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KDIGO Controversies Conference on Blood Pressure & Volume Management in Dialysis

**February 7-10, 2019
Lisbon, Portugal**

Kidney Disease: Improving Global Outcomes (KDIGO) is an international organization whose mission is to improve the care and outcomes of kidney disease patients worldwide by promoting coordination, collaboration, and integration of initiatives to develop and implement clinical practice guidelines. Periodically, KDIGO hosts conferences on topics of importance to patients with kidney disease. These conferences are designed to review the state of the art on a focused subject and to ask conference participants to determine what needs to be done in this area to improve patient care and outcomes. Sometimes the recommendations from these conferences lead to KDIGO guideline efforts and other times they highlight areas for which additional research is needed to produce evidence that might lead to guidelines in the future.

Background

Increasing evidence over the last decade has highlighted blood pressure (BP) and fluid volume status as key mediators of poor outcomes among individuals receiving maintenance dialysis.¹⁻⁶ Concomitantly, the dialysis community has begun to expand the definition of “adequate dialysis”, a concept traditionally defined by small molecule clearance, to other aspects of dialysis care, including BP and volume management.^{1,7} In the first of four planned KDIGO dialysis controversies conferences (Dialysis Initiation, January 2018), participants proposed a paradigm shift toward a culture of more individualized or personalized dialysis care. In this second dialysis conference, we will build on the Dialysis Initiation Conference by considering how BP and volume status management can be optimized and individualized across dialysis modalities and resource settings. In doing so, we will consider existing evidence and approaches but also look to the future to identify promising new technologies and gaps in knowledge that demand dedicated research.



Relevance of the Topic

Blood pressure and volume control are critical components of dialysis care. However the absence of widely available, accurate and objective measures of extracellular volume status in addition to the lack of high quality evidence for therapeutic interventions have hampered efforts to develop consensus best practices. As such, practice patterns related to BP (i.e. optimal BP targets, non-pharmacologic and pharmacologic management) and volume-related aspects of the dialysis prescription (i.e. treatment time, ultrafiltration rate, dialysate composition and extracellular volume status assessment) vary widely across the world. There is also substantial variation in uptake of volume-relevant dialysis technologies including but not limited to hemodiafiltration, temperature biofeedback, bioimpedance, blood volume monitors, and remote home treatment monitoring. Furthermore, qualitative data suggest that patients bear substantial symptom burdens that, in part, stem from suboptimal BP and volume management.^{8,9,10} Similarly, patients have cited dietary restrictions, common reflex volume mitigation strategies, as having deleterious effects on quality of life.¹¹ These volume-related patient burdens often go unrecognized by providers,^{9,12} suggesting that more individualized dialysis prescriptions must also account for patient symptoms and preferences.

Conference Overview

The KDIGO Controversies Conference on Blood Pressure (BP) and Volume Management in Dialysis will examine BP measurement and targets for individuals receiving maintenance dialysis; pharmacologic interventions for BP abnormalities; dialysis prescriptions as they relate to BP and volume; extracellular volume assessment and management with a focus on technology-based solutions; and volume-related patient symptoms and experiences. The objectives of this conference are to assess the current state of knowledge related to BP and volume management and identify existing and future opportunities to improve related clinical and patient-reported outcomes among individuals receiving maintenance dialysis.



Drs. Jenny Flythe (University of North Carolina, USA) and Kevan Polkinghorne (Monash University, Australia) will co-chair this conference. The format of the conference will involve topical plenary session presentations followed by focused discussion groups that will report back to the full group for consensus building. This highly interactive conference will invite key thought leaders and relevant stakeholders, including patients, in nephrology and other related disciplines who will comprehensively review the literature and current state of understanding in this area, and address clinical issue as outlined in the **Appendix: Scope of Coverage**. The conference output will include publication of a position statement that will help guide KDIGO and others on management and future research in this area. There will be four working groups that will each address:

Group 1	BP Measurement and Targets and Pharmacologic Approaches to BP and Volume Management Among Individuals Receiving Maintenance Dialysis
Group 2	The Dialysis Prescription as it Relates to BP and Volume
Group 3	Extracellular Volume Management and Technology-Based Considerations Relevant to Volume Management
Group 4	Volume-Related Patient Symptoms and Experiences and Non-pharmacologic Interventions for BP and Volume Abnormalities



APPENDIX: SCOPE OF COVERAGE

Group 1: Blood Pressure (BP) Measurement and Targets and Pharmacologic Approaches to BP and Volume Management Among Individuals Receiving Maintenance Dialysis

BP Measurement

1. How and when should BP be measured among individuals receiving dialysis?
 - a. What approach, if any, is considered the gold standard to measure BP among individuals receiving dialysis? What are the barriers to implementing the gold standard method of BP measurement?
 - b. When gold standard measurements are not available/feasible, what alternative BP measurements should be used to diagnose hypertension?
 - c. Do the answers to questions 1a-1b differ by dialysis modality (e.g., in-center hemodialysis (HD), home HD, peritoneal dialysis (PD))?

Definitions of Hypertension and Intradialytic Hypotension and Hypertension

2. What is the threshold for the diagnosis of hypertension among dialysis patients (include discussion of existing guideline definitions)?
 - a. Does this threshold vary depending on BP measurement technique?
 - b. Does this threshold apply irrespective of dialysis modality? Across all patients? If not, how should thresholds be individualized?
3. What is the optimal definition of intradialytic hypotension (include discussion of existing guideline definitions)? Based on what evidence?
 - a. Does this definition apply across dialysis modalities- HD and PD?
4. What is the optimal definition of intradialytic hypertension (include discussion of existing guideline definitions)? Based on what evidence?
 - a. Does this definition apply across dialysis modalities- HD and PD?
5. What is the definition of BP variability? Based on what evidence?
 - a. Does this definition apply across dialysis modalities- HD and PD?



- b. What approach, if any, is considered the gold standard approach to measuring BP variability? When gold standard measurements are not available/feasible, what alternative measurements should be used?
- c. What is the evidence supporting an association between BP variability and outcomes?
- d. Can and should BP variability be targeted for identification and intervention among dialysis patients?

Pharmacologic Approaches to BP and Volume Abnormalities

- 6. When should anti-hypertensive agents be used?
- 7. How should anti-hypertensive agents be selected?
 - a. Comparative effectiveness of anti-hypertensive agents?
 - b. What anti-hypertensive agents have been shown to improve cardiovascular outcomes (e.g. left ventricular hypertrophy/left ventricular mass, myocardial infarction, cardiovascular mortality) or all-cause mortality in patients receiving dialysis?
 - c. Regardless of their effect on BP, what is the role of diuretics in volume management?
 - d. How does dialysis modality factor into anti-hypertensive agent selection (e.g. removal by dialysis)?
 - e. What anti-hypertensive agent strategies should be used to treat intradialytic hypertension?
 - f. How can anti-hypertensive therapy strategies be individualized?
- 8. What is the optimal timing of anti-hypertensive administration?
 - a. How does dialysis modality factor into timing of anti-hypertensive agent administration?
- 9. What gaps remain in our understanding of antihypertensive medications in dialysis and what type(s) of research is (are) needed to fill these gaps?
- 10. Should pharmacologic agents be used to raise BP?

- a. If, yes, in what clinical situations and what agents? If, no, why, and what are alternative management strategies?
- b. Comparative effectiveness of BP-raising agents?

Group 2: The Dialysis Prescription as it Relates to BP and Volume

Prevention and Management of Intradialytic Hypotension and Hypertension

1. How might the hemodialysis (HD) prescription (centre HD and home HD) be modified to prevent intradialytic hypotension? *[Note: the definition of intradialytic hypotension will be covered by group 1 and should be omitted from discussion.]*
2. How might the peritoneal dialysis (PD) prescription be modified to prevent hypotension (chronic and acute)?
 - a. How should these strategies be individualized?
3. What are the current recommendations for non-pharmacologic management of intra-hemodialytic hypotension (centre HD and home HD)?
 - a. How should preventive intra-hemodialytic hypotension strategies be individualized?
4. How might the HD prescriptions (centre HD and home HD) be modified to prevent/control intradialytic hypertension? *[Note: the definition of intradialytic hypertension will be covered by group 1 and should be omitted from discussion.]*
5. How might the peritoneal dialysis (PD) prescription be modified to prevent/control hypertension?
 - a. How should these strategies be individualized?
6. Outside of dietary restrictions, what are the current recommendations for non-pharmacologic management of intra-hemodialytic hypertension (centre HD and home HD)?



- a. How should preventive intradialytic hypertension strategies be individualized?

Ultrafiltration Rate, Treatment Time and Residual Kidney Function

7. Is there an optimal ultrafiltration rate for HD?
 - a. What role, if any, is there for ultrafiltration profiling, and/or sequential therapy (ultrafiltration only, then ultrafiltration + dialysis) in HD?
 - b. How should the potential risks from higher HD ultrafiltration rates be balanced with the risks from volume overload (a potential consequence of lower ultrafiltration rates)?
 - c. What are the best strategies to lower ultrafiltration rates?
 - d. How can ultrafiltration rates be lowered in resource-constrained environments with limited run-times and few home therapy options?
8. What factors should be considered when prescribing HD treatment time?
 - a. Is there an optimal HD treatment time independent of ultrafiltration rate?
 - b. How does one reconcile the international differences in HD treatment times?
9. With regard to ultrafiltration in PD:
 - a. Is there an optimal ultrafiltration rate with the PD solutions of different glucose concentrations and glucose polymer PD solutions?
 - b. How does peritoneal membrane function factor into ultrafiltration? How should it be assessed?
 - c. How does choice of PD modalities (CAPD vs. automated PD) influence the ultrafiltration and factor into volume management?
10. How does residual kidney function (RKF) factor into volume management in both PD and HD?
 - a. Should RKF be measured routinely? If so, by what methods and how often?
 - b. What strategies can be used to preserve RKF (consider all modalities)?

Dialysate Composition and Prescription

11. What are the strategies for HD dialysate composition manipulation to optimize BP and volume control? [e.g. sodium, potassium, calcium, dialysate temperature]
12. What are the strategies for PD solution manipulation to optimize BP and volume control? [e.g. glucose concentration, non-glucose osmotic agents]

Group 3: Extracellular Volume Management and Technology-Based Considerations Relevant to Volume Management

Extracellular Volume Measurement

1. How should extracellular volume status be measured? [Consider in the absence of and presence of technology aids and consider all dialysis modalities]
 - a. How often? By whom? What training is required?
 - b. Does this differ across modalities?
 - c. Do comorbid medical conditions affect the accuracy extracellular volume status measurement and influence any associated clinical decision-making?
2. What are the existing and on-the-horizon tools for extracellular volume assessment?
 - a. What is the quality of their supporting evidence?
 - b. What are the barriers to their use in clinical practice and how can they be overcome?
 - c. What factors contribute to international differences in clinical uptake of such tools?
 - d. Are there inexpensive, readily available tools that could be implemented in resource-constrained environments? Are the relative cost effectiveness of different tools defined?



Intradialytic Volume-Related Technologies

3. How might different dialytic strategies be used for BP and volume management? When relevant, consider how such technologies might be implemented. *[Note: the dialysate composition will be covered by group 2 and should be omitted from discussion.]*
 - a. Hemodiafiltration (All forms including Pre, Post, Mixed, & Mid- Dilution, Mixed and Intermittent Infusion HDF?)
 - b. Temperature biofeedback?
 - c. Blood volume monitoring
 - d. Ultrafiltration profiling?
 - e. Isolated ultrafiltration?
 - f. Bioimpedance?
 - g. Others?

4. How might technology be used to reliably identify individuals at risk for impending clinical complications (e.g. intradialytic hypotension) and thereby reduce downstream clinical events including hospitalizations and death?

Home-Based Monitoring Technologies

5. How might home-based monitoring be used to improve BP and volume management among individuals on home-based therapies? Is there a role for home-based monitoring among centre-based patients?

6. What type of roles might wearable health technologies (existing or future) play in BP and volume management?

Group 4: Volume-Related Patient Symptoms and Experiences and Non-Pharmacologic Interventions for BP and Volume Abnormalities

1. What clinical symptoms plausibly relate to volume aberrations and/or BP aberrations among dialysis patients (consider all modalities; potential symptoms include: edema, breathlessness, thirst/dry mouth, cramping, etc.)?



- a. How strong is the evidence supporting these associations?
 - b. What types of additional research are needed to establish associations between symptoms and aspects of BP and/or volume management?
 - c. Do such symptoms vary by patient-specific factors and health conditions?
 - d. How should these symptoms be assessed/ measured? By whom? At what frequency?
 - e. How should these symptoms be managed?
2. How should volume-related symptom considerations be incorporated into dialysis prescriptions?
- a. How should patient-reported symptoms be factored into decisions about maximum volume removal, ultrafiltration rates or treatment time?
 - b. Could symptom-driven treatment decisions have unintended consequences for other aspects of BP and/or volume control?
 - c. How might the dialysis prescription (all modalities) be altered to mitigate symptoms?
 - d. How do we negotiate potential conflicts between meeting clinical benchmarks (e.g. clearance threshold) and patient symptoms (e.g. cramping or prolonged recovery time with longer treatments)?
 - e. How can the interdisciplinary care team be used to overcome these conflicts and challenges?
3. Should patient-reported outcomes/ experiences be used to rate the quality of volume management at a dialysis clinic/ program?
- a. Are there symptom measurement tools? (How should symptoms be assessed and with what instruments?)
 - b. How can metrics be individualized to avoid a “one-size-fits-all” approach?
4. What role do fluid and salt restrictions have in BP and/or volume management?
- a. What, if any, are the best evidence-based approaches for dietary restriction counseling/motivation/education?
 - b. How do dietary restrictions influence patient quality of life/ life satisfaction?



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- c. How might patients be empowered to adhere to dietary restrictions?

5. What role does exercise (interdialytic or intradialytic) have in BP and/or volume management?

6. How do we balance volume-related dietary restrictions and nutritional status?
 - a. Does the balance vary by patient characteristics (e.g. child, pregnancy, residual kidney function, frailty)?



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