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연령증가에 따른 지첨용적맥파의 주파수 영역에서의 변화

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Abstract

Age-related Changes of the Finger Photoplethysmogram in Frequency Domain Analysis

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Objectives

It is well known that some parameters of the photoplethysmogram (PPG) acquired by time domain contour analysis can be used as markers of vascular aging. But the previous studies that have been performed for frequency domain analysis of the PPG to date have provided only restrictive and fragmentary information. The aim of the present investigation was to determine whether the harmonics extracted from the PPG using a fast Fourier transformation could be used as an index of vascular aging.

Methods

The PPG was measured in 600 recruited subjects for 30 second durations. To grasp the gross age-related change of the PPG waveform, we grouped subjects according to gender and age and averaged the PPG signal of one pulse cycle. To calculate the conventional indices of vascular aging, we selected the 5−6 cycles of pulse that the baseline was relatively stable and then acquired the coordinates of the inflection points. For the frequency domain analysis we performed a power spectral analysis on the PPG signals for 30 seconds using a fast Fourier transformation and dissociated the harmonic components from the PPG signals.

Results

A final number of 390 subjects (174 males and 216 females) were included in the statistical analysis. The normalized power of the harmonics decreased with age and on a logarithmic scale reduction of the normalized power in the third ($r = -0.492$, $P < 0.0001$), fourth ($r = -0.621$, $P < 0.0001$) and fifth harmonic ($r = -0.487$, $P < 0.0001$) was prominent. From a multiple linear regression analysis, Stiffness index, reflection index and corrected up-stroke time influenced the normalized power of the harmonics on a logarithmic scale.

Conclusions

The normalized harmonic power decreased with age in healthy subjects and may be less error prone due to the essential attributes of frequency domain analysis. Therefore, we expect that the normalized harmonic power density can be useful as a vascular aging marker.

Key words

Photoplethysmography; Vascular aging; Spectrum analysis; Harmonics

INTRODUCTION

The finger photoplethysmogram (PPG) is obtained with a device that can measure pulsatile changes of the blood volume in the microvascular bed of the fingertip. The PPG based on an optical technology can provide valuable information about the characteristics of the cardiovascular system1). The PPG waveform is determined mainly by the characteristics of the systemic circulation, including the pressure wave reflection and the pulse wave velocity (PWV) of pressure waves in the aorta and large arteries2). In contour analysis, a characteristic change of the PPG waveform with advancing age, which is one of the major risk factors of cardiovascular disease, has been described. It is well known that some parameters of the PPG related with arterial stiffness and compliance can be used as markers of vascular aging3-5). The up-stroke time (UT)6), augmentation index (AIx)7), stiffness index (SI)8), reflection index (RI)9) and the second derivative of the finger photoplethysmogram (SDPTG) indices10) are representative markers of vascular aging obtained from contour analysis of the PPG.

Although an assessment of the arterial properties according to the contour analysis of the PPG is simple, convenient and non-invasive, the PPG has been less widely used due to influences of measurement errors. These errors result from the difficulty in automatic recognition of the inflection points caused by instability of the PPG signal and smooth waveform11-12), fluctuation of the baseline, variation of the pulse waveform by a discrepancy in the signal bandwidth5), and the influence of sympathetic activity and temperature variations. Especially, the difficulty to detect inflection points, the fluctuation of the baseline and the discrepancy in signal bandwidth are unconquerable problems in the contour analysis of the PPG.

Frequency domain analysis has the advantages that it provides a good differentiation between signal and noise and filtration is not necessary13).

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In addition the harmonics are conspicuous so that automatic recognition of the peak points can be easy in the spectral analysis of the PPG signal. The frequency spectrum analysis of the PPG is less error prone than the contour analysis.

However, the previous studies that have been performed for the frequency domain analysis of the PPG to date have provided only restrictive and fragmentary information. Therefore, we do not clearly understand how the specific Fourier components of the PPG change with advancing age, and which cardiovascular factors are related to these Fourier components. Considering that by the 1950s age-related changes of the amplitude of harmonic moduli of the arterial pressure wave were already investigated, it is surprising that there is insufficient information about the frequency domain information of the PPG14).

We hypothesized that if there is linear age-related change of the PPG in time domain, we may also found parallel change in frequency domain. To determine whether the harmonics dissociated from the finger photoplethysmogram using a fast Fourier transformation (FFT) can be used as an index of vascular aging, we surveyed age-related changes of the amplitude of harmonic moduli of the PPG and investigated the relationship of the harmonic components and the parameters used in the contour analysis.

METHODS

1. Study Subjects

We recruited 600 subjects in the health assessment center at Kyunghee University Medical Center. The PPG was included in the routine medical test program of our health assessment center. Subjects were presented with an informed consent prior to measurement. To provide a representative sample of a normal healthy population, subjects were excluded if any of the following exclusion criteria were present: current use of medication for hypertension, history of diabetes mellitus, cerebral vascular accident, ischemic heart disease, valvular heart disease, atrial fibrillation, frequent ventricular ectopic heartbeat, chronic renal failure, significant limb tremor, deformation of limbs and Raynaud's phenomenon.

2. Measurement of the PPG Signal

The subjects fasted for 12 hours before visiting the health assessment center. After comprehensive medical testing including blood test, the PPG was measured in the supine position at the cuticle of the second digit of the left hand wrapped with a black woven cuff to block off the outside light by use of a PT-300 instrument (Fukuda Denshi, Tokyo, Japan). All subjects refrained from smoking for at least 4 hours prior to the PPG measurement. The examination room was air-conditioned with a temperature of 24–26 oC, with a humidity of

45–65%. We acquired the PPG signal with a stabilization of respiration for 30 seconds. The analogue signals of the PPG were converted into digital signals with an MP100A instrument (BIOPAC Systems, Goleta, CA USA). The sampling frequency was 500 Hz. The digitalized signal data were transmitted to a personal computer for recording and subsequent off-line analysis. AcqKnowledge software (version 3.2.2, BIOPAC Systems, Goleta, CA USA) was used for filtration, coordinate acquisition of inflection points and FFT.

3. Age-related Changes of the PPG Waveform

To grasp the gross age-related change of the PPG waveform, subjects were grouped according to gender and age. The classification criteria of age were <30, 30–39, 40–49, 50–59 and ≥60 years. The recorded PPG signals were filtered with a band pass finite impulse response (FIR) filter to remove noise. We set up a cutoff frequency of 10 Hz and the number of coefficients as 200 for filtration. Only one pulse cycle, of which the baseline was stable in the filtered PPG signal for 30 seconds was selected and then was averaged with the use of MATLAB software (version 5.3.0, MathWorks Inc., Natick, MA USA). To compensate for a discrepancy in pulse cycles among the different individuals, we standardized the individual pulse cycles to the average pulse cycle on a per-group basis.

4. UT, SI, RI and SDPTG Indices

To calculate UT, SI and RI, we filtered the recorded PPG signals with the same method described above and selected the 5–6 cycles of pulse in which the baseline was relatively stable. We then acquired the coordinates of the start point, early systolic peak and early diastolic peak using the peak detector function of the AcqKnowledge software. The peak detector finds the highest or least valued point in the data between crossings when data crosses a threshold which the user inputs. To avoid a mistake in detecting inflection points, we acquired coordinate of each and every peak step-by-step changing the threshold manually. When the dicrotic notch was obscure, we found the diastolic peak point with the first derivative of PPG according to the use of Millasseau's method8). Finally the acquired coordinates were averaged.

UT was defined as the time elapsed from the start point to the systolic peak in the PPG. UT was corrected by the pulse rate to compensate for a discrepancy in pulse rate ($cUT=UT/\sqrt{a}$ cycle of the pulse)6). SI was defined as the height divided by the time delay between the systolic and diastolic peaks, and RI as the ratio of the diastolic peak to the systolic peak9). Fixing the cutoff frequency of 10 Hz, and the number of coefficients as 2, we performed the second derivation of the PPG signals to detect the SDPTG indices. We acquired the coordinates of the a, b, c, d and e wave peaks from the same pulse previously selected for UT, SI and RI, and calculated the aging index of the second derivative of the finger photoplethysmogram (SDPTG AI) according to Takazawa's definition10).

5. Frequency Spectrum Analysis of the PPG Signal

To remove 60 Hz electrical noise acquired along with PPG signal, the recorded PPG signals were filtered with a low pass FIR filter. We set up a cutoff frequency of 50 Hz and the number of coefficients as 200 for filtration, and then performed a power spectral analysis on the PPG signals for 30 seconds using FFT. The hamming window was applied to decrease the Gibb's phenomenon. The major peak of the fundamental frequency around the pulse rate in the spectrum and serial peaks around the multiples of the fundamental frequency were identified (Fig 1B, D). Only six harmonics were included in the statistical analysis because the spectral peaks beyond the sixth harmonic were too small to assess in the younger subjects (Fig 1B). The power spectrum was normalized by dividing the power at each harmonic by that of the fundamental.

The following terms and definitions were used in this study: Fk, the frequency at which the kth harmonic occurred; PWRk, amplitudeof the kth harmonic modulus nPWRk, amplitude of the kth harmonic modulus normalized to that of the fundamental (nPWRk=PWRk/PWR1); Ln(nPWRk), logarithmic scale of the normalized amplitude of the kth harmonic modulus.

6. Statistical Analysis

Statistical analyses were performed by using SPSS software (version 12.0.0, SPSS Inc., Chicago, IL USA). To provide an overview of the relationship between age and clinical characteristics, data were grouped according to age. One-way analysis of variance (ANOVA) and the chi-squared test were used to compare the clinical characteristics among the age groups. Independent student t-test was used to compare the clinical characteristics between men and women. The relationship between age and parameters of the PPG contour analysis including SI, RI, cUT and SDPTG indices was assessed by means of Pearson's correlation coefficient. The relationship between age and the parameters of PPG frequency analysis including the normalized amplitude of harmonics and its logarithmic scale was also assessed by Pearson's correlation coefficient. Thereafter, to determine the factors influencing the power density of harmonics, stepwise multiple linear regression analyses were performed with a logarithmic scale of the normalized amplitude of the harmonics as dependent variables and parameters mainly determined by the PPG contour including SI, RI and cUT as independent variables. All statistical tests were 2-sided, and a p-value less than 0.05 was considered as significant.

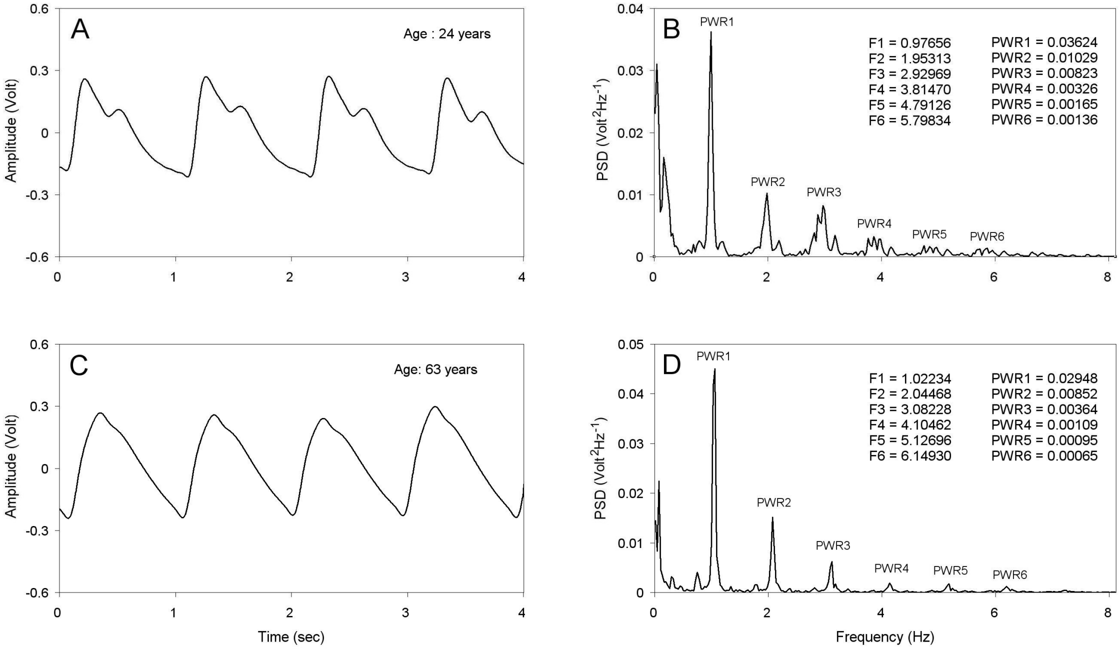

Fig. 1. PPG waveforms (A, C) recorded at the left index finger and power spectra (B, D) of the PPG waveforms for 30 seconds. The major peak as the first harmonic around the pulse rate in the spectrum and serial peaks around the multiples of the first harmonic frequency were identified as the second, third... harmonics. PSD, power spectral density; Hz, Hertz; Fk, the frequency of the kth harmonic; PWRk, amplitude of the kth harmonic modulus.

RESULTS

1. Clinical Characteristics of the Subjects

A final number of 390 subjects (174 males and 216 females) among the recruited 600 subjects were included in the statistical analysis. The age distribution was from 18 to 84 years. The clinical characteristics of the subjects are summarized in Table 1. The major reason for exclusion from the study included medication for hypertension (n = 159), history of ischemic heart disease (n = 9), diabetes mellitus (n = 27), cerebral vascular accident (n = 3) and valvular heart disease (n = 2). Other reasons for exclusion included atrial fibrillation, frequent ventricular ectopic heartbeat, chronic renal failure and significant limb tremor. Six subjects were excluded because the baselines of the PPG signals fluctuated widely and were unable to select 5~6 cycles of pulse for the contour analysis.

2. Gross Age-related Changes of the PPG Waveform

The gross age-related changes of the PPG

Table 1. Subject Characteristics According to Age Category

	≤30 years		30-39 years		40-49 years	
	Male	**Female**	**Male**	**Female**	**Male**	**Female**
Number of subjects	32	31	56	51	32	66
Age (years)	24.1±3.4	24.7±3.4	33.9±2.9	34.4±2.9	44.1±2.7	45.0±3.0
Height (cm)	172.8±6.0	161.8±5.0*	170.5±10.2	158.9±5.1*	167.5±12.0	157.3±5.0*
Weight (kg)	70.0±13.2	55.4±8.3*	74.1±11.7	55.6±8.0*	71.0±8.4	57.0±6.1*
Body mass index (kg/m2)	23.4±3.9	21.1±2.8*	25.8±5.4	22.0±2.8*	25.8±6.3	23.1±2.4*
Systolic BP (mmHg)	112.2±11.0	105.5±9.3*	118.4±15.9	106.5±12.0*	119.1±14.9	112.8±17.9
Diastolic BP (mmHg)	69.7±8.6	65.2±6.8*	71.3±8.1	67.5±8.0*	73.8±10.1	69.9±8.7
Pulse pressure (mmHg)	42.5±9.2	40.3±9.5	47.2±15.7	39.0±9.8*	45.3±12.2	42.9±14.1
Mean BP (mmHg)	83.9±8.4	78.6±6.3*	87.0±8.5	80.5±8.3*	88.9±10.4	84.2±10.6*
Pulse rate (beats/min)	65.8±10.2	65.5±6.6	69.3±9.6	68.1±9.0	69.4±9.5	65.7±9.4
Total cholesterol (mg/dl)	169.4±31.8	175.5±21.5	195.0±36.2	177.1±28.2*	189.6±34.4	188.0±32.2
Triglyceride (mg/dl)	101.4±60.3	81.7±36.5	166.6±103.4	107.8±69.8*	169.4±92.6	108.2±53.9*
Total lipid (mg/dl)	497.2±93.1	504.2±58.5	600.8±159.5	524.1±108.3*	606.2±127.6	548.0±93.6*
Phospholipid (mg/dl)	179.3±24.2	191.4±19.2*	200.9±36.4	191.0±26.8	200.6±29.5	201.3±29.0
HDL cholesterol (mg/dl)	45.8±8.8	54.4±12.2*	39.8±7.5	47.5±8.7*	40.8±8.6	49.7±13.2*
Glucose (mg/dl)	84.4±10.6	82.0±7.2	89.2±10.6	85.8±8.5	91.9±13.2	89.0±8.2
BUN (mg/dl)	12.8±3.1	10.6±2.2*	14.8±3.8	11.9±3.0*	14.0±4.4	12.5±3.6
creatinine (mg/dl)	0.96±0.11	0.73±0.07*	0.97±0.11	0.74±0.10*	0.96±0.11	0.77±0.13*
Hemoglobin (g/dl)	15.5±0.9	12.8±1.0*	15.4±1.1	12.7±1.0*	14.9±0.8	13.0±0.9*
Hematocrit (%)	44.6±2.7	37.4±2.8*	44.5±3.1	37.2±2.6*	43.3±2.5	37.5±2.5*

Values in the final column represent results of one-way analysis of variance (ANOVA) and chi-squared test for age. Data are mean±SD. BP, blood pressure.

*P<0.05 (Male vs Femal in each age group).

Table 1. Continued

	50-59 years		≥60 years		Significance
	Male	**Female**	**Male**	**Female**	
Number of subjects	33	43	21	25	P=0.0538
Age (years)	54.7±2.9	54.8±2.3	64.5±4.8	64.8±5.4	
Height (cm)	168.4±6.6	155.6±4.3*	166.1±6.6	152.3±5.1*	P<0.0001
Weight (kg)	68.5±9.4	60.2±7.6*	65.1±8.2	56.1±7.0*	P=0.0597
Body mass index (kg/m2)	24.2±3.4	24.9±3.4	23.6±2.6	24.2±3.1	P<0.05
Systolic BP (mmHg)	123.3±17.8	118.8±18.2	121.9±21.8	123.6±21.0	P<0.0001
Diastolic BP (mmHg)	72.1±9.9	71.6±9.2	72.9±11.9	73.6±10.8	P<0.01
Pulse pressure (mmHg)	51.2±13.4	47.2±13.5	49.0±12.6	50.0±16.8	P<0.01
Mean BP (mmHg)	89.2±11.5	87.4±11.2	89.2±14.8	90.3±12.7	P<0.0001
Pulse rate (beats/min)	67.8±11.4	66.3±8.1	65.6±9.7	70.2±10.7	P=0.1750
Total cholesterol (mg/dl)	201.6±35.8	207.5±28.1	189.1±37.9	200.5±30.5	P<0.0001
Triglyceride (mg/dl)	150.2±103.4	163.7±122.7	164.6±73.0	144.6±89.0	P<0.01
Total lipid (mg/dl)	601.3±128.4	637.2±145.1	583.3±126.9	598.8±116.3	P<0.0001
Phospholipid (mg/dl)	204.1±29.9	218.8±29.2*	197.5±34.0	210.1±28.1	P<0.0001
HDL cholesterol (mg/dl)	44.0±10.1	46.7±13.1	39.7±8.7	46.6±9.0*	P<0.01
Glucose (mg/dl)	100.0±31.8	94.7±23.1	93.4±16.8	96.5±22.0	P<0.0001
BUN (mg/dl)	14.1±3.4	14.4±4.5	16.0±3.6	15.3±4.5	P<0.0001
creatinine (mg/dl)	0.94±0.13	0.76±0.08*	1.00±0.29	0.76±0.11*	P=0.5711
Hemoglobin (g/dl)	15.0±1.1	13.3±0.9*	14.3±1.1	12.9±0.8*	P<0.05
Hematocrit (%)	43.1±3.2	38.8±2.6*	42.0±3.1	38.0±2.8*	P<0.05

waveform are shown in Figure 2. The rising edge of the systolic peak was sharp and the dicrotic notch was obvious in the representative waveform of men under 20 years of age. The edge of the systolic peak in women under 20 years of age was more flat than that in men. In

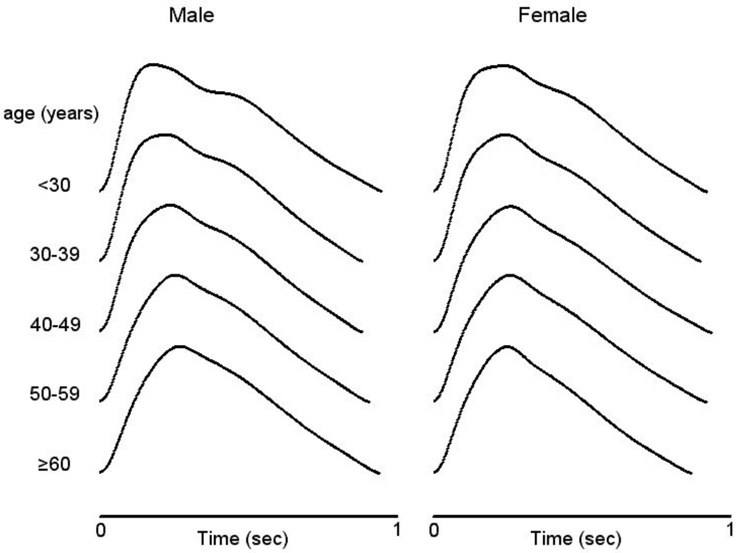

Fig. 2. Gross age-related changes of the PPG waveforms. We averaged the PPG waveforms after standardizing the respective pulse cycles to the average pulse cycle on a per-group basis.

middle age, the edge of the systolic peak became round and the dicrotic notch became obscure with advancing age. As described in a previous study5), in older subjects the contour of the PPG became smooth and the dicrotic notch diminished. Eventually the PPG waveform changed into a triangular and simple shape.

3. Relationships of SI, RI, cUT and SDPTG indices with age

SI (r = 0.430, P<0.0001), cUT (r = 0.542, P <0.0001), SDPTG AI (r = 0.786, P<0.0001), b/a (r = 0.747, P<0.0001) and d/a (r = -0.731, P<0.0001) were strongly correlated with age. However, RI (r = 0.121,P<0.05) was weakly correlated with age. From univariate analysis, the SI, RI, cUT and SDPTG indices were strongly correlated with each other. SI was correlated significantly with RI (r = 0.661, P<0.0001), cUT (r = 672, P<0.0001), SDPTG AI (r = 0.576, P<0.0001), b/a (r = 0.555, P<0.0001) and d/a (r = -0.632, P<0.0001).

4. Frequency Spectrum Analysis of the PPG Signal

1) Relationships of nPWRk and Ln(nPWRk) with age

$nPWR_2$ (r = -0.286, P < 0.0001), $nPWR_3$ (r = -0.482, P < 0.0001), $nPWR_4$ (r = -0.564, P < 0.0001), $nPWR_5$ (r = -0.467, P < 0.0001) and $nPWR_6$ (r = -0.263, P < 0.0001) were correlated with age.

A slightly higher correlation was obtained for the relationship between $Ln(nPWR_k)$ and age;

Ln($nPWR_2$) ($r = -0.281$, $P < 0.0001$), Ln($nPWR_3$) ($r = -0.492$, $P < 0.0001$), Ln($nPWR_4$) ($r = -0.621$, $P < 0.0001$), Ln($nPWR_5$) ($r = -0.487$, $P < 0.0001$) and Ln($nPWR_6$) ($r = -0.273$, $P < 0.0001$).

There is higher correlation between Ln ($nPWR_k$) and age in men than women; Ln ($nPWR_2$) (Male, $r = 0.375$, $P < 0.0001$; Female, $r = 0.158$, $P < 0.05$), Ln($nPWR_3$) (Male, $r = 0.577$, $P < 0.0001$; Female, $r = 0.405$, $P < 0.0001$), Ln($nPWR_4$) (Male, $r = 0.650$, $P < 0.0001$; Female, $r = 0.586$, $P < 0.0001$), Ln($nPWR_5$) (Male, $r = 0.582$, $P < 0.0001$; Female, $r = 0.389$, $P < 0.0001$) and Ln($nPWR_6$) (Male, $r = 0.340$, $P < 0.0001$; Female, $r = 0.389$, $P < 0.01$) (Fig 3-7).

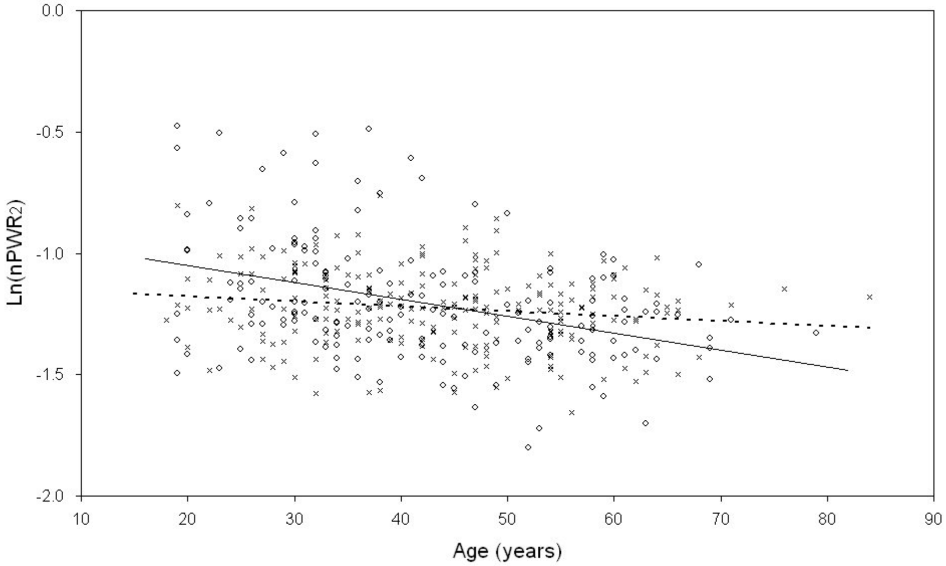

Fig. 3. Regression lines representing the effect of age on the logarithmic scale of the normalized amplitude of the second harmonic modulus for males (circles, solid line) and females (cross, dashed line).

Male Y=−0.0069X−0.9135 (r = 0.375, P<0.0001)

Female Y=−0.0020X−1.1395 (r = 0.158, P<0.05)

Ln(nPWR2), logarithmic scale of normalized amplitude of the second harmonic modulus.

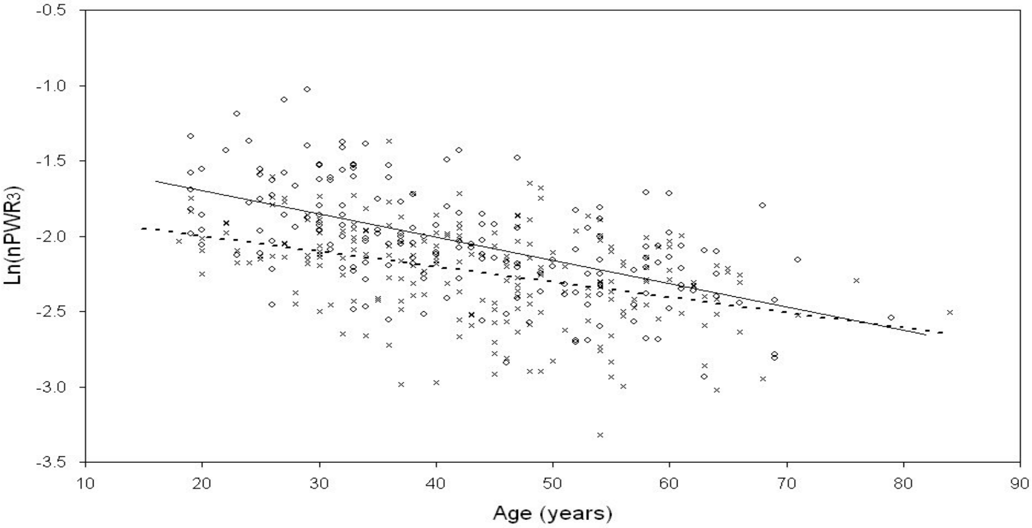

Fig. 4. Regression lines representing the effect of age on the logarithmic scale of the normalized amplitude of the third harmonic modulus for males (circles, solid line) and females (cross, dashed line).
Male Y=−0.0155X−1.3877 (r = 0.577, P〈0.0001)
Female Y=−0.0102X−1.7928 (r = 0.405, P〈0.0001)
Ln(nPWR3), logarithmic scale of normalized amplitude of the third harmonic modulus.

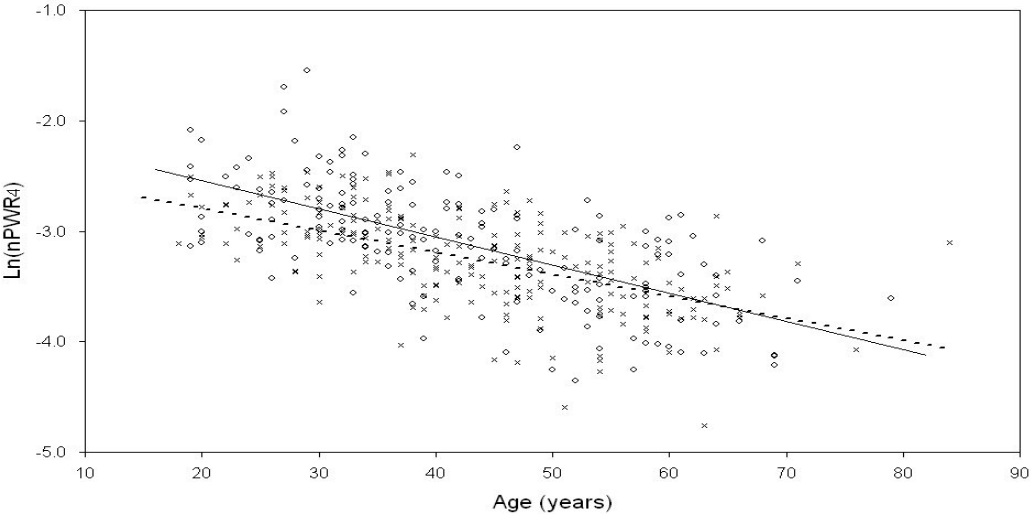

Fig. 5. Regression lines representing the effect of age on the logarithmic scale of the normalized amplitude of the fourth harmonic modulus for males (circles, solid line) and females (cross, dashed line).
Male Y=−0.0256X−2.0296 (r = 0.650, P〈0.0001)
Female Y=−0.0200X−2.3903 (r = 0.586, P〈0.0001)
Ln(nPWR4), logarithmic scale of normalized amplitude of the fourth harmonic modulus.

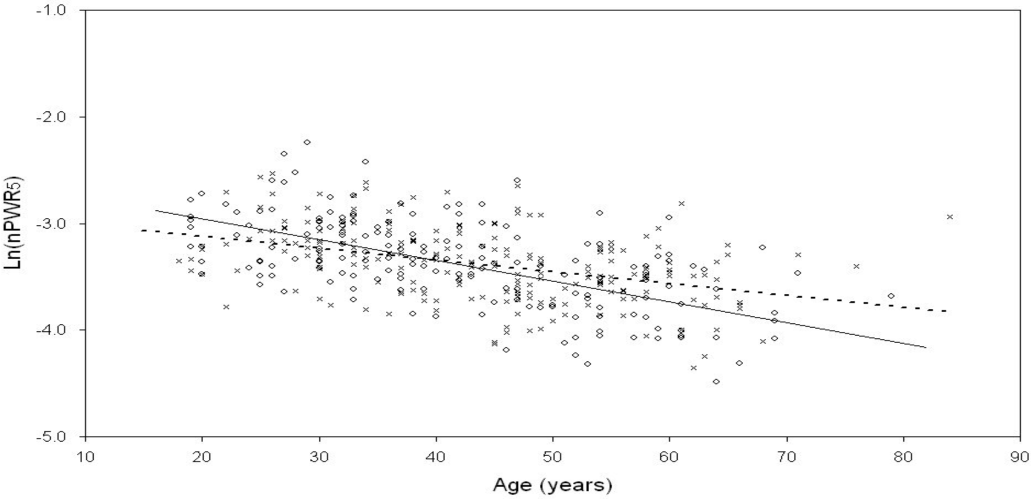

Fig. 6. Regression lines representing the effect of age on the logarithmic scale of the normalized amplitude of the fifth harmonic modulus for males (circles, solid line) and females (cross, dashed line).

Male Y=−0.0195X−2.5693 (r = 0.582, P<0.0001)

Female Y=−0.0112X−2.8975 (r = 0.389, P<0.0001)

Ln(nPWR5), logarithmic scale of normalized amplitude of the fifth harmonic modulus.

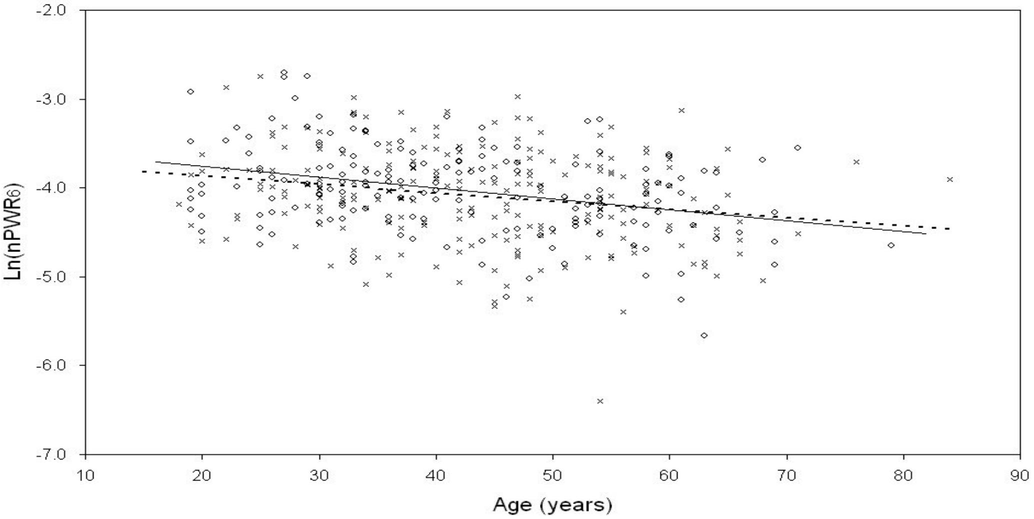

Fig. 7. Regression lines representing the effect of age on the logarithmic scale of the normalized amplitude of the sixth harmonic modulus for males (circles, solid line) and females (cross, dashed line).

Male Y=−0.0123X−3.5075 (r = 0.340, P<0.0001)

Female Y=−0.0092X−3.6879 (r = 0.389, P<0.01)

Ln(nPWR6), logarithmic scale of normalized amplitude of the sixth harmonic modulus.

2) Relationships of SI, RI, cUT and SDPTG indices with Ln(nPWRk)

From univariate analysis, the relationship of SI, RI, cUT and SDPTG indices with Ln(nPWR$_k$) are shown in Table 2. Ln(nPWR$_2$) was correlated significantly with SI (r = -0.533, P<0.0001), RI (r = -0.576, P<0.0001), cUT (r = -0.556, P<0.0001), SDPTG AI (r = -0.444, P<0.0001), b/a (r= -0.451, P<0.0001) and d/a (r = 0.465, P<0.0001). Ln(nPWR$_3$) was correlated significantly with SI (r = -0.465, P<0.0001), cUT (r = -0.657, P<0.0001), SDPTG AI (r= -0.692, P<0.0001), b/a (r = -0.669, P<0.0001) and d/a (r =0 .665, P<0.0001), and weakly with RI (r = -0.135, P<0.01). Ln(nPWR$_4$) was correlated significantly with SI (r = -0.526, P<0.0001), RI (r = -0.242, P<0.0001), cUT (r = -0.633, P<0.0001), SDPTG AI (r= -0.837, P<0.0001), b/a (r = -0.809, P<0.0001) and d/a (r = 0.818, P<0.0001). Ln(nPWR$_5$) was correlated significantly with SI (r = -0.380, P<0.0001), cUT (r = -0.463, P<0.0001), SDPTG AI (r = -0.713, P<0.0001), b/a (r = -0.701, P<0.0001) and d/a (r = 0.587, P<0.0001), and weakly with RI (r = -0.178, P<0.01). Ln(nPWR$_5$) was correlated significantly with cUT (r = -0.239, P<0.0001), SDPTG AI (r = -0.457, P<0.0001), b/a (r = -0.407, P<0.0001) and d/a (r = 0.285, P<0.0001), and weakly with RI (r = 0.229, P<0.01), but not with SI.

Ln(nPWR$_k$), logarithmic scale of normalized power of the k^{th} harmonics; SI, stiffness index; RI, reflection index; cUT, up-stroke time corrected by pulse rate; SDPTG AI, aging index of second derivative of the finger photoplthysmogram.

Table 2. Relationship Between the Parameters of PPG Frequency Analysis and Contour Analysis

	Ln(nPWR2)		**Ln(nPWR3)**		**Ln(nPWR4)**		**Ln(nPWR5)**		**Ln(nPWR6)**	
	r	**p value**	**r**	**p value**	**r**	**p value**	**r**	**p value**	**r**	**p value**
Age (years)	-0.281	<0.0001	-0.492	<0.0001	-0.621	<0.0001	-0.487	<0.0001	-0.273	<0.0001
SI (m/s)	-0.533	<0.0001	-0.465	<0.0001	-0.526	<0.0001	-0.380	<0.0001	-0.060	0.238
RI	-0.576	<0.0001	-0.135	<0.01	-0.242	<0.0001	-0.178	<0.01	0.229	<0.0001
cUT (sec)	-0.556	<0.0001	-0.657	<0.0001	-0.633	<0.0001	-0.465	<0.0001	-0.239	<0.0001
SDPTG AI	-0.444	<0.0001	-0.692	<0.0001	-0.837	<0.0001	-0.713	<0.0001	-0.457	<0.0001
b/a	-0.451	<0.0001	-0.669	<0.0001	-0.809	<0.0001	-0.701	<0.0001	-0.407	<0.0001
c/a	0.004	0.943	0.332	<0.0001	0.455	<0.0001	0.438	<0.0001	0.488	<0.0001
d/a	0.465	<0.0001	0.665	<0.0001	0.818	<0.0001	0.578	<0.0001	0.285	<0.0001
e/a	0.503	<0.0001	0.387	<0.0001	0.324	<0.0001	0.451	<0.0001	0.217	<0.0001

3) Multiple linear regression analysis

By multiple linear regression analysis with Ln($nPWR_k$) as an dependent variable and SI, RI and cUT as independent variables, the regression equation and R-squared values are shown in Table 3. Ln($nPWR_2$) (R-squared = 0.457), Ln($nPWR_3$) (R-squared = 0.471) and Ln($nPWR_4$) (R-squared = 0.432) strongly correlated with age and was well correlated with cUT, RI and SI in the model, whereas Ln($nPWR_5$) (R-squared = 0.232) and Ln($nPWR_6$) (R-squared = 0.183) were not well correlated.

Table 3. The Stepwise Regression Equation

	Independent variable	Regression coefficient	Standardized coefficient	p value
Ln(nPWR2)	Constant	0.0575		0.4293
	Up-stroke time	-2.0105	-0.3868	<0.0001
	Reflection index	-0.9685	-0.4202	<0.0001
			(model R-square = 0.457)	
Ln(nPWR3)	Constant	-1.3212		<0.0001
	Up-stroke time	-5.4392	-0.6084	<0.0001
	Reflection index	1.0354	0.2612	<0.0001
	Stiffness index	-0.0236	-0.2287	<0.0001
			(model R-square = 0.471)	
Ln(nPWR4)	Constant	-1.8175		<0.0001
	Up-stroke time	-6.1127	-0.4986	<0.0001
	Stiffness index	-0.0410	-0.2898	<0.0001
	Reflection index	0.8131	0.1496	<0.01
			(model R-square = 0.432)	
Ln(nPWR5)	Constant	-2.2281		<0.0001
	Up-stroke time	-3.9190	-0.3828	<0.0001
	Stiffness index	-0.0145	-0.1225	<0.05
			(model R-square = 0.225)	
Ln(nPWR6)	Constant	-4.5367		<0.0001
	Up-stroke time	-5.2001	-0.3946	<0.0001
	Reflection index	2.2654	0.3877	<0.0001
			(model R-square = 0.183)	

Abbreviations see in Table 2.

Discussion

Difficulty in automatic recognition of the inflection points11-12), fluctuation of the baseline and variation of the pulse waveform resulting from the discrepancy in signal bandwidth5) have been the main restrictions for the practical use of the PPG. Especially in older subjects with multiple risk factors for cardiovascular disease, the reflected wave arrives so early during systole that it becomes difficult to distinguish between the forward and reflected waves. A discrepancy in the filtering characteristics and signal bandwidth inducing a change of the PPG contour makes it difficult to interpret synthetically the results of previous studies5). The frequency domain analysis is relatively unrestricted from these error sources.

To better understand the cardiovascular properties with the PPG signal, a few studies analyzing the spectrum of various frequency components using the Fourier transformation have been performed15-18). In the frequency domain analysis of the PPG, Sherebrin and Sherebrin demonstrated that some harmonic components of the PPG were decreased in older subjects and that the decrease might be caused by loss of the dicrotic notch with age.17) Chuang et al demonstrated that the normalized power of the harmonics was shifted from high-frequency to low frequency in coronary artery disease patients after coronary artery bypass graft surgery, and the shift might be caused by a decrease of modulation activity in the autonomic nervous system.15) But information which the previous studies to date provided is too fragmentary for us to understand what the harmonics of the PPG mean and are associated with.

The present study showed that SI and cUT were strongly correlated with age. These results are consistent with results of the previous studies6),8),10). It is generally accepted that cUT increases with age in normal subjects and the increase of cUT results from increased arterial resistance and decreased vascular compliance5), and that the dicrotic notch becomes obscure with age8). The diminishing of the dicrotic notch in older subjects can be attributed to the reflected wave returning early to the fingertip due to increased pulse wave velocity and a merging with the forward wave2).

The SDPTG is well known as an index of vascular aging10),19). In our study, SDPTG indices were strongly correlated with age; SDPTG AI ($r = 0.786$, $P < 0.0001$), b/a ($r = 0.747$, $P < 0.0001$) and d/a ($r = -0.731$, $P < 0.0001$). Takazawa et al presumed that Age-related changes in the shallower b wave relative to the a wave might be caused by decreasing distensibility of the aorta and deepened d wave relative to a wave is caused mainly by increased reflection wave from the periphery10). But a late study showed that the correlations between PWV and these SDPTG indices were only weak in hypertensive patients and PWV and SDPTG might provide different information about arterial properties at central and peripheral sites20).

Our study showed that the amplitude of each harmonic modulus normalized to that of the fundamental decreased with age in the frequency domain analysis of the PPG signal. Since we identified that the dispersion of nPWRk in the younger group is larger than that in the older group and that nPWRk in the younger group falls off with advancing age more rapidly, we obtained a slightly higher correlation for the relationship between age and Ln(nPWRk). And we found that Ln(nPWRk) also decreased with age, especially when linear decreases of the third, fourth and fifth harmonic were prominent. The prominent decreases in the third, fourth and fifth harmonic did not coincide with the result of a study by Sherebrin and Sherebrin17) in that there were not significant differences of the normalized amplitude in the third, fourth and fifth harmonic modulus between the younger group and the older group. We believed that these differences might result from a small number of cases in the Sherebrin and Sherebrin study.

Although we clearly do not yet understand which physiological and clinical characteristics are related to the harmonic components dissociated from the PPG signal with Fourier transformation, we know that the decrease of the normalized harmonic power density with advancing age is dependent of the characteristic change of the PPG contour. From multiple linear regression analysis with Ln(nPWRk) as a dependent variable and cUT, SI and RI as independent variables, Ln(nPWR3) and Ln(nPWR4) strongly correlated with age and also well correlated with cUT, SI and RI in the model. According to the regression model, Ln(nPWR3) and Ln(nPWR4) were primarily affected by the time elapsed from the start point to the systolic peak as well as the time between the peak of the forward wave and the peak of the reflected wave. With advancing age, an increase of vascular resistance elongates the time between the start point and the peak of the forward wave6) and an increase of arterial stiffness reduces the time between the peak of the forward wave and the peak of the reflected wave5),8),21). These changes make the PPG waveform appear like an isosceles triangle. Therefore, we believe that the age-related change of the PPG waveform into a triangular, smooth and simple shape can be attributed to a decrease of the third and fourth harmonic components.

The present study has some limitations. First, the number of subjects over the age of 70 years was so small that it is impossible to precisely identify an age-related change in these older subjects. Considering that aortic PWV increases significantly in individuals over the age of approximately 50 years22), subjects over the age of 70 years should be included in the study to determine how precisely the specific Fourier components reflect the stiffness of the large arteries. Second, we did not sufficiently consider the effect of the autonomic nervous system on the power spectrum of the PPG. A decrease of heart rate variability with advancing age may concentrate the power of the harmonics15). To alleviate this problem, we normalized the power of each harmonic with that of the fundamental and did not choose the area under the spectrum curve but rather the amplitude of the harmonic modulus as a directing guide.

In conclusion, we have identified that the normalized harmonic power decreased with age in healthy subjects and that especially reduction in the third, fourth and fifth harmonic was prominent. The harmonic components dissociated from the PPG might be less error prone than the parameters used in contour analysis because of the essential attributes of frequency domain analysis (filters not necessary and better discrimination of noise). Therefore, we suggest that the normalized harmonic power density can be used as a new index of vascular aging. We expect that the harmonic components can be used for studying the elastic properties of the vascular system in subjects with risk factors for cardiovascular disease if it is revealed that the various cardiovascular factors are connected to specific harmonic components.

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연령증가에 따른 지첨용적맥파의 주파수 영역에서의 변화

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국문초록

연구배경과 목적

지첨용적맥파는 광학기술을 이용하여 손가락 끝에서 혈액용적의 변화를 측정하여 맥파를 검출하는 기술로서, 지첨용적맥파에 대한 시간영역 파형분석을 통해 혈관의 노화정도를 파악할 수 있음은 이미 잘 알려진 사실이다. 이에 본 연구자는 시간영역 파형분석을 통해 혈관노화지표를 얻을 수 있다면, 주파수영역분석법을 통해서도 혈관노화지표를 얻을 수 있을 것으로 가정하였다. 본 연구에서는 주파수영역에서 혈관노화지표를 찾기 위해 건강한 성인들을 대상으로 지첨용적맥파를 측정하고 주파수영역에서 분석하여 고조파가 혈관노화 지표로서 활용될 수 있는가 여부를 결정하고자 한다.

연구방법

건강인 390명(남자 174명과 여자 216명)을 대상으로 안정 후 앙와위에서 30초 동안 지첨용적맥파를 검출하였다. 검출한 맥파신호에서 기저선이 비교적 안정된 5-6개의 맥파주기를 선택하여 시간영역 파형분석을 통해 얻어지는 혈관노화지표인 승각시간, 경화지수, 반사지수, 가속도맥파를 구하였다. 주파수영역분석을 위해서는 빠른 퓨리에변환(FFT)를 실시하여 고조파 성분을 추출하였다. 특정점 검출을 위해서는 AcqKnowledge software의 peak detector 기능을 이용하였다.

연구결과

표준화된 고조파 파워는 연령증가에 따라 유의하게 감소하였다; nPWR2 ($r = -0.286$, $P < 0.0001$), nPWR3 ($r = -0.482$, $P<0.0001$), nPWR4 ($r = -0.564$, $P < 0.0001$), nPWR5 ($r = -0.467$, $P < 0.0001$) 및 nPWR6 ($r = -0.263$, $P<0.0001$).

표준화된 고조파 파워의 logarithmic scale에서 연령증가에 따라 보다 강한 선형적인 감소가 나타났다; Ln(nPWR2) ($r = -0.281$, $P<0.0001$), Ln(nPWR3) ($r = -0.492$, $P<0.0001$), Ln(nPWR4) ($r = -0.621$, $P<0.0001$), Ln(nPWR5) ($r = -0.487$, $P < 0.0001$) 및 Ln(nPWR6) ($r = -0.273$, $P<0.0001$).

승각시간, 반사지수, 경화지수를 독립변수로 한 중회귀분석에서 Ln(nPWR2) (R-squared = 0.457), Ln(nPWR3) (R-squared = 0.471) 및 Ln(nPWR4) (R-squared = 0.432)는 비교적 잘 설명되었으나, Ln(nPWR5) (R-squared = 0.232) 및 Ln(nPWR6) (R-squared = 0.183)는 비교적 잘 설명되지 않았다.

결론

건강인의 지첨용적맥파에서 기준 주파수로 표준화한 고조파 파워는 연령증가에 따라 감소였으며, 주파수영역분석이 가지는 특성을 고려해 볼 때 표준화된 고조파 파워는 기존의 시간영역 파형분석을 통해 얻어지는 혈관노화지표에 비해 잡음에 의한 오차가 보다 적을 것으로 기대된다. 따라서 우리는 표준화된 고조파 파워가 간편하고 용이하게 혈관노화를 반영하는 새로운 지표로서 활용될 수 있을 것으로 생각된다.

중심어

지첨용적맥파, 혈관노화, 주파수영역분석, 고조파

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