


SHORT REPORT

Inter-arm difference in blood pressure in patients referred to tertiary hypertension center: Prevalence, risk factors, and relevance to physicians

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Abstract

The prevalence of inter-arm BP difference is high in hypertension and is associated with adverse cardiovascular outcomes. We performed a retrospective chart review of prevalent patients in the Ottawa Hospital Hypertension Center to assess for prevalence, risk factors, and whether finding of inter-arm BP difference >10 mmHg leads to investigations of the aorta and aortic arch. Inter-arm BP difference among 493 patients was present in 16.2% (95% confidence interval [CI] 13.3-19.9%), and it was associated with presence of peripheral arterial disease. Physicians did not investigate ascending aorta and aortic arch for causes of the clinically significant inter-arm BP difference.

1 | INTRODUCTION

Prevalence of inter-arm blood pressure (BP) difference >10 mmHg is up to 39% in patients with hypertension, and it has major implications for diagnosis and management of hypertension.¹ Firstly, unrecognized inter-arm BP difference could lead to missed diagnosis of hypertension and/or under- or overtreatment of hypertension.² Second, recognized inter-arm BP difference is an important risk factor for adverse cardiovascular outcomes. In the meta-analysis of cohort studies by Zhou et al³, risk of fatal cardiovascular events increased with inter-arm difference in systolic BP >10 mmHg and >15 mmHg to 1.58 (95% CI 1.3-1.9) and to 1.88 (95% CI 1.3-2.6), respectively. In particular, presence of inter-arm BP difference >10 mmHg is associated with ruptured aortic aneurysms, aortic dissections, and cardiovascular death.⁴⁻⁶

Guidelines by national professional organizations recommend screening for inter-arm BP difference as it is relevant for diagnosis and management of hypertension.^{2,7-9} They however do not provide any further guidance concerning the investigations of ascending aorta and aortic root (and management) of patients with this condition known to be associated with an excess in hypertension-related adverse vascular outcomes.

The goal of the present study was to determine the prevalence and risk factors associated with inter-arm BP difference (>10 mmHg) in hypertensive patients referred to a tertiary care hospital-based hypertension centre. Finally, given the well documented association of inter-arm difference in BP and disease of the ascending aorta and aortic arch we also assessed physicians' awareness of this association based on the ordered investigations (or lack thereof) of patients with diagnosed inter-arm difference.

2 | MATERIAL AND METHODS

A retrospective chart review of all prevalent patients seen at The Ottawa Hospital Renal Hypertension Centre, Ontario, Canada between 2006 and July 2017 was performed. Casual sitting first single BP readings taken by one of 4 nurses specialized in hypertension and attending hypertension clinic on both arms sequentially (with no preference for which arm was measured first) using a mercury sphygmomanometer during their first clinic visit as per Hypertension Canada guidelines² were obtained from patient's charts, along with their age, height, weight, waist circumference, list of medications, past medical history, smoking status, and blood test results at the

time of their first visit. Information on investigations (or lack thereof) to further investigate for ascending aorta and aortic arch pathology such as ultrasound or computer axial tomography of the chest was obtained from patient's chart notes and electronic medical records. Patients with absent BP data and those discharged from the clinic were excluded.

We considered inter-arm difference in systolic BP in excess of 10 mmHg to be clinically significant. We defined proteinuria as a protein-creatinine ratio greater than 20 g/mol of creatinine. Demographic and clinical data are presented using means and standard deviation for quantitative data and as count (percentages) for nominal data. Univariate logistic regression was conducted to identify association of covariates with inter-arm difference. All covariates with $P \leq 0.1$ were then entered into a multivariable model using a stepwise method for backward elimination. All analysis was done using JMP (version 9.1, SAS Inc, Cary, NC).

3 | RESULTS

3.1 | Study population

There were 580 prevalent patients seen in the hypertension clinic between 2006 and July 2017 of which 488 were included in the final analysis after accounting for missing BP data and/or discharged patients. They were middle aged (59.4 ± 16.8 years) with additional cardiovascular risk factors and had difficulty to control hypertension as reflected by average of 3 BP-lowering drugs (Table 1).

3.2 | Prevalence of inter-arm BP difference

16.6% (81 patients, 95% confidence interval [CI] 13.3-19.9%) of the study population had a systolic inter-arm BP difference >10 mmHg. 5.9% (29 patients, 95% CI 3.8-8.0%), and 3.3% (16 patients, 95% CI 2.5-4.1%) had a systolic inter-arm BP difference >15 mmHg and 20 mmHg, respectively.

3.3 | Risk factors for inter-arm BP difference

Univariate analysis showed that patients with an inter-arm BP difference were more likely to be older males, but significance of this was lost in multivariate analysis.

3.4 | Hypothetical relevance of inter-arm BP difference for diagnosis of HTN

In our study, the diagnosis of hypertension would be completely missed based solely on BP readings from the arm with lower BP in 31 patients (38%, 95% CI 27.7-48.9%) diagnosed inter-arm BP difference.

3.5 | Relevance of diagnosed inter-arm BP difference for diagnostic imaging of aortic arch and ascending aorta pathology

None of the patients with confirmed inter-arm BP difference had been referred for investigations of the ascending aorta or aortic arch pathology.

4 | DISCUSSION

This retrospective study has two major findings. First, 16.6% of patients with hypertension referred to tertiary hospital-based hypertension center had de novo diagnosed inter-arm BP difference of >10 mmHg. Second, causes of the inter-arm BP difference are unknown as the result of considerable clinical inertia toward further investigations of ascending aorta and aortic arch.

4.1 | Comparison of prevalence of inter-arm BP difference to other studies

Prevalence of inter-arm systolic BP difference (>10 mmHg) differs considerably between the studies ranging from 1% to 39%^{4,10,11} These discrepancies in prevalence rates between studies are noted due to differing sample sizes, patient population (eg, hypertensive vs. non-hypertensive), associated comorbidities (eg, diabetes mellitus and obesity), setting (eg, inpatients vs. outpatient), age and methods of BP assessment (eg, mercury sphygmomanometry vs. automated oscillometric BP monitor).^{4,10,11} Our findings are in concert with data from systematic review by Clark et al⁴ reporting prevalence 19% for systolic inter-arm BP difference greater than 10 mmHg.

4.2 | Relevance of inter-arm BP difference for diagnosis and management of HTN

Our data suggest that still many physicians are not aware of high prevalence of inter-arm BP difference as it was de novo diagnosis identified in 16% referred patients. This is highly relevant for diagnosis of hypertension which would be potentially missed in 31 patients, as well as for the management of hypertension as BP readings from the arm with lower BP would lead to undertreatment of hypertension.^{2,7-9}

4.3 | Diagnostic imaging of the ascending aorta and aortic arch in patients with inter-arm BP difference

None of the patients with diagnosed inter-arm BP difference had further diagnostic testing for ascending aorta and aortic arch pathology. On one hand that is in line with the lack of specific

TABLE 1 Baseline demographic data of study participants

Demographics	All patients in Hypertension clinic included in study N = 488	Patients with inter-arm SBP difference \geq 10 mmHg N = 81 (16.6%)	Patients without inter-arm SBP difference \geq 10 mmHg N = 407 (83.4%)	P-value (Univariate regression analysis)
Males	236 (48.4%)	51 (63.0%)	185 (45.5%)	.004
Age (y)	59.4 \pm 16.8	63.3 \pm 16.6	58.7 \pm 16.8	.02
Body mass index (kg/m ²)	31.0 \pm 10.8	30.6 \pm 6.8	31.1 \pm 11.4	.67
Waist circumference (cm)	104.5 \pm 17.2	103.8 \pm 13.2	104.7 \pm 17.8	.68
Smokers ^a	193 (39.9%)	25 (30.9%)	168 (41.7%)	.07
Diabetes mellitus	149 (30.2%)	20 (25%)	129 (31.2%)	.38
Ischemic heart disease	68 (13.9%)	7 (8.6%)	61 (15.0%)	.03
Peripheral arterial disease	47 (9.7%)	7 (8.6%)	40 (9.8%)	.74
Cerebrovascular disease	52 (10.7%)	9 (11.1%)	43 (10.6%)	.89
Atrial Fibrillation	23 (4.8%)	2 (2.5%)	21 (5.2%)	.27
Congestive heart failure	18 (3.7%)	2 (2.5%)	16 (4.0%)	.51
Creatinine (mmol)	95.9 \pm 37.1	104.1 \pm 41.4	94.2 \pm 36.1	.05
LDL (mmol/L)	2.5 \pm 1.1	2.6 \pm 1.1	2.4 \pm 1.1	.44
Protein: Creatinine ratio (>20 g/mol)	189 (41.5%)	35 (47.3%)	154 (40.4%)	.27
Hypertension meds:	2.8 \pm 1.5	3.1 \pm 1.3	2.8 \pm 1.5	.09
Thiazide diuretic	253 (51.8%)	42 (51.9%)	211 (51.8%)	.99
RAAS inhibitor	387 (78.5%)	64 (80.0%)	323 (78.2%)	.91
Long-acting CCB	310 (63.3%)	52 (64.2%)	258 (63.4%)	.47
Alpha blocker	44 (9.0%)	10 (12.4%)	34 (8.4%)	.27
K-sparing diuretic	61 (12.5%)	9 (11.1%)	52 (12.8%)	.66
Beta blocker	225 (46.1%)	47 (58.0%)	178 (43.8%)	.05
Loop diuretic	37 (7.6%)	8 (9.9%)	29 (7.1%)	.41
Other	64 (13.1%)	12 (14.8%)	52 (12.7%)	.14
Lipid lowering therapy	219 (44.9%)	39 (48.2%)	180 (45.0%)	.38

All figures as mean \pm standard deviation or N (%).

Abbreviations: CCB, calcium channel blocker; DBP, diastolic blood pressure; LDL, low-density lipoprotein; RAAS, renin-angiotensin aldosterone system; SBP, systolic blood pressure.

^aSmokers = current or past smokers.

recommendation for further imaging of the ascending aorta and aortic arch in patients with inter-arm BP difference by guidelines by national professional organizations (Table 2). On the other hand, same guidelines recommend a referral to a specialist acknowledging the fact that inter-arm BP difference is associated with adverse hypertension-related outcomes. The evidence linking inter-arm BP difference to aortic arch and ascending aorta pathology and adverse cardiovascular outcomes is limited, but inertia toward further investigations of the aorta and aortic arch will certainly not lead to better understanding natural history of conditions presenting as inter-arm BP difference nor will lead to prevention of fatal adverse vascular outcomes such as ruptured ascending aortic aneurysm and ascending aorta dissection from underlying aortic pathology presenting as inter-arm BP difference.

Furthermore, it is possible that high inter-arm BP difference is a marker of an adverse vascular phenotype, as suggested from its stronger association with peripheral arterial disease (PAD) in previous studies.¹² Indeed, PAD has more recently emerged as a robust predictor of adverse cardiovascular outcomes.¹³ The presence of inter-arm BP difference could hence be considered as a trigger for greater awareness of evaluation and management of overall cardiovascular risk. It is indeed important to acknowledge that at the time of diagnosis of inter-arm BP difference only about 50% of patients were on treatment with lipid-lowering drugs. If these patients are truly considered of having high risk for adverse cardiovascular outcomes, one would assume a greater exposure to lipid-lowering drugs in line with recommendations by ACC/AHA guidelines.¹⁴

4.4 | Limitations of this study

Data from our study do not reflect prevalence of inter-arm BP difference in the general hypertensive population but rather referred patients with high prevalence of comorbidities such as diabetes mellitus and dyslipidemia. That also limits significance of correlation (or lack thereof) between inter-arm BP difference and these cardiovascular risk factors in our study. Furthermore, inter-arm BP difference is based on sequential BP assessment raising an issue of overestimated inter-arm BP difference caused by time gap between the two arm measurements. In this regard, use of simultaneous vs. consecutive of BP assessment by mercury sphygmomanometry did not yield difference in the prevalence of inter-arm difference among 1000 studied subjects by Kornis et al.¹⁵

4.5 | Conclusion

We report high prevalence of de novo diagnosed inter-arm BP difference among adult Canadians with hypertension referred to hypertension center indicating low awareness of this entity among physicians. Causes of the inter-arm BP difference in our patients are unknown as the result of current uncertainty about utility of further investigations. Given the association between inter-arm BP difference and adverse hypertension-related vascular outcomes, in our opinion, better awareness among the physicians leading to testing for inter-arm BP difference and investigations for causes of this entity could improve diagnosis and management of HTN and

Guideline Society	Guidelines regarding inter-arm BP difference
Hypertension Canada	"The appropriately sized cuff should be applied to the non-dominant arm unless the SBP difference between arms is >10 mm Hg, in which case the arm with the highest value obtained should be used" No recommendations about further investigations in patients with an inter-arm BP difference ²
American College of Cardiology/ American Heart Association	"At the first visit, record BP in both arms. Use the arm that gives the higher reading for subsequent readings" No recommendations about further investigations in patients with an inter-arm BP difference ⁸
National Institute for Health Care Excellence	"If the difference in readings between arms is more than 20 mmHg, repeat the measurements. If the difference in readings between arms remains more than 20 mmHg on the second measurement, measure subsequent blood pressures in the arm with the higher reading." No recommendations about further investigations in patients with an inter-arm BP difference ⁹
European Society of Cardiology and European Society of Hypertension	"BP should initially be measured in both upper arms, using an appropriate cuff size for the arm circumference. A consistent and significant SBP difference between arms (ie, >15 mmHg) is associated with an increased CV risk, most likely due to atheromatous vascular disease. Where there is a difference in BP between arms, ideally established by simultaneous measurement, the arm with the higher BP values should be used for all subsequent measurements." No recommendations about further investigations in patients with an inter-arm BP difference ⁷

TABLE 2 Summary of guidelines by national professional organizations regarding inter-arm BP difference

potentially prevent inter-arm BP difference related increase in adverse cardiovascular outcomes.

CONFLICT OF INTEREST

The authors have no conflict of interest to report.

AUTHOR CONTRIBUTIONS

M. Ruzicka conceived idea for analysis, wrote the paper, and made revisions. J. Jegatheswaran collected the data, generated tables, wrote the paper, and made revisions. S. Hiremath conceived idea, performed the statistical analysis, and provided editorial assistance for the final written paper. C. Edwards conceived idea and provided editorial assistance for the final written paper.

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