| Variables                      | Cohort 1 (N=49) | Cohort 2 (N=51) | p-value |
|--------------------------------|-----------------|-----------------|---------|
| Age                            | Median (N [IQR])| 53 (48-57)      | 52 (43-59) | 0.73 |
| Sex (N [%])                    | Male            | 38 (83)         | 37 (69)  | 0.10 |
|                                | Female          | 8 (17)          | 17 (31)  |       |
| Race (N [%])                   | White           | 11 (24)         | 31 (57)  | 0.004 |
|                                | Latino          | 17 (37)         | 8 (15)   |       |
|                                | Black           | 10 (22)         | 5 (9)    |       |
|                                | Native American | 1 (2)           | 3 (6)    |       |
|                                | Asian           | 7 (15)          | 5 (9)    |       |
| BMI (N [SD])                   | Mean            | 30.4 (27.8-35.5)| 32.1 (26.3-37.4) | 0.86 |
| Medical History (N [%])        | Obesity         | 18 (39)         | 32 (59)  | 0.045 |
|                                | Hypertension    | 21 (46)         | 11 (20)  | 0.007 |
|                                | Hyperlipidemia  | 13 (28)         | 15 (28)  | 0.96  |
|                                | Diabetes        | 18 (39)         | 14 (26)  | 0.16  |
|                                | Asthma/COPD     | 3 (7)           | 8 (15)   | 0.19  |
|                                | CAD             | 3 (7)           | 4 (7)    | 0.86  |
|                                | CKD             | 6 (13)          | 5 (9)    | 0.55  |
|                                | OSA             | 6 (13)          | 4 (7)    | 0.35  |
| ECMO Location                  | Center #1       | 12 (26)         | 13 (24)  | 0.81  |
|                                | Center #2       | 16 (35)         | 16 (30)  |       |
|                                | Center #3       | 9 (20)          | 10 (19)  |       |
|                                | Center #4       | 9 (20)          | 15 (28)  |       |
|                                | Transferred from Referral Hospital | 27 (59) | 44 (81)  | 0.012 |
| Ventilator Settings (Average [STD]) | FiO2           | 89.0 (14.4)     | 92.1 (13.7) | 0.28 |
|                                | PEEP            | 13.7 (3.4)      | 12.4 (2.9) | 0.046 |
|                                | Respiratory Rate| 25.9 (6.3)      | 23.8 (7.5) | 0.17  |
|                                | Tidal Volume    | 281.4 (181.7)   | 362.5 (101.5) | 0.017 |
|                                | Peak Pressure   | 34.2 (5.0)      | 32.2 (6.4) | 0.24  |
|                                | Plateau Pressure| 30.0 (4.4)      | 29.8 (6.2) | 0.88  |
| Arterial Blood Gas (Average [STD]) | pH             | 7.3 (0.1)       | 7.3 (0.1)  | 0.22  |
|                                | PCO2            | 62.2 (15.9)     | 64.2 (20.6) | 0.61  |
|                                | PaO2            | 56.5 (14.7)     | 57.1 (18.6) | 0.87  |
|                                | P/F Ratio       | 72.3 (22.7)     | 72.2341 (28.7) | 0.99  |
| Novel Therapeutics (N [%])     | Hydroxychloroquine +/- Azithromycin | 9 (20) | 14 (26)  | 0.45  |
|                                | Remdesivir      | 31 (67)         | 28 (52)  | 0.12  |
|                                | IL-6 Inhibitor  | 26 (57)         | 13 (24)  | <0.001 |
|                                | Convalescent Plasma | 22 (48) | 24 (44)  | 0.74  |
|                                | Steroids        | 33 (72)         | 53 (98)  | <0.001 |
|                                | Total Steroid Days (median [IQR]) | 6 (0-10) | 11 (10-14) | <0.001 |
| Renal Failure                  | Need for Renal Replacement (N [%]) | 21 (46) | 28 (52)  | 0.54  |
|                                | Total Renal Replacement, days (Average [STD]) | 21.9 (16.0) | 21.9 (15.8) | 1  |
| Transfusions (Average [SE])    | Total Units     | 11 (4-18)       | 11 (5-22) | 0.9   |
| SOFA Score (Average [STD])     | Prior to ECMO Cannulation | 7 (6-8) | 7 (2-8)  | 0.15  |
| ICU Treatments (N [%])         | Prone           | 41 (89)         | 48 (89)  | 0.97  |
|                                | Paralyzed       | 42 (91)         | 49 (91)  | 0.92  |
|                                | Vasopressor     | 33 (72)         | 35 (65)  | 0.46  |
Supplemental Table 1: Demographic, clinical, and ICU data for Cohort 1 and Cohort 2. BMI = body mass index; COPD = chronic obstructive pulmonary disease; CAD = coronary artery disease; CKD = chronic kidney disease; OSA = obstructive sleep apnea; SOFA = sequential organ failure assessment score