Parameters extracted from arterial pulse waves as markers of atherosclerotic changes: performance and repeatability

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Mikko Peltokangas Anca A. Telembeci, Jarmo Verho, Ville M. Mattila, Pekka Romsi, Antti Vehkaoja, Jukka Lekkala, and Niku Oksala

***Abstract*—Arterial diseases are significant and increasing cause of mortality and morbidity. In this study, we analyze and compare the discrimination capability of different arterial pulse wave (PW) based indices, both earlier proposed and novel ones, for describing the vascular health. The repeatability of the indices is also evaluated. Both volume PWs and dynamic pressure PWs are recorded by using photoplethysmographic and electromechanical film (EMFi) sensors connected to a wireless body sensor network. The study population consists of 82 subjects, 30 atherosclerotic patients and 52 control subjects. In addition, day-to-day variability of the derived indices is studied with 10 test subjects examined on three different days. The results are evaluated in terms of statistical tests and receiver operating characteristic (ROC) curves as well as coefficient of variation (CV) and intra-class correlation coefficient (ICC). Altogether 24 out of the evaluated 40 PW parameters showed statistical differences ($p < 0.05$ or less) between controls and atherosclerotic patients. Maximum area under curve was 0.88. Most of the indices had ICCs higher than 0.8 and average CVs less than 0.1. The study shows that the amplitude ratios and time intervals between different PW peaks could be a useful additional tool for the detection of atherosclerosis. The results encourage us for further studies in this field. Up to our knowledge, the performance and the repeatability of different PW derived indices have previously not been studied and compared with each other this extensively. Our findings also provide evidence for the utility of PW measurements for the detection of atherosclerotic changes.**

***Index Terms*—Atherosclerosis, Body sensor networks, Electromechanical film sensors, Photoplethysmography, Pulse wave measurements**

I. Introduction

Degenerative changes in the vasculature, such as atherosclerosis, are increasing causes of mortality and morbidity [1]. The major degenerative changes include stiffening of the arteries during aging, classically known as arteriosclerosis and thickening, stenosis or occlusion of the arteries due to accumulation of cholesterol, i.e. atherosclerosis. The relation of arterial stiffness and occlusive atherosclerosis, i.e. which of these is a marker or a cause is unclear [2], [3], [4], [5]. Clinically, both conditions are considered as a continuum of degenerative changes and indicators of increased risk for severe cardiovascular events, such as stroke and myocardial infarction.

There are various established methods for cardiovascular evaluation and risk assessment. Electrocardiogram (ECG) produces adequate information about the status and the electrical activity of the heart, but does not provide any information on the arterial tree. Oscillometric blood pressure measurement from brachial artery is well-known and widely-accepted method for assessing a cardiovascular risk, but it has several shortcomings: for example, the blood pressure exhibits both short- and long-term variation and spot blood pressure measurement is therefore prone to bias. In addition, as the cuff-based blood pressure measurement provides only the extremums of the pressure but no information how the PW behaves between them. Thus identical systolic and diastolic pressures in the brachial artery can be a result of completely different central blood pressure values [6]. Ankle-to-brachial pressure index (ABI) and doppler auscultation are utilized especially in the detection of advanced atheroscelorosis (peripheral arterial occlusive disease). However, the reported sensitivity and specificity of the ABI vary widely [7] especially with patients having medial sclerosis e.g. due to diabetes. Carotid-femoral pulse wave velocity and the intima media thickness of the carotid artery measured by using ultrasonic transducer have also been proposed for vascular risk characterization [2], [3], [4]. These methods, however, require a skilled operator, expensive equipment, relatively long time for a single result compared with the PW measurement and do not provide information on the actual PW that stresses the arterial walls. For these reasons, the existing methods are not necessarily suitable for rapid screening studies. At the present, to be able to detect especially subclinical atherosclerosis and to reduce morbidity and mortality, there is a growing need for alternative cost-effective, comfortable and rapid methods for monitoring the vasculature.

During the recent years, many research groups have reported measurement and analysis methods utilizing non-invasively

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recorded arterial pulse waves (PW) in the detection of vascular abnormalities. The peripheral PW consists of a heart beat induced percussion wave and its reflections from the impedance discontinuities of the arterial tree. The propagation of these waves depends on the arterial properties, including arterial wall properties, rheological properties of the blood, blood pressure and vascular resistance. Due to the complexity of the arterial system, there are several theories about the origin of the wave reflections and factors affecting them [5], [8], [9], [10].

Many kinds of PW-derived indices have been proposed for characterization of vascular status. The proposed indices have been either direct PW derived individual features, or e.g. classifiers combining many kinds of individual features and utilizing advanced data analysis methods [11], [12]. Common indices based on the PWs include a ratio of diastolic and systolic peak amplitudes and the time delay between these peaks. These features extracted from index finger photoplethysmographic (PPG) PWs have been shown to be dependent on the dose of glyceryl trinitrate (GTN) which affects the arterial stiffness and thus the blood pressure [13]. Both peripheral and central augmentation indices (AIx) as a ratio of systolic amplitudes have been proposed for the analysis of the PW signals recorded with different kinds of pressure transducers such as applanation tonometer [14]. Aging index, based on the second derivative of the index finger PPG, is well-known analysis method for the volume PW signals [15]. Different kinds of PW decompositions have been proposed by many authors for modeling and parametrizing the wave superposition of the observed PW [8], [16], [17].

Our studies aim for a development of a rapid and cost-effective measurement method that can be utilized e.g. in screening purposes in health centers. In the present study, we focus on evaluating the capability of simple direct PW-derived parameters most of which have earlier been proposed by other researchers to discriminate the test subjects into healthy controls and atherosclerotic patients as well as their repeatability.The performance of the studied parameters is compared with respect to the reference values found by the ABI measurement and a risk factor questionnaire. More detailed description of the evaluated parameters is found in section II-D. Based on our knowledge, the performance of different PW parameters has not been studied or compared this broadly for different measurement sites.

II. Materials and methods

A. Measurement hardware and sensor placement

All the volunteer test subjects participating in the study were examined in supine position and with the sensors connected to a wireless body sensor network presented earlier in [18]. Dynamic pressure PW signals were recorded by using sensors made of material called electromechanical film (EMFi), and volume PW signals were recorded by using PPG probes having an excitation wavelength of 905 nm. In addition, bipolar ECG was recorded from the subjects by conventional disposable ECG electrodes located under the clavicles or under the right clavicle and left lower abdomen.

The locations of the measurement points are illustrated in Fig. 1. Dynamic pressure signals were recorded preferably from the left wrist (distal antebrachium), bend of the arm (cubital fossa) and ankle (posterior tibial artery). PPG signals were recorded preferably from the left index finger and second toe. These locations were selected due to their easy access. The duration of each recording was approximately 15 min.

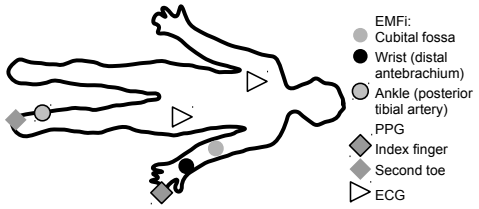

Figure 1. Placement of the PW sensors.

B. Study subjects

The clinical patient measurements were conducted in two Finnish university hospitals (Tampere and Oulu). The study subjects were divided into different groups as shown in more detail in Table I which shows the numbers of subjects having different risk factors in different groups, such as smoking, dyslipidemia (abnormal amount of lipids (e.g. cholesterol) in the blood), diabetes (high blood glucose levels over prolonged period), rheumatoid arthritis (autoimmune disorder affecting joints) and hypertension (high blood pressure). Group A consists of atherosclerotic patients having abnormal ABI ($ABI < 0.9$ or $ABI > 1.3$) and being older than 65 years. All the subjects in group A had atherosclerotic changes at least in iliac, femoral or crural regions which were verified by preoperative angiographic examination as a part of their normal treatment process. Group B consists of control subjects having normal ABI and being older than 70 years. Based on the risk factor questionaire and medical records, the control subjects had no history of the following symptoms or diagnosed cardiovascular diseases: cerebrovascular disease (amaurosis fugax, transient ischemic attack, ishcemic stroke), coronary artery

Table I
Different study groups and the number and proportion of test subjects having different cardiovascular risk factors.

Group	A (Atherosclerotic)	B (Old healthy)	C (Middle-aged)	D (Young)	B+C+D (All healthy)	A+B+C+D (All)	E (Day-to-day meas.)
Age*	74.8±7.5	76.5±5.2	61.5±6.9	29.6±4.6	60.2±19.1	65.6±17.3	26.9±3.7
N	30	21	19	12	52	82	10
Males	23 (77%)	7 (33%)	11 (58%)	12 (100%)	30 (58%)	53 (65%)	7 (70%)
Smoking	23 (77%)	4 (19%)	3 (16%)	0 (0%)	7 (14%)	30 (37%)	1 (10%)
Dyslip.	20 (67%)	3 (14%)	2 (11%)	0 (0%)	5 (10%)	25 (31%)	0 (0%)
Diabetes	15 (50%)	1 (5%)	0 (0%)	0 (0%)	1 (2%)	16 (20%)	1 (10%)
Rheum. arth.	1 (3%)	4 (19%)	1 (5%)	0 (0%)	5 (10%)	6 (7%)	1 (10%)
Hypertension	23 (77%)	4 (19%)	3 (16%)	0 (0%)	7 (14%)	30 (37%)	0 (0%)
Crea** μmol/l	48-60-76-99-173	47-60-77-78-107	-	-	-	-	-
SBP** (mmHg)	105-126-156-169-193	107-131-140-160-178	117-130-141-152-165	110-131-138-149-156	107-131-140-154-178	105-130-143-157-193	105-117-123-136-158
DBP** (mmHg)	53-63-71-87-120	63-76-80-89-99	64-79-82-95-106	58-76-80-85-97	58-75-81-88-106	53-68-80-88-120	62-74-80-83-97

*: mean±standard deviation, **: minimum - 25% quantile - 50% quantile - 75% quantile - maximum. Dyslip.: Dyslipidemia, Rheum. arth.: Rheumatoid arthritis, Crea: Plasma level of creatinine, SBP: Systolic blood pressure, DBP: Diastolic blood pressure.

disease (angina pectoris, myocardial infarction) or peripheral arterial disease (intermittent claudication, critical or acute limb ischemia).

The third and fourth groups, groups C (40–69 years) and D (less than 40 years), consist of younger test subjects with no aforementioned cardiovascular symptoms or diagnosed disorders. The measurement protocol was also similar with the test subjects in group E containing young (22–36 years) healthy subjects meeting the same criteria as the other control subjects in groups B–D, but the measurements were repeated on three different days for each test subject in order to study the day-to-day variations of the resulted parameters. Nine of the subjects in group C as well as all subjects in groups D and E were examined with the system in Tampere University of Technology (Tampere, Finland). The rest ten subjects in group C were examined in hospitals.

The distributions of systolic and diastolic blood pressures (SBP and DBP) for all the test subjects and plasma levels of creatinine (Crea) for patients under hospital treatment are shown in Table I by using the quantiles of 0% (minimum) 25%, 50% (median), 75%, and 100% (maximum). Non-parametric Kruskal-Wallis test is implemented for these distributions of different study groups, and statistically significant differences were not found in these variables ($p > 0.15$ for all these variables)

The study subjects were examined between 8 am and 4 pm, and their daily living (e.g. nutrition and smoking) was not restricted. For various reasons, there were from 0 to 16 test subjects per measurement point with no useful signal. Most common reasons were 1) low-amplitude PW signal (especially ankle PWs from atherosclerotic patients) (wrist 1, cubital fossa 2, ankle 8, finger 0, toe 1), 2) cannula or catheter at the wrist or cubital fossa or plastered limb, (wrist 3, cubital fossa 5, ankle 6, finger 0, toe 3), and 3) a technical problem, i.e. broken measurement wire or amplifier saturation due to high gain or leakage currents in the circuit board, or a changed frequency response of the EMFi sensor because of alcohol based liquid cleanser (wrist 2, cubital fossa 5, ankle 2, finger 0, toe 0).

C. Ethics and patient safety

The study was approved by the local ethical review boards of the hospital districts (R14096 (Pirkanmaa Hospital District) and 245 § 69/2014 (Northern Ostrobothnia Hospital District)), the Finnish National Supervisory Authority of Health and Welfare (Valvira) (ID 272) and the technical departments of the hospitals. All volunteer test subjects were informed on the purpose of the study and written informed consents were obtained. The subjects had also a chance to ask for additional information and interrupt their participation at any point.

D. Signal processing

The signal preprocessing and PW feature extraction were implemented as presented in [19]. Based on the found PWs and feature points illustrated in Fig. 2, altogether four different amplitude ratios (R_i) were defined for all the PW measurement points presented in Fig. 1. Ratio R_1, named as reflection index RI for index finger PPG in [13], is defined as a ratio of the amplitude of the diastolic wave B and the systolic peak $\max(P_1, P_2)$ as $R_1 = B/\max(P_1, P_2)$. However, depending on the shape of the PW, the diastolic wave is normalized either by the first or the second systolic peak when computing R_1. For this reason, we sought to study if the ratio of the diastolic wave and a particular systolic wave differs between atherosclerotic patients and healthy control subjects. Thus, ratio R_2 is defined as a ratio of the diastolic peak B and the first systolic peak P_1 as $R_2 = B/P_1$ and ratio R_3 as a ratio of the diastolic peak B and the second systolic peak P_2 as $R_3 = B/P_2$. The fourth tested amplitude ratio is peripheral augmentation index (pAIx), which is defined as a ratio of the late and the early systolic peaks as $R_4 = P_2/P_1$ [14].

Time delays between different peaks are also potential markers of atherosclerosis as the propagation velocity of the PW depends on arterial wall properties such as stiffness. Different peak-to-peak times T_i are computed as a time delay T_1 between the systolic maximum and the peak of the diastolic wave, time delay T_2 between the early systolic peak P_1 and the diastolic peak B, and time delay T_3 between the late systolic peak P_2 and the diastolic peak B. In addition to the amplitude ratios and the time intervals, aging index (AGI) is computed as $\mathrm{AGI} = (b-c-d-e)/a$ in which a is the maximum of the 2nd derivative of the PW and b, c, d and e are the following local extremities [15].

E. Evaluation of the results

The differences between the study groups are tested with two-tailed Mann-Whitney U-tests because of the low number of test subjects in different study groups. For those parameters having statistically significant differences between atherosclerotic patients and healthy subjects (i.e. $p < 0.05$), receiver operating characteristic (ROC) curves are drawn.

The repeatability of the results refers to the agreement of the obtained values of the measurand under same conditions, such as the same instrument, same observer and same location [20]. The repeatability of different ratio-scaled parameters (R_1–R_4 and T_1–T_3) is evaluated by computing (intra-subject) coefficients of variation (CV) based on their sample means m and sample standard deviations s as $\mathrm{CV} = s/m$ for the time series of parameters based on the PW signals recorded from each test subject. CV is not suitable repeatability indicator for interval-scaled AGI, so the one-way analysis of variance (ANOVA) based intra-class correlation coefficient (ICC) is computed. In general, the ICC is used to estimate the repeatability of the series of measurements and it is defined

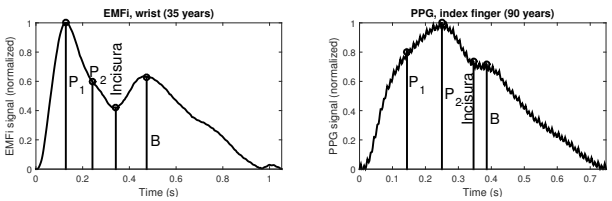

Figure 2. Examples of amplitude-normalized dynamic pressure and volume PWs having the early systolic peak P_1 higher than the late systolic peak P_2 (left panel) and the late systolic peak P_2 higher than the early systolic peak P_1 (right panel).

as a ratio of the between subject (group) variance and the sum of the between and within subject (group) variances [21], [22]. The ICC is computed for all the parameters as $\mathrm{ICC} = (\mathrm{MS_{bs}} - \mathrm{MS_{ws}})/(\mathrm{MS_{bs}} + (k-1)\mathrm{MS_{ws}})$ in which $\mathrm{MS_{bs}}$ is between-subject mean squares, $\mathrm{MS_{ws}}$ is within-subject mean squares from ANOVA table and k is the number of observations per subject and computed as in [21] in case of unequal numbers of observations per subjects.

III. Results

The distributions of different parameter values are shown in Fig. 3. As seen in Fig. 3, there are 24 parameters indicating statistically significant ($p < 0.05$) differences between the joint distribution of all healthy subjects (group B+C+D) and atherosclerotic patients (group A) and 10 parameters indicating statistically significant differences between atherosclerotic patients and all different age groups (i.e. group A vs. groups B, C and D separately). The classification performance of the 24 parameters having statistically significant differences between groups A and B+C+D is shown in Fig. 4 by using ROC-curves and area under curve (AUC) values.

For each test subject, CV is computed for the time series of each parameter in order to quantify the beat-to-beat variability of the parameters extracted from the PWs. These results are reported as mean value (m) and a sum of mean and standard deviation ($m+s$) in Fig. 5 for each parameter, measurement point and each study group. In addition to the beat-to-beat variability, Fig. 5 shows the average and standard deviation for the CVs (m and $m+s$) for the results based on the measurements carried out for the same subjects on three different days (study group E in Table I).

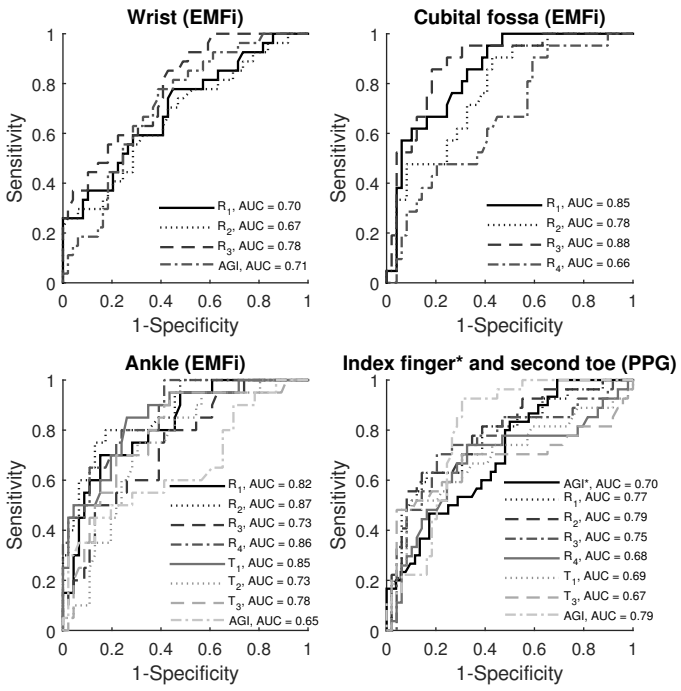

Figure 4. ROC-curves for the extracted parameters having statistically significant differences between atherosclerotic and healthy subjects. Asterisk (*) in the right lower panel indicates aging index from index finger, other curves in that panel are from the second toe.

ICCs are shown in Fig. 6a for different parameters and study groups based on the beat-to-beat time series of PW parameters. Similarly as in Fig. 6a, ICCs are shown in Fig. 6b for the averaged parameter values obtained from 10 equally distributed periods (20 PWs/period) per each test subject (i.e. 10 periods per each time series of each parameter). Fig. 6c shows the ICCs for the averages based on the measurements carried out with the same test subjects on three different days. The p-values are less than 0.0001 for all the ICCs shown in Figs. 6a and 6b. The p-values of statistically significant ($p < 0.05$) ICCs are shown in 6c for measurements conducted on three different days (group E).

IV. Discussion

Earlier we have reported single examples having up to 20% differences in the parameters extracted from successive PWs [18]. This suggests there is no sense to perform PW analysis based on a single PW due to random or temporary variations. On the other hand, particularly long recordings are not needed, as seen in Fig. 6b: ICC between the results extracted from periods of 20 PWs is higher than 0.95 with most of the parameters and study groups. Also the ICCs computed over beat-to-beat time series (Fig. 6a) are mostly higher than 0.8 and even close to 0.9.

A. Differences between the compared parameters

Figs. 3 and 4 indicate that the ankle is the best measurement point in terms of classification performance. However, day-to-day variations of the parameters extracted from the ankle PWs are large indicating poor performance in terms of repeatability (Figs. 5 and 6c). One explanation for this is that the signal-to-noise ratio (SNR) is commonly lowest in the signals recorded from the ankle due to low-amplitude pulsations. The low SNR causes also smaller number of detected PWs and thus fewer datapoints for the analysis. From this point of view, the analysis of ankle PW may not necessarily provide reliable results. On the other hand, according to simulated results presented in [23], the occlusions in the arterial pathway may cause oscillations in the pressure signal which can be interpreted as a signal having low SNR.

An interesting observation is that the parameters extracted from the PWs recorded from cubital fossa have better discrimination capability and practically equal or better repeatability than the parameters extracted from the wrist pulses (Figs. 3, 4, 5 and 6). The arterial pathway from the aorta to the wrist is longer than to the cubital fossa which may affect to the observed PW. The anatomic structures surrounding the radial artery at wrist and brachial artery at the cubital fossa are different and may therefore also affect PW morphology: in the wrist, the radial bone is located immediately adjacent to the artery while there is a significant amount of soft tissue adjacent to brachial artery at the cubital fossa. On the other hand, there are a couple of other possible reasons for the difference. First, the distal parts of the limbs are often more sensitive to the atherosclerotic changes. This may lead to a situation where the results obtained for the asymptomatic control subjects' wrist PWs reveal the latent degenerative changes seen as false

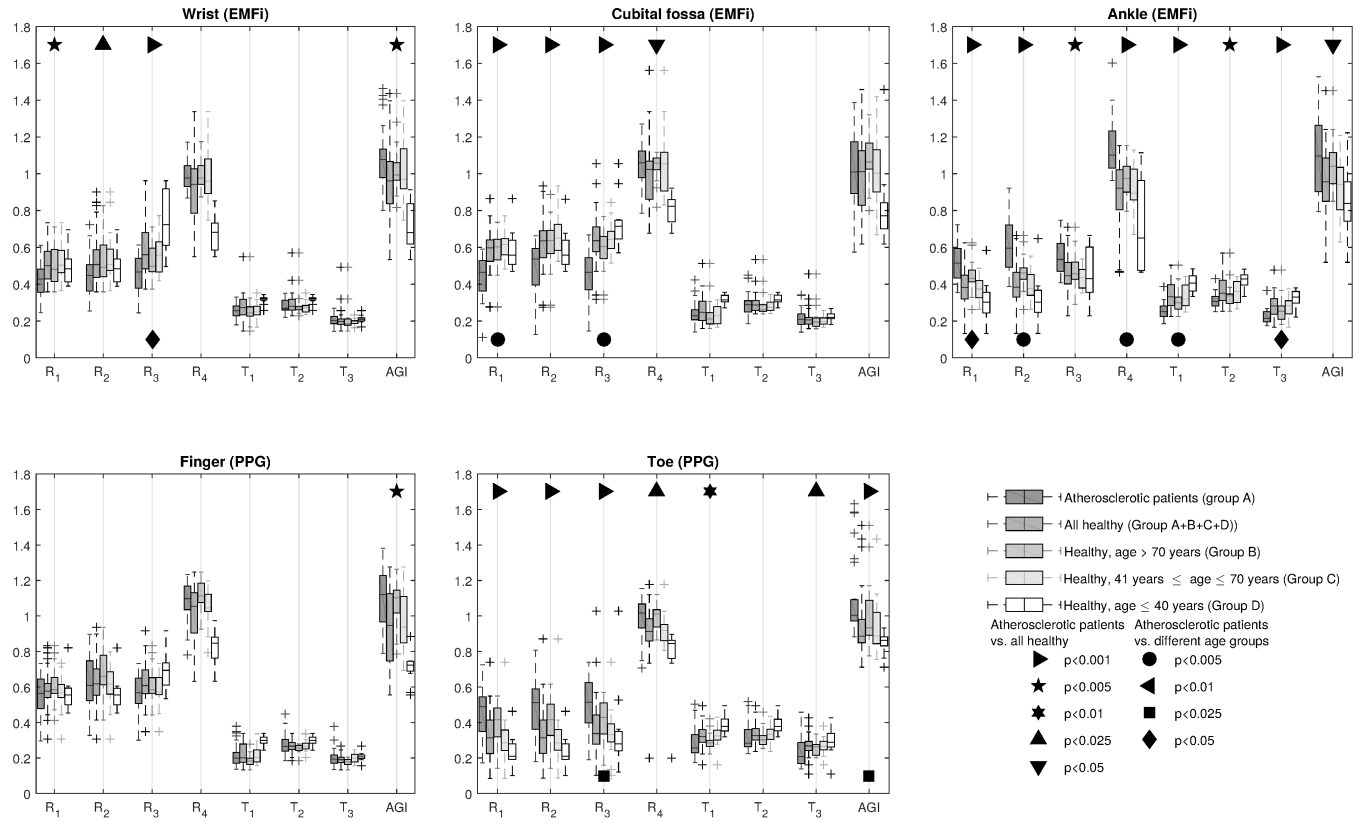

Figure 3. Distributions of the parameter values for the different study groups. Parameters R_1–R_4 are in relative scale and T_1–T_3 are in seconds. Values of aging index (AGI), that can also be negative, are scaled for the same range as R- and T-parameters in order to make the figure readable.

positive results whereas PWs recorded from cubital fossa do not. Second, the dominating artery in the forearm can be either radial or ulnar artery due to the anatomical differences in the structure of the upper limb [24].

The index finger PPG derived parameters are in general repeatable (Figs. 5 and 6), having high ICCs and small CVs. However, the consistent statistical differences between atherosclerotic patients (group A) and different control groups (B, C, D and B+C+D) were not found in this study, although the PW morphologies with young and older test subjects are clearly different in visual comparison.

The performance of tested novel parameters, R_2, R_3, T_2, and T_3 varies between different measurement sites (Figs. 3–6). However, especially the ratio of the amplitude of the diastolic wave and the second systolic peak, i.e. R_3, can be useful tool for analyzing PWs recorded from the wrist, cubital fossa and second toe, both in terms of repeatability and discrimination performance. The sensitivity (SE) and specificity (SP) of a diagnostic test depend on selected partition value. In this study, we did not fix or recommend any specific partition values, but the dependence between SE and SP can be seen in Fig 4. From Fig. 4, one can read at particular partition values providing e.g. SE = 0.95 and SP=0.69 for cubital fossa based R_3, SE=0.92 and SP=0.45 for second toe based R_2 and SE=0.92 and SP=0.37 for second toe based R_1.

B. Comparison with other studies

The repeatabilities and classification performances of all the computed parameters cannot be compared with any reference values found from the literature since many of the determined parameters are used only with a single measurement site and method in previous studies. Wang *et al.* [16] have reported ICCs of 0.91–0.96 and CVs of 0.029–0.043 for the non-invasively recorded radial artery based AIx which corresponds to R_4 in this study. Crilly *et al.* [25] have found ICCs of 0.93–0.96 for AIx values obtained from radial artery PW signals recorded with tonometric method. These values are approximately similar with the ones found in this study for not only the wrist but also the cubital fossa based R_4. The AIx values are related to aging [14], [19] but also to the cardiovascular risk factors [26].

The AUC value of 0.604 has been reported for the radial artery based AIx when discriminating subjects with and without coronary artery disease [26]. Our AUC value (0.66, Fig. 4) for the cubital fossa based R_4 is almost equal but not directly comparable because of different measurement sites and cardiovascular diseases behind the results. However, different cardiovascular risk factors are often concomitantly present.

The index finger PPG derived reflection index (R_1) and the peak-to-peak time (T_1) have been shown to be dependend on the dose of GTN so that the peak-to-peak time increases and reflection index decreases with the increasing dose of GTN and thus with increasing arterial elasticity [13]. In our

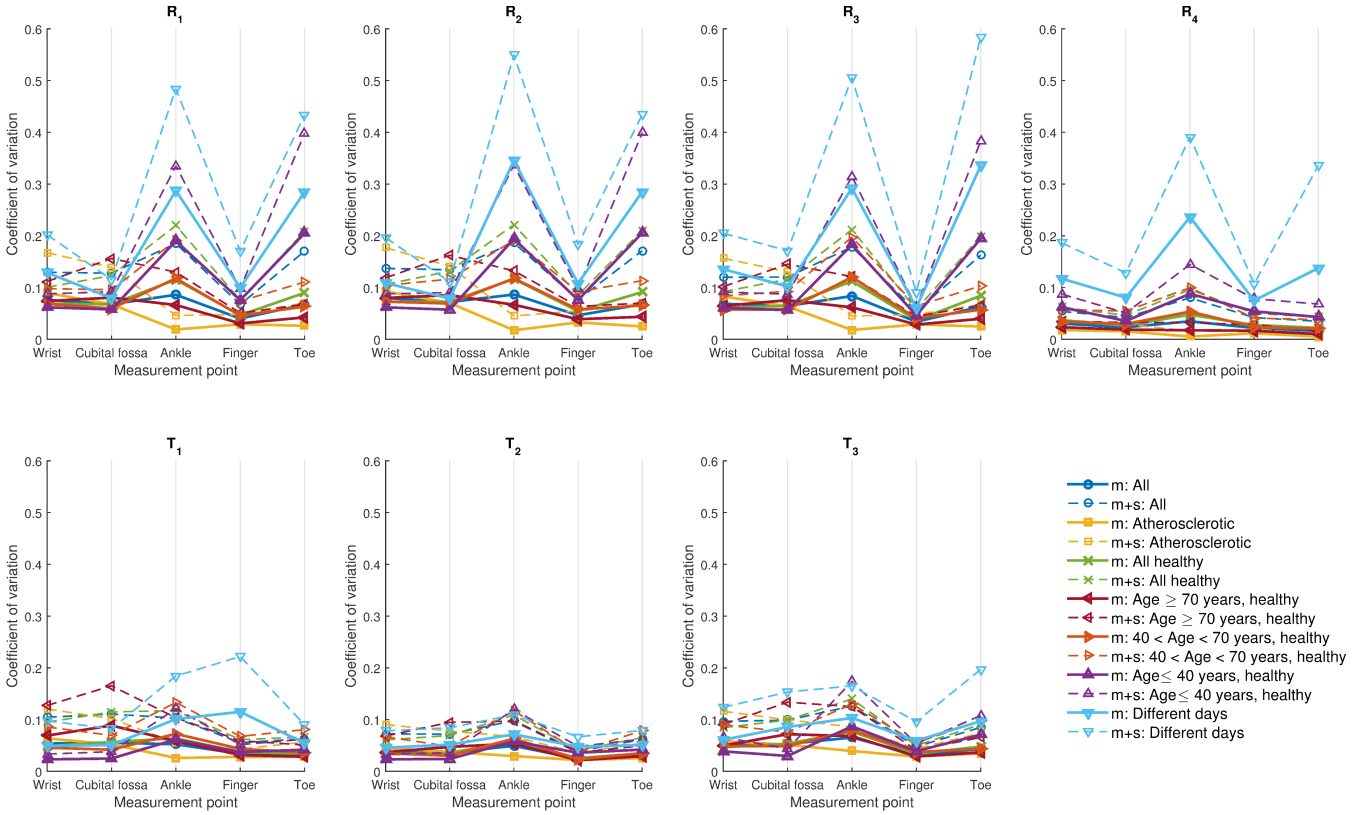

Figure 5. Average CVs (m) computed over the time series of each parameter of each test subject for each study group and measurement point. The sums of mean and standard deviation ($m+s$) are also shown in dashed lines. W = wrist, C = cubital fossa, A = ankle, F = finger, T = toe.

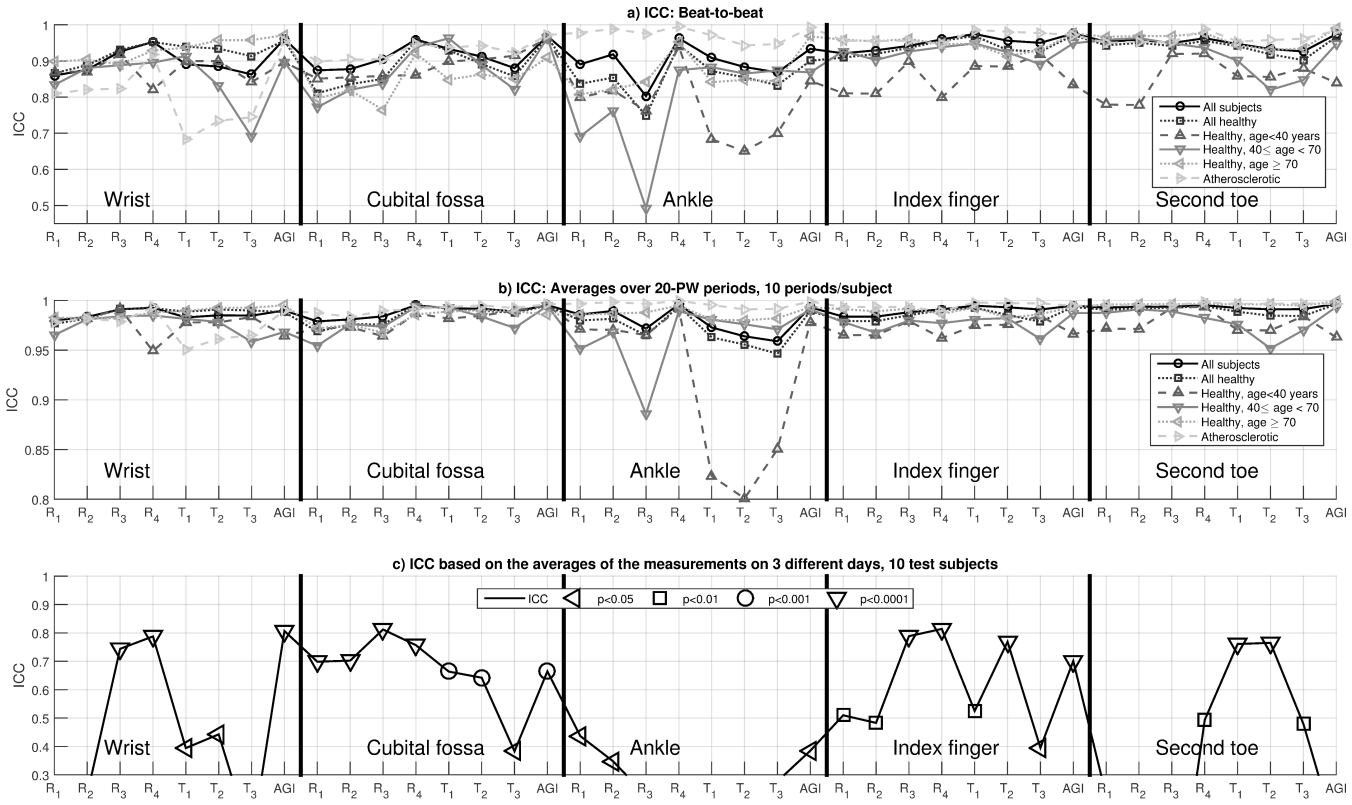

Figure 6. ICCs for beat-to-beat variability (a), averages over 20-PW periods (10 periods/subject) (b) and averages based on the measurement carried out on 3 different days (c). ICCs less than 0.3 are not shown in panel c).

results for the index finger PPG signals, the trend between the values of R_1 and study group as well as T_1 and study group are somewhat similar, but not statistically significant (Fig. 3). However, these differences are slightly more clear with second toe based R_1 and T_1. For upper limb and EMFi signal based R_1 values, the trend was opposite between the value of R_1 and study group, but statistically significant differences were not found between T_1 and study group. This may indicate increased systolic blood pressure due to earlier, high-amplitude and high-energy reflected wave during the systole which causes the low-energy diastolic wave.

For the index finger based aging index, Bortolotto *et al.* [15] have reported statistical differences ($p < 0.0001$, $n = 526$) between patients having atherosclerotic alterations and control subjects and significant age dependence. In our results, the values of AGI in Fig. 3 have increasing trends with age and arterial degeneration level, but statistically significant differences were not found between different groups with all the measurement points. One reason may be the signal pre-processing techniques used in our study, i.e. too heavy smoothing and filtering of the PW signals. The aging index is probably the most sensitive to the effects of over-smoothing since it is computed based on five amplitudes detected directly from the 2nd derivative of the PW. Still, even the day-to-day ICCs for the index finger PPG and the wrist PW based aging indices (Fig. 6c) are well comparable with the ICC of 0.84 reported in [27].

The reported specificity and sensitivity of our reference, ABI, vary widely from study to study: sensitivities of 15%–79% and specificities of 83.3%–99.0% were reported in [7]. In terms of repeatability, Atsma *et al.* [28] have reported ICCs of 0.72–0.85 and de Graaff *et al.* [29] ICCs of 0.87–0.98 for ABI, respectively. A comparison between the gold standard, ABI, and obtained parameter values shows that the studied methods could have comparable performance and the parameters derived from PWs could therefore work as an additional diagnostic help in patient screening.

The reported performance metrics for the advanced analysis methods that utilize e.g. machine learning techniques are often higher than the performances of the individual parameters reported in this study. Diagnostic accuracy (AC), sensitivity (SE) and specificity (SP) of 87.5% have been reported in [12] for the best-performing classifier utilizing support vector machine and index finger PPG. Typical AUCs higher than 0.9 have been reported for a linear discriminant analysis based method combining information from finger and toe PPGs in [11]. These results suggest that classifiers utilizing multidimensional or multichannel PW data could improve the discrimination capability, but as a drawback, they require sufficient and representative training data set.

C. Study limitations

The primary goal of this study was to evaluate and demonstrate the classification performance of relatively simple PW derived parameters including ones earlier proposed in literature and the repeatability of their measurement. Despite the promising results, there are some limitations in the study. First, the number of study subjects, 82 caucasians, is enough for finding statistical differences between the different groups, but prevents generalizing the results to the whole population in clinical point of view. Second, the recording of all the signals from all subjects was not successful, and thus the data used to compare the parameters with each other is not entirely from the same subject population. However, in practice, if recording of a PW signal is not possible due to low-amplitude pulsations, it is often a potential sign of a vascular disease since the low SNR is more common in atherosclerotic patients. The third limitation is our reference method, ABI and the results of risk factor questionaire, which were taken as the ground truth in the exclusion of the atherosclerotic changes although the ABI measurement has its own limitations [7], [30]. In order to validate and generalize the results, a study with larger number of test subjects and a more comprehensive reference method (e.g. magnetic resonance angiography) is needed, including both atherosclerotic patients and healthy control subjects.

V. Conclusions

According to authors' knowledge, this is the first study extensively comparing the classification performance of different PW derived parameters and their repeatability. We compared different individual parameters extracted from pulse waves recorded from the wrist, cubital fossa and ankle with the sensors made of EMFi as well as from index finger and second toe with PPG sensors.

The results indicate in both terms of classification performance and repeatability that there are potential parameters that can be utilized as diagnostic help in the detection of vascular abnormalities. Despite that the simple direct PW derived parameters could be utilized as an additional diagnostic strategy, a comparison between our results and the results found from literature for the classifiers based on simple machine learning techniques shows the superiority of the advanced analysis methods. Based on our results, the most appropriate locations for the detection of vascular abnormalities are wrist, cubital fossa and second toe whereas ankle PWs have poor repeatability and index finger PWs do not show statistically significant differences between atherosclerotic patients and control subjects. The results indicate also that increasing the duration of the measurement period (e.g. up to 15 minutes as in the present study) does not provide additional information compared with a short 20 second measurement period. The promising results encourage us for further studies related to the PW measurements and their usage in clinical diagnosis or screening of vascular changes.

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