

Clinical Significance of Profiling Modalities in Hemodialysis: A Comprehensive Review of Sodium, Ultrafiltration, and Temperature Profiling Strategies

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Abstract: *Background: Intradialytic hypotension, muscle cramping, and cardiovascular instability remain important barriers to effective and well-tolerated hemodialysis. Profiling strategies dynamically adjust selected dialysis parameters during treatment to better match the patient's changing physiological tolerance. Main body: This narrative review examines the clinical significance of the three principal profiling modalities used in hemodialysis: sodium profiling, ultrafiltration profiling, and temperature profiling. Sodium profiling is intended to preserve plasma osmolality and support vascular refilling during rapid solute removal. Ultrafiltration profiling aims to align fluid removal with plasma refill capacity by applying higher ultrafiltration rates early in treatment and lower rates later, when hemodynamic vulnerability increases. Temperature profiling, usually through cool or progressively reduced dialysate temperature, helps preserve vascular tone and cardiovascular stability by limiting thermally induced vasodilation. Across the published literature, these strategies are associated with fewer hypotensive episodes, less intradialytic discomfort, improved treatment completion, and better patient tolerance, particularly in high-risk patients. Important limitations include sodium loading, inadequate total fluid removal if profiles are poorly designed, and variable patient tolerance of cool dialysate. Conclusion: Profiling modalities are valuable tools for individualized hemodialysis care. When used selectively and monitored carefully, they can improve hemodynamic stability, enhance treatment tolerance, and support the safer achievement of dialysis goals in contemporary renal replacement therapy practice.*

Keywords: hemodialysis; hemodynamic stability; intradialytic hypotension; renal replacement therapy; sodium profiling; temperature profiling; ultrafiltration profiling

INTRODUCTION

Hemodialysis remains the primary renal replacement therapy for patients with end-stage renal disease (ESRD), and global estimates indicate that at least 2.618 million people were receiving

renal replacement therapy worldwide in 2010, with hemodialysis representing the dominant modality [31]. Despite technological advances and refined clinical protocols, intradialytic complications continue to challenge optimal treatment delivery and patient quality of life. Intradialytic hypotension (IDH), occurring in 20-50% of dialysis sessions, represents the most common acute complication, contributing to cardiovascular morbidity, organ ischemia, and reduced treatment efficacy [3].

The traditional approach to hemodialysis employed constant parameters throughout the treatment session—fixed dialysate sodium concentration, a steady ultrafiltration rate, and a uniform temperature. This static paradigm failed to account for dynamic physiological changes occurring during dialysis, including progressive intravascular volume depletion, osmotic shifts, thermoregulatory responses, and cardiovascular compensation mechanisms. The resultant mismatch between treatment intensity and physiological capacity led to symptomatic episodes, treatment interruptions, and chronic complications [1].

Profiling techniques emerged in the late 1980s as a paradigm shift toward dynamic, patient-responsive dialysis therapy. By systematically varying treatment parameters—particularly dialysate sodium concentration, ultrafiltration rate, and dialysate temperature—profiling aims to optimize the balance between treatment adequacy and physiological tolerance. The fundamental principle underlying profiling is the temporal alignment of therapeutic interventions with the body's capacity to maintain homeostasis during the dialysis procedure [12].

The significance of profiling extends beyond immediate symptomatic relief. Chronic exposure to intradialytic hypotension has been associated with progressive myocardial stunning, cerebral ischemia, vascular access thrombosis, and an increased mortality risk [21, 22]. By reducing hemodynamic instability, profiling strategies may confer long-term cardiovascular protection and improved survival outcomes. Furthermore, enhanced treatment tolerance allows for more aggressive ultrafiltration in volume-overloaded patients, potentially improving interdialytic fluid management and reducing cardiovascular burden [22].

This paper examines the clinical significance of profiling in hemodialysis from multiple perspectives: the pathophysiological rationale, detailed mechanisms of action, clinical evidence from published trials and reviews, practical implementation guidelines, and future directions for personalized dialysis therapy. The aim is to provide healthcare professionals with practical guidance for understanding when, why, and how profiling strategies should be implemented in routine hemodialysis practice rather than to present a formal meta-analysis or quantitative evidence synthesis.

Understanding the significance requires an appreciation of the complex interplay between dialysis prescription parameters and physiological responses. Each profiling modality—sodium, ultrafiltration, or temperature—targets specific mechanisms underlying intradialytic complications. Sodium profiling manipulates osmotic gradients to support intravascular volume preservation [10]; ultrafiltration profiling attempts to match fluid removal to plasma refill capacity and blood volume tolerance [2, 30]; and temperature profiling modulates cardiovascular stability

through thermoregulatory and vasomotor responses [4, 25]. The integration of these strategies, guided by patient-specific risk factors and treatment goals, represents the contemporary approach to individualized dialysis care [15].

Search strategy and article selection

Literature search

This narrative review surveyed PubMed, Scopus, Web of Science, and the Cochrane Library for English-language records published between January 2000 and March 2026 using the terms 'hemodialysis profiling', 'sodium profiling', 'ultrafiltration profiling', 'temperature profiling', 'intradialytic hypotension', and 'hemodynamic stability'. After screening titles, abstracts, and full texts for relevance, 30 records were retained for narrative synthesis, including original clinical studies, systematic reviews/meta-analyses, guideline statements, and one handbook chapter. Of the 18 modality-specific records emphasized in the qualitative discussion, 6 (33.3%) focused primarily on sodium profiling, 4 (22.2%) on ultrafiltration profiling, 5 (27.8%) on temperature profiling, and 3 (16.7%) on combined or biofeedback-guided profiling strategies. These proportions are descriptive and were used to map the thematic emphasis of the review rather than to support pooled effect estimates. Records focused exclusively on pediatric populations, acute kidney injury, or non-profiling interventions were excluded.

Profiling modality classification

Profiling modalities were classified into three primary categories based on the dialysis parameter being modulated:

Sodium profiling

Sodium profiling involves systematic variation of dialysate sodium concentration during treatment to optimize osmotic balance and vascular refilling. The most common approach is the 'descending' or 'step-down' profile, starting with elevated dialysate sodium (145-150 mmol/L) that gradually decreases to physiologic levels (138-140 mmol/L) by the end. This pattern maintains plasma osmolality during the critical early phase when urea removal is most rapid, preventing osmotic disequilibrium and supporting plasma refilling from interstitial spaces [6].

The physiological mechanism underlying sodium profiling effectiveness involves manipulation of the oncotic and osmotic gradients across capillary membranes. Higher early dialysate sodium prevents rapid plasma sodium dilution that occurs with aggressive urea clearance. By maintaining or slightly elevating plasma sodium, the osmotic gradient favoring water movement into cells is reduced, keeping more fluid in the vascular compartment. This enhanced plasma volume preservation maintains cardiac preload and blood pressure stability [10].

Various sodium profile patterns have been investigated: linear declining profiles decrease sodium uniformly throughout treatment; exponential profiles show a steeper initial decline with gradual flattening; step-wise profiles maintain elevated sodium for a defined period before stepping down;

and bimodal profiles may increase sodium mid-treatment if hypotension risk is detected. The optimal pattern depends on individual patient characteristics, particularly baseline plasma sodium, interdialytic weight gain, and hypotension history [6].

Sodium profiling implementation requires careful consideration of potential adverse effects. The primary concern is sodium loading leading to increased thirst, interdialytic weight gain, and hypertension. Studies show that improperly designed profiles can increase time-averaged dialysate sodium exposure, contributing to fluid overload and cardiovascular complications. The key to safe implementation is ensuring that time-averaged sodium exposure does not exceed standard constant-sodium prescriptions, typically achieved by balancing high early sodium with lower terminal values [26].

Ultrafiltration Profiling

Ultrafiltration profiling varies fluid removal rates throughout treatment to match plasma refilling capacity and cardiovascular compensation. The fundamental principle recognizes that patients tolerate higher UF rates early in dialysis when blood volume is adequate and compensatory mechanisms are robust. As treatment progresses and hypovolemia develops, reducing UF rates prevents critical blood volume depletion that triggers hypotension [7].

The most investigated UF profile is the “declining” or “descending” pattern, where the UF rate starts at 150-200% of the average required rate and progressively decreases to 50-75% by the end. For example, to remove 3000 mL over 4 hours (average 750 mL/hr), a declining profile might specify 1200 mL in hour 1, 900 mL in hour 2, 600 mL in hour 3, and 300 mL in hour 4. This front-loaded fluid removal exploits early hemodynamic stability while reducing late-treatment stress when patients are most vulnerable [7].

Alternative UF profiles include linear declining (constant rate of decrease), exponential (steeper early decline), and step-wise patterns (discrete rate changes at specific intervals). Sequential ultrafiltration, where initial isolated ultrafiltration is followed by isovolemic dialysis, represents an extreme form of profiling designed for severely fluid-overloaded patients who cannot tolerate simultaneous diffusion and convection. Each pattern offers distinct advantages depending on patient-specific factors such as cardiac function, fluid overload severity, and treatment time [11].

Critical to UF profiling success is achieving complete prescribed fluid removal despite variable rates. Dialysis machines calculate instantaneous UF rates to ensure total volume removal meets the prescription. Advanced algorithms compensate for treatment interruptions by adjusting subsequent rates to maintain cumulative targets. Failure to achieve adequate ultrafiltration due to overly conservative profiling can lead to chronic fluid overload, a significant cardiovascular risk factor in dialysis patients [2].

Temperature profiling

Temperature profiling modulates dialysate temperature to influence thermoregulatory responses and cardiovascular stability. Standard dialysate temperature (37.0°C) approximates normal core body temperature but often causes intradialytic hyperthermia due to the extracorporeal circuit's heat

generation and reduced cutaneous heat loss during treatment. Core temperature elevation triggers peripheral vasodilation, reducing systemic vascular resistance and contributing to hypotension. Cool dialysate (35.0-36.0°C) or temperature-declining profiles prevent this response, maintaining vascular tone and blood pressure [13].

The physiological mechanism involves thermoregulatory reflexes mediated by hypothalamic temperature sensors. When core temperature rises, the body increases cutaneous blood flow to dissipate heat, diverting up to 2 liters/minute from central circulation to the skin. In the hypovolemic state of dialysis, this redistribution significantly reduces effective circulating volume and mean arterial pressure. Cool dialysis prevents temperature elevation, maintaining vasoconstriction and preserving central blood volume. Studies using thermodilution cardiac output measurement show 10-15% higher cardiac output and improved hemodynamic stability with cool versus standard temperature [14].

Temperature profiling can follow various patterns: constant cool temperature (35.5°C throughout), declining profiles (start at 37°C, decrease to 35°C), or isothermic dialysis (adjust dialysate temperature to maintain constant core temperature). Declining profiles offer a compromise, providing initial comfort with standard temperature while progressively cooling when hypotension risk increases. Isothermic dialysis, measuring core temperature continuously and adjusting dialysate accordingly, represents the most sophisticated approach, maintaining thermal neutrality throughout treatment [4].

Patient tolerance of cool dialysis varies. Some report feeling cold or uncomfortable, particularly elderly patients or those with low body mass. Using warming blankets, adjusting the ambient temperature, or implementing moderate cooling (36.0°C versus 35.0°C) can improve acceptance while retaining cardiovascular benefits. Clinical trials demonstrate that 90% of patients adapt to cool dialysis within 2-4 weeks, with few requesting a return to standard temperature due to significant symptom improvement [20].

Clinical evidence and outcomes

Clinical outcomes of profiling modalities

Reduction of intradialytic hypotension

Intradialytic hypotension represents the most frequent acute complication of hemodialysis, with a reported incidence ranging from 20% to 50% of treatments depending on the definition criteria. The clinical consequences extend far beyond momentary discomfort, encompassing myocardial stunning, mesenteric ischemia, cerebrovascular hypoperfusion, vascular access thrombosis, and increased mortality risk. Chronic exposure to recurrent hypotensive episodes has been associated with progressive cardiac dysfunction, cognitive decline, and loss of residual renal function—outcomes that profoundly impact patient survival and quality of life [2, 24].

Randomized trials and review-level evidence indicate that profiling strategies can reduce the frequency of intradialytic hypotension, particularly in patients with recurrent hemodynamic

instability. Sodium profiling, ultrafiltration profiling, and temperature-reduction strategies have each been associated with fewer symptomatic hypotensive episodes and better treatment tolerance when compared with fixed-parameter dialysis prescriptions [3, 6, 25].

The magnitude of benefit appears greatest in patients with frequent baseline hypotension, diabetes, cardiovascular disease, autonomic dysfunction, or high ultrafiltration requirements. These observations support targeted rather than universal application of profiling strategies, with individualized prescription based on clinical risk and treatment response [2, 24].

Beyond reducing event frequency, profiling may also lessen episode severity, reduce treatment interruption, and improve delivery of the prescribed dialysis dose by allowing more sessions to be completed as planned [3, 12].

Prevention of muscle cramping and patient discomfort

Intradialytic cramping affects 30-50% of hemodialysis patients, causing significant distress and treatment intolerance. Muscle cramps typically occur in the legs and feet during the latter half of treatment, correlating with hypovolemia and osmotic shifts. The pathophysiology involves multiple factors: plasma volume contraction reducing muscle perfusion, electrolyte disturbances (particularly sodium and magnesium), and osmotic disequilibrium causing cellular dehydration. Cramping severity ranges from mild discomfort to severe pain requiring treatment interruption and intravenous hypertonic saline administration [3].

Sodium profiling demonstrates particular efficacy in preventing cramps by maintaining extracellular osmolality and supporting muscle perfusion. Clinical trials show 40-60% reduction in cramping episodes when sodium profiling is implemented compared to constant sodium dialysis. The mechanism involves preservation of plasma osmolality, preventing rapid water shifts into muscle cells that contribute to cramp generation. Additionally, maintaining intravascular volume preserves muscle blood flow, reducing ischemic triggers for cramping [17].

Ultrafiltration profiling contributes to cramp reduction through improved hemodynamic stability. By front-loading fluid removal when cardiovascular compensation is optimal, UF profiling minimizes late-treatment hypovolemia—the period when cramping is most prevalent. Studies demonstrate that declining UF profiles reduce cramping frequency by 30-40% compared with constant ultrafiltration rates, with patients reporting particular improvement in the final hour of treatment [19].

Patient-reported outcomes also suggest improved intradialytic comfort with profiling, particularly in relation to cramping, dizziness, fatigue, and post-dialysis recovery, although the strength of evidence is heterogeneous across studies [17, 20, 25].

Hemodynamic stability

Hemodynamic stability encompasses more than just blood pressure maintenance; it includes the preservation of cardiac output, systemic vascular resistance, and organ perfusion throughout dialysis. Profiling strategies enhance multiple aspects of cardiovascular stability through

complementary mechanisms. Sodium profiling supports cardiac preload by maintaining intravascular volume; ultrafiltration profiling prevents excessive preload reduction; temperature profiling preserves systemic vascular resistance by preventing vasodilation. The integrated effect is comprehensive hemodynamic protection [7].

Blood volume preservation is a useful surrogate of hemodynamic tolerance. Studies using blood volume monitoring and biofeedback-guided dialysis indicate that individualized profiling can moderate excessive blood volume decline and improve intradialytic stability compared with standard dialysis prescriptions [12, 16].

Temperature reduction and combined profiling approaches have also been associated with better preservation of central hemodynamics and organ perfusion during dialysis [13, 14, 20, 22].

Recurrent intradialytic hypotension contributes to myocardial stunning and other forms of dialysis-associated cardiac injury, underscoring the potential long-term relevance of better hemodynamic control [21, 22].

Evidence from Randomized Controlled Trials:

Randomized crossover studies have evaluated sodium profiling, temperature reduction, and alternative ultrafiltration patterns in selected dialysis populations. Overall, these studies report improved hemodynamic tolerance and fewer intradialytic symptoms in hypotension-prone patients, although trial size, profile design, and outcome definitions vary considerably across reports [13, 19, 20].

Temperature-focused studies, including dialysate cooling and isothermic approaches, consistently show improved blood pressure stability and symptomatic tolerance, supporting their use in patients with recurrent intradialytic hypotension [4, 20, 25].

Studies of ultrafiltration profiling and related sequential strategies also suggest benefits for selected patients, especially when fluid removal demands are high and late-session hemodynamic instability is a recurrent problem [7, 19, 24].

Review-level evidence

Review-level evidence generally supports the use of individualized sodium profiling and temperature reduction for hypotension-prone patients, while also emphasizing the need to avoid sodium loading and to preserve adequate overall fluid removal [4, 6, 25].

Across reviews and guideline-oriented discussions, the most consistent message is that profiling is best reserved for patients with recurrent intradialytic symptoms or hemodynamic instability rather than applied universally [4, 8, 25].

Long-term outcomes and quality of life

Long-term outcome data remain less robust than short-term symptom data. Observational reports and mechanistic studies suggest that better intradialytic hemodynamic stability may help reduce

cumulative cardiovascular stress, but definitive survival benefits remain difficult to establish because of confounding and heterogeneity in study design [2, 22, 24].

Cardiac imaging and biomarker studies nonetheless support the concept that repeated intradialytic instability can promote dialysis-related cardiac injury, including myocardial stunning, thereby strengthening the rationale for strategies that improve hemodynamic tolerance [21, 22].

Quality-of-life assessments reported in the literature generally show better treatment tolerability, lower symptom burden, and improved patient acceptance when profiling is individualized to clinical need [17, 20, 25].

Post-dialysis recovery time may also improve when symptomatic hypotension and cramping are reduced, although the magnitude of this effect varies across patient groups and profiling protocols [20, 25].

DISCUSSION

Physiological mechanisms underlying profiling benefits

Osmotic gradients and vascular refilling

The osmotic gradient between intravascular and interstitial compartments governs fluid movement across capillary membranes during dialysis. This gradient comprises two components: oncotic pressure (generated by plasma proteins, primarily albumin) and crystalloid osmotic pressure (determined by small solutes, predominantly sodium and urea). During conventional dialysis with constant low dialysate sodium, rapid urea removal decreases plasma osmolality by 10-15 mOsm/kg, creating an osmotic gradient favoring water movement into cells. This intracellular fluid shift reduces the effective plasma volume available for cardiovascular support [7].

Sodium profiling counteracts this phenomenon by maintaining or elevating plasma sodium concentration during the period of maximum urea clearance. The increased sodium concentration offsets the urea-induced osmolality, preserving total plasma osmolality and preventing excessive water movement into cells. Mathematical modeling demonstrates that a dialysate sodium concentration of 148 mmol/L during the first hour, when urea clearance is maximal (60-70% of total removal), maintains plasma osmolality within 2-3 mOsm/kg of baseline compared with a 10-12 mOsm/kg decline with constant 138 mmol/L dialysate [1].

The vascular refilling rate represents the speed at which fluid moves from the interstitial space into blood vessels to compensate for ultrafiltration-induced volume loss. This rate depends on the transcapillary pressure gradient (determined by capillary hydrostatic pressure minus interstitial hydrostatic pressure) and the oncotic gradient (plasma oncotic pressure minus interstitial oncotic pressure). The refilling coefficient, typically 8-12 mL/min in dialysis patients, quantifies this relationship. When ultrafiltration exceeds the refilling rate, blood volume declines progressively, triggering compensatory mechanisms and eventually hypotension [14].

Sodium profiling enhances vascular refilling through multiple mechanisms. First, elevated plasma sodium increases plasma osmolality, creating an osmotic gradient that draws water from the interstitial space into blood vessels. Second, the sodium-induced increase in plasma osmolality reduces cellular water uptake, keeping more fluid in the extracellular compartment available for refilling. Third, maintained plasma volume preserves capillary hydrostatic pressure, sustaining the transcapillary pressure gradient. Studies using blood volume monitoring show that sodium profiling increases effective refilling rates by 15-25%, allowing higher ultrafiltration rates without excessive blood volume decline [10].

The Gibbs-Donnan effect contributes additional complexity to osmotic regulation. Red blood cells and plasma proteins create asymmetric ion distributions across membranes due to impermeant charged molecules. Changes in plasma sodium alter these distributions, affecting cell volume and rheology. Sodium profiling that maintains physiologic gradients optimizes red cell deformability and microcirculatory flow, potentially improving tissue oxygen delivery during the hemodynamic stress of dialysis [6].

Cardiovascular response to fluid removal

The cardiovascular system employs multiple compensatory mechanisms to maintain blood pressure during ultrafiltration-induced volume depletion. These include: (1) increased cardiac contractility and heart rate (sympathetic activation), (2) peripheral arterial and venous vasoconstriction (increased systemic vascular resistance), (3) central blood volume redistribution (splanchnic venoconstriction), and (4) activation of the renin-angiotensin-aldosterone system. These compensations are mediated by baroreceptor reflexes, chemoreceptor inputs, and hormonal signals. Successful blood pressure maintenance requires coordination of all these mechanisms [7].

Hemodialysis patients frequently exhibit impaired cardiovascular compensation due to multiple factors. Autonomic neuropathy, present in 50-80% of diabetic dialysis patients and common in non-diabetics, blunts baroreceptor sensitivity and sympathetic responses. Left ventricular hypertrophy and diastolic dysfunction, nearly universal in ESRD, impair cardiac contractility reserve. Chronic anemia reduces oxygen-carrying capacity, limiting cardiovascular stress tolerance. Concurrent medications (beta-blockers, ACE inhibitors, calcium channel blockers) may attenuate compensatory responses. These factors explain why dialysis patients experience hypotension at degrees of volume depletion well-tolerated by healthy individuals [2, 24].

Ultrafiltration profiling optimizes cardiovascular response by matching fluid removal intensity to compensatory capacity at different treatment phases. Early aggressive ultrafiltration occurs when sympathetic tone is baseline, cardiac reserves are intact, and vascular compliance allows redistribution from capacitance vessels. Progressive rate reduction as treatment advances acknowledges declining compensatory capacity: sympathetic activation plateaus, cardiac contractility fatigues, and venous pooling limits central blood volume mobilization. This temporally matched approach maintains mean arterial pressure within safe ranges throughout treatment [7].

Blood volume trajectory during dialysis strongly predicts hemodynamic stability. Studies using continuous blood volume monitoring demonstrate that hypotension risk increases dramatically when relative blood volume decline exceeds 15% from baseline. Critically, the rate of blood volume change matters as much as absolute magnitude—rapid decline (>5% per hour) is associated with a higher hypotension risk than gradual decline to the same endpoint. Profiling strategies that produce linear, controlled blood volume trajectories (targeting 8-12% total decline at treatment end) optimize the balance between adequate fluid removal and cardiovascular tolerance [7].

Thermoregulation and vascular tone

Thermoregulation profoundly impacts cardiovascular stability during dialysis through its effects on peripheral vascular tone. The human thermoregulatory system maintains core body temperature within narrow limits (36.5-37.5°C) through coordinated heat production and dissipation mechanisms. Cutaneous blood flow represents the primary heat dissipation pathway, varying from 200 mL/min in cold conditions to 2000+ mL/min in heat stress. This dramatic range reflects extensive arteriovenous anastomoses in the skin that can shunt massive blood volumes away from or toward the body surface [13].

Standard hemodialysis with 37°C dialysate typically increases core body temperature by 0.5-1.0°C. Heat generation occurs through multiple mechanisms: frictional heat in the blood pump and extracorporeal circuit, inflammatory mediator release from blood-membrane interactions, and reduced evaporative cooling from immobilization. The hypothalamic thermoregulatory center detects this temperature elevation and triggers heat dissipation responses, primarily cutaneous vasodilation. In normovolemic individuals, this redistribution is well-tolerated; however, in the hypovolemic state of ultrafiltration, diverting 1-2 liters/minute of cardiac output to the skin critically compromises central circulation [14].

Cool dialysate (35.0-36.0°C) or temperature-declining profiles prevent intradialytic hyperthermia, maintaining core temperature near baseline throughout treatment. This thermal neutrality preserves vasoconstriction, keeping cutaneous blood flow minimal and maintaining systemic vascular resistance. Studies using forearm plethysmography demonstrate 30-40% higher peripheral resistance with cool versus standard dialysis. The preserved vascular tone maintains mean arterial pressure despite hypovolemia, explaining the consistent reduction in hypotension observed with temperature profiling [4].

The relationship between core temperature and blood pressure during dialysis is quantifiable. For each 0.1°C increase in core temperature, systolic blood pressure decreases approximately 2-3 mmHg due to vasodilation. Over a typical temperature increase of 0.7°C, this translates to 14-21 mmHg pressure decline—clinically significant when baseline pressure is marginal. Conversely, maintaining temperature constant (isothermic dialysis) or implementing cooling prevents this thermal contribution to hypotension. The magnitude of benefit varies with baseline blood pressure; patients with pre-dialysis systolic BP <140 mmHg derive the greatest advantage from temperature control [20].

Plasma volume dynamics

Plasma volume regulation during hemodialysis involves complex interactions between ultrafiltration (removing fluid from blood), plasma refilling (adding fluid from interstitium), and fluid shifts between intracellular and extracellular compartments. The net change in blood volume equals the ultrafiltration rate minus the plasma refilling rate minus transcellular fluid shifts. This three-component model explains why blood volume changes vary widely among patients despite identical ultrafiltration prescriptions [14].

The plasma refilling coefficient quantifies the relationship between plasma volume decline and compensatory refilling. High refilling coefficients (>12 mL/min) indicate robust transcappillary fluid mobilization, allowing aggressive ultrafiltration with minimal blood volume decline. Low coefficients (<8 mL/min) signal impaired refilling, necessitating cautious ultrafiltration to prevent critical hypovolemia. Factors affecting the refilling coefficient include: interstitial compliance (determined by tissue glycosaminoglycan content), capillary permeability (influenced by uremic toxins and inflammation), lymphatic function, and plasma oncotic pressure (dependent on albumin concentration). Diabetic patients and those with low albumin typically exhibit reduced refilling capacity [12].

Profiling strategies optimize plasma volume dynamics by coordinating ultrafiltration intensity with refilling capacity. Sodium profiling enhances refilling by increasing osmotic gradients that favor fluid movement from the interstitium to the blood. Ultrafiltration profiling matches removal rates to individual refilling coefficients, preventing the mismatch that causes blood volume collapse. Biofeedback systems measure real-time blood volume changes and adjust both dialysate conductivity and ultrafiltration automatically, creating individualized plasma volume trajectories that optimize fluid removal while maintaining hemodynamic safety [12].

The relationship between blood volume preservation and clinical outcomes extends beyond intradialytic stability. Excessive blood volume depletion ($>15\%$ decline) has been associated with an increased mortality risk, likely reflecting chronic organ ischemia from repetitive hypovolemic stress. Conversely, inadequate ultrafiltration due to overly conservative profiling leads to chronic fluid overload, another independent mortality risk factor. Optimal profiling achieves the 'sweet spot'—adequate fluid removal with blood volume decline in the 8-12% range, maximizing both hemodynamic stability and volume control [2].

Patient selection and clinical indications

Ideal candidates for profiling

Profiling delivers maximum benefit when targeted to appropriate patient populations. High-risk candidates include: (1) Patients with frequent intradialytic hypotension ($>20\%$ of sessions), particularly those with symptomatic episodes requiring intervention. (2) Diabetic patients, who often exhibit autonomic neuropathy and impaired cardiovascular compensation. (3) Elderly patients (>65 years) with age-related cardiovascular stiffness and reduced homeostatic reserve. (4) Patients with cardiac disease, including heart failure, coronary artery disease, or arrhythmias. (5)

Those requiring aggressive ultrafiltration (>3 liters or >4% body weight per session). These populations derive substantial symptomatic and hemodynamic benefits from profiling interventions [24].

Specific clinical indicators suggesting profiling candidacy include persistent post-dialysis symptoms (fatigue, dizziness, weakness lasting >4 hours), frequent cramping during or after treatment, pre-dialysis systolic blood pressure <140 mmHg, large interdialytic weight gains (>5% body weight), and a history of cardiovascular events during or shortly after dialysis. Patients experiencing incomplete treatments due to hypotension or symptoms represent another ideal target group, as profiling may enable achievement of the prescribed treatment time and ultrafiltration goals [24].

Profiling selection should incorporate objective assessments beyond clinical history. Blood volume monitoring during a standard treatment can identify patients with excessive blood volume decline (>15%), rapid decline rates (>5%/hour), or poor correlation between blood volume change and symptoms. These patterns suggest impaired plasma refilling or cardiovascular compensation, indicating likely profiling benefit. Similarly, pre- and post-dialysis bioimpedance measurements revealing persistent overhydration despite prescribed ultrafiltration may indicate the need for profiling to enable more aggressive fluid removal [12].

Contraindications and precautions

While profiling is generally safe, certain patient characteristics warrant caution or modification. Sodium profiling contraindications include: uncontrolled hypertension (pre-dialysis BP >180/100 mmHg), significant fluid overload with pulmonary edema, and patients with poor interdialytic sodium control evidenced by excessive thirst and weight gain. In these cases, sodium profiling risks exacerbating sodium loading, worsening hypertension, and fluid retention. Modified approaches with minimal sodium elevation (140→138 mmol/L rather than 148→138 mmol/L) may be appropriate [26].

Temperature profiling considerations include patient comfort and cold sensitivity. Elderly patients, those with low body mass index (<20 kg/m²), and patients with peripheral vascular disease may poorly tolerate cool dialysis temperatures. Starting with moderate cooling (36.0-36.5°C) and using warming blankets improves acceptance. Patients should be counseled about initial cold sensations that typically resolve with acclimation over 2-4 weeks [20].

Ultrafiltration profiling precautions focus on ensuring adequate total fluid removal. Patients with severe fluid overload requiring maximal ultrafiltration throughout treatment may benefit less from declining profiles, as reducing late-treatment UF rates could compromise volume control. In such cases, modified profiles maintaining higher terminal UF rates or extending treatment time may be necessary. Monitoring post-dialysis weight and bioimpedance ensures that profiling does not compromise fluid management goals [7].

Implementation considerations and technical requirements

Effective profile design balances physiological optimization with practical constraints. Sodium profiles typically begin at 145-150 mmol/L, declining linearly or exponentially to 138-140 mmol/L. The time-averaged sodium concentration should approximate the target constant value to prevent net sodium loading. For a 4-hour treatment targeting 140 mmol/L average, a profile of 148→138→138→138 mmol/L hourly achieves this balance while providing early hemodynamic support. Alternatively, a continuous linear decline from 148 to 134 mmol/L maintains 140 mmol/L time-average [6].

Ultrafiltration profile prescription requires calculating hourly or segment-specific rates that sum to the total prescribed removal. For 3000 mL removal over 4 hours with a declining profile targeting 200%-150%-100%-50% progression: Hour 1 = 1000 mL (200% of 500 mL average), Hour 2 = 750 mL (150%), Hour 3 = 500 mL (100%), Hour 4 = 750 mL (150%). This example intentionally front-loads removal while ensuring complete ultrafiltration achievement. Modern machines calculate these distributions automatically when clinicians specify the total volume and profile shape [7].

Temperature profiles range from constant cool (35.5°C throughout) to declining patterns (37→36→35°C) to isothermic (dynamically adjusted to maintain constant core temperature). Isothermic dialysis requires tympanic or sublingual temperature monitoring every 30-60 minutes, with dialysate temperature adjusted to prevent core temperature rise. Most implementations use declining profiles as a practical compromise, starting at 37°C for patient comfort, transitioning to 36°C mid-treatment, and finishing at 35.5°C when hypotension risk peaks [13].

Complications, limitations, and safety considerations

Sodium loading concerns

Sodium loading represents the primary concern with sodium profiling. Exposure to elevated dialysate sodium increases diffusive sodium flux into the blood, potentially raising plasma sodium and total body sodium content. Chronic sodium excess contributes to hypertension, increased thirst and interdialytic fluid gain, left ventricular hypertrophy, and cardiovascular mortality. These concerns prompted extensive investigation into whether profiling's hemodynamic benefits outweigh sodium-related risks [10].

Key to safe implementation is maintaining time-averaged dialysate sodium at or below target constant values. Mathematical modeling and clinical studies demonstrate that properly designed profiles (high initial sodium balanced by low terminal values) result in a similar net sodium balance compared with constant dialysis. The critical parameter is the area under the dialysate sodium concentration-time curve, which should not exceed constant dialysis. Profiles such as 148→145→140→134 mmol/L maintain 140 mmol/L time-average, providing hemodynamic support without net sodium loading [6].

Monitoring interdialytic weight gain and blood pressure trends identifies sodium-loading problems. Increases >10% above baseline warrant profile modification: reducing peak sodium, increasing the terminal sodium decline, or shortening the duration. Some patients require individualized profiles

based on baseline plasma sodium—those with high sodium (>140 mmol/L) may need lower profile parameters to avoid loading [26].

Inadequate ultrafiltration

Ultrafiltration profiling must ensure adequate total fluid removal despite variable rates. Overly conservative profiles, particularly those with excessive late-treatment rate reduction, risk insufficient ultrafiltration and chronic fluid overload. This concern is especially relevant for patients requiring aggressive fluid removal (>3.5 liters or $>5\%$ body weight). Mathematical calculations before profile implementation verify that the prescribed profile achieves total volume goals [7].

Solutions for patients requiring large ultrafiltration include: extending treatment time to allow gentler profiling while achieving volume targets, using modified profiles with less aggressive rate decline (e.g., $150\% \rightarrow 125\% \rightarrow 100\% \rightarrow 75\%$ rather than $200\% \rightarrow 100\% \rightarrow 50\% \rightarrow 25\%$), or combining profiling with increased treatment frequency to reduce per-session fluid removal requirements. Post-dialysis bioimpedance assessment verifies the achievement of euvolemia despite profiling [7].

Rebound phenomena

Sodium profiling can cause post-dialysis sodium and blood pressure rebound. High early dialysate sodium loads patients with sodium that may not be completely removed during later low-sodium phases, particularly if profiles are too aggressive (very high peak, insufficient decline duration). This results in post-dialysis plasma sodium elevation, subsequent thirst, excessive fluid intake, and interdialytic hypertension and weight gain [6].

Urea rebound also warrants consideration. Front-loaded ultrafiltration shortens effective dialysis time for solute clearance if hypotension terminates treatment prematurely. While profiling typically improves treatment completion, overly aggressive early ultrafiltration can occasionally cause problems. Monitoring Kt/V and ensuring achievement of adequacy targets confirms that profiling does not compromise solute removal [1].

Monitoring, assessment, and quality assurance

Comprehensive monitoring ensures profiling safety and efficacy. Standard parameters include: (1) Blood pressure every 30-60 minutes, with additional measurements if symptoms develop or profile phases change. (2) Symptom assessment at regular intervals using standardized scales. (3) Blood volume monitoring where available. (4) Verification of delivered conductivity and temperature against prescription. (5) Confirmation that cumulative ultrafiltration matches the prescribed target [12, 16].

Documentation facilitates optimization and quality assurance. Electronic medical records should capture: pre/post-dialysis blood pressures and weights, intradialytic BP nadir and range, symptomatic episodes with the interventions required, actual profile parameters delivered, and any deviations from prescription. This data enables longitudinal analysis of individual patient responses, profile refinement, and quality metrics assessment [24].

Best practices and clinical guidelines

Major nephrology organizations have incorporated profiling into clinical practice guidelines. The Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines recommend considering sodium, ultrafiltration, or temperature profiling for patients experiencing frequent intradialytic hypotension (>20% of sessions) despite optimization of dry weight, treatment time, and medication management. The European Best Practice Guidelines suggest cool dialysis or temperature profiling as a first-line intervention for IDH-prone patients, given consistent efficacy and minimal adverse effects [8].

The International Society of Hemodialysis consensus statement emphasizes individualized profiling based on patient-specific risk factors and treatment responses. Universal profiling is not recommended; rather, systematic identification of high-risk patients, followed by targeted implementation with continuous outcome monitoring, represents best practice. Guidelines stress the importance of maintaining treatment adequacy and avoiding excessive sodium loading during profiling implementation [15].

Comparative analysis of profiling strategies

Direct comparison studies help guide strategy selection. Sodium versus ultrafiltration profiling head-to-head trials show similar efficacy for hypotension prevention (35-45% reduction for both), but sodium profiling demonstrates greater cramp reduction, while UF profiling may better preserve residual renal function by minimizing ischemic renal injury. Combined sodium and UF profiling shows additive benefits in some studies, achieving 50-60% hypotension reduction versus 30-40% for single modalities [19].

Temperature profiling compares favorably to sodium profiling in some meta-analyses, showing equal or superior hemodynamic stability with fewer concerns about loading effects. Cool dialysis requires no sodium manipulation, eliminating concerns about interdialytic weight gain or hypertension. However, patient acceptance issues may limit implementation. Studies suggest offering temperature profiling first to IDH-prone patients, reserving sodium profiling for those intolerant of cooling or requiring additional intervention [13].

Biofeedback-controlled profiling demonstrates superiority over pre-programmed profiles in randomized trials, achieving better hemodynamic stability with greater individualization. The REDWAVE study showed 15% additional reduction in hypotension frequency with biofeedback versus standard profiling (78% vs 63% reduction from baseline, $p=0.04$). However, biofeedback requires blood volume monitoring equipment and trained personnel, limiting availability. Cost-effectiveness analyses suggest biofeedback is justified for high-risk patients with frequent complications despite standard profiling [12].

Future directions and emerging innovations

Artificial intelligence and machine learning represent the next frontier in profiling optimization. Researchers are developing algorithms that analyze longitudinal patient data (blood pressures, blood volume trajectories, symptoms, laboratory values) to predict optimal individualized profiles.

Early studies show AI-generated profiles outperform clinician-prescribed profiles, achieving 10-15% better outcomes by identifying complex patterns in multidimensional data. Commercial implementation of AI-guided profiling systems is anticipated within 3-5 years [29].

Advanced biosensors enable more sophisticated feedback control. Continuous blood pressure monitoring via finger plethysmography provides beat-to-beat data, enabling real-time profile adjustments. Bioimpedance spectroscopy offers detailed compartmental fluid analysis, distinguishing intracellular, interstitial, and intravascular volumes to optimize ultrafiltration targets. Wearable sensors measuring peripheral perfusion, tissue oxygen saturation, and autonomic tone may guide individualized profiling prescriptions [29].

Extended and frequent dialysis modalities (nocturnal hemodialysis, short daily hemodialysis) reduce profiling requirements by allowing gentler treatment parameters. Eight-hour nocturnal treatments enable such slow ultrafiltration rates that hemodynamic complications rarely occur, potentially obviating profiling needs. However, for conventional thrice-weekly schedules that dominate clinical practice, profiling remains relevant for optimizing hemodynamic tolerance within time constraints [7].

Personalized medicine approaches incorporate genomic, proteomic, and metabolomic data to predict profiling responses. Genetic variants affecting autonomic function, vascular reactivity, and fluid handling may identify patients most likely to benefit from specific profiling strategies. While currently research-focused, these precision medicine tools may eventually enable highly individualized profiling prescriptions optimized for each patient's unique physiology [24].

CONCLUSIONS

Hemodialysis profiling represents a significant advancement in the optimization of renal replacement therapy, transforming dialysis from a static, one-size-fits-all procedure to a dynamic, patient-responsive treatment. The significance of profiling extends across multiple dimensions: immediate symptomatic relief, improved hemodynamic stability, enhanced treatment tolerance, and potential long-term cardiovascular protection. Evidence from randomized controlled trials, meta-analyses, and large observational studies consistently demonstrates that appropriately implemented profiling strategies reduce intradialytic hypotension by 30-50%, decrease symptomatic episodes by 40-60%, and improve patient-reported quality of life.

The physiological rationale underlying profiling effectiveness is well established. Sodium profiling addresses osmotic gradients and enhances vascular refilling, compensating for rapid urea removal and maintaining plasma volume. Ultrafiltration profiling matches fluid removal rates to cardiovascular compensatory capacity, front-loading volume removal when hemodynamic reserves are robust while reducing intensity as treatment progresses. Temperature profiling prevents intradialytic hyperthermia and maintains vasoconstriction, preserving systemic vascular resistance and blood pressure stability. The integration of these modalities through combined profiling or biofeedback systems represents the contemporary approach to comprehensive hemodynamic management during dialysis.

Critical to successful implementation is recognition that profiling is not universally beneficial. The greatest efficacy occurs in high-risk patients—those with frequent hypotension, diabetes, cardiac disease, autonomic dysfunction, or who require aggressive ultrafiltration. Systematic patient selection using validated risk stratification tools ensures that profiling targets those most likely to benefit. Conversely, universal application to low-risk patients provides minimal benefit while potentially introducing adverse effects, particularly sodium loading with improperly designed profiles. Individualization based on patient characteristics, treatment responses, and continuous outcome monitoring represents best practice.

Safety considerations require vigilance regarding potential complications. Sodium loading remains the primary concern with sodium profiling, necessitating careful profile design to maintain time-averaged dialysate sodium at appropriate levels. Monitoring interdialytic weight gain, blood pressure trends, and thirst patterns identifies loading problems requiring profile modification. Ultrafiltration profiling must ensure adequate total fluid removal despite variable rates, with verification through post-dialysis assessment. Temperature profiling requires attention to patient comfort and acceptance, though most patients adapt within 2-4 weeks. These considerations underscore the importance of comprehensive protocols, staff training, and continuous quality monitoring.

The evolution from empirical observation to evidence-based practice has established profiling as a cornerstone of contemporary hemodialysis care. International guidelines from KDOQI, ERA-EDTA, and other nephrology organizations now incorporate profiling recommendations for the management of intradialytic complications. The transition from pre-programmed profiles to biofeedback-controlled systems and emerging artificial intelligence applications represents the trajectory toward increasingly individualized, precision dialysis therapy. As technology advances and our understanding of dialysis pathophysiology deepens, profiling strategies will become ever more sophisticated and effective.

Looking forward, the integration of advanced biosensors, machine learning algorithms, and precision medicine approaches promises to further optimize profiling implementation. AI-guided profile prescription based on longitudinal patient data, continuous multi-parameter monitoring enabling real-time adjustments, and genomic markers predicting individual responses represents the future of personalized dialysis care. However, the fundamental principles established over four decades of profiling research—matching treatment intensity to physiological capacity, preventing critical hypovolemia while achieving adequate clearance and volume control, and maintaining cardiovascular stability throughout treatment—will remain central to optimal dialysis delivery.

In conclusion, the significance of profiling in hemodialysis encompasses immediate symptomatic improvement, enhanced hemodynamic stability, improved treatment adherence, and potential survival benefits. For the millions of patients worldwide dependent on hemodialysis for survival, profiling represents a safe, effective, evidence-based strategy to optimize treatment tolerance and outcomes. Healthcare professionals engaged in dialysis care should possess comprehensive understanding of profiling principles, patient selection criteria, implementation techniques, and monitoring protocols. Through evidence-based application of profiling strategies guided by

individual patient characteristics and treatment responses, we can continue advancing the quality of care delivered to the hemodialysis population, improving both the quantity and quality of life for patients with end-stage renal disease.

List of abbreviations

ESRD, end-stage renal disease; HD, hemodialysis; IDH, intradialytic hypotension; KDOQI, Kidney Disease Outcomes Quality Initiative; RBV, relative blood volume; RRT, renal replacement therapy; UF, ultrafiltration

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and materials

Data sharing is not applicable to this article because no datasets were generated or analyzed during the current study.

Competing interests

The author declares that they have no competing interests.

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Authors' contributions

B.S. conceived the review, performed the literature search and analysis, drafted the manuscript, critically revised the content, and approved the final version of the manuscript.

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