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Carotid artery longitudinal wall motion alterations associated with metabolic syndrome and insulin resistance

Short title: Metabolic Syndrome and Longitudinal Motion of the Common Carotid Artery

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Summary

Background and aims: Our objective was to study relationships between the new biomarker of vascular health, carotid artery longitudinal wall motion (CALM) and metabolic syndrome (MetS).

Methods: Carotid ultrasound and assessment of MetS and its components were performed with 281 subjects aged 30–45 years. In the longitudinal motion analysis, the amplitude of motion and the antegrade-oriented and retrograde-oriented components of motion between the intima-media complex and adventitial layer of the common carotid artery wall were assessed.

Results: MetS, according to the harmonized criteria, was detected in 53 subjects (19%). MetS was significantly associated with increased antegrade and decreased retrograde longitudinal motion in the carotid artery wall. Augmented antegrade amplitude of longitudinal motion was associated with obesity ($\beta = 0.149$, $P < 0.05$) and low HDL-cholesterol ($\beta = 0.177$, $P < 0.01$). Attenuated retrograde amplitude of longitudinal motion was associated with hypertension ($\beta = -0.156$, $P < 0.05$), obesity ($\beta = -0.138$, $P < 0.05$) and hyperinsulinemia ($\beta = -0.158$, $P < 0.01$). Moreover, insulin resistance (homeostasis model assessment index above 2.44) was associated with adverse changes in CALM.

Conclusion: MetS and insulin resistance were associated with alterations in CALM. In particular, hypertension, obesity and hyperinsulinemia were associated with reduced total peak-to-peak amplitude as well as increased antegrade and reduced retrograde amplitudes, all of which might be markers of unfavourable vascular health.

Keywords: arterial stiffness, cardiovascular risk factors, hyperinsulinemia, hypertension, insulin resistance, motion tracking, ultrasound imaging.

Introduction

Metabolic syndrome (MetS) is a cluster of multiple cardiovascular risk factors such as central obesity, hypertension, dyslipidemia, glucose intolerance and insulin resistance (Eckel *et al.*, 2005). MetS is associated with increased risk of cardiovascular diseases and all-cause as well as cardiovascular disease mortality (Gami *et al*., 2007; Mottillo *et al*., 2010). Mechanisms through which MetS increases cardiovascular risk involve several pathophysiological changes in the arterial wall (Qiao *et al*., 2007). Although MetS components are interrelated, each component may act independently through different mechanisms, with adverse effects on the structure and function of the vascular system. Therefore, when investigating consequences of MetS, parallel use of methods that characterize the structure and function of blood vessels provides opportunity for a comprehensive evaluation of pathophysiological changes. Carotid artery longitudinal wall motion (CALM) is a relatively new biomarker reflecting vascular health that can be measured by using carotid ultrasound imaging together with assessment of carotid intima-media thickness and distensibility measurement in the same session (Yli-Ollila *et al*., 2013). CALM has not been studied systematically in subjects with MetS.

One important consequence of MetS is arterial stiffening, which is known to contribute to prognosis in diabetic patients (Prenner & Chirinos, 2015). Components of MetS have different associations with arterial stiffness parameters (Vagovicova *et al*., 2015). Furthermore, distinct clusters of components of MetS show differing patterns of associations with arterial stiffness (Scuteri *et al*., 2014). The results of our previous studies suggest that arterial stiffening is associated with alterations in CALM (Taivainen *et al*., 2015; Yli-Ollila *et al*., 2016; Yli-Ollila *et al*., 2016). Therefore, arterial stiffening is a potential link between CALM and MetS.

In addition to visceral adiposity, a key feature of MetS is insulin resistance (Salmenniemi *et al*., 2004). Insulin itself has obvious vascular effects (Yki-Järvinen, 2003). Insulin resistance is accompanied closely by endothelial dysfunction, which is thought to be an important mechanism through which insulin resistance results in harmful effects on the vasculature (Yki-Järvinen, 2003; Nesto, 2004). Adiponectin is an insulin-sensitizing and anti-inflammatory adipokine, the concentration of which decreases with weight gain; its levels are indirectly associated with insulin resistance (Trujillo & Scherer, 2005). Because adiponectin is protective against the development of arteriosclerosis, it is an interesting possible link between MetS and CALM.

To investigate associations between CALM parameters and components of MetS, we performed carotid ultrasound imaging and measured CALM in a large population of individual participants in the Cardiovascular Risk in Young Finns Study. Furthermore, CALM in association with insulin resistance, hyperinsulinemia and low adiponectin concentration was studied.

Methods

Subjects and study design

The Cardiovascular Risk in Young Finns Study is an ongoing, five-centre follow-up study of atherosclerosis risk factors in Finnish children and adolescents. The first cross-sectional survey was conducted in 1980, when 3596 3- to 18-year-old children and adolescents participated. Participants were randomly chosen from each area in Finland through a national register. With this cohort, follow-up studies were conducted regularly at intervals of from 3 to 6 years during the years 1980–2007 (Raitakari *et al*., 2008). The study was approved by the Ethics Committee, Hospital District of Southwest Finland. The participants provided written informed consent.

Kuopio University Hospital investigates the population of Eastern Finland and is one of the five centres involved. The present cross-sectional study consists of Kuopio centre data from 2007, when the subjects were 30 to 45 years of age. Vascular ultrasound studies were available for 465 subjects, and successful CALM analysis was performed for 292 subjects. Five female individuals were excluded due to pregnancy, and four individuals were excluded because of type 1 diabetes. Furthermore, there was a lack of anthropometric data for two individuals; thus, the final study population included 281 participants. Adiponectin data were lacking for seven participants. Hence, in the univariate analysis of CALM and adiponectin, 274 participants were analysed.

Assessment of risk factors

Height was measured to an accuracy of 1 cm and weight to an accuracy of 1 kg. Body mass index (BMI) was calculated as weight in kilograms divided by height in metres squared. Waist circumference was measured using an anthropometric tape at the end of expiration at the midpoint between the iliac crest and the lowest rib, with an accuracy of 0.1 cm, and the average of two measurements was used. Systolic and diastolic blood pressure were measured in the sitting position from the brachial artery using a random zero sphygmomanometer (Hawksley & Sons Ltd, Lancin, UK). The average of three measurements was used in the analysis. Cigarette smoking, medications, diagnosed diseases and pregnancy were measured with questionnaires, and smoking was processed as a dichotomous variable (smoking/non-smoking). Subjects smoking regularly daily were regarded as smokers.

Venous blood samples were drawn after an overnight 12 h fast for the determination of serum lipid, adiponectin, insulin and glucose levels. All measurements of lipid levels as well as glucose, insulin and adiponectin levels were performed in duplicate in the same laboratory. To measure levels of serum total cholesterol, triglycerides and high-density lipoprotein cholesterol (HDL-C), standard enzymatic methods were used. The Friedewald formula was used to calculate low-density lipoprotein cholesterol (LDL-C) concentration for participants with triglycerides <4 mmol/L. Details for these methods have been described previously (Juonala *et al*., 2004; Raiko *et al*., 2010). Serum insulin concentration was measured through microparticle enzyme immunoassay (IMx insulin reagent, Abbott Diagnostics, USA) on an IMx instrument, and glucose concentrations were analysed enzymatically (Raiko *et al*., 2010). The homeostasis model assessment (HOMA-IR) index was calculated using the following formula: fasting glucose (mmol/L) × fasting insulin (μU/mL)/22.5. Serum adiponectin concentrations were analysed through radioimmunoassay (Human Adiponectin and Leptin RIA kits, Linco Research, Inc, MO, USA; Saarikoski *et al*., 2010).

Definition of metabolic syndrome, hypertension, hyperglycaemia, hyperinsulinemia and insulin resistance

Metabolic syndrome was defined according to the harmonized criteria, and the definition included the following: waist circumference ≥88 cm in women and ≥102 cm in men; fasting plasma glucose ≥5.6 mmol/L or drug treatment; hypertriglyceridemia ≥1.7 mmol/L or treatment; HDL-C ≤1.3 mmol/L in women and 1.0 in men or drug treatment; and systolic blood

pressure ≥130 mmHg or diastolic blood pressure ≥85 mmHg or antihypertensive drug treatment. A diagnosis required that any three of the five criteria be present (Alberti *et al*., 2009). Hyperinsulinemia was defined as non-diabetic subjects having fasting insulin level in the highest quartile, where 11.06 mU/L was used as the cut-off point (cut-off point of the entire study population of the Young Finns Study, year 2007). Low adiponectin as a risk factor was defined according to the lowest quartile in this study population; the cut-off value was 6.22 μg/mL. High HOMA-IR as a risk factor was defined as the highest quartile in this study population and it was ≥2.44.

Carotid ultrasound imaging

Ultrasound studies were performed by trained sonographers following the standardized protocol described previously (Raitakari *et al*., 2003). Carotid artery imaging was performed using a Sequoia512 ultrasound scanner (Acuson, Mountain View, CA, USA) equipped with a 14 MHz linear array transducer. The ECG signal (modified chest lead 5) was recorded and presented alongside B-mode image sets. The left common carotid artery (CCA) was scanned using a resolution box function to record a 25 mm-wide and 15 mm-high image, including the beginning of the carotid bifurcation and the distal CCA. A 5-s cine loop (25 frames per second) was digitally stored for subsequent offline analysis.

Longitudinal motion

Assessment of CALM was performed in line with recently published practical guidelines (Rizi *et al*., 2020). Carotid artery wall motion analysis was performed using an in-house motion tracking program developed by our research group (Yli-Ollila *et al*., 2013). The software is written in MATLAB (2007b, The MathWorks Inc., Natic, MA, USA) and is capable of reading the graphical ECG-information of the ultrasound recording and simultaneously tracking the longitudinal and radial motions of the arterial wall. The basic method used in the motion tracking was a two-dimensional cross-correlation (block matching) enhanced with a contrast optimization technique to reduce noise from video.

In the longitudinal motion analysis, regions of interest were drawn on the ultrasound image on the intima-media complex, on the adventitial layer and on the surrounding tissue outside the adventitia. The motion tracking of the longitudinal motion was considered suitable for analysis

if the tracking successfully recorded at least two heart cycles, otherwise the motion data were discarded. Details of the method have been described (Yli-Ollila *et al*., 2013; Taivainen *et al*., 2015).

We measured longitudinal motion curves between the intima-media complex and the adventitial layer (IA). The curves of longitudinal motion have been previously shown to vary extensively between individuals (Yli-Ollila *et al*., 2013). We investigated the amplitude of the motion (IAampl), the forward-oriented (IAante) and the backward-oriented (IAretro) component of the motion between the different layers of the CCA wall. Furthermore, we evaluated the main deviation of the longitudinal motion (IAdev) between the arterial layers by computing the average of the motion curve over a cardiac cycle. A schematic figure showing the different measured parameters of carotid artery longitudinal wall motion in two original registrations is presented in Figure 1.

Statistical methods

Distributions of longitudinal motion parameters were only slightly skewed and residuals in models were normally distributed, thus parametric tests were considered acceptable to use. Independent samples *t*-test was used to determine the significance of differences between study groups with and without metabolic syndrome. Linear regression model adjusted for age and sex was used to define conformities between the indices of longitudinal motion and the components of metabolic syndrome, HOMA-IR as well as adiponectin. A multivariate regression model with stepwise method adjusted for age and sex was used to find independent effects of the individual components of metabolic syndrome and longitudinal motion parameters.

Results

Clinical characteristics of subjects with MetS (MetS+) and without (MetS−) are shown in Table 1. Significant differences between these two groups were found in all characteristic measures of MetS, including levels of insulin, glucose and adiponectin as well as in HOMA-IR. For smoking, age and sex, no statistically significant difference was found between the study groups. Differences in the CALM parameters between the MetS+ and MetS− groups are shown in Figure 2. Among the CALM parameters, significant differences between the MetS+ and MetS− groups were found in all examined parameters except IAampl. In subjects belonging to the MetS+ group, IAante was larger ($P < 0.01$) and IAretro was smaller ($P < 0.001$) than in the MetS− group. Individuals without MetS showed negative IAdev, whereas subjects in the MetS+ group had slightly positive values in IAdev. Representative examples of carotid artery longitudinal wall motion in a subject without MetS and with MetS are presented in Figure 1.

Table 2 presents associations (linear regression model adjusted for age and gender) between the CALM parameters and the components of MetS. IAdev showed positive and IAretro negative correlations with hypertension ($P < 0.05$ for both). No significant correlations were found between IAante, IAampl and hypertension. IAante and IAdev exhibited positive correlations with obesity ($P < 0.05$ for both). IAretro showed a negative correlation with obesity ($P < 0.05$). IAampl showed no significant correlation with obesity. No significant associations were found between CALM parameters and hypertriglyceridemia. Dyslipidemia, with low HDL-C a risk factor, showed a positive correlation ($P < 0.01$) with IAante, but there were no statistically significant associations with other CALM parameters. No significant correlations were observed between longitudinal motion parameters and either hyperglycaemia or adiponectin. IAretro and IAampl exhibited negative correlations with hyperinsulinemia ($P < 0.01$ and $P < 0.05$, respectively). IAretro and IAampl showed negative correlations with HOMA-IR ($P < 0.05$ for both).

In the multivariate analysis with a stepwise method, hypertension was associated with IAretro ($\beta = -0.175$, $P < 0.01$) and IAdev ($\beta = 0.145$, $P < 0.05$), but no other significant associations between CALM parameters and hypertension were seen. Low HDL-C was associated with IAante ($\beta = 0.164$, $P < 0.01$) and IAampl ($\beta = 0.126$, $P < 0.05$) but not with other CALM parameters. Hyperinsulinemia exhibited an inverse association with IAretro ($\beta = -0.124$, $P < 0.05$) and IAampl ($\beta = -0.156$, $P < 0.01$) but not with other CALM parameters.

Hyperglycaemia and obesity did not show any significant associations with CALM in these multivariate models.

Discussion

The novel finding of this study is that MetS is associated with alterations in CALM among young (30–45-year-old) adults. We found statistically significant differences between MetS+ and MetS− groups in all examined CALM parameters except IAampl. When studying separately associations of different components of MetS with CALM, statistically significant independent associations were found for hypertension, dyslipidemia and hyperinsulinemia. Hyperglycaemia or low adiponectin did not exhibit any significant associations with CALM parameters. In general, MetS and adverse profile in its components were associated with augmented antegrade and attenuated retrograde motion of intima-media complex in relation to the adventitia layer, which might be markers of unfavourable vascular health (Taivainen *et al*., 2015; Taivainen *et al*., 2018).

The relation between MetS and CALM parameters has not previously been systematically evaluated. However, there have been reports demonstrating significant associations between MetS and arterial stiffness (Li *et al*., 2005; Koskinen *et al*., 2009; Koskinen *et al*., 2010; Gomez-Sanchez *et al*., 2016; Vilmi-Kerälä *et al*., 2017; Topouchian *et al*., 2018). Thus, our finding of altered CALM in subjects with MetS is not surprising. One article reported CALM in type 2 diabetic subjects (Zahnd *et al*., 2011). In older type 2 diabetic subjects, mean amplitudes of CALM were lower than in young, healthy subjects. However, the study groups were not well comparable since, in older diabetic subjects, atherosclerotic process is more pronounced due to arterial ageing compared with a younger reference population. Therefore, it was not possible to detect a possible independent role of diabetes behind altered CALM. The influence of normal ageing process to CALM has been of interest to Cinthio and colleagues, who studied 150 healthy non-obese patients aged 20–76 years and determined that the antegrade-oriented phase of longitudinal motion increased with ageing and was earlier in men than in women (Cinthio *et al*., 2018). An important advantage of the present study is that MetS+ and MetS− groups were comparable with regard to age and sex distributions. Furthermore, statistically significant associations between MetS components and CALM were detected even after adjustment for age and sex.

We have reported previously relationships between CALM and cardiovascular risk factors in a study which is based on the same research population than this (Taivainen *et al*., 2018). In the present study, many of the same risk factors were included as components of MetS. In our previous study, systolic and diastolic blood pressure, BMI, total cholesterol and LDL-C showed significant associations with CALM (Taivainen *et al*., 2018). This is in line with the present study demonstrating changes in CALM to be associated with hypertension, obesity and dyslipidemia. When investigating the different MetS components of the harmonized criteria, the results were parallel to those of our previous study – antegrade longitudinal motion increased and retrograde longitudinal motion decreased with the existence of cardiovascular risk factors and, now, with MetS components (Taivainen *et al*., 2018).

The present study also included assessments of hyperinsulinemia, insulin resistance and low adiponectin, which are closely related to impaired glucose metabolism and therefore enable elaborate evaluation of metabolic disorders related to MetS. Novel findings are that hyperinsulinemia and insulin resistance also showed significant associations with CALM. No significant association was identified between hyperglycaemia and CALM in the present study, but reasonable, insulin-metabolism, and on demand hyperinsulinemia, regulates glucose levels and aim is to maintain euglycemia. Hyperinsulinemia is not included in all MetS criteria although it has been reported to be an important feature of MetS in the literature (e.g. Kassi *et al*., 2011).

Hyperinsulinemia is accepted to be essential in the pathophysiology of MetS, and an overabundance of free fatty acids is acknowledged to be a considerable contributor to the development of hyperinsulinemia (Eckel *et al*., 2005). In glucose metabolism, defects of insulin action contribute to glucose uptake and metabolism in insulin-sensitive tissues such as muscle and adipose tissue, and attenuates the insulin capability to suppress glucose production of the liver (Eckel *et al*., 2005). Furthermore, among some insulin-resistant individuals who secrete enough insulin to maintain near normal or normal glucose tolerance and do not acquire type 2 diabetes compensatory hyperinsulinemia can also act on in a way that predisposes the development of essential hypertension (Reaven, 2011). Some mechanisms behind essential hypertension in individuals with insulin resistance may arise from the fact that not all tissues are equally insulin-resistant; that is, the kidney is not resistant to the influence of insulin, and insulin enhances renal sodium retention in hyperinsulinemic/insulin-resistant individuals (Facchini *et al*., 1999). This could predispose to elevated blood pressure and in long term add risk to vascular changes.

In our study, adiponectin levels were significantly lower and HOMA-IR significantly higher in the MetS+ group compared with the MetS− group. Adiponectin levels decrease with visceral fat accumulation, and adiponectin has been found to protect against hypertension, type 2 diabetes, inflammation and atherosclerotic diseases (Matsuzawa, 2010; Ohashi *et al*., 2011). Among young adults in the Young Finns Study (n = 1693), high adiponectin levels were shown to associate with decreased incidence of MetS (Juonala *et al*., 2011). Despite significant univariate correlations with obesity, hypertension, hyperinsulinemia and insulin resistance, we did not find any significant correlations between adiponectin levels and CALM parameters.

Mechanisms underlying the relationship between MetS and CVD are likely to occur via direct or indirect influences of different components on endothelial function, the deposition of LDL cholesterol (LDL-C) or the recruitment, migration and proliferation of monocytes in smooth muscle cells in the arterial wall (Qiao *et al*., 2007). MetS can promote arterial stiffening through a variety of mechanisms including increased sympathetic activity, enhanced activity of the renin-angiotensin-aldosterone system, increased production of inflammatory cytokines and reactive oxygen species and reduction of nitric oxide availability (Saladini & Palatini, 2018). When evaluating the mechanisms behind the association between MetS and CALM, these same mechanisms should also be taken into consideration.

Our study was undertaken with a large, well-characterized study population comprising 30- to 45-year-old adults. The population consisted of white European subjects, and, for that reason, these results may not be generalizable to other ethnic groups. The size of the study population was large but notably smaller than in many other reports of The Cardiovascular Risk in Young Finns Study. Longitudinal motion analysis of CCA is challenging and requires good frame-to-frame image quality in ultrasound videos. In 2007, the ultrasound imaging protocol was optimized to measure carotid intima-media thickness and distensibility but not to assessments of CALM, and this is the reason for the relatively large number of unsuccessful scans, as described previously (Taivainen *et al*., 2018). However, the final number of study subjects in the study herein is large, and, for the majority, the signal quality of the data was good.

Conclusion

Our findings support the hypothesis that MetS alters CALM. In particular, hypertension, obesity and hyperinsulinemia were associated with reduced total peak-to-peak amplitude,

increased antegrade and reduced retrograde amplitudes, all of which might be markers of unfavourable vascular health.

Conflict of Interest

The authors have no conflict of interest.

Author Contributions

HT, HY, TML and TPL designed the experiment. HT, HY, TML and TPL contributed to the analysis and interpretation of data. HT, HY, TML, TPL, MJ, MK and OTR participated in the elaboration of the manuscript and gave final approval for its submission and publication, being accountable for all aspects of the work herein.

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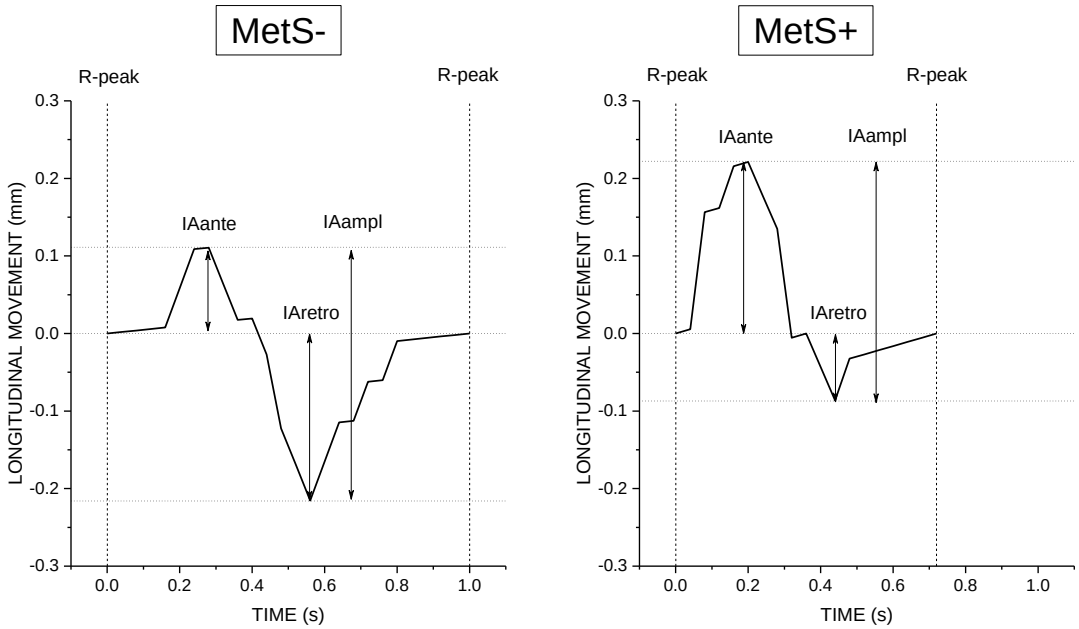

Figure 1. Representative examples of carotid artery longitudinal wall motion in a subject without metabolic syndrome (MetS-) and another with metabolic syndrome (MetS+). Time point 0.0 seconds corresponds to end-diastolic frame (incident with the R-wave on a continuously recorded electrocardiogram). In MetS+ antegrade oriented motion was larger and retrograde oriented was smaller than in MetS-. Abbreviations: IAante = Antegrade amplitude of the longitudinal motion between intima-media and adventitia layers, IAretro = Retrograde amplitude of the longitudinal motion between intima-media and adventitia layers, and IAampl = Peak-to-peak amplitude of the longitudinal motion between intima-media and adventitia layers.

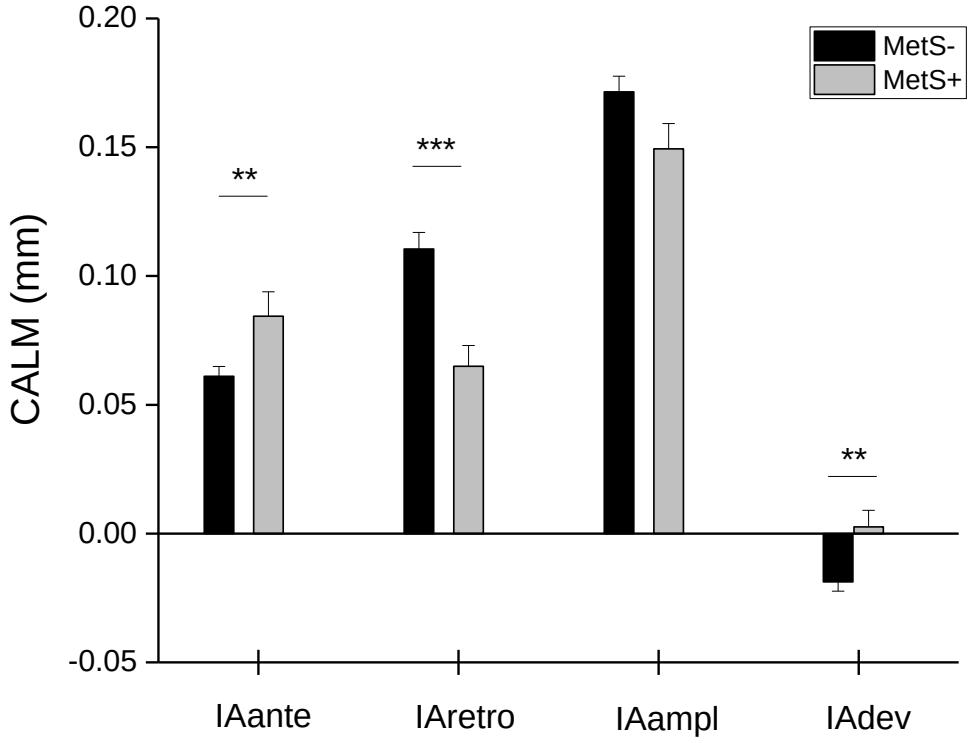

Figure 2. Carotid artery longitudinal motion (CALM) parameters between subjects without (MetS−) and with (MetS+) metabolic syndrome. IAante = Antegrade amplitude of the longitudinal motion between intima-media and adventitia layers, IAretro = Retrograde amplitude of the longitudinal motion between intima-media and adventitia layers, IAampl = Peak-to-peak amplitude of the longitudinal motion between intima-media and adventitia layers, IAdev = Average deviation of the longitudinal motion between intima-media and adventitia layers.

Table 1. Clinical characteristics of subjects without (MetS−) and with (MetS+) metabolic syndrome.

	MetS− (n = 228)	MetS+ (n = 53)
Age (years)	37.9 (4.9)	39.1 (4.5)
Sex (% women)	63.2%	49.1%
Smoking (%)	16.3%	22.6%
Body mass index (kg/m^2)	24.6 (3.7)	30.5 (5.2) ***
Waist circumference (cm)	83.1 (10.2)	101.1 (11.8) ***
Systolic blood pressure (mmHg)	126 (13)	137 (14) ***
Diastolic blood pressure (mmHg)	79 (9)	89 (9) ***
Total cholesterol (mmol/L)	4.95 (0.83)	5.49 (0.93) ***
Low-density lipoprotein cholesterol (mmol/L)	3.04 (0.73)	3.40 (0.81) **
High-density lipoprotein cholesterol (mmol/L)	1.42 (0.30)	1.20 (0.43) ***
Triglycerides (mmol/L)	1.08 (0.44)	2.05 (0.90) ***
Glucose (mmol/L)	5.20 (0.44)	5.75 (0.60) ***
Insulin (mU/L)	6.78 (4.70)	14.26 (7.96) ***
HOMA-IR	1.60 (1.26)	3.68 (2.17) ***
Adiponectin	10.90 (5.75)	7.11 (3.18) ***

Values are mean (SD) / %. Significances: ** = $P < 0.01$, *** = $P < 0.001$. Abbreviations: HOMA-IR = Homeostasis model assessment of insulin resistance.

Table 2. Age- and sex-adjusted relationships between components of metabolic syndrome and longitudinal motion parameters.

	B (SE)	Beta
Hypertension (Blood pressure ≥ 130/85 or medication)		
IAante	0.015 (0.008)	0.119
IAretro	−0.029 (0.012)	−0.156 *
IAampl	−0.015 (0.012)	−0.083
IAdev	0.014 (0.007)	0.131 *
Obesity (Waist circumference ≥ 102 cm in men and ≥ 88 cm in women)		
IAante	0.022 (0.009)	0.149 *
IAretro	−0.031 (0.013)	−0.138 *
IAampl	−0.009 (0.013)	−0.042
IAdev	0.018 (0.008)	0.136 *
Dyslipidemia (Triglycerides ≥ 1.7 mmol/L or medication):		
IAante	0.016 (0.009)	0.102
IAretro	−0.022 (0.014)	−0.093
IAampl	−0.006 (0.013)	−0.027
IAdev	0.006 (0.008)	0.045
Dyslipidemia (HDL-C < 1.00mmol/L in men and < 1.3 in women or medication)		
IAante	0.024 (0.008)	0.177 **
IAretro	−0.006 (0.012)	−0.029
IAampl	0.018 (0.012)	0.092
IAdev	0.014 (0.007)	0.114
Hyperglycemia (Glucose ≥ 5.6 mmol/L or treatment)		
IAante	0.010 (0.009)	0.070
IAretro	−0.018 (0.013)	−0.081
IAampl	−0.008 (0.013)	−0.037
IAdev	0.008 (0.008)	0.060

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Hyperinsulinemia (Insulin ≥ 11.06 mU/L)		
IAante	0.006 (0.009)	0.037
IAretro	−0.036 (0.013)	−0.158 **
IAampl	−0.030 (0.013)	−0.141 *
IAdev	0.014 (0.008)	0.109
Insulin resistance (HOMA-IR ≥ 2.44)		
IAante	0.003 (0.008)	0.024
IAretro	−0.031 (0.013)	−0.145 *
IAampl	−0.028 (0.012)	−0.136 *
IAdev	0.009 (0.007)	0.073
Low adiponectin (≤ 6.22 µg/mL)		
IAante	0.009 (0.009)	0.065
IAretro	0.002 (0.014)	0.007
IAampl	0.011 (0.013)	−0.052
IAdev	−0.003 (0.008)	−0.021

Significances: *P < 0.05, **P < 0.01. Abbreviations, IAante = Antegrade amplitude of the longitudinal motion between intima-media and adventitia layers, IAretro = Retrograde amplitude of the longitudinal motion between intima-media and adventitia layers, IAampl = Peak-to-peak amplitude of the longitudinal motion between intima-media and adventitia layers, and IAdev = Average deviation of the longitudinal motion between intima-media and adventitia layers, HDL-C = high-density lipoprotein cholesterol, HOMA-IR = Homeostasis model assessment of insulin resistance.

Table 3. Multivariate relationships between each component of metabolic syndrome and longitudinal motion parameters adjusted for age and sex.

	Hypertension B ± SE, Beta	Obesity B ± SE, Beta	Low HDL-C B ± SE, Beta	High triglycerides B ± SE, Beta	Hyperglycaemia B ± SE, Beta	Hyperinsulinemia B ± SE, Beta
IAante (mm)			0.02 ± 0.01, 0.164 **			
IAretro (mm)	−0.03 ± 0.01, −0.175 **					−0.03 ± 0.01, −0.124 *
IAampl (mm)			0.03 ± 0.01, 0.126 *			−0.03 ± 0.01, −0.156 **
IAdev (mm)	0.02 ± 0.01, 0.145 *					

Statistical significances: *P < 0.05, **P < 0.01, ***P < 0.001. Unstandardized coefficients B ± Std.Error, Beta, Sig. Abbreviations, IAante = Antegrade amplitude of the longitudinal motion between intima-media and adventitia layers, IAretro = Retrograde amplitude of the longitudinal motion between intima-media and adventitia layers, IAampl = Peak-to-peak amplitude of the longitudinal motion between intima-media and adventitia layers, and IAdev = Average deviation of the longitudinal motion between intima-media and adventitia layers, HDL-C = high-density lipoprotein cholesterol.

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