Dynamics of oxygen saturation, fluid and blood pressure during hemodialysis and their associations with clinical outcomes

Valorization

Valorization

Since the introduction of the Crit-Line monitor™ (CLM) in U.S. clinics of the Renal Research Institute, oxygen saturation and relative blood volume (RBV) can be easily and continuously obtained during hemodialysis (HD). Pre-HD, post-HD and peri-dialytic systolic blood pressure (SBP) are routinely collected by the dialysis staff. Incorporating all these measurements into clinical practice, our research shows that arterial and venous oxygen saturation, RBV, and peri-dialytic SBP changes are associated with hospitalization and mortality.

In this thesis, we researched a large cohort of chronic HD patients and found a high rate of intradialytic hypoxemic episodes and that 10% of the patients experienced a prolonged intradialytic hypoxemia (PIH, defined as hypoxemia > 1/3 of HD treatment time). PIH was significantly associated with higher all-cause hospitalization and mortality rates. We believe that what we have learned in this thesis will help us to identify PIH in patients with arterio-venous fistula or graft as vascular access. Building on that information, the nephrologist could then identify potential PIH causes that are amendable by adjusting the HD prescription (e.g. in cases of fluid overload), or that may require pulmonology consultation (e.g., in cases of sleep apnea). Sleep apnea is highly prevalent yet grossly underdiagnosed in HD patients. We see opportunities to develop machine learning algorithms to identify patterns in arterial oxygen saturation signals associated with sleep apnea syndrome.

We found that in chronic HD patients a low central venous oxygen saturation is associated with poor survival. In addition, we reported that patients with high ultrafiltration volume experienced a more pronounced decline of central venous oxygen saturation during HD. We hypothesize that ultrafiltration results in a reduced cardiac pre-load and cardiac output. A cardiac output reduction will result in a lower upper body blood flow and – under conditions of stable upper body oxygen consumption - a drop in central venous oxygen saturation. We propose that the central venous oxygen saturation is a surrogate marker of upper body blood flow and cardiac output. This insight allows us to utilize central venous oxygen saturation for hemodynamic monitoring during HD in patients with central venous catheter as vascular access. The real time monitoring of central venous oxygen saturation and calculation of estimated upper body blood flow could serve as an indicator of patient's hemodynamic. Coupled with alerts or e.g. ultrafiltration feedback control, these bio-signals can assist in preventing intradialytic complications such as intra-dialytic hypotension.

Another valuable clinical application of central venous oxygen saturation and the derived estimated upper body blood flow is the tracking of the hemodynamic response to the creation of an arterio-venous fistula (AVF). The trajectories of central venous

oxygen saturation and estimated upper body blood flow before and after AVF creation provide insights into the AVF maturation process and the associated hemodynamic response. These results help us to better understand if a patient has the ability to mount an appropriate increase in cardiac output in response to AVF creation and follow the AVF maturation process. This information has the potential to translate into a shorter time between AVF creation and successful cannulation and thus shorten the catheter residence time.

Intradialytic hypotension is frequently associated with a drop in blood volume due to ultrafiltration. Technologies have been developed to mitigate these effects by an automated ultrafiltration feedback control. Current technologies lack pre-defined targets that are associated with better outcomes, since there are limited researches into the relationship between attained RBV ranges during dialysis and patient outcomes. In our research we identified hourly intra-dialytic RBV ranges that are associated with significantly better patient survival. These RBV levels are 93-96% at the first hour, 89-94% at the second hour, and 86-92% at the third hour. Based on that research we have started with the development of an RBV-guided ultrafiltration feedback control system that aims to attain these “favourable” RBV ranges. The goal of such a control system is to eventually reduce morbidity and mortality.

In HD patients oxygen supply to tissues and organs is impaired due to multiple pathological alterations; the heart, gut, and brain are particularly susceptible organs. Fluid management and means to increase intradialytic hemodynamic stability (e.g. cool dialysate; feedback ultrafiltration control) are key to improve oxygen supply to tissues and organs. One potential intervention could be the administration of oxygen during dialysis. The real time monitoring of arterial or central venous oxygen saturation could provide us with data to trigger the administration of oxygen during dialysis.

Also, knowledge of real time oxygen saturation and RBV combined with patient demographic information and treatment data can be utilized to develop machine learning algorithm(s) to predict intradialytic complications such as intra-dialytic hypotension.

Lastly, several different approaches can be used for deriving "quasi pre-HD" hemoglobin levels from CLM data. These hemoglobin estimates could replace repeated blood draws and their associated blood loss, and logistic and staff costs.

A better understanding of the pathophysiology, clinical consequences and medical management requires future carefully designed clinical studies. Our results may serve as a guide for the development of prospective clinical studies. We believe that our results will motivate and encourage adequately equipped and trained clinical researchers to embark on future specialized studies.