White Paper

RFQIMT/RFQAS

Markers of early atherosclerosis in diabetology

esaote
Creativity in Healthcare

"RF-Data provides physicians with extra help to assess cardiovascular disease (CVD) risk and target organ damage (TOD). Accuracy, ease of use and reliability are the core of this innovative technological tool"

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Background

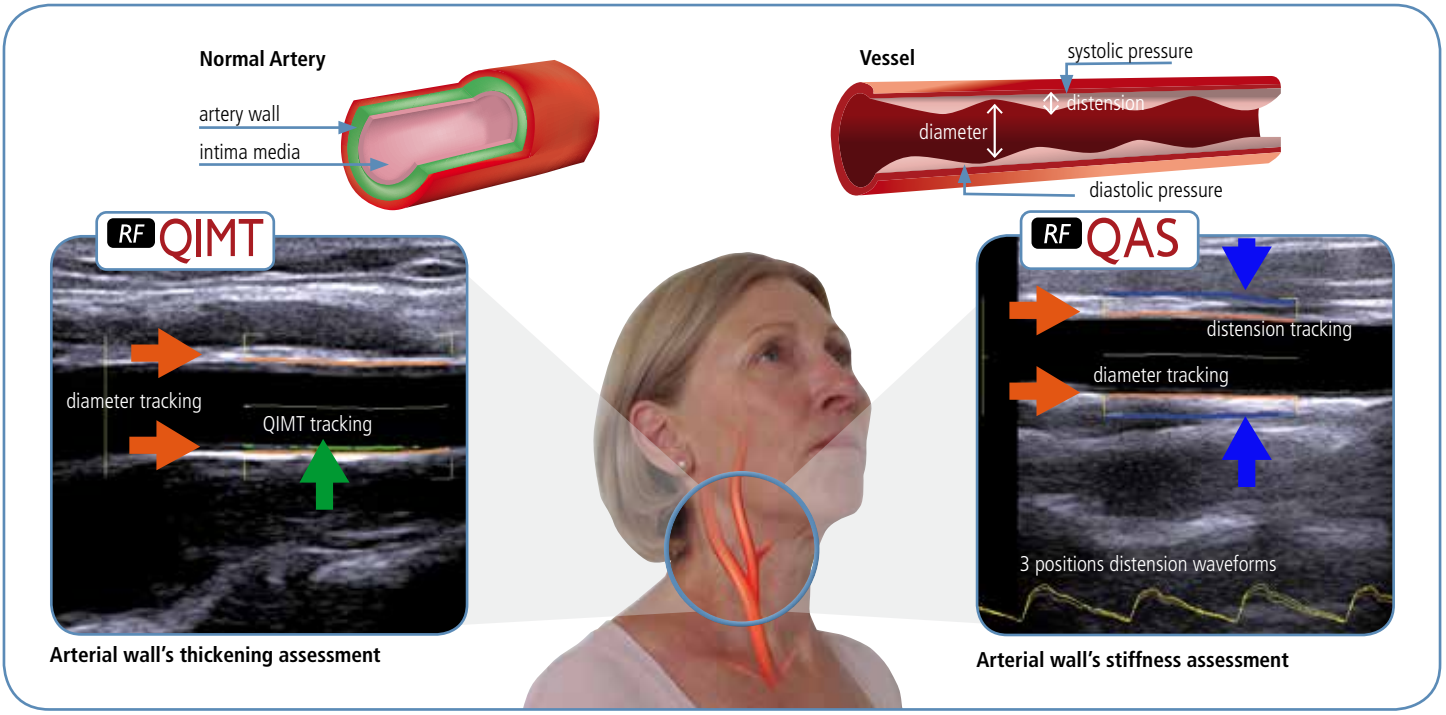
In addition to traditional parameters, such as cholesterol and blood pressure values, also intima media thickness ([RF]QIMT) and arterial stiffness ([RF]QAS) values are very useful in helping to understand arteriosclerosis, its severity and progression. An accurate cardiovascular management at an early stage, can provide an advantage to efficiently plan prevention and treatment. [RF]QAS and [RF]QIMT measurements are taken at the Common Carotid Artery, which represents a critical point in the vascular system.

Quality intima media thickness ([RF]QIMT)

[RF]QIMT measure carotid artery's wall thickness. Its ease of use combined with its real-time quality feedback, help the operator to achieve accurate and reproducible results. To assist physicians in their diagnostic and therapeutic procedure, the measures (even when taken at different examination times) can be reported on a normalised graph represented with plot indicators.

Quality Arterial Stiffness ([RF]QAS)

[RF]QAS measures carotid artery's wall stiffness. Arterial wall stiffness is expressed as the pulse wave velocity obtained from brachial blood pressure and the accurate measurements of diameter and change in diameter. Local blood pressure at the site of the ultrasound measurement is also supplied. Local blood pressure and stiffness are derived from quantification results based on sophisticated clinical studies.



RF-data
Both measurements are based on the Esaote RF-data technology

Quality
Very high accuracy (~20 µm) compared to standard video based processing

Ease of use
Comprehensive user interface for quick measurement (within 1 minute)

Real time
Easy and reliable real-time measurement with continuous feedback on the quality

Completeness
Clear visualization, extended measure output and complete report with IMT over age normal values

Innovation
Early detection of cardiovascular disease for preventive healthcare, cost reduction and improved quality of life

Case Study

RFQIMT/RFQAS - Markers of early atherosclerosis in T1DM

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New radio frequency echo-tracking technology provides real-time automated and highly accurate carotid intima-media thickness (IMT) and indices of large artery stiffness and endothelial function. In adolescents with type 1 diabetes mellitus (T1DM) this technique may be used to reveal very early atherosclerotic involvement, as well as to help monitoring adequacy of glycemic control and limiting incident cardiovascular complications.

Since incidence of cardiovascular complications in patients with type 1 diabetes mellitus (T1DM) is reported to be two to ten times greater than in healthy population[1] and inadequate glycemic control plays a major role in the development of vascular diseases, type 1 diabetes represents a major cause of cardiovascular disease.

Identifying preclinical alterations in the vascular system at a very early stage is thus crucial to prompt a more aggressive glycemic control and diminish incident cardiovascular complications[2].

A recent study indicates that young subjects with relatively long term T1DM with suboptimal glycemic control, free of clinical cardiovascular complications, display a significantly reduced count of circulating endothelial progenitor cells (EPCs), and therefore limited endothelial regenerating capacity, together with a generalized, although subtle, involvement of large artery structure and function compared to healthy controls. Increased radiofrequency-based common carotid intima-media thickness (QIMT™) is independently linked with lower circulating endothelial progenitor cells (EPC) and plasma adiponectin levels, while an impaired peripheral flow-mediated dilatation is associated with a poorer long-term glycemic control. Local carotid stiffness and pressure wave reflection appear primarily influenced by fasting plasma glucose, and aortic stiffness (carotid-femoral pulse wave velocity) by plasma LDL-cholesterol.

Radiofrequency echo-tracking is currently the most useful tool to detect and follow-up early vascular involvement in young subjects with T1DM, as well as to gain a deeper insight on the pathophysiologic mechanisms of vascular disease in this clinical setting[3]. MyLab70 RF echo-tracking system provides an accurate real-time assessment of vessel wall static and dynamic properties, through a quick measurement of local arterial stiffness and carotid IMT, representing a step ahead compared to other available similar techniques.

The vascular ultrasound parameters of 16 T1DM adolescents were compared to those of 26 healthy volunteers of similar age (Table 1 displays main clinical features) to evaluate known indices of large artery structure and function. Additionally, endothelial function was estimated by Reactive Hyperemia Index (RHI, Endopat, Itamar, Cesarea, Israel) and regenerating capacity by circulating EPCs count. The interactions between various large artery indices and EPCs, glycometabolic control, and atheroprotective adipokine adiponectin values were also evaluated.

T1DM adolescents were treated with a mixture of fast-acting basal insulin analogs (basal-bolus therapy optimized based on clinical evaluation and HbA1c).

Two hours after having ingested a light beverage based and caffeine free breakfast, each study participant completed an integrated examination of the vascular system.

A scan of the right carotid artery was acquired employing an ultrasound scanner operating with a linear 10 MHz probe (MyLab70 by Esaote, Genoa, Italy) and applying a previously validated RF-based tracking of arterial wall able to estimate in real time common carotid intima-media thickness (QIMT™) and distension (QAS™) with high spatial and temporal resolution[4].

Automatic measurement of far-wall IMT (C-IMT) and distension curves were acquired in a carotid segment ~1 cm before the flow divider. Maximum and minimum carotid diameters were acquired using the attained distension curves, and vascular stiffness parameters were calculated after calibration for blood pressure (BP).

A carotid local wave speed is automatically estimated by MyLab70 from the carotid distension curve and brachial blood pressure according to the Bramwell Hill equation.

Local carotid pulse pressure and augmentation index (AIx) were measured using applanation tonometry (PulsePen, Diatecne, Milan) while carotid-femoral pulse wave velocity (CF-PWV) to evaluate aortic stiffness index was taken with the Complior system (Alam, Paris).

Results

T1DM adolescents had considerably higher carotid Q-IMT (456 ±7 vs. 395 ±63 µm, $p < 0.005$), carotid WS ($p < 0.005$), PWV ($p = 0.01$), AIx ($p < 0.0001$) and central PP ($p < 0.01$), and lesser EPCs ($p = 0.02$) compared to controls (Fig. 1). Only diabetic patients with HbA1c ≥ 7.5% ($p < 0.05$) had lower RHI values.

The univariate associations between vascular parameters and plasma glucose, lipids, adiponectin and EPCs were analyzed to identify metabolic variables accounting for the significantly different vascular parameters among healthy and T1DM young subjects (Table 2).

Vascular parameters were entered as dependent variables, while sex, age, mean BP and all univariate metabolic correlates were entered as independent variables to carry out a multiple regression analysis (Table 3).

Multivariate models established that EPCs were independent determinants of carotid IMT, fasting plasma glucose was an independent determinants of carotid WS, AIx and central PP and EPCs were independent determinants of carotid IMT.

Tables

Table 1 Clinical and Metabolic Characteristics of Study Population

	Controls	T1DM	p
N	26	16	IMT (µm)
Sex (males, %)	58	68	= 0.47
Age (years)	19 ± 2	18 ± 2	= 0.12
Body mass index (kg/m^2)	21.6 ± 4.2	21.7 ± 6.2	= 0.82
Systolic BP (mmHg)	112 ± 10	118 ± 16	= 0.13
Diastolic BP (mmHg)	67 ± 5	66 ± 7	= 0.94
Mean BP (mmHg)	82 ± 5	83 ± 8	= 0.47
Heart rate (bpm)	70 ± 12	69 ± 11	= 0.88
Total cholesterol (mg/dL)	165 ± 22	170 ± 33	= 0.37
HDL-cholesterol (mg/dL)	58 ± 13	54 ± 8	= 0.36
LDL-cholesterol (mg/dL)	87 ± 19	100 ± 21	= 0.08
≀ Triglycerides (mg/dL)	71 [31]	75 [25]	= 0.94
≀ Adiponectin (mg/L)	18.5 [5.5]	19.0 [4.5]	= 0.09
Fasting plasma glucose (mg/dL)	***87 ± 7***	***178 ± 45***	***< 0.0001***
sRAGEs (pg/ml)	383 ± 152	464 ± 187	= 0.76
AGE-dependent AF (arbitrary units)	1.6 ± 0.3	1.7 ± 0.3	= 0.52
≀ EPCs (CD34+/KDR+/10^6 events*)	***74 [150]***	***39 [63]***	***= 0.02***

≀: skewed variables expressed as median [interquartile] range; * EPCs: log-transformed endothelial progenitor cells expressed as CD34+/KDR+ cells/10^6 cytometric events; p values after adjustment for sex and age. Statistically significant differences are highlighted in bold italic.

Table 2 Univariate Pearson Correlation Coefficients Between vascular Measures and Metabolic Parameters

	Central PP (mmHg)	AIx (%)	C-F PWV (m/s)	Carotid WS (m/s)	C-IMT (µm)	RHI score
Fasting plasma glucose (mg/dL)	***r = 0.36 (p < 0.05)***	***r = 0.47 (p < 0.005)***	***r = 0.33 (p < 0.05)***	***r = 0.4 (p < 0.01)***	r = 0.29 (p = 0.06)	r = 0.26 (p = 0.10)
HDL-cholesterol (mg/dL)	***r = 0.40 (p < 0.01)***	r = 0.17 (p = 0.31)	r = 0.16 (p = 0.33)	r = –0.09 (p = 0.59)	***r = 0.30 (p < 0.05)***	r = 0.24 (p = 0.14)
LDL-cholesterol (mg/dL)	r = 0.06 (p = 0.71)	r = 0.06 (p = 0.72)	***r = 0.35 (p < 0.05)***	r = 0.26 (p = 0.11)	r = 0.04 (p = 0.80)	r = –0.05 (p = 0.77)
≀ Adiponectin (mg/L)	r = 0.13 (p = 0.47)	***r = 0.44 (p < 0.01)***	r = –0.01 (p = 0.96)	r = –0.08 (p = 0.65)	***r = 0.36 (p < 0.05)***	r = 0.24 (p = 0.16)
≀ EPCs (CD34+/KDR+/10^6 events*)	r = 0.08 (p = 0.63)	r = –0.27 (p = 0.10)	r = –0.12 (p = 0.45)	r = –0.12 (p = 0.46)	***r = 0.31 (p < 0.05)***	r = 0.20 (p = 0.21)

≀: skewed variables log transformed; significant correlations are highlighted in bold italic.

Table 3 Independent Correlates of Vascular Parameters: Multiple Regression Model *(ß = standardized regression coefficient)

		*ß ± SE	p
Central PP (mmHg)			
	Sex (male)	***0.57 ± 0.15***	***p = < 0.0005***
	Age (years)	–0.07 ± 0.13	p = 0.60
	Mean BP (mmHg)	0.05 ± 0.13	p = 0.69
	HDL-cholesterol (mg/dL)	–0.01 ± 0.13	p = 0.96
	Fasting glucose (mg/dL)	***0.29 ± 0.12***	***p = 0.01***
Cumulative R^2		0.54	p < 0.0001
AIx (%)			
	Sex (male)	***0.57 ± 0.15***	***p = < 0.0005***
	Age (years)	–0.07 ± 0.13	p = 0.60
	Mean BP (mmHg)	0.05 ± 0.13	p = 0.69
	Fasting glucose (mg/dL)	***–0.01 ± 0.13***	***p = 0.96***
	≀ Adiponectin (mg/L)	***0.29 ± 0.12***	***p = 0.01***
Cumulative R^2		0.54	p < 0.0001
C-F PWC (m/s)			
	Sex (male)	***0.39 ± 0.16***	***p = < 0.05***
	Age (years)	0.30 ± 0.16	p = 0.06
	Mean BP (mmHg)	0.07 ± 0.15	p = 0.66
	LDL-cholesterol (mg/dL)	***0.36 ± 0.16***	***p = < 0.05***
	Fasting glucose (mg/dL)	0.24 ± 0.19	p = 0.13
Cumulative R^2		0.35	p < 0.01
Carotid WS (m/s)			
	Sex (male)	0.24 ± 0.16	p = 0.15
	Age (years)	0.26 ± 0.16	p = 0.13
	Mean BP (mmHg)	0.10 ± 0.16	p = 0.55
	Fasting glucose (mg/dL)	***0.46 ± 0.16***	***p = 0.01***
Cumulative R^2		0.29	p < 0.05
C-IMT (µm)			
	Sex (male)	***0.49 ± 0.17***	***p < 0.01***
	Age (years)	***0.39 ± 0.14***	***p < 0.01***
	Mean BP (mmHg)	0.14 ± 0.14	p = 0.30
	HDL-cholesterol (mg/dL)	–0.20 ± 0.15	p = 0.19
	≀ Adiponectin (mg/L)	***–0.35 ± 0.14***	***p = 0.01***
	≀ EPCs	***–0.48 ± 0.13***	***p = 0.001***
Cumulative R^2		0.57	p < 0.0005

2: skewed variables log transformed; independent correlates are highlighted in bold italic.

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