Tracking Arteriovenous Fistula Maturation: A Novel Approach

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Keywords

Arteriovenous fistula · Maturation · Central-venous oxygen saturation · Upper body blood flow · Vascular access

Abstract

Background: The time between the creation of an arteriovenous fistula (AVF) and its successful use is significantly longer in hemodialysis (HD) patients in the United States compared to those in other countries, and there is an urgent need to reduce the residence time of central-venous catheters (CVC).

Methods: Successful AVF creation and maturation results in typical hemodynamic changes, such as an increase in cardiac output and upper body blood flow (UBBF). In patients with CVC as vascular access, we measured once per minute intradialytic central-venous oxygen saturation (ScvO₂) and hemoglobin levels simultaneously using the Crit-Line Monitor. Under conditions of stable upper body oxygen consumption and arterial oxygen saturation, ScvO₂ and hemoglobin concentration allows the calculation of estimated UBBF (eUBBF). In a quality improvement project, we used ScvO₂ and eUBBF to track the hemodynamic changes accompanying AVF maturation. **Results:** Out of 11 patients (9 incident to HD, 1 female, age 61 ± 13 years), AVF maturation was successful in 9.

In 1 patient, the AVF did not mature. One patient died from sudden cardiac death with a maturing AVF. In the 9 patients with successful AVF maturation, ScvO₂ increased from 60.9 ± 2.7% prior to AVF creation to 73.4 ± 3.6% a week after AVF creation (19.6 ± 6.3% increase). eUBBF increased from 1.3 ± 0.3 to 2.2 ± 0.6 L/min (62.7 ± 37.5% increase); no material ScvO₂ or eUBBF changes occurred in the other 2 patients. **Conclusion:** Our results indicate the potential utility of ScvO₂ and eUBBF to track the hemodynamic response to AVF maturation. To what extent these insights translate into shortening of the time between AVF creation and successful cannulation warrants further investigations.

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Background

The creation of a native arteriovenous fistula (AVF) as a primary vascular access over AV grafts and central-venous catheters (CVC) in hemodialysis (HD) patients has been recommended for decades by the National Kidney Foundation – Kidney Disease Outcomes Quality Initiative and other group initiatives. An AVF is favored due to its advantage over CVC usage with respect to sur-

vival outcomes, hospitalization rates, and cost to the healthcare system [1–4]. Notwithstanding this evidence, most US incident patients start HD using a CVC [5–8]. Even though the use of AVF has notably improved in prevalent patients, the initiation of HD with an AVF continues to be low. In the United States, about 80% of patients initiate HD with a CVC as vascular access [9–11].

The time between AVF creation and first use depends on a successful AVF maturation, which varies significantly within and between countries [12, 13]. The Kidney Disease Outcomes Quality Initiative proposed opinion-based ultrasound criteria for successful AVF maturation of 600 mL/min blood flow rate, 0.6 cm diameter, and ≤ 0.6 cm depth from the skin (“rule of sixes”) [14], or empirically, as the ability to cannulate the AVF with 2 needles and obtain sufficient blood flow for adequate HD for at least 30 consecutive days [14–17]. Once an AVF has been cannulated successfully with 2 needles, the CVC can be removed. HD patients with a newly created AVF may continue to use CVCs for prolonged periods because of inappropriate maturation or failure to maintain patency. The extended use of a CVC is associated with adverse outcomes [12, 18–20].

The time to first AVF cannulation differs between countries and is longer in the United States than that in most other countries [1, 13]. Routine assessment of AVF maturation is largely subjective, based on clinical assessment performed by the nursing staff, whose experience and standards of practice may vary from clinic to clinic. A recent multicenter, observational cohort study in 602 participants identified AFV blood flow rate, diameter, and depth as moderate predictors of AVF maturation [21]. However, there are no generally agreed upon hemodynamic criteria for determining AVF maturity and cardiovascular adaptation to the AVF [22]. Additionally, there is no agreed upon process to follow fistula maturation and attempt cannulation based on prior hemodynamic information. Moreover, the approach to a timely fistula maturation and successful cannulation may be performed unreliably at some clinics [23].

Clinical studies have shown that cardiac output and upper body blood flow (UBBF) increase following AVF creation. This increased perfusion of the upper body can be expected to result in higher central-venous oxygen saturation ($ScvO_2$). Motivated by that physiological reasoning we embarked on a quality improvement program (QIP) to reduce CVC residence time by following AVF maturation using $ScvO_2$ and calculation of estimated UBBF (eUBBF).

Methods

This QIP took place at 2 Renal Research Institute clinics in New York City. The participation included incident and prevalent HD patients with a CVC as vascular access, with a newly created AVF between April 2017 and September 2018. In the short term, we considered AVF maturation as the time between AVF creation and first use, when the AVF allowed cannulation by 2 large bore needles, achieving sufficient blood flows for an adequate HD, and CVC removal was prospectively scheduled. The clinics use the Crit-Line Monitor (Fresenius Medical Care, Waltham, MA, USA) during HD as part of the standard of care. The Crit-Line Monitor is approved by the US Food and Drug Administration for measurement of hematocrits and oxygen saturation. All patients received bicarbonate dialysis and used polysulfone membranes.

The Crit-Line Monitor automatically and noninvasively measures oxygen saturation and hematocrit in the extracorporeal circuit during HD 9,000 times per minute and reports their respective average once per minute. Per manufacturer, the Crit-Line’s accuracy for oxygen saturation measurement is within 2%.

For estimation of upper body oxygen consumption we considered the brain and upper body skeletal muscle tissue, with the brain being by far the greatest consumer of oxygen at rest. Therefore, the upper body oxygen consumption was calculated as the sum of oxygen consumption of the brain and muscle. The respective brain tissue masses were calculated using anthropometric formulae [24]. Muscle mass was estimated as 2.3 kg in males and 1.2 kg in females. We then multiplied the estimated organ mass with organ-specific oxygen uptake rates, 3.5 of $O_2/100$ g brain tissue/min and 0.2 mL of $O_2/100$ g resting muscle tissue/min, respectively.

Ignoring the negligible amount of dissolved oxygen in the blood, the arterial oxygen content in mL of O_2 per liter of blood is defined as: (equation [1])

$$CaO_2 = 1.34 \times Hgb \times SaO_2$$

with 1.34 being the mL of O_2 that 1 g of Hgb can bind if fully saturated, Hgb being the hemoglobin concentration in g/L, and SaO_2 being the arterial blood oxygen saturation expressed as fraction.

Analogously, central-venous blood oxygen content in mL of O_2 per liter of blood is defined as: (equation [2])

$$CcvO_2 = 1.34 \times Hgb \times ScvO_2$$

The rate of oxygen delivery to the upper body is the product of arterial oxygen content and UBBF rate. Similarly, if a CVC resides in the superior vena cava, the rate of oxygen return from the upper body is the product of central-venous blood oxygen content and UBBF. The difference between the two equals the rate of oxygen consumption ($utilO_2$) by the tissues supplied by the UBBF. This is illustrated in the following mass balance equation: (equation [3]).

$$UBBF \times CaO_2 - utilO_2 = UBBF \times CcvO_2$$

with UBBF being the upper-body blood flow rate in L/min, $utilO_2$ being the rate of oxygen consumption in mL/min by the tissues supplied by the UBBF. Rearranging equation (3) to:

Fig. 1. Schematic representation of arterio-venous fistula (AVF) maturation tracking using central-venous oxygen saturation (ScvO₂). The green line represents adequate AVF maturation and adequate hemodynamic adaptation. Red lines depict inadequate AVF maturation and/or inadequate hemodynamic adaptation.

$$UBBF = \frac{\text{utilO}_2}{\text{CaO}_2 - \text{CcvO}_2}$$

Substituting equations (1) and (2) from above yields: (equation [4])

$$UBBF = \frac{\text{utilO}_2}{1.34 \times \text{Hgb} \times (\text{SaO}_2 - \text{ScvO}_2)}$$

To illustrate the relationship between ScvO₂ and the other parameters, the equation can be further rearranged as follows: (equation [5])

$$\text{ScvO}_2 = \text{SaO}_2 - \frac{\text{utilO}_2}{1.34 \times \text{Hgb} \times \text{UBBF}}$$

The UBBF equation above illustrates that in order to calculate UBBF, the following parameters are required: the rate of oxygen consumption by the tissues supplied by the UBBF, the Hgb concentration, SaO₂ and ScvO₂.

Arterial and central-venous Hgb concentration can be considered identical. In our study, we obtained ScvO₂ and simultaneous Hgb noninvasively using the Crit-Line Monitor. This input allows us together with reasonable assumptions regarding oxygen consumption and SaO₂ to calculate an estimated UBBF (eUBBF). To mitigate the impact of ultrafiltration on ScvO₂ and Hgb, we used data collected only between min 5 and 20 into the treatment.

Patients were followed with the Crit-Line Monitor while receiving HD through time periods before and after AVF creation. With normal AVF maturation and hemodynamic adaptation, the ScvO₂ and eUBBF are expected to increase. In contrast, AVF maturation failure and insufficient hemodynamic adaptation are expected to be blunted or absent from ScvO₂ and eUBBF increases (Fig. 1). It is important to point out that failure to increase ScvO₂ and eUBBF may indicate either failed AVF maturation or inadequate hemodynamic adaptation. Discriminating these pathologies requires additional investigations.

We report data as mean $\pm$ SD or percent. Because of the small number of patients, we refrained from formal statistical testing.

Results

We started the QIP in April 2017. There were 2 prevalent and 9 incident HD patients who underwent AVF creation. Their age was 61 ± 13 years, 10 males, 6 Whites, 4 African Americans, and 1 Asian. The HD vintage was 3.5 ± 7 years (range 0.1–17). The AVF location was brachiocephalic in 9 and radiocephalic in 2 patients.

Out of these 11 patients, AVF maturation was successful in 9. In these 9 patients, ScvO₂ increased from $60.9 \pm 2.7\%$ prior to AVF creation to $73.4 \pm 3.6\%$ a week later (increase by $19.6 \pm 6.3\%$; Fig. 2); eUBBF increased from 1.3 ± 0.3 to 2.2 ± 0.6 L/min (increase by $62.7 \pm 37.5\%$; Fig. 3). We saw no material ScvO₂ or eUBBF changes in the 2 patients who suffered from complications. One patient died from sudden cardiac death with a patent AVF in place. In the other patient the AVF failed to mature and assisted maturation procedures were required due to small and noncompliant vessels.

Discussion

The main finding of this pilot QIP is an increase of ScvO₂ and eUBBF in patients with uncomplicated AVF maturation; in contrast, these parameters remained essentially unchanged in patients who experienced complications (primary AVF maturation failure in 1 patient and presumably cardiac maladaptation after AVF placement in the other). Monitoring the dynamics of ScvO₂ and eUBBF may allow the early detection of insufficient AVF maturation and/or poor hemodynamic adaptation, whereas observing their expected increase may aid the

Fig. 2. a Time course of absolute ScvO₂ dynamics in 9 patients with normal AVF maturation (purple lines) and 2 patients with inadequate hemodynamic adaptation and failed AVF maturation respectively (red lines). **b** Time course of ScvO₂ (%) changes relative

to levels prior to AVF creation. The lines end at first successful AVF use (purple lines) or end of observation (red lines). The * denotes the deceased patient.

Fig. 3. a Time course of absolute eUBBF dynamics in 9 patients with normal AVF maturation (purple lines) and 2 patients with inadequate hemodynamic adaptation and failed AVF maturation respectively (red lines). **b** Time course of eUBBF changes relative

to levels prior to AVF creation. The lines end at first successful AVF use (purple lines) or end of observation (red lines). The * denotes the deceased patient.

decision to cannulate, which may serve to reduce CVC residence times.

There is unambiguous evidence from numerous studies that CVC use is associated with increased morbidity and mortality in maintenance HD patients. One obvious

way to reduce CVC use is to shorten the time between AVF creation and cannulation. In 2004, a DOPPS study indicated substantial differences in time to AVF cannulation between countries [25]. The fraction of patients having their AVF cannulated in the first month after creation

was 74% in Japan, 50% in Europe, and 2% in the United States. The respective numbers after 2 months were 98% (Japan), 79% (Europe), and 36% (US). In a recent study from the United States, Woodside et al. [5] used Crown-Web data to characterize time to the first use of newly created AVF as surrogate for successful AVF maturation. The authors identified 45,087 new AVFs that were placed in 39,820 prevalent HD patients in 2013. No evidence of AVF use was found in 36.2% of AVFs until December 31, 2014. Only 17.1% were cannulated by 2 months and 54.7% within 4 months. A time to first cannulation >10 months was reported in 6.6%.

Against this background, we explored the use of point-of-care measurement of ScvO₂ to provide caregivers with an actionable bio-signal that reflects the combined effects of AVF maturation and hemodynamic adaptation. The physiological reasoning underlying that approach is straight forward. A successful AVF maturation results in a drop in upper body peripheral vascular resistance and hence blood pressure, resulting in baroreceptor activation and subsequent hemodynamic adaptations, including a rise in cardiac output [26] and UBBF. While the relative distribution between UBBF and lower body blood flow in that situation has, to the best of our knowledge, not been studied systematically, it is reasonable to assume a directional agreement between UBBF and cardiac output. A higher UBBF results in an increased oxygen delivery to the upper body. Under conditions of constant tissue oxygen uptake, hemoglobin concentration and SaO₂, the ScvO₂ can be expected to increase, as shown in equation (5). For tracking UBBF from treatment to treatment, we must further assume that the oxygen consumption rate by the upper-body tissues remains constant over the period during which UBBF is assessed.

While it is difficult to assess upper body O₂ uptake in a patient on a routine clinical basis, it is important that no major changes in a stable patient at rest should be expected within a few weeks. While HD patients may have a lower brain oxygen consumption compared to healthy subjects [27], the assumption of a stable brain oxygen uptake in a given patient is reasonable, unless the mass of viable brain tissue changes substantially. The same applies to resting muscle oxygen uptake. In a clinically stable patient, changes in body composition take place on a time scale of months rather than days or weeks (the time expected for AVF maturation). In order to quantitate brain oxygen uptake, we estimated the respective brain mass using anthropometric formulae [24]. Factors that can change within minutes and thus affect ScvO₂ are SaO₂ and hemoglobin levels, the latter

particularly during ultrafiltration. The Crit-Line Monitor simultaneously measures the oxygen saturation and hemoglobin concentration, so that the dynamic hemoglobin changes can be factored into the calculation. Concurrent measurements of SaO₂ would be highly desirable because SaO₂ can change throughout HD [28, 29]. We recognize the absence of SaO₂ measurements as a limitation, and efforts to remedy this are underway. Arterial and central-venous Hgb concentration can be considered identical. In our study, we obtained ScvO₂ and Hgb noninvasively using the Crit-Line Monitor. In the absence of SaO₂ measurements, we assumed a constant value of 92.6% for every patient, which was recently described to be the average SaO₂ in a large population of HD patients [28]. It is important to appreciate that relative changes in ScvO₂ and eUBBF appear to be more informative than their absolute values, mitigating concerns that the calculation of eUBBF is based on patient-specific assumptions that may be difficult to ascertain in clinical practice.

It is interesting to observe that substantial changes in ScvO₂ and eUBBF are already present in the first week after AVF creation. These findings are in line with the rapid increase of AVF blood flow observed in ultrasound studies in patients following AVF creation [21]. In this study, the median (interquartile range) AVF flow increased in the full cohort from 604 (380–936; *n* = 539 patients) on day 1 after AVF creation to 801 (518–902; *n* = 527) mL/min in week 2. This ~30% increase in AVF blood flow within 2 weeks is less than the ~60% eUBBF increase we have observed between the period before AVF creation and the week thereafter, indicating that eUBBF may be a more pronounced signal.

The use of ScvO₂ and eUBBF monitoring to track AVF maturation and hemodynamic adaptation is also operationally attractive, since it can be automated and scaled to a large number of HD patients. Unlike ultrasound studies, this method is operator-independent and requires no additional personnel.

In summary, our findings indicate that normal AVF maturation is accompanied by an increase in ScvO₂ and eUBBF. Both ScvO₂ and Hgb are indispensable for eUBBF computation, and the advent of the Crit-Line Monitor has made routine, noninvasive and quasi-continuous measurements of these 2 parameters during HD a reality. Future detailed physiological studies including hemodynamic monitoring [30] and AVF flow measurement are required to better understand the maturation dynamics and the associated hemodynamic adaptation. Efforts should be made to characterize the expected trajectories

of ScvO₂ and eUBBF during adequate AVF maturation and cardiac adaptation. Application of the proposed method in a larger population is required to test the hypothesis that the CVC residence times can be reduced by a clinically relevant degree.

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