

# Central hemodynamics and the discrepancy between central blood pressure and brachial blood pressure

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## Abstract

Despite similar brachial blood pressure, central hemodynamics could be different. The objective of the present study was to investigate the factors, which could influence the discrepancy between central BP (cBP) and brachial blood pressure. Six hundred forty-seven patients (364 males, 48 ± 12 years old) were enrolled. Using applanation tonometry, cBP was noninvasively derived. The median difference between brachial systolic BP (bSBP) and central systolic BP (cSBP) was 8 mm Hg. We defined the discrepancy between bSBP and cSBP as differences >8 mm Hg. For adjustment of cBP, population was divided into 3 groups according to the cBP: group 1, <140 mm Hg of cSBP; group 2, 140 > cSBP < 160 mm Hg; group 3, =160 mm Hg of cSBP. All the central hemodynamic parameters of the patients, including augmentation pressure, augmentation index (AI), heart rate (75 bpm) adjusted augmentation index (AI@HR75), and subendocardial viability ratio, were measured. Using multivariate logistic regression analysis, we evaluated the factors which could influence the discrepancy between bSBP and cSBP. Age, gender, augmentation pressure, AI, and AI@HR75 were correlated with the discrepancy between bSBP and cSBP. AI@HR75 was significantly correlated with the discrepancy between bSBP and cSBP ( $\beta$ -coefficient = -0.376,  $P < .001$  in group 1;  $\beta$ -coefficient = -0.297,  $P < .001$  in group 2; and  $\beta$ -coefficient = -0.545,  $P < .001$  in group 3). In groups 1 and 2, male gender was significantly correlated with the discrepancy between bSBP and cSBP ( $\beta$ -coefficient = -0.857,  $P = .035$  in group 1;  $\beta$ -coefficient = -1.422,  $P = .039$  in group 2). In present study, arterial stiffness might affect the discrepancy between bSBP and cSBP. Also, male gender was closely related to the discrepancy between bSBP and cSBP especially with cSBP <160 mm Hg. Not only cSBP, the discrepancy between cSBP and bSBP should be considered for understanding the central hemodynamics.

**Abbreviations:** AI = augmentation index, AI@HR75 = heart rate (75bpm) adjusted augmentation index, bBP = brachial blood pressure, BP = blood pressure, cBP = central blood pressure, DBP = diastolic blood pressure, HTN = hypertension, PWA = pulse wave analysis, SBP = systolic blood pressure, SD = standard deviation, SEVR = subendocardial viability ratio.

**Key words:** central hemodynamics, gender difference, pulse wave analysis

## 1. Introduction

When blood pressure (BP) is measured conventionally over the brachial artery, it is assumed that these measurements accurately reflect pressures in the central circulation. Due to pulse pressure amplification, brachial BP (bBP) is higher than central BP

(cBP).<sup>[1]</sup> Despite similar bBP, central hemodynamics could be different.

Central hemodynamics have been known as a determinant of clinical outcomes. Owing to different effects on pressure wave reflection sites or timing of systolic ejection according to the different BP lowering drugs, there was discrepancy between cBP

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The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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and bBP. Differences in central aortic pressures was suggested as a potential mechanism of different clinical outcomes between the 2 BP treatment arms in the Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT).<sup>[2]</sup>

Without any effect of antihypertensive drug, discrepancy between cBP and bBP could be present. Although some reports have reported the phenomenon of normal cBP and elevated bBP in the youth,<sup>[3,4]</sup> there has been no proven data about possible underlying mechanisms of this phenomenon or its potential effect on cardiovascular outcomes. Pattern of BP amplification could be different according to many factors including well-known cardiovascular risk factors.<sup>[5]</sup> Also, arterial stiffness might be one of determinant factors of BP amplification.<sup>[6,7]</sup> Despite well-known prognostic value of cBP, cBP has not been applied to clinical practice due to many factors, including limited outcome-derived data and discrepancy between cBP and bBP. Understanding central hemodynamics might provide more information about future cardiovascular outcomes.

The objective of the present study was to investigate the factors, which could influence the discrepancy between cBP and bBP in patients with high normal BP or HTN.

## 2. Materials and methods

The study recruited patients aged  $\geq 18$  years with firstly diagnosed high normal BP or HTN at the outpatient clinic between June 2009 and May 2012. During period of 3 years, a prospective and cross-sectional design was used. The study included 773 patients (442 males,  $48 \pm 12$  year-old) with firstly diagnosed high normal BP or HTN, who were consecutively recruited in 11 university hospitals in Korea. After patients signed a written informed consent form for participation in this study, we enrolled the patients. As this was outpatient clinic-based study, no patient with acute disease affecting hemodynamic parameters was enrolled. As antihypertensive drug could affect central and peripheral pressure differently, we excluded the patients on medication.<sup>[8]</sup> Among the study population, 647 patients (364 males,  $48 \pm 12$  year-old) were finally enrolled in the present study. The study protocol and informed consent were reviewed and approved by the Institutional Review Board of each participating hospital.

Office BP measurements were taken from both arms 3 times by the study nurse using a validated oscillometric device (Omron HEM 747 ICN BP, Omron Healthcare Co., Kyoto, Japan) after 5 minutes of seated rest and at 2-minute intervals. Using office BP, high normal BP and HTN were defined according to 2013 ESH/ESC practice guidelines (High normal BP as SBP 130–139 mmHg and/or diastolic BP (DBP) 85–89 mmHg and HTN as SBP  $\geq 140$  mmHg and/or DBP  $\geq 90$  mmHg).<sup>[9]</sup>

Using commercially available applanation tonometry (SphygmoCor, AtCor Medical, Sydney, Australia), central hemodynamics, and parameters of arterial stiffness were assessed with pulse wave analysis of the radial artery. After 20 sequential waveforms had been acquired, a validated generalized transfer function was used to generate the corresponding central aortic pressure waveform.<sup>[10,11]</sup> Central systolic and diastolic BP, augmentation pressure (AP), augmentation index (AI), and subendocardial viability ratio (SEVR) were derived using the technique of pulse wave analysis. Augmentation pressure is the difference between the second and the first systolic peaks, and the AI is the ratio of AP to aortic pulse pressure calculated as the difference between respective systolic and diastolic pressure. As AI is influenced by heart rate,<sup>[12]</sup> an index adjusted for heart rate of 75 bpm (AI@HR75) was also calculated. SEVR was calculated as diastolic time integral divided by systolic time integral.<sup>[13]</sup>

The difference between office brachial SBP (bSBP) and central SBP (cSBP) was calculated. The median value of the difference between bSBP and cSBP was derived from the study population.

We defined the discrepancy between bSBP and cSBP as differences over the median value.

As cBP itself is closely related arterial stiffness, study population was classified according to the sCBP for minimizing the effect of cSBP itself on arterial stiffness. For adjustment of cSBP, population was classified into 3 groups according to the cSBP: group 1,  $< 140$  mmHg of cSBP, group 2,  $140 \leq$  cSBP  $< 160$  mmHg and group 3,  $\geq 160$  mmHg of cSBP.

SPSS 18.0 statistical software package (SPSS, Chicago, IL) was used for all calculations. Data are shown as the mean  $\pm$  standard deviation (SD) and the median values for continuous variables and as percentages for categorical variables. Comparisons were conducted by unpaired Student *t* test and ANOVA for continuous variables and Pearson chi-square test for categorical variables. In each group, multivariate analyses were performed using linear regression to evaluate the correlation of the discrepancy between bSBP and cSBP and baseline characteristics including central hemodynamics. To account for the effects of the factors including central hemodynamics on the discrepancy between bSBP and cSBP, multivariate logistic regression was used. Null hypotheses of no difference were rejected if *P* values were  $< 0.05$ .

## 3. Results

Among the study population, 647 patients (364 males,  $48 \pm 12$ -year-old) were finally enrolled in the present study. Median and mean difference between bSBP and cSBP of the 647 patients were 8 mmHg and  $9.1 \pm 6.6$  mmHg, respectively. We defined the discrepancy between bSBP and cSBP as differences over 8 mmHg. Baseline clinical characteristics according to the discrepancy between bSBP and cSBP are summarized in Table 1. The group with the discrepancy between bSBP and cSBP was consisted of 334 patients (236 males) with a mean age of  $45.8 \pm 12.3$  years. The group without the discrepancy between bSBP and cSBP was consisted of 313 patients (128 males) with a mean age of  $50.7 \pm 10.7$  years. Among these groups, age was significantly different ( $P < .001$ ). The parameters of arterial stiffness, AP, AI, and SEVR were also significantly different ( $P < .001$ ,  $< .001$ , and  $< .001$ , respectively). Despite the bSBP was higher in patients with the discrepancy, AI was lower than without in patients without discrepancy (Fig. 1).

For minimizing the effect of cSBP itself on arterial stiffness, total 647 patients were classified into 3 groups according to the cSBP: group 1 ( $n = 416$ , 247 males), group 2 ( $n = 196$ , 96 males) and group 3 ( $n = 35$ , 21 males). Baseline clinical characteristics of 3 groups are summarized in Table 2.

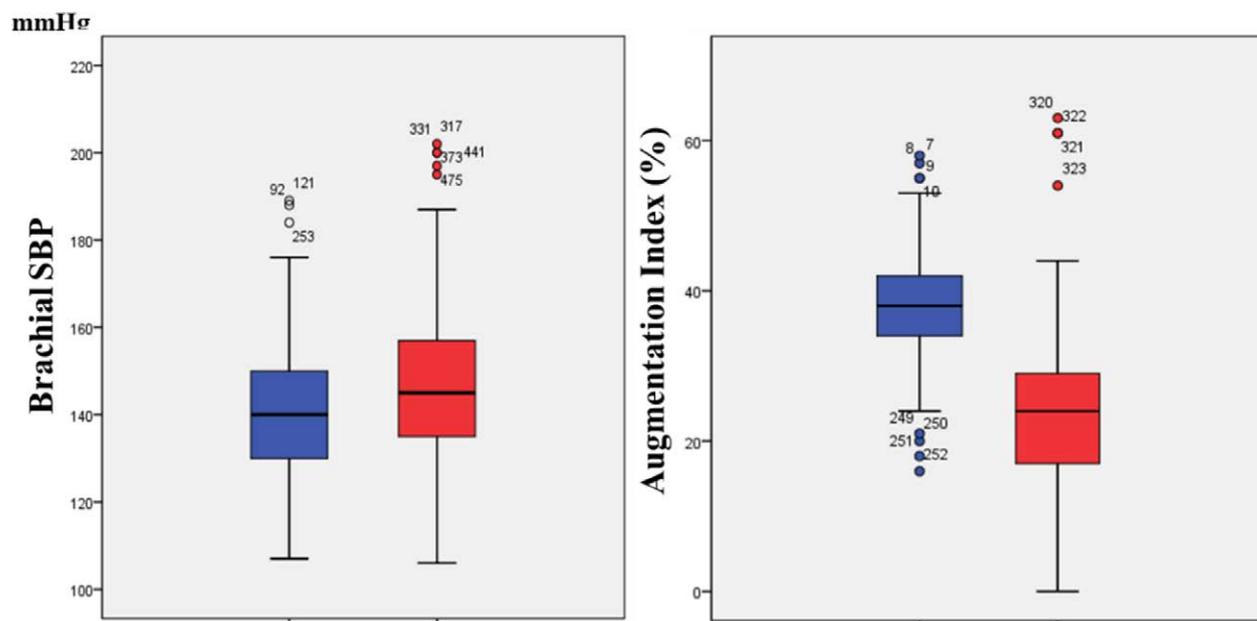
Multivariate analysis using linear regression demonstrated that age, gender, and arterial stiffness expressed as AP, AI and AI@HR75 were significantly different according to the discrepancy between bBP and cBP (Table 3). In all groups, the well-known cardiovascular risk factors were not statistically different according to the discrepancy between bSBP and cSBP.

Multivariate logistic regression analysis demonstrated that arterial stiffness expressed as AI@HR75 and SEVR showed significant negative correlation with the discrepancy between bSBP and cSBP in all 3 groups (Table 4). AI@HR75 was significantly negatively correlated with the discrepancy between bSBP and cSBP ( $\beta$ -coefficient =  $-0.376$ ,  $P < .001$  in group 1,  $\beta$ -coefficient =  $-0.297$ ,  $P < .001$  in group 2 and  $\beta$ -coefficient =  $-0.545$ ,  $P < .001$  in group 3). SEVR was also significantly negatively related to the discrepancy between bSBP and cSBP ( $\beta$ -coefficient =  $-0.087$ ,  $P < .001$  in group 1,  $\beta$ -coefficient =  $-0.089$ ,  $P < .001$  in group 2 and  $\beta$ -coefficient =  $-0.053$ ,  $P = .011$  in group 3). In groups 1 and 2, male gender was significantly correlated with the discrepancy between bSBP and cSBP ( $\beta$ -coefficient =  $-0.857$ ,  $P = .035$  in group 1,  $\beta$ -coefficient =  $-1.422$ ,  $P = .039$  in group 2).

**Table 1****Baseline characteristics according to the discrepancy between cSBP and bSBP.**

Variables	No discrepancy (n = 313)	Discrepancy (n = 334)	P
Age (year-old)	50.7 ± 10.7	45.8 ± 12.3	<.001
Men, n (%)	128 (40.9)	236 (70.7)	<.001
BMI (kg/m <sup>2</sup> )	24.2 ± 2.8	25.0 ± 2.9	<.001
bSBP (mm Hg)	139.9 ± 14.6	145.8 ± 16.9	<.001
bDBP (mm Hg)	91.2 ± 11.2	90.7 ± 13.2	.647
cSBP (mm Hg)	135.9 ± 14.3	132.0 ± 16.8	.002
cDBP (mm Hg)	87.2 ± 17.8	92.2 ± 13.4	<.001
AP (mm Hg)	16.5 ± 7.7	9.3 ± 7.0	<.001
AI (%)	37.9 ± 6.7	22.9 ± 10.2	<.001
AI@HR75 (%)	31.62 ± 9.0	20.6 ± 11.9	.54
SEVR (%)	164.3 ± 29.4	151.7 ± 27.3	<.001

BMI = body mass index, bSBP = brachial systolic blood pressure, bDBP = brachial diastolic BP, cSBP = central systolic blood pressure, cDBP = central diastolic BP, AP = augmentation pressure, AI = augmentation index, AI@HR75 = AI adjusted for heart rate of 75 bpm, SEVR = subendocardial viability ratio.



**Figure 1.** Brachial SBP and AI according to the discrepancy. Despite the brachial SBP is higher in patients with discrepancy (red column), AI was lower than in patients without discrepancy (blue column). AI = augmentation index; SBP = systolic blood pressure.

#### 4. Discussion and conclusions

The present study demonstrated the significant negative effect of arterial stiffness on the discrepancy between bSBP and cSBP in patients with high normal BP or HTN. In patients with cSBP under 160 mmHg, male gender was also closely related to the discrepancy between bSBP and cSBP.

Central hemodynamics have been known as a determinant of clinical outcomes. The results of the Conduit Artery Function Evaluation (CAFE) study suggested the potential superiority of cBP to bBP in cardiovascular prognostic value in the hypertensives.<sup>[2]</sup> As there was no established outcome-derived threshold for cBP, the application of cBP in clinical practice had been limited. The discrepancy between cBP and bBP might be also one of limitations of the application of cBP in clinical practice. Many data demonstrated that different antihypertensive drugs could affect pattern of BP amplification resulting discrepancy between cBP and bBP.<sup>[2,14,15]</sup> In the present study, there was discrepancy between cSBP and bSBP without effect of antihypertensive

drugs. The discrepancy between cSBP and bSBP was related to arterial stiffness itself and male gender.

In the present study, despite the bSBP was higher, reduced arterial stiffness was shown to be associated with discrepancy between bSBP and cSBP, compared with patients without discrepancy. The phenomenon of elevated bBP and normal cBP has been described as spurious systolic hypertension.<sup>[3,4]</sup> This phenomenon has been known to be predominantly found among the youth. In the present study, the mean age of enrolled population was 48 ± 12 year-old. It means that the discrepancy between cBP and bBP might not be confined to the youth. Rather, it might be closely related to arterial elasticity regardless of age. No study has demonstrated that young adults with spurious systolic hypertension had increased cardiovascular risk compared with normotensives or hypertensives.<sup>[4]</sup> As arterial stiffness is one of well-known risk factors for cardiovascular morbidity and mortality,<sup>[16–18]</sup> discrepancy between cBP and bBP, related to arterial elasticity, might suggest decreased future cardiovascular risk. There has been no proven data whether cBP

**Table 2****Baseline characteristics according to the groups.**

Variables	Group 1 (n = 416)	Group 2 (n = 196)	Group 3 (n = 35)
Age (yr old)	47 ± 12	50.3 ± 11.4	50.1 ± 9.5
Men, n (%)	247 (58.9)	96 (56.6)	21 (56)
BMI (kg/m <sup>2</sup> )	24.5 ± 2.8	24.7 ± 3.1	25.5 ± 2.9
bSBP (mm Hg)	134.4 ± 10.9	154.9 ± 8.1	177.7 ± 10.9
bDBP (mm Hg)	86.4 ± 10.4	97.0 ± 9.8	111 ± 14.3
cSBP (mm Hg)	124.8 ± 9.9	147 ± 5.1	169.3 ± 8.9
cDBP (mm Hg)	85.8 ± 13	94.4 ± 16.3	112 ± 16
AP (mm Hg)	10 ± 6.5	17 ± 8.1	22.4 ± 9.1
AI (%)	26.5 ± 17.6	38 ± 32.9	45.6 ± 36.1
AI@HR75 (%)	23.1 ± 12.1	30.7 ± 10.3	33 ± 7.2
SEVR (%)	157.9 ± 28.6	158.7 ± 29.4	152.4 ± 32

BMI = body mass index, bSBP = brachial systolic blood pressure, bDBP = brachial diastolic BP, cSBP = central systolic blood pressure, cDBP = central diastolic BP, AP = augmentation pressure, AI = augmentation index, AI@HR75 = AI adjusted for heart rate of 75 bpm, SEVR = subendocardial viability ratio.

**Table 3****Correlation of discrepancy between cSBP and bSBP with baseline characteristics including central hemodynamics.**

Variables	Group 1 Pearson correlation	P	Group 2 Pearson correlation	P	Group 3 Pearson correlation	P
Age	-0.388	<.001	-0.204	.004	-0.347	.041
Gender	-0.365	<.001	-0.325	<.001	-0.458	.006
BMI	0.150	.002	0.272	<.001	0.073	.677
bSBP	0.456	<.001	0.774	<.001	0.603	<.001
bDBP	-0.144	.003	0.056	.440	0.565	<.001
cSBP	-0.115	.062	-0.061	.394	0.198	.254
cDBP	0.112	.026	0.3869	<.001	0.643	<.001
AP	-0.553	<.001	-0.487	<.001	-0.521	<.001
AI	-0.642	<.001	-0.280	<.001	-0.244	.164
AI@HR75	-0.629	<.001	-0.516	<.001	-0.614	<.001
SEVR	-0.231	<.001	-0.319	<.001	-0.041	.817

BMI = body mass index, bSBP = brachial systolic blood pressure, bDBP = brachial diastolic BP, cSBP = central systolic blood pressure, cDBP = central diastolic BP, AP = augmentation pressure, AI = augmentation index, AI@HR75 = AI adjusted for heart rate of 75 bpm, SEVR = subendocardial viability ratio.

**Table 4****Multivariate analysis of discrepancy between cSBP and bSBP according to the groups.**

Variables	Group 1 β	P	Group 2 β	P	Group 3 β	P
Age	-0.055	.001	-0.019	.552	-0.047	.464
Gender	-0.857	.035	-1.422	.039	-1.151	.422
BMI	-0.001	.991	0.185	.093	-0.623	.014
AP	0.048	.412	-0.112	.085	-0.123	.178
AI	-0.031	.087	0.006	.575	0.021	.303
AI@HR75	-0.376	<.001	-0.297	<.001	-0.545	<.001
SEVR	-0.087	<.001	-0.089	<.001	-0.053	.011

BMI = body mass index, AP = augmentation pressure, AI = augmentation index, AI@HR75 = AI adjusted for heart rate of 75 bpm, SEVR = subendocardial viability ratio.

itself, the presence of the discrepancy between cBP and bBP or both is clinically relevant. The present study suggested that not only cBP, the discrepancy between cBP and bBP should be considered for understanding the central hemodynamics.

Gender difference was also one of factors affecting the discrepancy between bSBP and cSBP in the present study. Male gender tended to have correlation with the discrepancy between bSBP and cSBP. In females with hypertension, abnormal change of arterial elastance index during exercise, which may contribute

in development of heart failure and exercise intolerance, was demonstrated.<sup>[19]</sup> Different central hemodynamical change may contribute to the different compensatory response after the onset of heart failure between males and females. Despite similar peripheral pulse pressure, central hemodynamics reflecting arterial stiffness were different between males and females.<sup>[20]</sup> Although there is still controversy and inconsistent data, sex hormones including estradiol or follicle-stimulating hormone may associate with arterial stiffness.<sup>[21,22]</sup> Different central

hemodynamics according to the gender might affect the discrepancy between bBP and cBP.

This study has several limitations. As there is yet no criteria of hypertension or high normal BP according the cBP, the definition of the 3 groups were arbitrarily defined. Although some studies have tried to establish reference values for cBP,<sup>[5,23]</sup> there have been no widely sourced reference values for cBP. The present study suggested that not only cBP itself, understanding central hemodynamics, including the discrepancy between bBP and cBP, may increase clinical benefit by risk stratification in patients with high normal BP or HTN. As pattern of BP amplification were different according to many factors,<sup>[5]</sup> further studies might be needed to establish the diagnostic threshold of hypertension by cBP. Also, the definition of the discrepancy between bBP and cBP was arbitrarily defined to evaluate the relating factors on central hemodynamics in the certain recruited population in the present study. For defining the threshold for the discrepancy between bBP and cBP, further studies might be needed. Second, gender difference was related to the discrepancy between bBP and cBP in the present study. The result logically implied that sex hormones had a role. As the present study was not designed to evaluate the relationship between arterial stiffness and gender difference, menstrual cycle or menopausal status were not controlled in the statistics. To prove this, further studies might be needed. Third, cBP and other parameters of central hemodynamics were derived indirectly using radial artery tonometry. These parameters indirectly measured by radial tonometry were validated.<sup>[10–12]</sup> Also, these parameters have been widely used in clinical practice.

In conclusion, arterial stiffness might affect the discrepancy between bBP and cBP. Also, gender difference was closely related to the discrepancy between bBP and cBP especially with cBP under 160 mmHg. Not only cBP itself, the discrepancy between cBP and bBP should be considered for understanding the central hemodynamics. Understanding the central hemodynamics would be informative for more detailed cardiovascular risk stratification. As the present study was a cross-sectional study, not a cohort study, the definition of discrepancy could not be applied to the general population. For application to clinical practice, outcome-driven threshold should be determined.

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