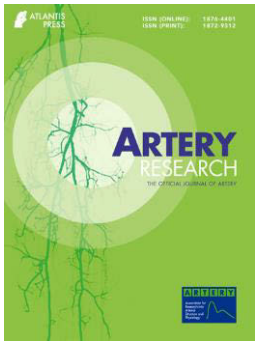

Artery Research

ISSN (Online): 1876-4401 **ISSN (Print): 1872-9312**
Journal Home Page: https://www.atlantis-press.com/journals/artres

Central blood pressure: A new vital sign?

Mary J. Roman

To cite this article: Mary J. Roman (2009) Central blood pressure: A new vital sign?, Artery Research 3:4, 125–127, DOI: https://doi.org/10.1016/j.artres.2009.10.179

To link to this article: https://doi.org/10.1016/j.artres.2009.10.179

Published online: 14 December 2019

Artery Research (2009) 3, 125–127

available at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/artres

Central blood pressure: A new vital sign?

Mary J. Roman*

Weill Cornell Medical College, 520 East 70th Street, New York, NY 10021, USA
Available online 28 October 2009

KEYWORDS
Central blood pressure;
Applanation tonometry;
Left ventricular hypertrophy;
Atherosclerosis;
Cardiovascular disease outcomes

The ongoing development of non-invasive technology to perform sophisticated pulse wave analysis and accurately determine central blood pressure has facilitated study of central blood pressure as a physiologic parameter or biomarker. It is now possible to systematically compare the magnitude of differences in central and brachial systolic and pulse pressures. Furthermore, the relative importance of central and brachial pressures in relation to both subclinical and clinical cardiovascular disease can now be assessed.

Central systolic and pulse pressures are systematically lower than their brachial counterparts due to pulse wave amplification. The major determinants of central systolic pressure include wave reflections, vascular stiffness, left ventricular contractility and heart rate. In theory, central pressure should provide a more accurate representation of the load imposed on the left ventricle and coronary and cerebral vasculature than brachial pressure due to its closer proximity. Arterial stiffening will result in higher central systolic pressure and thereby impose a greater afterload on the left ventricle whereas associated lower diastolic pressure may reduce coronary perfusion pressure. This article will review the evidence to support the adoption of central blood pressure as a new vital sign.

Although there is ample evidence of the use of biomarkers and other diagnostic testing without firm documentation of their clinical utility, present-day evidence-based medicine demands justification of use of any new biomarker, including comparison to 'gold' standards and, ultimately, cost-benefit analyses.[1] The first requirement of a new biomarker is that it be safe, accurate and reproducible. Applanation of an artery is safe and analogous to palpation of the pulse. Numerous studies have confirmed the accuracy of non-invasive central pressure measurement compared to simultaneous invasive measurements.[2–4] Reproducibility has likewise been documented[5] and may exceed that of brachial blood pressure determination.[6]

A second requirement of a new biomarker is that bear a relation to disease. We have examined the relation of central blood pressure to cardiovascular target organ damage in the Strong Heart Study. The Strong Heart Study (SHS) is a National Institutes of Health-funded population-based study of incident and prevalent cardiovascular disease in 4549 American Indians which was initiated in 1988.[7] In later phases of the study, echocardiography, carotid ultrasonography, radial applanation tonometry and genetic analyses have been added. One important aspect of

* Tel.: +1 212 746 4685; fax: +1 212 746 8561.
E-mail address: mroman@med.cornell.edu

1872-9312/$ – see front matter
doi:10.1016/j.artres.2009.10.179

the American Indian population is its high rates of obesity and diabetes mellitus which foreshadow the growing epidemic of these major public health issues in other ethnic groups and countries.[8]

We compared the relations of central and brachial blood pressures to measures of vascular hypertrophy (intimal-medial thickness and vascular mass [arterial cross-sectional area]) and extent of atherosclerosis (plaque score) in 3520 SHS participants who were studied in Exam 3.[9] The mean age of the group was 63 ± 8 years, 65% were women, 47% were diabetic and 52% were hypertensive. Brachial blood pressure was measured by cuff and mercury sphygmomanometry using a standard research protocol and central pressures were determined using radial tonometry (SphygmoCor). Brachial systolic pressure was, on average, 10 mmHg higher than central systolic pressure. Brachial and central systolic and pulse pressures were all significantly ($p < 0.001$) related to vascular hypertrophy and extent of atherosclerosis. By calculation of z statistics, we found that pulse pressures were more strongly related to vascular disease than were systolic pressures and that central pressures were more strongly related to vascular disease than were brachial pressures.

The relation of central and brachial pressures to left ventricular mass and geometry were analyzed in 2585 SHS participants in Exam 4.[10] Because of the addition of the Family Study, these participants were younger (40 ± 17 years) with lower prevalences of diabetes (21%) and hypertension (33%). Left ventricular mass was adjusted to its allometric relation to height (meters$^{2.7}$), an indexation which best adjusts for differences in body size when obesity is prevalent and improves prediction of cardiovascular risk.[11,12] Relative wall thickness was calculated as a measure of left ventricular geometry (higher values indicate concentric remodeling). Again, all blood pressure measures were strongly ($p < 0.001$) related to ventricular mass and relative wall thickness. In contrast to our finding with regard to vascular disease, systolic rather than pulse pressures were more strongly related to left ventricular hypertrophy and concentric geometry and, again, central pressures were more strongly related than brachial pressures.

These analyses support the hypothesis that central pressures are more strongly related to cardiovascular target organ damage than are brachial pressures. Furthermore, we may hypothesize that absolute (systolic) pressure is a more important stimulus to left ventricular hypertrophy and remodeling, whereas pulsatile stress (pulse pressure) is a more important stimulus to vascular hypertrophy and atherosclerosis. This hypothesis is supported by previous observations of stronger relations of brachial systolic than brachial pulse pressure to left ventricular mass.[13–15] In addition, a recent study in a healthy Taiwanese population noted that central pulse pressure was the strongest correlate of carotid intimal-medial thickness whereas central systolic pressure was the strongest correlate of left ventricular mass.[16]

A third, and more important, requirement of a new biomarker is that it predicts development of clinical disease. Several population-based studies provide support for this attribute. SHS participants who were free of prevalent cardiovascular disease ($n = 2{,}403$) were followed for a mean of 4.8 ± 1.3 years during which time 319 fatal and non-fatal cardiovascular events occurred.[9] In Cox regression analyses using pre-specified covariates, central pulse pressure was the strongest independent correlate of events among blood pressure variables. The Dicomano Study, a population-based study of elderly ($\geq$65 years of age) individuals, followed participants for 8 years and found that carotid pulse and systolic pressures but not brachial pressures predicted incident cardiovascular disease.[17] In the recent Taiwan study, 1272 healthy individuals were followed for 10 years. Although neither central nor brachial pressures were independently related to all-cause mortality, central pressures, particularly central systolic pressure, were related to cardiovascular mortality whereas brachial pressures were not.[16]

A threshold or partition value that predicts adverse cardiovascular outcomes would be of considerable clinical utility in providing a target for intervention strategies. As a first step in this process, we analyzed quartiles of central and brachial pulse pressures in SHS participants free of cardiovascular disease who were followed for a mean of 5.6 ± 1.7 years during which time 344 fatal and non-fatal cardiovascular events occurred.[18] In Cox regression models, brachial pulse pressure quartiles were of borderline significance ($p = 0.052$) in predicting outcomes whereas central pulse pressure quartiles were highly predictive ($p < 0.001$). The highest quartile of central pulse pressure ($\geq$50 mmHg) was the only quartile significantly related ($p = 0.003$) to outcome. Central pulse pressure $\geq$50 mmHg was significantly related to incident cardiovascular disease in both men and women, in diabetics and non-diabetics and in those above and below the ages of 60 or 65 years.

The ultimate requirement of a biomarker is that action taken to alter that biomarker improve clinical outcome and in a cost-effective manner. Suggestive but not definitive data exist to support this attribute. It is generally known that vasodilating drugs are more effective in lower central systolic pressure for a given brachial pressure than are diuretics or traditional beta-blocking agents. As a corollary, perindopril-based therapy resulted in greater lower of left ventricular mass than did atenolol-based therapy in the REASON study.[19] In the large ASCOT Study, the improved clinical outcomes noted in amlodipine-based based therapy compared to atenolol-based therapy were independent of greater blood pressure lowering in the amlodipine-based arm.[20] An explanation for this outcome may be found in the CAFÉ substudy wherein a subset of ASCOT participants underwent central blood pressure determination following one year of therapy.[21] Although brachial systolic and pulse pressures were lowered to a similar degree in both therapeutic arms, central systolic and pulse pressures were significantly lower (4 and 3 mmHg, respectively) with amlodipine-based therapy. Thus greater lowering of central blood pressure may explain overall results in the ASCOT Study. Similarly, the greater clinical benefit of losartan-based therapy compared to atenolol-based therapy noted in the LIFE Study, despite comparable lowering of brachial pressures, may be explained by greater lowering of central blood pressure by losartan.[22]

In order to firmly establish central blood pressure as a new vital sign and important biomarker, it will be necessary to establish normative values in large population-

based samples of healthy individuals over a broad age range, similar to efforts in the Anglo-Cardiff Collaborative Trial.[23] This study has clearly demonstrated that central systolic pressure cannot be inferred from brachial systolic pressures. In addition, conclusive documentation that lowering of central blood pressure improves clinical outcome, independent of lowering of brachial blood pressure, is required.

References

1. Hlatky MA, Greenland P, Arnett DK, Ballantyne CM, Criqui MH, Elkind MSV, et al. Criteria for evaluation of novel markers of cardiovascular risk: a scientific statement from the American Heart Association. *Circulation* 2009;**119**:2408—16.
2. Kelly R, Hayward C, Ganis J, Daley J, Avolio A, O'Rourke M. Noninvasive registration of the arterial pressure waveform using high-fidelity applanation tonometry. *J Vasc Med Biol* 1989;**1**:142—9.
3. Chen C-H, Ting CT, Nussbacher A, Nevo E, Kass DA, Pak P, et al. Validation of carotid artery tonometry as a means of estimating augmentation index of ascending aortic pressure. *Hypertension* 1996;**27**:168—75.
4. Pauca AL, O'Rourke MF, Kon ND. Prospective evaluation of a method for estimating ascending aortic pressure from the radial artery pressure waveform. *Hypertension* 2001;**38**:932—7.
5. Siebenhofer A, Kemp CRW, Sutton AJ, Williams B. The reproducibility of central aortic blood pressure measurements in healthy subjects using applanation tonometry and sphygmocardiography. *J Hum Hypertens* 1999;**13**:625—9.
6. Lane D, Beevers M, Barnes N, Bourne J, John A, Malins S, et al. Inter-arm differences in blood pressure: when are they clinically significant? *J Hypertens* 2002;**20**:1089—95.
7. Lee ET, Welty TK, Fabsitz RR, Cowan LD, Lee N-A, Oopik AJ, et al. The Strong Heart Study: a study of cardiovascular disease in American Indians: design and methods. *Am J Epidemiol* 1990;**132**:1141—55.
8. Fox CS, Coady S, Sorlie PD, D'Agostino Sr RB, Pencina MJ, Ramachandran RS, et al. Increasing cardiovascular disease burden due to diabetes mellitus: the Framingham Heart Study. *Circulation* 2007;**115**:1544—50.
9. Roman MJ, Devereux RB, Kizer JR, Lee ET, Galloway JM, Ali T, et al. Central pressure more strongly relates to vascular disease and outcome than does brachial pressure: the Strong Heart Study. *Hypertension* 2007;**50**:197—203.
10. Roman MJ, Okin PM, Kizer JR, Lee ET, Howard BV, Devereux RB. Relations of central and brachial blood pressure to left ventricular hypertrophy and geometry: the Strong Heart Study. J Hypertens, in press.
11. de Simone G, Kizer JR, Chinali M, Roman MJ, Bella JN, Best LG, et al. Normalization for body size and the population-attributable risk of left ventricular hypertrophy: the Strong Heart Study. *Am J Hypertens* 2005;**18**:191—6.
12. de Simone G, Devereux RB, Daniels SR, Koren MJ, Meyer RA, Laragh JH. Effect of growth on variability of allometric signals in adults and children and their capacity to predict cardiovascular risk. *J Am Coll Cardiol* 1995;**25**:1056—62.
13. Chen C-H, Ting C-T, Lin S-J, His T-L, Ho S-J, Chou P, et al. Which arterial and cardiac parameters best predict left ventricular mass? *Circulation* 1998;**98**:422—8.
14. Flack JM, Gardin JM, Yunis C for the CARDIA Research Group. Static and pulsatile blood pressure correlates of left ventricular structure and function in black and white young adults: the Cardia Study. *Am Heart J* 1999;**138**:856—64.
15. Verdecchia P, Schillaci G, Borgioni C, Gaatobigio R, Ambrosio G, Porcellati C. Prevalent influence of systolic over pulse pressure on left ventricular mass in essential hypertension. *Eur Heart J* 2002;**23**:658—65.
16. Wang K-L, Cheng H-M, Chuang S-Y, Spurgeon HA, Ting C-T, Lakatta EG, et al. Central or peripheral systolic or pulse pressure: which best relates to target organs and future mortality? *J Hypertens* 2009;**27**:461—7.
17. Pini R, Cavallini MC, Palmieri V, Marchionni N, Di Bari M, Devereux RB, et al. Central but not brachial blood pressure predicts cardiovascular events in an unselected geriatric population: the ICARe Dicomano Study. *J Am Coll Cardiol* 2008;**51**:2432—9.
18. Roman MJ, Devereux RB, Kizer JR, Okin PM, Lee ET, Wang W. High central pulse pressure is independently associated with adverse cardiovascular outcome: the Strong Heart Study. *J Am Coll Cardiol* 2009;**54**:1730—4;
    Roman MJ, Devereux RB, Kizer JR, Okin PM, Lee ET, Wang W. High central pulse pressure is independently associated with adverse cardiovascular outcome: the Strong Heart Study. J Am Coll Cardiol, 2009; 54:1730–4.
19. De Luca N, Asmar RG, London GM, O'Rourke MF, Safar on behalf of the REASON Project Investigators. Selective reduction of cardiac mass and central blood pressure on low-dose combination perindopril/indapamide in hypertensive subjects. *J Hypertens* 2004;**22**:1623—30.
20. Poulter NR, Weddel H, Dahlof B, Sever PS, Beevers DG, Caulfield M, et al. Role of blood pressure and other variables in the differential cardiovascular event rates noted in the anglo-scandinavian cardiac outcomes trial-blood pressure lowering arm (ASCOT-BPLA). *Lancet* 2005;**366**:907—13.
21. The CAFÉ Investigatorsfor the Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT) Investigators. Differential impact of blood pressure-lowering drugs on central aortic pressure and clinical outcomes. Principal results of the conduit artery function evaluation (CAFÉ) study. *Circulation* 2006;**113**:1213—25.
22. Dahlof B, Devereux RB, Kjeldsen SE, Julius S, Beevers G, de Faire U, et al. Cardiovascular morbidity and mortality in the losartan intervention for endpoint reduction in hypertension study (LIFE): a randomised trial against atenolol. *Lancet* 2002;**359**:995—1003.
23. McEniery CBM, Yasmin McDonnell B, Munnery M, Wallace SM, Rowe CV, et al on Behalf of the Anglo-Cardiff Collaborative Trial Investigators. Central pressure: variability and impact of cardiovascular risk factors: the anglo-cardiff collaborative trial II. *Hypertension* 2008;**51**:1476—82.