Review

Intima media thickness measurement in children: A statement from the Association for European Paediatric Cardiology (AEPC) Working Group on Cardiovascular Prevention endorsed by the Association for European Paediatric Cardiology

Robert Dalla Pozza a, *, Doris Ehringer-Schetitska b, Peter Fritsch c, Eero Jokinen d, Andreas Petropoulos e, Renate Oberhoffer f, on behalf of the Association for European Paediatric Cardiology Working Group Cardiovascular Prevention

a Department of Pediatric Cardiology, Ludwig Maximilians-University of Munich, Marchioninistr. 15, D-81377 Munich, Germany
b Dept. of Paediatrics, Landesklinikum Wiener Neustadt, Corvinusring 3-5, A-2700 Wiener Neustadt, Austria
c Dept. of Paediatric Cardiology, University Childrens Hospital, Auenbrugger Platz 34, A-8036 Graz, Austria
d Dept. of Paediatric Cardiology, Childrens Hospital, University of Helsinki, Stenbackinkatu 11, FIN-00029 Helsinki, Finland
e Merkezi Klinika, AZ 1005 Baku, Azerbaijan
f Institute of Preventive Paediatrics, Technical University of Munich, Uptown Munich, Georg-Brauchle-Ring 62, D-80992 Munich, Germany

ARTICLE INFO

Article history:
Received 9 August 2014
Received in revised form 27 November 2014
Accepted 14 December 2014
Available online 24 December 2014

Keywords:
Subclinical atherosclerosis
Intima media thickness
Carotid ultrasound
Preventive medicine

ABSTRACT

Atherosclerosis causing cardiovascular disease is the most common cause of death in the developed world. Early precursors of vascular changes – subclinical atherosclerosis – warrant special attention as this process can be stabilized or even reversed if treated in time. Sonographic Intima Media Thickness measurement of the carotid artery (cIMT: carotid Intima-Media-Thickness) is considered a valid surrogate marker for cardiovascular risk allowing assessment of atherosclerotic changes at a very early stage. It is easy to apply due to its non-invasive character. Moreover, cIMT has been proven to provide reliable and reproducible results both in adult and adolescent patients. For the paediatric age group, several characteristics deserve special consideration. The heterogeneity of techniques of scanning, measurement and interpretation impedes the comparison and interpretation of IMT values so far. Also, age- and sex-dependent normative data have to be considered for interpretation. Thus, the Association for European Paediatric Cardiology (AEPC) Working Group on Cardiovascular Prevention concludes to refer a statement on cIMT scanning, measurement and interpretation with special focus on paediatric patients. This statement includes an overview on normative data available as well as a practical guideline for the setting, scanning, measurement and interpretation of IMT values. Synchronizing different measurement methods will allow for comparing the results of several research centers. By that, in a large patient number, sufficient information may be given to assess the long-term endpoints of cardiovascular morbidity and mortality.

© 2014 Elsevier Ireland Ltd. All rights reserved.

1. Introduction

Atherosclerosis starts in childhood leading to cardiovascular disease in the adult patient [1,2]. Thus, early recognition of vascular changes to prevent cardiovascular sequelae is warranted [3]. One of the most commonly used non-invasive diagnostic methods is measurement of the Intima-Media-Thickness of the common carotid artery by ultrasound. Following the initial consideration as a surrogate marker for atherosclerosis (cIMT: carotid Intima-Media-Thickness), recent meta-analyses raised questions about the usefulness for the assessment of the vascular status in adult patients. Moreover, including carotid plaque screening seems to add valuable informations for the prediction of cardiovascular events more than IMT measurement alone in the adult patient [4–6].
Table 1: cIMT Measurement in Paediatric Patients with Elevated Cardiovascular Risk

<table>
<thead>
<tr>
<th>Condition</th>
<th>Reference</th>
<th>Result/Conclusion</th>
<th>Patients</th>
<th>Age (y)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Familial Hypercholesterolemia</td>
<td>Aggoun (2000) [32], Jarvaisalo (2001) [33], Koejvoets (2005) [34], Tonstad (1998) [35], Wiegmans (2004) [36], Narveerud (2014) [37]</td>
<td>cIMT: not increased in patients, but impaired endothelial function; Increased cIMT in patients (0.53 vs. 0.46 mm); Increased cIMT in children with null allele compared to children with receptor-defective mutation (0.52 vs. 0.50 mm); cIMT increased compared to controls (0.49 vs. 0.47 mm); cIMT increased compared to controls</td>
<td>n = 30 FH/n = 27 matched controls; n = 16 FH/n = 28 matched controls; n = 193 FH; n = 30 matched controls; n = 201 FH/n = 80 healthy siblings</td>
<td>11 ± 2 (range indicated); 11 ± 2 (range not indicated); 8–18.5; 10–19; 8–18</td>
</tr>
<tr>
<td>Arterial Hypertension</td>
<td>Lande (2006) [38], Sorof (2003) [39], Meyer (2006) [11], Woo (2004) [40], Jarvaisalo (2001) [33], Singh (2003) [41], Dalla Pozza (2007) [42], Dalla Pozza (2010) [43], Ianuzzi (2006) [44], Charakida (2005) [45]</td>
<td>cIMT: increased compared to controls (0.67 ± 0.54 mm); cIMT increased in 28% patients with increased cIMT had higher LVMI (0.52 ± 0.48 mm); cIMT increased in patients compared to controls (0.47 ± 0.42 mm); cIMT: increased compared to controls (0.47 ± 0.46 mm); cIMT: increased in patients compared to controls (0.47 ± 0.42 mm); cIMT thickening occurs early in the disease and might be partly reversed by Rx; cIMT increased compared to controls</td>
<td>n = 28 H T/n = 28 matched controls; n = 32; n = 36/n = 36 controls; n = 44 DM/n = 28 matched controls; n = 31/n = 35 controls; n = 150/n = 58 controls; n = 70; n = 38 obese with MS/n = 62 obese without MS (n = 61 boys/n = 39 girls); n = 83 HIV/n = 59 controls</td>
<td>10–18; 11.9 ± 2.7 (range not indicated); 9–12; 16.5 ± 4.1 (range not indicated); 10–18; 8–19.5; 12–18; 6–14; 11 ± 3.1 (range not indicated)</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>Woo (2004) [40], Jarvaisalo (2001) [33], Dalla Pozza (2007) [42], Dalla Pozza (2010) [43], Ianuzzi (2006) [44], Charakida (2005) [45]</td>
<td>cIMT: increased in patients compared to controls (0.47 ± 0.46 mm); cIMT: increased in patients compared to controls (0.47 ± 0.42 mm); cIMT thickening occurs early in the disease and might be partly reversed by Rx; cIMT increased compared to controls</td>
<td>n = 36/n = 36 controls; n = 44 DM/n = 28 matched controls; n = 31/n = 35 controls; n = 38 obese with MS/n = 62 obese without MS (n = 61 boys/n = 39 girls); n = 83 HIV/n = 59 controls</td>
<td>9–12; 11 ± 2 (range not indicated); 10–18; 6–14; 11 ± 3.1 (range not indicated)</td>
</tr>
<tr>
<td>Obesity</td>
<td>Meyer (2006) [11], Meyer (2006) [11], Woo (2004) [40], Jarvaisalo (2001) [33], Singh (2003) [41], Dalla Pozza (2007) [42], Dalla Pozza (2010) [43], Ianuzzi (2006) [44], Charakida (2005) [45]</td>
<td>cIMT: increased in obese children compared to controls with improvement after a 6-months exercise program (0.48 ± 0.44 mm); cIMT increased in patients compared to controls (0.47 ± 0.42 mm); cIMT increased in children with null allele compared to children with receptor-defective mutation (0.52 vs. 0.50 mm); cIMT thickening occurs early in the disease and might be partly reversed by Rx; cIMT increased compared to controls</td>
<td>n = 96/n = 35 controls; n = 32; n = 36/n = 36 controls; n = 31/n = 35 controls; n = 150/n = 58 controls; n = 70; n = 38 obese with MS/n = 62 obese without MS (n = 61 boys/n = 39 girls); n = 83 HIV/n = 59 controls</td>
<td>11–18; 11.9 ± 2.7 (range not indicated); 9–12; 16.5 ± 4.1 (range not indicated); 10–18; 6–14; 11 ± 3.1 (range not indicated)</td>
</tr>
<tr>
<td>Metabolic Syndrome</td>
<td>Ianuzzi (2006) [44], Charakida (2005) [45]</td>
<td>cIMT: increased in obese patients with MS compared to controls (0.55 vs. 0.54 mm); cIMT: increased in patients compared to controls (0.47 ± 0.42 mm); cIMT thickening occurs early in the disease and might be partly reversed by Rx; cIMT increased compared to controls</td>
<td>n = 38 obese with MS/n = 62 obese without MS (n = 61 boys/n = 39 girls); n = 83 HIV/n = 59 controls</td>
<td>6–14; 11 ± 3.1 (range not indicated)</td>
</tr>
<tr>
<td>HIV-Infection</td>
<td>Charakida (2005) [45], Dalla Pozza (2007) [48], Groothoff (2002) [49], Oh (2002) [50], Litwin (2005) [51], Meyer (2005) [52], Friend (2006) [53]. Oren (2003) [54], Jourdet (2011) [55], Salonen (2010) [56], Dalla Pozza (2011) [57]</td>
<td>cIMT: increased compared to controls (0.67 ± 0.47 mm); Increased cIMT correlated to arterial stiffening compared to controls (0.41 vs. 0.36 mm); Increased cIMT associated with inflammatory activity compared to patients with lower inflammatory activity (0.44 vs. 0.42 mm); Impaired endothelial function compared to controls; cIMT thickening occurs early in the disease and might be partly reversed by Rx; cIMT increased compared to controls (0.48 ± 0.38 mm); cIMT: increased compared to controls (0.57 vs. 0.49 mm); cIMT: increased in children with severe IUGR and exaggerated postnatal growth compared to children with IUGR and normal postnatal growth (0.48 vs. 0.43 mm); cIMT: lower in SGA than in obese children but not different from controls (0.44 vs. 0.46 vs. 0.44 mm); SGA children: unfavourable lipid profile; shorter birth length associated with increased cIMT compared to controls; Increased IMT associated with cardiac allograft vasculopathy compared to transplanted patients without cardiac allograft vasculopathy and to controls</td>
<td>n = 83 HIV/n = 59 controls; n = 72; n = 48/n = 28 controls; n = 130 patients/n = 48 controls; n = 55 patients/n = 270 controls; n = 28/n = 30 controls; n = 137 (80 boys/46 girls)/n = 46 controls; n = 750; n = 60 SGA/n = 49 obese/n = 55 controls; n = 35 patients/n = 35 controls; n = 22/n = 18 controls</td>
<td>11 ± 3.1 (range not indicated); 8.6 ± 2.8 (range not indicated); 6–23; 20.7–40.6; 19–39; 10–20; 12 ± 1 (range not indicated); 17–74; 27–30; 7–15; 20; 5–19.8</td>
</tr>
</tbody>
</table>

2. Background

Starting from 1986, the sonographic evaluation of Intimal-Medial-Thickening of the common carotid arteries has gained scientific and clinical significance [7]. In past years, cIMT measurement has been considered a surrogate marker of atherosclerosis [8]. Moreover, it seemed to be useful for the prediction of clinical cardiovascular events. Recent meta-analyses, however, concluded that...
IMT measurement alone could not predict cardiovascular events and showed that including carotid plaque detection the power of vascular assessment increased with regard to the prediction of cardiovascular events such as myocardial infarction, stroke, and peripheral arterial disease [9,10]. So, the value of IMT measurement for cardiovascular assessment is a matter of ongoing debate. Although these statements result from adult studies, in children, several conditions associated with increased cardiovascular risk and increased cIMT have been identified (Table 1) [3]. Increased cIMT leading to a preventive program showed a decrease when followed over a period of 6–12 months [11]. Also, cIMT measurement is suggested to assess the cardiovascular status in patients with elevated cardiovascular risk [1,3]. Thus, cIMT may have an important impact on the patient’s clinical management and the application of preventive strategies. Being a surrogate marker for the presence of cardiovascular changes, even small differences of the cIMT will be indicative for different counselling and management of the single patient [3,8]. Besides accurate measurement, it seems therefore essential to obtain precise, comparable and reproducible results for all age groups. It has to be stated that patients who benefit most of regular cIMT measurements and of cIMT guided preventive measures cannot be defined so far. Longitudinal data in the patient groups indicated above are lacking up to now [12]. Nevertheless, the cIMT measurement as a tool for enlightening, feedback to patients and caregivers and for scientific purposes provides enough information to justify the application in various centers [1]. And, as the cIMT measurement represents an additional tool to stratify the patients into different groups with different cardiovascular risk, it will be especially useful in the condition of patients whose cardiovascular risk and management are not well defined (i.e. children belonging to the groups with moderate cardiovascular risk and children at cardiovascular risk) [1]. Limiting factors for this approach are patient’s compliance which may be limited in younger children. In some circumstances, in very compliant patients, the authors have measured the cIMT also at an age of six years. It has to be noted, however, that most studies on normative data for comparison of the results are available only for older children starting with age groups around ten years of age [3]. Only one study included subjects starting at 6 years of age [13]. However, the number of subjects at the ages of 6/7 was too small to give normative data. So, the comparison of measured cIMT values may be limited for the younger age group.

The second limiting factor is related to anatomical conditions in which the length of the ultrasound transducer (“footprint”) may not fit to the length of the investigated region on the patient’s neck. So, data acquisition in smaller patients may be difficult or impossible.

Focal thickenings (plaques) are very uncommon in children but nevertheless are being observed in children with cardiovascular risk factors [14]. Most often these focal thickenings are found in the bifurcation and internal carotid segments and should be documented as they represent focal arterial damage and increased cardiovascular risk and are independent predictors of future cardiovascular events, better than IMT alone, in adult subjects [15].

3. Patient selection

In adult patients, cIMT measurement reflects the single patient’s vascular status. It seems wise to include in cIMT measurement programs all those paediatric patients at elevated cardiovascular risk [1,3]. Following the definition of the American Heart Association Expert Panel on Population and Prevention Science, paediatric patients with elevated cardiovascular risk can be divided into three groups [1]. Patients with high cardiovascular risk are patients with homozygous familial hypercholesterolemia, diabetes mellitus type 1, chronic kidney disease, patients after orthotopic heart transplantation, and patients after Kawasaki disease with current coronary aneurysms.

Patients with moderate cardiovascular risk are patients with heterozygous familial hypercholesterolemia, chronic inflammatory disease, patients after Kawasaki disease with regressed coronary aneurysms, and patients with diabetes mellitus type 2.

Patients at risk for cardiovascular disease are patients with congenital heart disease, patients after Kawasaki disease without coronary artery involvement, and patients after cancer treatment.

Additionally to these patient groups, the AEPC Working Group on Cardiovascular Prevention proposes also patients born small for gestational age (SGA), large for gestational age (LGA), and former

Table 3

<table>
<thead>
<tr>
<th>Action</th>
<th>Mannheim consensus</th>
<th>AEPC recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transverse Scan</td>
<td>Identify common carotid artery and bifurcation and internal search for plaques</td>
<td>Identical</td>
</tr>
<tr>
<td>Longitudinal Scan</td>
<td>Longitudinal view, carotid artery strictly perpendicular to the ultrasound beam, both walls clearly visible. Lateral probe angle recommended.</td>
<td>Position the common carotid in center of display, bifurcation at the left sidewalls horizontal, IMT on near and far wall visible. Visualize cIMT at least at two different angles. Record the angles from which the cIMT will be measured for follow up</td>
</tr>
<tr>
<td>On line measurement</td>
<td>IMT measured on the far wall. If IMT is measured near wall, should be measured separately from IMT of the far wall. IMT measured along a minimum of 10 mm length of an arterial segment.</td>
<td>Use on line cIMT tool to measure end-diastolic over 10 mm distance. Measure far wall common carotid artery target region over 10 mm length just before the start of the carotid bulb</td>
</tr>
<tr>
<td>Image storage for off line analysis</td>
<td>No recommendation</td>
<td>Record 5-beat cine-loops with simultaneous ECG, DICOM format</td>
</tr>
<tr>
<td>Measurement off line analysis using semi-automated software</td>
<td>Edge detection systems recommended. Manual reading only under rigorous quality control and quality assurance.</td>
<td>Select best end-diastolic frame out of loop. Identify carotid bifurcation. Set region of interest just before the start of the carotid bulb and extending proximally for 10 mm in the common carotid artery. Compare mean common cIMT results to age and sex-specific normative data for children. Plaques and cIMT outside the 75th percentile are considered abnormal</td>
</tr>
</tbody>
</table>

Table 2

| Patient groups to measure | Clinical condition: familial hypercholesterolemia, hypertension, obesity, diabetes mellitus, metabolic syndrome, Kawasaki syndrome, solid organ transplantation, chronic kidney disease, chronic inflammatory disease, post-cancer treatment survivors, children born small or large for gestational age |
| Setting | Patient supine, head extended and turned away from transducer |
| Ultrasound system | Ultrasound system with linear high frequency (>7.0 MHz) broadband transducer, digital (DICOM) data storage, ECG or other cardiac cycle tracking method |
DICOM format (Table 3). It has to be stated that ultrasound image for digital image acquisition, storage and review, preferably in a system using high-resolution broadband linear probes that allow measurement as early as possible in life to assess the vascular status at a very early stage [2].

3.2. Patient preparation

The cIMT measurement should be performed with the patient in the supine position with the neck slightly extended and turned 45° towards the opposite of the examined side to probe. The sonographer is positioned on the head of the patient with enough space to rest the elbow on the bed. For anatomical measurements only, no food or beverage restriction is applied. In cases of functional measurements (i.e. stiffness), abstinence of alcoholic and caffeine containing beverages and foods is recommended for the day of examination [18].

3.3. Scanning

The measurement should be performed with an ultrasound system using high-resolution broadband linear probes that allow for digital image acquisition, storage and review, preferably in a DICOM format (Table 3). It has to be stated that ultrasound image settings may significantly alter cIMT measurements [19]. Thus, the settings of dynamic range, gain and display depth should be standardized or documented when several measurements in an individual patient or in a patient group are performed. Also, especially if more than one investigator is involved, a well-standardized scan protocol to minimize differences of measurement should be defined.

The ultrasound system should operate a linear broadband transducer of above 7 MHz with a “footprint” of 3–4 cm. In smaller children, special transducers with higher frequencies may be used. The display depth and focus should not exceed 4 cm and should be adjusted to optimize the visualization of the boundaries and standardized for the typical patient group. The cIMT measurement should be performed in the end-diastolic phase for example by utilizing a 3-lead electrocardiogram (still frame at tip of R-wave) or other methods to monitor the cardiac cycle to ensure end diastolic measurements. The frame rate should be appropriate. Gain compensation should be optimized for cIMT measurements in the range of 60 dB or higher [14,19,20]. The neck vessels are shown first in a cross sectional plane with the common carotid artery in the center of the screen. Thereafter, the transducer is turned slowly clockwise to a longitudinal plane and the common carotid artery is displayed in its full length according to the footprint of the transducer. The perfect position of the transducer in relationship to the common carotid artery is when both the cIMT of the near and far wall are seen clearly throughout the artery and at least 10 mm of clear boundaries in the target segment are visible. The transducer is angled in an anterolateral and lateral view position to search for the most representative and clear cIMT boundaries. The angle that is used to measure cIMT should be documented for follow up. For off-line analysis preferably a clip of 5 s is recorded to allow the selection of the most appropriate frame for the cIMT measurement. It is important for clear detection of the cIMT boundaries that the carotid artery is well aligned; perpendicular to the ultrasound beam direction and that the region of the carotid bulb is visible at the left side of the image display for orientation (Fig. 1). Digital loops should be acquired from at least 1 or preferably 2 different scan angles and stored for analysis. The exam should be always performed at both sides. In addition the bifurcation and internal carotid segments are always inspected for early signs of focal vascular damage or atherosclerosis (plaques) regardless of age. When evaluating literature or using cIMT reference data, distinction needs to be made whether only the common carotid IMT (cIMT) or the composite IMT (composite cIMT) including other anatomical segments e.g. the bulb or internal carotid was measured. This may give very different results and is sometimes not clearly mentioned by the authors. As a minimum, 4 still frames (2 different views of the right and the left carotid artery, respectively) should be acquired and stored for offline-analysis.

3.4. Analysis

Analysis of the digitally stored loops should be performed preferably on a high-resolution monitor using validated dedicated software. The loop has to be evaluated throughout the entire cardiac cycle and the best end diastolic still frame (that means the still frame at the tip of the R-wave of the simultaneous ECG) will be considered for measurement. cIMT measurements are taken from the “far wall” of the common carotid artery as it is less susceptible to inter-observer variability and ultrasound system settings [3]. Within this wall, 2 bright lines separated by a darker area can be identified: the lumen-intima and the media-adventitia interface. cIMT is defined as the leading edge-to-leading edge distance between both bright interfaces. Measurement will be taken from the common carotid artery region proximal to the carotid bulb, not including the beginning of the bulb (Fig. 2). For full analysis, a region of interest of 10 mm will be selected. In children younger than ten years, a smaller region of interest may provide better analysis conditions. For measurement of the small distances, automated cIMT boundary detection software is preferred. In general, this software measures the distance on a pixel basis and calculates the mean value of multiple point measurements in the region of interest (Fig. 3). Most software systems also provide the maximal and minimal thickness from the region of interest. In a normal resolution ultrasound system screen, a region of interest of 10 mm length would contain 64 pixel measurements. Thus, the cIMT value calculated by the software would be based on 64 single measurements. In contrast, manual measurements would be subject to

**Fig. 1.** Measurement of the IMT of the common carotid artery. Target area is positioned just below the start of the bulb. CCA: common carotid artery; ICA: internal carotid artery; ECA: external carotid artery.
several sources of error like inappropriate manual tracing of the lines, or simply choosing one point to measure randomly within a region of interest. Especially in older children, where the cIMT is not homogeneously distributed among the region of interest, this may lead to significant over- or underestimation of the cIMT with the consequence that small differences in cIMT would result in a wrong classification of the individual patient. Newer cIMT parameters include “average”- cIMT as a result from several end-diastolic and end-systolic measurements during at least 3 heart cycles [21].

In case off line software is used ideally the cIMT value should be calculated from three separate video-loops from each common carotid artery and reported as mean cIMT separately for the right and left common carotid artery, as the values for the different vessels may differ [14].

For analysis, the inter- and intraobserver variability has to be assessed and an interscan/interreader variability of less than 0.055 mm and a coefficient of variation of less than 6% calculated as the SD divided by the mean using the root mean square approach and based on a minimum of 10 studies is required [18] (Table 4).

3.5. Normative data

Given the physiological progression of the cIMT throughout live, absolute cIMT measurement results will have to be compared to age- and sex-depending normative data [22]. So far, the AEPC Working Group on Cardiovascular Prevention is aware of several studies reporting normative values for children above the age of 10 years, but including less than 100 subjects (Table 5). Overall, several studies included more subjects and one study investigated also subjects at an age of less than ten years. One study reports on 160 subjects aged 10–18 years and a mean cIMT value between 0.48 ± 0.04 mm and 0.50 ± 0.04 mm. The authors do not state, however, how the measurements have been performed (manually or with computed system) [23]. Another study involved more than 200 subjects at an age of 10–20 years [24]. These authors measured the cIMT manually and report on cIMT values between 0.38 ± 0.04 mm and 0.40 ± 0.03 mm. One study included 267 subjects aged from 6 to 17 years and used a semi-automated edge detection system. The authors report on a cIMT between 0.48 ± 0.01 mm and 0.59 ± 0.08 mm [13]. Due to the small number of children under the age of 8 years, however, normative data are...
given starting from 8/9 years. Lastly, a study involving more than 1100 subjects from 6 to 17 years of age reports an cIMT between 0.36 mm (50th percentile at the age of 6 years) and 0.40 mm (50th percentile at the age of 18 years) [25]. For measurement of the cIMT, the caliper-method using manual tracing of the contours was adopted. One large study on more than 24,000 individuals included 1100 subjects from 6 to 17 years of age reports an cIMT between 0.38 ± 0.39 mm, female 0.39 ± 0.03 mm, female 0.39 ± 0.03 mm, female 0.39 ± 0.03 mm; 14–17 y: male 0.40 ± 0.04 mm, female 0.39 ± 0.05 mm; 17–20 y: male 0.39 ± 0.03 mm, female 0.40 ± 0.03 mm

### 4. Limitations

Although the cIMT measurement is widely used and — due to its non-invasive character — can be applied easily in the outpatient setting, the overall advantage of early recognition of increased cIMT has to be proven so far. Several studies have addressed the usefulness of preventive strategies in reducing increased cIMT values [11,27]. As the cIMT is considered a surrogate marker for atherosclerosis, a reduction in cIMT should indicate also a reduced risk for atherosclerosis. In adult patients, there are contradictory data regarding a reduction in cIMT and a reduction in coronary heart disease, cerebrovascular events and all-cause death [28]. Resulting from a recent meta-analysis, the IMT-progression and the risk for myocardial infarction and stroke do not show a linear relationship. The authors, however, conclude that further studies are necessary to investigate on the actual cardiovascular risk associated with increased IMT in young individuals and emphasize on adopting a uniform study and scanning protocol [10].

For children, furthermore, longitudinal data on cardiovascular morbidity and mortality which address the benefit of cIMT measurement are lacking so far even for selected patient groups. The longest study including cIMT measurement as an endpoint (though in childhood, IMT was not measured but cardiovascular risk factors were determined) is the Cardiovascular risk in Young Finns study, whose participants reached 45 years [29]. Thus, at present we cannot define the impact of cIMT measurements on the endpoint of cardiovascular morbidity and mortality in children. Also, we cannot define patient groups, which especially benefit from cIMT measurements. However, the members of the AEPC Working Group on Cardiovascular Prevention are deeply convinced that in future longitudinal data may enlighten the benefit of cIMT measurement. The greatest effect may come from sharing the cIMT scan results with the children’s parents to enhance compliancy of life style optimization and medication intake. In addition, treatment can be optimized attempting to stabilize or reverse the process in children that show clear evidence of early arterial damage or signs of sudden progression.

### 5. Summary and outlook

CIMT scanning and measurement offers noteworthy information about the cardiovascular risk if performed according to the requirements outlined in the present statement. Also for children, the cIMT may provide a reliable surrogate marker for vascular health. Considering the progression of vascular changes throughout life, it seems prudent to detect subclinical signs of arterial damage and atherosclerosis very early and relief atherosclerotic burden by preventive measures. Thus, especially in the paediatric age group, assessing the cardiovascular risk would be beneficial. The cIMT measurement offers, in addition to the conventional cardiovascular risk factors screening, direct information about the vascular status of the single child. It is easy to apply, fast, and reproducible. Therefore, the AEPC Working Group on Cardiovascular Prevention strongly recommends use cIMT in screening patients with elevated cardiovascular risk, even if the long-term benefit of IMT measurement on the single patient’s vascular health remains to be determined. To enable comparison of different measurements, standardized scanning settings and protocols are warranted. To enhance scientific research, normative data should be used for classification of the results.

Future perspectives include, beyond “simple” cIMT diameters, several new functional parameters derived from cIMT ultrasound images that are currently under investigation. I. e. 3D cIMT scanning would open the 3D-display of vessel wall structures and maybe add more information about intimal morphology [4,30]. 3D-cIMT scanning revealing carotid vessel wall volume (VWW) seems to provide useful informations about therapy response, even if also for this technique a standardized scanning protocol is warranted [5]. Some authors also suggest that 3D-vessel-volume measurement will overcome the heterogeneity of IMT-measurement and the problem of the limited dynamic range of IMT [5]. Also, the heterogeneity of the cIMT within a given region of interest, called IMT roughness, will contribute to a more differentiated view of intimal anatomy and very early changes in morphology [31]. The reflection pattern of the arterial muscular layer called the grayscale medium may also reveal information leading to better understanding of the atherosclerotic process. Lastly, the elasticity of the cIMT layer expressed as the difference between end diastolic and

<table>
<thead>
<tr>
<th>Study</th>
<th>Subjects</th>
<th>Normal value (mean IMT)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sass et al. [23]</td>
<td>160 (10–18 y) schoolchildren</td>
<td>Age and sex-dependent mean values, i. e. 10 y boy 0.49 ± 0.04 mm</td>
</tr>
<tr>
<td>Jourdan et al. [24]</td>
<td>247 (10–20 y) healthy adolescents excluding obese and hypertensive subjects</td>
<td>3 age groups: 10–13.9 y: male 0.38 ± 0.04 mm, female 0.38 ± 0.03 mm; 14–16.9 y: male 0.40 ± 0.04 mm, female 0.39 ± 0.05 mm; 17–20 y: male 0.39 ± 0.03 mm, female 0.40 ± 0.03 mm</td>
</tr>
<tr>
<td>Bohm et al. [13]</td>
<td>287 (6–17 y) German schoolchildren</td>
<td>Age- and sex dependent percentiles for 4 age groups; i. e. mean IMT for a 10 y boy 0.51 mm, 75th percentile 0.58 mm</td>
</tr>
<tr>
<td>Ried et al. [58]</td>
<td>397 (15.6 y) Danish adolescents from the European Youth Heart Study</td>
<td>Sex-dependent values: Male 0.57 ± 0.03 mm Female 0.55 ± 0.02 mm</td>
</tr>
<tr>
<td>Doyon et al. [25]</td>
<td>1155 (6–18 y) schoolchildren, excluded obese and hypertensive</td>
<td>Age- and sex dependent percentiles in 0.5 y steps, i. e. mean IMT for a 10 y boy 0.37 mm, 75th Percentile 0.40 mm</td>
</tr>
<tr>
<td>Engelen et al. [59]</td>
<td>24,871 (15–101 y), 263 healthy subjects 15–20 y</td>
<td>15 y boy: mean IMT 0.40 mm, 75th percentile 0.44 mm</td>
</tr>
</tbody>
</table>

### Table 4

Requirements for sonographers and readers modified from [18].

<table>
<thead>
<tr>
<th>Background</th>
<th>Theoretical training (min 8 h)</th>
<th>Scanning training (min 8 h)</th>
<th>Quality assurance and control (1/3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical doctor, sonographer, research nurse, medical technician, medical professional</td>
<td>Atherosclerosis, pathophysiology, CVD risk assessment, clinical use of carotid ultrasound, scanning technique, imaging, pitfalls</td>
<td>Protocol, image acquisition, reading, internal certification process</td>
<td>Min. 10 duplicate/repeat scans to assess inter/intra scan/reader variability (less than 6%) and difference (less than 0.055 mm). Retraining if not satisfactory</td>
</tr>
</tbody>
</table>

### Table 5

Normative cIMT data from larger studies in children.

<table>
<thead>
<tr>
<th>Study</th>
<th>Subjects</th>
<th>Normal value (mean IMT)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sass et al. [23]</td>
<td>160 (10–18 y) schoolchildren</td>
<td>Age and sex-dependent mean values, i. e. 10 y boy 0.49 ± 0.04 mm</td>
</tr>
<tr>
<td>Jourdan et al. [24]</td>
<td>247 (10–20 y) healthy adolescents excluding obese and hypertensive subjects</td>
<td>3 age groups: 10–13.9 y: male 0.38 ± 0.04 mm, female 0.38 ± 0.03 mm; 14–16.9 y: male 0.40 ± 0.04 mm, female 0.39 ± 0.05 mm; 17–20 y: male 0.39 ± 0.03 mm, female 0.40 ± 0.03 mm</td>
</tr>
<tr>
<td>Bohm et al. [13]</td>
<td>287 (6–17 y) German schoolchildren</td>
<td>Age- and sex dependent percentiles for 4 age groups; i. e. mean IMT for a 10 y boy 0.51 mm, 75th percentile 0.58 mm</td>
</tr>
<tr>
<td>Ried et al. [58]</td>
<td>397 (15.6 y) Danish adolescents from the European Youth Heart Study</td>
<td>Sex-dependent values: Male 0.57 ± 0.03 mm Female 0.55 ± 0.02 mm</td>
</tr>
<tr>
<td>Doyon et al. [25]</td>
<td>1155 (6–18 y) schoolchildren, excluded obese and hypertensive</td>
<td>Age- and sex dependent percentiles in 0.5 y steps, i. e. mean IMT for a 10 y boy 0.37 mm, 75th Percentile 0.40 mm</td>
</tr>
<tr>
<td>Engelen et al. [59]</td>
<td>24,871 (15–101 y), 263 healthy subjects 15–20 y</td>
<td>15 y boy: mean IMT 0.40 mm, 75th percentile 0.44 mm</td>
</tr>
</tbody>
</table>
end systolic cIMT may be used to assess the amount of early atherosclerotic changes within the intimal structure. The AEPC Working Group on Cardiovascular Prevention strongly recommends performing longitudinal studies to elucidate the endpoint of cIMT measurement and cIMT measurement guided preventive strategies: the relief of atherosclerotic burden and reduction of overall cardiovascular morbidity and mortality in the paediatric patient group.

Conflict of interests

R. Dalla Pozza: None.
D. Ehringer-Schetitska: None.
P. Fritsch: None.
E. Jokinen: None.
A. Petropoulos: None.
R. Oberhofer: None.

Acknowledgement

The authors want to appreciate the great contribution of J. Elmenhorst, B. Böhm and H. Weberruß (literature research); of V. Herceg-Cavak (manuscript edition), and of R. Meijer, M. Bots and J. Stein (external reviewers).

References

between childhood risk factors and carotid intima-media thickness in adulthood: the cardiovascular risk in young finns study, the childhood determinants of adult health study, the bogalusa heart study, and the muscatine study for the international childhood cardiovascular cohort (i3c) consortium, Circulation 122 (2010) 2514–2520.


