CHEST

Original Research

COPD

A Novel Extracorporeal CO_2 Removal System

Results of a Pilot Study of Hypercapnic Respiratory Failure in Patients With COPD

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***Background*: Hypercapnic respiratory failure in patients with COPD frequently requires mechanical ventilatory support. Extracorporeal CO_2 removal ($ECCO_2R$) techniques have not been systematically evaluated in these patients.**

***Methods*: This is a pilot study of a novel $ECCO_2R$ device that utilizes a single venous catheter with high CO_2 removal rates at low blood flows. Twenty hypercapnic patients with COPD received $ECCO_2R$. Group 1 (n = 7) consisted of patients receiving noninvasive ventilation with a high likelihood of requiring invasive ventilation, group 2 (n = 2) consisted of patients who could not be weaned from noninvasive ventilation, and group 3 (n = 11) consisted of patients on invasive ventilation who had failed attempts to wean.**

***Results:* The device was well tolerated, with complications and rates similar to those seen with central venous catheterization. Blood flow through the system was 430.5 ± 73.7 mL/min, and $ECCO_2R$ was 82.5 ± 15.6 mL/min and did not change significantly with time. Invasive ventilation was avoided in all patients in group 1 and both patients in group 2 were weaned; $Paco_2$ decreased significantly ($P < .003$) with application of the device from 78.9 ± 16.8 mm Hg to 65.9 ± 11.5 mm Hg. In group 3, three patients were weaned, while the level of invasive ventilatory support was reduced in three patients. One patient in group 3 died due to a retroperitoneal bleed following catheterization.**

***Conclusions:* This single-catheter, low-flow $ECCO_2R$ system provided clinically useful levels of CO_2 removal in these patients with COPD. The system appears to be a potentially valuable additional modality for the treatment of hypercapnic respiratory failure.**

***Trial registry:* ClinicalTrials.gov; No.: NCT00987740 and 01021605; URL: www.clinicaltrials.gov**

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Abbreviations: $ECCO_2R$ = extracorporeal CO_2 removal; IPPV = invasive positive pressure ventilation; NIPPV = noninvasive positive pressure ventilation; VAS = visual analog score

COPD causes significant morbidity and mortality, and is the fourth leading cause of death in the world.[1] Hypercapnic respiratory failure in COPD worsens the prognosis and increases the mortality.[2-5] Noninvasive positive pressure ventilation (NIPPV) is now established as the standard treatment of respiratory failure in acute exacerbation of COPD[6]; however, 26% to 54% of these patients still require invasive positive pressure ventilation (IPPV).[7,8] The prognosis for patients with COPD who require IPPV is poor with hospital survival ranging from 31% to 76%.[6,9,10]

As an adjunct to IPPV, extracorporeal CO_2 removal ($ECCO_2R$) techniques were first applied to patients with hypoxic respiratory failure over three decades ago[11,12] but have not achieved widespread use. Curiously, the application of $ECCO_2R$ specifically for hypercapnic respiratory failure has not been well studied. We describe here a pilot study of the application

of a novel, single venous catheter $ECCO_2R$ system in patients with COPD with hypercapnic respiratory failure conducted in India (single center) and in Germany (five centers).

Materials and Methods

$ECCO_2R$ Device

The $ECCO_2R$ device (Hemolung Respiratory Assist System; ALung Technologies Inc) was applied in three groups of patients with COPD with hypercapnic respiratory failure. This $ECCO_2R$ device has been described in detail previously and consists of a catheter, an integrated pump/gas-exchange cartridge, and a controller assembly.[13] The size 15.5F dual-lumen catheter is available in either a femoral or internal jugular configuration (Fig 1), and is inserted percutaneously and advanced to the inferior or superior vena cava. Venous blood is withdrawn through the double-lumen catheter by a centrifugal pump magnetically driven by the Hemolung controller unit, where it flows past a cylindrical bundle of hollow fibers assembled around a rotating core. Sweep gas (air or oxygen) is drawn through the hollow fibers by a vacuum pump (to prevent air embolism in the event of fiber breakage), creating a diffusion gradient for gas exchange across the membrane. The venous blood is returned to the patient through the double-lumen catheter. Unlike conventional passive oxygenators, the pump-driven enhanced flow past the membranes markedly increases gas-exchange efficiency, allowing for significant CO_2 removal at relatively low blood flow in the range of 300 to 500 mL/min. The rate of CO_2 removal is calculated and displayed on the controller monitor based on internal measurements of CO_2 percentage and flow in the hollow-fiber membrane sweep gas. This device has been studied in animals for up to 8 days, and was, therefore, limited in the clinical feasibility study to a maximum of 7 days (or 168 h) of therapy.

Subjects

Three groups of patients, aged 21 to 80 years, with COPD and hypercapnic respiratory failure ($Paco_2 > 50$ mm Hg, $pH < 7.3$) were considered eligible for study inclusion. Group 1 (n = 7) consisted of patients with acute exacerbation of COPD on NIPPV therapy with a very high likelihood (>50%) of requiring intubation and IPPV.[7,14] Patients in this group had been on NIPPV for at least 1 h with either $Paco_2 > 55$ mmHg and $pH < 7.25$ or $pH < 7.30$ and $Paco_2 > 55$ mm Hg, with < 5 mmHg $Paco_2$ decrease from baseline following NIPPV application. Group 2 (n = 2) consisted of patients with hypercapnic respiratory failure requiring NIPPV who had failed two weaning attempts and did not wish to be invasively mechanically ventilated. Group 3 (n = 11) consisted of patients with hypercapnic respiratory failure already on invasive mechanical ventilation who had either failed two or more weaning attempts or failed one weaning attempt and did not wish to continue invasive mechanical ventilation.

For each subject, written informed consent (as approved by each site's institutional review board) was obtained (institutional review board committee names and project approval numbers for all centers are included as a data supplement in e-Table 1). Consecutive patients with COPD presenting with hypercapnic respiratory failure were evaluated, and subjects meeting the inclusion criteria were enrolled. The diagnosis of COPD was based on medical history, physical examination, and pulmonary function tests indicating airways obstruction.[1] Patients with hemodynamic instability, sensitivity to heparin, recent major surgery, uncontrolled arrhythmia, thrombocytopenia (platelets < 100,000/mm^3), a bleeding diathesis, or coma from any cause were excluded from the study.

The double-lumen catheter was placed in either the femoral (n = 13) or jugular vein (n = 7) and advanced to the vena cava. A loading dose of heparin (80 units/kg) was administered, and the heparin dose was adjusted to maintain the activated partial thromboplastin time at 1.5 to 2.3 times baseline as long as the catheter was in situ. Blood flow through the catheter was initiated at 400 mL to 500 mL/min to achieve a CO_2 removal rate > 50 mL/min. The CO_2 removal rate and blood flow, displayed on the Hemolung controller, were continuously monitored and recorded. Baseline blood samples for measurements of hematologic parameters, electrolytes, and liver function tests, as well as arterial blood gas measurements, were made. These measurements were repeated serially at intervals throughout the period as long as the $ECCO_2R$ catheter was in situ. In addition, daily measurements of dyspnea using a visual analog scale (VAS) were made when possible.[15] Group 1 patients on $ECCO_2R$ and NIPPV were considered for intubation if there was a worsening or lack of improvement of the arterial blood gases, defined as an arterial $pH < 7.25$ or an increase in $Paco_2 > 10$ mmHg after 2 h of treatment, or worsening of respiratory distress, deterioration of neurologic status, intolerance of face/nasal mask, inability to clear secretions, or life-threatening cardiovascular instability. In each case, the final decision was made by the attending physician/principal investigator. All patients were followed to hospital discharge or 30 days after discontinuance of $ECCO_2R$.

Results

Twenty patients with COPD with hypercapnic respiratory failure received $ECCO_2R$ therapy (Table 1) for a mean of 104.2 ± 59.7 h (range, 0.2-192 h). The individual ventilatory parameters are shown in Table 2. The device was well tolerated by the patients and invasive ventilation was avoided in association with $ECCO_2R$ therapy in all patients in group 1; in one patient, $ECCO_2R$ was stopped after 20 min due to inadequate anticoagulation. Three patients in this group died within 30 days after completion of $ECCO_2R$ therapy

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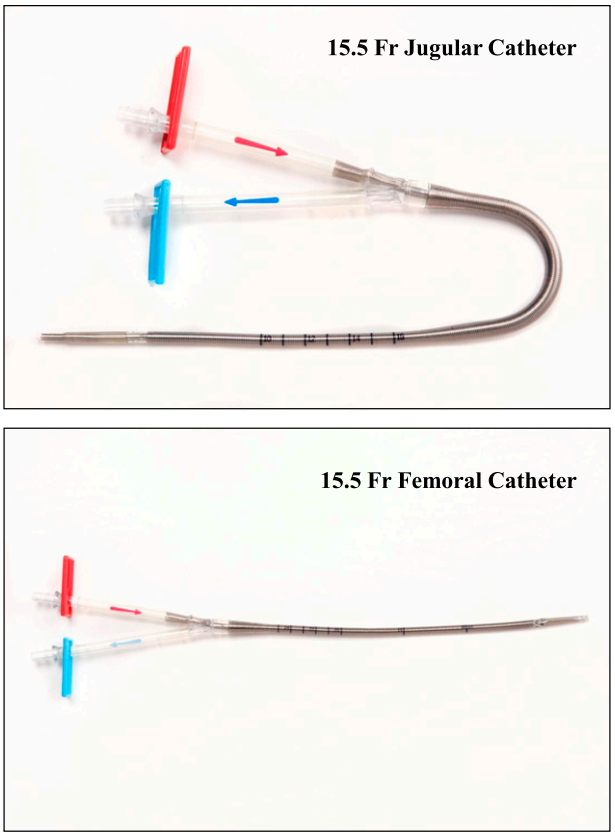

FIGURE 1. The Hemolung15.5F double-lumen extracorporeal CO_2 removal ($ECCO_2R$) catheter with an optional femoral or jugular configuration.

due to their underlying disease states. Both patients in group 2 were weaned off continuous NIPPV with the application of $ECCO_2R$, but remained on intermittent NIPPV support, and were alive 30 days after completion of therapy.

In group 3, nine of 11 patients had been on invasive mechanical ventilation for >15 days prior to $ECCO_2R$. Three patients were weaned off invasive mechanical ventilation, and in three further patients, the level of invasive ventilatory support was reduced. Only one patient remained on the same level of ventilatory support. One patient in group 3 died as a result of a retroperitoneal bleed following catheterization and received $ECCO_2R$ support for <3 h. At follow-up, after the cessation of $ECCO_2R$ therapy, seven patients died (Table 1). One patient in group 1 (patient 4, Table 1) suffered a cardiopulmonary arrest within 24 h of $ECCO_2R$ cessation, and the other patients died of varying causes between 7 and 26 days after completion of $ECCO_2R$. None of these deaths could be attributed to the $ECCO_2R$, and this mortality rate of 35% is not unexpected, given the severity of COPD and respiratory failure in these patients.[6,9,10] This mortality rate compares with in-hospital mortality rates of 29.3%,[6,10] and 1-year mortality of 49.1% to 62%[9,10] in similar patients.

The application of $ECCO_2R$ resulted in a decrease in the sensation of breathlessness. Systematic assessment of breathlessness by VAS was available in five subjects in whom there was a significant decrease in breathlessness: baseline VAS score, 7.2 ± 2.2 vs 3.56 ± 1.59 at 48 h ($n = 5$, $P < .027$).

Blood flow through the system (Fig 2) ranged between 117 and 587 mL/min (mean ± SD of 430.5 ± 73.7 mL/min). $ECCO_2R$ ranged from 14 to 121 mL/min (mean ± SD of 82.0 ± 16.3 mL/min) with the lower figures representing weaning from the device. Over the course of $ECCO_2R$ therapy, blood flow and CO_2 removal did not change significantly in these patients.

In patients from groups 1 and 2 on NIPPV, there was a significant decrease ($P < .003$, paired t test) in $PaCO_2$ within 1 h of the application of the device from 78.9 ± 16.8 mm Hg to 65.9 ± 11.5 mm Hg, and a significant increase ($P < .0002$, paired t test) in pH from 7.28 ± 0.08 to 7.34 ± 0.07. The effects of the application of $ECCO_2R$ in group 1 patients ($n = 6$) are shown in Figure 3, indicating continuing decrease in $PaCO_2$ and increase in pH with time. Arterial PO_2 was maintained within acceptable values with appropriate adjustment of the FIO_2. In group 3 patients, who were on invasive mechanical ventilation, precise changes in $PaCO_2$ and pH specifically due to the application of $ECCO_2R$ cannot be accurately assessed because of ventilator setting adjustments; nevertheless, the data on CO_2 removal rates (Fig 2) indicate that the $PaCO_2$ would very likely have decreased with constant ventilator settings.

There was no evidence of clinically significant hemolysis in any of the patients; liver and renal function were not adversely affected by the $ECCO_2R$ (e-Table 2). Plasma-free hemoglobin, an index of hemolysis, increased above 40 mg/100 mL in only two patients, in both of whom the increase was attributable to concomitant clinical events. Self-limited thrombocytopenia, most likely related to heparin use, was noted in eight patients. In only two patients did the platelet count drop transiently below 85,000/μL; none of the patients required platelet transfusion. A significant thrombocytopenia was seen posttherapy in one patient who received 3 units of plasma. Adverse events attributable to catheter placement consisted of one death secondary to blood loss from perforation of the left iliac vein (Table 1: group 3, subject 4), and one pneumothorax which resolved with treatment. In one subject a deep venous thrombosis was noted in the cannulated vein 3 days after the catheter had been removed, causing no further adverse effects.

Significant bleeding events requiring blood transfusion occurred in three patients: In two cases the bleeding was related to underlying disease and anticoagulation, and in one subject it was due to inadvertent

Table 1—*Study Groups*

Subject	Age, y (Sex)	FEV_1 % Predicted	FEV_1/FVC %	Clinical Data[a]	Days on NIPPV/IPPV Prior to $ECCO_2R$	Hours on $ECCO_2R$	Clinical Effects During $ECCO_2R$	Status 30 d Post-$ECCO_2R$
Group 1: Failing NIPPV								
1	76 (F)	...	...	Stage IV COPD, obesity, OSA, renal insufficiency	2	78	↓$PaCO_2$ ↓ dyspnea, remained on NIPPV	Died day 26: septic shock
2	69 (F)	38	50	Stage III COPD, no known comorbidities	4 h	66	↓$PaCO_2$ ↓dyspnea cessation of NIPPV support	On nocturnal NIPPV
3	68 (F)	18	27	Stage IV COPD with bilateral lower-lobe emphysema	7	142	↓$PaCO_2$ ↓dyspnea ↓NIPPV support	Died, day 1: cardiopulmonary arrest
4	72(M)	21	34	Stage IV COPD, LTOT > 2 y, bilateral LVRS 1 y	16	160	↓$PaCO_2$ ↓dyspnea	Died, day 10: respiratory failure, refused intubation
5	49 (M)	14	20	Stage IV COPD, resection bulla right upper lobe 1991, on lung transplant list 2 y	4	140	↓$PaCO_2$ ↓dyspnea ↓NIPPV support	Bilateral lung transplant day 31
6	50 (F)	...	...	Stage IV COPD, atypical mycobacterial infection (on antimicrobial therapy since 2009)	3	0.2	Catheter clotted, insufficient anticoagulation	On NIPPV
7	78 (M)	38	39	Stage III COPD, LTOT 1 y	1	41	↓$PaCO_2$ $ECCO_2R$ stopped because of ↓blood flow	Died, day 7: pneumonia, sepsis
Group 2: Unable to wean from NIPPV								
1	78 (M)	22	30	Stage IV COPD, right lung lobectomy 1998, polycystic kidney disease	1	48	↓$PaCO_2$ ↓dyspnea, stopped NIPPV	On intermittent NIPPV
2	59 (F)	18	53	Stage IV COPD, pulmonary hypertension LTOT 5 y, bilateral upper lobe endoscopic LVRS 2 y, compete endoscopic closure of right upper lobe 1 y	7	192	↓$PaCO_2$ ↓dyspnea,↓NIPPV support	On intermittent NIPPV
Group 3: Unable to wean from IPPV								
1	66 (M)	19	32	Stage IV COPD, LTOT 2 y, nocturnal NIPPV 1 y, endoscopic LVRS 4 y	9	168	↓$PaCO_2$ extubated day 2, reintubated after 37 h, tracheostomized and placed on NIPPV	On nocturnal NIPPV
2	64 (M)	13	28	Stage IV COPD, bullous emphysema, bilateral LVRS 2 y, on NIPPV 2 y, LTOT 2 y	4	177	Extubated in 3 h; reintubated after 94 h, then extubated	On intermittent NIPPV
3	61 (F)	28	31	Stage IV COPD, on lung transplant list since 2007	15	95	↓$PaCO_2$; remained on IPPV; $ECCO_2R$ discontinued because of coagulopathy (von Willebrand disease)	Died, day 17: pneumonia, septic shock

(Continued)

Table 1—*Continued*

Subject	Age, y (Sex)	FEV_1 % Predicted	FEV_1/FVC %	Clinical Data[a]	Days on NIPPV/IPPV Prior to $ECCO_2R$	Hours on $ECCO_2R$	Clinical Effects During $ECCO_2R$	Status 30 d Post-$ECCO_2R$
4	64 (F)	...	...	...	30	3	Vascular perforation during catheter placement	Died while on Hemolung at approximately 3 h
5	61 (M)	45	60	Stage III COPD, OSA on home NIPPV, myelodysplastic syndrome, cardiac arrest 1 mo prior, tracheostomy 18 d prior	30	79	↓$PaCO_2$ ↓dyspnea; spontaneous breathing	Extubated; on intermittent NIPPV
6	55 (F)	...	...	Stage III COPD, anxiety-panic disorder, hypertension, tracheostomy 10 d prior	17	168	↓$PaCO_2$ ↓dyspnea, ↓ventilator support	Continued IPPV with ↓ventilator support
7	73 (M)	...	...	Stage IV COPD, LTOT, hypertension, tracheostomy 2 mo prior	27	42	↓$PaCO_2$ ↓ventilator support	Continued IPPV with ↓ventilator support
8	46 (F)	12	52	Stage IV COPD, obesity, LTOT 10 y, on NIPPV 3 y	22	168	↓$PaCO_2$; remained on IPPV	Died, day 26: abdominal sepsis, respiratory failure
9	70 (M)	...	...	Stage IV COPD, Cor Pulmonale	62	118	↓$PaCO_2$; remained on IPPV; panic/anxiety attacks requiring sedation	Continued IPPV
10	67 (M)	28	45	Stage IV COPD	15	74	↓$PaCO_2$; ↓ ventilator support; ↓blood flow due to inadequate anticoagulation	Died, day 21: pneumonia, respiratory failure
11	71 (M)	16	34	Stage IV COPD, hypertension	72	129	↓$PaCO_2$ ↓dyspnea, extubated; reintubated day 4	Continued IPPV with ↓ventilator support

$ECCO_2R$ = extracorporeal CO_2 removal; F = female; IPPV = invasive positive pressure ventilation; LTOT = long-term oxygen therapy; LVRS = lung volume reduction; M = male; NIPPV = noninvasive positive pressure ventilation; OSA = obstructive sleep apnea.

[a]COPD stages based on the Global Initiative for Chronic Obstructive Lung Disease.[16]

Table 2—*Ventilatory Parameters*

	Group 1							Group 2		Group 3										
Subject	1	2	3	4	5	6	7	1	2	1	2	3	4	5	6	7	8	9	10	11
Minute ventilation, L/min																				
Baseline, pre-$ECCO_2R$	2.5	2.5	6.5	…	7.1	…	…	…	…	7.4	7.0	6.9	4.7	8.6	4.5	11.0	8.4	8.3	7.8	5.9
Time after $ECCO_2R$ application																				
1 h	2.0	3.4	4.0	15.0	6.0	…	…	6.8	9.7	8.0	6.9	3.7	3.5	…	6.8	10.1	7.7	7.1	6.8	9.7
2 h	4.0	3.5	8.0	16.0	8.0	…	…	7.3	10	6.6	7.3	3.5	3.41	…	3.8	6.8	5.5	…	7.3	10.2
Final	6.8	…	4.9	8.3	8.7	…	…	10.4	…	11.7	7.4	8.2	…	8.5	3.4	8.7	8.3	7.6	10.4	…
Frequency, min																				
Baseline, pre-$ECCO_2R$	18	20	18	22	16	18	…	25	15	15	16	19	15	16	16	20	23	22	25	15
Time after $ECCO_2R$ application																				
1 h	21	24	13	22	16	…		26	15	15	16	12	12	29	20	33	38	26	26	15
2 h	18	19	13	22	…	…	…	26	15	15	16	…	11	30	14	20	23	30	26	15
Final	23	24	20	22	…	…	…	26	16	24	11	16	…	11	20	20	24	25	26	16
FIO_2, %																				
Baseline, pre-$ECCO_2R$	…	…	30	44	28	30	44	40	35	35	35	45	35	30	30	40	50	32	36	30
Time after $ECCO_2R$ application																				
1 h	…	…	30	44	…	…	…	50	35	36	35	50	35	30	30	50	50	40	…	30
2 h	…	…	30	44	32	…	28	…	35	36	35	50	35	30	30	50	50	…	…	30
Final	…	…	30	80	28	…	40	40	35	45	40	75	35	35	30	30	40	40	44	30
IPAP, cm H_2O																				
Baseline pre-$ECCO_2R$	…	…	28	30	20	20	…	15	32	…	…	…	…	…	…	…	…	…	…	…
Time after $ECCO_2R$ application																				
1 h	…	…	…	…	20	…	…	…	32	…	…	…	…	…	…	…	…	…	…	…
2 h	…	…	12	…	20	…	…	24	32	…	…	…	…	…	…	…	…	…	…	…
Final	…	…	30	32	20	…	…	24	30	…	…	…	…	…	…	…	…	…	…	…
EPAP, cm H_2O																				
Baseline, pre-$ECCO_2R$	…	…	12	4	6	8	…	5	10	…	…	…	…	…	…	…	…	…	…	…
Time after $ECCO_2R$ application																				
1 h	…	…	…	…	6	…	…	…	10	…	…	…	…	…	…	…	…	…	…	…
2 h	…	…	12	…	6	…	…	5	10	…	…	…	…	…	…	…	…	…	…	…
Final	…	…	10	6	5	…	…	5	8	…	…	…	…	…	…	…	…	…	…	…
PEEP, cm H_2O																				
Baseline, pre-$ECCO_2R$	…	…	…	…	…	…	…	…	…	4	5	9	10	15	8	7	8	5	6	5
Time after $ECCO_2R$ application																				
1 h	…	…	…	…	…	…	…	…	…	4	5	…	10	15	8	10	8	5	6	5
2 h	…	…	…	…	…	…	…	…	…	4	6	8	9	15	10	10	8	5	6	5
Final	…	…	…	…	…	…	…	…	…	4	8	10	…	7	8	10	6	5	6	5

EPAP = expiratory positive airway pressure; IPAP = inspiratory positive airway pressure; PEEP = positive end-expiratory pressure. See Table 1 for expansion of other abbreviations.

excessive anticoagulation. In the two subjects with bleeding caused by their underlying disease, one (group 3, subject 3, Table 1) was attributed to a new diagnosis of von Willebrand disease, and the other (group 1, subject 3, Table 1) to an intestinal ulcer. In the patient who received excessive anticoagulation (group 1, subject 5, Table 1), bleeding occurred from the catheter insertion site and a preexisting thoracic drain.

Discussion

This pilot study supports the feasibility of using this single venous catheter $ECCO_2R$ device for removing CO_2 in hypercapnic patients with COPD, with side effects primarily related to and similar to those seen with central venous catheter placement used with extracorporeal therapies.[17] The device was consistently able to remove >80 mL/min of CO_2 over several days of continuous use at blood flow ranging between 300 and 550 mL/min through the extracorporeal circuit.

The overall mortality rate was very similar to that reported in comparable patients not receiving $ECCO_2R$,[6,9,10] and it could be argued that the absence of any significant improvement in mortality makes the value of this $ECCO_2R$ device questionable. However, this preliminary study was not planned to assess

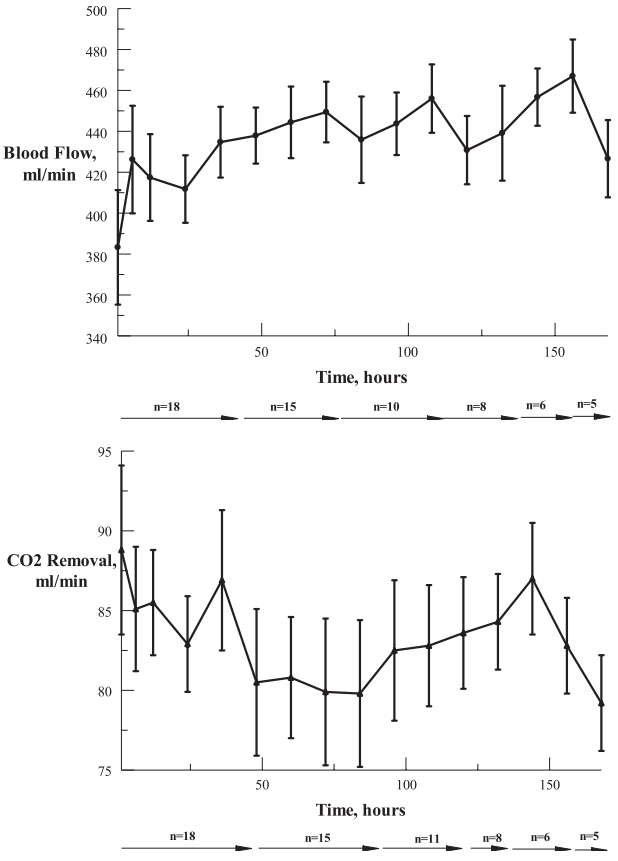

FIGURE 2. Blood flow (mean ± SEM) and CO_2 removal (mean ± SEM) through the catheter over time, where n = number of subjects at various time points.

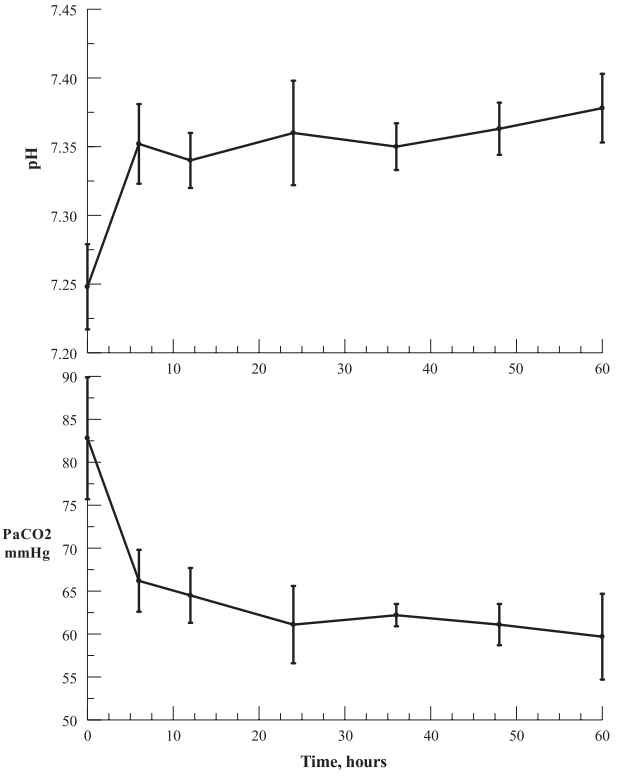

FIGURE 3. Changes in $PaCO_2$ (mean ± SEM) and pH (mean ± SEM) with $ECCO_2R$ in patients in group 1 (acute exacerbation of COPD on noninvasive positive pressure ventilation [NIPPV]). n = number of subjects; 0 h on abscissa represents baseline values. See Figure 1 legend for expansion of other abbreviations.

improvements in mortality outcomes, and the data are insufficient to provide definitive conclusions in this regard. On the other hand, mortality is significantly better in patients treated with NIPPV who avoid intubation and IPPV,[6] and it is possible that $ECCO_2R$ will have a beneficial effect on mortality; however, a definitive answer must await a larger, controlled, prospective study.

The most valid data for assessing the effect of the device are those seen in patients in group 1. In these patients who were on NIPPV, the device was capable of reducing the $PaCO_2$ and increasing pH (Fig 3), and none required invasive ventilation. We recognize that the decision to proceed to invasive ventilation is dependent on a number of factors and varies with the individual treating physician. Nevertheless, given the inclusion parameters for this group, the likelihood of these patients requiring invasive ventilation is predicted to be $>52\%$.[14] In group 3, it could be argued that the precise effects of the device could be confounded by the degree of mechanical ventilatory support and adjustments made by the investigator. However, in each case, the patients had been on standard treatment and the application of $ECCO_2R$ resulted in clinical improvement. The data indicate that the device application was associated with a decrease in the level of perceived dyspnea.

The single death directly attributable to the catheter placement was, as noted previously, due to internal hemorrhage from vessel perforation. This is a well-known adverse event with central venous catheter placement and is not unique to this device.[17] A more common side effect, thrombocytopenia, was likely related to heparin use. However, in the majority of cases, this was not associated with clinically significant bleeding. The current system is not an oxygenation device; in animal studies, the maximum oxygen uptake that can be achieved with the device at blood flow rates of 400 to 500 mL/min is 25 to 35 mL/min.

$ECCO_2R$ has been used as an adjunct to prevent lung damage in patients with ARDS.[12] The original technique required a pump-driven venovenous bypass, utilizing large catheters (21–28F size) and relatively high blood flows (25%–30% of cardiac output), with a high incidence of side effects.[18,19] These factors, as well as the negative results of a clinical trial,[20] prevented widespread clinical application of this technique.

Further innovations have led to the development of two different CO_2 removal techniques: a pumpless arteriovenous system, the interventional lung assist device (Novalung GmbH), and a pump-driven low

blood flow venovenous system (Hemodec s.r.l.). The pumpless device has been used primarily in patients with ARDS as an adjunct to mechanical ventilation.[21] Both an arterial and a venous catheter are required with high blood flows of 1.0 to 2.5L/min, ie, 25% to 50% of cardiac output, and concomitant use of norepinephrine to maintain the pressure gradient. Nevertheless, it is effective in CO_2 removal. Unfortunately, serious complications in 12% to 25% of patients, including limb ischemia, compartment syndrome, and amputation have been reported.[22] The pump-driven system uses a smaller catheter and lower blood flows (up to 400 mL/min). CO_2 exchange is increased by the use of a hemodialyzer in the circuit.[23] The actual CO_2 removal rates have not been stated in these studies.

The present pilot study establishes the feasibility of using this single venous catheter $ECCO_2R$ device for effective removal of CO_2 at relatively low blood flow rates in hypercapnic patients. It may be useful in the treatment of hypercapnic respiratory failure in patients with COPD and, possibly, may have a role in assisting protective ventilation in patients requiring extreme ventilatory support, such as in severe ARDS. A larger, prospective study may help to establish the efficacy and safety of the device and its role in the management of respiratory failure.

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