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Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active. MHz linear vascular probe of the BD Bard Site Rite5 ultrasound system (SomaTech Intl, Bloomfield, CT). At an image depth of 4.5 cm, needle puncture of the IJV was performed and the guidewire was inserted. When the ultrasound evaluation was performed to confirm the presence of the guidewire inside the IJV, three guidewires were visualized inside the lumen of the IJV in the short-axis view (Fig 1, A). The artifacts persisted when the image depth was increased to 6 cm (Fig 1, B). The artifacts disappeared and a single guidewire was visualized inside the lumen of the IJV when the image depth was reduced to 3 cm (Fig 1, C).

The Bard Site Rite 5 ultrasound system provides fixed focal points with each distinct image depth.<sup>2</sup> In our case, we encountered the side lobe artifacts because the focal points for the image depth of 4.5 cm and 6 cm were beyond the depth of the guidewire (about 1.2 cm). We avoided the side lobe artifacts by setting the focal point at or slightly beyond the target image.<sup>1</sup> The focal point may not be adjustable in all ultrasound machines and hence the operator needs to recognize this limitation to avoid side lobe artifacts.

# **Declaration of Competing Interest**

None.

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Effect of Ultraprotective Mechanical Ventilation on Right Ventricular Function During Extracorporeal Membrane Oxygenation in Adults With Acute Respiratory Distress Syndrome



#### To the Editor:

Right ventricular dysfunction (RVD) and acute cor pulmonale are frequent in patients with acute respiratory distress syndrome (ARDS) and may be associated with mortality.<sup>1</sup>

Venovenous extracorporeal membrane oxygenation (V-V ECMO) may allow the use of ultraprotective mechanical ventilation in the most severe cases of ARDS.<sup>2</sup> However, the effects of this mechanical ventilation strategy on right ventricle (RV) function are not well known. Indeed, alveolar collapse, increased pulmonary vascular resistance, and RVD may occur with these settings.<sup>3</sup> We conducted a retrospective observational study to assess the prevalence and evolution of RVD with echocardiography in patients supported with V-V ECMO for severe ARDS and ventilated with an ultraprotective ventilation strategy, including a driving pressure of 10 cmH<sub>2</sub>O. This study was approved by the Research Ethics Board of the University Health Network, Toronto, Canada, and performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Of the 153 patients who received V-V ECMO for severe ARDS between January 2014 and December 2017 at our institution, we included 18 patients (median age 43 years, eight women) who were assessed with echocardiography before and after cannulation. Before cannulation, RV dilatation was present in six of 16 (37%) and 10 of 17 (59%) patients, according to quantitative and qualitative assessment, respectively, and RVD was reported in nine of 14 (64%) patients, according to either measurement of RV systolic function (Table 1). Immediately after cannulation, tidal volume, plateau pressure, and driving pressure significantly decreased. RV size and systolic function were not significantly different after ECMO initiation, and the estimated right ventricular systolic pressure significantly decreased (Table 1). ECMO sweep gas flow showed an inverse correlation with right ventricular systolic pressure, and the arterial partial pressure of oxygen was correlated directly with RV fractional area change (Table 2). Although arterial oxygen saturation before cannulation was significantly lower in nonsurvivors, no other independent risk factor for RVD, RV dilatation, or mortality was identified in our population (data not reported).

This study had several limitations. It was a single-center, retrospective, observational study, with a small sample size; most patients were excluded because of missing echocardiograms or echocardiographic parameters. Moreover, considering that the echocardiograms were requested for clinical purposes rather than as part of a standardized serial protocol, we cannot exclude a selection bias for more severely ill patients and that patients' variable hemodynamic and respiratory conditions affected our findings.

In conclusion, RVD and dilatation were frequent before ECMO cannulation but were not associated with mortality. The extremely low tidal volumes during ECMO support did not cause a worsening of RV size and function or an increase of right ventricular systolic pressure, which was correlated inversely to the ECMO sweep gas flow. Prospective studies, including serial echocardiographic monitoring of RV function during V-V ECMO, are needed to assess the effect of lung rest ventilation on RV function and to clarify whether RVD in ARDS is a marker of a more severe underlying disease or an independent risk factor for mortality.

Table 1

Ventilatory, Hemodynamic, and Echocardiographic Data Before and After Venovenous Extracorporeal Membrane Oxygenation Cannulation

| Variables                             | Before V-V ECMO cannulation | After V-V ECMO cannulation | p value |
|---------------------------------------|-----------------------------|----------------------------|---------|
| Ventilatory variables                 |                             |                            |         |
| Minute ventilation (L/min)            | 10.8 (8.6-11.0)             | 1.3 (0.5-2.5)              | < 0.01  |
| Tidal volume (mL)                     | 380 (300-410)               | 150 (58-267)               | < 0.01  |
| Tidal volume (mL/kg PBW)              | 5.2 (5.0-6.2)               | 2.0 (0.9-3.6)              | < 0.01  |
| Respiratory rate (breaths/min)        | 30 (25-32)                  | 10 (10-10)                 | < 0.01  |
| Pplat (cm $H_2O$ )                    | 30 (30-34)                  | 20 (20-20)                 | < 0.01  |
| $\Delta P (cmH_2O)$                   | 18 (18-20)                  | 10 (10-10)                 | < 0.01  |
| PEEP ( $cmH_2O$ )                     | 10 (8-15)                   | 10 (10-10)                 | 0.45    |
| $Crs (mL/cmH_2O)^*$                   | 21 (19-23)                  | 9 (6-24)                   | 0.08    |
| $F_{I}O_{2}(\%)$                      | 100 (80-100)                | 50 (50-50)                 | < 0.01  |
| $PaO_2$ (mmHg)                        | 69 (62-77)                  | 92 (72-135)                | 0.02    |
| $PaO_2/F_1O_2$ (mmHg)                 | 80 (62-87)                  | n.a.                       | n.a.    |
| $SaO_2(\%)$                           | 93 (85-95)                  | 96 (94-97)                 | 0.02    |
| PaCO <sub>2</sub> (mmHg)              | 55 (49-69)                  | 47 (42-50)                 | 0.06    |
| pH                                    | 7.35 (7.19-7.44)            | 7.35 (7.30-7.39)           | 0.63    |
| Hemodynamic variables                 |                             |                            |         |
| Heart rate (beats/min)                | 105 (93-124)                | 95 (85-105)                | 0.18    |
| Mean arterial pressure (mmHg)         | 76 (68-81)                  | 76 (67-81)                 | 0.83    |
| Norepinephrine dose ( $\mu$ g/kg/min) | 0.00 (0.00-0.25)            | 0.14 (0.06-0.31)           | 0.04    |
| Vasopressin dose (U/h)                | 0 (0-0)                     | 0 (0-1)                    | 0.03    |
| Lactate (mmol/L)                      | 1.9 (1.6-3.5)               | 2.2 (1.8-4.3)              | 0.46    |
| Fluid balance $(mL)^{\dagger}$        | +1462 (653-3067)            | +838 (-37-2268)            | 0.55    |
| Echocardiographic variables           |                             |                            |         |
| RV basal diameter (cm) <sup>‡</sup>   | 3.9 (3.6-4.4)               | 4.3 (3.8-4.5)              | 0.29    |
| RV dilatation $(n/\%)^{\ddagger}$     | 6 (37)                      | 5 (55)                     | 0.16    |
| TAPSE (mm) <sup>§</sup>               | 15 (13-20)                  | 15 (13-18)                 | 0.41    |
| RV S' (cm/s)                          | 11.0 (9.0-12.0)             | 12.0 (9.5-13.5)            | 0.61    |
| RVFAC (%) <sup>¶</sup>                | 29 (22-34)                  | 23 (20-29)                 | 0.18    |
| RVD (n/%)**                           | 9 (64%)                     | 6 (50%)                    | 0.08    |
| RVSP (mmHg) <sup>††</sup>             | 58 (43-79)                  | 46 (34-62)                 | 0.02    |
| LVEF (%) <sup>‡‡</sup>                | 60 (60-63)                  | 60 (48-63)                 | 0.28    |

Data are reported as median (interquartile range) or number (percentage), as appropriate. Wilcoxon matched-pairs signed-rank test and McNemar test were applied, as appropriate; p values < 0.05 were considered significant.

Crs, static respiratory system compliance;  $\Delta P$ , driving pressure; F<sub>1</sub>O<sub>2</sub>, fraction of inspired oxygen; LVEF, left ventricular ejection fraction; n.a., not applicable due to difficulty in determining the capillary oxygen content without precise estimations of patient's cardiac output; PaCO<sub>2</sub>, arterial partial pressure of carbon dioxide; PaO<sub>2</sub>, arterial partial pressure of oxygen; PBW, predicted body weight; PEEP, positive end-expiratory pressure; Pplat, plateau pressure; RV, right ventricle; RVD, RV dysfunction; RVFAC, fractional area change of the RV; RV S', pulsed Doppler S wave of the RV; RVSP, RV systolic pressure; SaO<sub>2</sub>, arterial oxygen

saturation; TAPSE, tricuspid annular plane systolic excursion; V-V ECMO, venovenous extracorporeal membrane oxygenation.

\* Data available for 9 of 18 patients before cannulation and 17 of 18 patients after cannulation.

† Defined as 24-hour fluid balance for the midnight before the echocardiographic exam. Data available for 6 of 18 patients before cannulation and 13 of 18 patients after cannulation.

‡RV dilatation is defined as RV basal diameter > 4.1 cm (Lang et al.<sup>4</sup>). Data available for 16 of 18 patients before cannulation and 9/18 patients after cannulation.

§ Data available for 14 of 18 patients before cannulation and 12 of 18 patients after cannulation.

|| Data available for 11 of 18 patients before cannulation and 11 of 18 patients after cannulation.

¶ Data available for 6 of 18 patients before cannulation and 4 of 18 patients after cannulation.

\*\* Defined as TAPSE < 17 mm, RV S' < 9.5 cm/s, or RVFAC < 35% (Lang et al.<sup>4</sup>). Data available for 14/18 patients before cannulation and 12/18 patients after cannulation.

<sup>††</sup> RVSP was determined from peak tricuspid regurgitation jet velocity and an estimate of the right atrial pressure (Rudski et al.<sup>5</sup>). Data available for 11 of 18 patients before cannulation and 10/18 patients after cannulation.

<sup>‡‡</sup> Data available for 13 of 18 patients before cannulation and 13 of 18 patients after cannulation.

Table 2

| Echocardiographic Variables | ECMO Variables                  |         |                                 |         |  |  |  |  |
|-----------------------------|---------------------------------|---------|---------------------------------|---------|--|--|--|--|
|                             | ECMO blood flow                 | v       | ECMO sweep gas fl               | ow      |  |  |  |  |
|                             | Pearson correlation coefficient | p value | Pearson correlation coefficient | p value |  |  |  |  |
| RV basal diameter*          | -0.63                           | 0.10    | -0.44                           | 0.28    |  |  |  |  |
| TAPSE <sup>†</sup>          | 0.34                            | 0.30    | 0.07                            | 0.82    |  |  |  |  |
| RV S' <sup>‡</sup>          | 0.52                            | 0.10    | 0.46                            | 0.15    |  |  |  |  |
| RVFAC <sup>§</sup>          | 0.64                            | 0.36    | 0.77                            | 0.23    |  |  |  |  |
| RVSP                        | 0.44                            | 0.20    | -0.68                           | 0.03    |  |  |  |  |

| Echocardiographic variables | Gas exchange                    |         |                                 |         |                                 |         |  |  |
|-----------------------------|---------------------------------|---------|---------------------------------|---------|---------------------------------|---------|--|--|
|                             | PaO <sub>2</sub>                |         | PaCO <sub>2</sub>               |         | pH                              |         |  |  |
|                             | Pearson correlation coefficient | p value | Pearson correlation coefficient | p value | Pearson correlation coefficient | p value |  |  |
| RV basal diameter*          | 0.43                            | 0.29    | -0.49                           | 0.21    | 0.20                            | 0.63    |  |  |
| TAPSE <sup>†</sup>          | -0.03                           | 0.91    | 0.20                            | 0.52    | 0.03                            | 0.92    |  |  |
| RV S' <sup>‡</sup>          | -0.16                           | 0.63    | 0.58                            | 0.06    | 0.05                            | 0.88    |  |  |
| RVFAC <sup>§</sup>          | 0.95                            | 0.047   | 0.02                            | 0.98    | 0.94                            | 0.06    |  |  |
| RVSP                        | -0.53                           | 0.11    | 0.04                            | 0.91    | 0.18                            | 0.61    |  |  |

NOTE. Pearson correlation coefficient was calculated. p values < 0.05 were considered significant.

ECMO, extracorporeal membrane oxygenation; PaCO<sub>2</sub>, arterial partial pressure of carbon dioxide; PaO<sub>2</sub>, arterial partial pressure of oxygen; RV, right ventricle; RVFAC, fractional area change of the RV; RV S', pulsed Doppler S wave of the RV; RVSP, RV systolic pressure; TAPSE, tricuspid annular plane systolic excursion.

\* Data available for 16 of 18 patients before cannulation and 9 of 18 patients after cannulation.

<sup>†</sup>Data available for 14 of 18 patients before cannulation and 12 of 18 patients after cannulation.

<sup>‡</sup> Data available for 11 of 18 patients before cannulation and 11 of 18 patients after cannulation.

§ Data available for 6 of 18 patients before cannulation and 4 of 18 patients after cannulation.

|| Data available for 11 of 18 patients before cannulation and 10 of 18 patients after cannulation.

# **Conflict of Interest**

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