Does QRS Voltage Correction by Body Mass Index Improve the Accuracy of Electrocardiography in Detecting Left Ventricular Hypertrophy and Predicting Cardiovascular Events in a General Population?

Cesare Cuspidi, MD;[1,2] Rita Facchetti, MD;[1] Michele Bombelli, MD;[1] Carla Sala, MD;[3] Marijana Tadic, MD;[4] Guido Grassi, MD;[1,5] Giuseppe Mancia, MD[1,2]

From the Department of Health Science, University of Milano-Bicocca;[1] Istituto Auxologico Italiano IRCCS;[2] Department of Clinical Sciences and Community Health University of Milano and Fondazione Ospedale Maggiore Policlinico, Milano, Italy;[3] University Clinical Hospital Centre "Dragisa Misovic", Belgrade, Serbia;[4] and IRCCS Multimedica, Milano, Italy[5]

The authors assessed the value of body mass index (BMI) correction of two electrocardiographic criteria in improving detection of left ventricular hypertrophy (LVH) and prediction of cardiovascular and all-cause mortality in the Italian study Pressioni Arteriose Monitorate E Loro Associazioni (PAMELA) population. At entry, 1549 patients underwent diagnostic tests, 24-hour ambulatory blood pressure (BP) monitoring, standard electrocardiography, and echocardiography. The BMI-corrected Cornell voltage and Sokolow-Lyon voltage criteria provided better results for detection of echocardiographic LVH as compared with unadjusted electrocardiographic parameters. Cornell voltage index, but not Sokolow-Lyon index, was associated with an increased risk of cardiovascular events (and all-cause mortality). The adjusted risk of cardiovascular events related to one-standard deviation increment of BMI-corrected Cornell voltage was similar to that conferred by the uncorrected criterion in the total population, but outperformed in obese participants. These findings show that correction for BMI may improve the diagnostic accuracy of Cornell voltage index in detecting LVH and prediction of cardiovascular mortality in obese individuals. *J Clin Hypertens (Greenwich).* 2016;18:415–421. © 2015 Wiley Periodicals, Inc.

Left ventricular (LV) hypertrophy (LVH), either detected by electrocardiography or echocardiography, has been shown to be an independent predictor of nonfatal and fatal cardiovascular (CV) events as well as all-cause death in a variety of clinical settings including general population-based samples[1,2] and selected cohorts of hypertensive,[3–5] coronary artery disease,[6] chronic kidney disease,[7] and heart failure patients.[8] Thus, the accurate and cost-effective identification of LVH represents a clinical priority for stratifying individual CV risk.[9]

In current clinical practice, echocardiography is the reference method for detection of LVH because of its higher sensitivity/specificity compared with electrocardiographic (ECG) examination. The greater availability, lower cost, and relative simplicity of ECG recording, however, strongly support this diagnostic tool for LVH screening. LVH may affect normal ECG patterns by increasing QRS voltage and/or altering P waves, ST segments, and T waves.[10] ECG voltage criteria for LVH diagnosis have been used for more than 100 years owing to the pioneering observations by Lewis.[11] Although several ECG voltage (and nonvoltage) criteria have been proposed in the past century, the sensitivity of old and newer ECG criteria is limited, as reported in numerous studies based on the simultaneous estimation of LV mass (LVM) by echocardiography or less frequently by computerized tomography or magnetic resonance imaging.[12]

A consistent body of evidence supports the notion that overweight and obesity significantly reduce the accuracy of the most frequently used ECG criteria for detection of LVH such as Sololow-Lyon and Cornell voltage indexes because of the attenuating effects of increased chest wall and epicardial fat on QRS amplitudes.[13,14] Some authors have hypothesized that adjustment of ECG criteria for body mass index (BMI) may increase their diagnostic sensitivity for LVH.[15,16] This issue, however, remains largely underexplored and, more importantly, the value of BMI correction of ECG indexes in improving the prediction of CV events is unknown.

Thus, the present study was conducted to test whether adjusting established ECG criteria for BMI may improve their accuracy in detecting anatomical LVH, compared with echocardiographic LVM as a reference, and in predicting incident CV events. For this purpose, we analyzed the data obtained in the Pressioni Arteriose Monitorate E Loro Associazioni (PAMELA) study, a population study performed in Italy.

METHODS

Population

The PAMELA study was carried out in a sample of 3200 patients representative of the population of Monza (a town near Milan, Italy) for sex and age

Address for Correspondence: Cesare Cuspidi, MD, Istituto Auxologico Italiano, Clinical Research Unit, Viale della Resistenza 23, 20036 Meda, Italy
E-mail: cesare.cuspidi@unimib.it

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(25–74 years). The participation rate was 64%; thus, data were collected in 2051 patients. Demographic characteristics of nonparticipants and participants were similar. This was also the case for CV risk assessed by data collected via phone interview (data not shown).

Entry Data

The methods employed in the PAMELA study have been described in detail previously.[17] Briefly, after providing informed consent, patients were invited to undergo a comprehensive clinical evaluation at the outpatient clinic of the San Gerardo University Hospital of Monza in the morning of a working day. Collected data included a full medical history, blood and urine samples, physical examination, standard 12-lead electrocardiography, echocardiography, and three sphygmomanometric BP measurements in the sitting position. Body weight was recorded to the nearest 0.1 kg using a calibrated electronic scale with the patients wearing indoor clothing without shoes. Height was recorded to the nearest 0.5 cm using a standardized wall-mounted height board.

Patients were then fitted with an ambulatory BP monitoring device (Spacelabs 90207, Issaquah, WA) set to obtain automated BP and heart rate oscillometric readings every 20 minutes over 24 hours. During the monitoring period, the patients were asked to pursue their normal activities and to self-measure BP at home twice, namely at 9 AM and 9 PM, using a semiautomatic oscillometric device (Philips, model HP 5331, Royal Philips Electronics, Amsterdam, Netherlands) on the contralateral arm to the one used for ambulatory BP monitoring.

Electrocardiography

Standard 12-lead ECGs were recorded by our technical staff at 25 mm/s and 1 mV/cm calibration with equipment having frequency response characteristics in accordance with American Heart Association recommendations.[10] ECG findings were coded and assessed by two physicians blinded to clinical data. All R-wave and S-wave measurements were performed to the nearest 0.1 mV (ie, 1 mm) with calipers and metal rulers on three consecutive cycles. Patients with complete bundle branch block, previous myocardial infarction, Wolf-Parkinson-White syndrome were excluded from the analysis because of the interference of these abnormalities with LVH detection.

For the purpose of the present analysis, two largely used ECG criteria for LVH were tested at baseline examination: (1) Sokolow-Lyon voltage[18] and (2) sex-specific Cornell voltage.[19] ECG voltages were normalized to body size by the following formulae: Sokolow-Lyon-BMI product (mm × kg/m^2) = (S-wave amplitude in V_1 + R-wave amplitude in V_5 or V_6, whichever the larger) × BMI; Cornell voltage-BMI product (mm × kg/m^2) = (S-wave amplitude in V_3 + R-wave amplitude in aVL) × BMI.[16]

Echocardiography

Echocardiography was performed according to standardized procedures, as previously reported.[20] In brief, M-mode and two-dimensional echocardiographic examinations were carried out with a commercially available instrument (Acuson 128 CF, Computer Sonography, Mountain View, CA). End-diastolic (d) and end-systolic (s) LV internal diameters (LVIDs), interventricular septum thickness (IVS), and posterior wall thickness (PW) were measured by two-dimensional–guided M-mode tracings recorded at 50 cm/s to 100 cm/s speed, during at least three consecutive cycles according to Penn convention. Relative wall thickness was defined by the ratio of PW plus IVS thickness to LVIDd; LVM was estimated by using the corrected ASE method: $0.8 \times (1.04 \times [(IVSd+LVIDd+PWTd)^3 - LVIDd^3]) + 0.6$[21] and normalized to body surface area (BSA) or height$^{2.7}$. Echocardiographic tracings were obtained by two skilled operators and read by a third independent observer: the intraobserver coefficient of variation was 0.6% for LVIDd, 3.1% for IVSd thickness, and 3.2% for PWd thickness.

LVH was defined as LVM index ≥114 g/m^2 in men and ≥99 g/m^2 in women; these cutoffs are derived from sex-specific upper limits of normality (mean plus 1.96 standard deviation) for LVM indexed to BSA in 675 healthy individuals with sustained normotension.[20]

Follow-Up

Participants were followed from the time of the initial medical visit to October 1, 2004. Death certificates were coded using the *International Classification of Diseases, Tenth Revision* (*ICD-10*).[22] *ICD-10* codes 390 to 459 were considered as CV deaths. Nonfatal CV events were ascertained by hospital diagnosis using *ICD-10* codes.

Data Analysis

In each patient, three office BP measurements and two home BP measurements obtained at the initial visit were separately averaged. Ambulatory 24-hour BP readings were also averaged after editing for artifacts, based on preselected criteria.[23] The average of three measurements was used to define R-wave and S-wave voltages. Statistical analysis was performed by SAS (version 9.12; SAS Institute Inc, Cary, NC).

Cross-Sectional Analysis. Values are expressed as mean±standard deviation (SD) or percentage. Means were compared by Student *t* test for independent samples and categorical data were analyzed by chi-square test or Fisher exact test when appropriate. The strength of linear correlation between ECG voltages and BMI was tested by ordinary regression analysis. In order to identify the breakpoint where a significant change in the slope of the relationship between ECG voltages and BMI may take place, a piecewise regression analysis with an unknown knot location was performed.[24] Receiver operating characteristic (ROC) curve analyses were performed in order to evaluate the diagnostic

performance of absolute and BMI/adjusted ECG voltage criteria, treated as continuous variables, in detecting echocardiographic LVH defined by previous criteria. The area under the curve was used to assess the discriminant power of ECG parameters in predicting echocardiographic LVH.

Follow-Up Analysis. Hazard ratios of CV events (fatal and nonfatal) or all-cause mortality were calculated by Cox's proportional hazard model[25] and were calculated for a 1-SD increment of ECG criteria considered. Data were adjusted for age, sex, nighttime SBP, low-density lipoprotein and high-density lipoprotein cholesterol, serum glucose, BMI, smoking, and previous CV events. Finally, ROC curve analyses were performed in order to evaluate the diagnostic performance of ECG parameters in predicting CV prognosis. All tests were two-sided and $P<.05$ was considered statistically significant.

RESULTS

Demographic and Clinical Characteristics

Of 2051 patients included in the present analysis, 1549 had reliable ECG and echocardiographic tracings at baseline examination. As reported in Table I, average BMI and waist circumference at baseline were 25.4±4.2 kg/m^2 and 85±12 cm, respectively. Mean office BP was 132±21/83±11 mm Hg, mean 24-hour BP was 119±11/74±7 mm Hg, and mean home BP was 123±19/76±11 mm Hg. A total of 271 of 1549 patients (17.5%) were taking antihypertensive medications. Approximately 3.5% of the participants had a history of CV disease.

Up to 13% of the population sample was found to have echocardiographic LVH, according to the sex-specific thresholds indicated in the Methods section.

Prevalence rates of ECG LVH according to Sokolow-Lyon (S-wave amplitude in V_1 + R-wave amplitude in V_5 or V_6, whichever the larger, ≥35 mm) and Cornell voltage index criteria (S-wave amplitude in V_3 plus R-wave amplitude in aVL >20 mm in women and >28 mm in men) were 0.9% and 7.7%, respectively.

Correlation Analyses

Figure 1A reports the relationship between Cornell voltage and BMI. Piecewise regression analysis showed a significant change in slopes for the BMI value of 27.1 kg/m^2. The positive relationship between Cornell voltage and BMI for BMI values <27.1 kg/m^2 (r=0.15, $P<.0001$) was lost for BMI values ≥27.1 kg/m^2 (r=0.01, P=.82).

As depicted in Figure 1c, regression analysis for the relationship between Sokolow-Lyon voltage and BMI identified the BMI value of 27.7 kg/m^2 as the breakpoint for the slopes. In patients with BMI <27.7 kg/m^2, the Sokolow-Lyon voltage showed a direct relationship with BMI (r=0.15, $P<.0001$), whereas an inverse relationship was found between the two variables in patients with BMI ≥27.7 kg/m^2 (r=0.01, P=.83).

TABLE I. Clinical Characteristics of the Study Population at Initial Evaluation (N=1549)

Variables	
Age, y	50±13.5
Male sex, No. (%)	783 (50.55)
Body mass index, kg/m^2	25.4±4.2
Body surface area, m^2	1.75±0.19
Waist circumference, cm	85.1±12.2
Height, m	1.64±0.1
Office SBP, mm Hg	132±21
Office DBP, mm Hg	83±11
24-h SBP, mm Hg	119±11
24-h DBP, mm Hg	74±7
Home SBP, mm Hg	123±19
Home DBP, mm Hg	76±11
HDL cholesterol, mg/dL	55.6±15.5
Serum glucose, mg/dL	89.8±19.5
Triglycerides, mg/dL	113.5±76.9
Serum creatinine, mg/dL	0.88±0.17
Antihypertensive drugs, No. (%)	271 (17.5)
Office BP ≥40/90 mm Hg or antihypertensive drugs, No. (%)	674 (43.6)
History of CV events, No. (%)	52 (3.4)
Sokolow-Lyon index, mm	19.4±5.4
Sokolow-Lyon index* BMI, mm kg/m^2	495±161
Cornell voltage index, mm	15.2±5.7
Cornell voltage index* BMI, mm kg/m^2	391±169
LVM index, g/m^2	85.9±20.3

Abbreviations: BP, blood pressure; CV, cardiovascular; DBP, diastolic blood pressure; HDL, high-density lipoprotein; LVM, left ventricular mass; SBP, systolic blood pressure. Data are shown as mean±standard deviation, percentage, or absolute number. * = x.

Results of ROC Curves for Prediction of Echocardiographic LVH

The comparison of ROC curve areas of BMI-corrected and unadjusted ECG criteria (continuous variables) for LVH, defined by echocardiographic LVM indexed to BSA, is reported in Figure 2. The BMI-corrected Cornell voltage (Figure 2A) and BMI-corrected Sokolow-Lyon voltage (Figure 2B) criteria provided better results for detection of LVH as compared with their unadjusted ECG parameters in the total population, being associated with higher areas (P=.002, and $P<.001$, respectively).

In a sensitivity analysis using LVM normalized to height$^{2.7}$ in order to define LVH (LVM ≥51 g/h$^{2.7}$ in men and 47 g/h$^{2.7}$ in women), the BMI-corrected Cornell voltage and Solokow-Lyon turned out to be associated with significantly higher areas under the curve compared with the corresponding unadjusted ECG criteria (0.774 vs 0.696 [$P<.0001$] and 0.716 vs 0.598 [$P<.0001$], respectively).

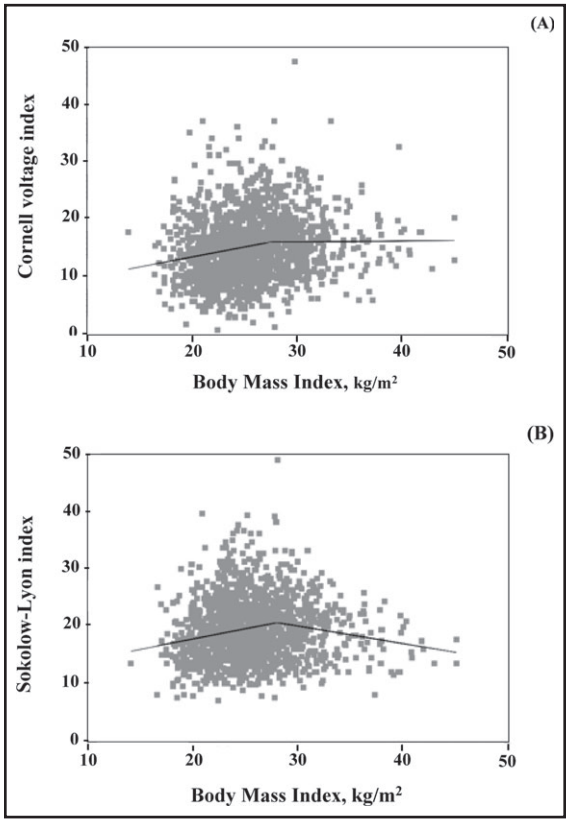

FIGURE 1. (A) Relationship between Cornell voltage and body mass index (BMI). Regression analysis showed a significant change in slopes for body mass index (BMI) ≥27.1 kg/m^2. (B) Relationship between Sokolow-Lyon voltage and BMI. Regression analysis showed a significant change in slopes for BMI ≥27.7 kg/m^2.

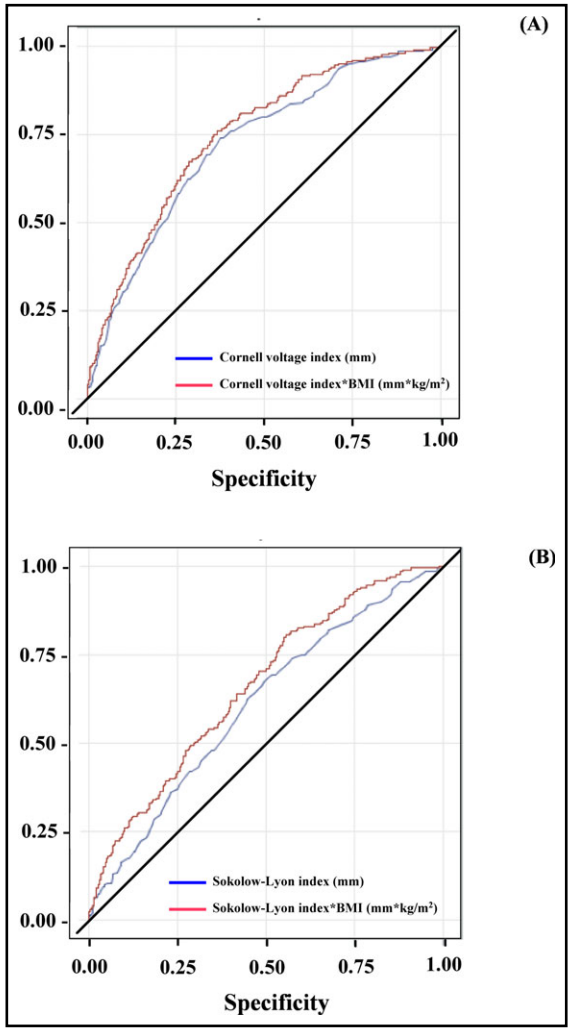

FIGURE 2. (A) Accuracy of uncorrected- and BMI-corrected Cornell voltage, estimated by receiver operating characteristic (ROC) curve analysis, in detecting echocardiographic left ventricular hypertrophy (LVH). The BMI-corrected Cornell voltage showed a significantly higher area under the curve (0.75 vs 0.72, *P*=.002) as compared to uncorrected criterion. (B) Accuracy of uncorrected and BMI-corrected Sokolow-Lyon voltage estimated by ROC curve analysis, in detecting echocardiographic LVH. The BMI-corrected Sokolow-Lyon voltage showed a significantly higher area under the curve (0.61 vs 0.66, *P*<.0001) as compared with uncorrected criterion.

In additional analyses performed in obese participants (BMI ≥30 kg/m^2), representing 11% of the entire sample, we found that areas under the curve were lower as compared with those obtained in the total population (data not shown). This finding confirms the concept that the accuracy of ECG criteria in detecting echocardiography LVH in obese patients is lower than in nonobese patients. BMI correction of ECG voltages increased areas under the curve of both criteria. The diagnostic improvement, however, reached statistical significance only for the Sokolow-Lyon index (0.615 vs 0.566, *P*=.002).

Prognostic Significance of Baseline ECG Voltages

During a mean follow-up of 149 months, a total 120 fatal and nonfatal CV events (7.7%) and 152 all-cause deaths (9.8%) were documented. Table II shows relative hazard ratios for the risk of CV mortality associated with a 1-SD increment in unadjusted and BMI-corrected Sokolow-Lyon and Cornell voltages. After adjustment for age, sex, nighttime SBP, low-density lipoprotein and high-density lipoprotein cholesterol, serum glucose, BMI, smoking, and previous CV events, either unadjusted and BMI-corrected Cornell voltage index but not unadjusted or BMI-corrected Sokolow-Lyon voltage predicted an increased risk of CV events.

The risk of nonfatal and fatal CV events increased by 50% for 1-SD increment of BMI-corrected Cornell voltage (*P*<.0001) and only by 43% for the unadjusted criterion (*P*=.001). Similar findings were found for the prediction of all-cause mortality (data not shown). ROC curves comparing the performance of unadjusted and BMI-corrected Cornell voltage and Sokolow-Lyon indexes in predicting CV and all-cause mortality did not show significant differences

As shown in Table III, in Cox regression analysis carried out in the obese fraction of the population,

TABLE II. Fatal CV Events Associated With a 1-Standard Deviation Increment of Cornell Voltage, BMI-Corrected Cornell Voltage, Sokolow-Lyon Index, and BMI-Corrected Sokolow-Lyon Index in the Total Population

CV Mortality	HR	95% CI		*P* Value	AIC
Cornell voltage					
Not adjusted	1.934	1.59	2.352	<.0001	1020.641
Age- and sex-adjusted	1.513	1.217	1.881	.0002	900.279
Fully adjusted	1.432	1.152	1.78	.0012	865.785
BMI-corrected Cornell voltage					
Not adjusted	2.072	1.743	2.463	<.0001	1005.023
Age- and sex-adjusted	1.607	1.323	1.951	<.0001	893.421
Fully adjusted	1.504	1.229	1.841	<.0001	863.28
Sokolow-Lyon index					
Not adjusted	1.479	1.215	1.8	<.0001	1046.174
Age- and sex-adjusted	1.094	0.873	1.369	.4355	913.139
Fully adjusted	1.087	0.859	1.374	.4872	875.339
BMI-corrected Sokolow-Lyon index					
Not adjusted	1.736	1.437	2.099	<.0001	1031.693
Age- and sex-adjusted	1.25	0.999	1.565	.0505	910.016
Fully adjusted	1.160	0.919	1.466	.2123	876.122

Abbreviations: AIC, Akaike information criterion; CI, confidence interval; HR, hazard ratio. Fully adjusted model: age, sex, body mass index (BMI), average nocturnal systolic blood pressure, fasting blood glucose, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, and previous cardiovascular (CV) disease.

TABLE III. Fatal Cardiovascular Events Associated With a 1-Standard Deviation Increment of Cornell Voltage, BMI-Corrected Cornell Voltage, Sokolow-Lyon Index, BMI-Corrected Sokolow Lyon Index in Obese Participants (N=194).

CV Mortality	HR	95% CI		*P* Value	AIC
Cornell voltage criteria					
Not adjusted	2.06	1.382	3.07	.0004	1020.641
Age- and sex-adjusted	1.778	1.155	2.738	.0089	900.279
Fully adjusted	1.599	1.02	2.507	.0496	865.785
Cornell voltage criteria × BMI					
Not adjusted	2.177	1.517	3.123	<.0001	1005.023
Age- and sex-adjusted	1.928	1.321	2.815	.0007	893.421
Fully adjusted	1.787	1.221	2.616	.0028	863.28
Sokolow-Lyon index					
Not adjusted	1.331	0.835	2.121	.2294	1046.174
Age- and sex-adjusted	1.047	0.646	1.697	.8516	913.139
Fully adjusted	1.593	0.814	3.12	.1742	875.339
Sokolow-Lyon index × BMI					
Not adjusted	1.644	1.015	2.662	.0432	1031.693
Age- and sex-adjusted	1.354	0.826	2.22	.2288	910.016
Fully adjusted	1.629	0.888	2.989	.1151	876.122

Abbreviations: AIC, Akaike information criterion; CI, confidence interval; HR, hazard ratio. Fully adjusted model: age, sex, body mass index (BMI), average nocturnal systolic blood pressure, fasting blood glucose, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, and previous cardiovascular (CV) disease.

uncorrected Cornell voltage showed an association with CV mortality of borderline statistical significance (*P*=.05), whereas the association was stronger (*P*=.003) with BMI-corrected Cornell voltage.

DISCUSSION

The main results of the present study conducted in a representative sample of the general population are the following: (1) correction of Cornell and Sokolow-Lyon voltage criteria by BMI improved the performance of both ECG criteria for detection of echocardiographic LVH, independently of the body size parameter used to normalize LVM; (2) Cornell voltage, but not Sokolow-Lyon index, was associated with an increased risk of CV events (and all-cause mortality), after adjusting for numerous confounding factors, including nighttime

SBP, a stronger predictor of CV prognosis than 24-hour or daytime BP; (3) correction of both Cornell voltage and Sokolow-Lyon index to BMI did not improve the value of such indexes in predicting CV and all-cause mortality as assessed by ROC curves; (4) the full-adjusted risk of CV events related to 1-SD increment of BMI-corrected Cornell voltage was 7% higher than that conferred by the uncorrected criterion in a Cox regression model (50% vs 43%, respectively); and (5) in obese participants, BMI-corrected Cornell voltage performed better than the unadjusted criterion in predicting CV fatal events

Several aspects of our cross-sectional and longitudinal analyses deserve comment. The prevalence of ECG LVH, as defined by two widely used criteria—Sokolow-Lyon and Cornell voltage—was markedly lower than echocardiographic LVH. The discrepancy between ECG and echocardiographic LVH prevalence rates depends on several factors. First, cardioelectric changes associated with the hypertrophic process (ie, amplitude of QRS voltage) do not closely correlate with LVM increments.[26] Second, the abnormal amount of thoracic adipose tissue in overweight and obese patients tends to reduce precordial ECG voltages by increasing the distance between cardiac mass and thoracic electrodes.[27] Third, precordial ECG voltages are known to be influenced by a variety of physiological and pathological conditions including lean body mass, female sex, chronic lung diseases, thorax deformations, and hypothyroidism. In our series, Cornell voltage outperformed Sokolow-Lyon criterion in detecting echocardiographic LVH being associated with higher area under the curve values (0.72 vs 0.61 for LVH/BSA, and 0.70 vs 0.60 for LVH/$h^{2.7}$). The better performance of Cornell voltage compared with Sokolow-Lyon is likely related to the fact that the former is partially independent of precordial voltages and, more importantly, the posterior-horizontal direction of electrical forces associated with LVH are better reflected by the amplitude of S wave in V3 and R wave in aVL.

In the PAMELA population, amplification of Cornell voltage and Sokolow-Lyon indexes by BMI enhanced ECG performances in detecting echocardiographic LVH, as shown by the increased area under the curve values. Improvement ranged from 4% (LVH/BSA) to 9% (LVH/$h^{2.7}$) for BMI-corrected Cornell voltage and from 7.5% to 17% for BMI-corrected Sokolow-Lyon index.

Our results are consistent with previous literature data. Pioneering findings from the Framingham Heart study suggested that Cornell voltage duration product adjusted for BMI (and age) significantly improved the detection of echocardiographic LVH across different subgroups of Caucasian adults with the exception of lean men.[28] In a group of 189 black African patients, sex-specific adjustment for BMI increased Cornell voltage and Sokolow-Lyon index sensitivity in identifying echocardiographic LVH from 37% to 69% ($P<.0001$), and from 26% to 58% ($P<.001$), respectively.[29]

In a recent study carried out in a large cohort of 2747 untreated hypertensive patients with a relatively high prevalence of echocardiographic LVH (36% according to non–sex-specific 51 g/$h^{2.7}$ criterion), Angeli and colleagues[16] were able to demonstrate that BMI-corrected Cornell voltage index increased the diagnostic accuracy of the traditional Perugia criterion and the new score exhibited the best performance in comparison to the remaining four ECG criteria examined.

The association of anatomic LVH with increased BMI and the lower sensitivity of several ECG criteria in overweight and obese patients may explain the improved ECG sensitivity for LVH after correction for BMI documented in the present and previous studies.

A meta-analysis of our group based on data from a pooled population of 4999 obese and 6623 nonobese patients showed that the likelihood of having LVH was much higher in obese patients than in their nonobese counterparts (odds ratio, 4.19; 95% confidence interval, 2.67–6.53; $P<.01$).[30] Despite the close link between obesity and LVH, a large amount of evidence indicates that sensitivity of several ECG criteria for LVH markedly decreases from normal-weight to overweight and obese patients. For instance, in the Losartan Intervention for Endpoint Reduction in Hypertension (LIFE) study, obese and overweight patients had a lower Sokolow-Lyon voltage compared with normal-weight patients and a lower prevalence of ECG LVH by Sokolow-Lyon criterion (10.9% vs 16.2% vs 31.4%, respectively; $P=.001$ for all).[31]

In order to provide a new piece of information on the potential advantages of BMI correction of ECG voltages in risk stratification,[32] we compared for the first time the prognostic value of uncorrected and BMI-corrected Sokolow-Lyon and Cornell voltage. During a 149-month follow-up period, uncorrected Cornell voltage, but not Sokolow-Lyon index, conferred an increased risk of fatal CV events (43% for 1-SD increment) and all-cause death (17% for 1-SD increment) after adjusting for traditional risk factors and ambulatory BP. After correction for BMI, a 1-SD increment of Cornell voltage was associated with a 50% higher risk of CV mortality and a 16% higher risk of all-cause mortality, respectively. The superiority of Cornell voltage over Sokolow-Lyon criterion for risk prediction is likely related to the fact that the former more closely reflects electrical changes induced by LVH. Although BMI correction improved diagnostic performance of Cornell voltage in detecting echocardiographic LVH, this was not the case for risk prediction in the total population. A notable finding of our study, however, was that BMI-corrected Cornell voltage performed better than the unadjusted criterion in predicting CV mortality in the obese fraction of the PAMELA population.

STUDY LIMITATIONS

Several limitations of the current analysis need to be mentioned. First, our ECG evaluation was restricted to QRS voltages and did not consider other variables such

as QRS duration and repolarization, which may have enhanced ECG sensitivity for LVH and ECG value in predicting outcomes. Second, our findings refer to white patients with a relatively low incidence of CV events and a low prevalence of obesity (11%); thus, they should not be extrapolated to different ethnic groups or populations with prevalent obesity or those at higher CV risk. Third, we corrected ECG voltages by BMI, a rough marker of obesity; other body size variables, such as adipose fat and fat-free body mass, have been shown to be strongly correlated with cardiac muscle mass.

CONCLUSIONS

Our observations support the notion that correction for BMI, a powerful determinant of LVM, may improve the diagnostic accuracy of Cornell voltage criterion in detecting LVH in a general population. The value of this correction in refining prediction of CV events may be relevant in obese individuals but needs to be further evaluated in populations with a high prevalence of obesity.

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