Extracorporeal Membrane Oxygenation in a 29-Year-Old Man with *Pneumocystis jirovecii* Respiratory Failure and AIDS

The use of extracorporeal membrane oxygenation (ECMO) in patients who have acute respiratory distress syndrome has been generally beneficial. However, because of various concerns, ECMO has rarely been used in patients who have human immunodeficiency virus infection with or without acquired immune deficiency syndrome.

We report our successful use of venovenous ECMO in a 29-year-old man who presented with severe respiratory distress secondary to *Pneumocystis jirovecii* pneumonia associated with undiagnosed infection with the human immunodeficiency virus and acquired immune deficiency syndrome. After highly active antiretroviral therapy was begun, acute immune reconstitution inflammatory syndrome developed. The patient’s respiratory condition deteriorated rapidly; he was placed on venovenous ECMO for 19 days and remained intubated thereafter. After a 65-day hospital stay and inpatient pulmonary rehabilitation, he recovered fully. In addition to presenting this case, we review the few previous reports and note the multidisciplinary medical and surgical support necessary to treat similar patients. *(Tex Heart Inst J 2018;45(4):254-9)*

Highly active retroviral therapy (HAART), combined with an early test-and-treat approach, has greatly reduced the incidence of human immunodeficiency virus (HIV) infection with progression to acquired immune deficiency syndrome (AIDS). However, despite improved surveillance and testing of at-risk populations, approximately 38,500 new HIV infections occurred in the United States in 2015. The prevalence of acute respiratory failure in these patients is high. Among patients with HIV admitted to intensive care for acute respiratory failure, 35% had *Pneumocystis jirovecii* (previously called *P. carinii*) pneumonia (PCP).

Extracorporeal membrane oxygenation (ECMO) has proved effective for treating respiratory failure of various causes. ECMO has typically been avoided in immunocompromised patients because it can further suppress immune function, and no clinical indications for HIV-infected or AIDS patients have been established. Nevertheless, there are currently no absolute contraindications to using ECMO in these patients.

Only a few case reports and a small case series have covered the use of ECMO in patients with HIV or AIDS as therapy for respiratory failure secondary to PCP. Of note, some patients with newly diagnosed HIV infection, AIDS, or both may develop immune reconstitution inflammatory syndrome (IRIS) after HAART initiation, resulting in PCP that leads to acute respiratory distress syndrome. In this report, we describe our use of venovenous ECMO in a patient who had all these conditions. In addition, we discuss the previous relevant cases.

**Case Report**

A previously healthy 29-year-old man (height, 61 in; weight, 132 lb) visited his primary care physician in July 2015 because of a 2-week history of severe shortness of breath associated with productive cough, headache, and body aches. His last physical examination (a routine wellness check) had been one year before. The patient now had ca-
chexia, diffuse crackles, oral thrush, pink papules on his knees, and purple nonpapular lesions on his face, trunk, and extremities. His severe dyspnea necessitated 4 L of oxygen delivered through a nasal cannula, so he was admitted to our institution for emergency evaluation of possible pneumonia. Notable laboratory results were a hemoglobin level of 9.6 g/dL, a hematocrit of 28.8%, and lymphocyte and monocyte levels of 0.8 g/L each. His chest radiograph was more consistent with PCP than with viral pneumonia. High-resolution computed tomograms revealed diffuse, patchy, ground-glass opacities with consolidation at the lung bases. Infection with PCP was confirmed by means of immunofluorescence during bronchoalveolar lavage. The patient’s persistent oxygen saturation in the mid- to low-80% range necessitated increased oxygen supplementation of 10 L/min delivered through a face mask. An arterial blood gas analysis revealed a PaO2 of 33 mmHg, a PaCO2 of 37 mmHg, and an alveolar–arterial gradient of 70 mmHg. Additional results after admission were an abnormally low CD4 count (4 cells/mm3) and a positive HIV polymerase chain reaction test (131,000 copies/mL). The patient reported no recent HIV testing or prior positive HIV test results.

Respiratory Status. The patient was transferred to the intensive care unit on hospital day (HD) 3 and was started on methylprednisolone and empiric intravenous trimethoprim/sulfamethoxazole. He needed intermittent bilevel positive airway pressure therapy for several days, but his condition slowly improved. On HD 10, a pneumomediastinum and small left pneumothorax developed; on HD 12, a small pigtail chest tube was placed for suction of a left upper pneumothorax.

Immune Status. On HD 4, we made the diagnosis of HIV infection with associated AIDS-defining characteristics, and on HD 5 we started the patient on HAART. Antiviral therapy consisted of a protease inhibitor (darunavir) and booster agent (ritonavir), and 2 nucleoside reverse transcriptase inhibitors (emtricitabine and tenofovir fumarate) coupled with an integrase strand transfer inhibitor (dolutegravir). By HD 16, the HIV viral load had markedly decreased (Table I). When results of HIV genotyping and phenotyping indicated susceptibility to all major classes of antiretroviral agents, darunavir and ritonavir were discontinued.

On HD 16, 10 days after HAART had begun, the patient underwent emergency intubation because of worsening respiratory function and severe hypoxemia. The ventilatory protocol included a pressure control rate of 25 breaths/min, a fraction of inspired oxygen (FiO2) of 90%, a positive end-expiratory pressure (PEEP) of 7 cm H2O, and a ΔP of 27 cm H2O. Despite therapeutic maneuvers such as prone positioning, lung-protective ventilation, administration of a neuromuscular blocking agent (cisatracurium), and initiation of inhaled nitric oxide, the patient’s respiratory status did not improve, and hypoxemia persisted (PaO2 <60 mmHg). Sputum cultures grew Mycobacterium avium-intracellulare; new infiltrates were noted on chest images, and we strongly suspected IRIS. Two days after the intubation, we held a multidisciplinary consultation conference. The infectious disease specialists, mechanical assist device sur-

| Variable* | July 2015 (admission) | Hospital Day | November 2015 (4 mo) | January 2016 (6 mo) | February 2016 (7 mo) | July 2017 (1 yr) |
|-----------|-----------------------|--------------|-----------------------|---------------------|---------------------|-----------------|
| HIV-1 RNA PCR (copies/mL) | 131,000 | 266 | 23 | 28 | 87 | 6,330 | ND | ND |
| HIV-1 RNA PCR log 10** (quantitative) | 5.12 | 2.42 | 1.36 | 1.44 | 1.94 | 3.8 | ND | ND |
| CD4 absolute count (511–2,245 cells/mm3) | 4 (L) | 1 (L) | 21 (L) | NR | NR | 73 (L) | NR | 207 (L) |
| CD8 absolute count (258–1,394 cells/mm3) | 165 (L) | 88 (L) | 322 (N) | NR | NR | 955 (N) | NR | 1,031 (N) |
| CD4/CD8 ratio (0.9–2.9) | 0.03 (L) | 0.01 (L) | 0.06 (L) | NR | NR | 0.08 (L) | NR | 0.2 (L) |
| HIV-1 genotyping | No resistance patterns to NRTIs, NNRTIs, or PIs | HIV subtype B | RT gene mutations: H208Y and R211K | — | — | — | — | — |

HIV = human immunodeficiency virus; L = low range; N = normal range; ND = not detectable; NNRTIs = nonnucleoside reverse transcriptase inhibitors; NR = not recorded; NRTIs = nucleoside reverse transcriptase inhibitors; PCR = polymerase chain reaction; PIs = protease inhibitors; RNA = ribonucleic acid; RT = reverse transcriptase

*Applicable reference ranges are in parentheses.

**COBAS™ AmpliPrep/COBAS™ TaqMan™ HIV-1 Test (Roche Molecular Systems, Inc.)
geon, intensivists, and cardiac anesthesiologists decided to initiate emergency venovenous ECMO because of the patient’s worsening hypoxemia.

On HD 18, ECMO cannulation proceeded as follows. Access to the right internal jugular vein was gained under ultrasonographic and fluoroscopic guidance with use of a 180-cm Amplatz Super Stiff guidewire (Boston Scientific Corporation), which was inserted into the inferior vena cava. The right internal jugular vein was serially dilated to 30F, and a 31F Avalon Elite® Bi-Caval Dual Lumen Cannula (MAQUET Cardiovascular) was inserted under transesophageal echocardiographic (TEE) and fluoroscopic guidance. Finally, venovenous ECMO was begun (flow rate, 4.5 L), and the ventilator settings were adjusted with decreases in FiO$_2$ from 100% to 60% and a PEEP of 7 cm H$_2$O. The patient’s postoperative course was complicated by episodes of delirium; cannula malpositioning, which necessitated 2 adjustments in the operating room under TEE guidance; and severe laceration of the uvula after TEE probe insertion, which necessitated operative repair. The general ECMO settings were as follows: flow rate, 3.5 to 5 L/min; sweep, 5.2 L/min; and FiO$_2$, 100%. On HD 38 (postoperative day 19), the cannulas were successfully removed; however, the patient needed prolonged ventilator support, and a tracheostomy was placed on HD 50.

The patient was progressively weaned to a tracheostomy collar during the next week. After 65 HDs, he was discharged to a long-term assisted care facility. During and after that hospitalization, he was treated for Kaposi sarcoma and was prescribed broad-spectrum antibiotics and antifungal agents long-term (Table II). His immune status slightly improved; after 14 months, he remained on HAART and anti-infective agents. His CD4 cell count progressively increased, and his HIV viral load suppression improved. By February 2016 (~7 mo after admission), his HIV viral load was undetectable, and his absolute CD4 cell count had improved to 207 cells/μL (close to a low-normal level).

The patient’s respiratory condition also steadily improved. Chest images after his initial hospitalization showed severe consolidation, interstitial changes, and scarring. Pulmonary function results indicated a severely restrictive ventilatory defect with greatly reduced diffusing capacity of the lungs for carbon monoxide (Dl$_{CO}$) (34% of predicted). His exercise tolerance was poor. After aggressive physical therapy and weaning from supplemental oxygen, he had dramatically improved breathing capacity and exercise tolerance. Computed tomograms of the chest showed resolution of the consolidation and vast improvement in the reticular changes. In July 2016, his lung volumes had increased from 3.53 to 5.21 L (71% of predicted), and Dl$_{CO}$ increased to 61% of predicted. He was able to exercise regularly and resumed his full-time career.

**Discussion**

We successfully used ECMO in a patient with respiratory failure secondary to PCP infection associated with undiagnosed HIV infection, AIDS, and IRIS. In the

| Drug               | Indication           | Therapy Duration (range) | Currently Prescribed |
|--------------------|----------------------|--------------------------|----------------------|
| Augmentin          | Antibiotic           | HD 25–29                 | No                   |
| Azithromycin       | MAC and prophylaxis  | HD 2–present             | Yes                  |
| Cefepime           | Antibiotic           | HD 17–24                 | No                   |
| Cefotaxime         | Antibiotic           | HD 2–5 and 46–48         | No                   |
| Clarithromycin     | MAC and prophylaxis  | HD 88–116                | No                   |
| Doxorubicin        | Kaposi sarcoma       | 3 doses after hospital discharge at 1-mo intervals | No |
| Ethambutol         | MAC and prophylaxis  | HD 16–present            | Yes                  |
| Fluconazole        | Thrush               | HD 6–37                  | No                   |
| Ganciclovir        | Cytomegalovirus      | HD 18–27                 | No                   |
| Imipenem           | Antibiotic           | HD 39–46                 | No                   |
| Levofloxacin       | MAC and prophylaxis  | After hospital discharge for 15 d | No |
| Metronidazole      | Antibiotic           | HD 26–46                 | No                   |
| Rifabutin          | MAC and prophylaxis  | HD 16–present            | Yes                  |
| Sulfamethoxazole/  | PCP and prophylaxis  | HD 2–present             | Yes                  |
| trimethoprim       |                      |                          |                      |

HD = hospital day; MAC = Mycobacterium avium complex; PCP = Pneumocystis jirovecii pneumonia
mid-1990s, P. carinii pneumonia (now called P. jirovecii) was recognized as the most prevalent and severe respiratory infection in HIV-infected patients. Indeed, PCP is still one of the first manifestations of advanced HIV infection and AIDS in more than 15% of cases. These patients have a 20% mortality rate at 3 months despite effective pneumonia prophylaxis and adjunctive steroidal therapy for mild to severe hypoxemia.18

Only a few patients with HIV infection or full-blown AIDS have been treated with ECMO (Table III).9-17 Because of low CD4 cell counts and at least one opportunistic infection, almost all had new diagnoses of HIV with AIDS. Initial concerns about using ECMO to treat HIV-infected or AIDS patients focused on possibly increasing immune suppression. However, over the last 25 years, long-term observational studies of HIV patients undergoing cardiac surgery with concomitant cardiopulmonary bypass have largely dispelled those concerns because bypass has posed no discernible risk of immune suppression or progression to AIDS.19,20

Our patient met the Centers for Disease Control criteria for stage 3 HIV infection and AIDS: HIV infection with a CD4 cell count <200 cells/mm³ and >2 opportunistic infections (Kaposi sarcoma, oral candidiasis, and PCP).3 The use of venovenous ECMO combined with antimicrobial therapy and HAART for PCP and AIDS gradually improved his respiratory function. Immune reconstitution inflammatory syndrome is a major concern during acute immune reconstitution after patients with HIV or AIDS begin HAART, and IRIS may ne-

**TABLE III. Summary of HIV-Positive Patients Undergoing ECMO for Respiratory Failure**

| Reference         | Pt. Age, Sex  | HIV Status | HIV Viral Loada | CD4 Countb | AIDS-Defining Diagnosesb | Time to ECMO Initiation (d) | ECMO Duration (d) | Type of ECMO | Outcome                  |
|-------------------|---------------|------------|-----------------|------------|--------------------------|----------------------------|-------------------|--------------|--------------------------|
| Gutermann H, et al.9 (2005) | 55, M New | 80,235 | 9 | Yes | After ECMO (21) | 4 | VA Alive 6 mo after DFH |
| Steppan J and Sikazwe I10 (2009) | 39, M Existing | NR | 69 | No | Before ECMO (NR) | 1 | VV Died during ECMO |
| Goodman JJ, et al.11 (2013) | 25, M New | 622,234 | 36 | Yes | After ECMO (NR) | 69 | VV Died during ECMO |
| 30, F New | 976,631 | 13 | Yes | After ECMO (3) | 7 | VV Alive 3 mo after DFH |
| Cawcutt K, et al.12 (2014) | 45, M New | NR | 33 | Yes | Before ECMO (NR) | 57 | VV Died 40 d after ECMO |
| De Rosa FG, et al.13 (2014) | 21, F Perinatal 118,330 | 2 | Yes | After ECMO (NR) | 20 | VV Alive 1 yr after DFH |
| 24, M New | 50,728 | 3 | Yes | During ECMO (8) | 24 | VV Died after ECMO |
| 38, F Existing | Suppressed | 200 | No | Before ECMO (NR; chronic HIV infection) | 13 | VV Alive 6 mo after DFH |
| Ali HS, et al.14 (2016) | 26, M New | 907,302 | 84 | Yes | After ECMO (NR) | 6 | VV DFH |
| Guedes M, et al.15 (2016) | 65, F New | 4,050,000 | 9 | Yes | After ECMO (17) | 10 | VV Alive 6 mo after DFH |
| Horikita S, et al.16 (2017) | 23, M New | 550,000 | 8.5 | Yes | Simultaneous with ECMO | 12 on, 2 off, 14 on | VV DFH |
| Lee N, et al.17 (2017) | 54, F New | 1,075,072 | 12 | Yes | During ECMO (12) | 31 | VV DFH |
| Current case (2018) | 29, M New | 131,000 | 4 | Yes | Before ECMO (2) | 19 | VV Alive 36 mo after DFH |

AIDS = acquired immune deficiency syndrome; DFH = discharge from hospital; ECMO = extracorporeal membrane oxygenation; F = female; HAART = highly active antiretroviral therapy; HIV = human immunodeficiency virus; M = male; NR = not recorded; Pt. = patient; VA = venoarterial; VV = venovenous

aAt time of admission or diagnosis
bAt time of admission
cAfter initiation of Pneumocystis jirovecii pneumonia therapy

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cessitate ECMO because acute respiratory distress syndrome can develop.\textsuperscript{21-23} Mycobacterial disease is typically associated with IRIS, as in our patient.

Our patient’s HIV genotype and phenotype analysis indicated susceptibility to all major classes and agents of HAART. However, many months passed before full immune reconstitution and HIV viral load suppression were achieved. Typically, CD4 cell repletion is notoriously slow, and our patient’s count did not reach normal levels even after one year of HAART. We continued HAART even during his intubation (this is possible enterally, through an orogastric or nasogastric tube).

Authors have noted the perceived futility of implementing ECMO in patients with advanced HIV infection or AIDS. Among the reported cases,\textsuperscript{9-17} 2 patients died during ECMO. Various complex factors contributed to those deaths and to the survival of the other patients. One eventual survivor had to be placed on venoarterial ECMO, a method not typically indicated for respiratory support. In no reported case when ECMO began was correlation apparent between the HIV viral load or CD4 cell count and the patient’s eventual survival or death. Our patient had a moderate HIV viral load and an almost nonexistent CD4 cell count. We prescribed HAART because these regimens have proved to be effective; the addition of ECMO support enabled full treatment.

Over decades of cardiac surgical experience, no contraindication to ECMO has arisen in terms of immunologic compromise in HIV-infected or AIDS patients. Improved HAART regimens have bolstered HIV patients’ long-term survival prospects,\textsuperscript{24} and HAART plus early ECMO for respiratory failure may achieve the same in patients like ours who have PCP secondary to HIV and AIDS. Of note, severely immunocompromised patients will need a wide range of resources for a long time, so they are best referred to centers experienced with HIV-infected patients who have undergone cardiac surgery, the implantation of mechanical respiratory devices, or both.

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