SUPPLEMENTARY ONLINE CONTENT

Krista Stephens, Nathan Mitchel, Sean Overton, Joseph E Tonna. On the transition from control modes to spontaneous modes during ECMO. A high-fidelity graphical analysis of ventilatory parameters and changes in pulmonary function among 419 patients.

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**Figure S6.** PaO2/FiO2 as a function of tidal volume and respiratory rate among patients with low compliance
Table S1. Ventilator parameters by support mode

| Variable                                      | All               | Control Modes | Spontaneous Modes | p-value<sup>2</sup> |
|-----------------------------------------------|-------------------|---------------|-------------------|---------------------|
| Tidal volume (mL)                            | 468 (360, 584)    | 428 (310, 534)| 513 (413, 633)    | <0.0001             |
| Respiratory rate (breaths per minute)        | 20 (15, 25)       | 18 (14, 22)   | 22 (18, 28)       | 0.32                |
| Peak inspiratory pressure (cmH₂O)            | 31 (21, 40)       | 35 (24, 40)   | 27 (16, 40)       | <0.0001             |
| Respiratory system compliance (mL/cmH₂O)     | 30.3 (22.2, 41)   | 27.6 (19.4, 37.2) | 34.7 (25.6, 43.9) | <0.0001             |
| Positive end expiratory pressure (cmH₂O)     | 8 (5, 10)         | 10 (8, 11)    | 5.4 (5, 8)        | <0.0001             |
| Elastic component of mechanical power (mL/(cmH₂O x min)) | 0.07 (0.04, 0.11) | 0.06 (0.03, 0.09) | 0.08 (0.05, 0.13) | <0.0001             |

<sup>1</sup> median, interquartile range (IQR)  
<sup>2</sup> p-value from univariate mixed effects panel regression model of one value per hour, clustered by patient.

Abbreviations: cmH₂O: centimeter of water; mL: milliliter; min: minute

Number of original observations: Tidal volume: 33,940; Respiratory rate: 36,882; Peak inspiratory pressure 33,655; Respiratory system compliance: 10,783; Positive end expiratory pressure: 36,045. Elastic component of mechanical power: 101,949 calculated observations.
### Table S2. Subset analysis of ventilator parameters by support mode, among patients with lung compliance <30 cmH2O

| Variable (Unit) | All (Median, IQR) | Control Modes (Median, IQR) | Spontaneous Modes (Median, IQR) | p-value^2 |
|----------------|-------------------|-----------------------------|-------------------------------|-----------|
| Tidal volume (mL) | 422 (320, 539)   | 375 (260, 480)              | 469 (383, 591)               | <0.0001   |
| Respiratory rate (breaths per minute) | 20 (16, 26)       | 18 (14, 22)                 | 23 (19, 28)                 | 0.29      |
| Peak inspiratory pressure (cmH2O) | 33 (21, 40)       | 35 (25, 40)                 | 27 (16, 40)                 | <0.0001   |
| Respiratory system compliance (mL/cmH2O) | 26.8 (19.1, 36)  | 23.7 (17, 31)               | 30.5 (23.4, 41.5)           | <0.0001   |
| Positive end expiratory pressure (cmH2O) | 8 (5, 10)         | 10 (8, 11)                  | 5.5 (5, 8)                  | <0.0001   |
| Elastic component of mechanical power (mL/(cmH2O x min)) | 0.07 (0.04, 0.10) | 0.05 (0.02, 0.09)           | 0.08 (0.05, 0.12)           | <0.0001   |

^1 median, interquartile range (IQR)

Abbreviations: cmH2O: centimeter of water; mL: milliliter; min: minute

Number of original observations: Tidal volume: 16,514; Respiratory rate: 18,025; Peak inspiratory pressure: 16,454; Respiratory system compliance: 5,496; Positive end expiratory pressure: 17,566. Elastic component of mechanical power: 51,694 calculated observations

^2 p value from univariate mixed effects panel regression model of one value per hour, clustered by patient.
Table S3. Multivariate analysis of the association between spontaneous mode and tidal volume during the period of transition

| Variable                                      | Coefficient | 95% CI       | p-value |
|------------------------------------------------|-------------|--------------|---------|
| Spontaneous Mode                             | 59.5        | (49.6 to 69.4) | <0.0001 |
| PEEP, per cmH2O                              | -0.1        | (-1.7 to 1.3)  | 0.85    |
| Compliance, per mL/cmH2O                     | 3.1         | (2.8 to 3.4)  | <0.0001 |
| Respiratory rate, per breath per minute       | -4.8        | (-5.3 to -4.3) | <0.0001 |
| Duration of time since switch to spontaneous, per hour | 1.1         | (0.6 to 1.5)  | <0.0001 |

Abbreviations: PEEP: positive end expiratory pressure; mL: milliliters; cmH2O: centimeter of water; Multivariate mixed effects panel regression model of one value per hour, clustered by patient.
Table S4. Multivariate analysis of the association between spontaneous mode and tidal volume during the period of transition, among patients with lung compliance <30 cmH2O

| Variable                               | Coefficient | 95% CI       | p-value |
|----------------------------------------|-------------|--------------|---------|
| Spontaneous Mode                       | 53.9        | (40.3 to 67.5) | <0.0001 |
| PEEP, per cmH2O                        | -1.6        | (-3.5 to 0.4) | 0.12    |
| Compliance, per mL/cmH2O               | 3.3         | (2.9 to 3.7)  | <0.0001 |
| Respiratory rate, per breath per minute| -3.6        | (-4.3 to -3.0)| <0.0001 |
| Duration of time since switch to spontaneous, per hour | 0.9         | (0.2 to 1.5)  | 0.007   |

Abbreviations: PEEP: positive end expiratory pressure; mL: milliliters; cmH2O: centimeter of water; Multivariate mixed effects panel regression model of one value per hour, clustered by patient.
Table S5. Multivariate analysis of the association between spontaneous mode and PEEP during the period of transition

| Variable                                      | Coefficient | 95% CI        | p-value   |
|-----------------------------------------------|-------------|---------------|-----------|
| Spontaneous Mode                             | -0.5        | (-0.6 to 0.4) | <0.0001   |
| Tidal volume, per mL                         | 0.0         | (0.0 to 0.0)  | 0.78      |
| Compliance, per mL/cmH2O                     | 0.0         | (0.0 to 0.0)  | <0.0001   |
| Respiratory rate, per breath per minute       | 0.1         | (0.0 to 0.0)  | 0.007     |
| Duration of time since switch to spontaneous, per hour | 0.0         | (0.0 to 0.0)  | <0.0001   |

Abbreviations: PEEP: positive end expiratory pressure; mL: milliliters; cmH2O: centimeter of water; Multivariate mixed effects panel regression model of one value per hour, clustered by patient.
Table S6. Multivariate analysis of the association between spontaneous mode and PEEP during the period of transition, among patients with lung compliance <30 cmH2O

| Variable                                      | Coefficient | 95% CI       | p-value |
|-----------------------------------------------|-------------|--------------|---------|
| Spontaneous Mode                              | -0.4        | (-0.6 to -0.1) | 0.02    |
| Tidal volume, per mL                          | 0.0         | (0.0 to 0.0)  | 0.09    |
| Compliance, per mL/cmH2O                      | 0.0         | (0.0 to 0.0)  | <0.0001 |
| Respiratory rate, per breath per minute       | 0.0         | (0.0 to 0.0)  | 0.58    |
| Duration of time since switch to spontaneous, per hour | 0.0         | (0.0 to 0.0)  | <0.0001 |

Abbreviations: PEEP: positive end expiratory pressure; mL: milliliters; cmH2O: centimeter of water; Multivariate mixed effects panel regression model of one value per hour, clustered by patient.
### Table S7. Multivariate analysis of the association between spontaneous mode and elastic component of mechanical power during the period of transition

| Variable                                           | Coefficient | 95% CI      | p-value  |
|----------------------------------------------------|-------------|-------------|----------|
| Spontaneous Mode                                   | 0.0         | (0.0 to 0.0) | <0.0001  |
| PEEP, per cmH2O                                    | 0.0         | (0.0 to 0.0) | 0.1      |
| Compliance, per mL/cmH2O                           | 0.0         | (0.0 to 0.0) | <0.0001  |
| Respiratory rate, per breath per minute            | 0.0         | (0.0 to 0.0) | <0.0001  |
| Duration of time since switch to spontaneous, per hour | 0.0         | (0.0 to 0.0) | <0.0001  |

Abbreviations: PEEP: positive end expiratory pressure; mL: milliliters; cmH2O: centimeter of water; Multivariate mixed effects panel regression model of one value per hour, clustered by patient.
Table S8. Multivariate analysis of the association between spontaneous mode and elastic component of mechanical power during the period of transition, among patients with lung compliance <30 cmH2O

| Variable                                      | Coefficient | 95% CI       | p-value  |
|-----------------------------------------------|-------------|--------------|----------|
| Spontaneous Mode                              | 0.0         | (0.0 to 0.0) | <0.0001  |
| PEEP, per cmH2O                               | 0.0         | (0.0 to 0.0) | 0.72     |
| Compliance, per mL/cmH2O                      | 0.0         | (0.0 to 0.0) | <0.0001  |
| Respiratory rate, per breath per minute       | 0.0         | (0.0 to 0.0) | <0.0001  |
| Duration of time since switch to spontaneous, per hour | 0.0         | (0.0 to 0.0) | 0.003    |

Abbreviations: PEEP: positive end expiratory pressure; mL: milliliters; cmH2O: centimeter of water; Multivariate mixed effects panel regression model of one value per hour, clustered by patient.
Table S9. Multivariate analysis of the association between duration of time since transition to spontaneous mode and respiratory rate during the period of transition

| Variable                                      | Coefficient | 95% CI          | p-value |
|------------------------------------------------|-------------|-----------------|---------|
| Duration of time since switch to spontaneous, per hour | 0.1         | (0.07 to 0.14)  | <0.0001 |
| PaO2/FiO2                                       | 0.0         | (0.0 to 0.0)    | <0.0001 |
| Compliance, per mL/cmH2O                        | 0.0         | (−0.1 to −0.06) | <0.0001 |
| PEEP, per cmH2O                                 | 0.16        | (0.02 to 0.0)   | 0.02    |

Abbreviations: PEEP: positive end expiratory pressure; mL: milliliters; cmH2O: centimeter of water; Multivariate mixed effects panel regression model of one value per hour, clustered by patient.
Table S10. Multivariate analysis of the association between duration of time since transition to spontaneous mode and respiratory rate during the period of transition, among patients with lung compliance <30 cmH2O

| Variable                              | Coefficient | 95% CI         | p-value   |
|---------------------------------------|-------------|----------------|-----------|
| Duration of time since switch to spontaneous, *per hour* | 0.14        | (0.1 to 0.2)   | <0.0001   |
| PaO2/FiO2                             | 0.0         | (0.0 to 0.0)   | 0.03      |
| Compliance, *per mL/cmH2O*            | -0.1        | (-0.1 to -0.04)| <0.0001   |
| PEEP, *per cmH2O*                     | 0.14        | (-0.07 to 0.35)| 0.2       |

Abbreviations: PEEP: positive end expiratory pressure; mL: milliliters; cmH2O: centimeter of water; Multivariate mixed effects panel regression model of one value per hour, clustered by patient.
Table S11. Multivariate analysis of the association between duration of time since transition to spontaneous mode and PaO2/FiO2 during the period of transition, among patients with tachypnea

| Variable                              | Coefficient | 95% CI       | p-value |
|---------------------------------------|-------------|--------------|---------|
| Duration of time since switch to spontaneous, *per hour* | -1.9        | (-3.1 to -0.7) | 0.001   |
| Compliance, *per mL/cmH2O*            | 0.1         | (-1 to 1)    | 0.89    |
| PEEP, *per cmH2O*                     | -8.0        | (-12.5 to -3.1) | 0.001   |
| Respiratory rate, *per breath per minute* | -3.7        | (-5.7 to -1.7) | <0.0001 |

Abbreviations: PEEP: positive end expiratory pressure; mL: milliliters; cmH2O: centimeter of water; Tachypnea defined as respiratory rate ≥30.
Multivariate mixed effects panel regression model of one value per hour, clustered by patient.
Table S12. Multivariate analysis of the association between duration of time since transition to spontaneous mode and PaO2/FiO2 during the period of transition, among patients without tachypnea

| Variable                                      | Coefficient | 95% CI        | p-value |
|-----------------------------------------------|-------------|----------------|---------|
| Duration of time since switch to spontaneous, per hour | 0.2         | (-0.3 to 0.7)  | 0.41    |
| Compliance, per mL/cmH2O                      | 1.3         | (0.9 to 1.7)   | <0.0001 |
| PEEP, per cmH2O                               | 0.1         | (-2.1 to 2.2)  | 0.95    |
| Respiratory rate, per breath per minute       | -1.2        | (-2.0 to 0.4)  | 0.002   |

Abbreviations: PEEP: positive end expiratory pressure; mL: milliliters; cmH2O: centimeter of water; Tachypnea defined as respiratory rate ≥30. Multivariate mixed effects panel regression model of one value per hour, clustered by patient.
Table S13. Multivariate analysis of the association between duration of time since transition to spontaneous mode and PaO2/FiO2 during the period of transition, among patients with tachypnea, low compliance subset

| Variable                  | Coefficient | 95% CI       | p-value |
|---------------------------|-------------|--------------|---------|
| Duration of time since switch to spontaneous, per hour | −1.7        | (−3.3 to −0.1) | 0.036   |
| Compliance, per mL/cmH2O | 0.19        | (−1.2 to 1.5)  | 0.89    |
| PEEP, per cmH2O          | −10.6       | (−16.3 to −4.9) | <0.0001 |
| Respiratory rate, per breath per minute | −1.6        | (−4.1 to 0.8)   | 0.196   |

Abbreviations: PEEP: positive end expiratory pressure; mL: milliliters; cmH2O: centimeter of water; Tachypnea defined as respiratory rate ≥30. Multivariate mixed effects panel regression model of one value per hour, clustered by patient.
| Variable                                      | Coefficient | 95% CI       | p-value |
|-----------------------------------------------|-------------|--------------|---------|
| Duration of time since switch to spontaneous, per hour | 0.9         | (0.14 to 1.6) | 0.019   |
| Compliance, per mL/cmH2O                      | 1.3         | (0.65 to 1.9) | <0.0001 |
| PEEP, per cmH2O                               | 5.56        | (2.2 to 8.7)  | 0.001   |
| Respiratory rate, per breath per minute       | -0.9        | (-2.2 to 0.3) | 0.125   |

Abbreviations: PEEP: positive end expiratory pressure; mL: milliliters; cmH2O: centimeter of water;
Tachypnea defined as respiratory rate ≥30.
Multivariate mixed effects panel regression model of one value per hour, clustered by patient.
| Variable                                      | Coefficient | 95% CI       | p-value   |
|-----------------------------------------------|-------------|--------------|-----------|
| Respiratory rate, per breath per minute       | −5.1        | (−7.6 to −2.5) | <0.0001   |
| Duration of time since switch to spontaneous, per hour | −10.5       | (−24.9 to 3.9) | 0.15      |
| Compliance, per mL/cmH2O                      | 0.26        | (−0.85 to 1.4) | 0.64      |
| PEEP, per cmH2O                               | −2.8        | (−8.8 to 3.1)  | 0.34      |

Abbreviations: PEEP: positive end expiratory pressure; mL: milliliters; cmH2O: centimeter of water;
Multivariate mixed effects panel regression model of one value per hour, clustered by patient.
| Variable                                         | Coefficient | 95% CI       | p-value |
|-------------------------------------------------|-------------|--------------|---------|
| Tidal volume, per mL                            | −0.17       | (−0.29 to −0.04) | 0.007   |
| Duration of time since switch to spontaneous, per hour | −1.8        | (−17.6 to 13.8) | 0.82    |
| Compliance, per mL/cmH2O                        | 1.8         | (−0.4 to 3.1) | 0.01    |
| PEEP, per cmH2O                                 | −1.5        | (−7.6 to 4.6) | 0.63    |

Abbreviations: PEEP: positive end expiratory pressure; mL: milliliters; cmH2O: centimeter of water; Multivariate mixed effects panel regression model of one value per hour, clustered by patient.
Table S17. Multivariate analysis of the association between respiratory rate and PaO2/FiO2 during the period of transition, among patients on control modes, low compliance subset

| Variable                                               | Coefficient | 95% CI      | p-value |
|--------------------------------------------------------|-------------|-------------|---------|
| Respiratory rate, per breath per minute                 | −9.2        | (−13.1 to −5.5) | <0.0001 |
| Duration of time since switch to spontaneous, per hour  | −23.6       | (−46.3 to −0.9) | 0.041   |
| Compliance, per mL/cmH2O                               | 0.08        | (−1.57 to 1.7) | 0.92    |
| PEEP, per cmH2O                                        | 1.0         | (−8.3 to 10.4) | 0.83    |

Abbreviations: PEEP: positive end expiratory pressure; mL: milliliters; cmH2O: centimeter of water; Multivariate mixed effects panel regression model of one value per hour, clustered by patient.
Table S18. Multivariate analysis of the association between tidal volume and PaO2/FiO2 during the period of transition, among patients on control modes, low compliance subset

| Variable                                      | Coefficient | 95% CI       | p-value |
|-----------------------------------------------|-------------|--------------|---------|
| Tidal volume, per mL                          | −0.3        | (−0.49 to −0.11) | 0.002   |
| Duration of time since switch to spontaneous, per hour | −10.6       | (−34.6 to 13.3) | 0.38    |
| Compliance, per mL/cmH2O                      | 2.8         | (0.5 to 5.1)  | 0.013   |
| PEEP, per cmH2O                               | −0.69       | (−13.1 to 6.2) | 0.49    |

Abbreviations: PEEP: positive end expiratory pressure; mL: milliliters; cmH2O: centimeter of water; Multivariate mixed effects panel regression model of one value per hour, clustered by patient.
Figure S1. Patient enrollment flowchart

483 patients in original dataset

64 excluded
- 34 patients did not receive mechanical ventilation
- 23 patients missing one variables completely
- 7 repeat encounters

419 patients analyzed
**Figure S2.** Adjusted increase in respiratory rate increases over time since the transition from control mode to spontaneous mode, among patients.
Figure S3. PaO₂/FiO₂ ratio (95% CI) over time among tachypneic patients (respiratory rate ≥30), low compliance subset.
Figure S4. PaO₂/FiO₂ ratio (95% CI) over time among patients without tachypnea (respiratory rate <30).

PaO₂ / FiO₂ over time among patients without tachypnea after a transition from control to spontaneous modes while on ECMO

NOTE:
Limited from 2 hours prior to until 24 hours after the switch to spontaneous breathing mode.
Limited to patients with respiratory rates < 30
P value from multivariate panel regression clustered by patient, adjusted for respiratory rate, lung compliance and positive end expiratory pressure.
**Figure S5.** PaO$_2$/FiO$_2$ ratio (95% CI) over time among patients *without* tachypnea (respiratory rate <30), low compliance subset

PaO$_2$/FiO$_2$ over time among patients *without* tachypnea after a transition from control to spontaneous modes while on ECMO, low compliance subset

NOTE:
Limit from 2 hours prior to until 24 hours after the switch to spontaneous breathing mode. Limited to patients with respiratory rates < 30

P value from multivariate panel regression clustered by patient, adjusted for respiratory rate, lung compliance and positive end expiratory pressure.
**Figure S6.** PaO₂/FiO₂ as a function of tidal volume and respiratory rate among patients with low compliance.