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Original Article

A study of renal function influence by integrating cloud-based manometers and physician order entry systems

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Abstract

Background: No evidence exists from randomized trials to support using cloud-based manometers integrated with available physician order entry systems for tracking patient blood pressure (BP) to assist in the control of renal function deterioration. We investigated how integrating cloud-based manometers with physician order entry systems benefits our outpatient chronic kidney disease patients compared with typical BP tracking systems.
Methods: We randomly assigned 36 chronic kidney disease patients to use cloud-based manometers integrated with physician order entry systems or typical BP recording sheets, and followed the patients for 6 months. The composite outcome was that the patients saw improvement both in BP and renal function.
Results: We compared the systolic and diastolic BP (SBP and DBP), and renal function of our patients at 0 months, 3 months, and 6 months after using the integrated manometers and typical BP monitoring sheets. Nighttime SBP and DBP were significantly lower in the study group compared with the control group. Serum creatinine level in the study group improved significantly compared with the control group after the end of Month 6 (2.83 ± 2.0 vs. 4.38 ± 3.0, $p = 0.018$). Proteinuria improved nonsignificantly in Month 6 in the study group compared with the control group (1.05 ± 0.9 vs. 1.90 ± 1.3, $p = 0.09$). Both SBP and DBP during the nighttime hours improved significantly in the study group compared with the baseline.
Conclusion: In pre–end-stage renal disease patients, regularly monitoring BP by integrating cloud-based manometers appears to result in a significant decrease in creatinine and improvement in nighttime BP control. Estimated glomerular filtration rate and proteinuria were found to be improved nonsignificantly, and thus, larger population and longer follow-up studies may be needed.

Keywords: blood pressure monitoring; chronic kidney disease; cloud-based manometers integrated to physician order entry systems; usual blood pressure record sheets

1. Introduction

Hypertension is the most common chronic disease that may lead to devastating organ damage including renal disease, stroke, and cardiovascular diseases. Hypertension and diabetes

Conflicts of interest: The authors declare that there are no conflicts of interest related to the subject matter or materials discussed in this article.

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mellitus are the two most common causes of chronic kidney disease (CKD) worldwide.[1] Poorly controlled blood pressure (BP) is well-known to be an independent predictor of progression to end-stage renal disease (ESRD) in CKD patients.[2,3] Even a mild to moderate elevation of baseline BP in CKD patients is a risk factor for ESRD. Thus, guidelines typically recommend strict and lower BP targets in CKD groups compared with those without CKD.[4,5] Intensified BP control with the objective of 130/80 mmHg is a crucial treatment strategy for slowing CKD progression, although it is achieved in only approximately 10% of patients. Moreover, diurnal BP changes are common in CKD patients, and recent studies have also revealed that the control of nighttime BP may reduce instances of cardiovascular events in these patients.[6] Therefore, it is critical for CKD patients to have the ability to accurately self-monitor their BP regularly in their homes, including nighttime BP.

The treatment and target for hypertension may be changing. However, the fact that patients should self-monitor their BP at home is the only factor that never changes, and this is always crucial. It can help physicians monitor and treat actual hypertension, despite treating the patients for clinical BP alone. Although cloud-based manometers have been developed, they still cannot be integrated with physician order entry systems. The ideal model of a BP measuring device is one that can integrate manometer data into physician order entry systems, and quickly assess patient BP when used at home. This would not require the need to log into other systems or serve any other function.

In a project coordinated with the National Taiwan University of Science and Technology, Taipei, Taiwan, we integrated cloud-based manometers with the order entry systems of nephrologists in treating CKD patients to help them maintain proper control over their BP. We also conducted a randomized controlled trial to investigate the relationship between intensive BP monitoring and CKD progression in this population. Our discussion explains the desirability of integrating cloud-based manometers into physician order entry systems using evidence-based medicine.

2. Methods

2.1. Participants

For our study, we recruited 36 participants who were CKD patients with hypertension, with an initial glomerular filtration rate (GFR) < 60 mL/minute/1.73 m^2 under typical antihypertensive medication. Our exclusion criteria included: (1) those patients who could not utilize the system effectively; (2) those with end-stage kidney disease undergoing renal replacement therapy; (3) those with an active infection or clinical congestive heart failure; or (4) a specific indication of, or contraindication, to the study procedure. The protocol and procedures of this study were approved by the Institutional Review Board of Taipei Medical University-Joint Institutional Review Board, and all the participants read and provided written informed consent. All participants were enrolled between September 2012 and March 2013, and we followed them until the end of the study, which lasted 6 months.

2.2. Study design

Study participants were randomly assigned to 1 of 2 recording systems. One group used cloud-based manometers integrated with physician order entry systems, and the other group used the regular BP recording sheets to track their BP. Daily recording and integration were performed in the integrated cloud-based manometer recording system group, and three monthly outpatient department follow-up readings were conducted at an outpatient clinic for the regular BP recording sheet group. The target BP in both groups was determined according to recent guidelines, which is < 130/80 mmHg for CKD patients with proteinuria.[4,5] Physicians verified patient BPs in their order entry system weekly, and more frequently if required as per the study group. Thus, the BP in the study group was more conveniently seen by their physicians, and patients were called back as needed to improve their BP control. In the control group, regular medication adjustments were conducted with every outpatient clinic follow-up visit, according to their BP record sheet.

2.3. Measurements and laboratory procedures

We assessed BP during outpatient clinic visits conducted at baseline and every 3 months during the first 6 months of follow-up. We arranged additional clinic visits with further BP assessments as required and titrated the antihypertensive medications so that we could shift the BP level within the target range in the study group. During each BP assessment, we obtained three consecutive seated BP measurements by using a clinic sphygmomanometer after the patients were at rest for at least 5 minutes, by using the mean of the last two readings recorded. We collected the morning spot urine for protein and creatinine, and available laboratory services were used to measure the serum and urinary levels of creatinine and protein as well as lipids during regular visits.

2.4. Outcomes

A composite endpoint was defined as the changes in each patient's BP as well as assessments of renal function, including changes to the estimated GFR (eGFR), creatinine, and urine protein excretion.

2.5. Statistical analysis

The summaries of clinical and demographic characteristics included the means and standard deviations of nominal variables that we analyzed using Chi-square tests. The repeated measure of analysis of variance (ANOVA) was used to evaluate the cross-sectional relationship between BP and the selected ratio variables, which included age, body mass index, eGFR, serum creatinine, and hematocrit.

3. Results

3.1. Patient characteristics

For the specific hypothesis tested here (i.e., the influence of the integrated BP monitoring system on renal function assessments), we assessed 60 volunteers for eligibility. Among them, 36 patients (22 men and 14 women with a mean age of 65.7 years in the study group and 69.8 years in the control group) provided all the required information for the study. The remaining 24 patients were excluded according to the stated criteria, and/or because of a lack of the required $\geq$ 3-month minimal follow-up (Fig. 1). Fourteen patients (39%) had CKD Stage 3, 10 patients (28%) had CKD Stage 4, and 12 patients (34%) had CKD Stage 5. Additional baseline demographic and clinical characteristics of the study participants are listed in Table 1. At baseline, no significant differences emerged in these characteristics between the two groups.

Table 1
Comparisons of patient characteristics between the two groups.

	Study (n = 18)	Control (n = 18)	p
Sex			0.171[a]
Male	9 (40.9)	13 (59.1)	
Female	9 (63.3)	5 (35.7)	
Age (y)	65.7 ± 11.4	69.8 ± 16.4	0.189[b]
Stage			0.693[a]
Stage 3	7 (50.0)	7 (50.0)	
Stage 4	6 (40.0)	4 (40.0)	
Stage 5	5 (41.7)	7 (58.3)	
Body mass index (kg/m^2)	26.0 ± 4.2	25.4 ± 4.3	0.812[b]
eGFR (mL/min)	29.8 ± 17.1	25.0 ± 14.7	0.411[b]
Creatinine (mg/dL)	3.21 ± 3.2	3.51 ± 2.0	0.223[b]
Hematocrit (%)	33.7 ± 6.4	31.7 ± 4.9	0.752[b]
Albumin (g/dL)	4.03 ± 0.5	3.92 ± 0.6	0.662[b]
Cholesterol (mg/dL)	183.0 ± 46.5	183.4 ± 42.4	0.927[b]
UTP/UCr	1.43 ± 1.3	1.43 ± 1.3	0.597[b]
SBP (morning)	137.7 ± 17.3	129.7 ± 9.4	0.211[b]
DBP (morning)	80.0 ± 6.6	76.0 ± 9.0	0.094[b]
SBP (night)	135.2 ± 14.5	134.8 ± 13.6	0.849[b]
DBP (night)	77.0 ± 6.5	75.4 ± 7.6	2.357[b]

Data are expressed as n (%) or mean ± standard deviation.
DBP = diastolic blood pressure; eGFR = estimated glomerular filtration rate.
[a] Chi-squared tests.
[b] Mann–Whitney test.

3.2. Association of BP monitoring with composite renal outcome

Table 2 shows a comparison of the BP and renal function tests between the two study groups at 0 months, 3 months, and 6 months. The nighttime systolic BP and diastolic BP were found to have decreased significantly in the study group compared with the control group (128.1 ± 13.5 mmHg vs. 138.7 ± 9.2 mmHg, $p < 0.05$ and 72.1 ± 5.5 mmHg vs. 75.9 ± 8.5 mmHg, $p < 0.05$). Serum creatinine level in the study group improved significantly compared with the control group after the end of Month 6 (2.83 ± 2.0 vs. 4.38 ± 3.0, $p = 0.018$). Proteinuria improved nonsignificantly at 6 months in the study group compared with the control group (1.05 ± 0.9 vs 1.90 ± 1.3, $p = 0.09$). Figs. 2 and 3 reveal BP and renal function test changes (vs. the baseline) between the two groups at 3 months and 6 months. Both systolic and diastolic BP during nighttime improved significantly in the study group compared with the baseline. Proteinuria changes from the baseline were also found to have decreased in the study group.

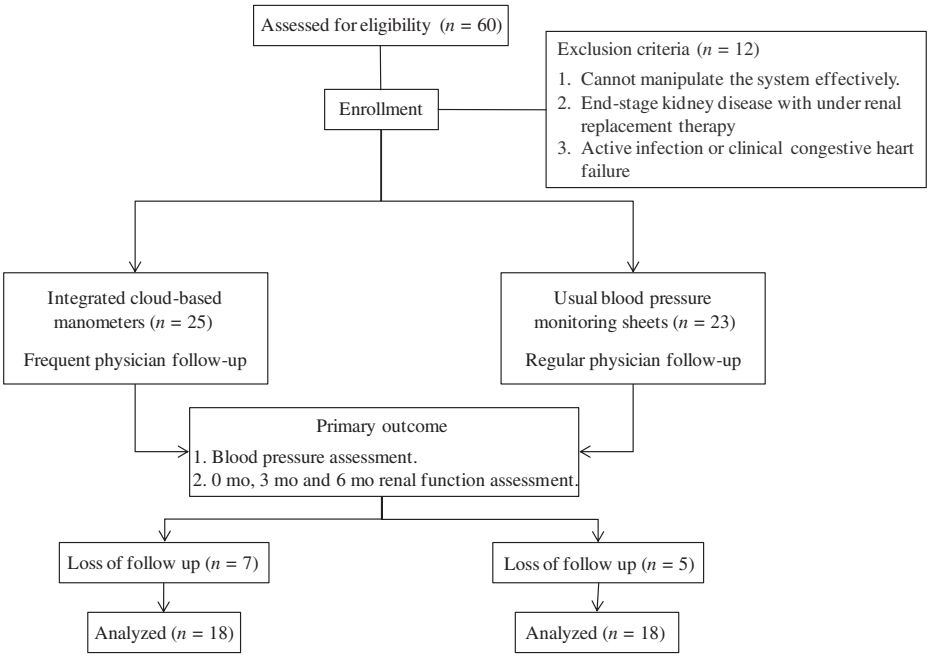

Fig. 1. Flowchart of patients participating in the study.

Table 2
Comparisons of blood pressure and renal function tests between the two groups at 0 months, 3 months, and 6 months.

	0 mo		3 mo		6 mo		
	Study (n = 18)	Control (n = 18)	Study (n = 18)	Control (n = 18)	Study (n = 18)	Control (n = 18)	p*
eGFR (mL/min)	29.8 ± 17.1	25.0 ± 14.7	30.7 ± 17.5	24.2 ± 14.7	31.1 ± 17.0	22.8 ± 15.3	0.087
Creatinine (mg/dL)	3.21 ± 3.2	3.51 ± 2.0	3.12 ± 2.9	3.86 ± 2.54	2.83 ± 2.0	4.38 ± 3.0	0.018
Hemoatocrit (%)	33.7 ± 6.4	31.7 ± 4.9	34.1 ± 5.0	31.5 ± 5.88	34.7 ± 4.7	31.7 ± 5.6	0.267
Albumin (g/dL)	4.03 ± 0.5	3.92 ± 0.6	4.00 ± 0.4	3.98 ± 0.42	4.16 ± 0.4	4.16 ± 0.3	0.602
Cholesterol (mg/dL)	183.0 ± 46.5	183.4 ± 42.4	201.8 ± 67.6	179.0 ± 26.9	193.4 ± 44.5	163.7 ± 32.0	0.855
UTP/UCr	1.43 ± 1.3	1.43 ± 1.3	1.29 ± 1.1	1.45 ± 1.04	1.05 ± 0.9	1.90 ± 1.3	0.095
SBP (morning)	137.7 ± 17.3	129.7 ± 9.4	138.3 ± 15.3	132.4 ± 14.0	134.5 ± 12.7	131.7 ± 12.2	0.189
DBP (morning)	80.0 ± 6.6	76.0 ± 9.0	79.6 ± 6.8	75.1 ± 13.2	77.2 ± 8.5	75.2 ± 11.8	0.351
SBP (night)	135.2 ± 14.5	134.8 ± 13.6	132.7 ± 11.7	137.3 ± 12.8	128.1 ± 13.5	138.7 ± 9.2	0.006
DBP (night)	77.0 ± 6.5	75.4 ± 7.6	74.8 ± 6.0	76.0 ± 9.2	72.1 ± 5.5	75.9 ± 8.5	0.016

Data are expressed as mean ± standard deviation.
* Repeated measure ANOVA, renal function test.
ANOVA = analysis of variance; DBP = diastolic blood pressure; eGFR = estimated glomerular filtration rate; SBP = systolic blood pressure; UTP/UCr = urine total protein/urine creatinine.

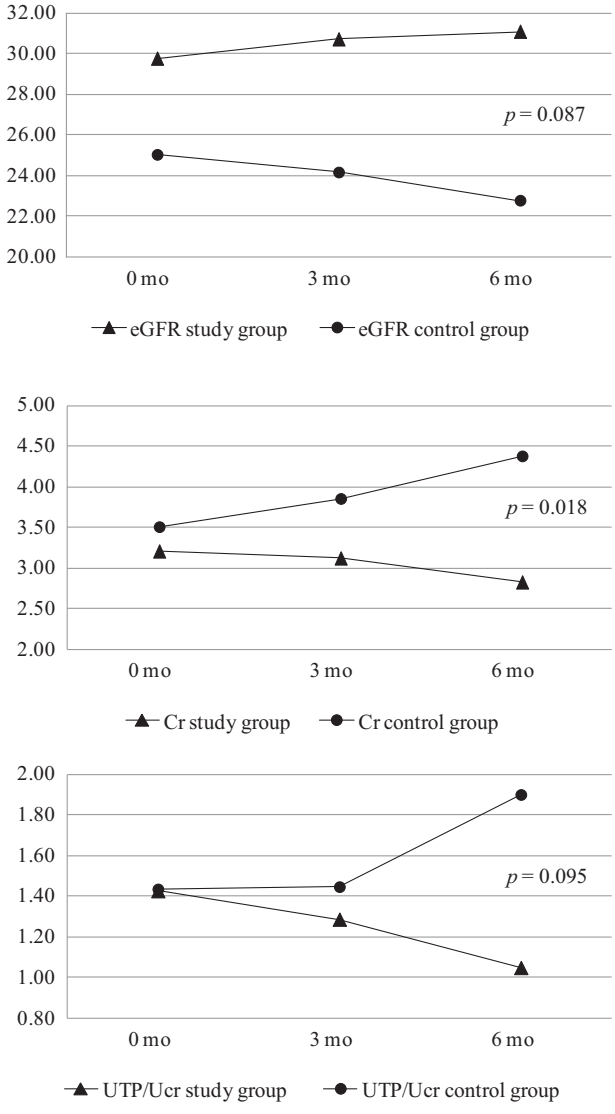

Fig. 2. Comparison of Month 0, Month 3, and Month 6 for estimated glomerular filtration rate (eGFR), creatinine (Cr), and renal function tests between the two groups. UTP/UCr = urine total protein/urine creatinine.

4. Discussion

This prospective, randomized study investigated how regular BP recording at home integrated into physician order entry systems impacts renal function deterioration in the later stages of CKD. We also examined the effect of the system on effective BP control in elderly patients with CKD. Our findings showed that nighttime BP decreased more in the study group compared with the control group at the end of 6 months, which is statistically significant (Table 2). Furthermore, nighttime systolic and diastolic BP had decreased significantly from baseline in the study group (Fig. 3). Agarwal and Andersen[7] showed that in CKD patients, nondipping BP (failure of falling in systolic BP at night) was common, and was an independent predictor of ESRD. Current international guidelines recommend long-acting, once-daily medications that provide smoother and more consistent BP control,[8] but these medications seem inappropriate for nondippers, especially early in the morning. Because nighttime high BP is also associated with a higher risk of cardiovascular disease,[9–11] a recent prospective MAPEC study[12] revealed that a bedtime ingestion of $\geq$ 1 hypertension medication is more effective for nondippers, and lowers CVD risk in these patients. In reviewing our patients' BP medications, we found that most of them use at least two antihypertensive agents (all of them including angiotensin-converting enzyme inhibitors/angiotensin receptor blockers and diuretics) in both the study and control groups. Therefore, an adequate control of BP in the study group may be due to physicians' frequent reminders and follow-ups in this group.

We found that the urine protein–creatinine ratio had decreased from baseline in the study group, which may be associated with improvements in nighttime BP in this group (Fig. 2). This finding is consistent with other trials that have documented that improvements in nighttime BP control may reduce urinary protein excretion.[13–15] A substantial amount of observational and experimental data has suggested that lowering BP prevents renal outcomes, and that the effect of intensive BP control is considerably greater with higher

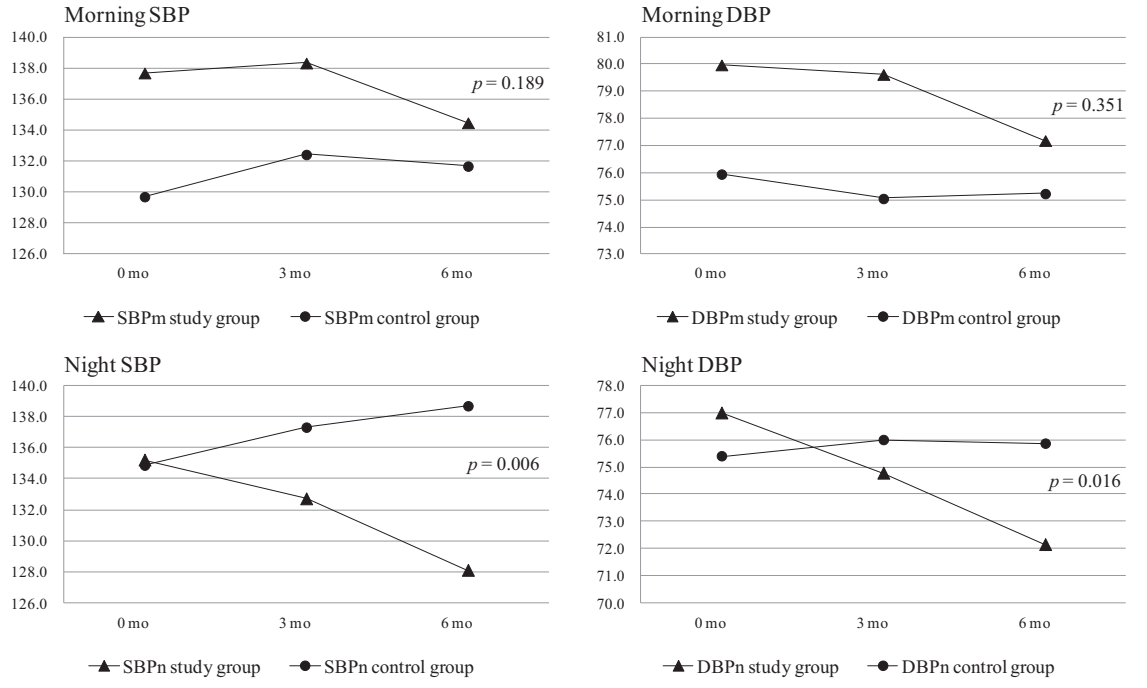

Fig. 3. Comparison of Month 0, Month 3, and Month 6 for morning (m) and night (n) systolic (SBP) and diastolic blood pressure (DBP) between the two groups.

proteinuria levels.[15] Because both of our study groups had urine protein > 1 g/g creatinine, their intensive BP control was effective in preventing progressive renal function impairment.

Over the past 2 decades, coexistent hypertension has been recognized to play a critical role in the progression of most diabetic and nondiabetic CKDs leading to ESRD,[16,17] even with mild to moderate elevations in BP. In experimental animal models with renal mass reduction, researchers found that renal dysautoregulation occurs with susceptibility to hypertensive injury.[18] This explains the markedly lower BP threshold in CKD patients in preventing further renal damage. Thus, medications that act as a blockade of the renin–angiotensin–aldosterone system are emphasized as the initial choice for these patients.[19] Several randomized controlled clinical trials in diabetic and nondiabetic CKD patients have proven greater renoprotection with medications for an RAS blockade compared with other antihypertensive regimens, with reductions in renal disease endpoints (doubling of serum creatinine, ESRD).[19–23] Moreover, in CKD patients, a study demonstrated that every 10 mmHg increase in systolic BP leads to a 35% increase in hospitalization resulting from cardiovascular and cerebrovascular events.[24] Recent studies have also demonstrated that BP control is also critical for hemodialysis patients, and may contribute to improved cardiovascular morbidity and mortality.[25]

In our study, reduction in eGFR in both groups was substantial because the patients were already in the pre-ESRD stage (eGFR < 45 mL/min/1.73 m^2), as shown in Table 2. However, we found that serum creatinine changed significantly at 6 months, and decreased from the baseline significantly in the study group (Fig. 2), which might reflect the improvement of the renal function test, attributable to improved BP control. Mourad et al[26] demonstrated in mild to moderate CKD patients that a reduction in their creatinine clearance was associated with an increased arterial stiffness of the central arteries, which was a result independent of their BP. Because our patients were in their later stages of CKD, their effects on eGFR reduction may have required more time for a follow-up. The wide-ranging variation in renal function may account for the insignificant results of renal function improvement in our study. Therefore, we may need a larger study population and a longer follow-up duration to observe the impact of integrated BP monitoring systems on cardiovascular events and ESRD outcomes in CKD patients.

4.1. Perspective

We believe that the blood recording system integrated into a physician order system in this high-risk, randomized population is crucial, and warrants further investigation for the following reasons: (1) to increase patient compliance, both regarding BP recording and regular medication consumption, because they would be aware that their physician is following their progression all the time, and are able to communicate with them anytime if their BP is unmanageable; (2) family participation and knowledge, because family members may need to participate in the process, and are knowledgeable in their family members' BP conditions; and (3) improved and earlier management by physicians according to the conditions of individual patients, which may prevent further adverse events, including hospitalization.

4.2. Limitations of the study

We faced obstacles in implementing integrated cloud-based manometer services such as costs, technical difficulties,

resource limitations including online assessments, and the process by which to best integrate BP data into the physician order system. We taught the study group to use the system every time they visited the outpatient clinic. This study also had limitations including a shorter follow-up duration and a small population size.

In conclusion, our study demonstrated a significant decrease in creatinine and night time BP in CKD patients by using an integrated BP monitoring system compared to the regular BP recording system. There was also a trend of improved eGFR and proteinuria in the study group. Whether this effect is associated with improved nighttime systolic BP control must still be determined with a longer follow-up duration. Thus, in order to ascertain whether an integrated BP monitoring system can be used to predict improved renal function preservation and cardiovascular outcomes requires additional and even larger high-risk population-based studies.

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