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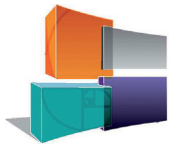
Anaesth Crit Care Pain Med 39 (2020) 886–887



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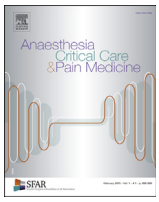

Letter to the Editor

Regional referral ECMO centre decision and mid-term mortality of patients suffering severe Acute Respiratory Distress Syndrome (ARDS)

Dear Editor,

The extracorporeal membrane oxygenation (ECMO) to Rescue Lung Injury in Severe Acute Respiratory Distress Syndrome (ARDS) (EOLIA) trial has recently investigated whether an early initiation of ECMO in patients suffering from severe ARDS may improve their outcomes. The results of this landmark trial are thrilling because the authors showed that the 60-day mortality rate in the ECMO group was not statistically different from the control group [1]. However, these results should be taken with caution because the ECMO was initiated as soon as the P_aO_2:FiO_2 ratio was below 80, while mechanical ventilation was not previously optimised in all patients (i.e. only barely more than half of patients assigned to the ECMO group were previously ventilated in a prone position) [1]. In our opinion, patients presenting with a P_aO_2:FiO_2 ratio between 60 and 80 could benefit more from an initial conservative approach based on patient-tailored mechanical ventilation settings. This latter statement is corroborated by the results obtained from our tertiary university teaching hospital selected as a regional referral ECMO centre by our regional health agency since 2009.

From 2012 to 2015, we have collected data obtained from calls received from peripheral hospitals' intensive care units (ICU) asking for an ECMO for patients with ARDS deemed refractory to conventional therapies. The indication for the ECMO was discussed between the primary care unit calling and our mobile respiratory assistance unit. ECMO was initiated as a rescue therapy (ECMO group) when the PaO_2:FiO_2 ratio was < 60 for three consecutive hours. ECMO was considered as "not-indicated" when the PaO_2:FiO_2 ratio was ≥ 60. Finally, ECMO was considered as "contraindicated" according to the CESAR trial criteria [2]. Independently of the decision made from our referral ECMO centre, mechanical ventilation optimisation including adjustment of the positive end expiratory pressure settings according to the EXPRESS protocol [3], continuous infusion of myorelaxant, inhaled nitric oxide and prone position was strongly recommended. At the time of the call, patients and clinical characteristics including respiratory parameters were noted in a dedicated medical file. The RESP score was calculated posteriori for each patient and, thus, did not influence the medical decision [3]. Because we work on a regular basis with the calling teams, the 90-day mortality was easily retrieved. Results are expressed as median [IQR]. A Kruskal–Wallis test or a Chi-square test according to the nature of the variables was used for multiple comparisons. A *P*-value < 0.05 was required to reject the null hypothesis.

As the study was purely observational and patients were treated according to normal standards of care in our institution, a waiver of patients informed consent was granted from the ethical board. Secondary processing of the data collected in this study was carried out at the University Hospital of Bordeaux in accordance with applicable legal and regulatory provisions, in particular General Data Protection Regulation No. 2016/679/EU of the 27th of April, 2016, and amended Act No. 78-17 of the 6th of January, 1978, on data processing files and freedoms. All data were collected and

Table 1
Patient characteristics (n = 71) at the time of the telephone call and outcomes.

	ECMO (n = 18)	"Non-indicated" (n = 19)	"Contraindicated" (n = 34)
Age, yr	33 [28–50]	42 [33–56]	58 [50–65]*
SAPS II	65 [60–66]	48 [42–60]	59 [44–80]
Duration of MV, days	1 [1–7]	1 [1–5]	7 [1–13]*
LODS score	3 [2–4]	3 [2–3]	3 [2–4]
Prone position	13 (72)	16 (80)	29 (88)
Myorelaxant use	18 (100)	20 (100)	31 (94)
pH	7.26 [7.15–7.30]	7.24 [7.20–7.34]	7.27 [7.22–7.34]
P_aCO_2, mmHg	58 [50–80]	52 [47–62]	54 [42–69]
P_{plat}, cmH_2O	32 [30–36]	29 [27–30]	30 [29–30]
PEEP, cmH_2O	12 [10–15]	12 [10–14]	12 [8–14]
Driving pressure, cmH_2O	19 [14–27]	15 [12–18]	18 [13–22]
Lactates, mmol L^{-1}	2.4 [1.8–3.9]	1.8 [1.6–2.5]	1.8 [1.2–4.7]
ICU length of stay, days	14 [5–58]	40 [14–53]*	8 [19–44]
Ventilator-free, days at 90-day	0 [0–60]	65 [56–77]*	0 [0–43]
RESP score, % predicted mortality	45 [20–50]	35 [20–50]*	50 [40–55]
90-day mortality	10 (53)	4 (20)*	24 (72)

Data are expressed as median [IQR] or n (% of patients). SAPS = simplified acute physiology score, MV = mechanical ventilation, LODS = logistic organ dysfunction system, P_{plat} = plateau pressure, PEEP = positive end expiratory pressure, ICU = intensive care unit, RESP = respiratory extracorporeal membrane oxygenation survival prediction. *: $P < 0.05$ *versus* both groups. The "non-indicated" group included patients with the PaO_2:FiO_2 ratio was ≥ 60. ECMO was considered as "contraindicated" in accordance to the CESAR trial criteria [4].

https://doi.org/10.1016/j.accpm.2020.05.019

analysed confidentially assigning an identification number to each patient.

During the study period, our regional referral ECMO centre received 85 calls from different peripheral hospital ICUs. Seventy-one (84%) of them were correctly registered and were successively analysed. In eighteen patients (25%), ECMO was initiated immediately as a rescue therapy (ECMO group). ECMO was considered as "not-indicated" and "contraindicated" in 19 (27%) and in 34 (48%) patients, respectively. Patients in "contraindicated" group were significantly older and were mechanically ventilated for a longer period (Table 1). In accordance to group's definition, PaO_2:FiO_2 ratio was significantly lower in the ECMO group compared to both the "non-indicated" and the "contraindicated" groups with ratios of 52 [45–63], 75 [62–83] and 69 [54–81], respectively ($P < 0.05$). Muscle relaxant drugs administration and prone position were prescribed in 97% (n = 69) and 82% (n = 58) of patients, respectively, with no statistical difference between groups. The 90-day mortality rate was significantly lower in the "non-indicated" group (Table 1). Despite of P_aO_2:FiO_2 ratio between 60 and 80, the 90-day mortality rate was 20% in the "non-indicated" group, whereas the predicted 90-day mortality rate under ECMO would have been 35% according to the RESP Score. However, early ECMO could have been proposed in that group according to the EOLIA criteria.

In conclusion, if ECMO is foreseen, physicians should evaluate attentively whether patients with severe ARDS could survive without ECMO. Because ECMO may be responsible for intrinsic morbidity, patient must be selected carefully. Our results strongly suggest that in these selected ARDS patients having a P_aO_2/FiO_2 ratio between 60 and 80, ECMO could be avoided and the mortality rate lowered if mechanical ventilation is strongly optimised [5].

Conflicts of interest

The authors of this paper do not have any conflict of interests to declare regarding any direct financial relation with the commercial identities mentioned in the paper.

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Available online 6 October 2020