

Prevention of Intradialytic Hypotension in Hemodialysis Patients: Current Challenges and Future Prospects

Seyed Mehrdad Hamrahan¹, Salem Vilayet², Johann Herberth^{2,3}, Tibor Fülöp^{2,3} 

¹Department of Medicine - Nephrology, Thomas Jefferson University, Philadelphia, PA, USA; ²Department of Medicine - Division of Nephrology, Medical University of South Carolina, Charleston, SC, USA; ³Medicine Services, Ralph H. Johnson VA Medical Center, Charleston, SC, USA

Correspondence: Tibor Fülöp, Department of Medicine - Division of Nephrology, Medical University of South Carolina, 96 Jonathan Lucas Street, Charleston, SC, 29525, USA, Tel +1 843 792-4123, Fax +1 843 792-2995, Email tiborfulop.nephro@gmail.com; fulopt@musc.edu

Abstract: Intradialytic hypotension, defined as rapid decrease in systolic blood pressure of greater than or equal to 20 mmHg or in mean arterial pressure of greater than or equal to 10 mmHg that results in end-organ ischemia and requires countermeasures such as ultrafiltration reduction or saline infusion to increase blood pressure to improve patient's symptoms, is a known complication of hemodialysis and is associated with several potential adverse outcomes. Its pathogenesis is complex and involves both patient-related factors such as age and comorbidities, as well as factors related to the dialysis prescription itself. Key factors include the need for volume removal during hemodialysis and a suboptimal vascular response which compromises the ability to compensate for acute intravascular volume loss. Inadequate vascular refill, incorrect assessment or unaccounted changes of target weight, acute illnesses and medication interference are further potential contributors. Intradialytic hypotension can lead to compromised tissue perfusion and end-organ damage, both acutely and over time, resulting in repetitive injuries. To address these problems, a careful assessment of subjective symptoms, minimizing interdialytic weight gains, individualizing dialysis prescription and adjusting the dialysis procedure based on patients' risk factors can mitigate negative outcomes.

Keywords: end-stage renal disease, dialysis, hemodialysis, hypotension, ultrafiltration

Introduction

Chronic kidney disease (CKD) is a significant global public health concern that often leads to end-stage renal disease (ESRD), requiring dialysis treatment or kidney transplantation.¹ Although the incidence of ESRD is reported to have plateaued in high-income countries, patient time spent receiving dialysis treatment is increasing due to longer patient survival on dialysis combined with limited availability of organ donors for the preferred modality of kidney transplantation.²⁻⁴ CKD and ESRD are often accompanied by hypertension, which increases in prevalence as glomerular filtration rate (GFR) declines.⁵ With the exception of specific comorbidities such as end-stage heart failure or advanced liver disease, practically all patients on hemodialysis (HD) have elevated blood pressure. This phenomenon is particularly prevalent prior to initiation of a dialysis session.^{6,7} While blood pressure monitoring during dialysis treatment is occurring primarily for safety reasons, the value of these measurements is limited for describing the burden of hypertension in-between treatments. Intradialytic hypotension (IDH) is a frequently observed complication of intermittent hemodialysis because relatively short treatment times necessitate rapid volume removal of excess fluid gains. IDH bears a broad overlap with intravascular hypovolemia that is also characterized by hypotension during treatment. Preventive measures can potentially reduce patient stress during HD treatment sessions, thus minimizing the potential risk of vascular access failure and associated cardiovascular mortality,⁸ even subtle asymptomatic blood pressure drops during HD treatment are potentially associated with significant end organ ischemia.⁹ The goal of this review is to provide a concise overview of IDH emphasizing its relevance to practicing clinicians.

Definition of Intra-Hemodialysis Hypotension

The incidence of IDH has been reported to vary between 5% and 40% in different ESRD patient populations.^{10,11} This wide range is in part due to the lack of data collection secondary to the absence of randomized controlled trials and lack of consensus on the definition of IDH among relevant organizations.^{12–15} In general, IDH is characterized by a rapid decrease in systolic blood pressure of greater than or equal to 20 mmHg and/or in mean arterial pressure (MAP) of greater than or equal to 10 mm Hg that results in end-organ ischemia and requires countermeasures such as ultrafiltration reduction or saline infusion to increase BP, to improve patient's symptoms. However, it should be noted that the correlation between blood pressure changes and clinical symptoms is poor, and some patients may exhibit signs of intravascular hypovolemia without a qualifying drop in blood pressure. Occasionally, a paradoxical rise in blood pressure may even be observed when physiologic compensatory mechanisms are vigorous.

Pathophysiology of Intra Hemodialysis Hypotension

Blood pressure monitoring during dialysis is performed primarily for safety reasons to alert care personnel for impending hemodynamic destabilization. The pathogenesis of IDH involves an interaction between ultrafiltration rate (UFR), cardiac output (CO), vascular resistance and the ability to refill volume from the extravascular space. Risk is increased by non-modifiable patient-related factors such as age and comorbidities like diabetes mellitus or cardiac diseases. Dialysis prescription-related risk factors include high UFR and dialysate temperature. In general, patients on intermittent HD are more sensitive to large shifts of volume during the relative short HD treatment time. The decline in relative blood volume induced by high UFR and limited plasma volume refill from the interstitial compartment plays a significant role in the pathogenesis of IDH.¹⁶ Volume removal during dialysis triggers cardiopulmonary receptors in the atria and baroreceptors in the aortic arch and carotid sinuses. Volume depletion results in activation of sympathetic nervous system (SNS) and stimulation of the renin-angiotensin-aldosterone system.¹⁷ Activation of SNS increases cardiac venous return by reducing venous capacitance in the splanchnic and cutaneous circulations in support of the central circulation.¹⁸ Simultaneously, there is an increase in heart rate, cardiac contractility and peripheral vascular resistance. The presence of diastolic dysfunction, a common finding in ESRD patient populations, increases the risk of IDH if cardiac venous return is compromised.¹⁹ Elevated levels of pro-inflammatory cytokines (TNF- α and IL-1 β) were reported in IDH and correlated with excessive BP drop during dialysis in vulnerable patients.²⁰ Reduced myocardial perfusion at the end of dialysis as a result of volume removal can lead to left ventricular dysfunction increasing the future risk of IDH,²¹ while high UFR-induced IDH itself is described as a predictor for cardiac remodeling.²²

Risk Factors of Intra Hemodialysis Hypotension

High Inter-Dialytic Weight Gain (IDWG)

Excessive fluid gains between HD sessions will lead to volume overload and increase the risk of mortality in ESRD.²³ Although IDWG is associated with a relatively modest increase in plasma volume, most of the combined salt and water fluid gain is sequestered in the extravascular and extracellular spaces. Additional intake of free water will also increase the intracellular fluid compartment volume because it affects the entire water compartment. During dialysis, net fluid removal reduces the central filling pressure and leads to a decrease in CO.²⁴ High IDWG requires higher UFR, which can overwhelm the physiologic compensatory mechanisms and increase the risk of IDH.²⁵ Furthermore, rapid UFR of >13 mL/kg/h is described to increase cardiovascular morbidity and mortality.²⁶ Even lower UFR can induce IDH in diabetics due to slow plasma refill and decreased vasoconstriction secondary to autonomic dysfunction.²⁷ In general, starting UF at a higher rate and then slowly decreasing it over the course of the dialysis session is associated with the lower risk of IDH.²⁸

Serum Osmolality

Another potential factor contributing to IDH associated with short HD treatment is the rapid clearance of urea. This can result in decreased plasma osmolality and the formation of transient osmotic gradients causing water to shift from the intravascular space to the intracellular and interstitial spaces.²⁹ The risk is higher in patients with higher pre-dialysis

calculated plasma osmolality undergoing shorter treatment.³⁰ Furthermore, it is possible that trends in the last few decades such as using larger surface filters and larger blood- and counter-current flow rates may have further exacerbated this phenomenon. In this context, sodium also plays an important role as the major component of plasma tonicity. Utilization of higher dialysate sodium without sodium profiling could potentially prevent rapid reduction in plasma osmolality and reduce the osmotic fluid shifts.³¹ Additionally, isolated UF that removes isotonic fluids without diffusive clearance maintains BP stability compared to usual HD.³² This strategy can be combined with regular HD in the special patient population presenting with high IDWG without a significantly abnormal pre-treatment elevated blood urea nitrogen level.

Electrolyte Abnormalities

Relatively large bicarbonate influx and overcorrection of metabolic acidosis may contribute to intradialytic blood pressure drop.^{33,34} This phenomenon may broadly overlap with acute, intradialytic drop of ionized calcium and clinical complaints of leg cramps during dialysis.^{34–36} Preventive measures may include mitigating predialysis acidosis with exogenous bicarbonate supplementation,^{37,38} but an effect on IDH has not been studied.

Decreased Cardiac Output

CKD is an independent non-modifiable risk factor for cardiovascular disease (CVD).³⁹ In ESRD patients, CVD-related morbidity and mortality are high even among younger individuals.⁴⁰ Multiple manifestations of cardiac diseases including low ejection fraction, diastolic dysfunction, valvular diseases, and arrhythmias are highly prevalent among ESRD patients. Heart failure and loss of contractility predispose the patient to IDH due to decreased cardiac output.⁴¹ Frequent episodes of IDH can also cause myocardial stunning resulting in progressive heart failure and increased risk of cardiovascular mortality.⁴²

Autonomic Dysfunction

The autonomic nervous system is a major component of the endogenous defense mechanism to prevent hypotension. Autonomic dysfunction is prevalent in diabetes mellitus, paraproteinemias and other comorbidities associated with CKD and ESRD and blunts the sympathetic activation in response to intravascular volume reduction during HD. This results in impaired compensatory arteriolar vasoconstriction and increased risk of IDH.^{43,44} Additionally, vascular calcification due to abnormal mineral metabolism is a common finding in patients on chronic dialysis.⁴⁵ The resultant arterial stiffness and associated endothelial dysfunction lead to insufficient vascular response to volume changes, increasing the risk of IDH.⁴⁶ Patients with vascular calcification and IDH are at higher risk for cardiovascular events.⁴⁷

Splanchnic Blood Flow Shifts

Food ingestion during hemodialysis treatment transiently decreases blood volume in the large vessels and can cause splanchnic sequestration and vaso-relaxation, predisposing the patient to IDH.^{48,49} This effect is less pronounced with high-protein meals, but more frequent in the presence of pre-existing autonomic dysfunction.^{50,51}

Dialysate Temperature

Increased temperature of the external environment and/or the core temperature to 37°C or above during intermittent HD results in a reduction of peripheral vascular resistance. This can cause redistribution of blood volume to the vasodilated skin vessels and increases the risk of IDH.⁵² Cooled dialysate below the patient's core temperature was shown to increase intradialytic MAP and to reduce the risk of IDH.⁵³

Body Mass Index

Patients undergoing hemodialysis are susceptible to sarcopenia, which is associated with an elevated ratio of extracellular to intracellular water. While reporting is inconsistent, an association between body mass index (BMI) and IDH was postulated in patients with lower lean tissue index because skeletal muscle serves as a water reservoir with approximately 20% of this being dynamically mobile.^{54,55} Other schools of thought propose the lean tissue index to fat tissue index ratio

as a better indicator of IDH than BMI alone because obesity and sarcopenia are known to have a synergistic and negative impact on performance status.⁵⁶

Antihypertensive Medication and IDH

The majority of ESRD patients on dialysis require the use of antihypertensive medications.⁵⁷ BP control is frequently complicated by IDH, especially when non-water-soluble drugs that are not cleared by HD are taken pre-HD. Nighttime dosing of these medications is being suggested to minimize the risk.⁵⁸ At the same time, use of antihypertensive drugs with negative chronotropic effects and alpha blockers are described to exacerbate IDH by impairing the compensatory responses.^{59,60} These effects are more significant in the setting of acidosis due to suppressed cardiac contractility.⁶¹

Modality of Chronic Dialysis

Hemodiafiltration with large volume post-filter infusion of ultrapure fluid is predominantly practiced in Europe and the Far East and may have a potential to reduce IDH, though remains debated.^{62,63} Part of the debate is centered around the possible cooling effect of post-filter infused fluid conferring the increased hemodynamic stability.⁶⁴ However, the evidence is questionable⁶⁵ and the technology is not uniformly available for all large dialysis provider chains, including not practiced in the United States. Moreover, on-line hemodiafiltration needs a somewhat different skill set for optimal patients management, which may not be intuitively immediately obvious.⁶⁶

Accurate Measurement of Volume Status

Accurately assessing a patient's volume status is a crucial aspect of managing fluid balance in patients undergoing hemodialysis.⁶⁷ However, there is a lack of reliable and easily available methods for assessing ideal volume status, which presents a significant challenge for clinicians and researchers alike. Additionally, there can be a large disconnect between total body salt-water status and central filling pressures, further complicating clinical judgement. Several methods for assessing volume status have been developed, but each has its implicit limitations that need to be considered before clinical use. Bioimpedance spectroscopy is one such method that provides an accurate measurement of specific volume spaces, including extra and intracellular spaces.^{68–70} However, this method can falsely suggest potentially removable fluid in error due to edemas mediated by low albumin states. Ultrasonographic assessment of lung B-lines is also helpful, but various technology platforms differ in accuracy and interpretation.^{71,72} Blood volume monitoring has recently been incorporated into dialysis platforms, which affords the potential to predict capillary refill failure and potentially decrease dialysis-related morbid events in general.⁷³ One of the most promising methods for assessing volume status is the bedside assessment of central venous filling, including the inferior vena cava (IVC) and neck central veins.⁷⁴ Despite technological simplifications and increasing availability of ultrasound, none of these sonographic approaches are currently routinely used in outpatient dialysis practices. Excessive fluctuation of BP during dialysis may contribute to access thrombosis, further highlighting the importance of accurately assessing volume status to minimize complications.⁷⁵ Therefore, there is a need for further research to identify reliable and easily accessible methods for assessing ideal volume status in hemodialysis patients to improve clinical outcomes.

Consequence

Blood pressure fall during HD can be a stressful experience for patients and can significantly affect their quality of life and cognitive function.^{76,77} This experience can result in an earlier termination of treatment, leading to inadequate volume and toxin removal.⁷⁸ Moreover, the frequency of IDH is associated with a longer dialysis recovery time.⁷⁹ IDH can cause end-organ ischemia, including myocardial stunning, and is associated with increased mortality.^{10,21} Impaired tissue perfusion is more significant in the absence of vital organs auto-regulatory vasodilation, as seen in diabetic patients.⁸⁰ This is particularly relevant with higher UFR at thresholds of 10 or 13 mL/kg/h.⁸¹ Furthermore, frequent IDH accelerates the loss of residual kidney function and increases mortality risk, as residual kidney function plays a significant role in fluid balance and toxin clearance, including bone mineral metabolites.⁸² Additionally, IDH is also associated with vascular access thrombosis, a critical point of vulnerability for patients on HD, with considerable

morbidity and additional costs associated with invasive procedures.⁸³ Therefore, managing and preventing IDH is crucial in improving the outcomes of patients on HD.

Prevention of IDH

Although the intermittent nature of HD treatments makes it less likely that IDH can be completely prevented, several strategies were described to decrease the frequency and severity of IDH, with the goal of reducing patient's stress and cardiovascular morbidity and mortality. Understanding the pathophysiology of IDH and using a modified and individualized dialysis prescription with or without pharmacological intervention are key components of this approach. Some of these strategies include:

1. Conducting a full assessment of cardiovascular status of at-risk patients, with or without significant cardiac history, to identify those who are most susceptible to IDH.⁸⁴
2. Frequently and precisely assessing the patient's estimated dry weight (EDW) to avoid excessive fluid removal during HD.⁸⁵
3. Restricting sodium in the diet to minimize interdialytic weight gain (IDWG) and the need for higher ultrafiltration rates (UFR).^{86,87}
4. Avoidance of food intake during treatment to lower the frequency of IDH without compromising overall nutritional status.⁸⁸
5. Adjusting sodium in the dialysate based on the patient's status to prevent significant IDWG as well as high UFR-associated IDH.⁸⁹
6. Avoidance of high UFR of >10 mL/kg/hr in general.⁹⁰
7. Conducting longer treatment sessions and slower reduction in plasma osmolality to mitigate hemodynamic instability.²⁹
8. Avoiding low calcium in dialysate to prevent decreased left ventricular contractility.⁹¹
9. Reducing dialysate temperature, if tolerated, may prevent thermally induced reflex vasodilation.⁹²
10. Using antihypertensive agents cautiously prior to dialysis based on pharmacodynamics.⁹³
11. Using alpha-1 receptor agonist, midodrine, cautiously if there is no cardiovascular contraindication.⁹⁴

Acute Treatment of IDH

Primary goal should be to address the patient's symptoms and discomfort while avoiding termination of treatment. This is crucial to ensure adequate clearance and prevent patients from leaving the dialysis unit volume overloaded or above their EDW. Several strategies can be employed to achieve this goal, including the following:

1. Stopping ultrafiltration: This can alleviate the decrease in intravascular volume and prevent further drop in BP during HD.
2. Placing the patient in Trendelenburg position: This can increase venous return and cardiac output, ultimately increasing BP.
3. Administering isotonic saline, if needed: This can help restore intravascular volume and prevent further hypotension.
4. Reassessing the prescription and UFR without terminating treatment: This can involve modifying the dialysis prescription to reduce the risk of IDH, such as reducing the target UFR or increasing the dialysate sodium concentration. It is important to note that any changes to the prescription should be done cautiously to prevent excessive ultrafiltration or electrolyte imbalances.

Research

The paucity of high-quality clinical trials limits strong recommendations for the prevention of IDH. The use of L-carnitine, a nutritional supplement that converts fatty acids to energy or online hemodiafiltration, as a convective blood purification technique to prevent IDH remain controversial strategies.^{65,95,96} However, large trials that are

increasingly unlikely to be funded in the era of shrinking resources limit the strong recommendation in prevention of IDH. More recently, machine-based learning methods now offer a fresh and potentially unbiased approach to tackling decades-old clinical problems. One large study reported that several variables, including pre-dialysis systolic BP, mean systolic BP during the previous HD session, UF target rate and IDH experience during the previous session were potentially predicting IDH.⁹⁷ Additionally, a Korean study demonstrated the efficacy of computer-derived deep learning in predicting IDH using data derived solely from the HD machine.⁹⁸ Further, a very recent paper described utilization of digitized EKG recording obtained within 48 h prior to dialysis session, to predict IDH.⁹⁹ Incorporating AI learning methods into dialysis supervision platforms could offer an advantage for the ongoing tasks of adjustment to and re-accommodation of local patterns and biases that impact care delivery. Thus, by leveraging machine-based learning methods, we can gain new insights into these clinical problems, leading to better prediction and prevention of complications during HD.

Conclusion

Despite numerous advances in dialysis management, IDH remains a pervasive problem. Due primarily to lack of a generally accepted definition, its true prevalence remains unclear. The clinical symptomatology of IDH broadly overlaps with effective intravascular volume depletion. It is associated with significant patient distress, recurrent episodes of transitory organ ischemia and an increased risk of immediate and future cardiovascular morbidity and mortality. A key pathological factor is the rapid fall in effective circulating volume with inadequate compensatory cardiovascular and neurohumoral response. Limiting weight gain between dialysis sessions, extending dialysis treatment time, reducing UFR and further individualizing HD prescription tailored to the patient's volume status could reduce both the frequency and severity of IDH. Implementing such interventions requires a multidisciplinary approach, including regular monitoring and timely adjustment of the HD prescription to optimize the patient's hemodynamic stability and a meaningful presence of nephrologists in the dialysis unit. The use of innovative technologies, such as machine-based learning, might aid in the detection and prediction of IDH, allowing for earlier interventions and improved patient outcomes.

Disclosure

Drs. Herberth and Fülöp are current employees of the United States Veterans Health Administration. However, the opinions and views expressed in this paper are the Authors' own and do not represent the official views or policies of the United States Veteran Health Administrations. Dr. Salem Vilayet is a current Fellow at the Department of Medicine - Division of Nephrology, Medical University of South Carolina (Class of 2024). The authors alone are responsible for the content and writing of the paper. The authors report no other conflicts of interest in this work.

References

1. Kalantar-Zadeh K, Jafar TH, Nitsch D, Neuen BL, Perkovic V. Chronic kidney disease. *Lancet*. 2021;398(10302):786–802. doi:10.1016/S0140-6736(21)00519-5
2. Thurlow JS, Joshi M, Yan G, et al. Global epidemiology of end-stage kidney disease and disparities in kidney replacement therapy. *Am J Nephrol*. 2021;52(2):98–107. doi:10.1159/000514550
3. Saran R, Robinson B, Abbott KC, et al. US renal data system 2016 annual data report: epidemiology of kidney disease in the United States. *Am J Kidney Dis*. 2017;69(3 Suppl 1):A7–A8. doi:10.1053/j.ajkd.2016.12.004
4. Hamrahian SM, Falkner B. Hypertension in chronic kidney disease. Hypertension: from basic research to clinical practice. *Adv Exp Med Biol*. 2017;956:307–325. doi:10.1007/5584_2016_84
5. Muntner P, Anderson A, Charleston J, et al. Hypertension awareness, treatment, and control in adults with CKD: results from the Chronic Renal Insufficiency Cohort (CRIC) Study. *Am J Kidney Dis*. 2010;55(3):441–451. doi:10.1053/j.ajkd.2009.09.014
6. Liang Y, Gan L, Shen Y, et al. Clinical characteristics and management of hemodialysis patients with pre-dialysis hypertension: a multicenter observational study. *Ren Fail*. 2022;44(1):1811–1818. doi:10.1080/0886022X.2022.2136527
7. Fulop T, Schmidt DW, Cosmin A, et al. Ambulatory blood pressure monitoring and peri-hemodialysis blood pressures in a southeast US hemodialysis unit. *Clin Nephrol*. 2012;77(5):383–391. doi:10.5414/CN107138
8. Flythe JE, Xue H, Lynch KE, Curhan GC, Brunelli SM. Association of mortality risk with various definitions of intradialytic hypotension. *J Am Soc Nephrol*. 2015;26(3):724–734. doi:10.1681/ASN.2014020222
9. Bradshaw W, Bennett PN. Asymptomatic intradialytic hypotension: the need for pre-emptive intervention. *Nephrol Nurs J*. 2015;42(5):479–85; quiz 86.
10. Chou JA, Kalantar-Zadeh K, Mathew AT. A brief review of intradialytic hypotension with a focus on survival. *Semin Dial*. 2017;30(6):473–480. doi:10.1111/sdi.12627

11. Kuipers J, Verboom LM, Ipema KJR, et al. The prevalence of intradialytic hypotension in patients on conventional hemodialysis: a systematic review with meta-analysis. *Am J Nephrol*. 2019;49(6):497–506. doi:10.1159/000500877
12. Workgroup KD. K/DOQI clinical practice guidelines for cardiovascular disease in dialysis patients. *Am J Kidney Dis*. 2005;45:S1–S153.
13. Ashby D, Borman N, Burton J, et al. Renal Association clinical practice guideline on haemodialysis. *BMC Nephrol*. 2019;20(1):379. doi:10.1186/s12882-019-1527-3
14. Kooman J, Basci A, Pizzarelli F, et al. EBP guideline on haemodynamic instability. *Nephrol Dial Transplant*. 2007;2(suppl_2):ii22–ii44.
15. Hirakata H, Nitta K, Inaba M, et al. Japanese society for dialysis therapy guidelines for management of cardiovascular diseases in patients on chronic hemodialysis. *Ther Apher Dial*. 2012;16(5):387–435. doi:10.1111/j.1744-9987.2012.01088.x
16. Fuertinger DH, Kappel F, Meyring-Wösten A, Thijssen S, Kotanko P. A physiologically based model of vascular refilling during ultrafiltration in hemodialysis. *J Theor Biol*. 2016;390:146–155. doi:10.1016/j.jtbi.2015.11.012
17. Rubinger D, Backenroth R, Sapoznikov D. Sympathetic nervous system function and dysfunction in chronic hemodialysis patients. *Semin Dial*. 2013;26(3):333–343. doi:10.1111/sdi.12093
18. Daugirdas JT. Intradialytic hypotension and splanchnic shifting: integrating an overlooked mechanism with the detection of ischemia-related signals during hemodialysis. *Semin Dial*. 2019;32(3):243–247. doi:10.1111/sdi.12781
19. Escoli R, Carvalho MJ, Cabrita A, Rodrigues A. Diastolic dysfunction, an underestimated new challenge in dialysis. *Ther Apher Dial*. 2019;23(2):108–117. doi:10.1111/1744-9987.12756
20. Yu J, Chen X, Li Y, et al. Pro-inflammatory cytokines as potential predictors for intradialytic hypotension. *Ren Fail*. 2021;43(1):198–205. doi:10.1080/0886022X.2021.1871921
21. Burton JO, Jefferies HJ, Selby NM, McIntyre CW. Hemodialysis-induced cardiac injury: determinants and associated outcomes. *Clin J Am Soc Nephrol*. 2009;4(5):914–920. doi:10.2215/CJN.03900808
22. Yu J, Chen X, Li Y, et al. High ultrafiltration rate induced intradialytic hypotension is a predictor for cardiac remodeling: a 5-year cohort study. *Ren Fail*. 2021;43(1):40–48. doi:10.1080/0886022X.2020.1853570
23. Zoccali C, Moissl U, Chazot C, et al. Chronic fluid overload and mortality in ESRD. *J Am Soc Nephrol*. 2017;28(8):2491–2497. doi:10.1681/ASN.2016121341
24. Levin NW, de Abreu M, Borges LE, et al. Hemodynamic response to fluid removal during hemodialysis: categorization of causes of intradialytic hypotension. *Nephrol Dial Transplant*. 2018;33(9):1643–1649. doi:10.1093/ndt/gfy048
25. Singh AT, Mc Causland FR. Osmolality and blood pressure stability during hemodialysis. *Semin Dial*. 2017;30(6):509–517. doi:10.1111/sdi.12629
26. Flythe JE, Kimmel SE, Brunelli SM. Rapid fluid removal during dialysis is associated with cardiovascular morbidity and mortality. *Kidney Int*. 2011;79(2):250–257. doi:10.1038/ki.2010.383
27. Calvo C, Maule S, Mecca F, Quadri R, Martina G, Cavallo Perin P. The influence of autonomic neuropathy on hypotension during hemodialysis. *Clin Auton Res*. 2002;12(2):84–87. doi:10.1007/s102860200025
28. Donauer J, Kölblin D, Bek M, Krause A, Böhler J. Ultrafiltration profiling and measurement of relative blood volume as strategies to reduce hemodialysis-related side effects. *Am J Kidney Dis*. 2000;36(1):115–123. doi:10.1053/ajkd.2000.8280
29. Mc Causland FR, Brunelli SM, Waikar SS. Dialysis dose and intradialytic hypotension: results from the HEMO study. *Am J Nephrol*. 2013;38(5):388–396. doi:10.1159/000355958
30. Mc Causland FR, Waikar SS. Association of predialysis calculated plasma osmolality with intradialytic blood pressure decline. *Am J Kidney Dis*. 2015;66(3):499–506. doi:10.1053/j.ajkd.2015.03.028
31. Tangvoraphonkchai K, Davenport A. Why does the choice of dialysate sodium concentration remain controversial? *Hemodial Int*. 2018;22(4):435–444. doi:10.1111/hdi.12645
32. Murugan R, Bellomo R, Palevsky PM, Kellum JA. Ultrafiltration in critically ill patients treated with kidney replacement therapy. *Nat Rev Nephrol*. 2021;17(4):262–276. doi:10.1038/s41581-020-00358-3
33. Gabutti L, Ferrari N, Giudici G, Mombelli G, Marone C. Unexpected haemodynamic instability associated with standard bicarbonate haemodialysis. *Nephrol Dial Transplant*. 2003;18(11):2369–2376. doi:10.1093/ndt/gfg383
34. Gabutti L, Bianchi G, Soldini D, Marone C, Burnier M. Haemodynamic consequences of changing bicarbonate and calcium concentrations in haemodialysis fluids. *Nephrol Dial Transplant*. 2009;24(3):973–981. doi:10.1093/ndt/gfn541
35. Takahashi A. The pathophysiology of leg cramping during dialysis and the use of carnitine in its treatment. *Physiol Rep*. 2021;9(21):e15114. doi:10.14814/phy2.15114
36. Soliman KM, Salim SA, Fülöp T. Hypocalcemia and cramping in dialysis patients. *J Parathyroid Dis*. 2019;7:16–18.
37. Wieliczko M, Malyszko J. Acid-base balance in hemodialysis patients in everyday practice. *Ren Fail*. 2022;44(1):1090–1097. doi:10.1080/0886022X.2022.2094805
38. Kourtellidou SI, Ashby DR, Johansson LR. Oral sodium bicarbonate in people on haemodialysis: a randomised controlled trial. *BMC Nephrol*. 2021;22(1):346. doi:10.1186/s12882-021-02549-x
39. Hamrahian SM. Hypertension and cardiovascular disease in patients with chronic kidney disease. In: *Approaches to Chronic Kidney Disease: A Guide for Primary Care Providers and Non-Nephrologists*. Springer; 2022:281–295.
40. Modi ZJ, Lu Y, Ji N, et al. Risk of cardiovascular disease and mortality in young adults with end-stage renal disease: an analysis of the US renal data system. *JAMA Cardiol*. 2019;4(4):353–362. doi:10.1001/jamacardio.2019.0375
41. Owen PJ, Priestman WS, Sigrist MK, et al. Myocardial contractile function and intradialytic hypotension. *Hemodial Int*. 2009;13(3):293–300. doi:10.1111/j.1542-4758.2009.00365.x
42. Dorairajan S, Chockalingam A, Misra M. Myocardial stunning in hemodialysis: what is the overall message? *Hemodial Int*. 2010;14(4):447–450. doi:10.1111/j.1542-4758.2010.00495.x
43. Nette RW, van den Dorpel MA, Krepel HP, et al. Hypotension during hemodialysis results from an impairment of arteriolar tone and left ventricular function. *Clin Nephrol*. 2005;63(4):276–283. doi:10.5414/CNP63276
44. Shafi T, Mullangi S, Jaar BG, Silber H. Autonomic dysfunction as a mechanism of intradialytic blood pressure instability. *Semin Dial*. 2017;30(6):537–544. doi:10.1111/sdi.12635
45. Adragao T, Herberth J, Monier-Faugere MC, et al. Low bone volume—a risk factor for coronary calcifications in hemodialysis patients. *Clin J Am Soc Nephrol*. 2009;4(2):450–455. doi:10.2215/CJN.01870408

46. Dubin R, Owens C, Gasper W, Ganz P, Johansen K. Associations of endothelial dysfunction and arterial stiffness with intradialytic hypotension and hypertension. *Hemodial Int*. 2011;15(3):350–358. doi:10.1111/j.1542-4758.2011.00560.x
47. Kim SY, Hong YA, Yoon HE, et al. Vascular calcification and intradialytic hypotension in hemodialysis patients: clinical relevance and impact on morbidity and mortality. *Int J Cardiol*. 2016;217:156–160. doi:10.1016/j.ijcard.2016.04.183
48. Shibagaki Y, Takaichi K. Significant reduction of the large-vessel blood volume by food intake during hemodialysis. *Clin Nephrol*. 1998;49(1):49–54.
49. Avci M, Arikian F. The effect of food intake during hemodialysis on blood pressure: a nonrandomized experimental trial. *Ther Apher Dial*. 2023;27(4):661–668. doi:10.1111/1744-9987.13967
50. Zoccali C, Mallamaci F, Ciccarelli M, Maggiore Q. Postprandial alterations in arterial pressure control during hemodialysis in uremic patients. *Clin Nephrol*. 1989;31(6):323–326.
51. Choi MS, Kistler B, Wiese GN, et al. Pilot Study of the effects of high-protein meals during hemodialysis on intradialytic hypotension in patients undergoing maintenance hemodialysis. *J Ren Nutr*. 2019;29(2):102–111. doi:10.1053/j.jrn.2018.06.002
52. Pizzarelli F. From cold dialysis to isothermic dialysis: a twenty-five year voyage. *Nephrol Dial Transplant*. 2007;22(4):1007–1012. doi:10.1093/ndt/gfl822
53. Mustafa RA, Bdaif F, Akl EA, et al. Effect of lowering the dialysate temperature in chronic hemodialysis: a systematic review and meta-analysis. *Clin J Am Soc Nephrol*. 2016;11(3):442–457. doi:10.2215/CJN.04580415
54. Lim Y, Yang G, Cho S, Kim SR, Lee Y-J. Association between ultrafiltration rate and clinical outcome is modified by muscle mass in hemodialysis patients. *Nephron*. 2020;144(9):447–452. doi:10.1159/000509350
55. Son HE, Ryu JY, Lee K, et al. The importance of muscle mass in predicting intradialytic hypotension in patients undergoing maintenance hemodialysis. *Kidney Res Clin Pract*. 2022;41(5):611–622. doi:10.23876/j.krcp.21.153
56. Tian M, Zha Y, Qie S, Lin X, Yuan J. Association of body composition and intradialytic hypotension in hemodialysis patients. *Blood Purif*. 2020;49(3):334–340. doi:10.1159/000504245
57. Sarafidis PA, Persu A, Agarwal R, et al. Hypertension in dialysis patients: a consensus document by the European Renal and Cardiovascular Medicine (EURECA-m) working group of the European Renal Association–European Dialysis and Transplant Association (ERA-EDTA) and the hypertension and the kidney working group of the European Society of Hypertension (ESH). *Nephrol Dial Transplant*. 2017;32(4):620–640.
58. Wang KM, Sirich TL, Chang TI. Timing of blood pressure medications and intradialytic hypotension. *Semin Dial*. 2019;32(3):201–204. doi:10.1111/sdi.12777
59. Assimon MM, Brookhart MA, Fine JP, Heiss G, Layton JB, Flythe JE. A comparative study of carvedilol versus metoprolol initiation and 1-year mortality among individuals receiving maintenance hemodialysis. *Am J Kidney Dis*. 2018;72(3):337–348. doi:10.1053/j.ajkd.2018.02.350
60. Denker MG, Cohen DL. Antihypertensive medications in end-stage renal disease. *Semin Dial*. 2015;28(4):330–336. doi:10.1111/sdi.12369
61. Mensack S. *Metabolic Acidosis*. Critical Care. Routledge; 2021:30–31.
62. Mora-Bravo FG, De-La-Cruz G, Rivera S, Ramirez AM, Raimann JG, Perez-Grovas H. Association of intradialytic hypotension and convective volume in hemodiafiltration: results from a retrospective cohort study. *BMC Nephrol*. 2012;13(1):106. doi:10.1186/1471-2369-13-106
63. Vilar E, Fry AC, Wellsted D, Tattersall JE, Greenwood RN, Farrington K. Long-term outcomes in online hemodiafiltration and high-flux hemodialysis: a comparative analysis. *Clin J Am Soc Nephrol*. 2009;4(12):1944–1953. doi:10.2215/CJN.05560809
64. Pinney JH, Oates T, Davenport A. Haemodiafiltration does not reduce the frequency of intradialytic hypotensive episodes when compared to cooled high-flux haemodialysis. *Nephron Clin Pract*. 2011;119(2):c138–c144. doi:10.1159/000324428
65. Tanemoto M, Ishimoto Y, Kosako Y, Okazaki Y. Comparison of intradialytic plasma volume change between online hemodiafiltration and standard hemodialysis. *Ren Replace Ther*. 2018;4(1):1–6. doi:10.1186/s41100-018-0188-1
66. Fülöp T, Tapolyai MB, Zsom L, et al. Successful practice transitioning between hemodialysis and hemodiafiltration in outpatient units: ten key issues for physicians to remember. *Artif Organs*. 2018;42(9):925–932. doi:10.1111/aor.13135
67. Canaud B, Chazot C, Koomans J, Collins A. Fluid and hemodynamic management in hemodialysis patients: challenges and opportunities. *J Bras Nefrol*. 2019;41(4):550–559. doi:10.1590/2175-8239-jbn-2019-0135
68. Tapolyai MB, Faludi M, Fülöp T, Dossabhoy NR, Szombathelyi A, Berta K. Which fluid space is affected by ultrafiltration during hemodiafiltration? *Hemodial Int*. 2014;18(2):384–390. doi:10.1111/hdi.12125
69. Tapolyai M, Faludi M, Reti V, Lengvarszky Z, Szarvas T, Berta K. Dialysis patients' fluid overload, antihypertensive medications, and obesity. *ASAIO J*. 2011;57(6):511–515. doi:10.1097/MAT.0b013e3182377216
70. Tapolyai M, Faludi M, Reti V, et al. Volume estimation in dialysis patients: the concordance of brain-type natriuretic peptide measurements and bioimpedance values. *Hemodial Int*. 2013;17(3):406–412. doi:10.1111/hdi.12023
71. Allinovi M, Palazzini G, Lugli G, et al. Pre-dialysis B-line quantification at lung ultrasound is a useful method for evaluating the dry weight and predicting the risk of intradialytic hypotension. *Diagnostics*. 2022;12(12):2990. doi:10.3390/diagnostics12122990
72. Kaptein EM, Cantillep A, Kaptein JS, et al. Comparison of respiratory variations of subclavian vein and inferior vena cava in hospitalized patients with kidney disease. *Int J Nephrol Renovasc Dis*. 2020;13:329–339. doi:10.2147/IJNRD.S280458
73. Zschätzsch S, Stauss-Grabo M, Gauly A, Braun J. Integrating monitoring of volume status and blood volume-controlled ultrafiltration into extracorporeal kidney replacement therapy. *Int J Nephrol Renovasc Dis*. 2021;349–358. doi:10.2147/IJNRD.S319911
74. Brennan JM, Ronan A, Goonewardena S, et al. Handcarried ultrasound measurement of the inferior vena cava for assessment of intravascular volume status in the outpatient hemodialysis clinic. *Clin J Am Soc Nephrol*. 2006;1(4):749–753. doi:10.2215/CJN.00310106
75. Hsieh MY, Cheng CH, Chen CH, et al. The association of long-term blood pressure variability with hemodialysis access thrombosis. *Front Cardiovasc Med*. 2022;9:881454. doi:10.3389/fcvm.2022.881454
76. Caplin B, Kumar S, Davenport A. Patients' perspective of haemodialysis-associated symptoms. *Nephrol Dial Transplant*. 2011;26(8):2656–2663. doi:10.1093/ndt/gfq763
77. Assimon MM, Wang L, Flythe JE. Cumulative exposure to frequent intradialytic hypotension associates with new-onset dementia among elderly hemodialysis patients. *Kidney Int Rep*. 2019;4(4):603. doi:10.1016/j.ekir.2019.01.001
78. Zsom L, Zsom M, Abdul Salim S, Fulop T. Subjective global assessment of nutrition, dialysis quality, and the theory of the scientific method in nephrology practice. *Artif Organs*. 2020;44(10):1021–1030. doi:10.1111/aor.13762

79. Guedes M, Pecoits-Filho R, Leme JEG, et al. Impacts of dialysis adequacy and intradialytic hypotension on changes in dialysis recovery time. *BMC Nephrol.* 2020;21(1):529. doi:10.1186/s12882-020-02187-9
80. Kim YS, Davis SC, Truijen J, Stok WJ, Secher NH, van Lieshout JJ. Intensive blood pressure control affects cerebral blood flow in type 2 diabetes mellitus patients. *Hypertension.* 2011;57(4):738–745. doi:10.1161/HYPERTENSIONAHA.110.160523
81. Assimon MM, Wenger JB, Wang L, Flythe JE. Ultrafiltration rate and mortality in maintenance hemodialysis patients. *Am J Kidney Dis.* 2016;68(6):911–922. doi:10.1053/j.ajkd.2016.06.020
82. Shemin D, Bostom AG, Laliberty P, Dworkin LD. Residual renal function and mortality risk in hemodialysis patients. *Am J Kidney Dis.* 2001;38(1):85–90. doi:10.1053/ajkd.2001.25198
83. Chang TI, Paik J, Greene T, et al. Intradialytic hypotension and vascular access thrombosis. *J Am Soc Nephrol.* 2011;22(8):1526–1533. doi:10.1681/ASN.2010101119
84. Furukawa K, Ikeda S, Naito T, et al. Cardiac function in dialysis patients evaluated by Doppler echocardiography and its relation to intradialytic hypotension: a new index combining systolic and diastolic function. *Clin Nephrol.* 2000;53(1):18–24.
85. Sinha AD, Agarwal R. Setting the dry weight and its cardiovascular implications. *Semin Dial.* 2017;30(6):481–488. doi:10.1111/sdi.12624
86. Tomson CR. Advising dialysis patients to restrict fluid intake without restricting sodium intake is not based on evidence and is a waste of time. *Nephrol Dial Transplant.* 2001;16(8):1538–1542. doi:10.1093/ndt/16.8.1538
87. Bossola M, Pepe G, Vulpio C. The frustrating attempt to limit the interdialytic weight gain in patients on chronic hemodialysis: new insights into an old problem. *J Ren Nutr.* 2018;28(5):293–301. doi:10.1053/j.jrn.2018.01.015
88. Jelacic I. Relationship of a food intake during hemodialysis and symptomatic intradialytic hypotension. *Hemodial Int.* 2021;25(3):333–337. doi:10.1111/hdi.12923
89. Hussein WF, Schiller B. Dialysate sodium and intradialytic hypotension. *Semin Dial.* 2017;30(6):492–500. doi:10.1111/sdi.12634
90. Aronoff GR. The effect of treatment time, dialysis frequency, and ultrafiltration rate on intradialytic hypotension. *Semin Dial.* 2017;30(6):489–491. doi:10.1111/sdi.12625
91. van der Sande FM, Cheriex EC, van Kuijk WH, Leunissen KM. Effect of dialysate calcium concentrations on intradialytic blood pressure course in cardiac-compromised patients. *Am J Kidney Dis.* 1998;32(1):125–131. doi:10.1053/ajkd.1998.v32.pm9669433
92. Tsujimoto Y, Tsujimoto H, Nakata Y, et al. Dialysate temperature reduction for intradialytic hypotension for people with chronic kidney disease requiring haemodialysis. *Cochrane Database Syst Rev.* 2019;7(7):CD012598. doi:10.1002/14651858.CD012598.pub2
93. Chang TI. Impact of drugs on intradialytic hypotension: antihypertensives and vasoconstrictors. *Semin Dial.* 2017;30(6):532–536. doi:10.1111/sdi.12633
94. Brunelli SM, Cohen DE, Marlowe G, Van Wyck D. The impact of midodrine on outcomes in patients with intradialytic hypotension. *Am J Nephrol.* 2018;48(5):381–388. doi:10.1159/000494806
95. Wasserstein AG. L-carnitine supplementation in dialysis: treatment in quest of disease. *Semin Dial.* 2013;26(1):11–15. doi:10.1111/sdi.12041
96. Chewcharat A, Chewcharat P, Liu W, et al. The effect of levocarnitine supplementation on dialysis-related hypotension: a systematic review, meta-analysis, and trial sequential analysis. *PLoS One.* 2022;17(7):e0271307. doi:10.1371/journal.pone.0271307
97. Lee H, Moon SJ, Kim SW, et al. Prediction of intradialytic hypotension using pre-dialysis features - a deep learning-based artificial intelligence model. *Nephrol Dial Transplant.* 2023;gfa064. doi:10.1093/ndt/gfa064
98. Kim HW, Heo SJ, Kim M, et al. Deep learning model for predicting intradialytic hypotension without privacy infringement: a retrospective two-center study. *Front Med.* 2022;9:878858. doi:10.3389/fmed.2022.878858
99. Vaid A, Takkavatakam K, Divers J, Charytan DM, Chan L, Nadkarni GN. Deep learning on electrocardiograms for prediction of in-hospital intradialytic hypotension in ESKD patients. *Kidney360.* 2023;10–34067. doi:10.34067/KID.0000092022