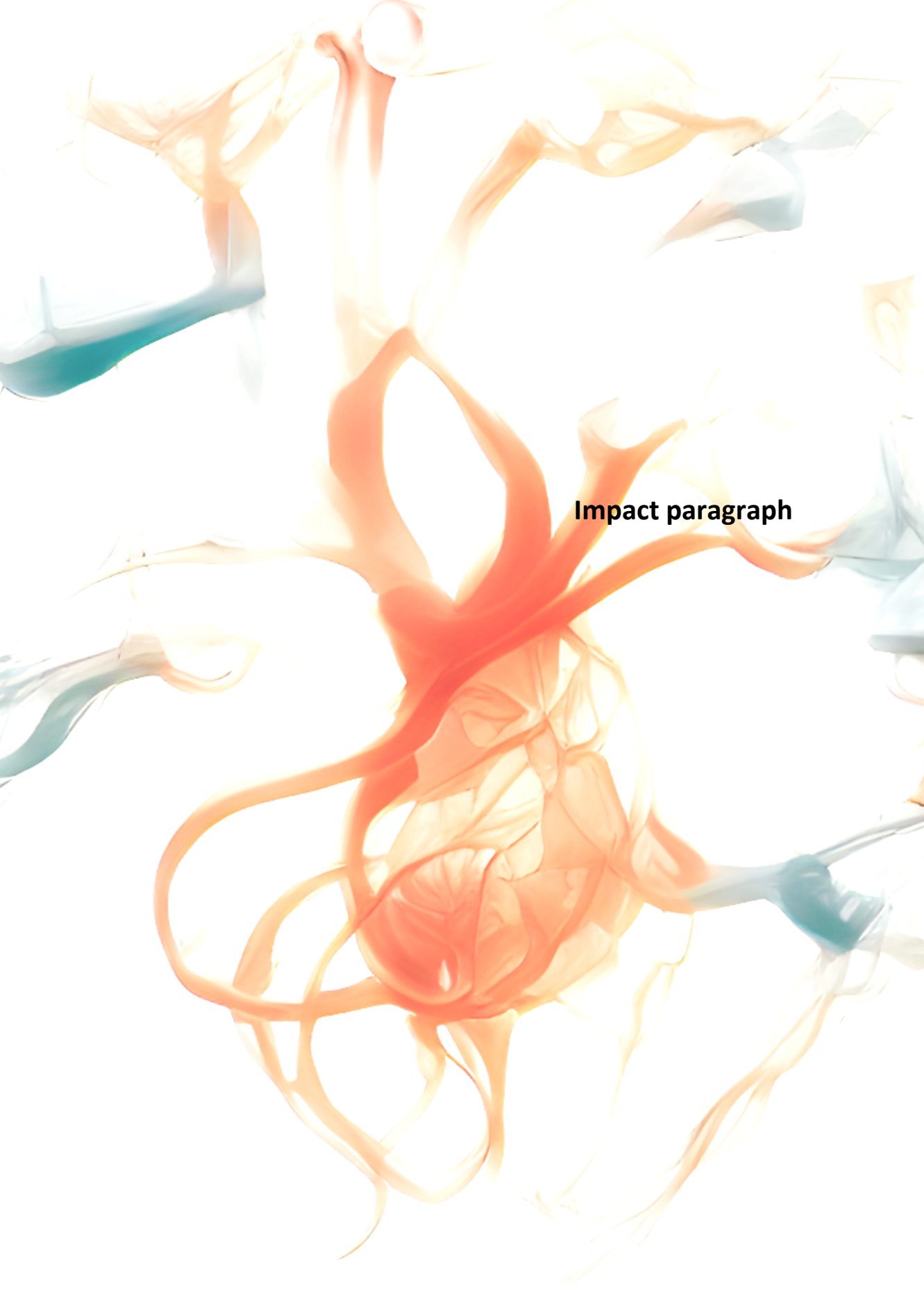
Intradialytic monitoring of blood pressure, oxygen saturation and relative blood volume



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The routine use of the Crit-Line monitor™ (CLM) during hemodialysis (HD) allows for continuing intradialytic hemodynamic monitoring of key parameters including relative blood volume (RBV) and arterial and central venous oxygen saturation (SaO_2 and $ScvO_2$, respectively based on the patient's vascular access type). Blood pressure is routinely collected by the dialysis staff during treatments and peridialytic systolic blood pressure (SBP) can be easily calculated with these measurements. The research in this thesis showed that peridialytic SBP changes, RBV and both SaO_2 and $ScvO_2$ are associated with clinical outcomes.

The association of pre-HD SBP levels and the peridialytic SBP change with all-cause mortality was studied in a large population of maintenance HD patients. It was found that a peridialytic SBP rise combined with high pre-HD SBP was associated with higher mortality. In contrast, when concurrent with low pre-HD SBP, a peridialytic SBP rise was associated with better survival. The findings from this research will help clinical staff to identify patients in which either SBP increases or decreases are associated with improved outcomes and thus may aid individualized treatment prescriptions. It would also help to identify patients that might have a higher risk of complications that will benefit from further and closest follow-up and in whom more intensive hemodynamic monitoring might result in improved patient care.

This research found that specific intradialytic hourly RBV ranges are associated with significantly lower all-cause mortality in HD patients. Notably patients who attained these favorable 3-hours RBV range in our study did not experience higher rates of intradialytic hypotension (IDH), despite higher ultrafiltration rates (UFR). Patients who didn't attain these ranges might represent a more vulnerable population that might not tolerate higher fluid removal, or it could highlight increased caution among clinicians to avoid complications. Patients with lower RBV changes may benefit from higher ultrafiltration volumes which should however be combined with closely monitoring of hemodynamic parameters during treatment. These results may serve as foundation for future clinical trials assessing the relationship between RBV profiles, fluid status and patient outcomes. These findings also served as basis for the development of a real time ultrafiltration rate feedback control that aims to attain these favorable RBV ranges that will be integrated in the CLM to be utilized routinely in HD clinics across the US.

Furthermore, this thesis showed that intradialytic mean $ScvO_2$ levels in patient with central vascular catheters (CVCs) are a major explanatory determinant of the

association of intradialytic RBV changes and clinical outcomes. Mortality risk is increased in patients with concurrent low $ScvO_2$ and small RBV changes. These results add to the pathophysiological understanding and could be used to trigger alerts by the current available technology or could be integrated in potential ultrafiltration feedback controllers, the integration of multiple bio-signals can assist in preventing intradialytic complications and to eventually reduce morbidity and mortality.

Monitoring of $ScvO_2$ in patients with CVCs who also had an arterio-venous fistula (AVF) created also tracks the hemodynamic response and provide a window into the maturation process of the AVF, as it is expected that cardiac output to increase when AVFs are maturing successfully. This approach could result in the identification of failed AVFs and faster referrals to vascular surgeons. Furthermore, it would result in early identification of mature AVFs that are ready for cannulation decreasing the time to first successful cannulation. Indeed, a recent quality improvement project showed that the use of $ScvO_2$ measurements for this application enabled the faster removal of CVC after access creation, possibly enabling a reduction of CVC related complications such as infections.

Patients on HD are a vulnerable population that is at higher risk of morbidity and mortality as observed during the COVID-19 pandemic. Previous studies showed that intradialytic monitoring of SaO_2 levels could aid in the identification of patients with prolonged intradialytic hypoxemia that its associated with increased mortality and which may provide a rationale for interventions, such as oxygen supplementation protocols during HD. As shown by the research in this thesis, intradialytic monitoring of SaO_2 could also support early detection of patients with COVID-19 or other respiratory illnesses that are at risk for complications. In the case of respiratory infections, it might also support early diagnosis ensuring proper distancing protocols to avoid infection spreading within the clinics.