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Association between Brachial-ankle pulse wave velocity and Composite carotid/coronary atherosclerosis in a middle-aged asymptomatic population

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Background

- Atherosclerosis has been associated with insidious vascular pathologies. After a latent period, atherosclerotic vessels can cause acute critical cerebrocardiac events, including stroke and acute myocardial infarction, as well as somewhat stable medical conditions including dizziness and angina pectoris.

- Many clinical studies have demonstrated poor clinical outcomes in asymptomatic populations with subclinical atherosclerotic vascular changes.

→ ***Early detection of atherosclerotic vascular changes before clinical manifestations*** **could be important to prevent future vascular events.**

Background

- To examine atherosclerotic vascular change, many non-invasive imaging technologies have been introduced.

  ① **Carotid ultrasound** is used to examine atherosclerotic vascular changes of carotid arteries by measuring carotid intima media thickness (CIMT) and to detect carotid atherosclerotic plaques (CAP).

  ② **Coronary computed tomography (CT)** is also used to examine coronary arteries by measuring coronary artery calcium (CAC) and coronary artery stenosis (CAS).

- Although these imaging modalities have the potential to accurately detect vascular atherosclerotic changes, *discordance among CIMT, CAP, CAC, and CAS* might cause some discrepancy to evaluate the overall atherosclerotic vascular burden.

- Moreover, *high medical cost, use of a nephrotoxic contrast dye, and extensive radiation exposure* limit their wide use in screening subclinical atherosclerotic vascular changes in the asymptomatic population.

Background

- **Brachial-ankle pulse wave velocity (baPWV)** is a non-invasive hemodynamic parameter that represents arterial stiffness. Previous studies have demonstrated that measuring non-invasive hemodynamic parameters could be useful for screening subclinical atherosclerosis. These parameters have also been reported to be associated with future cardiovascular events.
- *However, at present, few data are available on the relationship between these parameters and subclinical coronary or carotid atherosclerosis.*

Purpose of the study

In the present study, we investigated the differences among CIMT, CAP, CAC, and CAS, and explored the potential role of baPWV to screen both carotid and coronary atherosclerotic changes in a community-based asymptomatic population.

Method

Study design

- One thousand one hundred thirty participants, who were previously registered for metabolic syndrome at 25 public health centers in Seoul, were randomly selected.
- Subjects with a previous history of angina pectoris, myocardial infarction, stroke, or any revascularization were excluded.
- Medical exams, blood samples, non-invasive hemodynamic parameters, carotid ultrasonogram, and coronary computed tomography were performed from January to September 2014.
- After excluding subjects with missing data for any of those exams, 773 subjects were analyzed.

Method

Brachial-ankle pulse wave velocity and augmentation index

Brachial-ankle pulse wave velocity (baPWV) and ankle-brachial index (ABI) were measured by using an oscillometric sphygmomanometer (VP-1000 plus; Omron Colin, Kyoto, Japan). Central systolic blood pressure (cSBP), augmentation index (AIx), and AIx@75 were measured by using applanation tonometry (HEM9000A1; Omron Colin, Kyoto, Japan). All measurements were performed by trained nurses in accordance with the manufacturer′s recommendations.

Carotid ultrasonography

Carotid artery imaging was obtained by experienced clinicians by using a B-mod tomographic ultrasound system (VIVID Q, GE, USA) with a linear 6.0-13.0 MHz probe. Carotid intima media thickness (CIMT) was measured 1.0 cm distal to both common carotid artery bifurcations. The presence of carotid artery plaque was determined when the local CIMT was greater than 1.5 mm or 50% of the surrounding area.

Method

Coronary computed tomography

Cardiac CT examinations were performed by using a second-generation dual-source CT scanner (Somatom Definition Flash; Siemens Healthcare, Forchheim, Germany) with a 2 ×128 × 0.6 mm3 section collimation and a 280 msec ration time.

The CAC score, calculated according to modified Agatston units, was categorized as 0 (0 Agatston score), mildly increased (1 to 99) and moderately increased (≥100).

Coronary artery stenosis was evaluated for 4 major coronary arteries: right coronary artery, left circumflex artery, left anterior descending artery and left main artery. Coronary arteries with more than 50% diameter stenosis were considered significant CAS and counted.

Method

Statistical analysis

Categorical variables were reported as count (percentage) and continuous variables as the mean ± standard deviation. Independence of categorical variables was analyzed by the chi-square test. Continuous variables were analyzed by the Student t-test. To identify risk predictors for the composite endpoint of coronary and carotid atherosclerosis, the selected variables were tested with a multivariate logistic regression analysis by univariate analysis (p<0.10). An odds ratio with a 95% confidence interval and p-value are reported. Receiver operating characteristic (ROC) curves of baPWV were constructed for a diagnosis of coronary and carotid atherosclerosis. Only p-values less than 0.05 were considered statistically significant. All statistical analyses were performed using SAS (v9.3, SAS institute Inc., USA).

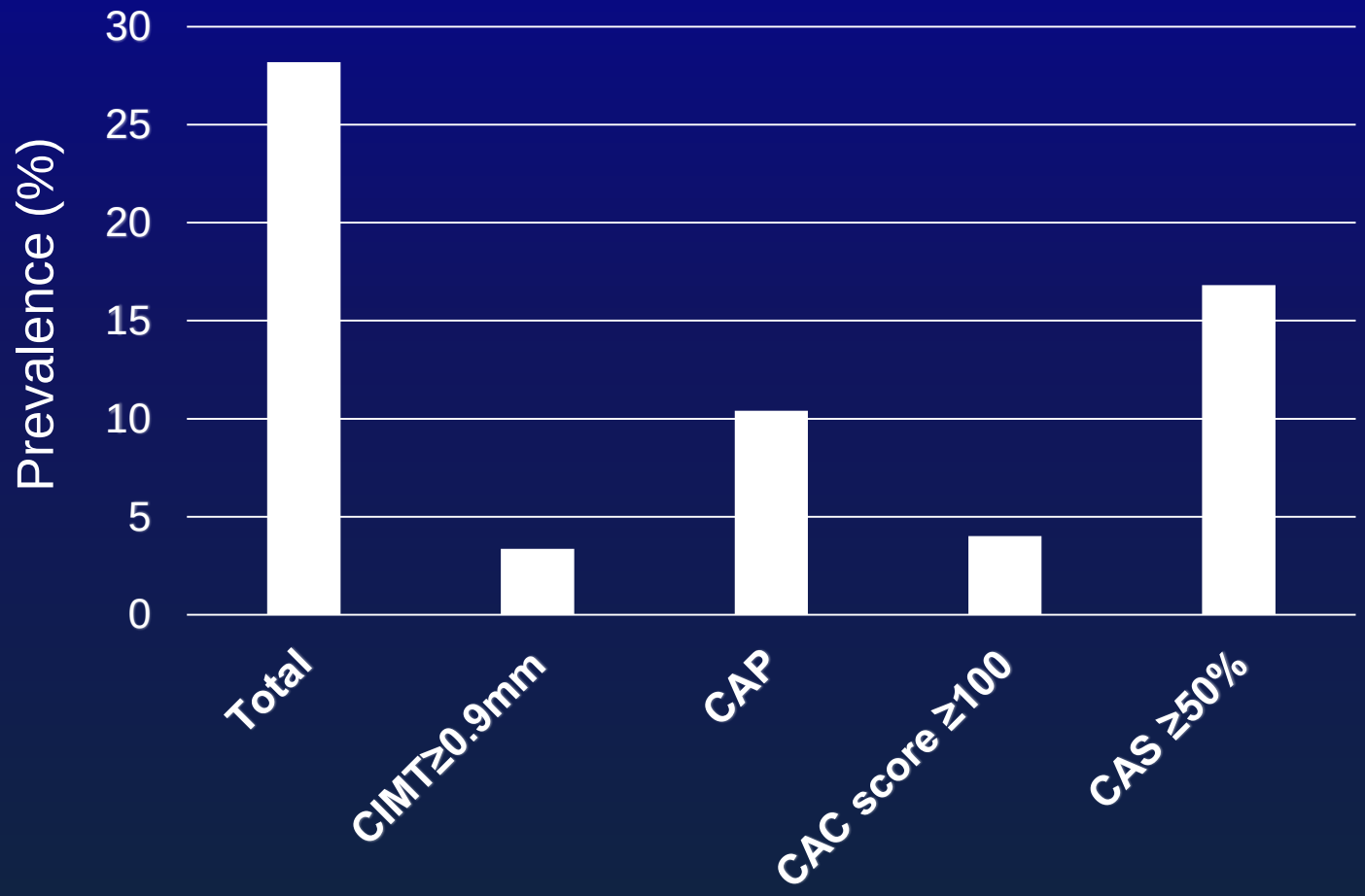
Baseline characteristics

	Q1 (n = 194)	Q2 (n = 193)	Q3 (n = 193)	Q4 (n = 193)	*p*-value
Age (year)	51.40 ± 8.22	54.16 ± 6.83	55.27 ± 5.99	57.38 ± 5.58	< 0.0001
Men	78 (40.21)	87 (45.08)	109 (56.48)	103 (53.37)	0.0016
BMI	26.47 ± 3.01	25.60 ± 2.63	25.71 ± 2.96	25.08 ± 2.81	< 0.0001
Current smoking	38 (19.59)	29 (15.1)	43 (22.28)	46 (23.96)	0.1398
Hypertension	39 (20.1)	57 (29.53)	91 (47.15)	120 (62.18)	< 0.0001
Diabetes	24 (12.37)	18 (9.33)	25 (12.95)	45 (23.32)	0.0013
Dyslipidemia	70 (36.08)	73 (37.82)	68 (35.23)	72 (37.31)	0.9442
Metabolic syndrome components					
Waist (cm)	88.31 ± 8.07	87.18 ± 7.59	87.88 ± 7.68	86.56 ± 7.63	0.1238
Systolic BP (mmHg)	119.05 ± 11.89	123.83 ± 12.31	130.56 ± 13.52	137.70 ± 14.02	< 0.0001
Diastolic BP (mmHg)	77.18 ± 8.68	80.18 ± 8.45	84.88 ± 9.10	87.46 ± 9.21	< 0.0001
Triglyceride (mg/dL)	145.78 ± 93.90	161.18 ± 88.63	156.26 ± 98.69	158.16 ± 102.0	0.42
HDL-cholesterol (mg/dL)	50.12 ± 11.09	50.37 ± 13.06	51.87 ± 13.74	53.49 ± 12.70	0.034
Glucose (mg/dL)	96.91 ± 11.36	98.88 ± 11.84	100.78 ± 21.60	104.75 ± 22.76	0.0001
Metabolic syndrome	59 (30.41)	79 (40.93)	73 (37.82)	87 (45.08)	0.009

Baseline characteristics

	Q1 (n = 194)	Q2 (n = 193)	Q3 (n = 193)	Q4 (n = 193)	*p*-value
Laboratory findings					
Hemoglobin (g/dL)	14.01 ± 1.26	14.18 ± 1.35	14.45 ± 1.35	14.51 ± 1.24	0.0003
Total cholesterol (mg/dL)	197.06 ± 32.06	202.05 ± 34.91	197.22 ± 35.07	204.88 ± 35.64	0.0678
LDL-cholesterol (mg/dL)	130.25 ± 30.23	132.16 ± 34.07	127.18 ± 33.90	132.69 ± 33.80	0.3496
hsCRP (mg/dL)	1.64 ± 3.51	1.73 ± 7.89	1.15 ± 1.46	1.47 ± 2.34	0.6119
Apolipoprotein A1 (mg/dL)	138.92 ± 20.42	141.30 ± 23.99	143.39 ± 25.10	147.57 ± 24.53	0.003
Apolipoprotein B (mg/dL)	101.23 ± 21.61	104.11 ± 22.63	99.95 ± 24.68	104.41 ± 23.32	0.1599
Non-invasive hemodynamic parameters					
baPWV (mean, cm/sec)	1150.2 ± 71.8	1296.7 ± 33.4	1420.5 ± 37.6	1681.7 ± 173.9	< 0.0001
ABI (mean)	1.07 ± 0.09	1.08 ± 0.08	1.09 ± 0.09	1.11 ± 0.08	< 0.0001
cSBP (mmHg)	122.05 ± 13.42	128.58 ± 13.54	135.16 ± 15.50	143.14 ± 16.38	< 0.0001
AIx	74.61 ± 16.47	78.62 ± 15.16	78.23 ± 15.14	80.13 ± 13.63	0.0033
AIx@75	74.75 ± 13.51	78.08 ± 12.47	78.31 ± 12.34	80.49 ± 10.71	< 0.0001
Coronary artery calcium (CAC) and carotid intima medial thickness (CIMT)					
CAC score	9.68 ± 44.51	12.92 ± 46.58	15.59 ± 55.72	29.28 ± 110.92	0.0326
CIMT (mean, mm)	0.62 ± 0.11	0.65 ± 0.13	0.65 ± 0.11	0.69 ± 0.11	< 0.0001

Prevalence of subclinical atherosclerosis



CAC, coronary artery calcium; CAS, coronary artery stenosis; CIMT, carotid intima media thickness; CAP, carotid artery plaque.

Primary endpoint

	Q1 (n = 194)	Q2 (n = 193)	Q3 (n = 193)	Q4 (n = 193)	*p*-value
CAC score ≥ 100	4 (2.06)	6 (3.11)	10 (5.18)	11 (5.7)	0.0397
CAS ≥ 50%	24 (12.37)	31 (16.06)	37 (19.17)	38 (19.69)	0.0372
CIMT ≥ 0.9mm	3 (1.55)	9 (4.66)	5 (2.59)	9 (4.66)	0.2089
Presence of CAP	14 (7.25)	13 (6.77)	21 (10.94)	32 (16.67)	0.001
Composite coronary/carotid atherosclerosis	41 (21.13)	48 (24.87)	61 (31.61)	68 (35.23)	0.0007

Data are presented as the number (%). CAC, coronary artery calcium; CAS, coronary artery stenosis; CIMT, carotid intima media thickness; CAP, carotid artery plaque.

Severity of the composite atherosclerosis

	Number of positive tests for the composite coronary and carotid atherosclerosis			*p*-value
	0	1	≥ 2	
baPWV (cm/sec)	1365.84 ± 204.30	1417.92 ± 228.05	1537.27 ± 276.21	< 0.0001
AI@75	78.26 ± 12.53	77.20 ± 12.51	76.12 ± 11.04	0.3901
cSBP (mmHg)	131.82 ± 16.80	133.34 ± 17.13	132.74 ± 12.90	0.5629

Data are presented as the mean ± SD. baPWV, brachial-ankle pulse wave velocity; AIx@75, augmentation index at 75 beats/min; cSBP, central systolic blood pressure.

Correlation between coronary and carotid atherosclerosis

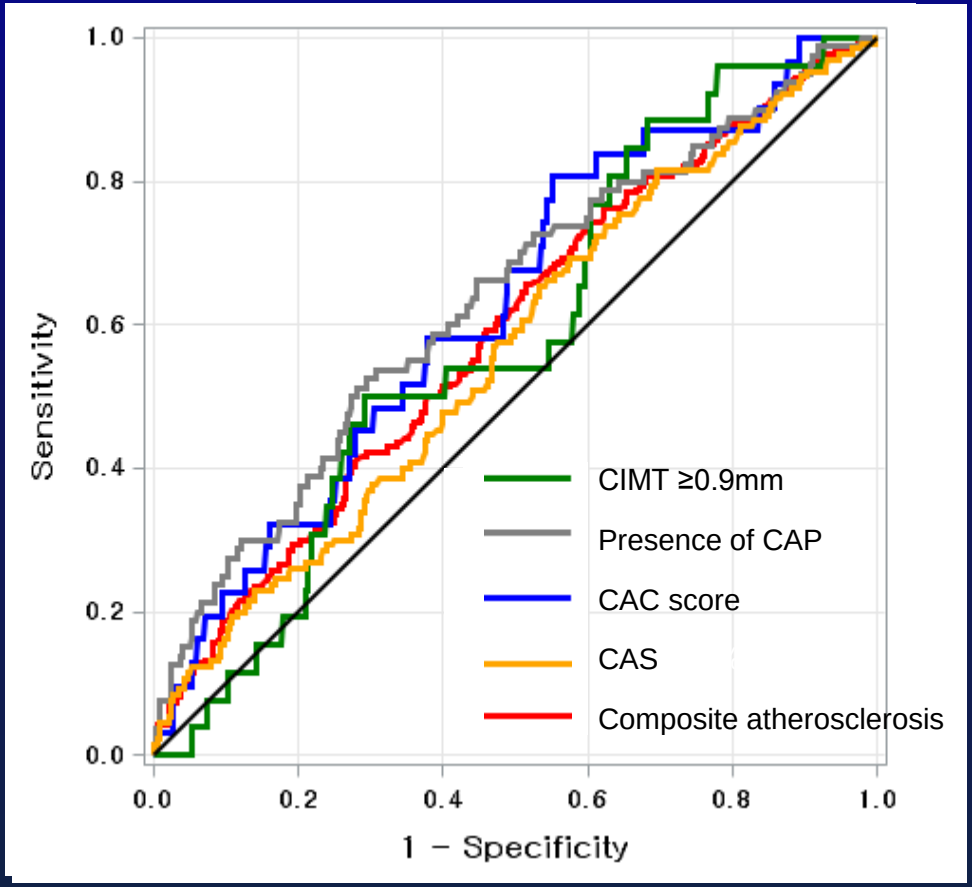
	CAC score			*p*-value
	0	1-99	≥ 100	
CIMT ≥ 0.9 mm	12 (2.07)	13 (8.02)	1 (3.23)	0.0054
Presence of CAP	44 (7.61)	25 (15.53)	11 (36.67)	<0.0001
	CAS (%)			*p*-value
	< 30	30-50	≥ 50	
CIMT ≥ 0.9 mm	12 (2.45)	9 (5.84)	5 (3.85)	0.1859
Presence of CAP	39 (8.04)	22 (14.29)	19 (14.62)	0.0091

Data are presented as the number (%). CAC, coronary artery calcium; CAS, coronary artery stenosis; CIMT, carotid intima media thickness; CAP, carotid artery plaque.

Risk predictors for composite coronary/carotid atherosclerosis

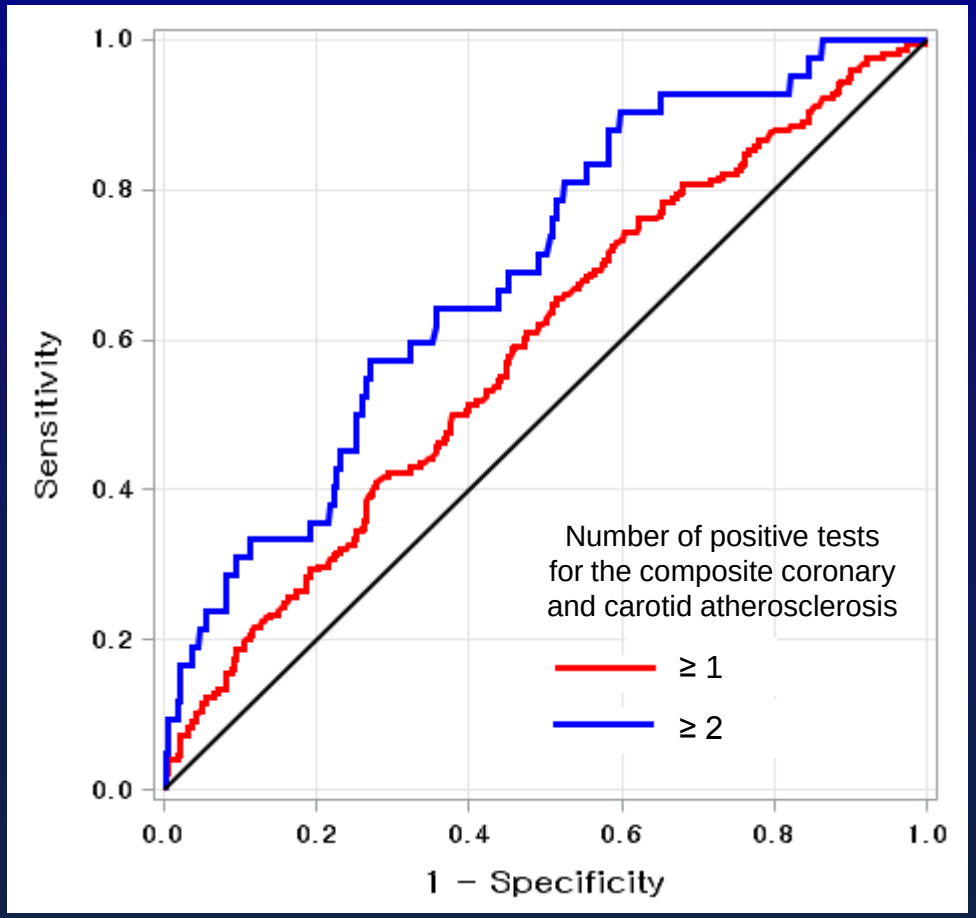
Risk Factor	Univariate analysis			Multivariate analysis		
	beta	OR (95% CI)	*p*-value	*beta*	OR (95% CI)	*p*-value
Age	0.0642	1.066 (1.039-1.095)	< 0.001	0.071	1.074 (1.043-1.106)	< 0.001
Men	0.3987	2.22 (1.609-3.063)	< 0.001	0.3764	2.123 (1.454-3.099)	< 0.001
BMI	-0.019	0.981 (0.929-1.036)	0.4947			
Current smoking	0.1878	1.456 (1.001-2.119)	0.0497	0.0359	1.074 (0.691-1.67)	0.7498
Hypertension	0.1246	1.283 (0.934-1.762)	0.1242			
Diabetes mellitus	0.2971	1.811 (1.194-2.748)	0.0052	0.166	1.394 (0.849-2.288)	0.1891
Dyslipidemia	0.098	1.216 (0.881-1.679)	0.2333			
Waist	0.012	1.012 (0.992-1.033)	0.2435			
Systolic BP	0.0117	1.012 (1.001-1.023)	0.0296	0.00549	1.006 (0.992-1.019)	0.4242
Diastolic BP	0.0159	1.016 (1-1.033)	0.0533			
Triglyceride	0.00183	1.002 (1-1.003)	0.0213	0.000873	1.001 (0.999-1.003)	0.3808
HDL-Cholesterol	-0.0171	0.983 (0.97-0.996)	0.0106	-0.0124	0.988 (0.973-1.003)	0.1054
Glucose	0.0119	1.012 (1.003-1.021)	0.0071	0.00202	1.002 (0.992-1.012)	0.6958
LDL-cholesterol	-0.00215	0.998 (0.993-1.003)	0.3767			
hsCRP	-0.0276	0.973 (0.915-1.034)	0.3768			
Apolipoprotein A1	-0.00201	0.998 (0.991-1.005)	0.5536			
Apolipoprotein B	0.0037	1.004 (0.997-1.011)	0.2836			
baPWV	0.00153	1.002 (1.001-1.002)	< 0.0001			
cSBP	0.005	1.005 (0.996-1.014)	0.2928			
AI@75	-0.0101	0.99 (0.98-1.00)	0.0533			

Diagnostic potential of baPWV for the composite atherosclerosis (I)



	AUC (95% CI)
CIMT ≥0.9mm	0.582 (0.4828-0.6820)
Presence of CAP	0.634 (0.5672-0.7014)
CAC score ≥100	0.626 (0.5278-0.7241)
CAS ≥50%	0.565 (0.5114-0.6189)
the composite coronary and carotid atherosclerosis	0.589 (0.5447-0.6334)

Diagnostic potential of baPWV for the composite atherosclerosis (II)



Number of positive tests for the composite coronary and carotid atherosclerosis		
≥ 1	AUC (95% CI)	0.589 (0.5447-0.6334)
	Cut-off value	1347.5
	Sensitivity	0.6101
	Specificity	0.5243
≥ 2	AUC (95% CI)	0.692 (0.6127-0.7709)
	Cut-off value	1413.5
	Sensitivity	0.6429
	Specificity	0.6432

Summary

(1) 28.2% of asymptomatic subjects with previously screened metabolic syndrome met at least one of the composite coronary and carotid atherosclerosis criteria (CIMT ≥0.9mm, CAC ≥100, or the presence of CAP or CAS).

(2) There were significant associations between CIMT and CAC score and between CAP and CAS.

(3) Subjects with a higher baPWV had a significantly higher prevalence of composite coronary and carotid atherosclerosis.

(4) baPWV had moderate diagnostic potential to detect more than 2 positive tests in composite coronary and carotid atherosclerosis.

Conclusion

In a community-based population, baPWV was significantly higher in asymptomatic individuals with composite coronary and carotid atherosclerosis, as determined by CAC, CAS, CIMT, and CAP. However, baPWV might be of limited value in identifying subjects at risk for subclinical coronary and carotid atherosclerosis.

Thank you for your attention