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Assessment of Volume Status Using Body Composition Monitor for Blood Pressure Control in Patients Undergoing Maintenance Hemodialysis: A Randomized Controlled Trial

Niraj Dhakal, Nisha K Sapkota, Mahesh R Sigdel

Author(s) affiliation

Department of Nephrology and Transplant Medicine, Maharajgunj Medical Campus, Tribhuvan University Teaching Hospital, Institute of Medicine, Maharajgunj, Kathmandu, Nepal

Corresponding author

Niraj Dhakal, MD, DM
drnirajdhakal@gmail.com

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ABSTRACT

Introduction

Optimal fluid balance and blood pressure control have been shown to improve outcomes in hemodialysis population. We investigated the effectiveness of body composition monitor (BCM) to target dry weight in maintenance hemodialysis (MHD) patients for blood pressure (BP) control and intradialytic adverse events.

Methods

A total of 61 consenting adults under MHD were randomly allocated into either BCM group or Clinical Method group. Target dry weight was set every 4-weekly based on BCM report or clinical assessment; dry weight was adjusted with 200-500 ml/session reduction or increment of ultrafiltration in addition to interdialytic weight gain. Outcomes were analyzed in terms of BP control, anti-hypertensive medicine score, and intradialytic adverse events.

Results

During 12 weeks of study period, systolic blood pressure ($p<0.001$), diastolic blood pressure ($p=0.01$) and mean arterial pressure ($p<0.001$) significantly decreased from baseline in BCM group but there were no significant changes in Clinical Method group. Lower blood pressure was achieved in BCM group as compared to Clinical Method group. There was a significant decrease from baseline in anti-hypertensive medicine score in the BCM group ($p<0.001$) but not in the clinical method group ($p=0.34$). There were significantly fewer events of cramps in the BCM group as compared to the Clinical Method group ($p=0.04$).

Conclusion

BCM guided volume management in MHD patients was more effective than volume management based on clinical judgment only in controlling blood pressure and decreasing anti-hypertensive medicine burden and intradialytic cramps.

Keywords
Body composition monitor; hemodialysis; hypertension

INTRODUCTION

Chronic volume overload in patients on maintenance hemodialysis (MHD) leads to uncontrolled blood pressure (BP) and has significant impact on patients' survival with a 12% excess risk of death.[1–3]

Clinical judgment that has been practiced to assess fluid balance in MHD population is far from perfect.[4] Achieving dry weight becomes difficult at times and inaccurate estimation of ultrafiltration (UF) can sometimes lead to uncontrolled hypertension and intradialytic adverse events.[5] Optimized volume status in MHD patients lead to better control of BP and reduced intradialytic events.[6–8] Body Composition Monitor (BCM) is one of the emerging validated method for fluid assessment that is easy to perform, and non-invasive.[9] However, to date, BCM is not a part of regular clinical practice due to absence of compelling supportive evidence.

This study investigated the effectiveness of use of BCM to target dry weight for achievement of better BP control and reduce intradialytic adverse events in MHD patients.

METHODS

This was an open-label, parallel-group randomized controlled trial (RCT) conducted in patients undergoing MHD in Tribhuvan University Teaching Hospital (TUTH), Kathmandu. Prior ethical approval from Institutional Review Committee of Institute of Medicine [Ref no: 103(6-11) E2 077/078] and Ethical Review Board of Nepal Health Research Council [ERB protocol no: 587/2020] were obtained. Duration of the study was three months after randomization. Consenting adults patients more than 16 years who were on outpatient MHD for more than three months were enrolled. Patients with metallic devices like a pacemaker, coronary stent, prosthetic joints, or pins or having amputation of the limb, pregnancy, decompensated liver disease or heart failure or having volume monitored with BCM within one month before randomization were excluded. Patients were then randomized into either BCM group or Clinical Method group with simple randomization technique using computer-generated random numbers with equal allocation into two groups.

All patients in the study received standard care as per kidney disease initiative global outcome (KDIGO) guideline 2012[10] as well as institutional practice. A portable multi-frequency whole-body BCM machine (Fresenius medical care, Germany, Serial number: 0BJA6281) was used to assess the volume. Hydration status was expressed as liters over or underhydration.

All the patients were advised for less than 2 gm/day of salt intake and less than 500ml/day of fluid intake in addition to the volume of urine output.

In the BCM group, BCM was done every four weeks' pre-dialysis and target dry weight was set as per the BCM report. In the Clinical Method group, dry weight was set by the primary investigator as per clinical assessment i.e., intradialytic weight gain, BP, edema, jugular venous pulsation, tachypnea, and basilar crepitation every 4 weeks.

Target dry weight was probed with the gradual change in post-dialysis weight with target UF of interdialytic weight gain (IDWG) ±200-500 ml/dialysis session until body weight was ± 500 kg of target dry weight. If UF was not tolerated because of hypovolemic symptoms (such as muscle cramps, need for excessive saline, or symptomatic hypotension), adverse events were recorded, and the set target dry weight was adjusted by plus 500 gm. and if participants experienced hypervolemic events (congestive heart failure, pulmonary edema), adverse events were recorded, and the set target dry weight was adjusted by minus 500 gm. until the next assessment to set target dry weight by primary investigator either clinically or as per BCM report according to the assigned group. When the patient experienced the same adverse effect of dry weight change for three consecutive visits, s/he was dropped from the study because of the adverse event. The patients were followed up by the primary investigator in the hemodialysis (HD) ward every 4 weekly ± 7 days i.e. at weeks 4, 8, and 12.

The sample size was calculated with 80% power and 95% confidence interval with two tail alpha levels of 0.05, using the following formula:

$$n = \frac{2\,[(\alpha+\beta)^2\,\sigma^2]}{(\mu_1-\mu_2)^2}$$

where,

- n : sample size in each group
- μ_1 : population mean in treatment Group 1
- μ_2 : population mean in treatment Group 2
- σ : population variance
- $\mu_1-\mu_2$: difference the investigator wishes to detect
- α : conventional multiplier for alpha=0.05
- β : conventional multiplier for power=0.80

In the study of Patel et al mean reduction in mean arterial pressure (MAP) was 5.97 mmHg in the BCM group and 1.98 mmHg in the control group, with a mean difference of 3.99 mmHg and with a pool standard deviation (SD) of 6.01.[7] Using a clinically significant difference of 5 mmHg, we calculated our required sample size to be 23 in each group. Considering an attrition rate of 10% for death, renal transplant, and loss to follow up our required sample size was 26 in each group.

Data were collected as per the predetermined Proforma at baseline and every 4 weeks. Demographic data were collected by direct patient interview, clinical and investigational data that included records of BP, weight, adverse events, treatment provided during dialysis, patients' daily medicine, and deviation from treatment protocol were collected from patients' dialysis record book. Data were entered in IBM SPSS software. Baseline characteristics, and differences or changes in parameters between or within the groups were analysed by descriptive and inferential statistics using SPSS version 20.11

The outcome of the study was measured at 12 weeks in terms of BP control, antihypertensive medicine burden, and volume-related adverse events. A score was given to quantify the burden of antihypertensive drugs; the maximum dose was scored as 1 and the dose of antihypertensive was calculated as a fraction thereof if the patient was not taking the maximum dose of the given medications. Based on the published drug dose guideline, the maximum dosage of each antihypertensive drug was determined.[12]

Missing data were managed with multiple imputation techniques. The Shapiro Wilk test was used to check for the normality of data. For categorical variables percentage or proportion was used and for continuous variables mean ± SD was used for normally distributed data and median with interquartile range (IQR) was used for skewed distribution

In inferential statistics, the Independent Sample t-Test or Mann Whitney U test was used to compare the mean difference in parameters between the BCM group and Clinical Method group according to the distribution of data. Chi-Square Test or Fishers' Exact Test was used to analyze categorical variables. Paired Sample t-Test or Wilcoxon Signed Rank Test was used to compare the changes in parameters within the groups at baseline and after 3 months. Outcomes were analyzed as an intention to treat analysis. All tests of significance were two-tailed and a p-value less than 0·05 was considered significant.

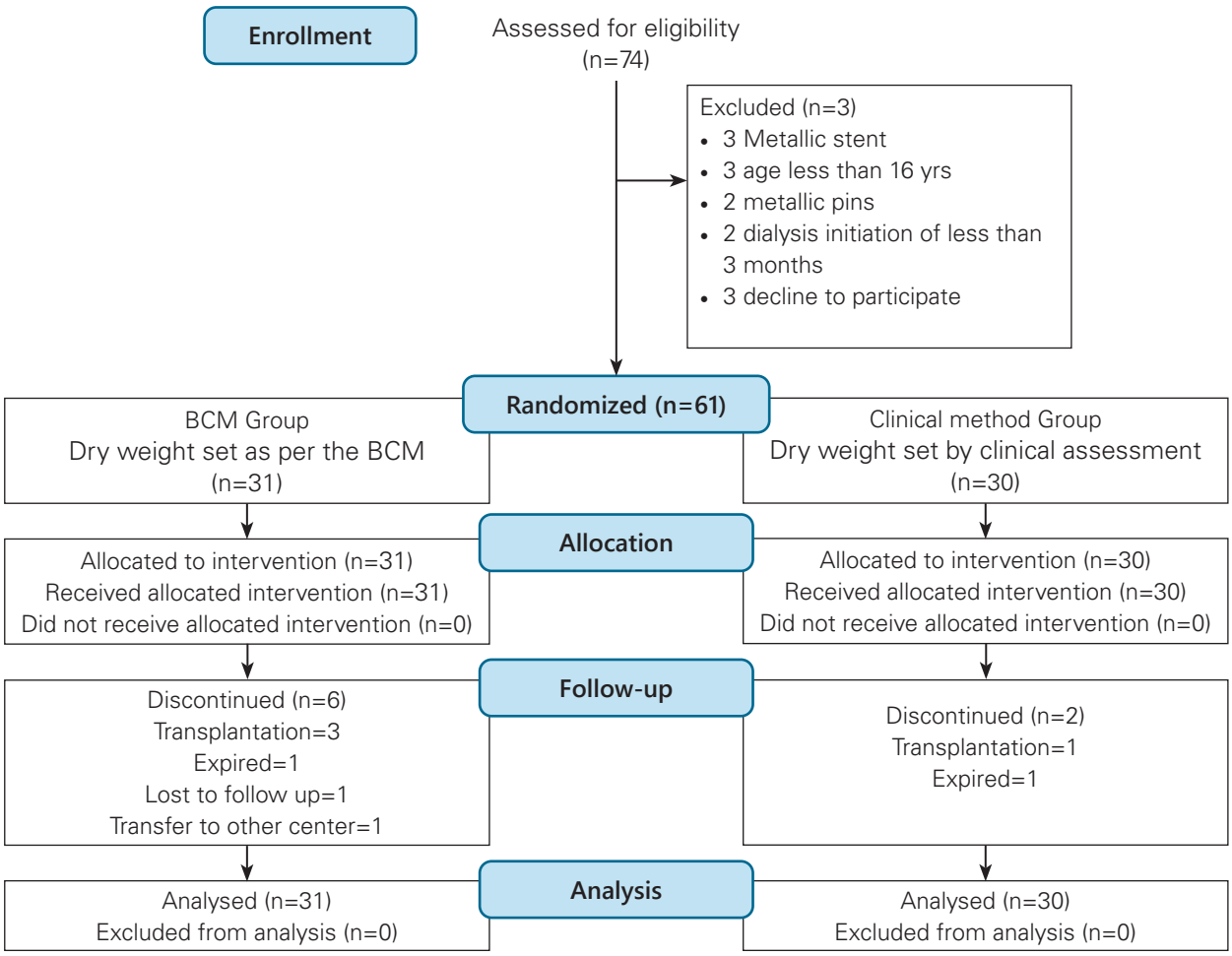

Figure 1. CONSORT flow diagram

RESULTS

During the enrolment period, 74 patients on MHD were assessed for eligibility. Sixty-one patients fulfilled the inclusion criteria and were randomized to the BCM group (n=31) and the Clinical Method group (n=30), and all received allocated intervention. Eight patients, 6 in the BCM group and 2 in the Clinical Method group did not complete the study and the reasons for dropout are shown in Figure 1.

Blood pressure values over different time points and their comparisons between groups are shown in Table 2.

There was significant difference in systolic blood pressure (SBP) among groups at first month, second month, and third month with participants in the BCM group attaining lower SBP than Clinical Method Group (Table 2). At second month diastolic blood pressure (DBP) was significantly lower in BCM group as compared to Clinical method group. However, the same was not observed at first and third month.

Mean arterial pressure (MAP) between groups did not differ significantly at first month in BCM group and Clinical Method group. Subsequently, at second and third months, MAP was significantly lower in the BCM group.

There was significant decrease in SBP, DBP and MAP with mean difference of 12.21 mmHg, 3.71 mmHg, and 6.53 mmHg, respectively from baseline to third month in BCM group (Figure 2, 3 and 4). However, there were no significant changes in SBP, DBP and

Table 1. Baseline characteristics of study participants

Baseline Characteristics	All patients (n=61)	BCM group (n=31)	Clinical Method Group (n=30)	p value
Age (years)	43.31±14.96	40.87±12.79	45.83±17.75	0.19[a]
Gender (M: F)	43:18	21:10	22: 8	0.63[b]
Cause of CKD				
Primary GN	9(14.7%)	4(12.9%)	5(16.6%)	0.57[b]
AAV	1(1.6%)	-	1(3.3%)	
Diabetes Nephropathy	7(11.5%)	3(9.7%)	4(13.3%)	
HTN Nephrosclerosis	2(3.3%)	-	2(6.7%)	
ADPKD	3(4.9%)	2(6.5%)	1(3.3%)	
Obstructive	2(3.3%)	1(3.2%)	1(3.3%)	
Chronic Pyelonephritis	1(1.6%)	1(3.2%)	-	
Undetermined	36(59%)	21(67.7%)	15(50%)	
Comorbidities				
HTN	57(93.4%)	28(90.3%)	29(96.7%)	0.61[c]
Diabetes	8(13.1%)	2(6.5%)	6(20%)	0.15[c]
CAD	4(6.6%)	1(3.2%)	3(10%)	0.61[c]
PVD	1(1.6%)	-	1(3.3%)	0.49[c]
Dialysis Vintage (months)	25(IQR:11-36)	19(IQR: 11-35)	27(IQR: 15-41)	0.36[d]
Access				
AVF	58(95.1%)	29(93.5%)	29(96.7%)	1.0[c]
Tunneled cuff catheter	3(4.9%)	2(6.5%)	1(3.3%)	
MHD frequency				
Twice/week	37(60.7%)	20(64.5%)	17(56.7%)	0.53[b]
Thrice/week	22(36.1%)	11(35.5%)	11(36.7%)	0.92[b]
Urine output				
Less than 500ml	48(78.7%)	23(74.2%)	25(83.3%)	0.38[b]
More than 500ml	13(21.3%)	8(25.8%)	5(16.7%)	
Mean Weight (Kg)	58.33±10.54	57.71±10.85	58.97±10.35	0.65[a]
BP				
Mean SBP (mmHg)	157.38±18.88	155.16±16.11	159.67±21.41	0.36[a]
Mean DBP (mmHg)	88.61±8.88	89.52±7.63	87.67±10.06	0.56[a]
Mean MAP(mmHg)	111.53±10.67	111.41±9.13	111.67±12.22	0.87[a]
Median antihypertensive Score	0.5(IQR: 0.25-1.16)	0.67(IQR: 0.25-1.33)	0.5(IQR: 0-1.18)	0.67[d]

(a: T-test, b: Chi-square test, c: Fisher's Exact test, d: Mann-Whitney U test)

Table 2. Comparison of blood pressure at different points between BCM and Clinical Method groups

BP	BCM groups (n=31) (Mean ± SD)	Clinical Method Groups(n=30) (Mean ± SD)	p value [95% Confidence Interval]
Mean SBP			
SBP at 1st month	155.09±18.83	165.97±21.96	0.04 [-21.35 to -0.41]
SBP at 2nd month	150.95±16.09	169.97±22.33	0.001 [-29.35 to -8.69]
SBP at 3rd month	142.96±15.11	159.01±22.08	0.002 [-25.72 to -6.38]
Mean DBP			
DBP at 1st month	90.50±12.83	89.60±10.89	0.76 [-5.22 to 7.03]
DBP at 2nd month	87.70±7.14	91.64±7.64	0.04 [-7.72 to -0.15]
DBP at 3rd month	85.82±5.42	88.43±6.12	0.08 [-5.56 to 0.35]
Mean MAP			
MAP at 1st month	112.03±12.69	115.06±12.48	0.35 [-9.47 to 3.42]
MAP at 2nd month	108.78±8.97	117.75±11.95	0.002 [-14.40 to -3.53]
MAP at 3rd month	104.87±6.81	111.96±10.46	0.003[-11.59 to-2.58]

DBP, diastolic blood pressure; MAP, mean arterial pressure; SBP, systolic blood pressure

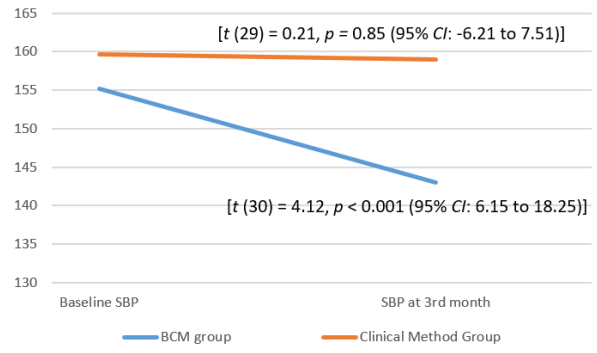

Figure 2. Comparison between baseline and 3rd-month systolic blood pressure within groups

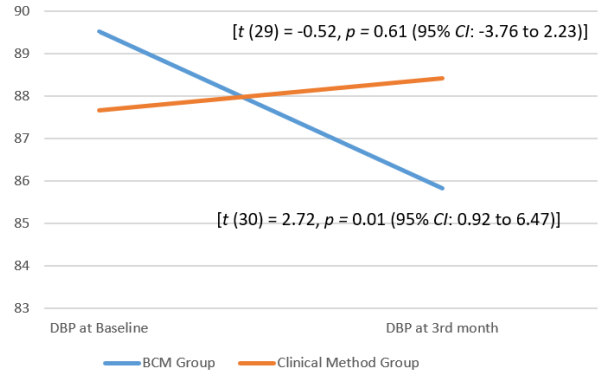

Figure 3. Comparison between baseline and 3rd-month diastolic blood pressure within groups

MAP with mean difference of 0.65 mmHg, -0.76 mmHg, and -0.29 mmHg, respectively in Clinical Method Group from baseline to third month.

At third month, we observed a significant decrease

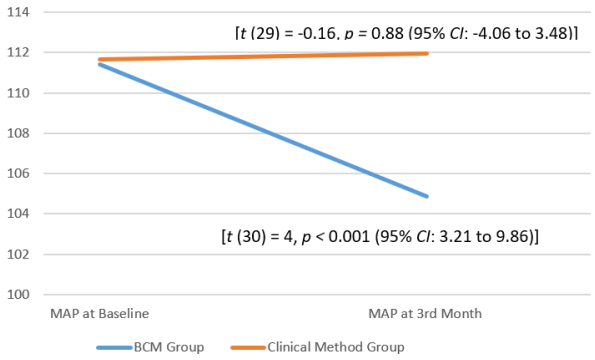

Figure 4. Comparison between baseline and 3rd-month mean arterial pressure within groups

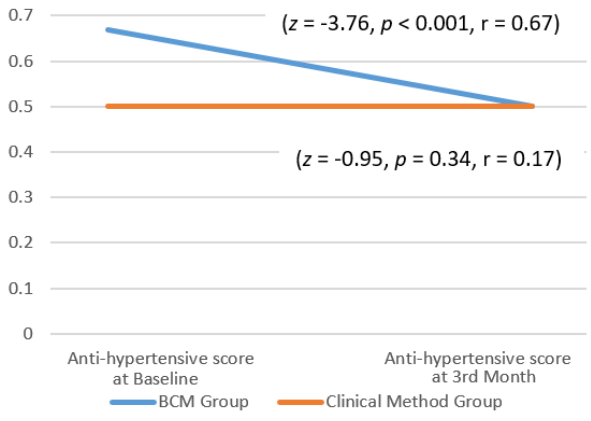

Figure 5. Comparison between baseline and 3rd-month anti-hypertensive medicine score within groups

from baseline in the anti-hypertensive medicine score in the BCM group but not in the Clinical Method group (Figure 5).

Table 3. Comparison of adverse event rates between BCM and Clinical Method groups

Adverse event	BCM group (n=31)		Clinical Method group (n=30)		p-value
	Event Rate (event/session/ 3 month)	Number of Total Events	Event Rate (event/session/ 3 month)	Number of Total Events	
Headache	0.15	118	0.16	125	0.60
Cramps	0.11	75	0.16	122	0.04
Dizziness	0.03	23	0.04	28	0.74
Nausea	0.12	91	0.08	66	0.31
Vomiting	0.09	66	0.06	47	0.39
Intradialytic Hypertension	0.06	50	0.09	74	0.87
Intradialytic Hypotension	0.04	28	0.06	43	0.05
Pulmonary Edema	0.01	11	0.01	8	0.56
Total	0.61	462	0.66	513	0.7

In the study period, total of 1,554 sessions of hemodialysis (HD) was performed with 774 sessions in BCM group and 780 sessions in Clinical Method group. There were total of 0.63 events/ HD session/ 3 months. Comparison of events between groups is shown in Table 3.

The most common event was headache with a rate of 0.16 events/ HD session/ 3 months followed by cramps, 0.13 events/ HD session/ 3 months and nausea, 0.1 events/ HD session/ 3 months. The event rate for intradialytic hypertension, intradialytic hypotension, vomiting, dizziness, pulmonary edema was less than 0.1 events/ HD session/ 3 months. There was no episode of access thrombosis and there was no dropout related to volume-related adverse events during the study period. There was significantly fewer occurrence of cramps in the BCM group compared with the Clinical Method group, whereas there was no significant difference in other adverse events (Table 3).

There were five hospital admissions during the study period all due to infectious complications, two in the BCM group both due to COVID pneumonia and three in the Clinical Method group, two due to COVID pneumonia, and one due to sepsis. Two death occurred during the study one in each group. None was related to volume-related adverse events. One patient in the BCM group died due to COVID pneumonia and the other death in the Clinical Method group was due to sepsis.

DISCUSSION

Dialysis adequacy is not only the clearance of solutes but also involves providing correct ultrafiltration to render a euvolemic state and patient wellbeing at the end of dialysis.[13] The concept of dry weight has been practiced since the introduction of dialysis and control of volume overload has been shown to have a better outcome in terms of improved left ventricular mass index, blood pressure, arterial wall stiffness, quality of life, and mortality.[1,6,14–16]

In our study, we compared effect of BCM guided dry weight titration as compared to dry weight probing by clinical assessment in terms of BP control, antihypertensive medicine burden and intradialytic adverse events. At baseline, there was no significant difference in SBP, DBP, and MAP between groups. During follow up there was a significant decrease over time in SBP, DBP, and MAP in the BCM group but there was no significant change in these parameters in the Clinical Method group. In the BCM group, SBP was significantly lower than the Clinical Method group after baseline during first, second and third months. Diastolic BP was significantly lower in BCM group at second month. Mean arterial pressure was significantly lower in BCM group after first month. The antihypertensive burden expressed as antihypertensive medicine score also decreased over time in BCM group.

Similar to our findings, Onofriescu et al, in their observation found a significant reduction in BP in the BCM group, and also there was an increase in the number of patients not using any antihypertensive agents after 2.5 years.[6] Recently Patel et al, have shown BCM guided fluid management to have the benefit of significantly reducing MAP over six months, and also there was a trend toward reduction in SBP and DBP at sixth month compared to baseline. In their study, the anti-hypertensive medicine score also significantly decreased in the BCM group.[7] Huan-Sheng et al, in their RCT done in the Asian MHD population, found that there was a significant reduction in pre-dialysis SBP in an overhydrated patient in the BCM group but not in the control group.[8] Machek et al, in their prospective trial they observed a significant reduction in SBP by 25 mmHg in the hyperhydrated group after a decrease in volume overload. Additionally, there was the

achievement of a 35% reduction in anti-hypertensive medication which was significant.[17] Most common cause for hypertension in chronic kidney disease (CKD) is volume overload, thus, it is advised first to control volume status before the escalation of anti-hypertensive medicine in CKD patients.[13,18] Thus, in our and other studies mentioned above better control of BP and reduction in anti-hypertensive burden observed may be explained by the effect of better control of overhydration due to objective assessment of dry weight by BCM.

However, in the recently published RCT by Sommerer et al, there was no significant reduction in BP over time in both the groups and no significant difference was observed in BP reading between BCM or control group.[19] This was contradictory to our observation and it could be explained by the fact that their study participants were relatively older with a mean age of around 70 years, had longer dialysis vintage and almost half of their patients had diabetes, which combined there was increased risk for progression of atherosclerosis in their patients. Thus we must also account for other causes of hypertension besides volume overload.

In our study, there was a significant difference in the occurrence of cramps with fewer cramps occurring in the BCM group than Clinical Method group, however other volume-related adverse events in both the groups didn't differ significantly though numerically more number of events such as headache, dizziness, intradialytic hypertension, and intradialytic hypotension were seen in Clinical method group.

Similar to our finding there were significantly fewer cramps in the BCM group in the observation by Patel et al.[7] In their study, patients in the clinical judgment arm had more events of hypotension and dizziness which was statistically significant. But the difference in our study didn't reach the level of significance. This may be due to the shorter duration of follow-up in our study and we might have observed significant differences if our study was to be continued beyond three months.

Contradictory to our findings, the observation done by Sommerer et al,[19] showed significantly more cramps and hypotension in BCM guided volume management group and in the study by Huan-Sheng et al,[8] there was significantly more proportion of headache in addition to cramps and hypotension in BCM group. These deviations from our observation may be explained by the fact that their study population was older and baseline blood pressure in their study was lower than in our study. We can rationalize that in elderly MHD patients, other factors like cardiovascular disease must be accounted for during volume management and increasing dialysis duration rather than UF rate may provide adequate time for plasma refill and volume management without adverse events.[13]

Volume management guided by BCM in addition to clinical judgment may be helpful for achievement of appropriate dry weight in MHD patients which was shown in our study to have better control of BP, reduced antihypertensive medicine burden and intradialytic cramps in MHD patients. In future, study with larger sample population of MHD patients with extended follow up is required to answer the cardiovascular outcome and mortality benefit of BCM guided dry weight probing, so that, BCM measurement would be a part of patient monitoring in hemodialysis units.

CONCLUSION

BCM guided volume management of patients in MHD led to better blood pressure control, reduced antihypertensive pill burden and reduced cramps. BCM could compliment clinical assessment in volume management of MHD patients.

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CONFLICT OF INTEREST

The authors declare that they have no competing interests.

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