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Letter to the Editor

Concomitant insulin resistance and impaired vascular function is associated with increased coronary artery calcification

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Abstract

Background: Digital Thermal Monitoring (DTM) of vascular function has been shown to correlate well with the Framingham risk score (FRS) and coronary artery calcium (CAC) score. This study investigates whether vascular dysfunction measured by DTM is associated with insulin resistance (IR).
Methods: 326 consecutive asymptomatic subjects (age 55±10 years, 73% male), without CAD, diabetes or NCEP defined metabolic syndrome, underwent DTM, CAC and IR calculation. DTM measurements were obtained during and after a 5-minute supra systolic arm-cuff occlusion. Post cuff-deflation temperature rebound (TR) and AUC (area under the temperature curve) were measured and correlated with IR defined by the ratio of triglyceride to HDL ≥ 3.8.
Results: There was no significant difference between patients with and without IR in Lipoprotein (a), C-reactive protein and homocysteine ($p > 0.05$). TR decreased from the normal cohort (1.68±0.25) to IR (1.07±0.18) to CAC ≥ 100 (0.94±0.21) to FRS ≥ 20% (0.77±0.21) to IR & CAC ≥ 100 (0.68±0.16) ($p = 0.001$). After adjustment for age, gender and traditional cardiac risk factors, the odds ratio of reduced TR and CAC ≥ 100 was 2.46, and 2.10 in IR compared to those without IR.
Conclusion: 1) Vascular dysfunction measured by DTM is strongly associated with IR. 2) IR Patients with concomitant high FRS and or high CAC exhibit severe vascular dysfunction.

Keywords: Digital thermal monitoring; Framingham risk score; Insulin resistance

Insulin resistance (IR) increases atherogenesis and atherosclerotic plaque instability by inducing proinflammatory activities in vascular and immune cells [1]. Increased triglycerides (TG) and decreased high density cholesterol (HDL) as reflected in the TG/HDL ratio, has proved to be a simple measure of insulin resistance and strongly associated with cardio-metabolic risk in IR patients [2].

Digital Thermal Monitoring (DTM) of vascular reactivity is a new non-invasive test based on changes in fingertip temperature during and after a transient arm-cuff occlusion and release procedure. DTM has been shown to correlate with coronary artery calcium score in asymptomatic patients. The present study investigated the correlation of vascular dysfunction measured by DTM with the TG/HDL-C and coronary artery calcium (CAC) in asymptomatic adults.

1. Methods

The study population consisted of 326 consecutive asymptomatic patients (age >35 years) who underwent CAC scanning and DTM. Subjects with established cardiovascular disease, stroke, diabetes, NCEP defined metabolic syndrome, Raynaud's syndrome, infection,

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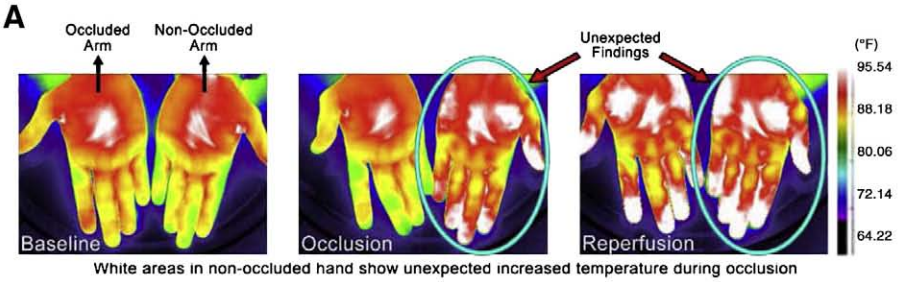

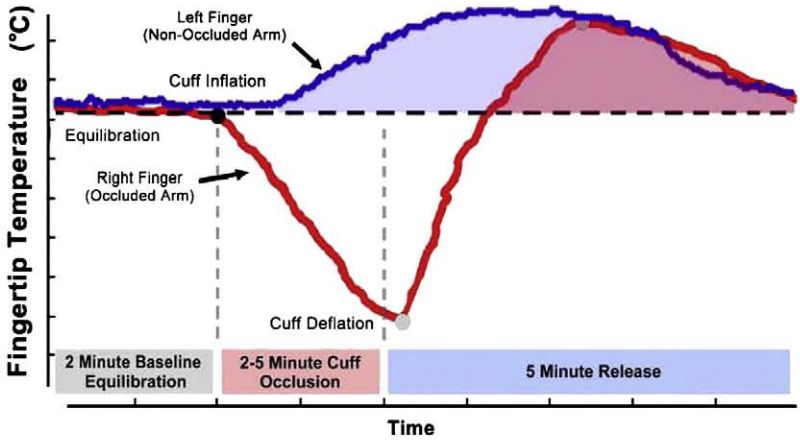

DTM Indices of Vascular Reactivity (Occluded Arm)

Temperature Rebound (TR) = Post cuff deflation Temperature Max – Temperature initial

Area Under the temperature Curve (AUC) = Post cuff deflation Area Under the Curve

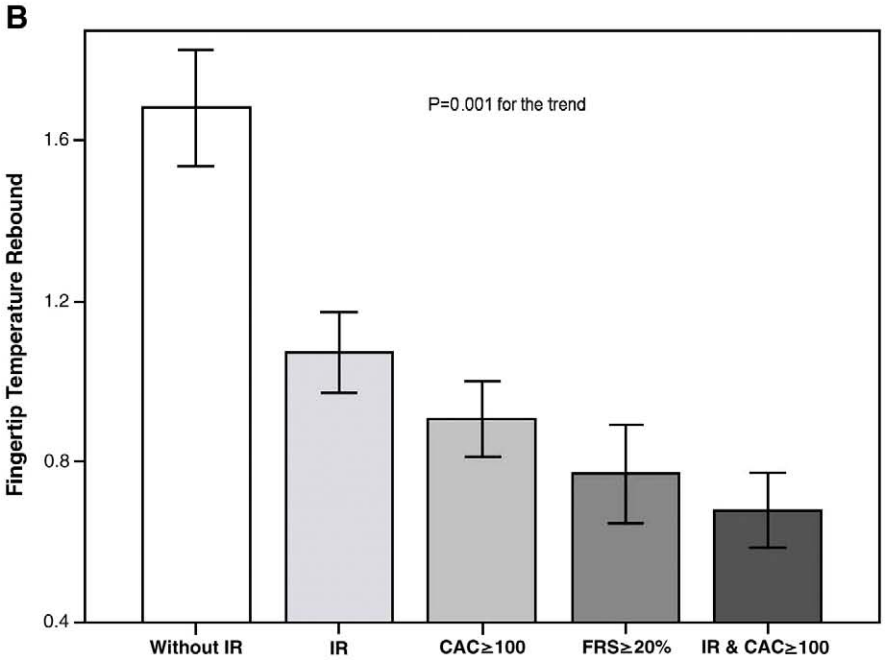

Fig. 1. A) Fingertip skin temperature changes before and during post-occlusive reactive hyperemia, as shown by infrared imaging and Digital Thermal Monitoring (DTM). B) Vascular dysfunction of digital thermal monitoring increases with severity of metabolic status and burden of atherosclerosis.

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Table 1
Relationship between insulin resistance, cardiovascular risk factors and DTM

Variable	Normal cohort	Insulin resistance	p value
	N=214	N=112	
Age (years)	56±10	54±11	0.03
Gender (male)	67%(143)	81%(99)	0.01
Smoking	40%(85)	41%(45)	0.9
Hypertension	29%(62)	40%(49)	0.04
Hypercholesterolemia	52%(111)	63%(77)	0.06
Family history of premature CHD‖	51%(109)	52%(64)	0.7
Body mass index (kg/m^2)	26.9±4.1	28.3±5.7	0.04
Coronary artery calcium score	184±25	323±49	0.005
Fasting blood sugar (mg/dL)	93±5	95±5	0.5
Total cholesterol (mg/dL)	198±40	210±45	0.01
HDL-C (mg/dL)	55±16	36±7	0.0001
LDL-C (mg/dL)	126±37	134±42	0.3
Triglyceride (mg/dL)	99±39	200±45	0.0001
Lipoprotein (a) (mg/dL)	6.3±0.7	7.5±0.4	0.05
Framingham risk score (%)	7.6±6	11±8	0.002
C-reactive protein (mg/dL)	2.7±0.9	3.6±1.3	0.5
Homocysteine (umol/L)	11.7±1.8	12.6±3.2	0.4
Temperature rebound (TR)	1.68±0.25	1.07±0.18	0.001
Area under curve (AUC)	429±18	342±20	0.001

HDL-C=high density lipoprotein cholesterol.
LDL-C=low density lipoprotein cholesterol.
‖ first degree relative; female <65 years, male <55 years.

cancer, immunosuppression, systemic inflammation status, and end-stage renal or liver diseases were excluded. IR, defined as TG/HDL-C>3.8 [2], and Framingham 10 year risk of CVD were calculated [3].

CAC Scanning was performed with an E-Speed electron beam scanner (GE-Imatron, Calif., USA) with 30-40 contiguous ≥3 mm slices. CAC was quantified using the previously described Agatston scoring method [4].

DTM was performed in the morning in a quiet, dimmed room at a controlled ambient temperature between 23.5 °C and 25.0 °C. Studies were conducted after an overnight fast of at least 10 h and abstinence from tobacco, alcohol, caffeine, vasoactive medications, exercise, high-fat foods and vitamin C. The measurements were obtained with the subjects supine and after 30 min of rest. Each patient's blood pressure in the left arm was recorded in a sitting position 5 min before the DTM test (Omron HEM 705 CP semi-automated sphygmomanometer, Bannockburn, IL, USA). DTM of both hands was obtained during 5 min stabilization, 5 min cuff inflation to 50 mmHg greater than systolic blood pressure, and 5 min deflation using an automated, operator-independent protocol (VENDYS, Endothelix Inc., Houston, TX). Fig. 1.A shows DTM indices of vascular reactivity based on the extent of temperature rebound (TR) and area under the temperature curve (TMP-AUC) in the fingertip of the occluded arm.

2. Results

There were no significant differences in CRP, homocysteine, and smoking between the cohorts. CAC, Lipoprotein (a) and FRS were significantly higher in the IR group. Similarly, TR and AUC were significantly reduced in IR groups (Table 1). TR significantly decreased from normal to IR to concomitant increased CAC and IR (Fig. 1.B).

After adjustment for age, gender and traditional cardiac risk factors by logistic regression, the odds ratios of CAC≥100, reduced TR and increased lipoprotein (a) were 2.46 (95% CI 1.23–4.92, $p=0.01$), 2.10 (95% CI 1.10–3.91, $p=0.01$), and 1.31(95% CI 1.09–1.58, $p=0.03$), respectively, in IR compared to the normal cohort, respectively. There were no significant differences between the cohorts for CRP and homocystiene after adjustment for age, gender and traditional cardiac risk factors.

3. Discussion

Previous studies reported that the triglyceride/HDL cholesterol ratio is an independent predictor of the presence of coronary atherosclerotic lesions [5–9] also is a strong predictor of myocardial infarction. In addition, there are numerous studies confirming the strong predictive power of CAC as an excellent marker of overall atherosclerotic burden for clinical events in asymptomatic patients [10].

This study demonstrates that insulin resistance, measured as TG/HDL-C ratio>3.8, is associated with vascular dysfunction, significant CAC, and increased lipoprotein (a) in subjects with no prior history of coronary artery disease, diabetes or metabolic syndrome. Furthermore, vascular dysfunction measured by DTM increased with the combination of IR and significant CAC.

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The authors of this manuscript have certified that they comply with the Principles of Ethical Publishing in the International Journal of Cardiology [11].

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