A Novel Hypertension Management Algorithm Guided by Hemodynamic Data

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INTRODUCTION

Hypertension affects approximately one-third of adult Americans (~67 million). Only an estimated 43.7% of patients with hypertension achieve target blood pressure (BP).1 This number is significantly lower for patients with chronic kidney disease (CKD) and resistant hypertension.2 Current hypertension management guidelines permit a range of options regarding the selection of antihypertensive agents which contributes to variable practice patterns.3,4 Moreover, practitioners usually adopt suboptimal trial and error approaches when treating patients with hypertension. In addition, patients with hypertension do not respond uniformly to antihypertensive therapies because hypertension is a heterogeneous hemodynamic disorder.5

Bioimpedance or impedance cardiography (IC) is a novel tool in the management of hypertension with most of these studies using thoracic IC technology.6 Unfortunately, patients with CKD have been excluded from most of these reports. To address this gap, we undertook a pragmatic continuous quality improvement project in a real-world nephrology practice setting evaluating the use of hemodynamic parameters obtained using NICaS (a noninvasive cardiac system; Supplementary Appendix S1), a regional IC technology, to individualize the management of patients with hypertension and CKD.

RESULTS

A total of 93 patients were included in the analysis: 73 in the study group and 20 controls. Demographic characteristics did not differ significantly between the groups (Supplementary Table S1). The mean (SD) age was 60.5 (16.4) years for the study patients and 63.3 (10.7) years for the controls. Diabetes was present in 38.4% of the study patients and 30.0% of the controls, and approximately two-thirds had CKD stage 2. By design, the study patients had a significantly higher mean number of NICaS tests than the controls: 2.6 vs. 2.0, \( P < 0.001 \). For the study group, hemodynamic data obtained using NICaS were used in the selection and titration of antihypertensive medications according to a predetermined algorithm (Supplementary Table S2).

The hemodynamic profiles of the groups at baseline and final time points are illustrated in Supplementary Figure S1. At baseline, 41.1% of the study group patients had vasoconstricted physiology, 41.1% had mixed hemodynamics, and 17.8% were hyperdynamic. There were no significant differences in baseline hemodynamic profiles. At final analysis, 68.5% (50 of 73) of the study group patients achieved a normal physiological profile compared with 35.0% (7 of 20) of the controls (\( P = 0.006 \)).

Table 1 reveals a comparison of baseline and final BP and hemodynamic parameters. Figure 1 illustrates the percentage of patients who met their respective BP goal at the final analysis. Given the “real world” nature of this project, BP values clinically close to the “hard” target of 130/80 mm Hg (e.g., 133/83 mm Hg) could be deemed acceptable with no change in treatment. Patients meeting these doctor-adjudicated situations were considered to meet their “soft target.” Mean baseline BP for both groups was statistically similar: 161.2/89.8 mm Hg (study) versus 163.4/89.8 mm Hg (control). There was a significantly greater drop in systolic, diastolic, and mean BP from baseline for the study patients than the controls. The study patients had a
mean (SD) decrease in systolic BP of 24.2 (15.6) mm Hg compared with 14.5 (21.4) mm Hg in the controls (P = 0.025) along with a significantly greater mean (SD) decrease in diastolic BP of 12.8 (10.1) mm Hg versus 7.3 (9.7) mm Hg, P = 0.031 and mean arterial pressure of 16.4 (10.8) mm Hg versus 9.5 (12.7) mm Hg, P = 0.018. Significantly more patients in the study group met the hard target criteria: 57.53% versus 25.00%, P = 0.010, and for the soft target of 130/80 mm Hg at 50.88% versus 15.38%, P = 0.029 (Supplementary Table S3). Compared with the controls, a greater percentage of patients without CKD achieved the target: 81.25% versus 28.57% (P = 0.026). Within-group vital signs and hemodynamic data at baseline and final time points are found in Supplementary Table S4. Changes in central hemodynamic parameters are reported in Supplementary Tables S5 and S6.

The percentage of study group patients who had resistant hypertension, defined by uncontrolled BP despite 3 antihypertensives including a diuretic, was 13.7% versus 15.0% in the control group. There were no differences between the groups at study end regarding medication classes or number of antihypertensive medications (Supplementary Table S7). Nevertheless, significantly more patients in the study group compared with baseline were on select medications. There were no significant differences in the percentage of patients at baseline and final analysis in either group treated with thiazide or loop diuretics.

**DISCUSSION**

Previous studies suggested that management strategies incorporating hemodynamic data may be superior to standard care.51-53 Our findings confirm these results and reveal the feasibility and effectiveness of incorporating hemodynamic data derived from the validated7-9 NICaS bioimpedance system in the management of hypertension in patients with and without CKD in a clinical practice setting. The NICaS bioimpedance technology has greater accuracy and9 provides somewhat different hemodynamic information compared to thoracic IC because it measures blood flow and arterial resistance in the periphery rather than centrally. Neither technology accurately measures blood volume. The hemodynamic patterns observed here are notably heterogeneous.54 Further research is needed to reveal whether normalization of hemodynamic parameters confers additional cardiovascular benefits beyond those of BP control.

We did not observe an increase in the use of thiazide or loop diuretics at the final period in contrast with the findings of Taler et al.51 The difference may be partly explained by differences in the cohorts; our cohort had a smaller proportion of patients with resistant hypertension.

**Table 1. Blood pressure and hemodynamic variables within the study and control groups at baseline and final time points**

| Variables, mean (SD) or n (%) | Study group at baseline n = 73 | Study group at final point n = 73 | P values comparing study group baseline with final points | Control group at baseline n = 20 | Control group at final point n = 20 | P values comparing control group baseline with final point |
|-----------------------------|-------------------------------|---------------------------------|----------------------------------------------------------|-------------------------------|-------------------------------|----------------------------------------------------------|
| SBP                         | 161.2 (15.6)                 | 137.0 (15.4)                   | <0.001                                                   | 163.4 (16.4)                 | 148.9 (18.9)                 | 0.007                                                   |
| DBP                         | 89.8 (12.0)                  | 77.0 (11.7)                    | <0.001                                                   | 88.8 (11.6)                 | 82.5 (18)                    | 0.003                                                   |
| MAP                         | 113.3 (9.9)                  | 97.0 (11.0)                    | <0.001                                                   | 113.9 (9.1)                 | 104.4 (10.7)                 | 0.003                                                   |
| HR                          | 78.0 (13.0)                  | 76.5 (11.2)                    | 0.301                                                    | 74.2 (17.8)                 | 74.9 (12.4)                  | 0.840                                                   |
| BMI                         | 31.1 (7.8)                   | 31.4 (8.1)                     | 0.271                                                    | 31.3 (5.3)                  | 31.3 (5.3)                   | 0.466                                                   |
| SI                          | 39.0 (8.8)                   | 41.9 (11.0)                    | 0.020                                                    | 38.2 (9.5)                  | 39.7 (7.6)                   | 0.466                                                   |
| CI                          | 3.0 (0.9)                    | 3.2 (1.0)                      | 0.216                                                    | 2.8 (0.8)                   | 3.0 (0.7)                    | 0.295                                                   |
| CPI                         | 0.8 (0.2)                    | 0.7 (0.2)                      | 0.009                                                    | 0.7 (0.2)                   | 0.7 (0.2)                    | 0.677                                                   |
| TPRI                        | 3193.3 (863.1)               | 2612.3 (755.8)                 | <0.001                                                   | 3549.8 (1151.9)             | 2972.3 (779.1)               | 0.002                                                   |

BMI, body mass index; CI, cardiac index; CPI, cardiac power index; DBP, diastolic blood pressure; HR, heart rate; MAP, mean arterial pressure; SBP, systolic blood pressure; SI, stroke index; TPRI, total peripheral resistance.

**Figure 1.** The graph illustrates the % of patients who met their respective hard or soft blood pressure goal at the final time point of the study period.
hypertension. Yet, given the significant percentage with CKD in our study, it is still surprising. It is possible that the assessment of total body water and effective volume status using the regional versus thoracic IC techniques provided conflicting data regarding fluid status. We observed a significant increase in the use of angiotensin receptor blockers in the treatment arm. We also noted significantly underpowered though we observed statistically control group is small and our inferences were potentially underpowered though we observed statistically significant differences between groups in many key variables. This pragmatic project includes the possibility of bias based on physician practice styles and treatment effect. Another limitation is that the assessment of volume status using IC has not been validated in hypertensive cohorts. Therefore, it is possible that our definition of hypervolemia underestimated the percentage who may have responded to diuretic therapy. Finally, we did not exclude patients with congestive heart failure whose management is complicated by episodes of decompensation with more loop diuretics and/or holding renin angiotensin system inhibitors with increasing creatinine and/or potassium. Consequently, our findings may not be generalizable to this subpopulation of patients with hypertension.

In summary, this pragmatic continuous quality improvement program reveals the feasibility and effectiveness of a hemodynamically directed management algorithm to individualize hypertension management in a busy nephrology practice. This approach was associated with improved brachial and central BP control and normalization of cardiovascular hemodynamics in a cohort of patients with and without CKD. Although this study is hypothesis generating, the results suggest that hemodynamically guided hypertension management may result in more patients achieving target BP and improved physiology.

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**AVAILABILITY OF DATA AND MATERIALS**

Data and materials may be made available on written request to the corresponding author.

**AUTHOR CONTRIBUTIONS**

MJG, BAC, and YC designed the project. MJG and BAC supervised the clinical aspects of the project. YC collected and validated the data. BHN performed the statistical analysis. MJG, BAC, and YC drafted the manuscript. All authors reviewed the manuscript and contributed important intellectual portions of the study. All authors approved the final version of the manuscript.

**SUPPLEMENTARY MATERIAL**

Supplementary File (PDF)

Supplemental Methods.

Appendix S1. Regional bioimpedance cardiography (NiCaS) measurements.

Table S1. Demographics of the study cohort.

Table S2. Algorithm for the management of hypertension by hemodynamic profile.

Table S3. In-target blood pressure results at baseline and final time points.

Table S4. Vital signs and hemodynamic data at baseline and final time points.

Table S5. Comparisons of central blood pressure and pulse wave analysis results within the study and control groups at baseline and final time points.

Table S6. Central blood pressure and pulse wave analysis at baseline and final time points.

Table S7. Antihypertensive medication classes within the study and control groups at baseline and final time points.

Figure S1. Hemodynamic profiles of the study and control groups at baseline and final time points. Red triangles, black circles, and blue squares represent means of SBP, MAP, and DBP for the entire group (irrespective of BP target), respectively.

**Supplementary References.**

**REFERENCES**

1. Muntner P, Harding ST, Fine LJ, et al. Trends in blood pressure control among US adults with hypertension, 1999-2000 to 2017-2018. J Am Med Assoc. 2020;324:1190-1200. https://doi.org/10.1001/jama.2020.14545

2. Braam B, Taler S, Rahman M, et al. Recognition and management of resistant hypertension. Clin J Am Soc Nephrol. 2017;12:524-535. https://doi.org/10.2215/CJN.06180616

**DISCLOSURE**

BG and MJG report receiving funding, through their medical practice, from NiMed. All the other authors declared no competing interests.
3. Unger T, Borghi C, Charchar F, et al. 2020 International Society of Hypertension Global Hypertension Practice Guidelines. Hypertension. 2020;75:1334–1357. https://doi.org/10.1161/HYERTENSIONAHA.120.15026

4. Whelton PK, Carey RM, Aronow WS, et al. 2017. ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines [published correction appears in J Am Coll Cardiol. 2018;71:2275–2279]. J Am Coll Cardiol. 2018;71:e127–e248. https://doi.org/10.1016/j.jacc.2017.11.006

5. Dhruva SS, Huang C, Spatz ES, et al. Heterogeneity in early responses in ALLHAT (Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial). Hypertension. 2017;70:90–102. https://doi.org/10.1161/HYERTENSIONAHA.117.09221

6. Ferrario CM, Flack JM, Strobeck JE, Smits G, Peters C. Individualizing hypertension treatment with impedance cardiography: a meta-analysis of published trials. Ther Adv Cardiovasc Dis. 2010;4:5–16. https://doi.org/10.1177/1753944709348236

7. Paredes O, Shite J, Shinke T, et al. Impedance cardiography for cardiac output estimation: reliability of wrist to ankle electrode configuration. Circ J. 2006;70:1164–1168. https://doi.org/10.1253/circj.70.1164

8. Cotter G, Moshkovitz U, Kaluski E, et al. Accurate, noninvasive continuous monitoring of cardiac output by whole-body electrical bio-impedance. Chest. 2004;125:1431–1440. https://doi.org/10.1378/chest.125.4.1431

9. Cotter G, Schachner A, Sasson L, Dekel H, Moshkovitz Y. Impedance cardiography revisited. Physiol. Meas. 2006;27:817–827. https://doi.org/10.1088/0967-3334/27/9/005