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Reduction of ventilator settings allowed by intravenous oxygenator (IVOX) in ARDS patients

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Abstract *Objective:* To evaluate the possibility of reducing ventilator settings to "safe" levels by extrapulmonary gas exchange with IVOX in ARDS patients.
Design: Uncontrolled open clinical study.
Setting: Medical Intensive Care Unit of a University Hospital.
Patients: 6 patients with ARDS who entered into IVOX phase II clinical trials.
Interventions: The end-point of this study was to reduce ventilator settings from the initial values, recorded on the day of inclusion, to the following: peak inspiratory pressure <40 cmH_2O, mean airway pressure <25 cmH_2O and tidal volume <10 ml/kg. Trials to achieve this goal were made on volume-controlled ventilation within the 24 h before and after IVOX insertion. Comparison of the results achieved during these trials used Wilcoxon test.
Results: Before IVOX implantation reduction of ventilator settings was not possible in the 6 patients, despite a non-significant increase in PaO_2/FIO_2 was achieved. IVOX permitted significant decrease in $PaCO_2$ (from 60.5 ± 15 to 52 ± 11 mmHg; $p = 0.02$) before any modification of the ventilatory mode. After IVOX insertion, a significant decrease of the ventilator settings was performed: peak and mean airway pressures dropped from 44 ± 10 to 36.8 ± 6.7; $p = 0.02$ and from 26.3 ± 5.6 to 22.5 ± 3.9 cmH_2O; $p = 0.02$, respectively. Concommitantly, $PaCO_2$ remained unchanged and PaO_2/FIO_2 increased significantly from 93 ± 28 to 117 ± 52; $p = 0.04$. The interruption of oxygen flow on IVOX was associated with a slight decrease of the oxygen variables. Tolerance of IVOX was satisfactory. However, a significant decrease both in cardiac index and in pulmonary wedge pressures (from 4.5 ± 1.2 to 3.4 ± 9; $p = 0.03$ and from 16 ± 5 to 11 ± 2; $p = 0.04$, respectively) was observed.
Conclusion: Gas exchange achieved by IVOX allowed reduction of ventilator settings in 6 ARDS patients in whom previous attempts have failed. CO_2 removal by the device, may explain these results. Efficacy of IVOX on arterial oxygenation was uncertain.

Key words Adult respiratory distress syndrome · Extra lung support · Pulmonary barotrauma · Intravascular oxygenator

Introduction

Since the first description by Ashbaugh et al. [1], the mortality of the adult respiratory distress syndrome (ARDS) remains high despite a better understanding of the pathogenesis of this condition and improved management in intensive care units [2–4]. Therapy is essentially supportive and consists mainly of mechanical ventilation with positive-end expiratory pressure to achieve arterial oxygenation. This support, however, requires high airway pressures and volumes to achieve gas exchange and may worsen the lung injury [5, 6]. Indeed the lungs are not uniformly stiff, as was demonstrated by CT-scan analysis [7], and the ventilator may cause overinflation of compliant regions of the lungs [8]. Extra pulmonary methods to supplement gas exchange may help to "rest the lungs" during the acute phase of the disease. Extracorporeal support using artificial lung membranes have been proposed to decrease both pulmonary barotrauma and oxygen toxicity from the ventilator [9, 10]. However, they require high resources to permit prolonged extracorporeal assistance and can be sources of hemorrhagic complications. A new extrapulmonary but intracorporeal gas exchanger (IVOX, Cardiopulmonics, Salt Lake City, UT) has been recently proposed by Mortensen et al. [11]. The gas transfer allowed by this device depends on the size of the device, gas tension gradients, cardiac output, blood hemoglobin concentration and intra-device gas flow rate. The safety and efficacy of this device have been established in animal models and more recently in humans [12–15]. However, gas transfer reported in these studies remained low. Until now, clinical consequences of IVOX and, in particular decrease in ventilator requirements, remain uncertain [13, 14]. The goal of this open clinical study was to determine the effects of IVOX on gas exchange and reduction of ventilator settings in 6 patients with severe ARDS, by comparing the results with those obtained before IVOX insertion.

Patients and methods

Patients

The use of IVOX was part of a phase II study approved by the Food and Drug Administration. This study was also aproved by the "French Minister of Health" and by the Ethics committee of our institution. Informed consent was obtained from the patients or from their closest relatives. Patients with ARDS entered into this study when 1) they had a Murray score [16] higher than 2.5; 2) they met IVOX phase II clinical trials blood gas entry criteria: $PaO_2 \leq 60$ mmHg with $FIO_2 \geq 0.5$ and PEEP ≥ 10 cmH_2O or PIP ≥ 45 cmH_2O or MAP ≥ 30 cmH_2O. Alternatively, with the minute volume of respiratory gas at 150 ml/min/kg body weight or higher, if the patient's PCO_2 was higher than 40 mmHg and 3) they failed to improve their respiratory variables despite trying different modes of mechanical ventilation, i.e. volume controlled, pressure controlled-inverse ratio ventilation, and permissive hypercapnia. The PEEP level used during this period of initial evaluation was determined as the minimal pressure at which the slope of the total respiratory pressure-volume curve becomes linear [17]. When this point was not available, the best PEEP was defined by oxygen delivery and best compliance [18]. The patients were sedated by a continuous infusion of midazolam and fentanyl, whereas muscle relaxation was maintained with a constant infusion of pancuronium bromide.

Protocol of evaluation

The end point of this study was to reduce ventilator settings from the initial values, recorded on the day of inclusion, to the following: peak inspiratory pressure ≤ 40 cmH_2O, mean airway pressure ≤ 25 cmH_2O and tidal volume ≤ 10 ml/kg. Trials to achieve this goal were made within the 24 hours before and after IVOX insertion. Four steps of data collection were chosen: point 1, on inclusion; point 2, just before IVOX (not recorded during the period of instability following reduction of ventilator support but after stabilization of the patient on optimized levels of airway pressures and volumes); point 3, after IVOX insertion and before ventilator modifications and point 4, 24 h after insertion. The possibility of decreasing ventilator variables was assessed on clinical tolerance and repeated blood gas measurements aiming to maintain $PaO_2 > 50$ mmHg. The delay of 24 h was set to limit the role of evolution of the lung disease on the results. Gas transfer was interrupted to evaluate performance of the device by measuring gas transfer rates and modification of respiratory variables. During these gas flow interruption periods, mechanical ventilator settings and hemodynamic support remained unchanged. These trials were made during short periods of time (10–15 min) to avoid prolonged instability related to hemodynamic and gasometric effects in severely ill patients. Carbon dioxide transfer was determined from the product of IVOX exhaust gas CO_2 concentration, determined by capnometry, and IVOX exhaust gas flow rate.

The safety of IVOX insertion, chronic implantation and removal was also addressed by clinical assessment, monitoring of cardiovascular variables and repeated blood gas analysis.

IVOX procedure

The Intravascular Oxygenator (IVOX®), provided by Cardio Pulmonics inc., Salt Lake City UT) contained multiple (590–1100), crimped hollow fibers (length 55–65 cm) consisting of an ultra-thin (1 mm) gas-permeable siloxane polymer membrane supported by a skeleton of microporous polypropylene. Devices of size #7– #10 were furled to an outer diameter of 1.1–1.5 cm and inserted through a femoral venotomy to lie through both vena cava and the right atrium, where they were unfurled to attain a surface area of 0.21–0.52 m^2. Insertion of the devices was performed as described previously [13–15], according to recommendations from the company. The introducers used for IVOX insertion into the right common femoral vein were in the shape of a hollow, truncated ram's horn. They were inserted surgically as follows: a 10-cm incision was made over the right common femoral vein, the vessel was dissected free and ligatures were placed proximally and distally to control bleeding while the venotomy was made. The patients were given 400 u/kg heparin via a central venous catheter. A guide wire was inserted through the introducer into the vena cava, and the IVOX was slid over the guide wire such that the tip of the device was located in the inferior portion of the superior vena cava, as determined by fluoroscopy. Diffusional gas exchange then occurs between 100% O_2 flowing under negative pressure (between -300 and -500 cmH_2O) inside the hollow fibers and blood flowing through the meshed device in the central venous system, achieving continu-

ous in vivo blood oxygenation and CO_2 extraction. Carbon dioxide elimination was constantly monitored by a capnometer. The subatmospheric pressure was used to avoid the risk of gas embolism in cases of fiber rupture. The devices were maintained in place during the acute phase of the disease and gas transfer was interrupted only during a short period of time every few days, to evaluate performances of the device. During the time IVOX was implanted, anticoagulation was obtained by continuous infusion of heparin to maintain a PTT at 1.5–2 times the normal values, with heparin concentrations measured by anti Xa higher than 0.2. When appropriate they received antibiotics to treat documented infections and vancomycin was always added after IVOX insertion and given during the whole period of implantation. Removal of the devices was performed surgically with repair of the common femoral vein. Anticoagulation was sustained during 7 days after removal of the device and the venous bed integrity was controlled by echo-doppler.

Statistical analysis

Comparisons between the respiratory variables were performed with a non-parametic Wilcoxon test. Three types of comparisons were made: between point 1 and 2; between points 2 and 4 and between points 3 and 4. Results are expressed as mean ± standard deviation and $p<0.05$ was taken as significant.

Results

From March 1992 to January 1993, six patients were enrolled into the protocol. Two survived and were finally discharged from the hospital, two died 17 and 32 days after removal of IVOX. All of them had severe ARDS, without prior history of chronic lung disease and with a Murray score ranging from 2.75–4 (Table 1). They had following severity scores: mean values for SAPS [19] and OSF [20] 20 and 2, respectively. Predisposing factors for ARDS were pulmonary infection in 5 and large blood transfusions in one. Previous duration of ARDS and mechanical ventilation ranged from 2–23 days.

Before IVOX implantation, there was no statistical difference between the variables recorded before and after trying to reduce ventilator settings, although a moderate and non-significant increase in PaO_2/FIO_2 from 72±25 to 93±28, was achieved (Table 2, comparing point 1 and 2).

Insertion of the devices was performed easily (insertion time averaged 50 min) and gas transfer was achieved. CO_2 elimination ranged from 13–74 ml·min^{-1} with an average of 43 ml·min^{-1} and increased with the size of the device: 74 ml·min^{-1} for size # 10. However, in two patients (3 and 5) an incomplete unfurling of the devices was observed with reduction of surface exchange area. Moreover, in patient 5, a few fibers were broken during the insertion and, as recommended by the company, negative pressure and oxygen flow were slightly decreased with subsequently low gas transfer (VCO_2: 13–21 ml·min^{-1}, despite the size # 9 of the device).

After IVOX insertion, a significant decrease of the ventilator settings was possible: peak and mean airways pressures dropped from 44±10 to 36.8±6.7, $p = 0.02$; and from 26.3±5.6 to 22.5±3.9 cmH_2O, $p = 0.02$, respectively. This decrease in pressures was associated with a non-significant decrease of tidal volume (from 10.2±1 to 9.6±1.2 ml/kg).

The mean carbon dioxide removal achieved by IVOX permitted an immediate significant decrease in $PaCO_2$ (from 60.5±15 to 52±11 mmHg, $p = 0.02$) before any modifications of the ventilatory mode and allowed subsequent reduction of ventilator settings without significant increase in $PaCO_2$ (Table 2). During the interruption of gas flow on IVOX, a significant increase in $PaCO_2$ was observed (from 54.5±12 to 62.5±16, $p = 0.02$) which resolved after restarting oxygen administration on the device (Table 3).

The effects of IVOX on oxygen variables were as follows: i) just after IVOX insertion there was no change in PaO_2/FIO_2 (from 93±28.2 to 90.2±35.2); ii) 24 h after IVOX insertion, PaO_2/FIO_2 improved significantly from 93±28.2 to 117.2±51.5, $p = 0.04$ and iii) during gas flow interruption on IVOX there was a very small, but significant decrease in PaO_2/FIO_2 from 115±57 to 110±56,

Table 1 Characteristics of patients treated with IVOX

No.	Age	Sex	Etiology of ARDS	SAPS[a]	OSF[b]	Murray[c]	Ventilation[d] (days)	Final outcome[e]
1	23	M	Pulmonary infection	19	4	3.75	6	D
2	57	F	Pulmonary infection	21	1	2.75	2	D*
3	58	M	Blood transfusion	14	1	3.25	2	S
4	61	M	Pulmonary infection	21	3	4	3	D
5	28	M	Pulmonary infection	14	1	3.75	23	S
6	65	M	Pulmonary infection	24	2	4	9	D**

[a] *SAPS* Simplified Acute Physiologic Score [19]
[b] *OSF* Organ System Failure score as described by Knaus [20]
[c] *Murray* The score as described by Murray [16]
[d] Duration in days of mechanical ventilation before IVOX implantation
[e] *S* Survival; *D** death occurred 32 days after IVOX ; *D***, death occurred 17 days after IVOX

Table 2 Modification of respiratory parameters. (All patients were ventilated with volume-controlled mode. Measures were made in steady state. *Point 1* data on inclusion, *point 2* data just before IVOX, after stabilization of the patients on optimized ventilation, *point 3* data after IVOX insertion and before ventilator modifications, *point 4* data obtained 24 h after IVOX insertion, *PIP* Peak Inspiratory Pressure, *MPaw* mean airway pressure, *PEEP* Positive End Expiratory Pressure. Comparison was made using Wilcoxon test and $p<0.05$ was taken as significant)

Patient	PIP (cmH_2O)			MPaw (cmH_2O)			PEEP (cmH_2O)			Minute ventilation (l/min)			PaO_2/FIO_2				$PaCO_2$ (mmHg)			
Point	1	2/3	4	1	2/3	4	1	2/3	4	1	2/3	4	1	2	3	4	1	2	3	4
1	60	59	41	34	32	24	14	12	10	13	14	12	77	111	118	116	101	85	69	69
2	36	41	35	18	27	25	18	14	12	12.5	17	13.5	50	67	63	74	61	41	38	38
3	35	33	28	21	18	16	15	10	10	11	11.5	11	88	106	126	165	66	51	45	42
4	52	50	46	31	30	27	18	17	17	16.5	16	13	42	51	37	47	52	58	50	54
5	35	32	31	23	21	20	11	11	11	15	17	17	112	98	113	119	60	56	52	48
6	46	49	40	29	30	23	14	14	14	13	13.5	10.2	63	125	184	182	77	73	59	69
Mean	44	44	37**	25	26	22.5**	15	13	12.3	13.7	14.8	12.7	72	93	90	117**	70	60.5	52*	53**
±SD	±10.5	±10.6	±6.7	±6.5	±5.6	±3.9	±2.7	±2.5	±2.7	±2.1	±2.3	±2.4	±26	±28	±35	±52	±17.5	±15	±11	±13

* $p<0.05$ between point 2 and point 3
** $p<0.05$ between point 2 and point 4

with no difference in PvO_2, SvO_2 and intrapulmonary shunt (Table 3).

The tolerance of IVOX was satisfactory and no serious complication was noted. However, IVOX insertion was constantly followed by an important and significant decrease in cardiac index from 4.5 ± 1.2 to 3.4 ± 9, $p=0.03$ (Table 4), associated with a significant decrease in pulmonary wedge pressures with no change in heart rate (inotropic and vasopressive treatment was unchanged during this period of time). Only one patient (patient 2) had blood loss during IVOX insertion enough to cause hypovolemia; about 500 ml of blood loss requiring transfusion of two red blood packed cells. In 3 patients a decrease in cardiac index may have been due to impaired venous return by IVOX, clinically suspected by bilateral leg edema and ultrasound findings (patients 1, 3, 6).

Mild hematoma of the insertion sites were noted in 3 patients (patients 2, 3, 6), but disappeared spontaneously. A small drop in platelet counts were observed in 3 patients (patients 1, 3, 6), but the decrease was small ($<10\%$) and did not require platelet transfusion. During prolonged IVOX implantation there were no signs of hemolysis or hyperfibrinolytic activity. No device related infection was noted during the implantation period. However, 2 patients had local inflammation of the scar with no positive cultures on repeated samples. Lastly, cultures of the fibers from the explanted devices were always germfree. There was no sign of deep venous thrombosis and no sign of pulmonary embolism during implantation and after removal of IVOX on clinical and Doppler analysis. There was no thrombus in the repaired vein or in the vena cava, and no evidence of IVOX-thromboembolic pulmonary infarction confirmed by autopsy findings in 3 patients.

Discussion

This preliminary study demonstrated the possibility to reduce ventilator settings in 6 patients with ARDS in whom similar reduction was not possible just before implantation of the device. This result was obtained despite IVOX achieving rather low gas transfer, especially in 2 patients (patients 3 and 5), in whom early partial rupture and incomplete unfurling decreased performance of the device. Similar experiences with IVOX have already been reported in preliminary studies [13, 14]. Conrad et al. [13] reported in 2 patients significant reductions in ventilatory support. Unfortunately, mean and peak pressures were not available and the second patient was treated with high-frequency positive pressure ventilation combined with IVOX. High et al. (14] observed that small changes in ventilatory settings were possible, but only in 2 of the 5 patients studied. Moreover, the precise degree to which mechanical ventilator settings were reduced was also

Table 3 Effect of IVOX on oxygenation variables[a]. (*PvO_2* Mixed venous oxygen pressured, *SvO_2* mixed venous oxygen saturation, *Qv/Qt* intrapulmonary shunt calculated with the standard formula, *CI* cardiac index. Means and standard deviation were compared with Wilcoxon test and $p<0.05$ was taken as significant)

No.	PaO_2/FIO_2 On/off		PvO_2 (mmHg) On/off		SvO_2 (%) On/off		Qv/Qt (%) On/off			CI (l/min/m^2) On/off		$PaCO_2$ On/off
1	57	54	38	37	53	55	34	34	4.6	4.5	67	73
2	93	85	39	37	62	57	30	30	3.3	3.4	40	4.5
3	185	174	36	36	68	65	19	18	3.3	3.3	44	50
4	47	44	30	27	48	46	33	30	3.7	3.8	59	74
5	157	157	44	45	74	75	29	28	5.1	5.2	48	51
6	151	149	36	35	67	63	23	20	3.0	2.9	69	82
Mean ± SD	115 ± 57	110 ± 56	37 ± 4.6	36 ± 5.7	62 ± 9.8	60 ± 9.9	28 ± 5.9	27 ± 6.3	3.8 ± 0.8	3.9 ± 0.8	54.5 ± 12	62.5 ± 16
p		0.04		NS		NS		NS		NS		0.02

[a] Numbers represent the means obtained during short period of flow interruption in the device

Table 4 Cardiovascular modification after IVOX implantation[a]. (*CI* Cardiac index, *MAP* mean artery pressure, *MPAP* mean pulmonary artery pressure, *RAP* right atrial pressure, *PWP* pulmonary wedge pressure, *HR* heart rate in beats by minute. Means and standard deviation were compared with Wilcoxon test and $p<0.05$ was taken as significant)

Patient	CI (l/min/m^2)		MAP (mmHg)		MPAP (mmHg)		RAP (cmH_2O)		PWP (cmH_2O)		HR (b/min)	
1	5.4	3.7	113	98	43	36	13	15	8	9	102	106
2	3.9	3.4	106	91	39	32	20	19	20	13	126	118
3	4	3	97	76	26	23	13	8	13	11	109	119
4	4.2	3.2	74	64	29	25	14	13	14	11	103	120
5	6.5	5	90	82	40	28	18	22	18	8	119	137
6	3.1	2.2	80	86	34	27	12	10	21	13	99	112
Mean ± SD	4.5 ± 1.2	3.4 ± 0.9	93.3 ± 15	82.8 ± 11.9	35.2 ± 6.7	28.5 ± 4.8	15.7 ± 3.2	14.5 ± 5.3	15.7 ± 4.9	10.8 ± 2	110 ± 10.7	119 ± 10.4
p		0.03		0.04		0.03		NS		0.04		NS

[a] This table represents the hemodynamic changes obtained just before and just after the IVOX implantation

missing. In the present study, the decrease in airway pressures was significant and both peak and mean airway pressures reached the previously determined levels in 5 out of 6 patients. The carbon dioxide removal by IVOX may explain this results and the reduction in ventilator settings was not associated with an increase in $PaCO_2$. All patients were ventilated with permissive hypercapnia on inclusion and further reduction in ventilatory support was prevented by worsening $PaCO_2$ and pH before IVOX implantation. CO_2 elimination by IVOX was immediately observed after IVOX insertion and persisted during the whole time of implantation as confirmed by constant increase of $PaCO_2$ observed during the periods of gas flow interruption on the device. The possibility to increase gas transfer by increasing gas tension gradients has already been reported [14] and may explain why $PaCO_2$ did not increase despite reduction of respiratory support. IVOX may be helpful in ARDS patients treated with permissive hypoventilation [23] by reducing deleterious effects of hypercapnia and/or by allowing increased reduction in ventilatory support for the same level of $PaCO_2$. Spontaneous improvement of underlying lung disease could also explain the possibility to reduce ventilatory. However, the short period of time between the two phases of evaluation and the absence of clinical and radiological changes do not support this hypothesis. As previously reported, changing the mode of ventilation may permit decrease in airway pressures and volumes with improved arterial oxygenation [21, 22]. To eliminate such bias in this study, the same mode of volume-controlled ventilation was used before and after insertion of IVOX. When a significant decrease in ventilatory requirements was obtained by using IVOX, clinical benefits remained uncertain. Indeed, in the 4 patients who required high airway pressures before IVOX insertion, peak and mean pressures remained high and possible sources of persistant pulmonary barotrauma [24, 25]. Moreover, it has been recently reported that barotrauma may be volotrauma [26] and IVOX did not allow significant reduction of tidal volume.

In comparison with extracorporeal support ECMO and $ECCO_2R$ [9, 10, 27, 28], the efficacy of IVOX on oxygenation was poor. In particular, it was not possible to improve PaO_2 with this device in 2 patients (patients 2 and 4). There was no improvement in arterial oxygenation observed immediately after IVOX insertion despite $PaCO_2$ decreasing rapidly. Gas flow interruption on the device was associated with a very small decrease in PaO_2/FIO_2. However, changes in PaO_2 might be obscured by spontaneous variations of PaO_2 during the period of gas flow interruption, which in turn induces modifications of regional intrapulmonary shunt by changing the amplitude of hypoxic vasoconstriction. Even when mean pulmonary artery pressure (MPAP) significantly decreased after IVOX implantation, no change in PvO_2 or in intrapulmonary shunt during interruption of gas flow on IVOX was seen. Precise evaluation of oxygen transfer rates from the device is known to be difficult [13, 14]. Changes in intra-luminal O_2 concentrations during passage through the device are slight, and they are mostly due to saturation of the exhaust gases with water vapor. Since it is not technically feasible to quantify IVOX O_2 supply by monitoring exhaust from the device, Bagley et al. [29] have used the product of cardiac output and the differences in O_2 content of mixed venous blood during ON and OFF periods. While applying this method we found large deviations resulting from spontaneous fluctuations in mixed venous blood hemoglobin oxygen saturations and flow rates emptying into the inferior vena cava, as previously reported [14]. By using extrapolation from animal experiments, O_2 supply form IVOX ranged from $10-15\ ml \cdot min^{-1}$ and remained low, even with larger devices. High et al. using a more sophisticated method of measurement of oxygen transfer [14], found similar results and questioned the usefulness of the small quantity of oxygen supplied in the venous circulation, mainly in the inferior vena cava. In the present study, it was difficult to conclude that the increase in PaO_2/FIO_2 obtained 24 h after IVOX insertion was due to this small oxygen supply. Indeed changes in ventilatory mode and the evolution of the underlying disease may participate to this improvement.

Tolerance of IVOX was rather satisfactory in this small group of patients. IVOX implantation and explantation proved to be simple and straightforward procedures. In particular, the absence of infection related to the devices and the low frequency of hemorrhagic complications were remarkable when considering the size and location of the device chronically implanted in patients with severe conditions. However, we constantly observed a decrease in cardiac index within the first 24 h, which could be due to reduction of venous return and hypovolemia. The latter was probably due to blood loss during insertion, at least in one patient, and this possible event was described in the guidelines provided by the company. This side effect was not clearly reported in the previous studies [13, 14]. In 3 patients a decrease of venous return was clinically suspected and confirmed by ultrasonic examination. Impaired venous return by obstruction due to the device was not reported in animal models. Caval obstruction was previously reported in one patient with a small vena cava [14], but the size of the vena cava was normal on ultrasound examination in our patients. Previous correction of hypovolemia, performed just before IVOX insertion may be a good solution to improve hemodynamic tolerance, but fluid challenge in ARDS patients may worsen the lung injury [30] and has to be carefully considered. The incomplete unfurling of the device, was suspected in patients 3 and 5, but it was clearly established only when the devices were removed. This incomplete expansion of the device in the central venous system resulted in less efficient gas exchange and hampered reduction in ventilator support. It could also contribute to the formation of blood clots or bacterial adherence over the device. Therefore, early detection of such technical problems has to be achieved to improve safety of the future devices.

In conclusion carbon dioxide removal constantly achieved by IVOX allowed reduction in ventilator settings in six patients with ARDS. The effects of this gas exchanger on oxygenation were small and controversial. These preliminary results must be confirmed by a randomized study comparing permissive hypoventilation with and without IVOX in patients with ARDS.

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