Relation Between Body Fat–Corrected ECG Voltage and Ambulatory Blood Pressure in Patients With Essential Hypertension

Osamu Tochikubo, Eiji Miyajima, Tomohiko Shigemasa, Masao Ishii

Abstract—Because adipose tissue has high electric resistance, the amount of body fat influences ECG voltage. In this study, body fat weight of patients with essential hypertension was measured by means of the impedance method and was used to correct mean ECG voltage. Then the relation between body fat–corrected mean ECG voltage ($V_{fm}$) and ambulatory blood pressure (BP) was investigated. The subjects were 172 patients with essential hypertension (88 men, 84 women, none receiving medication) between the ages of 30 and 75 years. Ambulatory BP was measured by a multi-biomedical recorder. Minimum sleep-time BP (base BP) was calculated to correspond with minimum sleep-time heart rate. The tetrapolar bioelectric impedance method was used to measure body fat (kg). Left ventricular mass (LVM) was obtained by echocardiography. Then comparisons were made with standard 12-lead ECG, and the statistical mean ECG voltage ($V_m$) and $V_{fm}$ were derived by multivariate statistical analysis. The following formula was devised to obtain $V_{fm}$ resulting from the multivariate analysis that demonstrated a high correlation with LVM ($r = 0.85$): $V_{fm} = 0.175(Body\ Fat)^{1/3} \times V_m + 0.5$ (mV). The coefficient of correlation ($r$) between $V_{fm}$ and ambulatory BP was not smaller than that between LVM and ambulatory BP. Base systolic BP demonstrated a significantly higher $r$ value ($r = 0.83$) with $V_{fm}/BSA^{1/2}$ (where BSA is body surface area) than mean daytime SBP ($r = 0.65$). In many subjects with white-coat hypertension, $V_{fm}/BSA^{1/2}$ was $1.33\ mV/m$ (34 of 38 cases; sensitivity, 89%; specificity, 89%). These results indicate that $V_{fm}$ is a better indicator of hypertensive left ventricular hypertrophy and that it may be useful in estimating minimum sleep-time systolic BP and in diagnosing white-coat hypertension in the outpatient clinic. (Hypertension. 1999;33:1159-1163.)

Key Words: hypertrophy, left ventricular • electrocardiography • sleep • blood pressure monitoring, ambulatory • hypertension, white-coat

Clinically, ECG detection of left ventricular hypertrophy (LVH) employs criteria of R-wave and S-wave amplitudes1–3 and QRS duration.4 ECG accuracy in detecting LVH, however, is inferior to that of the echocardiographic method.1,2 Many factors such as body weight (BW), lung tissue changes, and amount of subcutaneous fat influence the voltage of the ECG wave.5,6 Because fat is electrically resistant, when a thick layer of subcutaneous fat lies between the heart and the ECG electrodes, cardiac electric potential (voltage) attenuates before reaching the electrode. To compensate for this phenomenon, we measured body fat by means of the impedance method,7,8 and then we corrected the mean amplitude of the ECG voltage by means of body fat value to produce the optimum correlation with echocardiographic left ventricular mass (LVM) by multivariate analysis. Next, we investigated the correlation between body fat–corrected mean ECG voltage ($V_{fm}$) and ambulatory blood pressure (BP).

Methods

Patients

The subjects were 192 patients (98 men and 94 women) not receiving medication and ranging in age from 30 to 75 years. BP, measured by the auscultatory method 3 times on 3 different days, was $\geq 140$ mm Hg for systolic BP (SBP) and $\geq 90$ mm Hg for diastolic BP (DBP; Korotkoff phase V). All subjects underwent a routine examination, and only those patients with essential hypertension were selected for the study. Because no definite relation between their ECG findings and echocardiographic LVM could be found, the following were eliminated from the study: 4 patients demonstrating right bundle branch block, 2 patients with left bundle branch block, 3 patients with renal complications accompanied by edema, 3 patients with old myocardial infarction, and 1 patient with pulmonary emphysema. Seven other patients with poor echocardiographic recordings were also eliminated. The final experimental group consisted of 172 subjects (88 men and 84 women; mean $\pm$ SD age, $56 \pm 12$ years). Patients with cardiac valvular disease, pericardial effusion, anemia, or cardiomyopathy were not included.

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Subjects were subdivided into 3 groups (Table 1). The following 16 patients were included in the severe hypertension group with target organ damage: 7 patients with hypertensive retinopathy (Keith-Wagner category 3), 4 patients with hypertensive congestive heart failure, and 5 patients with renal failure (serum creatinine concentration 177 to 354 μmol/L). Eleven patients in this group had abdominal (visceral fat) obesity. The 38 subjects whose mean 24-hour BP was in the vicinity of 133/82 mm Hg were included in the white-coat hypertension group. Numerous other reports as well as the 95th percentile of mean 24-hour BP for normotensive subjects (n = 180; age range, 30 to 75 years) at our facility have established 133/82 mm Hg as the criterion for white-coat hypertension. The remaining 17 patients were classified in the sustained hypertension group (Table 1). The examinations were performed before any antihypertensive medication was administered. The study was approved by the ethical committee of our institute, and all subjects gave written informed consent.

### Ambulatory BP Methodology

The multi-biomedical recorder1 (TM2425, A&D Co) was used simultaneously records indirect BP by the cuff method, heart rate (heart rate=60/R-R) from ECG R-R interval, body motion (acceleration), ambient temperature, and body position (sitting or standing). In this study, the BP of all subjects was measured for 24 hours at 30-minute intervals. The nighttime (sleep-time) data derive from the subjects’ diaries. All remaining time was counted as waking time or daytime. Because such factors as depth of sleep and rapid eye movement sleep influence BP, it is impossible to be certain that nighttime BP readings represent true sleep-time BP.1 Therefore, we took the minimum sleep-time BP (base BP) as a representative sleep-time BP. Base BP was obtained statistically13 to correspond to minimum sleep-time heart rate value with the use of the multi-biomedical recorder.

### ECG Methodology

A programmable ECG analyzer (Cardio Base FCP-4731, Fukuda Denshi Co, Ltd) was used to obtain standard 12-lead ECG. A 10-second segment of simultaneous ECG lead recordings was sampled at a rate of 1000 samples per second per lead. We measured mean R- and S-wave amplitudes (mV) with a 10-second mean ECG waveform. According to the method described below, 12-lead R- and S-wave representative values were taken as statistical mean ECG voltage (Vm). Because unipolar leads have lower standardization than bipolar leads, we first obtained Re (length of Einthoven arrow) to represent R- and S-wave amplitudes for the 6 limb leads. Then we obtained the electric axis, the angle of which was termed θ. Because this θ value tends to decrease (left axis deviation) as LVH increases,2 we devised the following formula to correct Re for θ (Equation 1).

$$Re = \frac{Re}{\cos(60° - \theta)^{1/2}}$$

When θ is >60°, cos(60° - θ)^{1/2} is set at 1. When θ is <0°, this value is set at 0.5. Equation 1 was determined for the following reasons. The Einthoven vector (Re) is a frontal-plane vector. When the size of a hypothetical 3-dimensional vector of LVM action potential is taken as Rec, it can be inferred to be part of the following relation: Re=Re/|A|×LVM, where A is the proportional constant, cos $\phi$=Re/|A|×LVM is <1 (Re=|A|×LVM). Therefore, from these conditions, inferring the value of A from the distribution of Re (mV) and LVM (g) gives $~10^{-2}$ mV/g. The value for $\phi$ is obtained from the following formula: $\phi$=cos$^{-1}$ (Re/LVM×10$^{-2}$). We next investigated the relation between $\phi$ and θ (Figure 1). In cases of θ=60°, $\phi$ is in the vicinity of 0. In cases of 0°<$\phi$<60°, $\phi$ and θ are distributed in the vicinity of the relationship $\theta=\phi=60°$. Equation 1 was derived from this relation.

Precordial lead ECG voltages related to LVH are SV1, SV2, SV3, RV5, and RV6. As a result of principal components analysis, SV1 and SV3 were gated the relation between $\phi$ and θ (Figure 1). In cases of θ=60°, $\phi$ is in the vicinity of 0. In cases of 0°<$\phi$<60°, $\phi$ and θ are distributed in the vicinity of the relationship $\theta=\phi=60°$. Equation 1 was derived from this relation.

![Figure 1. Relation between $\theta$ (axis deviation) and $\phi$ (angle between Einthoven vector and hypothetical LVM vector; LVM×10$^{-2}$ mV/g) in each patient.](image-url)
RVs were selected as representative precordial lead voltages strongly related to LVM. The following model formula was used as a representative mean electric potential ($V_m$) of the 12 leads:

$$V_m = (RV_1 + m \times REC + n \times SV_3)/3.$$  

where $m$ and $n$ are weight-determining coefficients in relation to LVM, RV1 is R-wave voltage in lead V1, and SV3 is absolute S-wave voltage in lead V3. Their sizes ($m=2$, $n=3$) were inferred from multivariate linear regression analysis between echocardiographic LVM and $V_m$ ($LVM = 1.4 \times (RV_1 + 2.2 \times REC + 3.0 \times SV_3 + 34)$, multiple correlation coefficient=0.76).

**Echocardiographic Methodology**

Standard M-mode 2-dimensional echocardiograms were recorded with a cardiac ultrasound machine (SONOS2500, Hewlett Packard Inc) by a cardiologist. Left ventricular dimensions were measured from 2-dimensionally guided M-mode tracings according to the recommendations of the American Society of Echocardiography. LVM was calculated from Penn conversion8 by the following formula: $LVM = 1.04(LVID + PWT + IVS) - (LVID)^2 = 13.6$ (g), where LVID is left ventricular internal dimension, PWT is posterior wall thickness, and IVS is interventricular septal thickness. The following formula was used to estimate body surface area (BSA) from BW (kg) and height (H) (cm): $BSA = 0.007184 \times BW^{0.425} \times H^{0.725}$. These criteria consisted of 156 patients without severe hypertension.

**Comparison Between Mean ECG Voltage and Echocardiographic LVM**

The sum of the myocardial electric potentials influences ECG voltage. However, considering it possible that the greater the amount of body fat, the greater the attenuation of voltage at ECG electrodes, we devised the following model expression:

$$LVM = a(Body Fat)^b \times V_m + \gamma.$$  

Estimates of body fat amount were made by means of the tetrapolar bioelectric impedance method. Measurements were performed by means of an impedance meter (AD6311, A&D Co) with a 4-electrode arrangement that introduces a painless signal (800 mA, 50 kHz) on the basis of electric resistance between the joints of the upper limbs. The equipment used automatically computes body fat weight (kg) from gender, height, weight, and impedance ($\Omega$) values. In the past, numerous reports1 – 6 have dealt with comparisons between ECG LVM criteria and echocardiographic LVM. Voltage criteria included Sokolow-Lyon voltage15, Cornell voltage, Robert’s total QRS sum voltage, uncorrected Einthoven vector corrected by corrective factors (REC) 0.366 0.261, and Cornell voltage1. These criteria also examined the correlation coefficients with echocardiographic LVM in this study.

**Statistical Analysis**

Standard statistical methods, including unpaired t test and ANOVA, were used. A program from the Social Survey Research Information Co. Ltd was used to perform multiple linear regression analysis, discriminant analysis, and multiple principal components analysis. The cutoff value between groups was determined by discriminant analysis to discriminate well between the groups, and sensitivity and specificity were calculated. Nonlinear data such as $a(Body Fat)^b \times V_m + \gamma$ were converted into natural logarithms and analyzed. Data are expressed as mean±SD. Coefficients of correlation (r) were compared statistically with 2-tailed Fisher z transformation. A level of $P<0.05$ was considered statistically significant.

**Results**

**Fat-Corrected ECG Voltage**

Use of the model equation $a(Body Fat)^b \times V_m + \gamma$ to arrive at regression coefficients ($\alpha=0.175$, $\beta=0.27$, $\gamma=0.48$) among echocardiographic LVM (g), body fat (kg), and $V_m$ (mV) by means of multiple regression analysis led to the following relationship expression (correlation for both was $r=0.846$): $LVM = 100 \times V_m$, $V_m = 0.175(Body Fat)^{b/3} \times V_m + 0.5$ (mV). The relation between echocardiographic LVM and $V_m$ is shown in Figure 2. Table 2 shows correlation coefficients between echocardiographic LVM and Sokolow-Lyon voltage, Cornell voltage, Robert’s 12-lead QRS sum voltage, CHS model, and $V_m$ in the subjects investigated in this study. The highest coefficient of correlation was between $V_m$ and LVM in both total and World Health Organization I and II groups.

**Relationship Between $V_m$ and Ambulatory BP**

Table 3 shows coefficients of correlation (r) for mean 24-hour BP, daytime BP, nighttime BP, minimum sleep-time BP (base BP), and LVM and $V_m$.

The $V_m$ demonstrated higher or approximately the same r values with ambulatory BP values as those demonstrated by echocardiographic LVM. SBP demonstrated a higher coefficient.

**TABLE 2. Correlation Coefficients Between Echocardiographic LVM and ECG Criteria**

<table>
<thead>
<tr>
<th>Category</th>
<th>Total</th>
<th>WHO I and II</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n=172)</td>
<td>(n=156)</td>
</tr>
<tr>
<td>Sokolow-Lyon voltage³</td>
<td>0.621</td>
<td>0.406</td>
</tr>
<tr>
<td>Cornell voltage¹</td>
<td>0.661</td>
<td>0.590</td>
</tr>
<tr>
<td>Robert’s total QRS sum voltage¹⁶</td>
<td>0.726</td>
<td>0.645</td>
</tr>
<tr>
<td>CHS model⁶</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>0.701</td>
<td>0.604</td>
</tr>
<tr>
<td>Women</td>
<td>0.686</td>
<td>0.641</td>
</tr>
<tr>
<td>Einthoven vector (RE)</td>
<td>0.366</td>
<td>0.261</td>
</tr>
<tr>
<td>Einthoven vector corrected by $\theta$ (REC)</td>
<td>0.601</td>
<td>0.456</td>
</tr>
<tr>
<td>$V_m$</td>
<td>0.846</td>
<td>0.754</td>
</tr>
<tr>
<td>Men</td>
<td>0.859†</td>
<td>0.763*</td>
</tr>
<tr>
<td>Women</td>
<td>0.832†</td>
<td>0.742</td>
</tr>
</tbody>
</table>

* $P<0.05$, † $P<0.01$ vs CHS model.
TABLE 3. Correlation Coefficients (r) Between Vfm (LVM) and Ambulatory BP Parameters

<table>
<thead>
<tr>
<th>Ambulatory BP</th>
<th>LVM</th>
<th>Vfm</th>
<th>Vfm/BSA</th>
<th>Vfm/BSA^1/2</th>
</tr>
</thead>
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<tr>
<td>Mean 24-h BP</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP</td>
<td>0.603</td>
<td>0.705</td>
<td>0.658</td>
<td>0.708</td>
</tr>
<tr>
<td>DBP</td>
<td>0.428</td>
<td>0.503</td>
<td>0.379</td>
<td>0.458</td>
</tr>
<tr>
<td>Mean daytime BP</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP</td>
<td>0.528</td>
<td>0.645</td>
<td>0.606</td>
<td>0.646</td>
</tr>
<tr>
<td>DBP</td>
<td>0.490</td>
<td>0.402</td>
<td>0.281</td>
<td>0.356</td>
</tr>
<tr>
<td>Mean nighttime BP</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP</td>
<td>0.639</td>
<td>0.723</td>
<td>0.680</td>
<td>0.724</td>
</tr>
<tr>
<td>DBP</td>
<td>0.490</td>
<td>0.515</td>
<td>0.415</td>
<td>0.482</td>
</tr>
<tr>
<td>Minimum sleep-time BP</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP</td>
<td>0.721</td>
<td>0.821</td>
<td>0.788</td>
<td>0.834</td>
</tr>
<tr>
<td>DBP</td>
<td>0.539</td>
<td>0.572</td>
<td>0.492</td>
<td>0.552</td>
</tr>
</tbody>
</table>

*P<0.05 vs r values between LVM and ambulatory BP parameters.

cient of correlation with Vfm than DBP, and the highest correlation coefficient among the BP values was between base SBP and Vfm (r=0.821). When LVM and Vfm were corrected for BSA, Vfm/BSA^1/2 demonstrated a high coefficient of correlation with ambulatory SBP value and a significantly higher coefficient (r=0.834) with base SBP than with mean daytime SBP (r=0.646, P<0.01) (Table 3, Figure 3).

In many cases of white-coat hypertension, Vfm/BSA^1/2 was <1.33 mV/m (34 of 38 cases; sensitivity, 89%; specificity, 89%) (Figure 3). Vfm/BSA^1/2 was >1.91 mV/m in many cases of severe hypertension (13 of 16 cases; sensitivity, 81%; specificity, 97%) (Figure 3) (cutoff values of 1.33 and 1.91 mV/m were determined by discriminant analysis to discriminate well between the groups).

**Discussion**

Detection of LVH is of the greatest importance in estimating hypertension severity and predicting the prognosis in patients with hypertension.17–20 In the clinic, LVH is detected on the basis of echocardiograms. Despite the advantages of echocardiography, cost and operational considerations and its reproducibility tend to limit its utility. In addition, compared with the results of MRI,20 echocardiographic LVM tends to overestimate LVM detected by MRI method. On the other hand, ECG is a more practical method and its measurements are highly reproducible, but its evaluation of LVH is not accurate.21–23 As is well known, R- and S-wave voltages are decreased in cases of emphysema and obesity.5,6 Although electric resistance between the heart and the electrodes is influenced by various factors, owing to the high electric resistance of adipose tissue, body fat makes correction necessary. With this in mind, we developed a model expression for inferring the total myocardial action potential: α(Body Fat)^β×V_m + γ, in which α(Body Fat)^β is taken as the electric resistance factor. However, V_m cannot be measured in cases of right and left bundle branch block. Moreover, this method has limitations: in cases of old myocardial infarction or complications associated with pulmonary emphysema and edema, V_m tends to produce values smaller than those of echocardiographic LVM.

**Figure 3.** Correlations between mean daytime SBP and Vfm/BSA^1/2 and between minimum sleep-time (base) SBP and Vfm/BSA^1/2. The symbol □ indicates white-coat hypertension, in which the cutoff point (1.33 mV) was determined by discriminant function to discriminate well between white-coat hypertension and other groups (Dw≤−0.09×1.2, when Dw=0, x=1.33, and sensitivity and specificity of discrimination were 13/16×100% and 119/134×100%, respectively); ●, sustained hypertension; and □, severe hypertension. The cutoff point (1.91 mV) was also determined between severe HT and other groups (Ds≥−0.9x+1.9, when Ds=0, x=1.91 mV, and sensitivity and specificity of discrimination were 13/16×100% and 151/156×100%, respectively). Dw indicates discriminant function for white-coat hypertension; Ds, discriminant function for severe hypertension.

Echocardiographic LVM and ECG voltage reflect different pathological features. Not only hypertrophy of cardiac muscle cells but also increases in such interstitial substances as fibroblasts and collagen play a part in increases of LVM. Therefore, LVM as demonstrated by echocardiography and MRI provides a good opportunity to examine not only cardiac muscle cells but total interstitial substances as well. However, with such methods, the sum total of pure cardiac muscle cells cannot always be determined. Because R- and S-wave voltages observed on ECG are related to cardiac muscle cell potential, ECG may possibly be superior for revealing cardiac muscle hypertrophy caused by high-pressure loads.

The second problem was determining whether the formula used in this study is appropriate for inferring V_m. Numerous inference formulas are available for ECG voltage: methods entail calculating the means of all R and S waves from total 12-lead QRS amplitude,16 SV_1+RV_3, RaVL+SV_3, CHS
model, maximal spatial vector of vector cardiography, and the Novacode program based on statistical multivariate models for estimation of echocardiographic LVM. The formula proposed in this study was used to improve and simplify these methods. Because differences in race, gender, and age may occur, however, the formula should be used with larger numbers of subjects to improve its applicability.

The method used to estimate amount of body fat entails another problem. Because it is an experimental estimation, it cannot be used in cases of edema or in conditions accompanied by pericardial effusion. In this study, however, with the use of an impedance meter jointly employing electrodes attached to both arms, measurement of body fat was possible. In addition, our method proved practical because it can automatically calculate both V_m and V_fm by means of a computer and impedance meter built into the ECG equipment.

Another goal of this study was to determine whether V_fm is more strongly related to base BP or to daytime BP. We found that V_m had a higher correlation with SBP than with DBP. In addition, correlation with base SBP was significantly higher than correlation with daytime SBP (Table 3). Because LVM is influenced by BSA, the formula V_m/BSA^{1/2} produces the highest coefficient of correlation with base SBP (Figure 3). In other words, it is possible that the sum of myocardial action manifests itself during deep sleep when metabolic activities are at a minimum, is little influenced by environmental factors and can be thought to express the true basal BP advocated by Smirk et al. Base BP is more reproducible than either daytime or nighttime BP and has a high coefficient of correlation with base SBP. These findings suggest that V_m may be an indicator of cardiac muscle hypertrophy induced by increased afterload.

From the opposite standpoint, V_m is useful in estimating base SBP and therefore may be helpful in discriminating between sustained hypertension and white-coat hypertension or severe hypertension in the outpatient clinic.

Acknowledgment

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References

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