ULTRASONIC AND COMPUTED TOMOGRAPHIC BIOMARKERS IN THE DIAGNOSIS OF ATHEROSCLEROSIS

Ph.D. Thesis Summary

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Introduction

Cardiovascular disease is the leading cause of death in Hungary. The standardized death rate for circulation disease is 779.4 deaths per 100 000 inhabitants, which is the 6th worst data in the European statistics. The data is even worse in case of ischemic heart disease. In case of ischemic heart disease the standardized death rate is 400.1 deaths per 100 000 inhabitants, which is a weak data as compared to the average standardized death rate in Europe which is 137 deaths per 100 000 inhabitants.

The most common cause of the cardiovascular disease is the arteriosclerosis and within this broader category the atherosclerosis. Atherosclerosis is a progressive disease and only some of its risk factors are modifiable or can be eliminated. The primary prevention has a high significance in the outcome of the disease. Therefore the early diagnose of atherosclerosis and those non-invasively determined biomarkers, which can improve the personal risk stratification, are come into prominence.

The early diagnose of atherosclerosis is part of the cardiovascular primary prevention. The screening covers epidemiological risk stratification, physical examinations, laboratory tests, and some non-invasive scanners and methods are in used. The most important non-invasive methods are the B-mode ultrasound examination of the vessel wall, the different measurements of stiffness parameters and the evaluation of Agatston score in non-contrast enhanced CT images.

1. Determination of normal β values via radio frequency echo-Tracking technique

Nowadays there are many different devices with different technical background available on the market for the evaluation of vascular stiffness. Most of these equipments determinate the changes of vascular stiffness based on the measurement of PWV and AI value. With RF echo-Tracking, besides these two parameters, the β stiffness parameter and pressure-strain elasticity modulus (E_p) and arterial compliance (AC) value are determined. These three parameters are calculated from the blood pressure and the diameter changes of the vessel (Table 1.). The E_p and AC values strongly depend on blood pressure because the diameter-pressure relationship is non-linear. The β stiffness value is less blood pressure dependent because of its calculation method. And it is blood pressure independent in case of normotension.

1.1. Objectives

To the best of our knowledge, our team is the first that determined normal values of β stiffness parameter and PWV via RF echo-Tracking in a healthy Central European population during the years

2005 and 2006. The PWV parameter was chosen, because it is an accepted independent predictive factor in the risk assessment of atherosclerosis with an ascertained cut off value, which was determined with other methods of stiffness measurements. The β stiffness was examined because it is less blood pressure dependent than the other stiffness parameters, and we found no normal values of β stiffness parameter in European population in the literature. One of our cases (discussed in the next section) had been suggested that the determination of normal β value in different age groups in both genders was necessary in domestic population for the appropriate clinical application of the method, because our findings were showed that there might be a significant difference in normal values of healthy Asian and health European population.

1/a. **Ep (pressure-strain elasticity modulus): representing the arterial stiffness** **Ep = (Ps-Pd)/[(Ds-Dd)/Dd]** **β (stiffness parameter): representing the arterial stiffness** **β = ln(Ps-Pd)/[(Ds-Dd)/Dd]** **Blood pressure dependency is lower than that of Ep.** **AC (arterial compliance): representing vessel compliance** **AC = π(Ds×Ds-Dd×Dd)/[4(Ps-Pd)]**
1/b. **AI**: augmentation index **PWV**: pulse wave velocity

Table 1. Parameters are representing properties of vessel wall and are calculated automatically by the E-Tracking software. 1/a. These parameters are calculated from systolic and diastolic blood pressure values and from the systolic and diastolic diameters of the examined vessel 1/b. These parameters are automatically calculated by the analysis of the detected sphygmogram.

1.2. Methods

For the measurement of stiffness parameters ALOKA USV 5410 ultrasound equipment with linear transducer (3-10 MHz) and with special software for the RF e-Tracking option had been used. To standardize the measurement the examinations were performed by two experts at the same time of the day, in the same air-conditioned room after 5-10 minutes of rest.

1.3. Patient population

Our team examined all together 146 volunteers of different age groups between 3 and 65 years in both sex (male n=51, female n=95). These volunteers had no remarkable changes in their laboratory findings, their body mass index (BMI) were in normal range and had not got any modifiable risk factors of vascular and cardiovascular diseases. We exclude those volunteers who had high blood pressure (140/90 mmHg<) or abnormal IMT (0.8mm <) on site.

1.4. Results

We analyzed the PWV and β stiffness parameters in five different age groups (≤25 ys, 26-35 ys, 36-45 ys, 46-55 ys and 56-65 ys) in both genders. We found that the values of β stiffness parameter and

PWV show slightly elevation during the aging in both genders (Table 2, Fig. 1). The intraobserver coefficient of variation was 6.9% for β-stiffness and 3.5% for PWV. The interobserver coefficient of variation was 8.8% for β-stiffness and 4.6% for PWV.

Age (years)	beta mean ± SD		PWV (m/s) mean ± SD		BP (mmHg) SBP mean ± SD/ DBP mean ± SD		HR (bpm) mean ± SD	
	male	female	male	female	male	female	male	female
≤ 25	3.78 ± 0.76	4.46 ± 0.9	4.37 ± 0.52	4.48 ± 0.35	127±21.08/ 80±8.79	115±9.44/ 73±7.55	78±10.85	75±11.65
26-35	5 ± 1.98	5.89±1.3	5.17 ± 0.77	5.39 ± 0.57	130±3.1/ 88±10.05	124±9.0/ 79±5.0	70±24.63	66±7.23
36-45	7.14 ± 1.15	7.28 ± 1.83	6.19 ± 0.54	6 ±0.57	130±8.38/ 84±7.31	120±15.92 / 78±16.28	75±9.62	73±6.89
46-55	7.95 ± 1.73	9.11 ± 1.82	6.7 ± 0.94	6.82 ± 0.82	138±16.38/ 89±9.43	127±11.5/ 81±8.1	74±15.45	69±8.51
56-65	8.14 ± 1.05	9.93 ± 2.92	6.61 ± 0.42	7.2 ± 1.18	134±9.33/ 85±8.6	129±6.03/ 83±7.37	70±6.59	62±13.23

Table 2. The normal values of β stiffness and PWV parameters were determined via RF echo-tracking method. 146 healthy volunteers (51 males and 95 females, 3 - 65 year-olds) were examined in five different age groups. Data are presented as mean ± SD (standard deviation). Mean and SD of blood pressure (BP) and heart (HR) for each age groups were calculated as well.

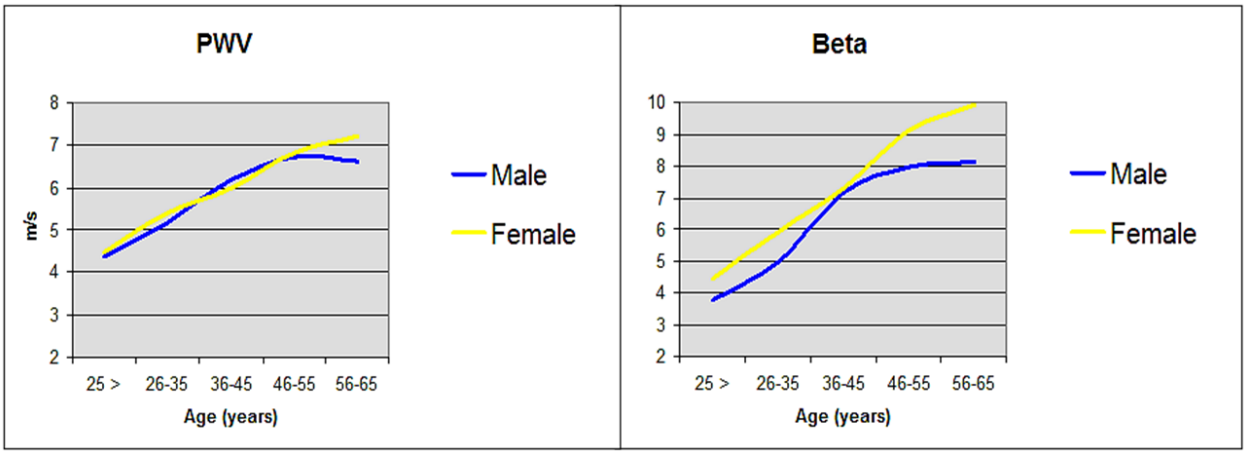

Figure 1. Diagrams show that normal values of β and PWV parameters slightly increase with aging

1.5. Conclusions

Results of intra- and interobserver studies show that RF e-Tracking technique is a reliable and reproducible method of vascular stiffness measurement. One of the obtained parameters was the β stiffness parameter. In case of normotensive population this parameter is non-blood pressure dependent unlike PWV and AI with, therefore it may show stronger correlation with the rigidity of the vessel wall. Based on our data the vascular stiffness slightly increases with aging in both sexes. One of the possible explanations is that the healthy population had a clinically non manifest or early

form of atherosclerosis which means that there are no non-invasively visible changes on the arterial wall. The other interpretation can be the relative or absolute decreasing of elastic vascular components during the normal aging. The invasive, histological examination was not part of our investigation; therefore we cannot tell which idea is correct.

2. Clinical application of RF e-Tracking in case of a patient with progeria

Hutchinson-Gilford progeria syndrome (HGPS) is an extremely rare genetic condition. The reported incidence is 1:8 million, estimated incidence is about 1:4 million since the first cases were reported in 1898 by Hutchinson and in 1902 by Gilford. The reason of this disease was unknown until 2003, when a de novo point mutation in the lamin A gene had been determined as the most common reason. This gene encodes a protein that helps to maintain the structural integrity of the cell nucleus. Patients with this disorder suffer from symptoms of accelerated aging, such as thin and wrinkled skin, hair loss, osteoporosis and most notably vascular disease (atherosclerosis). Appearance and progression of vascular disease determinates the quality and the term of their life. Atherosclerosis causes stroke and/or myocardial infarction during its progression which leads to death of these patients by the end of their second decade of life. Early diagnosis and treatment of atherosclerosis may increase therapy effectiveness.

Our patient was a 9-year-old male. In his case the progeria syndrome was diagnosed in the first year of his life. The genetic abnormality was determined at the age of 9. He had some symptoms of premature aging. His mental development was normal and he had no signs or symptoms of vascular disease. Laboratory, ECG, echocardiography, carotid arteries B- and duplex-scan findings were unremarkable. His blood pressure was within the normal range. The aim of our ultrasound examination was to determinate the vascular age of the patient and diagnose the early stage of atherosclerosis if it was present.

The appearance of the common carotid arteries was normal on B-scan and there were no detectable sings of any stenosis by using duplex Doppler technique. Our examination revealed a blood-pressure of 111/69 mmHg, a 5.19 mm maximal and 4.97 mm minimal vessel diameter on the left side, and a 6.20 mm maximal and 5.94 mm minimal vessel diameter on the right side. The measured β values were 10.8 in case of the left, and 11.0 in case of the right CCA, which corresponds to the 36-45-year-old healthy population group and suggests an early stage of atherosclerosis. Our patient's β value was threefold higher compared to his own age: our data (Fig. 2, 3) suggests that under the age of 15, the normal β value is 3.46 ± 0.71 (n=7).

Regarding our data we have demonstrated that our patient biological age was significantly higher than his chronological age. Compare his stiffness parameters to the normal values of an Asian population his biological age was 45 years. Compare to our normal values of a domestic population his biological age was even higher. It was more than the determined highest normal value which can be explained by the presence of early stage of atherosclerosis. Though the measured PWV β (6.9 m/s) did not reach the widely accepted cut off value (10 m/s) of the PWV it was quite close.

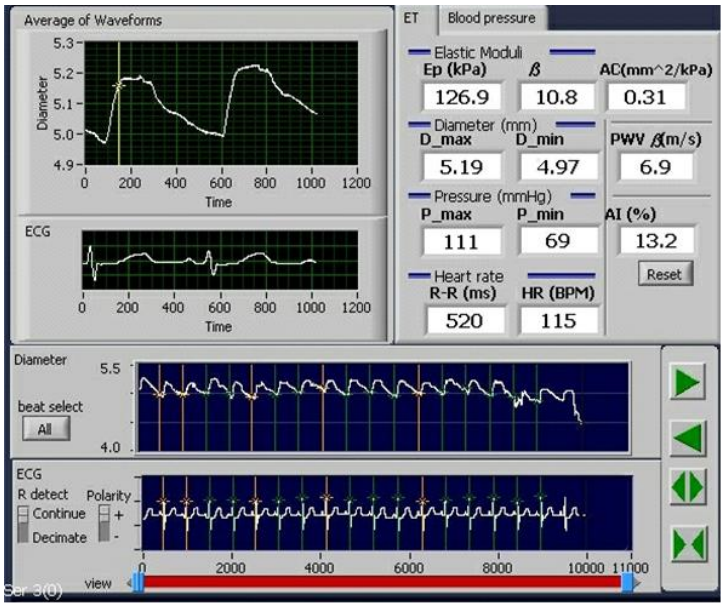

Figure 2 Original registrant of the measurement in case of the left common carotid artery of a 9 year-old child with progeria syndrome

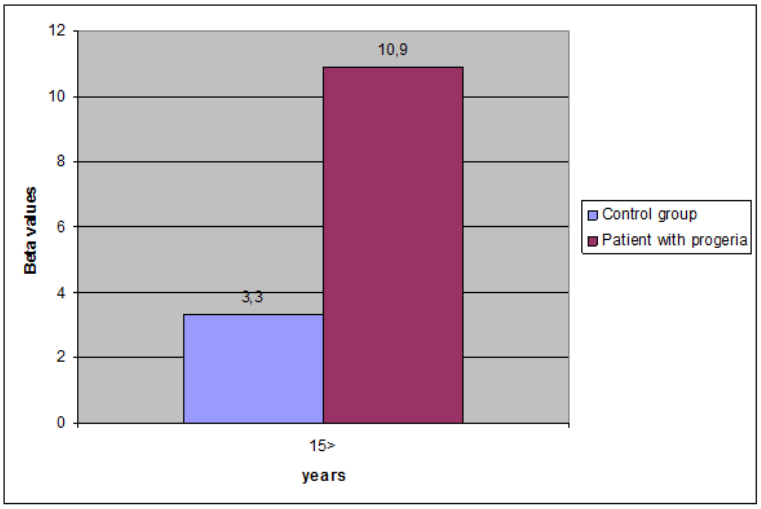

Figure 3 Patient's main β value was more than threefold higher than the normal of his own age group: under age 15 the normal β is 3.46 ± 0.71 (n=7).

3. Evaluation of epicardial fat volume, Agatston-score and stiffness parameters in patients with CAD

In the first decade of the 21st century epicardial fat volume (EFV), besides the Agatston-score and the stiffness parameters, has come to the fore in the risk assessment of CAD. EFV can be easily measured by a semi-automatic software in the non-contrast enhanced cardiac CT images, which were reconstructed for the evaluation of Agatston score (coronary artery calcium score (CACS)). The larger volume of epicardial fat results in increased coronary artery disease (CAD) risk because in case of higher epicardial fat volume (EFV) the atherogenic factors of the epicardial fat become predominant.

3.1. Objectives

The aim of our study was to find connections between EFV, Agatston- score and the stiffness parameters (measured with Arteriograph) in patients with known CAD. Most of our patient underwent coronary CT angiography (CCTA) examination too. In this group of patients the connections between the severity of CAD and the EFV and the stiffness parameters were examined as well.

3.2. Methods

For CT imaging 64 slice dual-source CT (Somatom Definition; Siemens Medical Solutions, Forchheim, Germany) scanner with ECG dependent tube current modulation (Care Dose 4D) had been used with 0.33 s of rotation time. Depending on the patient's heart rate prospective ECG-triggering (HR <60 bpm) or retrospective ECG-gating (HR > 60 bpm or arrhythmia) was applied. Pharmacologic heart rate modulation was necessary with administration of β-blocker (metoprolol orally [50 mg] or intravenously [5-10 mg]) when the patient's heart rate was higher than 95 bpm before scanning. Orally nitroglycerin (0.8 mg) was also administered before the CT imaging procedure.

Non-contrast and contrast enhanced images were acquired between the level of tracheal bifurcation and the diaphragm during a single breath-hold. Following a native scan contrast enhanced image acquisition was performed by using bolus tracking technique. In all cases we used iomeprol intra venous contrast material with 350 mg/mL iodine content.

Native scan's data sets were reconstructed with B35f convolution kernel, 3 mm effective slice thickness and 1.5 mm increment for calcium score measurements. Contrast enhanced data sets were reconstructed with B26f convolution kernel, 0.75 mm effective slice thickness and 0.4 mm increment for quantitative coronary analysis. All of these reconstructions were performed in overlapping mode. The reconstruction window was at 70% of the cardiac cycle in case of prospective ECG triggering. In case of retrospective ECG gating the reconstruction window was depend on heart rate. To quantify the calcium content of coronary arteries the Agatston scoring method had been used. The software tool (Syngo CAC, Siemens Medical Solutions, Forcheim, Germany) automatically marked out every contiguous three pixels with a density of above 130 HU. Those marks which cover coronary arteries (RCA, LM, LAD and Cx) were selected manually. Than the software tool calculated the score by multiplying the area of the marked lesion by a density factor obtained from the maximum HU in the lesion. Total calcium score is the sum of individual lesion scores. For the measurement of epicardial fat volume axial slices of non-contrast enhanced MDCT images were analyzed. In our definition epicardial fat is the adipose tissue which is situated between the visceral layer of pericardium and the myocardium. The pericardium was traced semi automatically in 3D by a dedicated software tool (Syngo Volume, Siemens Medical Solutions, Forchheim, Germany) between the level of the pulmonary trunk's bifurcation and the diaphragm. Manual optimization of the pericardial borders in multiple planes was performed if it was necessary. To separate fat from other tissues in the region of interest enclosed by the pericardium thresholds of -30 to -190 HU were chosen. The total volume of epicardial fat was reported in cm^3 at the end of the measurement.

For the analysis of coronary CT angiogram another dedicated (Syngo Circulation, Siemens Medical Solutions, Forchheim, Germany) software had been used. The threshold of significant area stenosis was 75%.

Regional stiffness parameters had been measured in standard conditions with arteriograph (Arteriograph, TensioMed, Budapest, Hungary) right before the CT examination. With a short compression and fast decompression of the brachial artery the pulse wave was registered oscillometric. The PWV and AI were calculated by the analysis of the nicely separated anterograde and the retrograde waves and with the measurement of the distance between pubic symphysis and jugular notch.

3.3. Patient population

To find relationship between arterial stiffness parameters, Agatston score and EFV 158 consecutive outpatients who had been referred for cardiac CT and simultaneously underwent both cardiac CT examination and oscillometric pulse wave analysis were enrolled. Among these patients there were 111 who underwent CCTA as well. Thus the examination of connections between the EFV, stiffness parameters and the degree of the coronary artery stenosis became possible. A written informed consent was signed by each of the enrolled patients.

3.4. Results

As for the stiffness parameters, both AIx and PWVao were significantly higher ($p \leq 0.01$) in CAD patient group than in the control group. In the CAD patient group the average value of AIx was 34.5 ± 14.7% and the average value of the PWVao was 10.2 ± 2.3 m/s. In case of healthy population the average value was 30.2 ± 12.8% for AIx and it was 9.5 ± 1.6 m/s for PWVao (based on former data of work-group). Compared our examined parameters (AIx, PWVao, EFV and Agatston score) we found significant differences between average values of EFV and Agatston score of the CAD and the control group($p \leq 0.01$). EFV value was 121.1 ± 69.8 cm^3 in CAD patient group and it was 83.7 ± 39.3 cm^3 in the control group. The mean value of the Agatston score was 207 (0-1327) in CAD patient group and 5.3 (0-146) in the control group.

The mean value of Agatston score was significantly higher ($p<0.05$) in both male (424.27) and female (94.39) patients group with coronary stenosis. The highest mean values were measured in the patient groups (male: 1002.35, female: 605.5) with significant coronary artery stenosis.

Normal mean values of EFV were detected in case of patient group without coronary artery stenosis in both sex (male: 98.16 cm^3, female: 76.04 cm^3), and the highest mean values were found in the patient group with significant coronary artery stenosis in both sex (male: 152.35 cm^3, female: 100.78 cm^3). But the data of male patients alone showed a significant difference in this respect.

3.5. Conclusions

Our results suggest that the Agatston score and EFV measured with semiautomatic software in appropriately reconstructed cardiac CT images and the oscillometric detected stiffness parameters are important biomarkers of CAD, because all of these parameters were significantly higher in CAD patient group compared to the control group. There were significantly higher Agatston score and in case of male patients significantly higher - and based on literature abnormal - EFV in case of the

patient group with significant coronary artery stenosis. Though in case of female patients we did not found significant connection between EFV and severe coronary artery stenosis and the mean value of EFV was lower than the abnormal, but it might caused by the low number of patients.

Our results showed weak correlation between EFV and Agatston score which suggests that these parameters might be independent predictive parameters of CAD. It is possible that the different dominant risk factors of CAD can bias different examined parameters. But because of the relatively low number of the enrolled patients we had no chance to subdivide the patient groups into further distinct groups based on the dominant risk factors. In a subsequent study we examined whether one of the major CAD risk factor - the type 2 diabetes mellitus - has any effect on the EFV and Agatston score values.

4. Evaluation of epicardial fat volume, Agatston-score, BMI and hepatic density values in patients with type 2 diabetes mellitus

4.1. Objectives

Based on the literature our research group was the first who studied the relationship between BMI, Agatston score, EFV and hepatic density in type 2 diabetic patient group and control group in domestic population by a retrospective, cross-sectional correlation analysis.

4.2. Methods

For cardiac imaging 64 slice DSCT scanner (Somatom Definition; Siemens Medical Solutions, Forchheim, Germany) had been used. We analyzed appropriately reconstructed non contrast images for the evaluation of Agatston score and EFV as described above. And hepatic density in Hounsfield units (HU) had been measured in the same reconstructed non contrast images with the same size and shape of ROI (region of interest) at level of 8^{th} hepatic segment. The mean density of healthy liver is 50-70 HU. In case of diffuse hepatic steatosis the mean density of the liver is less than 40 HU. Body mass index (BMI) had been calculated as body weight in kilograms divided by body height in meter squared.

4.3. Patient population

In this clinical study 158 (73 male and 85 female) of our patients, who underwent cardiac CT examination in 2014 - 2015, were enrolled. These patients were referred for cardiac CT examination either to assessment of CAD or planning and guiding of catheter ablation therapy with 3D reconstructions. In our patient population two patient groups, type 2 diabetic patient group (n=60, male: 30, female: 30) and control group (n=98, male: 43, female: 55), were formed.

4.4. Results

Comparing the diabetic and non-diabetic patient group the mean value of EFV was appreciably higher in diabetic (180.2±69.7 cm3) than in non-diabetic patient group (140.1±65.1 cm3). The mean of Agatston score was also remarkably higher in diabetic patient group (383.8±915.8) than in the control group (149±33.3). The mean value of hepatic density was lower in diabetic patient group (47.2±14.3 HU) compared with the control group (50.8±15.28 HU). The mean of BMI was higher than the normal both in diabetic (31.2±5.34) and non-diabetic (28.2±5.18) patient group (Table 3.) Gender

comparison showed that the mean of BMI, EFV and Agatston score values are higher and the mean hepatic density value is lower in diabetic than in non-diabetic patient group in both genders.

	Type 2 diabetes	Control
Age (years)	62±9.5	60.16±11.8
BMI (kg/m^2)	31.2±5.34	28.2±5.18
Agatston score	381.8±915.8	149±33.3
EFV (m^3)	180.2±69.7	140.1±65.1
Hepatic density (HU)	47.2±14.3	50.8±15.28

Table 1 Mean values with standard deviations of age, BMI, Agatston score, EFV and hepatic density in type 2 diabetic patient group (n=60) and control, non-diabetic patient group (n=98)

Based on the results of two-sample T test in case of EFV there is a significant difference ($p<0.001$) between the mean values of the two patient groups. As for the hepatic density mean values there is no significant difference ($p=0.140$) between the patient groups. Statistical analysis with Mann-Whitney test showed a significant difference ($p=0.038$) between the mean values of Agatston score of diabetic and non-diabetic patient group. Separating according to genders there was significant difference ($p=0.001$) between the male diabetic and non-diabetic patient group's mean Agatston score values. But there were no significant differences between the gender groups in case of other examined parameters.

In our correlation study BMI and age were independent variables, EFV, hepatic density and Agatston score were dependent variables. With linear regression analysis we found a statistically significant ($p<0.001$) strong moderate linear correlation between EFV and BMI ($r=0.569$) and between EFV and age ($r=0.465$) in case of the control group. In case of diabetic patent group a significant ($p=0.001$) weak ($r=0.385$) correlation was found between EFV and BMI. But there was no correlation between the age and BMI ($p=0.110$). There were a negative significant weak correlation between hepatic density and BMI both in diabetic ($p=0.012$, $r=-0.298$) and non-diabetic ($p<0.001$, $r=-0.337$) patient group. There was a non-significant linear correlation ($p=0.314$) between the hepatic density and age in the control group. In case of the diabetic patient group there was a weak ($r=0.232$), significant ($p=0.040$) linear correlation. With Spearman's correlation in case of control group there were weak significant correlations between the Agatston score and BMI ($r=0.183$, $p=0.040$) and between the Agatston score and EFV ($r=0.323$, $p=0.001$). Between the Agatston score and age there was a strong moderate ($r=0.440$) significant ($p<0.001$) correlation. In case of the diabetic patient group there were no statistically significant correlations between the Agatston score and BMI ($p=0.258$) and between Agatston score and EFV ($p=0.099$). However there was a weak ($r=0.297$) significant (0.011) correlation between Agatston score and age.

4.5. Conclusions

Based on the statistical analysis we came to the conclusion that BMI has a stronger influence on EFV than the age, and the higher the BMI the lower the hepatic density both in diabetic and control group. The diabetic patient group has a lower hepatic density and a higher EFV than the other group. These statistical findings support our idea that with the adequate analysis of non-contrast cardiac CT images we can demonstrate the accumulation of ectopic fat (intrahepatic and epicardial fat) on account of obesity in diabetic patients. Agatston score increases with aging in diabetic and non-

diabetic patient group as well. In case of diabetic patients the calcium content of the coronary artery is higher. This suggests that increased EFV promotes changes of the perivascular milieu of the coronary arteries and the proinflammatory, atherogenic biochemical and enzymatic agents become dominant.

Interestingly in case of the non-diabetic patient group the EFV and Agatston score are paralelly changing parameters, but in case of the diabetic patient group it is not so. One of the possible reasons of that can be the relatively small number of enrolled patients and a large standard deviation. The other explanation is the well-known fact that in the early phase of diabetes the microangiopathy is the dominant vascular change. Later on the macrovascular changes become typical with climbing calcium content in the wall of the large and medium sized arteries including coronary arteries which results in increasing Agatston score values. But at this point unfortunately our study has certain limitations: We had no chance to exam duration of diabetes. The type or length of the applied pharmaceutical therapy had not been analyzed yet, neither in diabetic nor in non-diabetic patients group. Most of the type 2 diabetic patients have elevated blood lipid levels and because of elevated LDL cholesterol and triglyceride levels therefore in this patient group statin therapy is widely used. The statins can stabilize the vulnerable plaques while they may increase the calcium content of the vessel wall. Statins may have positive impact on hepatic steatosis.

5. Application of ECG gated angiography in planning and guiding of therapeutic procedures based on a case study of a catheter ablation of a cardiac arrhythmia

In our clinical practice the most common indication of cardiac CT examination is coronary artery imaging, however there are other indications. The multiplanar or 3D reconstructed images of an ECG gated CT angiography can assist in planning and guiding of several catheter and surgical therapies (e.g.: catheter ablation of cardiac arrhythmias, TAVI procedures, coronary stent placement, and surgery of aortic or left ventricle aneurysms) alone and by 3D printing or by hybrid imaging as well.

From the examples above imaging prior to catheter ablation of arrhythmogenic foci is the most common indication. Merging of the activation map and the 3D CT image and the real time intracardiac echocardiogram (ICE) of the left atrium helps to localize and to visualize continuously the arrhythmogenic foci during the ablation procedures. In the case of ventricular arrhythmias arising from the left ventricle outflow track 3D electro-anatomy mapping is a highly important option as it was confirmed by the following case-study.

A 54-year-old female patient was hospitalized with 2 years history of premature ventricular complexes (PVC) and clinical symptoms of dyspnea and tachycardia and palpitation. Her main complaints were palpitations, and occasional dyspnea, enhanced by physical exercise. Premature ventricular complexes on surface ECG showed that PVCs had LVOT origin. With stress testing PVCs in bigeminal fashion and a 3 sec non-sustained ventricular tachycardia were observed. Echocardiography showed concentric left ventricular hypertrophy, moderate diffuse hypokinesis and an ejection fraction of 43%. Previous medications had not provided any symptomatic improvement therefore catheter ablation therapy of arrhythmogenic foci became the promising option.

Retrospective ECG gated, contrast-enhanced cardiac CT was performed with 64 slice DSCT (Somatom Definition; Siemens Medical Solutions, Forchheim, Germany) a week before ablation. There were two purposes of the CT examination. One of them was to rule out CAD as a reason of arrhythmia. The other was the imaging of the left ventricle, the aortic root and the coronary ostia all together for the complex electro-anatomy mapping during the ablation to prevent some complications e.g. narrowing or occlusion of coronary ostia. The CT image reconstruction for the evaluation of coronary arteries and coronary analysis were performed as subscribed above (Syngo Circulation, Siemens Medical Solutions, Forchheim, Germany). The CT image reconstruction for the evaluation of coronary arteries and coronary analysis were performed as subscribed above (Syngo Circulation, Siemens Medical Solutions, Forchheim, Germay). It revealed slight calcification in the left main coronary artery and in the left anterior descending artery. Three-dimensional (3D) electro-anatomical reconstructions of the left ventricle CartoSound system (Biosense Webster, Inc, Diamond Bar, CA, USA) had been used. This system automatically makes the segmentation of the left ventricle, the aorta and the coronary arteries from the reconstructed CT images. An intracardiac echocardiography catheter (ICE, Sound Star) was inserted into the right atrium via femoral venous approach. The endocardial contours of the left ventricle, the aortic root, and the right coronary artery were traced on the ICE images at the time of the onset of the QRS, and merged with the 3D reconstructed CT image. With electro-anatomic mapping, the source of PVCs was identified, which was located in the left sinus of Valsalva, 18 mm below the left main coronary orificium. With continuous ICE visualization of the ablation catheter (Navistar) a sufficient RF ablation (30W, 1 min, 50°C) was performed. At the end of the procedure programmed stimulation could not trigger PVCs.
This case demonstrates the advantages of using data sets of cardiac CT during catheter ablation procedures. The hybrid imaging provides the opportunity of a safe and effective catheter ablation of the left ventricle outflow track arrhythmogenic foci which could not be possible with ICE guiding alone.

Summary

In my clinical research I studied ultrasonic, oscollometric and computed tomography biomarkers of atherosclerosis.
Initially I stated to work with RF echo-Tracking method, which was a new technical tool for detection vascular stiffness parameters. These parameters seemed to be useful data in diagnosis of early stage atherosclerosis. We tested the reliability of this method at first. Than our research group was the first to determinate the normal values of the less blood pressure dependent β stiffness parameter in different age groups of healthy volunteers in both genders with this method in Central European population. As a control the PWV value was also measured in the same groups. As we expected the mean values of both parameters were slightly increasing with aging. A possible clinical application of this method was demonstrated and the prognostic value of stiffness parameters was emphasized in a case report of a patient with progeria syndrome.

In our following research besides the stiffness parameters Agatston score and epicardial fat volume (EFV) were studied first in a Hungarian CAD patient group and control group. In this study stiffness parameters (AIx and PWVao) were oscillometric measured and Agatston score and EFV values were collected with the evaluation of cardiac CT images. All of these parameters were higher in CAD

patient group than in control group and they are important markers of atherosclerosis. We found weak or no correlation between these parameters. It has been suggested that these parameters have independent predictive value and the different back ground of the CAD might be important. The different dominant risk factors could be the reason of the unequal increase of the studied parameters in CAD patient group.

In our further research we studied the Agatston score, EFV, hepatic density and BMI values in type 2 diabetic patient groups, again firstly in domestic population. Based on our results the measurement of these parameters during the analysis of native cardiac CT images can improve the personal risk assessment of CAD in type 2 diabetic patients without further examinations or further radiation exposure.

And finally we demonstrated the effectiveness and advantages of hybrid imaging in cardiac catheter ablation therapies of arrhythmias and showed the function of merged cardiac CT images in 3D electro-anatomic mapping with a case report. ECG gated CT examinations provide further opportunities for planning and guiding of catheter and surgical procedures. Beyond catheter ablation of arrhythmias, the 3D imaging of the aorta and the heart is crucial in TAVI (transcatheter aortic valve implantation) procedure and in morphological correction of cardiac chambers. Moreover 3D printing of these structures is became possible with ECG gated CT imaging.

Novel findings

In Central European region firstly we determinate the normal values of PWV and β stiffness parameter with RF echo-Tracking technic. We also studied the intra- and inter observer reliability of this method. And with the publication of a case-report of a patient with progeria syndrome a special clinical application of RF echo-Tracking method was presented.

We were first to study the connections between stiffness parameters and Agatston score and EFV together in CAD patient group.

Also we were first to study the connection between Agatston score, EFV, hepatic density and BMI parameters in type 2 diabetic patients in Hungary.

We demonstrated the important role of cardiac CT examination and hybrid imaging in catheter ablation therapy of cardiac arrhythmias with a case-report.

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