



# Implementation of a regional multidisciplinary veno-venous extracorporeal membrane oxygenation unit improved survival: a historical cohort study

## Amélioration de la survie grâce à la création d'une unité régionale multidisciplinaire d'oxygénation par membrane extracorporelle veino-veineuse : une étude de cohorte historique

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### Abstract

**Purpose** Veno-venous extracorporeal membrane oxygenation (vvECMO) is a highly invasive technique with a high risk of mortality. Based on reports of improved outcomes in high-volume ECMO centers, we established a regional vvECMO unit. The objective of this study was to evaluate how the vvECMO unit affected patient mortality rates.

**Methods** This was a historical cohort study of all patients admitted to Dijon University Hospital and supported by

vvECMO between January 2011 and June 2021. Patients managed with the vvECMO unit were compared with patients managed with non-vvECMO units. The primary outcome was 90-day mortality.

**Results** Of 172 patients treated using vvECMO, 69% were men, and the median [interquartile range] age was 59 [48–66] yr. Of the 172 patients, 35 were treated in the vvECMO unit and 137 were treated elsewhere (110/137 before the unit was established and 27/137 after). Ninety-day mortality was lower in patients managed in the vvECMO unit (15/35, 43% vs 92/137, 67%;  $P = 0.005$ ). Within the vvECMO unit, mortality rates were also lower for the subgroup of patients managed after the specialized

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unit was established (15/35, 43% vs 20/27, 74%;  $P = 0.002$ ). After adjusting for baseline severity of illness at vvECMO initiation, the vvECMO unit was independently associated with a lower 90-day mortality rate (hazard ratio, 0.41; 95% confidence interval, 0.21 to 0.80).

**Conclusion** The establishment of a vvECMO unit was associated with reduced 90-day mortality. This improved survival may relate to patient selection, more specialized mechanical ventilation support, and/or improvement of vvECMO care.

## Résumé

**Objectif** L'oxygénation par membrane extracorporelle veino-veineuse (ECMO-VV) est une technique hautement invasive qui s'accompagne d'un risque élevé de mortalité. Sur la base de comptes rendus faisant état d'améliorations des devenir dans les centres pratiquant un volume important d'ECMO, nous avons mis en place une unité régionale d'ECMO-VV. L'objectif de cette étude était d'évaluer l'impact de l'unité d'ECMO-VV sur les taux de mortalité des patients.

**Méthode** Nous avons réalisé une étude de cohorte historique incluant tous les patients admis au CHU de Dijon et traités par ECMO-VV entre janvier 2011 et juin 2021. Les patients pris en charge par l'unité d'ECMO-VV ont été comparés aux patients pris en charge par d'autres unités. Le critère d'évaluation principal était la mortalité à 90 jours.

**Résultats** Sur 172 patients traités par ECMO-VV, 69 % étaient des hommes et l'âge médian [écart interquartile] était de 59 [48-66] ans. Sur les 172 patients, 35 ont été traités par l'unité d'ECMO-VV et 137 ont été traités ailleurs (110/137 avant la création de l'unité et 27/137 après). La mortalité à 90 jours était plus faible chez les patients pris en charge par l'unité d'ECMO-VV (15/35, 43 % vs 92/137, 67 %;  $P = 0,005$ ). Au sein de l'unité d'ECMO-VV, les taux de mortalité étaient également plus faibles pour le sous-groupe de patients pris en charge après la création de l'unité spécialisée (15/35, 43 % vs 20/27, 74 %;  $P = 0,002$ ). Après ajustement pour tenir compte de la gravité initiale de la maladie à la mise en place de l'ECMO-VV, l'unité d'ECMO-VV était indépendamment associée à un taux de mortalité plus faible à 90 jours (rapport de risque, 0,41; intervalle de confiance à 95 %, 0,21 à 0,80).

**Conclusion** La mise en place d'une unité d'ECMO-VV a été associée à une réduction de la mortalité à 90 jours. Cette amélioration de la survie peut être liée à la sélection des patients, à un soutien par ventilation mécanique plus spécialisé et/ou à l'amélioration des soins d'ECMO-VV.

**Keywords** ARDS · critical care outcomes · extracorporeal membrane oxygenation · mortality · patient care team · respiratory failure · sepsis

Acute respiratory distress syndrome (ARDS) is associated with high rates of mortality despite recent advances in therapy.<sup>1</sup> In the most severe cases of ARDS, veno-venous extracorporeal oxygenation (vvECMO) support can partially restore blood oxygenation despite highly impaired alveolar gas exchange. It can also be used as a rescue therapy to limit ventilator-induced lung injury.<sup>2</sup>

With the onset of the COVID-19 pandemic, and the publication of several randomized studies, this technique is now increasingly used for intensive care unit (ICU) care of patients with severe ARDS. Implementation of ECMO centers during the COVID-19 pandemic has been associated with good outcomes in highly selected patients.<sup>3</sup> Nevertheless, despite improved vvECMO techniques, management, and knowledge, morbidity and mortality remain high among patients supported by vvECMO.<sup>4</sup>

Extracorporeal membrane oxygenation is an intensive and costly technique requiring specific skills and training. A recent retrospective analysis of the Extracorporeal Life Support Organization (ELSO) registry of COVID-19 patients treated with ECMO indicates a volume-outcome relationship favoring high-volume centers.<sup>4</sup> This finding aligns with guidelines and expert reports that argue for a regional network approach to managing patients who need ECMO support.<sup>5</sup>

Previously, several ICUs performed vvECMO at our institution. Because of the cost of this technique and in accordance with the relevant literature and expert opinion, we established a referral vvECMO unit in 2019. Because of referral errors and/or bed availability issues, some patients continued to be treated in other units.

The objective of the present study was to evaluate the effect of the implementation of our referral vvECMO unit on 90-day mortality. We hypothesized that treatment in a dedicated vvECMO unit would reduce mortality by improving patient selection and care.

## Methods

### Selection and description of participants

This historical cohort study at Dijon University Hospital was approved by the Institutional Review Board (IRB 00010254-2021-186). Patients' informed consent was required. All patients received written information of

their inclusion in the study. The cohort included all patients admitted to an ICU for vvECMO treatment and all those for whom vvECMO treatment was initiated during their stay (following ICU admission) between 1 January 2011 and 30 June 2021. All patients in the cohort received vvECMO. Patients admitted to the pediatric ICU were excluded. This report was drafted in accordance with the STROBE statement.<sup>6</sup>

### Protocol

Our regional healthcare territory with a population of 2,785,900 is served by one tertiary hospital with four ICUs (total bed capacity, 64) and five peripheral ICUs. Only the tertiary hospital offers vvECMO. Prior to the implementation of the vvECMO unit, any intensive care physician from the tertiary hospital (any of the four ICUs) could determine vvECMO indication; the physician contacted the cardiac surgical team, and patients were placed on vvECMO and managed in that unit.

The regional vvECMO unit was implemented on 1 January 2019 for intra- and inter-hospital transfer involving a referring ICU and a multidisciplinary team including critical care physicians, cardiothoracic surgeons, anaesthesiologists, perfusionists, and ICU nurses. Indication, contraindication, management, and weaning of vvECMO patients were standardized (Electronic Supplementary Material [ESM], eAppendix). The unit has a direct internal and external 24/7 phone line dedicated to vvECMO. Any physician within the region who is considering vvECMO initiation can use this line to contact an intensive care physician from the vvECMO unit. They will receive therapeutic advice regarding ARDS, including mechanical ventilation strategy and a clear indication for or against vvECMO. In cases of severe ARDS where indication for vvECMO is unclear, patients are admitted to the vvECMO unit for further evaluation. All indications for vvECMO are discussed by the unit's multidisciplinary team. If appropriate, vvECMO is initiated by the cardiothoracic surgeon, using the percutaneous method according to a standardized protocol (ESM eAppendix).

ICU and vvECMO care follow international guidelines for ECMO care<sup>7</sup> and ventilation.<sup>8</sup> Prone positioning, early interruption of neuromuscular blockers, and judicious sedation are encouraged. The multidisciplinary team (ICU physician, nurses, and perfusionists) completes several daily rounds to assess clinical evolution, correct vvECMO functioning, and any complications. All intrahospital transport is performed by the ECMO team; vvECMO weaning is evaluated daily, and ECMO is explanted by the ICU team following the first successful weaning trial (ESM eAppendix). The dedicated medical

and paramedical staff undergo regular training in vvECMO-specific technical and nontechnical skills.

### Data collection

All data were abstracted from patient medical records, including demographics, comorbidities, injury severity scores (Respiratory Extracorporeal Membrane Oxygenation Survival Prediction [RESP]<sup>9</sup> and Sequential Organ Failure Assessment [SOFA]),<sup>10</sup> organ failures and supports, physical location of cannulation, etiology of respiratory failure, ventilatory parameters and procedures, blood gas parameters, intubation duration, vvECMO support duration, vasopressor and inotropic therapy, medication use during ICU stay, length of ICU stay, complications, length of hospital stay, and death.

### Definitions

A patient was considered as managed by the vvECMO unit if they had been managed by the unit. Clinical and vvECMO-related complications were defined in accordance with international and ELSO guidelines.<sup>7</sup> Acute kidney injury was defined in accordance with the KDIGO classification.<sup>11</sup> Only adverse events diagnosed while under vvECMO support were collected. Polytransfusion was defined as receipt of more than eight red blood units while under vvECMO.

### Endpoints

The primary endpoint was 90-day mortality. Secondary endpoints included duration of mechanical ventilation, duration of ECMO, ICU length of stay, hospital length of stay, and ECMO-related adverse events occurring during vvECMO support (classified as hemorrhagic, thrombotic, acute kidney injury, neurologic adverse event, tamponade, cardiac arrest, infectious adverse event, or mechanical adverse event).

### Statistical analysis

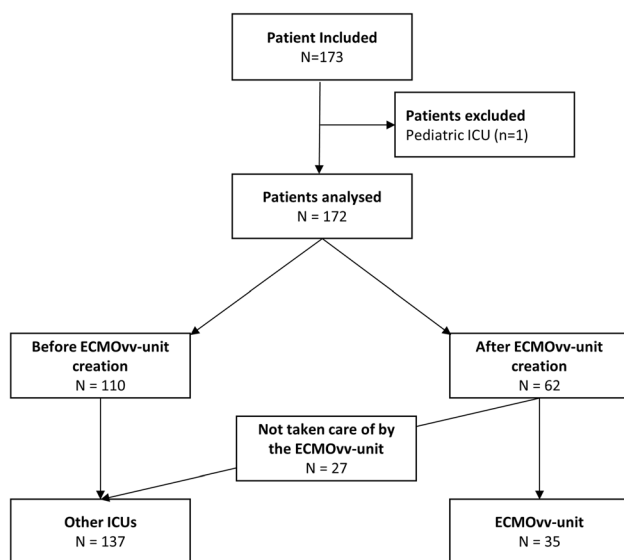
We compared patients managed in the vvECMO unit with those managed outside the unit. Normality was assessed using the Shapiro–Wilk test; quantitative data were compared using Student's *t* test or the Kruskal–Wallis nonparametric test and are presented as means (standard deviation) or median [interquartile range (IQR)]. Categorical, ordinal, and binary data were compared using Chi-squared or Fisher's exact tests if the conditions of validity were not fulfilled and are reported as frequencies and percentages. Censored data are represented on Kaplan–Meier curves; for comparison, we used the log-rank test.

We identified potential confounders from the bivariate analysis ( $P$  value  $< 0.05$ ) and the literature (known mortality risk factors), and tested relevant confounders with the use of a multivariable Cox proportional hazards model. After stepwise selection, the retained confounders were 1) precannulation risk of mortality (RESP score<sup>9</sup> and SOFA<sup>10</sup>) and 2) COVID-19-related respiratory failure (as ECMO was frequently used for viral pneumonia within the specialized unit, and the scores were validated before the COVID-19 pandemic). The proportional hazards assumption was assessed graphically. Missing data were considered to be random and were omitted from the analysis. The total numbers of observations are indicated when more than 10% ( $n < 155$ ) are missing for a single variable. All analyses were performed using R software (R Foundation for Statistical Computing, Vienna, Austria).

## Results

### Population and baseline characteristics

Of the 172 patients that received vvECMO included in the analysis (Fig. 1), 69% were men, and the median [IQR] age was 59 [48–66] yr. Of these, 105/172 (61%) were cannulated at the tertiary hospital center. Overall, 107/172 patients (62%) died within 90 days of commencing vvECMO therapy. In total, 35/172 patients were managed in the vvECMO unit and 137/172 were not; of these, 110/137 were managed prior to establishment of the vvECMO unit



**Fig. 1** Study flow chart. *Before vvECMO unit creation* refers to the period 2011–2018; *After vvECMO-unit creation* refers to the period 2019–2021 (June). ICU = intensive care unit; vvECMO = veno-venous extracorporeal membrane oxygenation

and 27/137 were managed by other ICUs at the tertiary center following its establishment (Fig. 1).

Baseline characteristics depending on admission to the vvECMO unit are presented in Table 1. Most patients in the vvECMO unit (74%) were supported for viral pneumonia, and SOFA and RESP scores indicated lower severity (higher RESP score indicate higher survival probability). More patients in the vvECMO unit were placed in the prone position prior to vvECMO initiation, and patients exhibited significantly higher positive end-expiratory pressure (PEEP) at ECMO initiation (median [IQR], 12 [11–14] vs 10 [6–12] cm H<sub>2</sub>O;  $P = 0.02$ ) (Table 2). A higher proportion of patients in the vvECMO unit were prone while on vvECMO (21/35 (60%) vs 37/137 (27%),  $P < 0.001$ ).

Patients characteristics by 90-day mortality are presented in ESM eTable 1. Patients alive after 90 days were younger (median [IQR] age, 54 [41–62] yr vs 62 [51–69] yr;  $P < 0.001$ ) and were rated as lower risk on the predictive scoring systems (median [IQR] RESP score, 2 [-1 to 4] vs 0 [-3 to 2];  $P < 0.001$ ).

Management and organ support at vvECMO initiation by 90-day mortality are presented in ESM eTable 2. Patients alive at 90 days had shorter a duration of mechanical ventilation before ECMO support (median [IQR], 1 [0–5] days vs 4 [1–9] days;  $P = 0.003$ ). By bivariate analysis, the cause of respiratory failure was not associated with 90-day mortality.

### Primary outcome

Patients managed in the vvECMO unit had lower 90-day mortality (15/35 (43%) vs 92/137 (67%); unadjusted risk difference, 0.24 (95% confidence interval [CI], 0.42 to 0.06;  $P = 0.005$ ) (Fig. 2A and Table 3). Mortality was also lower for the subgroup of patients in the vvECMO unit treated following establishment of the structured care unit (15/35 (43%) vs 20/27 (74%);  $P = 0.002$ ) (Fig. 2B). Multivariate analysis confirmed an independent association between the vvECMO unit and 90-day mortality (hazard ratio, 0.41; 95% CI, 0.21 to 0.80;  $P = 0.008$ ) (Table 4). The mortality rate for patients with ECMO support for SARS-CoV-2 infection was 54% in the vvECMO unit and 81% in other ICUs ( $P < 0.01$ ).

### Secondary outcomes

There were no significant differences between groups in terms of length of ICU or hospital stay (Table 3). Adverse events that occurred under ECMO are presented in ESM eTable 3. Patients who were managed in the vvECMO unit exhibited lower occurrence of acute kidney injury (17/35 [49%] vs 99/137 [73%];  $P = 0.03$ ).

**Table 1** Baseline characteristics depending on management in the vvECMO unit

Variable	Other ICU N = 137	vvECMO unit N = 35	P value
Age (yr), median [IQR]	58 [47–67]	60 [54–65]	0.67
Female sex, n/total N (%)	42/137 (31%)	11/35 (31%)	0.93
BMI (kg·m <sup>-2</sup> ), median [IQR]	30 [25–35]	32 [27–42]	0.12
<b>Medical history, n/total N (%)</b>			
Hypertension	57/136 (42%)	19/35 (54%)	0.19
Diabetes	21/137 (15%)	14/35 (40%)	0.001
Active smoking	31/137 (22%)	3/35 (9%)	0.06
Dyslipidemia	30/137 (22%)	14/35 (40%)	0.049
COPD	11/137 (8%)	3/35 (9%)	1.00
Chronic renal failure	8/137 (6%)	1/35 (3%)	0.69
Solid cancer	25/137 (8%)	2/35 (6%)	0.07
Blood cancer	2/137 (1%)	2/35 (6%)	0.18
<b>Cannulation in the referral unit, n/total N (%)</b>	93/137 (68%)	12/35 (34%)	< 0.001
<b>Cause of respiratory failure, n/total N (%)</b>			
Viral infection	33/137 (24%)	26/35 (74%)	< 0.001
Bacterial infection	46/137 (34%)	3/35 (9%)	
Other	58/137 (42%)	6/35 (17%)	
<b>SARS-CoV-2 infection, n/total N (%)</b>	16/137 (12%)	26/35 (74%)	< 0.001
<b>Severity score</b>			
SOFA score, median [IQR]	9 [7–12]	7 [4–9]	0.002
RESP score, median [IQR]	0 [-3 to 2]	2 [0 to 4]	0.005
<b>Organ support, n/total N (%)</b>			
RRT before ECMO	27/133 (20%)	1/34 (3%)	0.02
Norepinephrine at initiation	101/136 (74%)	19/34 (56%)	0.04

P values refer to between-group comparisons

BMI = body mass index; COPD = chronic obstructive pulmonary disease; ICU = intensive care unit; IQR = interquartile range; RESP = Respiratory Extracorporeal Membrane Oxygenation Survival Prediction; RRT = renal replacement therapy; SOFA = Sequential Organ Failure Assessment; vvECMO = veno-venous extracorporeal membrane oxygenation

## Discussion

Our main finding is that management in a specialized multidisciplinary vvECMO unit was associated with lower 90-day mortality. The improved survival rate may relate to patient selection (better prognosis at vvECMO initiation), more specialized mechanical ventilation support, and/or better vvECMO management (improved care, high volume, multidisciplinary team, specialized center).

Overall, we observed a significant reduction in 90-day mortality in patients treated in the dedicated vvECMO unit. Little is known about patient outcomes following the creation of such a referral unit. Two historical cohort studies have reported better outcomes following the establishment of ECMO teams.<sup>12, 13</sup> The high mortality rate observed before implementation of a referral unit may partly explain the significant effect of the intervention. Our research augments existing evidence by showing that

patients treated outside of the specialized unit after its establishment had worse outcomes.

Several factors may contribute to the improved outcomes of patients who receive vvECMO support in specialized units. First, our results align with the existing evidence of better outcomes in high-volume centers.<sup>4, 14–16</sup> Indeed, before the vvECMO unit was established, several units in the hospital performed vvECMO, and some may only have completed a low number of vvECMO runs per year.

Patient selection may also contribute to improved survival (i.e., poor prognosis prior to ECMO) as suggested by higher injury severity scores. Due to the highly invasive nature of vvECMO, and the resources mobilized for this intervention, it is important to select patients who are most likely to benefit from vvECMO (i.e., those with a reasonable probability of recovery or as a bridge to transplant).<sup>17</sup> In the present study, the

**Table 2** Respiratory characteristics before vvECMO depending on management in the vvECMO unit

Variable	Other ICU <i>N</i> = 137	vvECMO unit <i>N</i> = 35	<i>P</i> value
<b>Blood gas analysis, median [IQR]</b>			
Lowest PaO <sub>2</sub> to F <sub>i</sub> O <sub>2</sub> (mm Hg) <sup>a</sup>	60 [50–80]	75 [59–85]	0.02
PaCO <sub>2</sub> at implantation (mm Hg) <sup>b</sup>	60 [47–72]	54 [45–66]	0.18
pH at implantation <sup>c</sup>	7.22 [0.15]	7.30 [0.13]	0.02
<b>Noninvasive ventilation management, <i>n</i>/total <i>N</i> (%)</b>			< 0.001
NIV	50/137 (37%)	20/35 (57%)	
HFNO (without NIV)	14/137 (10%)	9/35 (26%)	
None	73/137 (53%)	6/35 (17%)	
<b>Invasive management</b>			
PEEP (cm H <sub>2</sub> O), median [IQR] ( <i>n</i> = 134)	10 [6–12]	12 [11–14]	0.02
Tidal volume (mL·kg <sup>-1</sup> ), mean (SD) ( <i>n</i> = 106)	5.9 [1.1]	6.4 [0.7]	0.047
Neuromuscular blockers, <i>n</i> /total <i>N</i> (%)	132/136 (97%)	35/35 (100%)	0.58
Prone positioning, <i>n</i> /total <i>N</i> (%)	82/137 (60%)	28/35 (80%)	0.03
Nitrous oxide, <i>n</i> /total <i>N</i> (%)	81/131 (62%)	10/31 (32%)	0.005
Duration of MV before ECMO (days), median [IQR]	3 [1–8]	4 [1–7]	0.81

*P* values refer to between-group comparisons

F<sub>i</sub>O<sub>2</sub> = fraction of inspired oxygen; ICU = intensive care unit; IQR = interquartile range; HFNO = high-flow nasal oxygen; MV = mechanical ventilation; NIV = noninvasive ventilation; PaCO<sub>2</sub> = arterial partial arterial pressure of carbon dioxide; PaO<sub>2</sub> = arterial partial pressure of oxygen; PEEP = positive end-expiratory pressure; vvECMO = veno-venous extracorporeal membrane oxygenation

<sup>a</sup> *N* = 157

<sup>b</sup> *N* = 133

<sup>c</sup> *N* = 131

multidisciplinary team setting promoted discussion and multidisciplinary decision-making regarding vvECMO indication. We also observed an improvement in preinitiation patient care in terms of stricter implementation of the international guidelines on ARDS (prone positioning) before ECMO initiation.<sup>5, 18</sup>

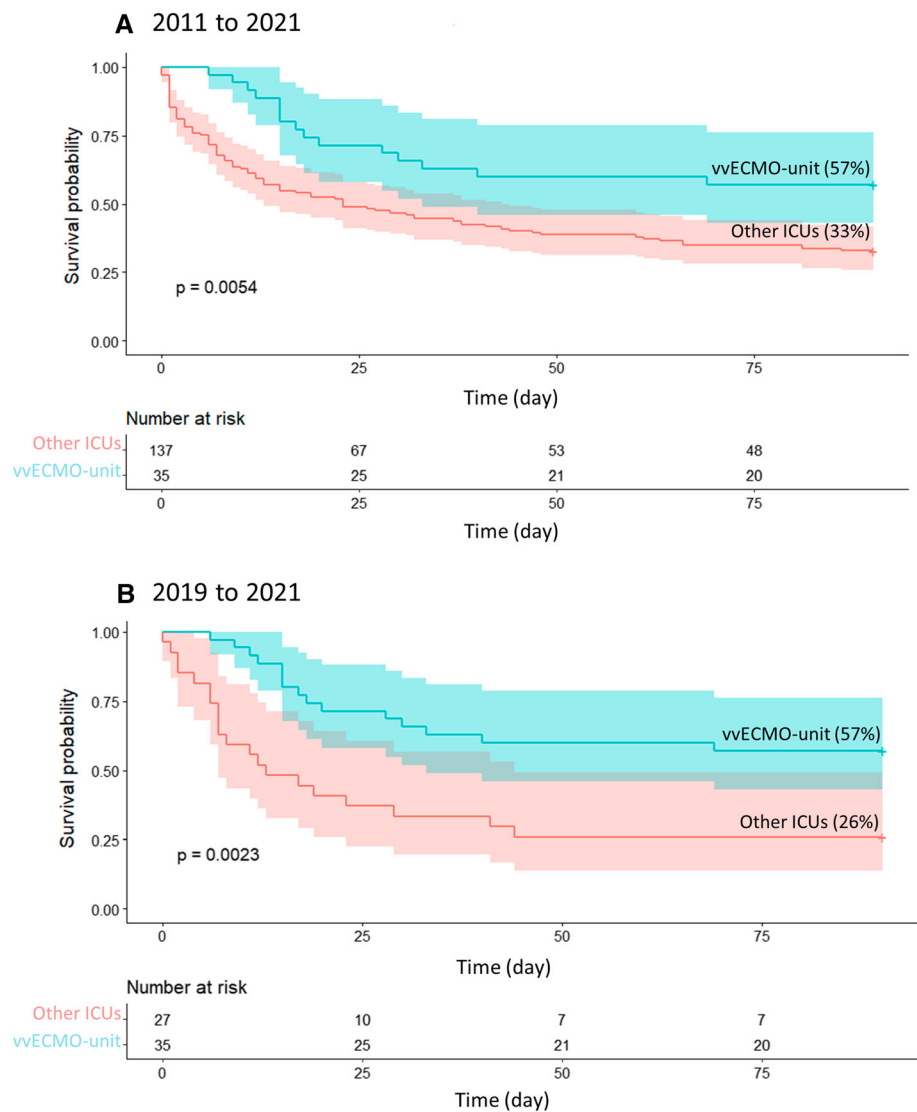
Finally, the observed improvement in survival rates may be linked to enhanced management of patients under vvECMO (improved respiratory management and/or improved vvECMO management). Indeed, treatment in a specialized unit helps to ensure a standardized approach to daily procedure and challenging situations such as vvECMO weaning.<sup>19</sup> To determine whether improved care bundling also contributed to lower mortality rates, we performed a multivariate analysis adjusted for RESP and SOFA scores to minimize the effect of selecting patients at higher risk of death.<sup>9</sup> The analysis suggest that being cared for in the vvECMO unit reduced mortality among patients at similar risk of death prior to ECMO initiation, supporting the hypothesis that higher volume improves care and reduces 90-day mortality. This is further supported by the higher rate of prone positioning and the lower rate of acute kidney injury in patients admitted to the vvECMO unit. Prone positioning is thought to have

physiologic benefits and to improve oxygenation without increasing adverse effects.<sup>20, 21</sup> In summary, we believe that the benefits of the vvECMO unit are more likely to be explained by a combination of elements that improve care, rather than by any single factor.

The effects of the intervention seem unrelated to universal changes in practice or better technologies. While some patients continued to be admitted to non-vvECMO units, the mortality rate was lower among patients treated in the dedicated vvECMO unit during the same time period. Similarly, mortality rates were higher among patients supported by vvECMO for COVID-19-related ARDS who were treated outside the specialized unit.

This study has several limitations. Because the study was retrospective, some mechanical ventilation parameters could not be investigated due to a high rate of missing data. In particular, the absence of plateau pressure data meant that pulmonary compliance could not be analyzed. Additionally, while data collection commenced in 2011, patients were only admitted to the vvECMO unit from 2019. Nevertheless, our results remain significant for the subgroup of patients admitted from 2019 onwards. Despite multivariable analysis, there is likely residual and

**Fig. 2** Kaplan–Meier curves for 90-day mortality by vvECMO unit management: (A) complete population; (B) subgroup of patients admitted from 2019. *P* values refer to between-group comparisons (log rank test). vvECMO = veno-venous extracorporeal membrane oxygenation



**Table 3** Primary and secondary outcomes depending on management in the vvECMO unit

Outcomes	Other ICU <i>N</i> = 137	vvECMO unit <i>N</i> = 35	Unadjusted risk difference (95% CI)
<b>Primary outcome</b>			
90-day mortality, <i>n</i> /total <i>N</i> (%)	92/137 (67%)	15/35 (43%)	0.24 (0.42 to 0.06)
<b>Secondary outcomes</b>			
ECMO duration (days), median [IQR]	8 [4–14]	12 [6–15]	−0.9 (−5.5 to 3.8)
Duration of MV (days), median [IQR]	20 [9–36]	26 [15–33]	−0.7 (−10.4 to 9.1)
ICU length of stay (days), median [IQR]	24 [12–40]	28 [17–38]	1.2 (−8.5 to 10.9)
Hospital length of stay (days), median [IQR]	31 [1–55]	37 [24–57]	0.7 (−22.3 to 23.7)

*P* values refer to between-group comparisons

CI = confidence interval; ICU = intensive care unit; IQR = interquartile range; MV = mechanical ventilation; vvECMO = veno-venous extracorporeal membrane oxygenation

**Table 4** Multivariate analysis for 90-day mortality

Variable	Adjusted HR (95% CI)	P value
vvECMO unit	0.41 (0.21 to 0.80)	0.008
RESP score	0.93 (0.88 to 0.98)	0.004
SOFA score	1.1 (1.1 to 1.2)	< 0.001
SARS-CoV-2 infection	2.5 (1.3 to 4.2)	0.003

CI = confidence interval; HR = hazard ratio; RESP = Respiratory Extracorporeal Membrane Oxygenation Survival Prediction; SOFA = Sequential Organ Failure Assessment; vvECMO = veno-venous extracorporeal membrane oxygenation

unmeasured confounding and the observed result may be due to patient selection. As the vvECMO unit was established in 2019, it was not possible to determine whether mortality would have been lower before that date. Nevertheless, our results suggest that this unit has had beneficial effects in line with the current literature and guidelines. While the low number of outcome events in the vvECMO unit may have reduced the power of the study, the large effect means that the results remain significant. Finally, the etiology of ARDS is associated with mortality, and these trends can change over time. Nevertheless, the analysis was adjusted for the diagnosis of COVID-19, and on the RESP score that incorporates etiology.

In conclusion, the establishment of a vvECMO unit was associated with reduced 90-day mortality, supporting the view that vvECMO should be managed in specialized units by multidisciplinary teams. Our results provide empirical evidence strongly supporting the global trend toward referral of vvECMO to high-volume centers as recommended by international guidelines.

**Author contributions** Maxime Nguyen, Pierre-Grégoire Guinot, Belaid Bouhemad, Marie-Catherine Morgant, Olivier Bouchot, Vivien Berthoud, and Valentin Kabbout contributed to drafting the article. Maxime Nguyen, Pierre-Grégoire Guinot, Belaid Bouhemad, Isabelle Gounot, Ophélie Dransart-Raye, Christophe Douguet, Vivien Berthoud, and Valentin Kabbout contributed to the conception and design of the study. Valentin Kabbout, Vivien Berthoud, and Pierre-Grégoire Guinot contributed to the acquisition of data. Pierre-Grégoire Guinot and Maxime Nguyen contributed to the analysis of data. Pierre-Grégoire Guinot, Maxime Nguyen, and Vivien Berthoud contributed to the interpretation of data.

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