INFOGRAPHIC

Using an in-office passive leg raise to identify older adults with suboptimal blood pressure control

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Introduction: Passive leg raise (PLR) is a simple, dynamic maneuver that has been used to increase preload to the heart. We hypothesize that PLR may offer a new and efficient office-based tool for assessing blood pressure (BP) control in older adults.

Methods: One hundred and three veterans (≥60 years old) without known cardiovascular disease and varying degrees of blood pressure control were included in this cross-sectional cohort study. Twenty-four hour ambulatory BP monitoring identified Veterans with optimal and suboptimal BP control (≥125/75 mmHg). Bioimpedance electrodes (Baxter Medical, Deerfield, Illinois, USA) and brachial BP were used to calculate hemodynamic parameter changes across PLR states [pre-PLR, active PLR (3 min), and post-PLR]. Multiple linear regression was used to assess associations between BP control status with changes in hemodynamic parameters between PLR states.

Results: The 24-h ambulatory BP monitoring identified 43 (42%) older Veterans with optimal BP control (mean age of 70.5 ± 7.0 years) and 55 (54%) with suboptimal BP (mean age of 71.3 ± 8.7 years). Veterans with suboptimal BP control had significantly reduced change in total peripheral resistance (ΔTPR) (7.0 ± 156.0 vs. 127.3 ± 145.6 dynes s/cm^5; $P = 0.002$) following PLR compared with Veterans with optimal BP control. Suboptimal BP control ($\beta = -0.35$, $P = 0.004$) had a significant association with reduced ΔTPR, even after adjusting for demographic variables.

Conclusion: Measuring PLR-induced hemodynamic changes in the office setting may represent an alternative way to identify older adults with suboptimal BP control when 24-h ambulatory BP monitoring is not available.

Graphical abstract: http://links.lww.com/HJH/C557

Keywords: blood pressure, hemodynamics, older adults, passive leg raise

Abbreviations: Δ, change in; ABPM, ambulatory blood pressure monitoring; BP, blood pressure; BSA, body surface area; *CO*, cardiac output; HR, heart rate; HTN, hypertension; MABP, mean arterial blood pressure; NTN, normotension; OBP, optimal blood pressure; PLR, passive leg raise; SOBP, suboptimal blood pressure; SV, stroke volume; TPR, total peripheral resistance

INTRODUCTION

Approximately 50% of adults in the United States over the age of 20 years suffer from hypertension, and the prevalence rises with advancing age [1,2]. According to the current guidelines, a diagnosis of hypertension in adults is defined as a resting, in-office SBP above 130 mmHg and/or DBP above 80 mmHg that is measured on two separate occasions using an upper arm brachial BP cuff [3]. Though used regularly in the ambulatory setting, this method can lead to the misdiagnosis of hypertension [4,5]. The potential pitfalls of diagnostic inaccuracy have led to more reliance on home BP monitoring and 24-h ambulatory blood pressure monitoring (ABPM), which have been adopted into guidelines [6–21]. Although these additional tools can be helpful and cost-effective, potential drawbacks include participant buy-in, additional time to complete testing, and reliance on data provided by the user.

Additional straightforward in-office tests or physiologic maneuvers that can be used to diagnose hypertension in the clinical setting could help improve cardiovascular health, especially in older adults. One potential maneuver previously used to assess volume status in the ICU is the passive leg raise (PLR) [22]. PLR is performed by having the patient lie supine and passively having both legs raised above the level of the heart. PLR increases preload to the heart and augments cardiac output; however, no studies have evaluated if PLR-induced preload augmentation can offer insight into the effect of suboptimal BP control on cardiac function and vascular adaptation in older adults [23].

METHODS

The University of Wisconsin Madison and the Madison Veteran's Hospital Institutional Review Boards reviewed

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and approved this prospective cohort trial. Written informed consent was collected from all participants.

Study participants

Figure 1 provides an illustrative representation of participant enrollment, exclusion criteria, and allocation into study groups that were further analyzed.

The analysis included 103 ambulatory, community-dwelling, older (≥ 60 years old) Veteran participants. Each participant was initially identified as 'normotensive' or 'hypertensive' at study entry based on self-report or current antihypertensive medication use (44 normotensive controls and 59 patients reported hypertension). Self-reported hypertensive status was confirmed by evidence of two or more office BP readings with a SBP greater than 140 mmHg or ongoing use of antihypertensive medication. Reasons for exclusion were established cardiovascular disease, chronic kidney disease, hypoxemic pulmonary disease, secondary hypertension, and recent hospitalization in the past month for any reason.

After entry into the study, regardless of self-reported normotensive/hypertensive status, 24-h ABPM was used to

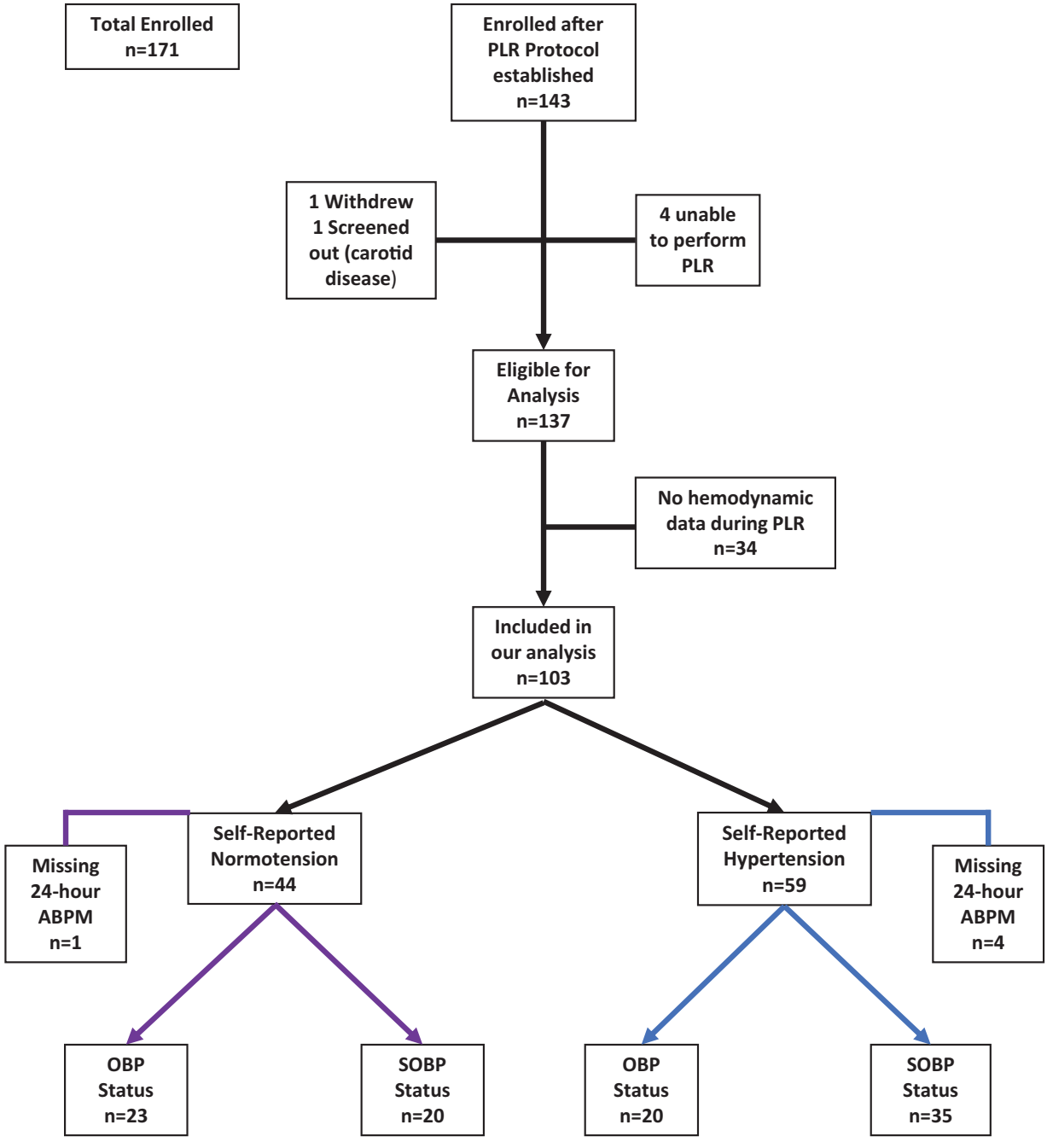

FIGURE 1 Flowsheet of participant enrollment, exclusion criteria, and allocation into study groups that were further analyzed. 24-h ambulatory BP monitoring (ABPM) determined allocation into optimal blood pressure (OBP) and suboptimal BP (SOBP) groups. PLR, passive leg raise.

identify participants with optimal blood pressure (OBP) control versus sub-OBP (SOBP) control by using the average of all BP recordings during both day and night between days 1 and 2 of the study protocol. SOBP was defined as a mean SBP at least 125 mmHg or a mean DBP at least 75 mmHg.

Study protocol

On visit day 1, participants were fitted with 24-h ABPM (SpaceLabs Healthcare, Snoqualmie, Washington, USA) and were asked to wear the monitor until they returned for their study visit the following day. Typical bedtime and waketime was reported by the participants. BP was recorded every 30 min during wake periods and every 60 min during sleep periods. The ABPM was returned at the start of day 2, and all recorded BP values were used in calculating the average 24-h BP for each participant.

On visit day 2, participants were asked to fast 8 h from eating (hydration with water and de-caffeinated coffee was permitted) before the study day began and hold their antihypertensive medication until after the protocol was completed. Participants rested in a supine position in a temperature-controlled room for 10 min (pre-PLR). Serial sphygmomanometer derived mean arterial BP (MABP), heart rate (HR), noninvasive stroke volume (SV), and noninvasive cardiac output (*CO*) measurements (Cheetah Starling Fluid Management System, Baxter Healthcare, Deerfield, Illinois, USA) were collected using clinically validated bioimpedance electrodes [24]. Total peripheral resistance (TPR) was derived from the following equation: $TPR = 80 \times (MAPB/CO)$. Following initial data collection for 10 min, PLR was completed by elevating the participant's lower extremities to an angle of 45° for 3 min using an angled ramp (active PLR). Hemodynamic parameters during PLR were calculated from maximum percentage change in SV index, which typically occurred during the first 120 s of the PLR. Following the 3 min PLR, the participant was placed back in a supine position for between 7 and 10 min. Hemodynamics and BP measurements were repeated during each condition (pre-PLR, active PLR, post-PLR).

Statistical analyses

Data was analyzed using SPSS (Version 27, IBM SPSS, Armonk, New York, USA). Categorical data were summarized in terms of frequencies and percentages whereas continuous data were described using means and standard deviations. Demographic data was described for five groups: All participants, self-reported hypertensive participants, self-reported normotensive participants, participants with SOBP, and participants with OBP. Baseline data were compared between self-reported hypertensive and normotensive participants as well as between SOBP and OBP participants using independent sample *t* tests (continuous data) or χ^2 tests (categorical data). Absolute hemodynamic parameters (MABP, HR, *CO*, SV, and TPR) during each PLR state as well as differences in hemodynamic parameters between pre-PLR to active PLR and active PLR to post-PLR were calculated for all five participant groups. These data were also compared between self-reported hypertensive/normotensive participants and between SOBP/OBP participants using independent sample *t* tests.

Simple linear regression modeling was used to analyze possible univariate associations between demographic data [age, sex, race, body surface area (BSA), sleep apnea diagnosis, and antihypertensive medication use], self-reported hypertensive status, 24-h ABPM-measured SBP/DBP, and SOBP status with hemodynamic parameters during and between each PLR state. Multiple linear regression modeling was used for multivariate analysis, adjusting for the above demographic data. The multivariate model assumptions were validated by assessment of associated residual plots.

All reported *P* values are two-sided and *P* less than 0.05 was used to define statistical significance.

RESULTS

Study populations and baseline characteristics

Table 1 shows demographic and hemodynamic parameter data of all participants ($n = 103$), self-reported normotensive participants ($n = 44$), self-reported hypertensive participants ($n = 59$), participants with OBP ($n = 43$), and participants with SOBP ($n = 55$).

Between self-reported hypertensive and normotensive participants, there was similar ($P > 0.05$) average age, self-reported white race, positive diabetes status, positive sleep apnea diagnosis, and current smoking status. However, participants with self-reported hypertension had higher average BSA and were more likely to be male compared with participants with reported normotension ($P < 0.05$).

Between SOBP and OBP participants, there was similar ($P > 0.05$) average age, self-reported white race, male sex, positive diabetes status, antihypertensive medication use, and current tobacco use. However, participants with SOBP were more likely to have a diagnosis of sleep apnea and higher BSA ($P < 0.05$). Participants with SOBP had higher self-reported hypertension status but did not meet significance ($P = 0.09$).

There was considerable disagreement between self-reported hypertensive status and BP control status determined by 24-h ABPM. Of 43 participants who had self-reported normotension at study onset, 20 were identified to have SOBP based on 24-h ABPM. Of 55 participants with self-reported hypertension at study onset, only 35 were found to have SOBP.

Univariate analyses of hypertension/normotension status and suboptimal blood pressure/optimal blood pressure status with hemodynamic parameters across passive leg raise states

Figure 2 illustrates the effects of PLR on hemodynamic parameters during (pre-PLR, active PLR, and post-PLR) and between (pre-PLR to active PLR and active PLR to post-PLR) each PLR state. Differences in these values were compared between self-reported normotensive/hypertensive populations and OBP/SOBP populations using independent sample *t* tests. This data is characterized in further detail within Supplemental Table 1, http://links.lww.com/HJH/C556.

Self-reported hypertensive and SOBP participants had significantly higher MABP during all PLR states compared

TABLE 1. Characteristics of participants stratified by reported hypertension and blood pressure control status determined by 24-h ambulatory blood pressure monitoring

Demographic	All ($n=103$)	Reported NTN ($n=44$)	Reported HTN ($n=59$)	*P* value	OBP ($n=43$)	SOBP[a] ($n=55$)	*P* value
Age (years)							
Mean	70.8	70.1	71.3	0.46	70.5	71.3	0.62
SD	7.8	8.1	7.7		7.0	8.7	
BSA (m^2)							
Mean	2.0	1.9	2.1	0.003	1.9	2.1	0.001
SD	0.2	0.2	0.2		0.2	0.2	
Male sex							
No. (%)	71 (68.9)	24 (54.5)	47 (79.7)	0.006	25 (58.1)	42 (76.4)	0.054
Race (white)[b]							
No. (%)	93 (90.3)	41 (93.2)	52 (88.1)	0.39	40 (93.0)	49 (89.1)	0.50
Diabetes							
No. (%)	17 (16.5)	4 (9.1)	13 (22.0)	0.080	4 (9.3)	9 (16.4)	0.31
Sleep apnea							
No. (%)	19 (18.4)	5 (11.4)	14 (23.7)	0.11	3 (7.0)	13 (23.6)	0.030
Current tobacco use							
No. (%)	10 (9.7)	2 (4.5)	8 (13.6)	0.13	4 (9.3)	6 (10.9)	0.79
BP Med							
No. (%)	53 (51.5)	0 (0)	53 (89.8)	<0.001	18 (41.9)	31 (56.4)	0.15
Reported HTN							
No. (%)	59 (57.3)	0 (0)	59 (100)	-	20 (46.5)	35 (63.6)	0.090
24-h ABPM SBP							
Mean	123.7	119.2	127.2	0.001	113.6	131.6	<0.001
SD	12.2	11.5	11.6		7.4	8.8	
24-h ABPM DBP							
Mean	72.0	71.3	73.9	0.10	67.8	76.7	<0.001
SD	7.5	6.2	8.2		4.3	7.1	
SOBP[a]							
No. (%)	55 (56.1)	20 (45.5)	35 (59.3)	0.090	0 (0)	55 (100)	-

Statistical analyses: *P* values were derived from independent sample *t* tests or χ^2 tests based on continuous and categorical data, respectively. 24-h ABPM, 24-h ambulatory blood pressure monitoring; BP med, antihypertensive medication use; BSA, body surface area; HTN, hypertension; NTN, normotension; OBP, optimal blood pressure control; SOBP, suboptimal blood pressure control.
[a]Suboptimal blood pressure control is derived from 24-h ABPM $\geq$ 125/75 mmHg.
[b]White and nonwhite distinction was used given overwhelming majority of participants were white with the remaining ~10% representing self-reported black participants.

with normotensive and OBP participants, respectively. Self-reported hypertensive patients also had higher *CO* during post-PLR compared with normotensive participants. There were no other hemodynamic parameters significantly different between self-reported hypertensive and normotensive participants. However, SOBP participants had multiple hemodynamic parameters significantly different from OBP participants during each PLR state. Participants with SOBP had no difference in TPR values during pre-PLR, active-PLR, or post-PLR compared with participants with OBP ($P > 0.05$).

There was no difference in ΔMABP, ΔHR, Δ*CO*, ΔSV, or ΔTPR from either pre-PLR to active PLR or active PLR to post-PLR between self-reported hypertensive and normotensive participants. However, participants with SOBP had reduced changes in *CO* and SV from pre-PLR to active PLR and active PLR to post-PLR (trending toward significance) compared with participants with OBP. Participants with SOBP had increased TPR from pre-PLR to active PLR while participants with OBP had decreased TPR (11.6 ± 147.9 vs. -56.1 ± 106.4 dynes s/cm^5, $P = 0.04$). Additionally, SOBP participants had a reduced change in TPR from active PLR to post-PLR (7.0 ± 156.0 vs. 127.3 ± 145.6 dynes s/cm^5; $P = 0.002$) compared with OBP participants.

Association of participant demographics with hemodynamic parameters across passive leg raise states

The associations of demographics with hemodynamic parameters during pre-PLR, active PLR, and post-PLR (Supplemental Table 2, http://links.lww.com/HJH/C556) were analyzed using simple linear regression. Multiple linear regression models were also used to adjust for other demographic variables (age, BSA, sex, race, sleep apnea diagnosis, and antihypertensive medication use). MABP, HR, *CO*, SV, and TPR were all strongly associated with BSA during every PLR state, even after adjustment.

The associations of demographics with hemodynamic parameters between PLR states (Table 2) were analyzed using simple linear regression and multiple linear regression modeling as above. Increase in TPR from pre-PLR to active PLR was associated with reported white race after adjustment. Decrease in MABP from active PLR to post-PLR was associated with higher BSA and female sex. Decrease in HR from active PLR to post-PLR was associated with reported white race. Decrease in TPR from active PLR to post-PLR was strongly associated with higher BSA.

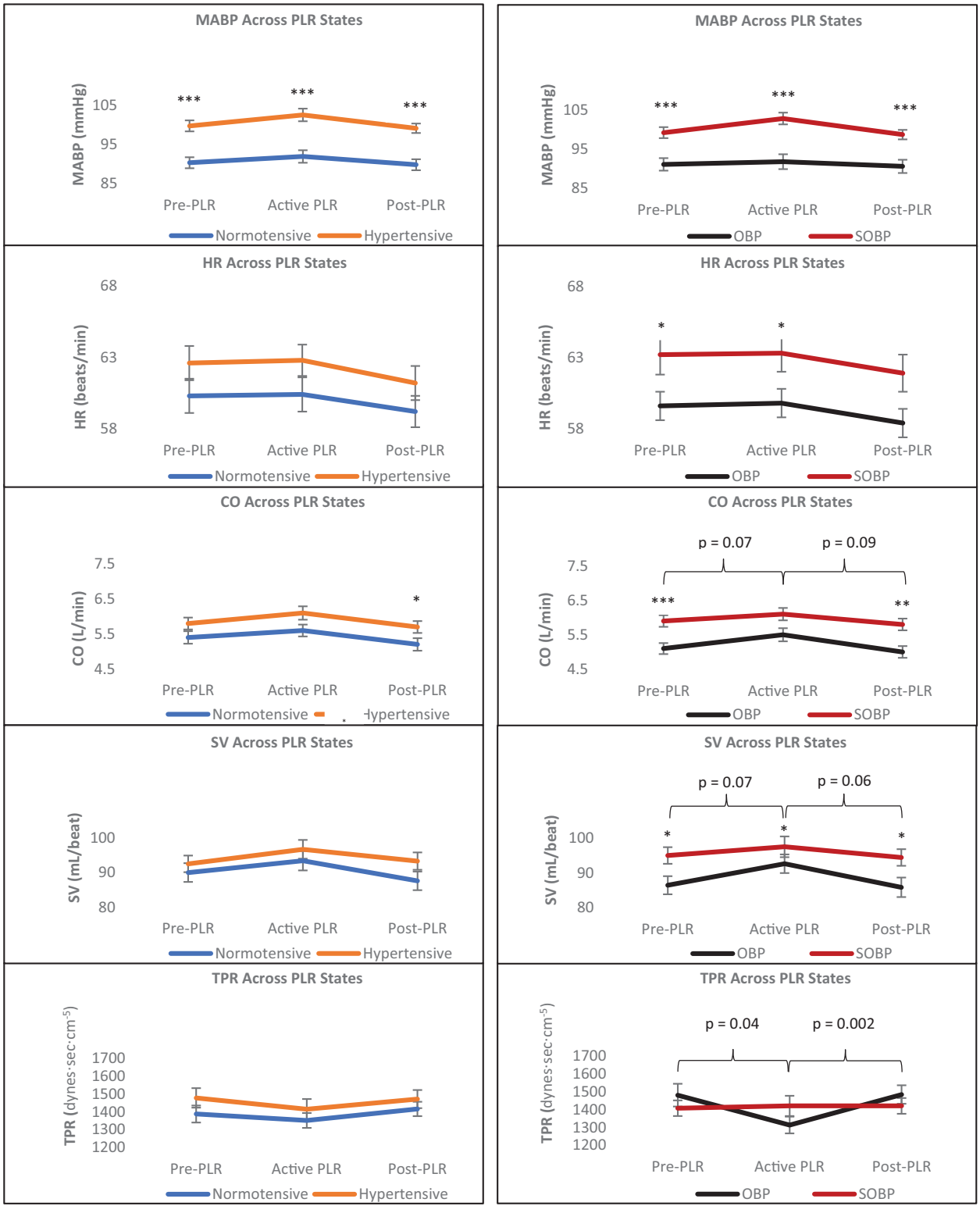

FIGURE 2 Change in hemodynamics during a passive leg raise. Noninvasively measured hemodynamic parameters across passive leg raise (PLR) states (pre-PLR, active PLR, and post-PLR) for self-reported normotensive/hypertensive populations and 24-h ambulatory blood pressure monitoring determined optimal blood pressure (OBP)/suboptimal blood pressure control (SOBP) populations. Independent sample *t* tests assessed differences during each state of PLR as well as across PLR states. *CO*, cardiac output; HR, heart rate; MABP, mean arterial blood pressure; PLR, passive leg raise; SV, stroke volume; TPR, total peripheral resistance. Error bars are standard errors. Significance: $^{*}P < 0.05$, $^{**}P < 0.01$, $^{***}P < 0.001$.

TABLE 2. The associations between demographic variables and change in hemodynamic parameters across passive leg raise states (pre-passive leg raise to active passive leg raise/active passive leg raise to post-passive leg raise)

	Pre-PLR to active PLR									
	ΔMABP		ΔHR		ΔCO		ΔSV		ΔTPR	
Demographic	*β*	*P* value	*β*	*P* value	*β*	*P* value	*β*	*P* value	*β*	*P* value
Univariate[a]										
Age	0.07	0.64	0.08	0.41	−0.16	0.11	−0.18	0.066	0.16	0.18
BSA	0.13	0.27	0.03	0.80	−0.01	0.95	−0.05	0.59	0.20	0.097
Male sex	−0.01	0.96	0.04	0.71	−0.13	0.19	−0.14	0.15	0.19	0.11
Race (white)	0.18	0.12	0.10	0.34	−0.12	0.22	−0.17	0.081	0.25	0.036
Sleep apnea	0.08	0.50	0.11	0.26	0.14	0.17	0.08	0.45	0.02	0.86
BP Med	0.02	0.89	0.05	0.65	0.09	0.35	0.07	0.50	−0.04	0.72
Multivariable[b]										
Age	0.08	0.54	0.10	0.38	−0.07	0.56	−0.11	0.35	0.09	0.50
BSA	0.18	0.23	0.00	0.99	0.01	0.92	−0.04	0.75	0.16	0.26
Male sex	−0.11	0.45	−0.03	0.83	−0.15	0.28	−0.10	0.45	0.11	0.46
Race (white)	0.18	0.15	0.09	0.40	−0.11	0.30	−0.16	0.12	0.25	0.035
Sleep apnea	0.07	0.58	0.13	0.25	0.13	0.21	0.08	0.48	0.01	0.91
BP Med	0.01	0.065	0.04	0.71	0.08	0.42	0.06	0.53	−0.05	0.67
	Active PLR to post-PLR									
	ΔMABP		ΔHR		ΔCO		ΔSV		ΔTPR	
Demographic	*β*	*P* value	*β*	*P* value	*β*	*P* value	*β*	*P* value	*β*	*P* value
Univariate[a]										
Age	−0.17	0.16	0.02	0.81	0.23	0.023	0.19	0.050	−0.20	0.087
BSA	−0.16	0.18	−0.01	0.95	0.07	0.46	0.11	0.28	−0.32	0.006
Male sex	0.13	0.26	−0.02	0.87	0.12	0.24	0.13	0.20	−0.18	0.13
Race (white)	−0.13	0.28	−0.20	0.043	0.06	0.57	0.11	0.26	−0.08	0.52
Sleep apnea	0.21	0.069	−0.04	0.69	−0.03	0.78	−0.00	0.97	−0.01	0.94
BP Med	−0.04	0.72	0.01	0.96	0.10	0.33	0.09	0.35	−0.07	0.57
Multivariable[b]										
Age	−0.22	0.076	0.07	0.57	0.23	0.049	0.19	0.11	−0.20	0.13
BSA	−0.41	0.002	0.02	0.91	0.08	0.55	0.11	0.40	−0.36	0.011
Male sex	−0.38	0.006	−0.05	0.73	−0.03	0.84	−0.02	0.91	0.05	0.71
Race (white)	−0.11	0.32	−0.21	0.042	0.04	0.70	0.10	0.31	−0.10	0.41
Sleep apnea	0.25	0.04	−0.03	0.78	−0.03	0.78	−0.02	0.85	0.04	0.75
BP Med	−0.10	0.36	0.00	0.99	0.10	0.32	0.09	0.37	−0.06	0.62

BP Med; antihypertensive medication use; BSA, body surface area; *CO*, cardiac output; HR, heart rate; MABP, mean arterial blood pressure; PLR, passive leg raise; SV, stroke volume; TPR, total peripheral resistance.
[a]Univariate analysis was completed with simple linear regression modeling.
[b]Multivariable analysis was completed with multiple linear regression modeling using all other demographic variables.

Association of participant blood pressures, self-reported hypertensive status, and suboptimal blood pressure status with hemodynamic parameters across passive leg raise states

When assessing for potential associations between self-reported hypertension/24-h ABPM measured average BPs/SOBP status and hemodynamic parameters during pre-PLR, active PLR, and post-PLR (Supplemental Table 3, http://links.lww.com/HJH/C556), multiple linear regression models were used to adjust for demographic variables (age, BSA, sex, race, sleep apnea diagnosis, and antihypertensive medication use). Increased MABP was strongly associated with self-reported hypertension, 24-h ABPM measured high SBP, high DBP, and SOBP status during all PLR states after multivariate adjustment.

When assessing for potential associations between self-reported hypertension/24-h ABPM measured average BPs/SOBP status with hemodynamic parameters between PLR states (Table 3), multiple linear regression models were used as above. Decreased MABP from active PLR to post-PLR was associated with SOBP status after adjustment. Decreased *CO* from pre-PLR to active PLR was strongly associated with 24-h ABPM measured high SBP, high DBP, and SOBP status. However, increased *CO* from active PLR to post-PLR was only associated with 24-h ABPM measured DBP. Change in HR across PLR states had no association with self-reported hypertension, 24-h ABPM-measured SBP/DBP, or SOBP status. Increased TPR from pre-PLR to active PLR was strongly associated with 24-h ABPM-measured high SBP, high DBP, and SOBP status. Similarly, decreased TPR from active PLR to post-PLR was strongly associated with these same BP categories.

DISCUSSION

We show that PLR is a practical, office-based test that offers measurable dynamic hemodynamic parameters that

TABLE 3. Associations between reported hypertension and 24-h ambulatory blood pressure monitoring-measured blood pressure/suboptimal blood pressure status with hemodynamic changes across passive leg raise states

	Pre-PLR to active PLR									
	ΔMABP		ΔHR		ΔCO		ΔSV		ΔTPR	
BP and BP statuses	*β*	*P* value	*β*	*P* value	*β*	*P* value	*β*	*P* value	*β*	*P* value
Unadjusted										
Reported HTN	0.03	0.82	0.01	0.92	0.08	0.44	0.05	0.59	−0.05	0.69
24-h ABPM SBP	0.15	0.22	0.07	0.51	−0.19	0.066	−0.23	0.021	0.26	0.032
24-h ABPM DBP	0.08	0.50	−0.04	0.73	−0.21	0.043	−0.22	0.032	0.26	0.028
SOBP[b]	0.19	0.13	−0.02	0.84	−0.18	0.074	−0.18	0.074	0.25	0.041
Adjusted[a]										
Reported HTN	−0.00	0.98	−0.08	0.62	0.06	0.70	0.07	0.66	−0.10	0.58
24-h ABPM SBP	0.12	0.35	0.06	0.59	−0.24	0.028	−0.27	0.010	0.26	0.035
24-h ABPM DBP	0.09	0.53	−0.03	0.78	−0.34	0.002	−0.35	0.001	0.37	0.004
SOBP[b]	0.16	0.25	−0.05	0.68	−0.24	0.026	−0.22	0.036	0.25	0.050
	Active PLR to post-PLR									
	ΔMABP		ΔHR		ΔCO		ΔSV		ΔTPR	
BP and BP statuses	*β*	*P* value	*β*	*P* value	*β*	*P* value	*β*	*P* value	*β*	*P* value
Unadjusted										
Reported HTN	−0.06	0.63	−0.08	0.42	0.07	0.50	0.11	0.29	−0.07	0.55
24-h ABPM SBP	−0.26	0.031	−0.03	0.75	0.22	0.028	0.24	0.018	−0.35	0.003
24-h ABPM DBP	−0.07	0.58	−0.05	0.65	0.16	0.11	0.20	0.044	−0.20	0.094
SOBP[b]	−0.20	0.11	−0.01	0.94	0.17	0.090	0.19	0.067	−0.37	0.002
Adjusted[a]										
Reported HTN	−0.03	0.84	−0.23	0.15	−0.09	0.59	0.02	0.92	0.05	0.78
24-h ABPM SBP	−0.22	0.065	−0.06	0.62	0.20	0.074	0.22	0.048	−0.30	0.013
24-h ABPM DBP	−0.20	0.11	−0.05	0.67	0.27	0.018	0.29	0.008	−0.28	0.030
SOBP[b]	−0.23	0.049	−0.01	0.91	0.18	0.10	0.19	0.082	−0.35	0.004

ABPM, ambulatory blood pressure monitoring; *CO*, cardiac output; HR, heart rate; HTN, hypertension; MABP, mean arterial blood pressure; PLR, passive leg raise; SV, stroke volume; TPR, total peripheral resistance.
[a]Adjusted for age, body surface area, sex, race (white vs. nonwhite), sleep apnea, and antihypertensive medication use.
[b]SOBP status is suboptimal blood pressure control measured from average 24-h ABPM ≥ 125/75 mmHg.

correlate with 24-h ABPM-measured higher SBP, higher DBP, and SOBP status within the older adult (≥60 years) population. When comparing self-reported hypertensive/normotensive status, only MABP was consistently different. Interestingly, multiple hemodynamic parameter differences were found to be associated with BP control status based on 24-h ABPM standards, regardless of self-reported hypertensive status. After adjusting for confounding variables (age, BSA, sex, race, sleep apnea, and antihypertensive medication use), our results showed that a reduction in TPR from active PLR to post-PLR was strongly associated with 24-h ABPM-measured higher SBP, higher DBP, and SOBP status.

Previous research has shown 24-h ABPM is superior to office BP measurements when considering both diagnostic accuracy and correlation to end-organ damage (evidenced by increased left ventricular mass index changes and carotid intima thickness associated with long-standing hypertension) [6,18,25]. Despite these important benefits, 24-h ABPM it is often considered impractical for routinely diagnosing hypertension and has largely been usurped by self-measured home BP monitoring [26,27]. Still, home BP monitoring relies on patient compliance and proper technique and may not be reliable in older adults because of disability or potential cognitive impairment [27]. Interestingly, our data shows notable discordance between reported hypertension status and BP control status based on 24-h ABPM. This may partially be because of antihypertensive medication effect, but diagnostic inaccuracy of self-reported BP status is likely playing a role. Ultimately, our data suggests hemodynamic changes measured during PLR correlate to the more accurate 24-h ABPM data rather than self-reported hypertensive status.

PLR acutely impacts hemodynamics by transferring venous volume from the legs to the intrathoracic cavity [28,29], increasing right and left ventricular preload [30,31]. The effect of PLR on *CO* can have individual variability, and prior evidence suggests this is due to differences in cardiac preload reserve [32]. Our data showed PLR-induced changes in *CO* were blunted for participants with SOBP compared with participants with OBP from pre-PLR to active PLR, even after adjusting for demographic variables and antihypertensive medication use (Fig. 2 and Table 3). The normal physiologic effect of PLR on TPR has also been previously characterized. A study by Nemoto *et al.* [33] showed an overall trend of transient decline in TPR at the beginning of active PLR and post-PLR followed by an increasing magnitude that continued through post-PLR in eight healthy adults. Older participants with OBP in our study followed this same pattern. However, we found that participants with SOBP control had blunted changes in TPR throughout PLR compared with OBP participants, even after adjusting for demographics and antihypertensive

medication use (Fig. 2 and Table 3). Our results suggest that participants who cannot augment *CO* and TPR changes in response to PLR may be, at least in part, because of poor BP control. Although many pathophysiologic factors such as reduced venous capacitance may contribute to these findings, arterial stiffness has been shown to precede hypertension and may decrease vascular adaptability due to both intrinsic and load-dependent vessel wall changes [34].

Even after adjustment for demographic variables, higher BSA was associated with higher *CO* and lower TPR during each PLR state. Similar associations between weight and *CO*/SVR were found in a study by Li *et al.* [35] where hemodynamic data was derived using cardiac MRI. Interestingly, we found that increasing BSA also has a significant association with reduction in TPR from active PLR to post-PLR after adjustment for other demographic variables. Despite this strong association with BSA, 24-h ABPM measured high SBP, high DBP, and SOBP status also remained strongly associated with reduced TPR from active PLR to post-PLR after multivariate adjustment.

There is increasing evidence of heterogeneity in hemodynamic profiles within the hypertensive population, and these changes may eventually lead to more personalized hypertension treatment.[25–26] For example, Mahajan *et al.* [36] showed that within a cohort of 33 414 hypertensive individuals, 70% had high TPR with normal cardiac index, 15% with high cardiac index and normal TPR, and 15% with low/normal cardiac index and TPR. These measurements were all completed at rest. Our SOBP group fit into the group with higher *CO* (5.9 ± 1.3 vs. 5.0 ± 1.0, $P = 0.001$) but similar TPR (1407.2 ± 320.0 vs. 1480.7 ± 413.7, $P = 0.33$) at baseline. Results from our study show that changes in MABP, *CO*, SV, and TPR across PLR states are significantly associated with higher 24-h ABPM measured SBP, DBP, or SOBP status. Therefore, a preload augmentation model of assessing hemodynamic parameters like PLR may offer helpful information in further developing complete hemodynamic profiles that would offer additional insight into how we treat these individuals.

Limitations

This was a single-center cohort study with a sample population limited to predominantly white/Caucasian (~90%) Veteran participants over the age of 60 years and older. Impedance cardiography was used, which has lower utility in patients with arrhythmias, shunts, and valvular pathologies, though is ideal for healthy older adults who are free of known cardiovascular disease. These analyses were performed on a subset of participants enrolled who underwent PLR and had hemodynamic data available. PLR in our study was carried out from a supine position rather than a semi-recumbent position. Starting in a semi-recumbent position allows for lowering of the torso, which may increase venous return more than the supine position because of additional blood volume from the splanchnic system [22,37]. Starting in a supine vs. semi-recumbent position could have impacted the differences, we observed in TPR based on BP status as TPR is a directly related ratio of MABP and *CO*. Changes in hemodynamic parameters with PLR were a secondary outcome, thus the study was not specifically powered to detect changes based on BP control status. Similarly, baseline characteristics of the groups were different, which is reflected in significant differences in sex, BSA, and sleep apnea incidence between groups (Table 1), though we attempted to account for this with multivariate analyses. The cross-sectional cohort design of the study did not allow us to prospectively follow participants to determine if blood pressure control was sustained. Finally, the office-setting implementation of PLR with noninvasive impedance cardiography does come with challenges including the time required to complete the test (~20 to 30 min), the necessity for a patient to be present at an office visit (unable to provide this test during a virtual visit), costs associated with procurement of necessary testing equipment (impedance cardiography system/sensors, testing software, BP cuff, etc.), and the need to train personnel to oversee the testing protocol.

CONCLUSION

Changes in hemodynamic parameters due to preload augmentation with a PLR may lead to development of future tests that efficiently identify older adults with SOBP control when 24-h ABPM is not available. Noninvasively measured change in total peripheral resistance throughout a PLR maneuver was significantly reduced in older participants with SOBP control compared with those with OBP control. Further prospective studies are needed to confirm the utility of our findings.

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Conflicts of interest

There are no conflicts of interest.

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