68] 17 5.7% 0.90 [0.70;1.00] 0.62 [0.47;0.78] 17 5.7% 0.70 [0.40;1.00] 0.82 [0.68;0.92] 24 7.2% 0.80 [0.50;1.00] 0.68;0.93] 24 4.6% 0.70 [0.40;1.00] [0.55;0.85] 31 4.3% 0.70 [0.12;0.88] 0.94 [0.86;1.00]	Respiratory rate [min ⁻¹] Optimal threshold ⁷ Sensitivity Specificity AUC 10 7.9% 0.80 [0.50;1.00] 0.65 [0.50;0.80] 0.73 [0.57;0.90] 10 6.9% 0.70 [0.50;1.00] 0.72 [0.56;0.85] 0.68 [0.47;0.89] 10 5.9% 0.70 [0.40;1.00] 0.74 [0.61;0.87] 0.77 [0.61;0.93] 10 3.1% 0.80 [0.50;1.00] 0.50 [0.35;0.68] 0.67 [0.47;0.86] 17 5.7% 0.90 [0.70;1.00] 0.62 [0.47;0.78] 0.75 [0.55;0.91] 17 5.7% 0.70 [0.40;1.00] 0.80 [0.68;0.92] 0.74 [0.56;0.91] 24 7.2% 0.80 [0.50;1.00] 0.70 [0.68;0.93] 0.51;0.97] 24 4.6% 0.70 [0.40;1.00] 0.70 [0.55;0.85] 0.51;0.90] 31 7.7% 0.50 [0.40;1.00] 0.94 [0.86;1.00] 0.065	Respiratory rate [min¹¹] Optimal threshold¹ Sensitivity Specificity AUC Optimal threshold¹ 10 7.9% 0.80 [0.50;1.00] 0.65 [0.50;0.80] 0.73 [0.57;0.90] 11.4% 10 6.9% 0.70 [0.50;1.00] 0.72 [0.56;0.85] 0.68 [0.47;0.89] 8.1% 10 5.9% 0.70 [0.40;1.00] 0.74 [0.61;0.87] 0.61;0.93] 5.8% 10 3.1% 0.80 [0.50;1.00] 0.50 [0.61;0.87] 0.67 [0.47;0.86] 4.9% 17 5.7% 0.90 [0.50;1.00] 0.62 [0.47;0.78] 0.74 [0.55;0.91] 4.4% 17 5.7% 0.70 [0.40;1.00] 0.82 [0.56;0.91] 0.74 [0.56;0.91] 4.4% 24 7.2% 0.80 [0.50;1.00] 0.68;0.93] 0.74 [0.51;0.97] 6.7% 24 4.6% 0.70 [0.50;1.00] 0.70 [0.55;0.85] [0.51;0.90] 4.1% 31 7.7% 0.50 [0.12;0.88] 0.86;1.00] 0.70 [0.46;0.94] 5.0%	Respiratory rate [min-1] Optimal threshold? Sensitivity Specificity AUC Optimal threshold? Sensitivity 10 7.9% 0.80 [0.50;1.00] 0.65 [0.50;0.80] 0.73 [0.57;0.90] 11.4% 0.60 [0.30;0.90] 10 6.9% 0.70 [0.40;1.00] 0.72 [0.56;0.85] 0.68 [0.47;0.89] 8.1% 0.60 [0.30;0.90] 10 5.9% 0.70 [0.40;1.00] 0.74 [0.61;0.87] 0.77 [0.61;0.93] 5.8% 0.90 [0.70;1.00] 10 3.1% 0.80 [0.50;1.00] 0.62 [0.35;0.68] 0.67 [0.47;0.86] 4.9% 0.80 [0.50;1.00] 17 5.7% 0.90 [0.70;1.00] 0.62 [0.47;0.78] 0.73 [0.55;0.91] 4.9% 0.90 [0.70;1.00] 17 5.7% 0.70 [0.40;1.00] 0.82 [0.55;0.91] 4.4% 0.90 [0.70;1.00] 24 7.2% 0.80 [0.50;1.00] 0.80 [0.58;0.93] 0.74 [0.56;0.91] 4.1% 0.70 [0.40;1.00] 24 4.6% 0.70 [0.50;1.00] 0.70 [0.55;0.85] 0.70 [0.51;0.90] 4.1% 0.80 [0.50;1.00] 31 4.3% 0.70 [0.12;0.88]	Respiratory rate [min**] Optimal threshold* Sensitivity Specificity AUC Optimal threshold* Sensitivity Specificity 10 7.9% 0.80 [0.50;1.00] 0.65 [0.50;0.80] 0.73 [0.57;0.90] 11.4% 0.60 [0.30;0.90] 0.88 [0.70;0.97] 10 6.9% 0.70 [0.40;1.00] 0.72 [0.66;0.85] 0.68 [0.47;0.89] 8.1% 0.60 [0.30;0.90] 0.82 [0.69;0.92] 10 5.9% 0.70 [0.40;1.00] 0.74 [0.61;0.87] 0.77 [0.61;0.93] 5.8% 0.90 [0.70;1.00] 0.74 [0.61;0.87] 10 3.1% 0.80 [0.50;1.00] 0.50 [0.47;0.86] 4.9% 0.90 [0.62;0.90] 0.78 [0.62;0.90] 17 5.7% 0.90 [0.47;0.00] 0.62 [0.47;0.78] 0.73 [0.47;0.86] 4.9% 0.90 [0.70;1.00] 0.62;0.90] 17 5.7% 0.70 [0.40;1.00] 0.82 [0.47;0.78] 0.74 [0.47;0.86] 4.9% 0.90 [0.70;1.00] 0.57;0.90] 17 5.7% 0.70 [0.40;1.00] 0.68;0.92] 0.74 [0.56;0.91] 4.4% 0.90 [0.70;1.00] 0.71 [0.58;0.84] 24 7.2%