Intradialytic Hypoxemia in Chronic Hemodialysis Patients

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Key Words

Oxygen saturation · Oxygen status · Chronic kidney disease · End-stage renal disease · Hypoxia · Cardio-pulmonary-renal syndrome

Abstract

When kidney failure occurs, patients are at risk for fluid overload states, which can cause pulmonary edema, pleural effusions, and upper airway obstruction. Kidney disease is also associated with impaired respiratory function, as in central sleep apnea or chronic obstructive pulmonary disease. Hence, respiratory and renal diseases are frequently coexisting. Hypoxemia is the terminal pathway of a multitude of respiratory pathologies. The measurement of oxygen saturation (SO₂) is a basic and commonly used tool in clinical practice. Both arterial oxygen saturation (SaO₂) and central venous oxygen saturation (ScvO₂) can be easily obtained in hemodialysis (HD) patients, SaO₂ from an arteriovenous access and ScvO₂ from a central catheter. Here, we give a brief overview of the anatomy and physiology of the respiratory system, and the different technologies that are currently available to measure oxygen status in dialysis patients. We then focus on literature regarding intradialytic SaO₂ and ScvO₂. Lastly, we present clinical vignettes of intradialytic drops in SaO₂ and ScvO₂ in association with different symptoms and clinical scenarios with an emphasis on the pathophysiology of these cases. Given the fact that in the general population

hypoxemia is associated with adverse outcomes, including increased mortality, cardiac arrhythmias and cardiovascular events, we posit that intradialytic SO₂ may serve as a potential marker to identify HD patients at increased risk for morbidity and mortality.

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Introduction

Patients with chronic kidney disease (CKD) show a vast spectrum of signs and symptoms as a result of damage in different organs. Recently, pulmonary manifestations associated with CKD gained increased attention in clinical practice and research. Studies are focusing on the links between pulmonary function and renal damage, and it has been proposed to classify these clinical manifestations as ‘cardio-pulmonary-renal’ syndrome [1].

For the study of respiratory pathologies in hemodialysis (HD) patients, the measurement of the hemoglobin (Hgb) oxygen saturation (SO₂) has been shown to be valuable. More than 20 years ago, it has been demonstrated that SaO₂ decreases during extracorporeal renal replacement therapy [2], and recently, a comparable obser-

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vation has been made for ScvO₂ [3]. The purpose of this review is to provide an overview about intradialytic SaO₂ and ScvO₂ during HD and its clinical correlates.

Pulmonary Gas Exchange

Structure of the Respiratory System

Disturbances of oxygenation can occur at any level of the cardio-pulmonary system and evaluation of oxygen status must take a variety of different factors into account. The respiratory system is a complex set of organs with the main purpose of delivering oxygen to the blood and removing carbon dioxide.

On its way to the lungs, air passes through the epipharynx, trachea, and two principal bronchi, which then further divide into lobular, segmental and terminal bronchioles. This portion of the respiratory tract holds approximately 150 ml and is known as 'anatomic dead space', because there is no gas exchange. The terminal bronchioles then branch off into the respiratory bronchioles, which are the transition zone between the upper and the lower airways. The lower respiratory tract is the air exchange compartment and consists of the respiratory bronchioles and alveolar ducts, which are full of alveolar sacs. This compartment can hold a volume of 2.5–3 liters (fig. 1). The alveolar sacs are complex structures that form the air–blood interface with a surface area of about 75 m² in healthy adults [4].

Gas Exchange

Respiration is the result of three principal mechanisms: ventilation, diffusion and perfusion [1]. Ventilation is the transport of air into the lungs, which is driven by respiratory muscles and regulated primarily by the respiratory center in the brain stem [5]. The respiratory center integrates neural, chemical and hormonal signals and controls the rate and depth of respiratory movements of respiratory muscles. Chemoreceptors measure chemical signals such as changes in pH, carbon dioxide and oxygen concentration in the blood. These signals are then relayed to the respiratory center. Additionally, baroreceptors in the chest may affect ventilation patterns [6]. Alterations in ventilation can be due to disturbances at the neural level, of respiratory muscles, of chest bones or of airways [7]. The pulmonary perfusion is in series to the right heart and depends on the cardiac output. The relationship between alveolar ventilation and perfusion is a key determinant of gas exchange, and diffusion is the principal mechanism of gas exchange at the air–gas interface.

Fig. 1. Airway anatomy.

Oxygenation

Once oxygen has entered the blood by diffusion across the alveolar membranes it is either reversibly bound to Hgb in the red blood cells or dissolved in the plasma. The amount of dissolved oxygen depends on the oxygen partial pressure (PaO₂; also called oxygen tension) and the solubility coefficient of oxygen (0.0031 ml/dl/mm Hg). The fraction of Hgb molecules carrying oxygen (SO₂) depends on the partial pressure of oxygen and the Hgb oxygen affinity. The latter is modified by the blood pH (Bohr effect), partial pressure of carbon dioxide (Haldane effect), 2,3-diphosphoglycerate (2,3-DPG) levels inside erythrocytes, and blood temperature. All of those factors may change during dialysis [8–10]. The blood oxygen-carrying capacity (CaO₂) depends on the concentration of Hgb and its affinity to oxygen [11]. One gram of Hgb is able to carry approximately 1.34 ml of oxygen [12]. At sea level, around 98% of the oxygen in the blood is bound to Hgb and 2% dissolved in the plasma.

Fig. 2. Interactions between ventilation, diffusion, perfusion and oxygen-carrying capacity. All these factors affect the blood oxygen content. CNS = Central nervous system.

CaO₂ is calculated as follows:

$$\text{CaO}_2 \text{ (ml O}_2\text{/dl blood)} = 1.34 \text{ (ml/g)} \times \text{Hgb concentration (g/dl)} \times \text{SaO}_2 \text{ (\%)} / 100 + 0.0031 \text{ (ml/dl/mm Hg)} \times \text{PaO}_2 \text{ (mm Hg)}$$

In a healthy subject, a single erythrocyte carries around 250–300 million Hgb molecules, resulting in a Hgb concentration inside the cell of around 330 g/l. This means that at a hematocrit of 45%, the Hgb concentration is 150 g/l [8]. Therefore, in healthy subjects, 100 ml of blood has the capacity to bind approximately 20 ml of oxygen. However, carbon monoxide and methemoglobin render Hgb incapable of binding oxygen, thereby reducing the oxygen-carrying capacity.

Thus, the content of oxygen in the blood depends not only on the aforementioned ventilation, diffusion and perfusion but also on the oxygen-carrying capacity of the blood. The oxygen content of the venous blood depends additionally on the extraction of oxygen at the tissue level. Sufficient delivery of oxygen to tissues depends on a well-regulated interplay between these factors (fig. 2).

Acid Base Status and Effect on Ventilation

The normal arterial pH of 7.35–7.45 is carefully maintained by the lungs, kidneys and plasma buffers. The predominant buffering mechanism is the carbonic acid/bicarbonate system [13]. Other major buffers include plas-

ma proteins and phosphate ions [14]. When the hydrogen (H⁺) content in the blood increases, it combines with bicarbonate (HCO₃⁻) to become carbonic acid (H₂CO₃⁻).

Carbonic acid breaks down into water and carbon dioxide; the carbon dioxide diffuses into the lung alveoli and is exhaled. An increase in CO₂ triggers the central and peripheral chemoreceptors and thus stimulates ventilation [15]. Reduced central nervous respiratory drive, impaired gas diffusion, or neuromuscular disorders that affect ventilation may result in respiratory acidosis. Conversely, hyperventilation results in respiratory alkalosis. Dialysis patients often suffer from acidosis, which is corrected during HD by the influx of bicarbonate from the dialysate.

Hypoxia

Hypoxia indicates an inadequate tissue oxygen supply. In HD patients, several types of hypoxia can be differentiated. Anemic hypoxia is caused by a decreased concentration of functional Hgb or a reduced number of red blood cells. Hypoxic hypoxia results from impaired pulmonary blood oxygenation, abnormal pulmonary function, airway obstruction, or cardiac right-to-left shunt. Ischemic hypoxia is characterized by tissue oligemia and may be caused by reduced tissue perfusion due to vasculopathies [16].

Table 1. Devices for measuring SO₂ in HD

Device	Measurement principle	Reported parameter
Pulse oximeter	Different light-absorption spectra for HgbO ₂ and deoxygenated Hgb	% hemoglobin oxygen saturation
Near-infrared spectroscopy	Different light-absorption spectra for HgbO ₂ and deoxygenated Hgb in the infrared spectrum	% oxygen linked to Hgb, myoglobin and CrOx in tissue
CritLine Monitor TM	Different light-absorption spectra for HgbO ₂ and deoxygenated Hgb	% hemoglobin oxygen saturation
Blood gas analyzer	PaO ₂ is obtained by an electrode that measures electrical currents generated by oxidation-reduction reactions; % hemoglobin oxygen saturation is then computed based on empiric algorithms which may differ between manufacturers	PaO ₂ and % hemoglobin oxygen saturation

HgbO₂ = Oxygenated hemoglobin; CrOx = cytochrome oxidase.

The 2 primary means to assess oxygen status are the measurement of PaO₂ and SaO₂. Normal values for PaO₂ range from 85 to 100 mm Hg [17]. Values between 60 and 80 mm Hg are considered 'mild hypoxia', values between 40 and 60 mm Hg 'moderate hypoxia' and values <40 mm Hg indicate 'severe hypoxia' [16]. An arterial SaO₂ >95% is considered normal at an altitude below 1,000 m [17]. Although there is no universally agreed-upon definition, most sources define hypoxemia as SaO₂ ≤90% [18–20]. The arterial oxygen status is primarily indicative of the respiratory function, although nonrespiratory pathologies may also play a role.

Current Technologies for the Measurement of Blood Oxygenation

A number of devices allow clinicians to assess the blood oxygen status (table 1). Blood gas analyzers measure partial pressure (PaO₂) of oxygen in blood samples using an electrode to measure the electric currents generated from a set of oxidation–reduction reactions. Once PaO₂ is obtained, the analyzer calculates the SO₂ using empiric models, which may differ between manufacturers [21]. SO₂ can be measured noninvasively by optical methods utilizing the fact that oxygenated and deoxygenated Hgb have different light absorption characteristics. Pulse-oximetry probes are usually attached to a finger to measure SO₂ either in a static and continuous fashion [22, 23]. Near-infrared spectroscopy is used for the measurement of regional tissue SO₂ [24, 25]. Of particular relevance to the dialysis field is the measurement of SO₂ in the extracorporal

real circuit during dialysis (CritLine MonitorTM; CLM). This device obtains SO₂ using different wavelengths and absorption-based algorithms. Depending on the vascular access type, SaO₂ or ScvO₂ is measured.

Arterial Oxygenation during HD

In HD patients with arteriovenous vascular access, SaO₂ can be determined from measurements in the arterial blood line of the extracorporeal circuit. Nielsen and Jensen [16] reported a high correlation between blood gases in the radial artery and the arterial line of HD patients with a well-functioning fistula. However, a few points deserve consideration when interpreting the arterial oxygen status in a HD patient. Anemia may lead to a reduced arterial oxygen content, which escapes detection when considering SaO₂ or PaO₂ only. Further, an increase in pH during dialysis causes a left shift of the oxygen disassociation curve, reducing oxygen release in the tissue. Erythrocyte 2,3-DPG levels may decline during dialysis and thus increase the Hgb oxygen affinity [9].

A low arterial oxygen status is the common terminal pathway of multiple functional and structural pathologies; sleep apnea, chronic obstructive pulmonary disease, pulmonary edema, and pulmonary calcification are particularly prevalent in HD patients [26–30]. Munger et al. [31] monitored SO₂, arrhythmias and silent ischemia in 10 ESRD males and found that all subjects demonstrated intradialytic hypoxemia. All patients had episodes of cardiac ectopy and 5 subjects had a total of 89 episodes of silent ischemia. They postulated that the hypoxia likely

Fig. 3. Time course of mean SaO₂ and 95% CI in chronic HD patients with arteriovenous access.

contributed to the incidence of arrhythmias and silent ischemia [31]. Sleep apnea syndromes are associated with ventricular arrhythmias, ventricular tachycardia, atrial fibrillation and bradyarrhythmias [32]. In healthy men who are subjected to acute hypoxia, there is an increase in myocardial oxygen extraction, and increased coronary blood flow [33]. However, the incidence of coronary artery disease is high in the ESRD population, and as previously discussed, the SO₂ curve shifts to the left during dialysis, decreasing Hgb oxygen disassociation, potentially affecting adversely the patient's ability to cope with the hemodynamic stress during HD. Recently we assessed intradialytic SaO₂ in a large cohort of chronic HD patients [34]. In 8% of patients, the mean intradialytic SaO₂ was below 90% and 12% had an intradialytic SaO₂ below 90% for more than a third of their treatment time, a condition we labeled 'prolonged intradialytic hypoxemia'. We found that prolonged intradialytic hypoxemia was associated with an inflammatory phenotype [35]. Longitudinal studies are necessary to examine the long-term effects of intradialytic hypoxia.

Other studies demonstrated a drop of PaO₂ as well as SaO₂ at the beginning of HD treatments reaching a nadir after 30–60 min and then returning to pre-dialysis levels or even rising slightly above starting values toward the end of HD [36, 37]. We were able to corroborate these findings (fig. 3). This phenomenon generated much interest in the early days of dialysis; the causes remain unclear until today and seem to be multifactorial. The mag-

Fig. 4. Causes of hypoxemia.

Fig. 5. Time course of mean ScvO₂ and 95% CI in 25 chronic HD patients with central venous catheters as access.

nitude of the PaO₂ decline varies depending on the type of dialysis membrane and dialysate composition. A proposed mechanism is a complement-mediated leukostasis in small pulmonary vessels caused by bioincompatible dialysis membranes leading to an alveolar ventilation/perfusion mismatch. Further, bicarbonate influx during HD leads to an increase of pH and subsequent hypoventilation and possibly also hypoxemia [38]. In addition, fluid overload may adversely impact alveolar oxygen diffusion,

Clinical Vignette 1. This patient reported dyspnea on exertion between dialysis treatments. The ultrafiltration volume was 5 liters. At dialysis initiation, the SaO_2 was 86%. The significance of excessive fluid gains on the patient's respiratory system is demonstrated following a review of the patient's SaO_2 levels during a HD session. During the treatment, one can see the steady improvement of SaO_2 when the patient approached estimated dry weight. Note that the CLM also reports changes in RBV ($\% \text{BV}\Delta$) that are computed from the hematocrit increase. The slope of the $\% \text{BV}\Delta$ curve indicates the rate of blood volume reduction.

resulting in reduced blood oxygenation (fig. 4). Approaching dry weight should decrease the diffusion distance and thus improve blood oxygenation. In fact, Anand et al. [39] found a positive relationship between the slope of the relative blood volume (RBV) curve, an indirect marker of volume status, and change in SaO_2 indicating a contribution of volume overload to hypoxemia. Clinical Vignette 1 exemplifies this phenomenon.

Most patients sleep at some point during dialysis. Clinical Vignette 2 illustrates intradialytic SaO_2 drop while the patient was sleeping. During the sleep hours, the central respiratory control is not as tightly regulated as when awake. In dialysis patients, uremic destabilization of the central respiratory control, as well as fluid status related narrowing of the upper airway may be additional factors contributing to episodes of sleep apnea and low SaO_2 during dialysis treatments [40]. The incidence of sleep apnea syndromes is much higher in the dialysis population, compared to the general population [41]. Moreover, age-related changes of the respiratory system, such as a weakening of the neuro-mechanical link between chemosensors, brain stem and respiratory muscles, may lead to a reduced ability to maintain blood gas homeostasis in elderly chronic HD patients [42].

Clinical Vignette 2. In this clinical vignette the patient fell asleep in the first treatment hour. Note the sharp decline and high variation of SaO_2 while the patient was sleeping. The patient awoke after two hours and shortly thereafter had a blood pressure of 88/50 mm Hg, a RBV reduction by 9%, with an UFR of 470 ml/h and a SaO_2 of 88%. Ultrafiltration was reduced and supplemental oxygen administered.

Clinical observations indicate that low SaO_2 can be associated with a rapid increase in hematocrit during HD, indicative of a reduced vascular refill (Clinical Vignette 3). However, the underlying pathophysiology is not fully elucidated. The physiological responses to intradialytic blood volume reduction resemble to some extent those seen with hemorrhage. First, the reduction in blood volume leads to a reduction in venous return, resulting in a decrease of cardiac output and mean arterial pressure. This is compensated by an increased heart rate and arterial and venous constriction, resulting in increased total peripheral resistance and enhanced venous return. The arteriolar constriction leads to a reduced blood flow in capillaries and thereby a reduced capillary hydraulic pressure, promoting fluid absorption from the interstitium into the capillaries (vascular refill). However, the reduction of blood flow also results in the reduction of oxygen delivery and accumulation of metabolic waste products such as adenosine and lactic acid, which cause vasodilation of arterioles. This vasodilation restores oxygen delivery and blood flow in the capillaries but also leads to an increase of hydraulic capillary pressure and a decrease in vascular refill [43]. An increase of blood oxygen content, for example, by the administration of supplemental oxygen may have the potential to mitigate a drop in blood volume.

Clinical Vignette 3. SaO_2 was assessed at 50 min into the treatment and noted to be 83%. Supplemental oxygen was initiated at 2 liters per minute via nasal cannula and the SaO_2 rose to 95%. The RBV increased immediately from a 5% reduction to a 1% reduction despite no change in the UFR. Over the next one and a half hours, the blood volume decreased by 5%. At 2 and one half hours, the patient took supplemental oxygen off which was followed by an immediate decrease in both the SaO_2 to 86% and the RBV showing a steep slope to a reduction of 7.5%. At the vital sign check, the nurse noted the low oxygen level, steep RBV slope and asked the patient to put the oxygen back on. Near the end of the third hour the patient took oxygen off again and a similar drop in SaO_2 and blood volume occurred. Finally, the patient requested to end the treatment 20 min early because of hypotension instead of having normal saline given. The patient had removed the nasal cannula a third time approximately 10 min prior to the request for early sign off and a similar steep slope in the blood volume and decrease in SaO_2 occurred.

Clinical Vignettes 4 and 5 demonstrate that drops in SaO_2 and ScvO_2 , respectively and may coincide with muscle cramps, a frequent intradialytic morbid event [44]. Again, the pathophysiology underlying these observations is not clear [45]. There is a dearth of studies on the association between hypoxia and muscle cramps. Of note, it has been shown in patients with obstructive sleep apnea that continuous positive airway pressure improved or resolved nocturnal leg cramping [46, 47]. Clinical observations made authors of this study indicate that the application of oxygen already at the beginning of the treatment prevents or reduces cramps in many patients who frequently experience cramps during HD.

While little is known about the relationship between intradialytic and interdialytic SaO_2 , it is interesting to note that hypoxia may continue for hours even after HD is completed. Dhakal et al. [48] studied 10 maintenance

Clinical Vignette 4. This patient had a history of sleeping during dialysis and often awakened with severe cramping. The starting SaO_2 was 95%, the ultrafiltration volume 3.8 liters. Near the end of the first hour the SaO_2 decreased to 90% and remained at 89–90% during most of the second hour. At 1 h 45 min into the treatment the patient complained of slight cramps. At this time the blood volume was reduced by 5%. Due to patient symptoms the ultrafiltration was turned off. While the ultrafiltration was off the patient's blood volume began gradually increasing to -3% and the blood pressure remained unchanged. The cramping subsided and the patient was able to fall to sleep near the end of the second hour. While sleeping, the SaO_2 dropped to 81% and the patient awakened with severe cramps. The patient's blood volume showed a minimal change to -4%. Upon awakening, the SaO_2 returned to 95% and the cramping gradually subsided. The blood volume change demonstrated a gradual slope that never decreased more than -6% throughout this treatment.

HD patients, and continuously monitored their SO_2 up to 4 h post-HD. In this study, hypoxic episodes were observed as late as 4 h after dialysis.

Central Venous Oxygenation during HD

ScvO_2 represents the SO_2 of blood drawn from the superior vena cava. ScvO_2 is easily obtained in HD patients with central venous catheters, as the catheter tip is usually located at the cavoatrial junction. ScvO_2 is clinically valuable as it is a surrogate of pulmonary artery mixed venous oxygen saturation (SvO_2), which reflects cardiac output, tissue oxygen delivery, and tissue oxygen extraction [49]. There has been much debate regarding the use of ScvO_2 as a surrogate for SvO_2 . Animal studies in dogs and pigs have demonstrated a good correlation between

Clinical Vignette 5. This patient had 2.5 kg of fluid to be removed during the treatment. The ScvO₂ at the start of the treatment was 60%. By the end of the first hour, the ScvO₂ had decreased to 51%. Over the second hour the SO₂ continued decreasing and showed a severe drop 40 min into the second hour to 33%. The blood volume gradually decreased to -5%. The estimated dry weight was not yet met at the time of the symptoms. The blood pressure had not changed but the patient complained of severe cramping. The ultrafiltration was temporarily discontinued and a bolus of normal saline was administered. The cramping was relieved and ScvO₂ increased to 61% and the ultrafiltration was resumed. Note that at 2.5 h into the treatment the ScvO₂ decreased again and severely dropped to 32.9% at 3 h and 10 min into the treatment. The patient complained of severe cramps and blood pressure remained unchanged. A second bolus of normal saline was administered and the patient was taken off treatment. The estimated dry weight was not met.

ScvO₂ and SvO₂ [50, 51]. Human studies have also shown a linear association; however, SvO₂ measurements are consistently lower than ScvO₂ [52]. This is likely due to the fact that the ScvO₂ is mostly a measure of upper body oxygen consumption, while the SvO₂ includes deoxygenated blood from the lower body and coronary sinus [53]. In addition, during sepsis or heart failure, ScvO₂ tends to be higher than SvO₂ because of decreased extraction at peripheral tissue, and increased oxygen delivery to the upper body. While the absolute numbers did not correlate, the changes in SvO₂ reflected changes in ScvO₂ [53, 54].

ScvO₂ measurement is currently used in critical care and post-surgery monitoring. Rivers et al. [55] have advocated for early goal directed care in sepsis, with measurement of ScvO₂ as one of these measures. Obtaining ScvO₂ >70% was associated with improved outcomes. Studies showed benefits of monitoring ScvO₂ during high-risk

surgery, where ScvO₂-guided fluid and volume resuscitation were associated with improvements in length of intensive care unit stay, morbidity and mortality [56, 57]. Low ScvO₂ or SvO₂ indicate inadequate tissue oxygenation, either from decreased cardiac output and oxygen delivery or high extraction of oxygen at the tissue level. Despite a body of literature showing the utility of ScvO₂ monitoring, data in the dialysis population are scarce.

Eating is generally discouraged during HD, given the concern for hypotension. In healthy subjects eating increases both splanchnic and hepatic blood flow [58]. There is a drop in systemic vascular resistance, accompanied by an increase in both heart rate and cardiac output to maintain blood pressure [59–61]. However, postprandial hypotension is seen particularly in patients with autonomic dysfunction, patients with hypertension, elderly patients, patients with cardiovascular disease, and patients with renal failure on HD [62]. The hypotension seen in this patient population is partially explained by an inadequate sympathetic response; the heart rate, cardiac output, and peripheral vasoconstriction do not increase appropriately to the drop in systemic vascular resistance and splanchnic blood pooling [59, 63]. Dialysis further limits the cardiovascular systems' ability to compensate, as it decreases blood volume and right ventricular refill due to ultrafiltration, potentially further decreasing cardiac output. Clinical Vignette 6 highlights these points, as approximately 30 min into the meal, the patient's blood volume drops, cardiac output presumably fails to increase appropriately, as demonstrated by a drop in ScvO₂, and hypotension ensues.

Cordtz et al. [64] were the first to evaluate ScvO₂ in 20 HD patients who were classified as either hypotension prone (HP) or hypotension resistant (HR). While both patient groups started at the same ScvO₂ (HP 52.2 ± 6.7% vs. HR 49.7 ± 6.9%), intradialytic ScvO₂ only decreased in the HP group. Harrison et al. [3] further expanded on the topic by examining ScvO₂ in 18 prevalent dialysis patients. In their study population, they found a strong inverse correlation between ultrafiltration rate (UFR) and ScvO₂ ($r = -0.680$). Clinical Vignette 7 illustrates these findings. This patient had a low baseline ScvO₂, and with increasing ultrafiltration, ScvO₂ dropped further; finally, saline was administered because of hypotension. Hypotension on dialysis is a common occurrence and it is linked to decreased blood volume and decreased cardiac output [65]. HD is also associated with decreased myocardial blood flow and an increased incidence of regional wall motion abnormalities (RWMA), which further decrease cardiac output [66, 67]. One study found that in-

Clinical Vignette 6. This patient had a history of eating during treatment and then often became symptomatic with hypotension which was treated with boluses of saline and periodic cessation of the ultrafiltration resulting in inability to achieve the estimated dry weight. This patient was eating before treatment and continued after the treatment was initiated. Note that there was a sharp downward slope of his blood volume to -10% and ScvO_2 to 34.4% during the first 30 min. At the beginning of the treatment the ScvO_2 was 61% . When the nurse noted the blood volume to be at a -10% decrease at 35 min into the treatment, ultrafiltration was stopped to reduce the potential for symptoms related to hypovolemia.

creasing UF during HD was associated with increased odds of developing RWMA's [68]. In clinical Clinical Vignette 7, 3 h into HD blood volume had decreased to such an extent that apparent cardio-vascular compensatory mechanisms could no longer maintain cardiac output, as reflected by a decrease in ScvO_2 . With fluid bolus administration, the blood volume increased, and cardiac output, blood pressure, and ScvO_2 improved.

We assessed ScvO_2 in 25 patients during 294 HD treatments using CLM. In our population, a majority of patients spent the dialysis treatments with mean ScvO_2 between 50 and 60% , lower than 70% , which is generally considered normal [49]. Of note, other studies in HD patients have also shown a mean $\text{ScvO}_2 < 70\%$ [3, 64]. In our patient cohort, a ScvO_2 increase in the first hour was followed by a steady decline to levels well below those at HD start (fig. 5). The etiology of these findings is unclear. However, the incidence of congestive heart failure is high in HD patients, and patients usually start HD sessions fluid overloaded. We speculate that the initial ultrafiltration may improve cardiac contractility, cardiac output and tissue perfusion. However, as more fluid is removed, a decrease in cardiac refill and cardiac output may result in poor tissue perfusion and subsequent ScvO_2 decline.

Clinical Vignette 7. This patient had a history of cardiomyopathy and symptoms on HD ranging from hypotension to 'a funny feeling' at various times during treatment. The patient had previously been identified as having a low ScvO_2 and used oxygen with each HD treatment, most often with a mask instead of a nasal cannula due to nostril irritation. This patient's fluid gains were typically 1–2 kg between dialysis sessions. On the example exhibit the patient had a stable ScvO_2 ranging from 55 to 58% with 2 liters of oxygen per minute but in the beginning of the third hour there was a sharp decrease in the ScvO_2 along with symptoms of hypotension and lightheadedness. A 100 ml bolus of normal saline improved the symptoms and the ScvO_2 for the remaining hour and a half. This patient had a history of having unexplained symptoms often in the middle of the treatment and the estimated dry weight was raised several times. Symptoms were lessened when the staff reacted to the decreasing ScvO_2 by reducing the ultrafiltration.

ScvO_2 has long been used in critical care settings as a marker of adequate tissue perfusion and appropriate resuscitation. Systematically collected data on ScvO_2 and HD are scarce; however, some data suggest the low ScvO_2 is associated with intradialytic hypotension (IDH) and high UFR. Both IDH and high UFR are associated with increased incidence of cardiac events [67–69]. ScvO_2 may be a useful monitoring tool to identify high-risk patients; however, further studies are needed to explore that notion.

Conclusions and Perspectives

Respiratory system integrity and function are susceptible to malfunction in CKD and dialysis patients. In addition to pulmonary edema, pleural effusions, and pulmonary calcifications, respiratory control pathways are frequently affected, such as in sleep apnea syndrome. Hy-

poxemia is a frequent terminal pathway of respiratory pathologies. Current technologies allow continuous measurement of SO₂ during routine HD. Clinical observations suggest that intradialytic hypoxemia is associated with intradialytic morbid events, such as hypotension and cramping. While these are important hypothesis-generating clinical observations, further investigations are necessary to define causal pathways.

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Disclosure Statement

P.K. holds stock in Fresenius Medical Care.

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