



Thinking Volume First: Developing a Multifaceted Systematic Approach to Volume Management in Hemodialysis

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Abstract

Purpose of review: Volume overload and hypovolemia-induced symptoms are common in the hemodialysis (HD) population and frequently result in emergency department visits and hospitalization. A structured strategy for the reporting, evaluation, and management of disordered volume status may improve clinical outcomes and the patient experience. We developed a new strategy that systematically addresses volume issues by leveraging the electronic medical record, technological adjuncts, and multidisciplinary expertise to institute new processes of care in our HD unit.

Sources of information: This initiative was implemented in a unit located in an urban academic hospital where 250 patients receive maintenance HD. This initiative involved a multidisciplinary team of health professionals including physicians, nurse practitioners, social workers, and dietitians.

Methods: We generated volume metrics for HD recipients based on routinely collected data from the unit's electronic medical record. We then engaged stakeholders in a root cause analysis to identify the major causes of abnormal volume metrics locally. We subsequently developed interventions that were designed to address each of the major causes in a pragmatic and sustainable program.

Key findings: The final product was a local volume management program with 3 components. First, we integrated volume metric reporting into the routine surveillance bloodwork reports across our unit. This enabled the clinical teams to more easily target patients at risk for volume-related adverse events and provide them with closer surveillance. Those identified with abnormal volume metrics were then evaluated with the use of technologic adjuncts such as lung ultrasound and bioimpedance spectroscopy to complement traditional assessments of volume status. Finally, those with abnormal volume metrics underwent rigorous interdisciplinary review for potential nutritional/social interventions.

Limitations: While we report the successful initial implementation of the program within a single center, it remains unclear whether this initiative will lead to meaningful benefits for HD recipients, be readily applicable in other centers, or be sustainable in the long term.

Implications: This volume management program will need further evaluation linked to outcome assessment and feasibility in other centers before wider adoption is advocated.

Abrégé

Contexte motivant la revue: La surcharge volémique et les symptômes induits par l'hypovolémie sont fréquents chez les patients hémodialysés (HD) et entraînent souvent des visites aux urgences et des hospitalisations. Une stratégie structurée de notification, d'évaluation et de gestion des déséquilibres hydriques peut améliorer les résultats cliniques et l'expérience du patient. Nous avons développé une nouvelle stratégie qui aborde systématiquement les problèmes de volémie en exploitant les dossiers médicaux électroniques, les auxiliaires technologiques et une expertise multidisciplinaire pour instaurer de nouvelles procédures de soins dans notre unité d'hémodialyse.

Sources: Cette initiative a été mise en œuvre dans l'unité de dialyse d'un centre hospitalier universitaire en milieu urbain, dans lequel 250 patients reçoivent des traitements d'HD périodiques. Une équipe multidisciplinaire constituée de médecins, d'infirmières-praticiennes, de travailleurs sociaux et de nutritionnistes a participé à l'initiative.

Méthodologie: Nous avons généré des données de volémie pour les patients hémodialysés à partir des données recueillies sur une base régulière dans le dossier médical informatisé de l'unité. Nous avons ensuite fait participer les différents intervenants à l'analyse des causes profondes afin de déterminer les principales causes des anomalies volémiques observées dans notre unité. Enfin, nous avons développé des interventions pour traiter chacune des principales causes à l'aide d'un programme viable et pragmatique.



Principaux résultats: Le résultat est un programme local de prise en charge de la volémie à trois composants. Premièrement, nous avons intégré la mesure de la volémie dans les rapports d'analyses sanguines de surveillance de routine dans toute l'unité. Cela a permis aux équipes soignantes de cibler plus facilement les patients susceptibles de subir des manifestations indésirables liées à la volémie et de les surveiller de plus près. Les patients présentant une mesure de volémie anormale ont ensuite été évalués à l'aide d'auxiliaires technologiques tels que l'ultrasonographie pulmonaire et la spectroscopie de bioimpédance, en complément de l'évaluation traditionnelle du statut volémique. Enfin, les patients présentant des anomalies volémiques ont fait l'objet d'un examen interdisciplinaire rigoureux en vue de potentielles interventions nutritionnelles/sociales.

Limites: Bien que nous rapportons le succès de la mise en œuvre initiale du programme dans un centre, nous ignorons si cette initiative apportera des bienfaits significatifs aux patients hémodialisés, si elle s'appliquera facilement à d'autres centres ou si elle est viable à long terme.

Conclusion: Ce programme de gestion de la volémie devra faire l'objet d'une évaluation plus poussée quant à l'examen des résultats cliniques et à sa faisabilité dans d'autres centres avant que son adoption à d'autres centres ne soit préconisée.

Keywords

hemodialysis, volume, quality improvement, bioimpedance, electronic medical records

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What was known before

Despite the best efforts of practitioners, symptoms and resource-use related to volume overload and hypovolemia remain frequent among hemodialysis recipients.

What this adds

This article describes a novel strategy to systematically address volume issues by leveraging the electronic medical record, technological adjuncts, and multidisciplinary expertise to institute new processes of care in the hemodialysis unit.

Case Presentation

Mr E is a 75-year-old male who receives maintenance hemodialysis (HD) 3 times per week via a tunneled right jugular central venous catheter. His medical history is significant for end-stage kidney disease from ischemic nephropathy, ischemic cardiomyopathy with a reduced ejection fraction of 25%, and ventricular tachycardia for which he has an implantable cardiac defibrillator (ICD). Three months ago, he was admitted for 3 days for acute pulmonary edema. On the 4 days per week that he does not receive dialysis, he has no functional limitations; however, during the evenings that follow each dialysis session, he has severe fatigue that prevents him from leaving his bed.

His predialysis blood pressure ranges from 110 to 120 systolic over 65 to 70 diastolic, he has no peripheral edema, and he has no crackles on pulmonary auscultation.

Introduction: Volume Dysfunction in Recipients of HD

For recipients of maintenance HD, finding the balance between volume overload and hypovolemia is paramount. In the case of volume overload, symptomatic heart failure and severe hypertension can result in dyspnea, cardiac events, left ventricular remodeling, and death.¹⁻³ On the contrary, hypovolemia can result in ischemic organ injury⁴⁻⁷ and debilitating symptoms including cramping, postdialysis fatigue, and cognitive changes.⁴⁻¹¹ Although possibly limited by residual confounding, a growing evidence base comprising observational studies has demonstrated associations between a variety of volume-linked metrics and adverse outcomes.^{4,8-14}

To optimize volume status among HD recipients, clinicians have depended on clinical assessment to inform an individualized ultrafiltration (UF) target that aims to have patients achieve postdialysis "dry weight" that should theoretically reflect euvolemia. Conventional practice synthesizes patient history, clinical exam, and blood pressure measurements to guide volume assessment. However, these tools are rudimentary and may provide misleading information on a patient's true volume status. We believe

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that given the high rate of hospital encounters for volume overload,¹⁵ and the high burden of hypovolemia-induced symptoms in the HD population,¹⁶ reliance on these “traditional” markers needs reevaluation. A new strategy that systematically addresses volume issues may lead to a reduction in adverse outcomes.¹⁷

Based on emerging data in the literature, we believe that volume assessment could be improved by implementing a protocolized unit-wide volume management strategy. This strategy could leverage multiple resources. First, an electronic dialysis facility record can be used to systematically identify individuals at risk of volume-related adverse events. Next, promising technological adjuncts for the assessment of volume status such as bioimpedance spectroscopy (BIS) and lung ultrasound (LUS) can be used to complement routine clinical assessment of those individuals at highest risk. Bioimpedance spectroscopy and LUS are easy-to-use techniques that are already available at our hospital and at many other HD centers, although there is no clear guidance from the literature about how these should be used in clinical practice. Finally, an interdisciplinary approach can be deployed to address proximal causes of suboptimal fluid balance that relate to nonadherence with the prescribed dialysis duration and/or dietary recommendations.

Accordingly, we designed a local volume management program with 3 components: the integration of volume metric reporting into the routine surveillance bloodwork reports, the use of technologic adjuncts to aid clinicians in volume assessment, and rigorous interdisciplinary review for those with abnormal volume metrics.

Developing Volume First! at St. Michael's Hospital

The in-center HD unit at our hospital consists of 6 daytime shifts and 2 overnight nocturnal shifts, Monday through Saturday. Each patient receives care by 1 of 4 nurse practitioners and 1 of 9 nephrologists. Dialysis pharmacists, dietitians and social workers, are deeply embedded in patient care and join nurse practitioners and physicians every 6 weeks for a detailed review of routine blood work and other dialysis-related issues at an interdisciplinary conference.

Dialysis prescriptions are adjusted as required by the primary clinical team, but the facility practice is for all patients to receive a personalized dialysate temperature that is cooled to 0.5°C below their body temperature, consistent with the protocol of the MyTEMP trial (clinical trials.gov NCT: NCT02628366).

In the summer of 2018, stakeholders were engaged in a root cause analysis to identify major causes of abnormal volume metrics in our HD unit. The output of these stakeholder interviews was a fishbone diagram, shown in Figure 1. Following this exercise, we audited our local unit to identify the frequency of each of the proposed root causes. From a sample of 4 conventional HD shifts

(approximately 140 patients), we identified 16 patients with at least 1 abnormal volume metric. We then probed each of the 16 patients (and their clinicians) to attribute the volume dysfunction to 1 to 2 proximal causes. We then created a Pareto diagram as shown in Figure 2. Three key root causes were identified as proximal causes of an abnormal volume metric in 85% of cases in the sample: high interdialytic weight gain, incorrect target weight, and missed HD sessions/cut time.

To target locally relevant root causes of volume dysfunction in our HD unit, we developed and deployed the multifaceted change strategy outlined in Figure 3 and described extensively in this report.

Since we launched this initiative unit-wide in October 2018, we have prospectively tracked the number of patients above threshold for each volume metric at 6-week intervals with an eye toward reducing the overall prevalence of patients with at least 1 abnormal volume metric over time. We are currently planning further improvement cycles focusing on ensuring consistent implementation of this multifaceted intervention.

Core Elements of the Volume First Initiative

Automatic Reporting of Volume Metrics

As part of routine clinical care, a series of blood tests are drawn at 6-weekly intervals for every outpatient receiving HD at our institution. For each dialysis shift of patients, a table is automatically generated for the interdisciplinary team to review: each row represents 1 patient, and each column contains imported lab data which aid in the routine assessment of dialysis adequacy and include traditional hematologic and biochemical markers that are of relevance to dialysis recipients. We leveraged the routine interdisciplinary review of bloodwork parameters to incorporate a review of easily measured markers of volume dysfunction.

Multiple parameters related to volume status have been shown to be associated with adverse outcomes. Of these, 3 in particular are consistently linked with important outcomes while being easy to generate from routinely collected data. These metrics include intradialytic hypotension (IDH), weight-adjusted net ultrafiltration rate (UFR), and failed target weight achievement (FTWA). The 3 metrics are partially interrelated and are listed with their prognostic implications from the published literature in Table 1.

1. Intradialytic hypotension is defined as a systolic blood pressure nadir less than 90 mm Hg affecting 40% or more HD sessions and has been identified as a high-risk prognostic marker associated with mortality, hospitalization, and incident dementia.^{4,8-11} The associated risks are higher when IDH

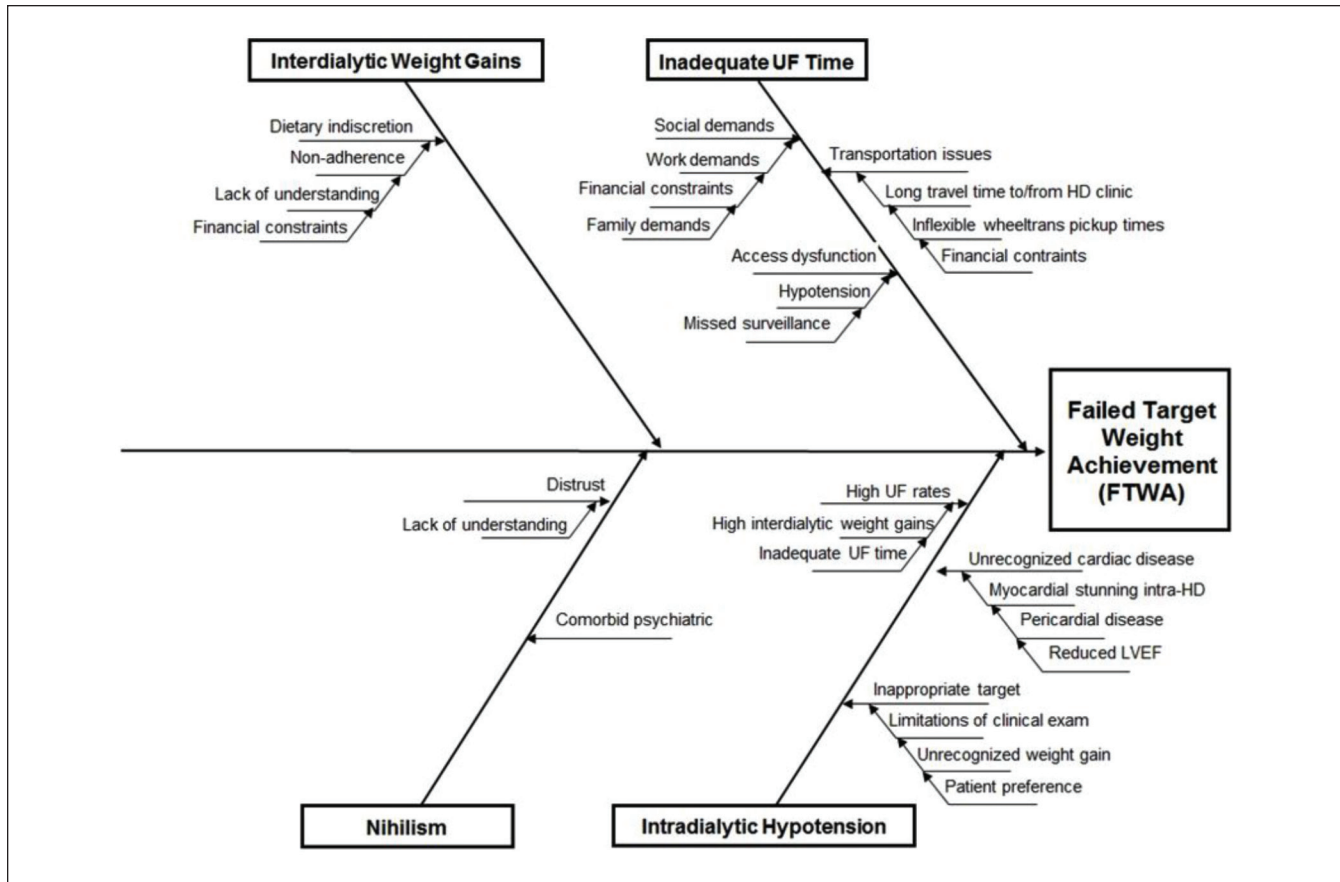


Figure 1. Fishbone (Ishikawa) diagram outlining the major root causes of abnormal volume metrics, as identified by local stakeholders. Note. HD = hemodialysis; UF = ultrafiltration.

occurs more frequently, as the risks of repeated ischemic injuries on the various organs are cumulative. Although there are a number of definitions of IDH in the literature, we selected the aforementioned definition for our initiative as it is clearly linked with outcomes (valid), easily measurable (feasible and reliable), actionable, and not gameable, which are all characteristics of a good quality metric.^{18,19}

2. Ultrafiltration rate is calculated by averaging each session-related weight-adjusted net UFR over a fixed time period (we used discrete 6-week intervals). Higher UFR has been linked to mortality, with the risk increasing exponentially when UFR is between 10 and 13 mL/h/kg and the highest risk group having UFR greater than 13 mL/h/kg.¹² High UFR, especially when it exceeds the rate of plasma refill from peripheral tissues, has been purported to induce a circulatory stress leading to ischemic injuries and contributing to poor outcomes.²⁰ This metric is valid, reliable, and actionable.
3. Failed target weight achievement, defined as having a postdialysis weight greater than 1 kg above

the ordered target weight affecting 30% or more of sessions, has been linked to both mortality and hospitalizations.^{13,14} Failed target weight achievement may occur when the estimated target weight is inappropriately low (eg, due to occult lean tissue weight gain) thus leading to hypovolemia during HD and resultant end-organ hypoperfusion; FTWA may also occur as a result of either or both of IDH and high UFR. Failed target weight achievement is valid, reliable, actionable, and acts as a safeguard to UFR which may be partially gameable. For example, to achieve a more acceptable average UFR metric, one might consider simply reducing the UFR; however, if this intervention is not coupled with an increase in treatment time or a decrease in interdialytic weight gain, FTWA will result. Thus, used together, UFR and FTWA are far less gameable than using either metric alone.

We used data that are routinely captured within our electronic medical record (NephroCare, Fresenius) to reliably generate these metrics and display them alongside routine parameters of dialysis adequacy. Patients with metrics above

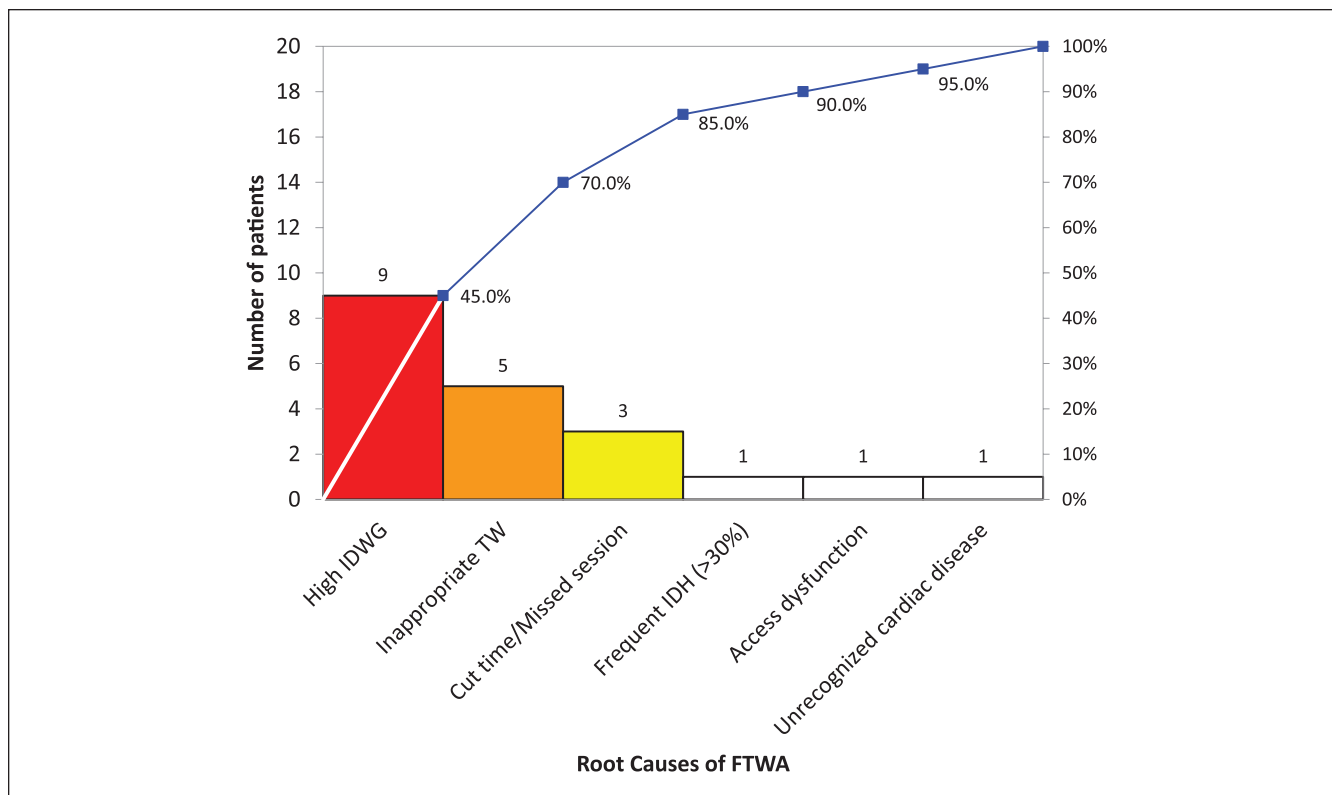


Figure 2. Pareto diagram depicting the frequency of the root causes of volume dysfunction in a sample of patients from 4 HD shifts prior to the launch of any specific interventions.

Note. HD = hemodialysis; IDWG = interdialytic weight gain (high defined as >4% of target weight); TW = target weight; IDH = intradialytic hypotension; FTWA = failed target weight achievement; UF = ultrafiltration.

any of the previously described thresholds for IDH, UFR, and FTWA can be easily identified and flagged for intervention. An example of a report provided to the interdisciplinary team at 6-week intervals is provided in Figure 4.

Returning to the Case

On the latest 6-weekly report, Mr E is found to have had IDH during 72% of sessions, a UFR of 8 mL/h/kg, and an FTWA frequency of 50%. The clinical team suspects that his severe postdialysis fatigue is related to his frequent IDH and that they could help him feel better if they could reduce this occurrence safely. Moreover, they suspect a non-UFR-related mechanism of IDH resulting in FTWA in his case. There are a number of possible non-UFR-related mechanisms that might explain his IDH including unrecognized lean tissue weight gain (ie, excessive UF goal), reduced total peripheral resistance during dialysis, and poor cardiac reserve (due to use of nondialyzable antihypertensives prescribed to treat his cardiomyopathy, his underlying poor cardiac functional status, or both). The clinical team decides to address issues of volume first and return to the bedside for a repeat clinical assessment aided by adjunctive technology.

Use of Adjunct Technologies for Fluid Status Assessment

Recently, we performed a meta-analysis of randomized control trials assessing the utility of tool-assisted volume assessment.²¹ This study showed a signal toward improved blood pressure control among patients with tool-assisted assessments. The study also showed a nonstatistically significant trend toward fewer hospitalizations, cardiovascular events, and mortality, with the use of certain tools.²¹ We were interested in technologies for which a strong rationale existed and which were readily accessible in our dialysis unit, specifically BIS and LUS.

Bioimpedance spectroscopy is a technology that may help identify subclinical extracellular volume (ECV) expansion. The output from this technology is a measure, in liters, of the extent of additional ECV water that is present beyond the expected lean tissue mass. An example of the BIS output is shown in Figure 5. Observational data suggest that the presence of BIS-measured relative ECV expansion of >15% for a dialysis recipient is associated with decreased survival as compared with a dialysis recipient with <15% relative ECV expansion.² However, only 1 interventional study using BIS to guide UF targets among HD recipients was associated

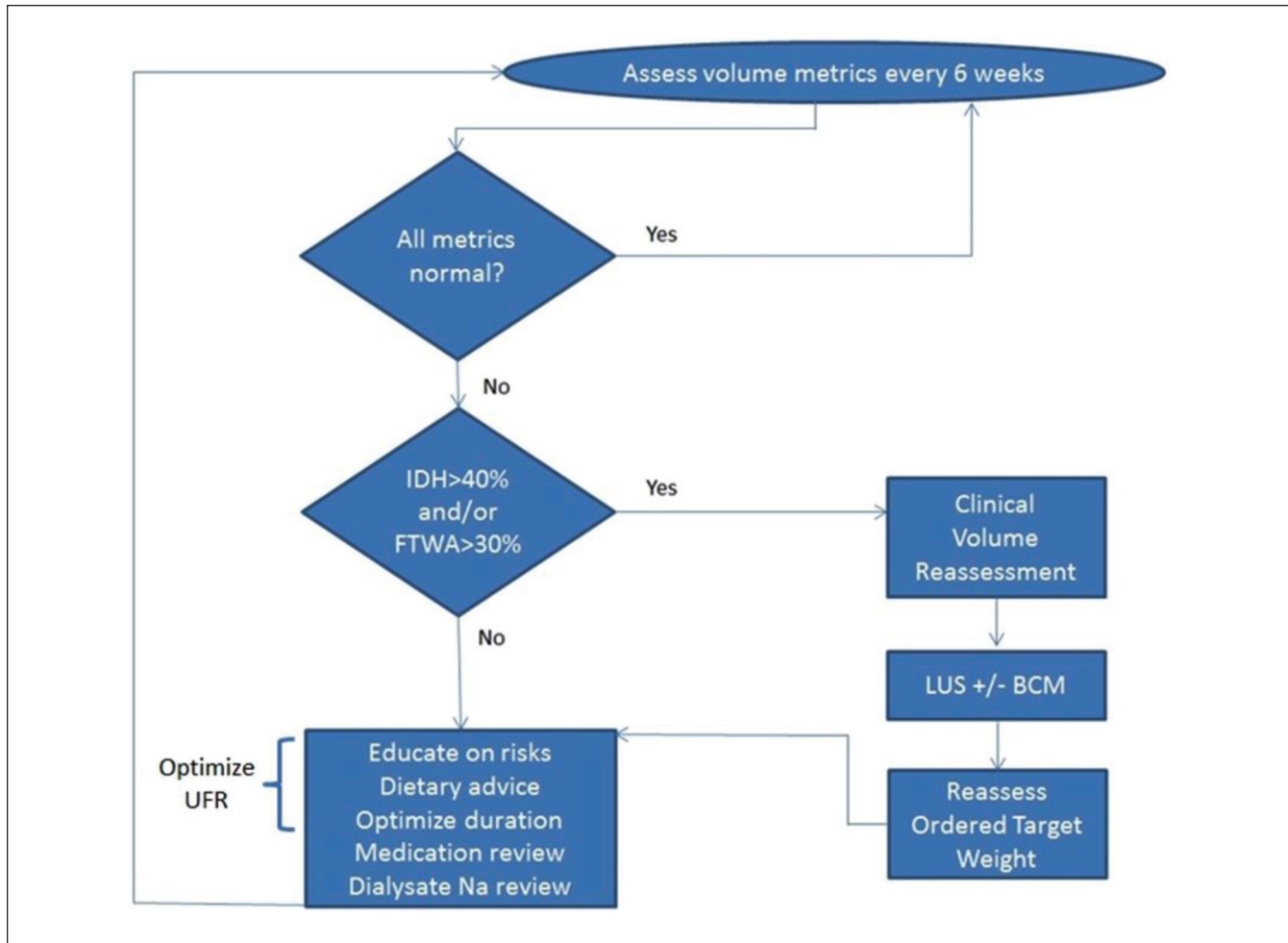


Figure 3. High-level process map detailing the approach to patients receiving maintenance in-center hemodialysis at our hospital. Note. IDH = intradialytic hypotension; FTWA = failed target weight achievement; LUS = lung ultrasound; BCM = body composition monitor (a type of bioimpedance spectroscopy used at our site); UFR = ultrafiltration rate; Na = sodium.

Table 1. Volume Metrics and Their Associated Links With Poor Outcomes When Exceeding Alarm Thresholds.

Volume metric	Alarm threshold	Associations with clinical events
Frequency of IDH	>40% of sessions >35% of sessions >30% of sessions	1.49 adjusted hazard ratio for death at 5 years ⁹ 1.5 hospitalizations per patient per year ⁴ 1.13-1.36 adjusted hazard ratio for dementia at 5 years ¹¹
Average UFR	>13 mL/kg/h	1.31 adjusted hazard ratio for death at median 2.3 years ¹²
Frequency of FTWA	>30% of sessions	1.17 adjusted hazard ratio for death at median 2.1 years ¹³ 2.3% absolute risk increase for emergency room visit within 30 days ¹⁴

Note. IDH = intradialytic hypotension defined as systolic blood pressure <90 mm Hg; UFR = ultrafiltration rate defined as ((preweight – postweight) / duration) / postweight; FTWA = failed target weight achievement defined as postweight > 1 kg above target weight.

with improved survival,²² and this has not been reproduced to date.

Lung ultrasound is another technology that may help identify subclinical volume expansion by detecting extravascular lung water which manifests as multiple “B-lines.” An example of B-lines seen on LUS is shown in Figure 6. The presence of greater than 15 B-lines in a

dialysis recipient is associated with shorter survival time as compared with a dialysis recipient with fewer than 15 B-lines.¹ Research protocols focused on using LUS to assess 28 zones, prior to dialysis, which is not pragmatic and is a barrier to its current use in routine practice despite the widespread availability of ultrasounds in dialysis clinics in Canada.

Name	Date	Avg PRU	Urea Kt/V	Urea Pre	Urea Post	Cre Pre	Alb	Ca	PO4	Na	K	Total CO2	BS	HGB	WBC	PLT	IDH	UFR	FTWA
		n/a	1.3	20.8	n/a	534	31	2.16	2.05	136	4.7	22	7.1	123	9.15	194	47%	5	7%
	69	1.1	31.3	9.7	1064	35	1.82	2.72	134	5.3	22	23.2	113	5.96	237	11%	6	11%	
	72	1.3	21.2	6	986	35	1.91	2.29	136	4.8	23	9.5	108	4.98	258	0%	6	0%	
	69	1.1	12.6	3.9	668	39	2.16	1.1	136	3.6	27	14.7	127	5.02	198	12%	4	6%	
	85	1.5	24.2	3.7	474	35	2.28	2.29	133	5.7	25	18.2	130	7.95	195	6%	8	0%	
	69	1.0	23.5	7.4	676	40	2.33	1.2	143	5.9	25	5	115	6.73	223	36%	4	31%	
	68	1.1	26.8	8.6	551	30	2.16	2.14	132	5.8	25	19.7	106	5.95	184	11%	16	17%	
	88	1.3	23.8	2.9	453	36	2.08	1.38	142	3.9	23	6.1	90	11.14	284	0%	3	0%	
	75	1.4	33.1	8.3	668	39	2.13	2.61	127	5.4	22	24.8	108	10.34	243	12%	8	38%	
	88	1.8	13.9	1.7	655	37	2.2	1.08	138	3.5	24	13.2	113	11.4	210	0%	7	0%	

Figure 4. An example of a de-identified volume metrics report.

Note. PRU = percent reduction of urea; Avg Kt/V = average on-line Kt/V readings; Alb = albumin; Ca = calcium; PO₄ = phosphate; Na = sodium; K = potassium; CO₂ = bicarbonate; BS = blood sugar; HGB = hemoglobin; WBC = white blood cell count; PLT = platelet count; IDH = intradialytic hypotension; UFR = average ultrafiltration rate in mL/h/kg; FTWA = failed target weight achievement. Bold values indicate that the metric is above an alarm threshold.

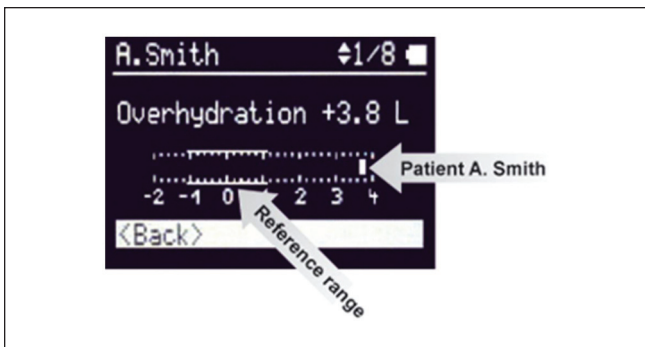


Figure 5. Output displayed for patient A Smith following BIS performed with the Body Composition Monitor (Fresenius Medical Care).

Source. Image was obtained from the Fresenius Medical Care website <http://www.bcm-fresenius.com/>.

Note. This BIS suggests that patient A Smith has a dry weight that is 3.8 L below his or her current weight. BIS = bioimpedance spectroscopy.

There has not been systematic uptake of either of these tools for several reasons: limited accessibility to appropriate devices, limited training in the proper use of these devices, limited awareness by practitioners regarding the utility of these technologies, and the absence of definitive evidence that these tools provide incremental knowledge

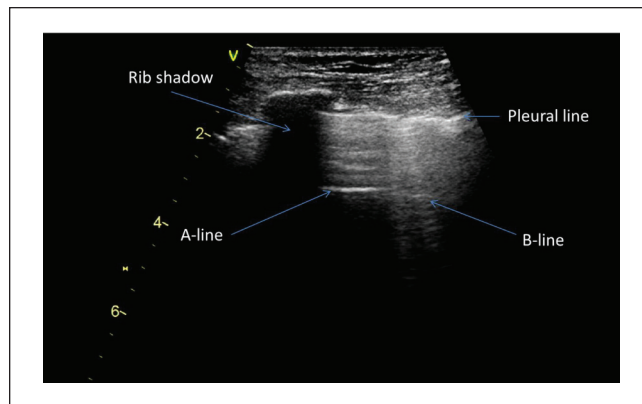


Figure 6. An image obtained from bedside lung ultrasound.

Note. Two B-lines are apparent as they radiate downward from the pleural line, obliterating the horizontal A-line.

over standard clinical assessment to reduce adverse outcomes.

Within our local volume management program, patients with IDH >40% or FTWA >30% are flagged for clinical volume reassessment with the aid of adjunctive technologies; in other words, for these high-risk patients, 1 or both of BIS and LUS are performed to help guide UF goals and target weight assessment. Bioimpedance spectroscopy is

performed just prior to the start of HD by the dietician, physician, nurse practitioner, or dialysis nurse. The BIS device estimates how far away the patient is from their dry weight. This result can be used by the clinician to help guide volume targets. The entire BIS process takes 10 to 15 minutes to complete, and training time is minimal. Bioimpedance spectroscopy is typically not performed on individuals with amputations and implanted metallic devices, although it can be safely performed for patients with ICDs.²³ Lung ultrasound is performed by the clinician using a linear or phased-array probe to detect the presence of B-lines. The presence of many B-lines increases the likelihood that a patient is above their dry weight. This result can be used by the clinician to help guide volume targets. Performance of the traditional 28-zone technique can be cumbersome and time consuming, and simplifications in other clinical settings have been shown to be equally valid.^{24,25} In our unit, we use a simplified semiquantitative eight-zone assessment which takes less than 3 minutes to perform and can be completed while the patient is receiving HD with minimal disruption. We assume extravascular lung water is present when 3 or more B-lines are seen in 3 or more of the eight lung zones, assuming at least one affected zone is present bilaterally. Fellows and new nurse practitioners are taught how to use point-of-care LUS, and we support these clinicians to improve their image acquisition and interpretation skills with oversight by a local nephrologist who has extensive training in lung ultrasonography (W.B.-S.).

For HD recipients with UFR >13 mL/kg/h who do not experience frequent IDH or frequent FTWA, a different intervention focused on interdisciplinary assessment is deployed first.

Returning to the Case

Mr E's ordered target weight is 63 kg, although at half of his sessions he leaves at 64 kg or higher. In retrospect, his target weight has remained unchanged for the last 12 weeks; it was last adjusted 1 week following hospital discharge 3 months ago. Upon clinical reassessment, he appears euvolemic. His pre-HD blood pressure is 120/80, his jugular venous pressure (JVP) is 3 cm above the sternal angle, he has no peripheral edema, and he has no crackles on auscultation. He arrives at HD weighing 65 kg. Bioimpedance spectroscopy is performed prior to HD and reports overhydration of 1 L, suggesting that his dry weight may be closer to 64 kg. Lung ultrasound is then performed just after the start of HD and only 1 single B-line in total is identified among the 8 lung zones assessed. The clinical team suspects that he has had unrecognized weight gain in the interval since his discharge from hospital. They adjust his ordered target weight to 64 kg and his session-related UF goal is accordingly adjusted downward. In the 6 HD sessions of the following 2 weeks,

he has only 1 episode of IDH. Two weeks later, he reports no additional dyspnea and notes that his post-HD fatigue has improved in that he now only rests in bed for 3 hours after HD in the evenings following dialysis.

Interdisciplinary Assessment

As the last component of our volume management program, for all patients with at least 1 abnormal volume metric, an interdisciplinary approach is deployed with the intention of educating and empowering patients to improve their individual volume-related risk. Beyond education, specific prompts act as reminders for clinicians to (1) provide individualized dietary advice on sodium and water restriction, (2) address barriers to adherence with dialysis duration (and consider extended hours of HD if appropriate and available), (3) review medications for those that may stimulate thirst (eg, medications with anticholinergic effects such as dimenhydrinate or diphenhydramine) or contribute to hypotension during HD (eg, nondialyzable antihypertensive agents such as carvedilol), and (4) review dialysate Na prescription to avoid Na loading or profiling which may contribute to excess interdialytic weight gain (with a prompt to consider matching dialysate Na to the most recently measured serum Na).

The interdisciplinary intervention is detailed along with each component of our volume management program within the high-level process map shown in Figure 3.

Returning to the Case

Mr E meets with the interdisciplinary team and is educated on the risks of volume dysfunction. His interdialytic fluid gains are noted to be consistently 2% of total body weight which is less than 4% and therefore not considered excessive. He is offered extended hours of HD in the hopes that the remaining episodes of IDH would resolve by further reducing his UFR; he declines, telling the clinical team that he already spends enough time in the HD unit. The team reviews his medications and notes that he takes carvedilol, a nondialyzable and possibly cardioprotective beta-blocker and antiarrhythmic. They then engage him and his usual cardiologist in a discussion of the risks and benefits of switching to a more dialyzable beta-blocker such as metoprolol or bisoprolol to further minimize IDH. Although there is some older evidence that carvedilol may improve outcomes among dialysis recipients with reduced ejection fraction,²⁶ more recent data suggest that carvedilol use may result in more frequent IDH and reduced survival as compared with metoprolol.²⁷ In the subsequent 6-week interval, Mr E's IDH frequency drops to 27%, UFR remains 8 mL/h/kg, and FTWA falls to 15%; he reports that his postdialysis fatigue has improved to the point he could now host guests in his home on the evenings following dialysis.

Discussion

Although observational studies convincingly demonstrate that abnormal volume metrics are associated with adverse outcomes, we are unaware of any programs to systematically address volume dysfunction in Canada. We describe the design and implementation of a multistep program to manage volume dysfunction that comprises systematic reporting, investigation, and intervention.

We used routinely collected data from the electronic record to generate volume metrics of clinical significance. By linking review of these metrics to well-established reviews of surveillance bloodwork, we have developed a context to heighten awareness of frequent IDH, high UFR, and frequent FTWA. Although we encourage clinicians to routinely monitor for IDH and other markers of volume dysfunction, generating summary metrics at 6-week intervals has provided a failsafe for quality control and an opportunity for a structured review of volume data that did not previously exist.

We provided precise guidance to clinicians for the systematic evaluation of patients with abnormal volume metrics that incorporated BIS and LUS as adjunctive technologies. Although the current evidence base has not definitively shown that using these technological adjuncts improve clinical outcomes among all-comers receiving HD, we believe that when properly applied, these techniques can enhance the information provided by history and physical exam, which represent the current standard of care for determination of volume status. As applying BIS and LUS to every patient in the unit is neither practicable nor necessary, we targeted assessments to individuals with abnormal volume metrics, in whom the findings are most likely to inform decision-making.

Our protocol marshals the complementary expertise of the different health disciplines who care for HD recipients. Education on the risks of fluid excess, dietary advice to limit high interdialytic fluid gains, and evaluating and addressing the root causes of shortened HD durations are essential strategies that can lower a patient's average net UFR. Reviewing the indication and timing of antihypertensive medications and reassessing, the dialysate composition can avoid iatrogenic causes of frequent IDH and high interdialytic fluid gains. Our local experience has confirmed the feasibility of incorporating adjunctive technologies, such as BIS and LUS, into local practice.

Our program has a number of limitations. First, our system-wide identification of patients with volume dysfunction occurs at 6-week intervals and not in "real-time"; this may delay the identification of patients with de novo abnormal metrics and the reassessment of patients with known volume dysfunction. Second, the alarm threshold values for each volume metric is supported by observational data and it is possible that closer attention to individuals whose values do not exceed these thresholds

would result in better outcomes. Third, our use of adjunctive technologies is based on a belief that these tools are likely to have benefit in those with abnormal volume metrics. It is possible that systematic assessment of all patients (eg, monthly BIS) in a dialysis program, irrespective of volume metrics, would provide actionable information that would alter prescriptions and improve outcomes. Fourth, the performance and interpretation of LUS is dependent on both the availability of ultrasound and the technical skills of the operators which may impact the immediate generalizability of our program to other centers in Canada. Fifth, our focus on avoiding volume dysfunction may have unintended consequences; for example, in some cases, we may be trading a reduction in IDH for an increase in interdialytic ambulatory blood pressure. Based on the current evidence base, it is unclear whether this trade-off leads to improved clinical outcomes. Last, our experience is limited by the fact we work at a single center, and it is likely that the root causes of volume dysfunction at other facilities will be different than those at our own.

To our knowledge, there are 2 trials that are currently recruiting patients to investigate tools used to guide UF targets. The Using Intradialytic Blood Pressure Slopes to Guide Ultrafiltration (IBPS, NCT03303391) trial is testing whether using relative blood volume (RBV) technology to guide UF targets can improve ambulatory blood pressure control. Although RBV technology is promising, a crossover trial from a Canadian group showed that RBV biofeedback was ineffective at preventing IDH.²⁸ The Lung Water by Ultrasound Guided Treatment in Hemodialysis Patients (The LUST Study, NCT02310061) is the second interventional trial currently recruiting patients. This trial is testing whether using predialysis point-of-care LUS to guide UF targets can reduce the risk of death, myocardial infarction, heart failure, and hospitalizations. A substudy of the LUST trial was recently published²⁹ which showed that LUS-guided UF prescriptions can reduce home blood pressures over the course of 8 weeks among a group of HD recipients with uncontrolled ambulatory hypertension; interestingly, in achieving better control of ambulatory blood pressure, there was no increase in the number of episodes of IDH.

One multicenter randomized trial sought to assess whether BIS-guided fluid management would improve survival and reduce the risk of major vascular events and heart failure (BOCOMO, NCT01509937); however, no results have been published despite the study's completion in 2015.

To our knowledge, we are the first program in Canada to go beyond a simple policy for reassessment of UF targets and incorporate routine volume metric reporting into standard practice with an eye toward reducing its prevalence in a systematic way. Although reducing the prevalence of abnormal volume metrics has not been definitively shown to improve

clinical outcomes, we believe that there is robust rationale for our approach. We look forward to conducting rigorous testing in the future to demonstrate our program's effect on important patient outcomes such as quality of life, hospitalizations, cardiovascular events, and mortality.

Ethics Approval and Consent to Participate

This initiative was formally reviewed by institutional authorities at St. Michael's Hospital and deemed to neither require Research Ethics Board approval nor written informed consent from participants.

Consent for Publication

All authors consent to the publication of this study.

Availability of Data and Materials

Materials related to this initiative can be made available by the authors upon email request.

Declaration of Conflicting Interests

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