Echo-Tracking Is a Novel Technology to Assess Structural and Functional Properties of Carotid Arteries (Review)

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The problem of searching and large-scale implementation of early diagnostic techniques of cardiovascular diseases at the stage of preclinical failure is still relevant. Novel methods for vessel stiffness assessment to stratify cardiovascular risk and determine the aim of treatment intervention are certain to provoke interest.

The review considers the modern aspects of local stiffness of an arterial wall, and presents comparative data on ultrasound capabilities when using a standard B-mode and a new technique: echo-tracking. Software echo-tracking applications (QIMT and QAS) are described. We analyzed the parameters characterizing local rigidity. Obtaining measurement data minimally dependent on researcher's attitude was found to be an evident advantage of echo-tracking. The paper gives the guide values of a norm for the parameters under study in different age subgroups, and demonstrates diagnostic and prognostic value of the obtained parameters and their dynamics during the drug therapy.

Key words: echo-tracking; arterial stiffness; carotid arteries; atherosclerosis.

Despite certain advances in medical science, incidence, disability and mortality from cardiovascular pathology are still high worldwide. There is fragrant necessity to search and implement widely early diagnostic techniques for cardiovascular diseases as early as at the stage of preclinical involvement, and develop a common algorithm of preventive examination to stratify risk groups and develop their further management [1–3]. The alteration of aorta, carotid and femoral arteries is a significant marker of cardiovascular events. Elastic arteries provide both: blood carrying to periphery, and also damping of pressure wave forming due to cardiac output [4–8]. The diagnostics of arterial wall properties altered is of great importance for medical practice. Most patients with arterial hypertension (AH), who are under care of a primary care physician, are those suffering from moderately expressed carotid atherosclerosis (carotid artery narrowing is under 50%) [9]. According to different authors, combined atherosclerotic involvement of coronary, carotid and peripheral arteries occurs in 30–65% cases [7, 10–12]. Therefore, the determination of elastic properties of carotid arteries is of special concern, and used in numerous studies, as well as recommended to be used by general practitioners [1, 2, 4].

Radiofrequency analysis peculiarities of carotid arteries

Currently, there are a lot of techniques, which enable to estimate the arterial bed state. Ultrasound investigation (US) of arteries of different localization is highly informative and the most common diagnostic procedure. Routine US enables to determine rather quickly and invasively the atherosclerosis of surface arteries including carotid ones. The increase in carotid intima-media thickness (CIMT) and atheroma detection in carotid arteries are known to increase significantly cardiovascular risk, and require patient's management and combination therapy [13]. In accordance with Mannheim protocol, carotid arteries US for CIMT measurement is performed 1.5–2.0 cm proximal of the bifurcation of common carotid artery, the upper normal level being determined as 0.9 mm [14–18]. However, there are evidences that this index value (0.9 mm) cannot be considered as a norm for patients of different ages, sex and nationalities [19, 20]. Currently, there are imaging techniques, which enable to measure CIMT to greater accuracy.

Among these techniques there is a relatively new echo-tracking program available in US scanners

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MyLab25/30, MyLab50, MyLab60/70/90/XVG (Esaote, Italy), as well as in some Aloka modifications (Hitachi, Japan). The program is based on standard B-mode with the integrated radiofrequency "filling" of a signal, it consisting in echo-contrast boundary monitoring that enables to track the altered artery diameter during different cardiac cycle phases [7, 19, 20]. Radiofrequency analysis minimizes data loss compared to the systems using video image analysis.

The technique was first mentioned in foreign literature

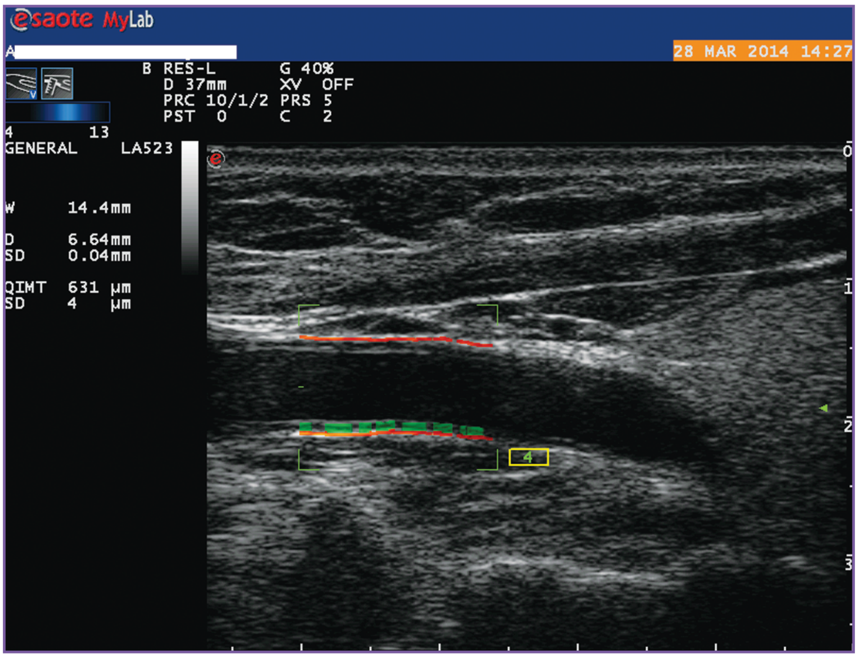
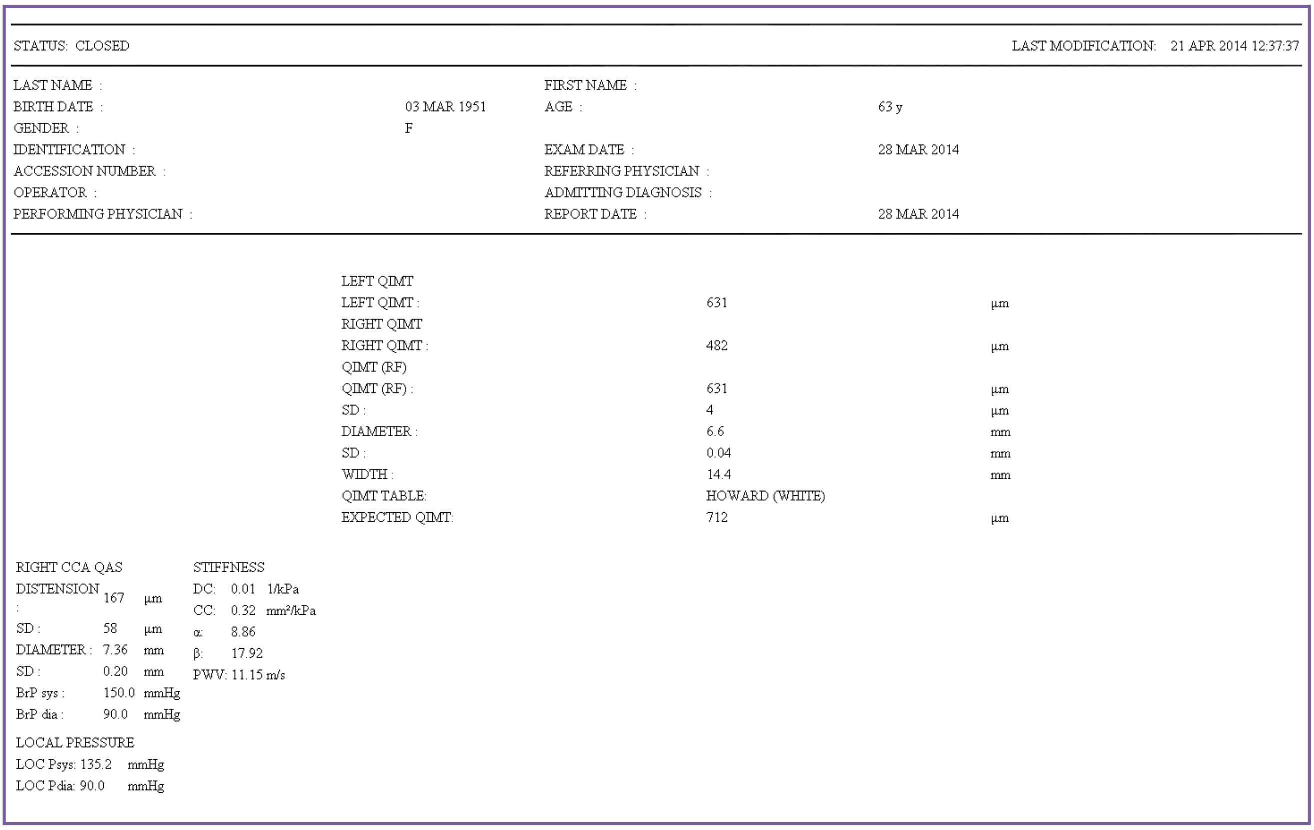


Figure 1. The measurement of carotid intima-media thickness by real-time echo-tracking (our study findings); *D* is artery diameter; *SD* is standard deviation; *QIMT* is Quality Intima-Media Thickness



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LEFT QIMT		
LEFT QIMT :	631	µm
RIGHT QIMT		
RIGHT QIMT :	482	µm
QIMT (RF)		
QIMT (RF) :	631	µm
SD :	4	µm
DIAMETER :	6.6	mm
SD :	0.04	mm
WIDTH :	14.4	mm
QIMT TABLE:	HOWARD (WHITE)	
EXPECTED QIMT:	712	µm

RIGHT CCA QAS			STIFFNESS		
DISTENSION :	167	µm	DC:	0.01	1/kPa
SD :	58	µm	CC:	0.32	mm²/kPa
DIAMETER :	7.36	mm	α:	8.86	
SD :	0.20	mm	β:	17.92	
BrP sys :	150.0	mmHg	PWV:	11.15 m/s	
BrP dia :	90.0	mmHg			

LOCAL PRESSURE
LOC Psys: 135.2 mmHg
LOC Pdia: 90.0 mmHg

Figure 2. Image of measurement results of carotid intima-media thickness and local rigidity parameters (our study findings)

in 2001 [21]. In Russian Federation echo-tracking technology has become available since 2011 in US scanners MyLab (Esaote).

Currently, it is possible to use two software applications for echo-tracking: QIMT (Quality Intima-Media Thickness) and QAS (Quality Arterial Stiffness). Since all measurements are real-time, their further processing is unnecessary that minimizes an impact of a medical researcher on the findings. The accuracy of the equipment units based on radiofrequency usage is 6–10 times higher compared to those based on video image analysis. The measurement of absolute distance of standard deviation (SD) for devices based on video image analysis was found to be 54–60 μm; the same parameter for echo-tracking varies within 9–25 μm [22–26]. Echo-tracking software provides measurement findings minimally dependent on researcher's attitude, which in routine practice can be corrected by a sonologist (e.g., an angle under study, scanning depth, image magnification, etc.) (Figure 1).

CIMT calculations performed by the first application of echo-tracking function (QIMT program) is fully automatic, a researcher just mounts a sensor on an artery view region, and starts up a program. A frame of "measurement gates" appears on a display, and automatically outlines a vessel wall to automatically measure its thickness. To assess the validity of program operation and control the accuracy of measurements there is a number of control characteristics, such as SD: the results are considered correct if SD is in the range of 5–15 μm. Resolution of the technique reaches 10 μm, technical errors being less than 17 μm *in vitro* and 30 μm *in vivo* [26] (Figure 2).

US scanners with echo-tracking function have integrated Howard table showing CIMT dependence on age and sex, and are based on the results of a prospective epidemiological ARIC Study, which enrolled about 15,792 healthy subjects of different age groups [27, 28].

The second echo-tracking application — QAS program — enables to estimate local rigidity of vessels [29, 30]. The operation principle is to determine the amplitude of vessel wall movement during a pulse wave, and record the alterations of inside and outside diameters, as well as vessel volume in systole and diastole.

Local characteristics of rigidity assessed by echo-tracking

Calculation formulas integrated in the unit enable to assess some local characteristics of rigidity of the arteries under study: artery distensibility, pulse wave velocity, rigidity index, etc.

Let us take a detailed look at these parameters. *Artery distensibility* during the left ventricular systole is known to depend on vessel wall elastic properties and local pressure value in a vessel. The relationship can be expressed as $C=\Delta V/\Delta P$, where C is compliance; ΔV is systolic and diastolic changes of vessel segment volume, ΔP is pulse pressure [7, 31–36]. Considering that arterial wall compliance does not depend on

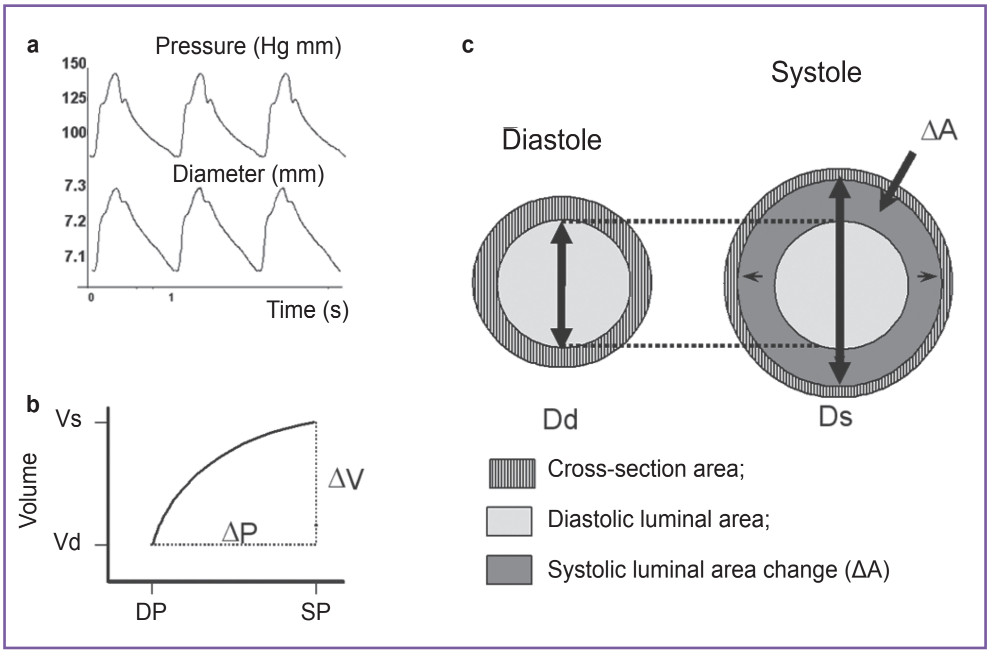

Figure 3. Local arterial distensibility: (a) simultaneous recording of changes in pressure amplitude and diameter; (b) pressure–volume curve; (c) schematic diagram of cross-section lumen changes

pressure level in a vessel, we can devise a formula of compliance coefficient (*CC*) of a vessel wall:

$$CC=\Delta A/\Delta p=[3.14\cdot Dd(Ds–Dd)/2]/\Delta p \text{ (mm}^2\text{/kPa)},$$

where ΔA is vessel cross-section variation in systole; Δp is pulse pressure; *Ds* is artery diameter in systole; *Dd* is artery diameter in diastole (Figure 3).

Arterial wall compliance characterizes the vessel capability to transform a pulsatile flow into a continuous flow.

Arterial distensibility, i.e. the wall capability to resist blood pressure wave, is estimated by a cross-section distensibility coefficient (*DC*) formula:

$$DC=\frac{\Delta A}{A\cdot\Delta p}=2[(Ds–Dd)/Dd]\Delta p \text{ (1/kPa)}.$$

Pulse wave velocity (PWV) is a common parameter characterizing the arterial bed condition. Its value increases proportionally with vessel wall rigidity. Echo-tracking technology enables to calculate local PWV in any arterial system area that can be visualized. The calculation is automatic according to the following formula:

$$\text{PWV}=\frac{1}{\sqrt{\rho\cdot DC}}=\sqrt{\frac{D^2\cdot\Delta p}{\rho(2\cdot D\cdot\Delta D+\Delta D^2)}},$$

where *D* is diastolic diameter; Δ*D* is diameter alteration in systole; *DC* is distensibility coefficient; Δ*p* is local pulse pressure; ρ is blood density.

There is one more index of arterial condition, which echo-tracking can calculate. It is *stiffness index β*. It reflects the vessel wall capability to resist deformities: the higher *β* value, the higher the wall rigidity:

$$\beta=\int(SP/DP)D/\Delta D.$$

where *SP* is systolic, *DP* is diastolic pressure in the carotid artery.

Index α characterizes the vessel cross-section variation in pulse wave:

$$\alpha=Ad\cdot\int(SP/DP)/(As-Ad),$$

where *As* and *Ad* is the vessel cross-section area in systole and diastole, respectively.

Augmentation index (Aix) is a parameter dependent on pressure value in local area of bloodstream. It shows the difference between the first and the second systolic peaks in a vessel; its level is partially due to return time and reflected wave amplitude:

$$Aix=[AP/(SP–DP)]100\%,$$

where *AP* is augmentation pressure, *SP and DP* is local systolic/diastolic pressure [38–41].

Local rigidity and CIMT values according to current research data

Relative novelty of the technique is explained by the absence of tight standards for parameters obtained by echo-tracking. However, increasingly more researchers give preference to the local rigidity study of carotid arteries using this program that is due to both: the simplicity and the accuracy of the technique, and also a close anatomical position of carotid arteries to aorta, and their surface position and accessibility [42–46].

In 2008 there were published the results of carotid arteries elasticity properties studied by echo-tracking in Chinese population [47]. The study included 4,812 healthy subjects (1,971 — men, 2,841 — women) aged from 5 to 80 years (mean age is 33.7±10.8 years). All subjects enrolled in the study were non-smokers, had no previous complaints of cardiovascular events, their lipid metabolism and blood pressure indices conformed with norms, common CIMT was ⩽0.1 cm. Rigidity index *β* at the age of 30–39 years was found to be 6.55±2.0, and then increased proportionally to age, in a group of people over 60 it being 10.71±3.9. Local PWV in carotid arteries in subjects of similar age groups was 5.42±2.0 and 6.99±1.4 m/s. *CC* in people under 30 years had maximal values: 1.18±0.4, and in healthy subjects over 60 years it decreased up to 0.73±0.3. Considering the scope of research, the findings enable to consider conventionally these indices in age subgroups to be guide values for this method. The research results showed such parameters as rigidity index *β* and local PWV to increase with age, while *CC*, on the contrary, tended to decrease. It can be explained by chronological aging of a vessel wall. The specified parameters demonstrated high reliable correlation in all age subgroups, while local augmentation index *Aix* showed weak correlation with other indices, and, respectively, low prognostic value.

Further investigation in Chinese population showed index *β* and local PWV to increase significantly in smokers compared to non-smokers (regardless the presence of other risk factors of cardiovascular complications), while *Aix* index appeared to be significantly lower than that in smokers with AH, dislipidemy and hyperglycemia [48]. Moreover, in three mentioned groups systolic and diastolic diameters of carotid arteries differed significantly, while the subjects with several risk factors turned out to have significantly higher systolic and diastolic pressure in common carotid artery.

A team of Italian researchers [49] published the findings of their pilot study aimed at searching and evaluating differences in rigidity indices of carotid arteries measured by echo-tracking, among healthy subjects and human immunodeficiency virus (HIV) patients with no cardiovascular events. They examined 54 healthy subjects, and 54 HIV patients, the groups being compatible in age, sex and other anthropometric parameters. It should be noted that the differences between the groups in local rigidity and CIMT did not reach their statistical significance. *CC* values only appeared to be reliably lower in HIV patients. Mean age of controls was 48 years, *β* index was 6.61 (5.45–8.90), *CC* was 0.95 (0.78–1.23), local *Aix* was 15.40 (9.15–23.20)%, carotid PWV was 5.8 (5.32–6.40) m/s, common CIMT was 690 (540–800) µm. Local rigidity indices in both groups showed positive significant correlation with age, and negative significant correlation of age with *CC* due to reduced carotid arterial compliance at ageing, which are consistent with the results obtained by other researchers. In addition, arterial compliance reduction did not depend on antiretroviral therapy regimen [49, 50].

The data on carotid arteries obtained by echo-tracking in patients with retarded coronary flow is of particular interest [51]. The research included the patients with normal (n=50) and pathological (n=50) coronoangiography findings. Index *β* and local PWV appeared to be significantly higher when coronary flow velocity decreased that can indirectly indicate a microvascular event, endothelial dysfunction, atherosclerosis of small and epicardial arteries. The findings reliably correlated with the level of high sensitivity C-reactive protein.

Predictive role of aortal rigidity in the prognosis of general and cardiovascular mortality was proved in patients with AH [52–55], diabetes mellitus [56, 57], terminal renal failure, as well as in elderly people [52, 55]. Most studies assessed rigidity by carotid-femoral PWV as an index indicating the state of elastic arteries. Arterial involvement of various localization is known to differ in AH patients, and with age [58–60]. So, peripheral arteries, primarily, muscular ones, such as brachial, radial, and femoral, to a lesser degree, are subjects to alterations due to the above described factors. Prognostic value of carotid rigidity was determined in cardiovascular complications developing in patients with terminal renal failure and after renal transplantation [61–68]. CIMT of common carotid artery is a proved predictor of cardiovascular events in different patients' groups [7, 26, 30, 69–74].

Three groups of patients underwent a comparative examination in order to determine the relationships between arterial fluid parameters locally measured in carotid artery (echo-tracking), and aortal fluid estimated by carotid and femoral PWV [75]. Among 463 subjects under study there were 94 healthy subjects, 243 patients with essential AH, and 126 patients with AH combined with type 2 diabetes mellitus. The distensibility of carotid arteries were found to be significantly lower, and local PWV was higher in AH patients (isolated AH, and AH in combination with type 2 diabetes mellitus) compared to normotensive subjects. The correlation analysis of aortal and carotid PWV parameters showed positive reliable findings in a group in general ($r=0.34$; $p<0.001$), and in each subgroup, in particular. The strongest correlations between the indices of two type rigidity were found in healthy subjects. These findings confirm the results of other studies on a predictive role of carotid fluid determination in groups of patients without concomitant cardiovascular pathology [75–83].

Beaussier et al. [84, 85] showed using echo-tracking that if AH patients have atherosclerotic plaques in carotid arteries, the arterial wall becomes less elastic in the place of plaque localization than that in superjacent areas resulting in carotid artery extension inside the atherosclerotic involvement. It can lead to "a mechanical fatigue" and provoke its rupture. The assessment of plaque structure using magnetic resonance tomography in addition to echo-tracking enabled to conclude that the altered shift of carotid artery wall depends on both: the plaque presence, and also its structure that enables to distinguish high-risk plaques [85–90].

The method is certain to be unable to replace routine US of carotid arteries [37, 91–94], in particular, when determining surgical indications. However, even now it enables to estimate the efficiency of drug therapy provided. According to Russian researchers, against the background of 24-week therapy with angiotensin receptor blockers as a part of a combined therapy in patients with coronary heart disease and AH, echo-tracking showed significant CIMT decrease, as well as the improvement of most characteristics of local rigidity, in particular, *SP* and *DP*, index *β*, *CC*, carotid artery PWV [95].

Further investigations are certain to be required to determine all the capabilities of echo-tracking in arterial wall involvement diagnosis. However, it is obvious even now that the technique due to its peculiarities is very promising for the determination of a long-term prognosis and the efficacy assessment of drug therapy provided [96–99].

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