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A NOVEL GEOMETRICAL ANALYSIS OF THE ARTERIAL PULSE BASED ON THE GOLDEN RATIO φ (*PHI*): ASSOCIATION WITH HEART RATE VARIABILITY

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Abstract

Purpose. This study aimed to quantify the deviation of an arterial pulse (pressure wave) from the „golden" or „divine" pulse, defined according to the golden ratio φ (*phi*), and to investigate whether the extent of this deviation is related to the function of autonomic nervous system (ANS) as assessed by 24-hr heart rate variability (HRV).
Methods. Seventy-two healthy subjects underwent 24-hr continuous monitoring of ECG. Applanation tonometry of the radial artery and pulse wave analysis of peripheral and central (mathematically derived) aortic pressure waveforms were performed in all subjects. Time- and frequency domain indices of HRV were computed together with nonlinear dynamic parameters. Two novel indices were computed primarily based on pressure (systolic and diastolic pressure; mmHg) and time (ejection and diastolic durations-intervals; msec) values extracted from the recorded pressure waves.
Results. The new phenotypic, geometrical biomarkers based on the golden ratio (φ) were associated with

Résumé

Une nouvelle analyse géométrique de l'impulsion artérielle basée sur le nombre d'or φ (phi): association avec la variabilité de la fréquence cardiaque

Objectif. Cette étude visait de quantifier la déviation du pouls artériel (onde de pression) à partir du pouls „doré" ou „divin", défini selon le nombre d'or φ (phi), et de trouver si l'étendue de cette déviation est liée à la fonction du système nerveux autonome (SNA), évaluée par la variabilité de fréquence cardiaque pendant 24 heures (VRC).
Méthodes. Soixante-douze sujets en bonne santé ont été mis en surveillance continue de l'ECG pendant 24 heures. La tonométrie par aplanissement de l'artère radiale et l'analyse des ondes de pouls des formes d'ondes de pression aortiques périphériques et centrales (dérivées mathématiquement) ont été réalisées chez tous les sujets. Les indices de temps et de fréquence de VFC ont été calculés avec des paramètres dynamiques non linéaires. Deux nouveaux indices ont

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HRV indices and especially with those computed at the frequency domain. These associations were independent from age, gender, body mass index, mean arterial pressure, pulse pressure and mean 24-hr heart rate.
Conclusion. The new proposed geometrical analysis of the arterial pulse reflects/characterizes specific 24-hr HRV features and is independently related with ANS function. Although the potential pathophysiological, underlying mechanisms of this association can be hardly explained by this study, the application of the golden ratio φ for the analysis of the arterial pulse merits further investigation and may open a new window for the evaluation of cardiovascular risk.

Keywords: arterial pressure, pulse wave analysis, brachial artery, hemodynamics, aorta, blood pressure.

Abbreviations
HRV = Heart rate variability
PWA = Pulse Wave Analysis
CV = Cardiovascular
ApEn = Approximate Entropy
DFA = Detrended Fluctuation Analysis
SBP = Systolic blood pressure
DBP = Diastolic blood pressure
PP = Pulse pressure
MAP = Mean arterial pressure
ED = Ejection duration
DD = Diastolic duration
ANS = Autonomic nervous system

été calculés principalement sur la base des valeurs de pression (pressions systolique et diastolique, mmHg) et de temps (éjection et durée diastolique-intervalle, msec) extraites des ondes de pression enregistrées.
Résultats. Les nouveaux marqueurs phénotypiques et géométriques basés sur le nombre d'or (φ) ont été associés aux indices VRC et en particulier à ceux calculés sur le domaine fréquentiel. Ces associations étaient indépendantes de l'âge, du sexe, de l'indice de masse corporelle, de la pression artérielle moyenne, de la pression artérielle et de la fréquence cardiaque moyenne pendant 24 heures.
Conclusion. La nouvelle analyse géométrique proposée de l'impulsion artérielle reflète / caractérise des caractéristiques VRC spécifiques pendant 24 heures et elle est indépendamment liée à la fonction SNA. Bien que les mécanismes physiopathologiques potentiels de cette association puissent être expliqués difficilement par cette étude, l'application du nombre d'or φ pour l'analyse de l'impulsion artérielle mérite d'être étudiée puisqu'elle pourra ouvrir une nouvelle „fenêtre" vers l'évaluation du risque cardiovasculaire.

Mots-clés: pression artérielle, analyse de l'onde pulsative, artère brachiale, hémodynamique, aorte, tension artérielle.

Introduction

The last few decades scientists began to appreciate the pivotal role of heart rate variability (HRV) in clinical research. HRV describes the variations of both instantaneous heart rate and RR intervals and it has prevailed, as a term, instead of cycle length variability, heart period variability, RR variability, and RR interval tachogram. HRV is increasingly recognized for its ability to indicate or predict various health problems such as autonomic nervous system dysfunction, cardiovascular disorders, fetal distress, anxiety, depression, asthma, diabetes and other diseases. Basically, HRV assesses the balance between the sympathetic and the parasympathetic nervous system and it can provide additional valuable information concerning pathophysiological conditions as well as risk stratification and prediction. A milestone in the clinical significance of HRV was reached in 1980s when it was confirmed that HRV was a strong and independent predictor of mortality after an acute myocardial infarction[1-3]. Until now several other studies have demonstrated that HRV can predict mortality in other populations as well[4-7].

Several different methods and techniques are available for (i) the recording of cardiac cycle length (period) and (ii) for the processing and analysis of the acquired time-series (i.e. ECG, pressure, blood flow or other bio signals) for the quantification and assessment of HRV[1]. Time-domain and spectral (or frequency-domain) analyses are the most commonly used methods for the computation of numerous indices of HRV[8]. Other geometrical parameters and more recently dynamics have been also applied for HRV assessment often yielding promising diagnostic and prognostic results[9-11].

On the other hand, the arterial pulse and more specifically the morphology of the pressure waves has been also extensively analyzed and widely used for the study and diagnosis of several cardiovascular and other pathophysiological conditions. With the advent of technological innovations accurate and non-invasive recording of arterial pressure waves is now possible using high-fidelity sensors such as those implemented in applanation tonometry or photo plethysmography.

In parallel, several computational methods have been proposed for Pulse Wave Analysis (PWA), each one aiming to determine different facets and underlying mechanisms related to pressure wave phenotypes such as pressure and time related characteristics. Beyond the measurement of peak (systolic and diastolic) BP values, pressure waves can be further analyzed for the evaluation of wave reflections, arterial stiffness, arterio-ventricular coupling and cardiac output. The pathophysiological and clinical relevance of wave reflections[12-17] and arterial stiffness[18-20] surrogates has been extensively examined and quite established the last three decades as predictors of CV risk.

However, the relationship between pulse wave morphology and HRV is still unexplored. Although geometrical methods have been used for HRV analysis[8], there are limited applications of such geometrical approaches on PWA. One of the most mysterious and absorbing numbers in the history of mathematics, beyond the well known number *pi* (3.14), is the „mean and extreme ratio" or else „divine proportions", „golden section", „golden ratio" or „golden number" most often denoted by the Greek symbol-letter φ (*phi*). This element represents an ancient concept probably known by Babylonians and Egyptians more than 2500 years BC ago, but it was theoretically described by the mathematician and philosopher Pythagoras (ca 580BC – 500BC) and his School, while it was further established by the mathematician Euclid of Alexandria (Mid-4th century – Mid-3rd century BC) as reported in his work *The Elements*.

The golden ratio is defined by the proportion of two quantities (α and β) where the ratio of the sum of the quantities ($\alpha + \beta$) to the larger quantity (α) equals the ratio of the larger quantity (α) to the smaller one (β), according to the equation:

$$\frac{\alpha}{\beta} = \frac{(\alpha + \beta)}{\alpha} \stackrel{\text{def}}{=} \phi$$

[eq. 1], where ϕ is the golden number which approximates 1.618.

A philosophically and historically based concept (rather than clinical), of the „golden" or „divine" arterial pulse, is described in this paper. The main purpose is to quantify the deviation of an arterial pulse from the „golden pulse" and to further explore whether the extent of this deviation is related to the function of autonomic nervous system as assessed by HRV. The possibility to detect or predict specific HRV characteristics via a simple phenotypical, geometrical, analysis of a single arterial pulse wave using the golden ratio φ, either in pressure or time scale (axes), is a challenging and novel hypothesis with substantial clinical relevance.

Methods

Study population

The study included healthy subjects who underwent a preventive cardiovascular check-up. Exclusion criteria were drug administration for chronic diseases, diabetes, cardiovascular disease, heart failure, renal failure and obesity. A total of 72 subjects were finally examined (mean age 39.6 ± 13.9 years, 28 females and 44 males). Thirty- one subjects were non-smokers, 35 were smokers and 6 ex-smokers. All subjects underwent non-invasive hemodynamic assessment and 24 hours monitoring of heart rate variability as previously described [21].

Twenty-four hours recording of ECG

A continuous electrocardiogram (ECG) was recorded for 24-hours at ambulatory conditions using a Holter device (Synescope, version 3.1, ELA Medical, France). The recording was acceptable if its minimum time duration was 18 hours, necessarily including sleep. All subjects were advised to follow their regular daily schedule at the day of ECG recording. The sampling frequency and time resolution was 500 Hz and 1ms respectively. The ECG data were digitized by the apparatus and the recorded RR interval series were exported and transferred to a computer for further offline analysis.

Assessment and analysis of Heart Rate Variability

Initially the RR-interval time series were analyzed by the software of the Holter device. Manual editing by visual inspection was performed to eliminate noise, premature/ectopic beats and artifacts. Only recordings with >90% normal sinus beats were included in the study and further analyzed.

Time- and frequency-domain analysis was performed by the Synescope software for the calculation of several indices (Table 1). Analysis of heart rate dynamics by methods based on chaos theory and nonlinear system theory was also performed. Four nonlinear dynamic indices were computed: (i) Approximate Entropy (ApEn) and (ii) time scale correlation features ($\alpha 1$, $\alpha 2$) derived from Detrended Fluctuation Analysis (DFA). Nonlinear indices were computed using our custom made nonlinear dynamics tool as previously described[22]. For each nonlinear measure the RR time series was segmented in accordance to previous studies[23-25] and the average values for each index were computed from segments containing 4000 RR intervals. The RR interval series was extracted from Synescope in a „.txt" file format and used as an input for our computational tool.

Table 1. Conventional Heart Rate Variability parameters

Definition	*Abbreviation*	*Units*
Time domain		
Average heart rate for the entire 24-hr recording	HR_{24hr}	bpm
Standard deviation (SD) of all RR intervals	SDNN	ms
SD of the averages of RR intervals for all 5 min segments of the entire recording	SDANN	ms
Mean of the SD of RR intervals for all 5min segments in the entire recording	ASDNN	ms
Square root of the mean sum of squared differences between adjacent RR intervals	RMSSD	ms
The percentage of adjacent RR pairs differing more than 50ms	pNN50	%
Frequency domain		
Total Power (Variance of all RR intervals) ≤ 0.4Hz	TP	ms^2
Natural logarithm of TP	TP_{log}	
Power in the very low frequency range 0.003-0.04Hz	VLF	ms^2
Natural logarithm of VLF	VLF_{log}	
Power in the low frequency range 0.04-0.15Hz	LF	ms^2
Natural logarithm of LF	LF_{log}	
LF as a percentage of TP	$LF_{\%}$	%
Normalized LF as a percentage of TP-VLF	LF_{norm}	n.u.
Power in the high frequency range 0.15-0.4Hz	HF	ms^2
Natural logarithm of HF	HF_{log}	
HF as a percentage of TP	$HF_{\%}$	%
HF as a percentage of TP-VLF	HF_{norm}	n.u.
LF to HF ratio	LF/HF	
Nonlinear		
Approximate Entropy	ApEn	
Short-term scaling exponent derived from Detrended Fluctuation Analysis	α_1	
Long term scaling exponent derived from Detrended Fluctuation Analysis	α_2	

Non-invasive recording of the arterial pressure wave

The arterial pulse was recorded at every subject by applanation tonometry of the radial artery as previously described[26]. Each subject rested for at least 10min before the measurement which was performed in the supine position. The subjects were examined in a quiet room with constant temperature (~ 21-23 °C), at least 12 hours from their last meal, coffee or cigarette. Recording and analysis of the peripheral (radial) and aortic pressure waves were performed by using the SphygmoCor apparatus (AtCor Medical Pty. Ltd, Sydney, Australia). In brief, peripheral pressure waves were recorded at the radial artery by applanation tonometry and a single averaged pressure waveform was obtained from approximately 10-20 waveforms. Pressure waves were calibrated using brachial SBP and DBP values. Each recoding was assessed by specific quality control criteria according to the manufacturer's instructions (quality index≥85%). Three measurements with acceptable quality index were averaged to calculate the hemodynamic parameters used in the study. The apparatus software mathematically transformed the radial pressure waveforms by using transfer functions to derive the respective aortic pressure waves and further analyzed them as previously described[27]. The determined pressure and time-related parameters are reported at table 2.

Pulse wave analysis based on the golden ratio φ (phi)

The golden ratio or divine proportions between two elements α and b that fulfill the equation [1] can be applied for the analysis of the arterial pulse wave at the pressure and time dimension. According to this concept, BP values, namely DBP, pulse pressure (PP), and SBP may correspond to the elements α, α+β and β as illustrated at figure 1. Similarly, at the time scale (axis), the diastolic duration (DD), ejection duration (ED) and cardiac period can be expressed by three lines α, β and α+β, respectively. Theoretically, by this geometrical analysis, the „golden" or „divine"

Table 2. Descriptive, hemodynamic and heart rate variability characteristics of the study population.

Parameter	
Age (years)	39.6±13.9
Height (cm)	173±9
Weight (kg)	77.9±15.8
BMI (kg/m^2)	25.9±4
Gender (males, n, %)	44 (61.1%)
Smoking status	
Smoker, %	31 (43.1%)
Non-smoker, %	35 (48.6%)
Ex-smoker, %	6 (8.3%)
Brachial SBP (mmHg)	124.7±21.5
Brachial DBP (mmHg)	80.3±10.6
Brachial PP (mmHg)	44.4±18.7
Mean pressure (mmHg)	95.3±12.6
Aortic SBP (mmHg)	112.2±17
Aortic DBP (mmHg)	81.2±10.7
Aortic PP (mmHg)	30.9±12.3
Ejection Duration (msec)	328±19
Diastolic Duration (msec)	575±129
Cardiac Period (msec)	903±143

Values are expressed as mean±standard deviation for continuous variables or as absolute number and percentage for categorical variables. BMI: body mass index, SBP: systolic pressure, DBP: diastolic blood pressure, PP: pulse pressure.

Table 3. Linear and nonlinear indices of 24 hours heart rate variability.

Heart Rate Variability indices	
Time domain	
HR24 (bpm)	76.1±9.6
SDNN (ms)	154.2±46.2
SDANN (ms)	137±39.8
ASDNN (ms)	65.4±31.5
RMSSD (ms)	39.2±38.8
PNN50 (%)	11.7±13.8
Frequency domain	
TP (ms^2)	4985±5471
TP_{log}	3. 6±0.3
VLF (ms^2)	2761±2070
VLF_{log}	3.3±0.3
LF (ms^2)	1417±2066
LF_{log}	3.0±0.4
$LF_{\%}$ (%)	26.4±6.3
LF_{norm} (n.u.)	68.8±8.6
HF (ms^2)	611±1871
HF_{log}	2.4±0.5
$HF_{\%}$ (%)	8±5.6
HF_{norm} (n.u.)	19.6±8.4
LF/HF	4.3±2.2
Nonlinear dynamics	
ApEn	1.026±0.219
α1	1.276±0.175
α2	1.009±0.109

Abbreviations are defined in table 1.

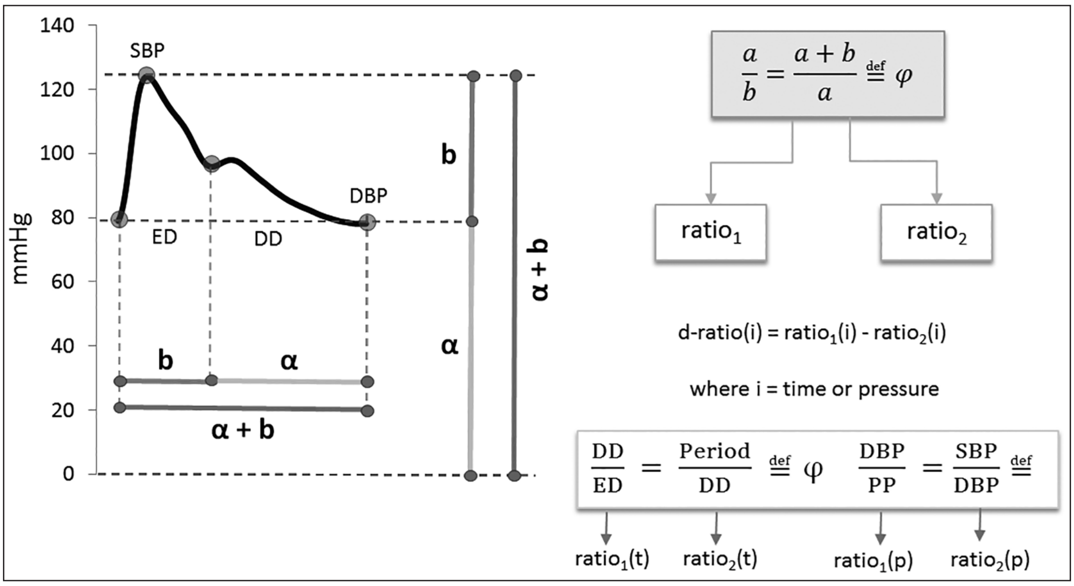

Figure 1. Analysis of the arterial pressure wave using the golden ratio φ (phi). SBP: systolic blood pressure, DBP: diastolic blood pressure, PP: pulse pressure, ED: ejection duration, DD: diastolic duration, Period: duration of the cardiac cycle.

Table 4: Bivariate linear correlations of the absolute differences of (a) the two time ratios and (b) the two pressure ratios for both brachial and aortic pressure waves with demographic, hemodynamic and heart rate variability parameters.

	Pearson Correlation Coefficients		
	Radial d-ratio(P)	***Aortic d-ratio(P)***	***d-ratio(t)***
Age	−0.117	−0.393**	−0.220
Height	0.111	0.232*	−0.017
Weight	0.025	0.046	−0.052
Body mass index	−0.057	−0.103	−0.059
Hemodynamic Parameters derived by Pulse Wave Analysis			
Brachial SBP	0.083	−0.259*	0.036
Brachial DBP	0.061	0.224	−0.027
Mean pressure	0.042	−0.060	−0.038
Brachial PP	0.060	−0.425**	0.057
Aortic SBP	0.030	−0.281*	−0.016
Aortic DBP	0.059	0.214	−0.035
Aortic PP	−0.007	−0.574**	0.010
Ejection duration	0.028	−0.144	0.239*
Diastolic duration	0.009	−0.149	0.487**
Cardiac period	0.012	−0.154	0.472**
Indices of Heart Rate Variability			
ApEn	0.124	0.062	0.024
α1	−0.020	0.096	−0.166
α2	0.000	−0.158	0.070
HR_{24hr}	−0.062	0.245	−0.366**
SDNN	0.076	0.049	0.439**
SDANN	0.055	0.053	0.456**
ASDNN	0.078	0.052	0.265*
RMSSD	0.076	0.041	0.123
PNN50	0.098	0.070	0.326**
TP	0.083	0.038	0.187
TP_{log}	0.049	0.089	0.330**
VLF	0.108	0.029	0.425**
VLF_{log}	0.053	0.064	0.387**
LF	0.040	0.038	0.062
LF_{log}	0.043	0.128	0.220
$LF_{\%}$	−0.025	0.143	−0.173
LF_{norm}	0.015	0.061	−0.317**
HF	0.064	0.034	−0.009
HF_{log}	0.020	0.091	0.323**
$HF_{\%}$	0.039	0.132	0.162
HF_{norm}	0.027	0.070	0.339**
LF/HF	0.097	0.083	−0.302**

* and ** indicate that correlation is significant at the 0.05 and 0.01 level, respectively

SBP, DBP: systolic and diastolic blood pressure respectively, PP: pulse pressure. Abbreviations of heart rate variability indices are defined in table 1.

pressure and time ratios of an arterial pressure waveform should follow the golden ratio φ (phi) according to the equations:

$$\frac{DD}{ED} = \frac{Period}{DD} \stackrel{\text{def}}{=} \varphi \quad and \quad \frac{DBP}{PP} = \frac{SBP}{DBP} \stackrel{\text{def}}{=} \varphi$$

[eq. 2], where φ ≈1.618

Pulse waveforms that deviate from the „golden" pulse will exhibit pressure or time ratios that differ from 1.618. In order to quantify this deviation we determined the absolute difference between the two pressure and time ratios as following:

d-ratio(p) = abs [(DBP/PP) – (SBP/DBP)], [eq. 3]

d-ratio(t) = abs [(DD/ED) – (Period/DD)], [eq. 4]

The net values of the above differences were also determined. Absolute differences close to zero (0) indicate an equality of the two ratios meaning that the pressure or time proportions are equal by definition to the golden number 1.618. As the absolute differences increase then the pressure or time proportions deviate from the golden ratio and thus the pulse differs from the theoretical „golden" pulse.

Results

The main demographic and hemodynamic characteristics of the study population are reported in Table 2. The linear (time- and frequency-domain) as well as the nonlinear dynamic indices of 24-hr HRV are reported in Table 3.

The absolute differences between (a) the two time ratios and (b) the two pressure ratios for both radial and aortic pressure waves (figure 1) were analyzed by bivariate correlation coefficients versus demographic, hemodynamic and HRV parameters (Table 3).

It is notable that the absolute difference between the time ratios derived from the radial pressure waves (figure 1) recorded by applanation tonometry were associated significantly with most of the time-domain and frequency domain indices of HRV. More specifically positive correlations were found for SDNN, SDANN, ASDNN, PNN50, HF_{log} and HF_{norm}, whereas negative correlations were observed for HR_{24hr}, LF_{norm} and LF/HF (Table 4). The respective absolute difference between the two pressure ratios had no significant correlation with the computed HRV indices.

Multiple Linear Regression Analysis

By multivariate linear regression analysis we further examined whether the observed associations with d-ratio(t) remained significant after adjustment for the potential confounding effect of age, gender, BMI and blood pressure (mean pressure and pulse pressure). It was found that d-ratio(t) was still significantly related with SDNN (b=0.363, p<0.001), SDANN (b=0.402, p<0.001), PNN50 (b=0.233, p=0.03), HR_{24hr} (b=-0.369, p=0.001), TP_{log} (b=0.215, p=0.028), VLF (b=0.322, p=0.001), VLF_{log} (b=0.281, p=0.004), LF_{norm} (b=-0.324, p=0.007), HF_{log} (b=0.203, p=0.042), HF_{norm} (b=0.274, p=0.019), and LF/HF (b=-0.256, p=0.031), independently of age, gender, BMI, MAP and brachial PP. The strongest independent association was observed between d-ratio(t) and SDANN with the former index explaining almost the 16% of SDANN variation regardless from age, gender, BMI, MAP and PP.

Still, a critical question is whether the observed associations of HRV indices with d-ratio(t) are superior than the associations of ED, DD, cardiac period with HRV indices, per se.

The absolute difference d-ratio(t) between the $ratio_1$(t) and the $ratio_2$(t) (equation 4) which expresses the deviation of the time-intervals' proportions from the golden number 1.618, has no collinearity with ED (r=0.239), DD (r=0.487) and cardiac period (r=0.472).

The HRV indices which are significantly correlated with d-ratio(t) as reported in table 4, were adjusted for ED and DD in a separate multiple regression model (table 5). Surprisingly, it is shown that the d-ratio(t) is associated with SDNN, SDANN, VLF, LF_{norm}, HF_{log}, HF_{norm}, and LF/HF independently of ED and DD (table 5).

Discussion

The functional characteristics of the autonomic nervous system and the hemodynamic profile of systemic circulation are both critical factors modulating and reflecting the cardiovascular health. Analysis of HRV and arterial pulse wave morphology provide valuable information concerning ANS function and systemic circulation respectively. For the first time a new geometrical analysis was applied on non-invasively recorded peripheral (radial) and central (aortic) arterial pressure waves revealing some novel pressure wave phenotypes. It was demonstrated that the new phenotypic, geometrical biomarkers based on the golden ratio (φ) or divine proportions were significantly and independently associated with HRV indices and especially those computed at the frequency domain in healthy subjects. Specifically the absolute difference of the time ratios DD/ED and Period/DD (d-ratio(t)) of the arterial pressure wave was a

Table 5. Correlation coefficients of specific time measures used for the calculation of d-ratio(t) which indicates the deviation from the golden ratio (φ) versus heart rate variability indices.

	ED	*DD*	*Period*	*ratio$_1$(t)*	*ratio$_2$(t)*	*Net d-ratio(t)*	*d-ratio(t)*
SDNN	0.309**	0.483**	0.478**	0.463**	−0.362**	0.441**	0.439** § †
SDANN	0.330**	0.485**	0.483**	0.458**	−0.358**	0.436**	0.456** § †
ASDNN	0.173	0.329**	0.320**	0.333**	−0.269*	0.319**	0.265*
PNN50	0.131	0.315**	0.302**	0.323**	−0.232*	0.302**	0.326** §
HR_{24hr}	−0.423**	−0.605**	−0.604**	−0.587**	0.534**	−0.579**	−0.366** §
TP_{log}	0.229	0.383**	0.377**	0.379**	−0.303**	0.363**	0.330** §
VLF	0.226	0.468**	0.454**	0.475**	−0.374**	0.453**	0.425** § †
VLF_{log}	0.276*	0.458**	0.451**	0.452**	−0.369**	0.434**	0.387** §
LF_{norm}	−0.021	−0.123	−0.114	−0.118	0.011	−0.090	−0.317** § †
HF_{log}	0.152	0.251*	0.248*	0.242*	−0.150	0.220	0.323** § †
HF_{norm}	0.006	0.066	0.061	0.058	0.061	0.027	0.339** § †
LF/HF	−0.100	−0.114	−0.116	−0.085	−0.014	−0.059	−0.302** § †

ED: ejection duration, DD: diastolic duration, ratio1(t)=DD/ED, ratio$_2$(t)=Period/DD, d-ratio(t): the absolute difference between ratio$_1$(t) and ratio$_2$(t). Abbreviations of heart rate variability indices are defined in table1.
§ remained significant ($p<0.05$) in a multivariate regression model adjusting for age, gender, mean arterial pressure, brachial pulse pressure and body mass index.
† remained significant ($p<0.05$) in a multivariate regression model adjusting for ejection (ED) and diastolic (DD) duration.

significant predictor of SDNN, SDANN, PNN50, HR_{24hr}, TP_{log}, VLF, VLF_{log}, LFnorm, HF_{log}, HF_{norm} and LF/HF independently of age, gender, BMI, mean arterial pressure and brachial pulse pressure.

The arterial pulse and particularly the pressure wave is commonly examined: (a) at the brachial artery with the main purpose to determine its maximum and minimum pressure levels using cuff-based sphygmomanometers and (b) at the radial artery by palpation in order to determine its frequency via the measurement of heart beats per minute and consequently to estimate the pulse period. Gradually, the classic, traditional sphygmomanometric techniques[28] are transforming to more advanced technologies offering the recording and computation of a plethora of hemodynamic biomarkers others than SBP, DBP, MAP and heart rate such as central (aortic) blood pressure[29], wave reflection indices (augmentation index, reflection timing and magnitude), pulse transit time[30] and arterial stiffness[31], cardiac output[32-34] and others[35, 36]. More interestingly wearable devices have been also developed thus providing the possibility of ambulatory monitoring of the above mentioned parameters[37, 38].

Nonetheless, there is limited information concerning the association of pressure wave features with HRV indices especially in healthy subjects. Although a relationship between arterial stiffness (assessed by pulse wave velocity) and HRV has been reported in diabetic patients[39,40] the potential association of HRV indices with pressure wave characteristics is still cloudy. In a previous study of healthy subjects, it was observed that traditional cardiovascular disease factors (i.e. age and heart rate) rather than hemodynamic parameters predominantly influenced long-term, time- and frequency-domain HRV indices[21]. This was also apparent for several pressure markers derived by PWA including central pressure and augmentation index.

In the present study we applied for the first time the golden ratio φ (phi) on peripheral and central pressure waveforms recorded non-invasively in healthy subjects. Deviation of the arterial pulse from the concept of the „golden“ pulse was quantified in both the pressure dimension (using the pressure ratios DBP/PP and SBP/DBP and their absolute difference) and the time dimension (using the ratios DD/ED, Period/DD and their absolute difference). Greater differences between these ratios indicate a greater deviation from the golden ratio φ. The most striking observation of this study is the significant correlation of d-ratio(t) with the frequency domain indices of HRV regardless of age, gender, blood pressure levels and BMI. In contrast, BP markers and pulse wave time indices (ED and DD) were not related to most of the spectral characteristics of HRV.

Conclusions

This finding implies that the specific geometrical analysis of the peripheral arterial pulse reflects or characterizes specific HRV features. The potential pathophysiological background and the underling mechanisms of this association can be hardly explained by the current study design. Also, it is not possible yet to discriminate hemodynamic, autonomic nervous function or mathematical/statistical influences that might contribute to this finding. Undoubtedly, the concept of the „golden" or „divine" pulse and its potential research or clinical utility and relevance is very challenging. The application of the golden ratio φ for the analysis of the arterial pulse merits further investigation and may open a new window to the evaluation of the cardiovascular and autonomic nervous systems.

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Compliance with Ethics Requirements:

„The authors declare no conflict of interest regarding this article"

„The authors declare that all the procedures and experiments of this study respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008(5), as well as the national law. Informed consent was obtained from all the patients included in the study"

„All institutional and national guidelines for the care and use of laboratory animals were followed"

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