Correlation Relationship Assessment between Left Ventricular Hypertrophy Voltage Criteria and Body Mass Index in 41,806 Swiss Conscripts

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Introduction: Electrocardiographic criteria for left ventricular hypertrophy (LVH) have been limited by low sensitivity at acceptable levels of specificity. A number of studies have demonstrated that body mass index (BMI) is associated with decreased sensitivity of ECG LVH classification in hypertensive patients. The objective of this study is to investigate the correlation relationship between LVH voltage criteria and BMI in Swiss conscripts.

Methods: A database of 41,806 young Swiss people, who underwent compulsory conscription for the Swiss Army, was compiled. Along with other medical data, an ECG was taken. Statistical analyses, such as linear regression and calculation of correlation coefficient, were carried out between LVH voltage criteria and BMI.

Results: The mean age in the studied population was 19.2 ± 1.1 years with a median age of 19 years (range from 17 to 38 years). We found an overweight prevalence of 25.1%. The results showed that body habitus had significant association with Sokolow-Lyon voltages. A mean decrease of 13%, 5%, 19%, 14%, and 12% for the five studied Sokolow-Lyon indexes were found between normal range subjects ($18.5 \leq \text{BMI} < 25$) and obese subjects ($25 \leq \text{BMI}$).

Conclusions: Our study confirms the hypothesis that people with higher BMI, a growing section of the population, have lower ECG amplitudes. Therefore, the Sokolow-Lyon voltage criteria may underestimate the presence of LVH for subjects with higher BMI, which is not the case for the Cornell voltage. Our analysis suggests that computerized electrocardiography for the diagnosis of left ventricular hypertrophy based on Sokolow-Lyon voltages should incorporate the BMI factor.

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Left ventricular hypertrophy (LVH), characterized by an increase in chamber mass produced largely by an increase in the size of cardiomyocytes, is a reaction to any form of stress that can be reversed and normalized. In some cases, however, the hypertrophy involves fibroblasts with the expression of additional and not necessarily normal collagen. LVH due to an advanced number of fibroblasts and collagen expression has been demonstrated as an independent and important risk factor for cardiovascular diseases. It is associ-

ated with increased cardiovascular morbidity, mortality, and hypertension, as a major predictor.^{1–6}

Conventional electrocardiographic diagnosis criteria for detection of LVH introduced after the general acceptance of the standard 12-lead ECG, include the mostly accepted Sokolow-Lyon voltage index introduced in 1949,⁷ the recently introduced Cornell voltage index or Cornell voltage-duration product,^{8–10} and the Romhilt-Estes point score system.¹¹ These criteria have been limited by low sensitivity at acceptable levels of specificity.^{8,10,12–19}

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The sensitivity is usually less than 50% while the specificity is often in the range of 85–90%.²⁰ Several extracardiac factors including age, gender, race, and body habitus may have an impact on ECG-based LVH classification.^{8,12,13,15,18–32}

Obesity, that may be characterized by body mass index (BMI),¹⁹ has been revealed to be associated with the presence of LVH^{21,22} and with decreased sensitivity of electrocardiographic criteria based on ECG amplitudes for LVH classification.^{6,12,15,23,24} However, many of these studies have only been performed on hypertensive subjects, and limited on small population sample (several hundreds or thousands of subjects). Few articles have assessed relationships between ECG criteria and BMI in a quantitative manner for a medically unselected population.

Focusing on body habitus, known as one of the extracardiac factors influencing diagnostic criteria of LVH, the object of this study is to investigate the correlation between BMI and LVH voltage criteria, with the aim of establishing more accurate voltage criteria for screening of LVH, taking into account BMI factor. Statistical studies were carried out on a very large population sample.

MATERIAL AND METHODS

Study Population

In Switzerland, young male citizens normally have to undergo compulsory military service in the Swiss Army from the age of 18 years. Female citizens may be volunteers for the military service. For every conscript, a medical history is obtained, a physical examination and an ECG measurement are performed, and in the end a status of "medically fit for military service" or "unfit for military service" is assigned. This population constitutes an excellent basis for studies on screening and studies on medically unselected populations as every young, male Swiss citizen, whatever his medical status is (no disease, disease that may affect the heart or other), does undergo the conscription process.³³ In this context, we compiled a database of 41,806 young people, who underwent medical examination in all Swiss recruitment centers between March 1, 2004 and July 31, 2006 without any exclusion of measurements except due to technical problems (i.e., no possible readout of data due to file corruption or similar).

Electrocardiography

A standard resting 12-lead ECG was recorded for each subject using the AT-104 PC (SCHILLER AG, Baar, Switzerland). Data acquisition was performed at a sampling frequency of 1 kHz with a bandwidth of 0.05, 350 Hz and with a resolution of 5 μ V/bit. For data storage, the ECGs were down-sampled to 500 Hz with corresponding prefiltering. Weight, height, blood pressure, and other parameters were recorded at the same time. All data were stored in the data management software SEMA-200 V2.45 (SCHILLER AG).

Statistical Analysis

The amplitude of S waves in leads V₁ and V₂ and that of R waves in leads V₅ and V₆ were extracted from SEMA-200. Five different variants of the Sokolow-Lyon voltage (four possible combinations of SV₁, SV₂, RV₅, RV₆, and the most widely used one)^{6,7,18} and the Cornell voltage⁹ were calculated for each ECG (Table 2). Weight and height of all subjects were extracted in order to perform an allometric analysis (possible data reduction) and calculate the BMI.¹⁹ Data were statistically analyzed by means of MATLAB programs (The MathWorks Inc., Natick, MA, USA) version R2006a written for this task. First, an allometric analysis of the weight and the height of all subjects was carried out in order to get an idea of how well the BMI would describe the body habitus in the studied population and how well the BMI (instead of the single parameters, height and weight) will perform.

Second, we investigated the effect of body habitus on the Sokolow-Lyon voltages and on the Cornell voltage. The subjects were divided into four groups according to their body habitus. We used the BMI cutoff as recommended by NHLBI, NIDDK and others.^{27–29} We defined underweight as a BMI < 18.5, normal weight as a BMI $\geq$ 18.5 to less than 25, overweight as a BMI $\geq$ 25 to less than 30 and obesity as a BMI $\geq$ 30. The mean value and standard deviation (SD) of each group were calculated. The P value was determined according to the Student's *t*-test principle.³⁰ The null hypothesis was rejected at 2-tailed $\alpha \leq 0.05$.

Third, in order to assess more precisely the contribution of BMI to the Sokolow-Lyon voltage and to the Cornell voltage, all subjects were divided into subgroups according to BMI value, with an interval of 1 kg/m². Correlation analysis and linear

Table 1. Demographic Characteristics of Swiss Conscripts. Data have been Acquired at the Swiss Recruitment Centers between March 1, 2004 and July 31, 2006

Demographic Characteristic	Definition	Number of Subjects	Percentage of Subjects
Age (year)			
	<18	221	0.5%
	18–20	35,993	86.1%
	21–25	3369	8.1%
	>25	2223	5.3%
BMI (kg/m ²)			
Underweight	<18.5	1969	4.7%
Normal	18.5–24.9	29,346	70.2%
Overweight	25–29.9	8317	19.9%
Obese	≥30	2174	5.2%

regression estimation were performed by examining the distribution of Sokolow voltage and Cornell voltage with respect to BMI. The mean and SD values were calculated for each BMI group. Furthermore, a correlation test was performed according to Marques de Sá³⁴ based on Student's *t*-test with a null hypothesis that the correlation coefficient $\rho = 0$ (no correlation) and a significance level of $\alpha = 0.01$.

RESULTS

Forty-one thousand eight hundred and six ECGs were analyzed with 41,648 ECGs of male conscripts (99.6%), and 158 of female conscripts (0.4%). The mean age was 19.2 ± 1.1 years with the median age of 19 years (range 17–38 years). A total of 86.1% of conscripts were aged from 18 to 20 years (Table 1).

The allometric analysis between the height and weight of the study's subjects gave an $\alpha = 24.0$

and $\delta = 1.9$ when $y_i = \alpha x_i^\delta$ where y_i is the weight in kilograms and x_i is the corresponding height in meters. This suggests that the BMI (which has a δ value of 2.0) is the closest (most reasonable) body habitus descriptor.

The subjects were then divided into four groups according to their BMI. It was shown that 4.7% of the subjects in the studied population were underweight, 70.2% had normal weight, and 25.1% were overweight or obese (Table 1).

Effect of Body Habitus on Sokolow-Lyon Voltage and on Cornell Voltage

The Sokolow-Lyon voltages and the Cornell voltage in normal weight, overweight, and obese subjects are presented in Table 2. Differences between each group were statistically significant (all $P < 0.0001$).

It is shown that body habitus yields significant association with Sokolow-Lyon voltage, in particular in the cases of Sokolow 1, Sokolow 3, Sokolow 4, and Sokolow 5. Compared to normal-weight subjects, lower mean values of Sokolow-Lyon voltage were obviously exhibited in overweight and obese subjects ($BMI \geq 25$). For Sokolow 1, the mean value decreased 13% from 3.1 of normal weight to 2.7 of obese subjects, and 5%, 19%, 14%, 12%, respectively, for Sokolow 2, Sokolow 3, Sokolow 4, and Sokolow 5. Sokolow 2 voltage of normal-weight subjects and that of overweight subjects remains nearly the same. Meanwhile for obese subjects, the voltage decreases significantly. However, there is no obvious correlation between the Cornell voltage and BMI. Indeed, the mean value decreased from 1.61 of normal-weight to 1.55 of overweight subjects, but then increased from 1.55 to 1.58 to obese subjects.

Table 2. Calculation of the Five Sokolow-Lyon Voltage Variants and the Cornell Voltage in Normal Weight, Overweight, and Obese Subjects

ECG Criteria	Definition	Normal Weight (n = 29,346)	P Value	Overweight (n = 8317)	P Value	Obese (n = 2174)
Sokolow 1	SV1 + RV5	3.08 ± 0.87	<0.0001	3.00 ± 0.80	<0.0001	2.69 ± 0.69
Sokolow 2	SV1 + RV6	2.62 ± 0.77	<0.0001	2.64 ± 0.73	<0.0001	2.48 ± 0.67
Sokolow 3	SV2 + RV5	3.97 ± 1.00	<0.0001	3.74 ± 0.90	<0.0001	3.23 ± 0.75
Sokolow 4	SV2 + RV6	3.50 ± 0.93	<0.0001	3.38 ± 0.75	<0.0001	3.01 ± 0.75
Sokolow 5	SV1 + max(RV5, RV6)	3.09 ± 0.86	<0.0001	3.03 ± 0.80	<0.0001	2.72 ± 0.69
Cornell voltage	RaVL + SV3	1.61 ± 0.71	<0.0001	1.55 ± 0.63	<0.0001	1.58 ± 0.56

The P values between normal weight and overweight subjects and between overweight and obese subjects are calculated as well. The voltages are expressed as mean $\pm$ SD, in mV and *n* is the number of population sample.

Figure 1. Two-dimensional plot of the statistical distribution for each of the five variants of Sokolow-Lyon voltage criteria and of Cornell voltage criteria against BMI showing the corresponding linear regression model.

Distribution of Sokolow-Lyon Voltage and Cornell Voltage against BMI

The distribution of each Sokolow-Lyon voltage and of the Cornell voltage with respect to BMI was evaluated, as depicted in Figure 1. The contour of each curve demonstrates the tendency of distribution with smaller Sokolow-Lyon voltage for higher BMI. This statistical distribution (in the x-axis direction) shows a lognorm-, gamma-, or beta-type behavior.³⁴ The Kolmogorov-Smirnoff test³⁴ was performed on the distributions of the Sokolow-Lyon voltages and of the Cornell voltage with a significance level of $\alpha = 0.05$. The result shows that the statistical distributions of the Sokolow-Lyon voltages and of the Cornell voltage yield a Gaussian behavior. Therefore, a linear regression analysis (in the form of $y = ax + b$, with coefficient of correlation R) is valid in our case as the behavior of the error to be minimized in such a model has to have a Gaussian-like distribution in the y-axis direction.³⁴ Furthermore, one can perform a regression test in order to prove significance for the linear regression model.³⁴ The null hypothesis $\rho = 0$ (no linear regression) could be rejected. In

the first view, quite small R values (-0.08 , -0.01 , -0.17 , -0.12 , -0.07 , and -0.04 , respectively, for five variants of the Sokolow-Lyon voltage and for the Cornell voltage) of the linear regression model (Fig. 1) are, in fact, large enough to give rise of significance at a level of $\alpha = 0.01$ for a large population such as ours. Other types of regression estimation (i.e., potential, exponential, logarithmic, or polynomial) all showed a correlation coefficient lower than found for linear regression.

The estimated regression coefficients of -0.018 , -0.002 , -0.047 , -0.030 , and -0.017 , respectively, for the five variants of the Sokolow-Lyon voltage are all negative, revealing thus a negative correlation between BMI and the Sokolow-Lyon voltage criteria, whatever the variant. Meanwhile, the estimated regression coefficient for the Cornell voltage (-0.008) is much smaller than that for the Sokolow-Lyon voltages except for the Sokolow 2. These distributions correspond to the previous analysis showing effect of body habitus on Sokolow-Lyon voltage and on Cornell voltage.

Figure 2 shows the mean and SD values with respect to BMI. In a statistical point of view, the tendency of Sokolow-Lyon voltage formed by the

Figure 2. Mean $\pm$ SD values of Sokolow-Lyon voltages and Cornell voltage according to BMI.

mean $\pm$ SD value confirms the previous observations revealed by Figure 1, demonstrating that Sokolow voltage decreased with higher BMI. For instance, the Sokolow 1 voltage was 3.1 ± 0.8 mV for BMI = 24 and was 2.1 ± 0.6 mV for BMI = 44. Nevertheless, in the case of Sokolow 2, this tendency is less obvious than others, which corresponds to the smallest regression coefficient (absolute value) shown in Figure 1. While for the Cornell voltage, the mean $\pm$ SD value remains almost unchanged against increased BMI. For instance, the Cornell voltage was 1.6 ± 0.7 mV for BMI = 24 and was 1.5 ± 0.5 mV for BMI = 44.

Discussion

As already mentioned in the introduction, the known extracardiac factors influencing the Sokolow-Lyon voltage criteria include age, gender, race, and body habitus. In the studied population, the mean age is 19.2 ± 1.1 years. The fact that the subjects belong to the same age category could eliminate effect of age on ECG criteria for the diagnostic of LVH. Similarly, the factors of gender

and race can also be neglected since the population is based on Swiss conscripts and only 0.4% of them are females. Therefore, the results represent a young, medically unselected population of males, aged mainly between 18 and 20 years.

The allometric analysis underlines the use of BMI as a descriptor for body habits. The coefficient δ being the exponent (power dependency) is with a value of 1.9 really near the value of 2 used for the BMI ($= \text{height}/\text{weight}^2$). Our optimal estimator/normalization factor for body habitus being $y = \text{height}/\text{weight}^{1.9}$ can therefore be approximated by the generally accepted BMI. The results corresponds well to the suggestion by Norman et al.¹⁶ who found in the Framingham study that BMI can be used as body habitus descriptor instead of height and weight as single correction variable and who use the BMI to improve the LHV algorithm proposed by them. The α -value found to be 24.0 is near the upper limit of normal weight range (remembering that normal weight is defined as a BMI value between 18.5 and 24.9). Knowing that the prevalence of overweight and obesity in young men is growing, an upper limit of 24.0 for the α -value

is reasonable. We found 25.1% of all Swiss conscripts to be overweight and 5.2% obese. These impressive results have clinically important consequences^{27,31,32,35} and match other studies. Papdimitrou,³⁶ Padez,³⁷ and Neovius³⁸ have found similar results—in young Greeks, a prevalence of 28.5% for overweight (10.4% obese), in Portuguese conscripts, 21.3% (4.2% obese), and in Swedish conscripts, 16.3% (3.2% obese), respectively.

The hypothesis of negative correlation relationship between ECG criteria and BMI has been assessed by a number of studies over the last decade. Levy et al. found a negative association between sensitivity of predominantly precordial lead voltage criteria and quartile of BMI in 4684 subjects who underwent echocardiographic study for LVH in the Framingham Heart Study.¹⁵ The same conclusion was drawn by Norman et al. who also found that for both genders, BMI was negatively correlated with precordial lead ECG voltages in 3351 adults from the Framingham Heart Study.¹⁹ Many other studies have only been led in hypertensive patients. Okin et al. pointed out that in 8417 hypertensive patients for the LIFE study, increased BMI has significantly effect on ECG LVH by Sokolow-Lyon criteria and thus Sokolow-Lyon voltage criteria underestimate the prevalence of anatomic LVH in the presence of obesity.¹² Abergel et al. found in a population of 380 hypertensive patients sensitivity of Sokolow-Lyon voltage to be significantly lower in obese hypertensive patients than in nonobese patients.³⁹

The sensitivity of precordial lead voltage criteria for detecting LVH has been reported to be lower in subjects with higher BMI because of the waning of QRS voltage in such individuals. Waning of QRS voltage has been demonstrated to occur in those subjects because the distance between the electrode and the left ventricle tends to become greater.^{12,15,18,19,40} Indeed, a bioelectrical model of double-layer sources has been established and analyzed⁴⁰ where it is demonstrated that the change in cardiac body surface potentials is inversely proportional to the distance between the double-layer sources and the thorax. Our investigation confirms and extends these observations to a much larger and medically unselected population (more than 40,000 subjects mainly males and mainly aged from 18 to 20 years), demonstrating a negative correlation of BMI with Sokolow-Lyon voltages, therefore, an underestimation of LVH in subject with higher

BMI. Looking at the number (regression model) in more detail, one could conclude that the calculation error of the Sokolow-Lyon voltage (as an indicator for LVH) between a small (ex. 20) and a large BMI (ex. 35) is 0.27, 0.07, 0.71, 0.45 and 0.26 mV or even 0.36, 0.04, 0.94, 0.60, and 0.34 mV when taking a BMI of 40 for the five studied Sokolow-Lyon indexes. These values cannot be neglected compared to the limit of 3.5 mV for LVH classification. Furthermore, it is interesting to see that the five studied Sokolow-Lyon indexes do not have identical negative voltage drop for increasing BMI (13% for V_1/V_5 vs 5% for V_1/V_6 , 19% for V_2/V_5 , 14% for V_2/V_6 and 12% for standard Sokolow-Lyon index). Comparing the numbers more closely suggests that the precordial voltage from electrode V_2 is more sensitive than V_1 (being more sensitive than V_5) and V_5 more sensitive than V_6 for voltage waning with increased BMI.

However, some variations can also be observed in Figure 2 for underweight subjects corresponding to small BMI (less than 18.5) and obese subjects corresponding to high BMI (more than 35). Keeping the same tendency as other BMI groups, their Sokolow-Lyon voltages do not vary in the same way but exhibit fluctuation. This may be due to small number of subjects of these BMI groups. For instance, we only have 100 subjects for BMI = 16 and 38 subjects for BMI = 40, which is statistically not sufficient compared to the total number of studied persons.

Compared to the Sokolow-Lyon voltage indexes, the Cornell voltage index exhibits much less dependence on BMI. The linear regression model shows that the variation of the Cornell voltage is only 0.05 mV between a small BMI (ex. 18) and a normal BMI (ex. 24) and is 0.14 mV between a small BMI (ex. 18) and a large BMI (ex. 35). These values could be neglected regarding the LVH classification.

It is also known that obesity is associated with an increased prevalence of anatomic LVH. The prevalence of 25.1% of overweights in such a young population certainly is not a good sign for public health in future. It has been demonstrated that among the main independent predictors such as male gender, systolic blood pressure, valvular heart disease, cardiovascular disease, and antihypertensive medication, high BMI is the most important variable risk indicator of LVH. Furthermore, the prevalence of LVH is proportional to BMI in a general population.^{1,12,41}

CONCLUSION

The study was based on a very large population of more than 40,000 medically unselected subjects (99.6% male, mainly aged between 18 and 20 years). We demonstrated that the conventional Sokolow-Lyon voltage based ECG criteria for classification of LVH have negative correlation relationship with BMI in the studied population, which is not the case for the Cornell voltage criterion.

The prevalence of being overweight was 25.1% (including 5.2% obese). These numbers are alarming (high BMI increases prevalence of LVH) and match other, smaller and more restrictive studies. Thus, the BMI can be used to adjust the Sokolow-Lyon voltage criteria in order to take into account the fact that the prevalence of LVH is proportional to the BMI.

Furthermore, the detection of LVH based on the Sokolow-Lyon voltage criteria is underestimated in overweight and obese subjects. Therefore, it is important to take BMI into account and adjust Sokolow-Lyon criteria in order to correct for smaller ECG amplitudes obtained for persons with higher BMI, which in case of Swiss conscripts (young people) is already every fourth person.

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