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Correction of QRS voltage for body mass index does not improve the prediction of fatal and nonfatal cardiovascular events. The Moli-sani study

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Abstract *Background and aims:* The diagnosis of LVH by ECG may particularly difficult in obese individuals. The aim of this study was to prospectively investigate whether the correction for body mass index (BMI) might improve the prognostic significance for cerebro and cardiovascular events of two electrocardiographic (ECG) criteria for left ventricular hypertrophy (LVH) in a large cohort of Italian adults.

Methods and results: In 18,330 adults (54 ± 11 years, 55% women) from the Moli-sani cohort, obesity was defined using the ATPIII criteria. The Sokolow–Lyon (SL) and Cornell Voltage (CV) criteria were used for ECG–LVH. In overweight and obese subjects, as compared with normal weight, the prevalence of ECG–LVH by the SL index was lower. During follow-up (median 4.3 yrs), 503 cerebro and cardiovascular events occurred. One standard deviation (1-SD) increment in uncorrected and in BMI-corrected SL index and CV was associated with an increased risk of events (HR 1.12, 95% CI 1.02–1.22 and HR 1.16, 95% CI 1.06–1.26 and HR 1.12, 95% CI 1.03–1.23 and HR 1.17, 95% CI 1.07–1.27, respectively for SL and CV). In obese subjects, 1-SD increment in uncorrected CV and in BMI-corrected CV was not associated to a significant risk of events (HR 1.05, 95% CI 0.910–1.22 and HR 1.08, 95% CI 0.95–1.23 respectively). Uncorrected SL index showed a significant association with events, which was marginally stronger with BMI-corrected SL voltage (HR 1.18, 95% CI 1.02–1.37 and HR 1.17, 95% CI 1.04–1.33 respectively, Akaike information criterion change from 3220 to 3218).

Conclusions: BMI correction of ECG LVH voltage criteria does not significantly improve the prediction of cerebro and cardiovascular events in obese patients in a large cohort at low cardiovascular risk.

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Introduction

The detection of left ventricular hypertrophy (LVH) carries important prognostic information for future cardiovascular morbidity/mortality [1,2] independent of hypertension and other risk factors, in the general population and in different clinical settings [3,4]. The robust evidence that regression of ECG–LVH, induced by treatment, results in improved cardiovascular prognosis [5–12] have indicated that the detection of cardiac hypertrophy represents a major task in the use of clinical electrocardiography.

The association of obesity with cardiac remodeling and with subclinical abnormalities in myocardial function and diastolic filling [13] has been frequently reported, possibly explaining the increased risk for cardiovascular morbidity. In addition obesity is associated with other diseases, such as diabetes mellitus, metabolic syndrome or hypertension, associated to a high risk of LVH development [14].

Even in hypertrophic cardiomyopathy (the most common genetic heart disease), cardiac phenotype and clinical course are influenced by the presence of overweight and obesity [15].

The diagnosis of LVH by ECG may be particularly difficult in obese individuals [16]. Conflicting results were obtained in studies comparing the accuracy of several ECG criteria for LVH (including voltage criteria) to echocardiographic [17–20] or to MRI LV mass measurements and calculation in obese individuals. The diagnostic performance of LVH of ECG criteria based on precordial voltages is clearly poor in obese patients and alternative criteria such as the Cornell voltage, the Cornell voltage product or the voltage of R wave in lead aVL [21] have been also shown to be unsatisfactory [22].

The Moli-sani project (http://www.moli-sani.org) is a population-based cohort study aiming at evaluating the risk factors linked to chronic-degenerative disease with particular regard to cerebrovascular, cardiovascular and cancer and intermediate metabolic phenotypes such as hypertension, dyslipidemia, diabetes, obesity, and metabolic syndrome [23–25] in which a computerized ECG acquisition and interpretation was performed. In this large adult low cardiovascular risk Italian population, we have previously shown that the use of several ECG criteria may give different prognostic information in normal weight, overweight or obese patients [26]. In the presence of obesity none of the ECG–LVH criteria suggested by European guidelines reached a predictive significance of cardiovascular events, being body mass index (BMI) a powerful determinant of true LV mass.

Some authors have suggested that correction of ECG voltages by measures of body size might improve the accuracy of electrocardiography for the diagnosis of LVH [27–29], although the value of adjustment for BMI of ECG indexes in improving the prediction of cardiovascular events has been poorly investigated [30].

Thus, we considered worthwhile to investigate the prevalence and the prognostic significance for fatal and nonfatal cerebrovascular and cardiovascular events of different ECG voltages criteria for LVH, indexed by BMI in normal weight, overweight and obese subjects in a large community sample of the Italian adult population in the framework of the Moli-sani Study.

Methods

The Moli-sani study is a large population-based cohort study that recruited subjects from the general population of the Molise region, a central-southern area of Italy [31]. Individuals were enrolled from March 2005 to April 2010 and were followed up for mortality for a median of 4.3 years (interquartile range: 3.5–5.3 years, 79,121 person/years). Exclusion criteria were pregnancy at the time of recruitment, disturbances in understanding or willingness, current poly-traumas or coma, or refusal to sign the informed consent. Between March 2005 and April 2010, 24,325 subjects were recruited by accurately trained research personnel. The recruitment strategies were carefully defined and standardized; structured digitalized questionnaires were administered to collect personal and clinical information. Primary fatal and nonfatal incident cases of coronary heart disease (CHD, i.e., unstable angina, myocardial infarction, coronary revascularization and sudden death for unspecified cardiac event) and cerebrovascular disease that occurred in the cohort during follow-up were ascertained by linkage of the study cohort to the hospital discharge files and to the regional ReNCaM registry and, by using the International Classification of Diseases, ninth revision(ICD-9). For CHD, ICD 9 codes 410–414 and/or reperfusion procedure (ICD-9 codes 36.0–36.9) and for cerebrovascular disease, ICD9 codes 430–432, 434, 436–438 or procedure codes for carotid revascularization (ICD 9 code 38.12) were considered. Suspected CHD deaths were identified when ICD-9 codes 410–414 or 798 and 799 were reported as the underlying cause of death or codes 250, 401–405, 420–429 as the underlying cause of death, associated with codes 410–414 as a secondary cause of death. Suspected cerebrovascular deaths were identified when ICD 9 codes 430–438 were reported as the underlying, antecedent, or direct cause of death. All events were validated using procedures of the American Heart Association (AHA), World Heart Federation (WHF), European Society of Cardiology (ESC), Centers for Disease Control (CDC) and National Heart, Lung and Blood Institute (NHLBI) for epidemiology and clinical research studies [33]. Heart Failure (HF) incidence was identified by direct linkage with hospital discharge forms or ReNCaM registry, according to the ICD-9-CM code: 428 (“Heart failure”) when it was present in the main and in first 2 concomitant admission diagnoses and in the underlying cause of death, respectively. Time to event was calculated until the date of diagnosis of CVD, or the date of death, or the date of the last contact prior to December 2011.

A critical evaluation of the diagnosis was performed, by analyzing hospital medical records for hospital deaths and for other deceased patients if previously hospitalized during the follow-up. The process of ascertainment of death causes was conducted by qualified personnel

blinded to the present analyses. The procedures followed were in accordance with institutional guidelines, and informed consent was obtained from each participant. The study protocol was in accordance with the ethical guidelines of 1975 the Declaration of Helsinki, and approved by the local institution's Human Research Committee (Catholic University ethical committee).

Anthropometric, blood pressure (BP) measurements and definition of risk factors

Body weight and height were measured on a standard beam balance scale with an attached ruler with subjects wearing no shoes and only light indoor clothing. BMI was calculated as kg/m^2. Participants were classified as normal weight (BMI range <25 kg/m^2), over-weight (25–30 kg/m^2), and with obesity (class 1–3, i.e. BMI 30–34.9 kg/m^2 or >35 kg/m^2) according to WHO definition [32]. Blood pressure (BP) was measured by an automatic device (OMRON-HEM-705CP) three times on the nondominant arm and the average of the last two values was taken as the BP [33]. Hypertension was defined as systolic BP > 140 mmHg or diastolic BP > 90 mmHg, or using pharmacological treatment. Hypertensive patients were classified according to systolic and/or diastolic BP values in to Grade 1 (>140–159 and/or >90–99 mmHg), grade 2 (160–179 and/or 100–109 mmHg) and grade 3 (>180 and/or >110 mmHg) [33]. Diabetes was defined as blood glucose >126 mg/dL or using pharmacological treatment. Hypercholesterolemia was considered as cholesterol >240 mg/dL or using pharmacological treatment. Serum lipids and glucose were assayed by enzymatic reaction methods using an automatic analyzer (ILab 350, Instrumentation laboratory (IL), Milan, Italy). LDL-cholesterol was calculated according to Friedewald formula Physical activity was assessed by a structured questionnaire (24 questions on working time, leisure time and sport participation) and expressed as daily energy expenditure in metabolic equivalent task-hours (MET/h). Subjects were classified as non-smokers if they had smoked less than 100 cigarettes long-life or they had never smoked cigarettes, ex-smokers if they had smoked cigarettes in the past and had stopped smoking for at least 1 year, and current smokers those who reported having smoked at least 100 cigarettes in their lifetime and still smoked or had quit smoking within the preceding year.

Education was based on the highest qualification attained and was categorized as low (secondary school or lower) or high (high school or higher). Household income was divided into four categories as low (≤10,000 Euros/year), low-medium (>10,000 ≤ 25,000 Euros/year), medium–high (>25,000 ≤ 40,000 Euros/year) and high (>40,000 Euros/year).

Electrocardiographic LVH

LVH was measured from the standard 12-lead resting ECG. ECG tracings were measured using a Cardiette_ar2100-view electrocardiograph storing ECG in SCP *(Standard Communication Protocol)* format. QRS duration was calculated by the electrocardiograph according to a standardized formula.

The presence of LVH was defined according to different criteria, as suggested by 2013 ESH/ESC guidelines [33]. ECG–LVH was determined using Sokolow–Lyon voltage index (SV1 + RV in V5 or V6, which-ever is larger, with a cut-off value of 3.5 mV). The Cornell voltage was calculated as by the sum of R in aVL and S in V3 with cut-off values of >2.8 mV in men and >2.0 mV in women.

Statistical analysis

Values for continuous variables are means ± standard deviation (SD) or as percentage. Means were compared by the Student's *t*-test for independent samples, and categorical data were analyzed by the chi-square test or Fisher's exact test when appropriate.

ANOVA for continuous or categorical variables was used to identify variables associated with the different body weight categories (normal, overweight, and obesity class 1–3) and included socio9 demographic variables (age, sex, smoking habit, income, education and occupational class, physical activity), hypertension (as a dichotomic and also by 3 strata), systolic and diastolic BP, hypercholesterolemia, diabetes and blood glucose. Associations with *P* value < 0.10 were used in the multivariable model.

The potential predictors tested for association with presence/absence of LVH for each electrocardiographic criterion included socio-demographic variables [age, sex, income, education, occupational class, smoking habit, physical activity, hypercholesterolemia, hypertension (as a dichotomic and also by 3 strata), diabetes and BMI categories]. Hazard ratios with corresponding 95% confidence intervals of cardiovascular events were calculated by the Cox's proportional hazard model to quantify the association of different LVH criteria uncorrected and BMI corrected with the occurrence of events in the whole population and according to different BMI strata. Appropriate interaction terms were calculated to test for differences of the effect.

The Akaike Information Criterion (AIC) was used as a measure of model accuracy. The delta AIC statistic was used to evaluate the difference between AIC values for two tested models.

The data analysis was generated using SAS/STAT software, Version 9.1.3 of the SAS System for Windows_2009. SAS Institute Inc. and SAS are registered trademarks of SAS Institute Inc., Cary, NC, USA.

Results

For the present analysis 18,330 subjects (10,033 women and 8297 men) were analyzed. Subjects with incomplete questionnaire (n = 235), history of cardiovascular disease, including heart failure (n = 1140) and with a BMI < 18.5 kg/m^2 (n = 74) were excluded. Subjects

Table 1 General characteristics of the study population.

No. of subjects, %	18,330 (100%)
Sex (men; *n*, %)	8297 (45.3%)
Age [year; mean (95% CI)]	54.4 (54.2–54.5)
Smokers (*n*, %)	4309 (23.5%)
Total physical activity [MET-h; mean (95% CI)]	43.3 (43.1–43.4)
BMI [kg/m^2; mean (95% CI)]	28.0 (27.9–28.1)
Obesity (*n*, %)	5286 (28.8%)
Overweight (*n*, %)	7956 (43.4%)
Normal weight (*n*, %)	5088 (27.8%)
Normotension (*n*, %)	8442 (46.1%)
Grade 1 Hypertension (*n*, %)	3690 (20.1%)
Grade 2 Hypertension(*n*, %)	526 (28.9%)
Grade 3 Hypertension(*n*, %)	782 (4.3%)
Diabetes (*n*, %)	1459 (8.0%)
Heart rate [bpm; mean (95% CI)]	67.2 (67.1–67.4)
QRS duration [ms; mean (95% CI)]	88.8 (88.7–89.0)

underweight (BMI $<$ 18 kg/m^2) showed a greater prevalence of female sex and history of cancer, and were younger. In addition, subjects with missing ECG data (N = 3007) or with ECG features that could not allow the diagnosis of LVH, such complete left or right bundle branch block (n = 859), and diagnosis of anterior (n = 17) or posterior infarction (n = 663) were excluded from this analysis.

General characteristics of men and women included in the study are illustrated in Table 1.

Few subjects (n = 342, 1.9%) had class 3 obesity and were considered in a unique group with class 1 (n = 3866, 21.1%) and 2 (n = 1078, 5.9%) obese subjects.

Prevalence of ECG–LVH The prevalence of ECG–LVH ranged from 0.31% (identified by the Sokolow–Lyon) to 0.96% (based on the Cornell Voltage) in the whole population (Table 2).

In overweight (n = 7956) and in obese (n = 5286) patients, as compared with normal weight subjects (n = 5088), a progressively lower age and sex adjusted prevalence of ECG–LVH was observed when the Sokolow–Lyon voltage criterion was used, while a higher prevalence was shown by using the Cornell Voltage. ECG–LVH prevalence was not statistically different among the different groups when the Cornell voltage criteria were used.

Cardiovascular events During follow-up (median 4.3 yrs), there were 503 new cerebrovascular and cardiovascular events (n = 77 fatal and n = 436 non-fatal; n = 216 coronary heart disease, n = 51 stroke and n = 307 heart failure; some individuals experienced more than one event; 79,121 person years). The overall event rate was 6.38/1000 participants per year, reflecting the low risk for cardiovascular events in this population.

The age and sex adjusted incidence of events was significantly higher in subjects with ECG–LVH according to the Cornell-Voltage criteria (HR 1.89, 95% CI 1.05–3.39), but not for the Sokolow–Lyon (HR 1.67, 95% CI 0.54–5.20).

After adjusting for different confounders (age, sex, cigarette, hypertension, hypercholesterolemia, diabetes, income, education, occupational class, physical activity) 1-SD increment in the Cornell Voltage index and the BMI-corrected Cornell voltage was also associated with an increased risk of cardiovascular events (HR 1.12, 95% CI 1.03–1.23 and HR 1.17, 95% CI 1.07–1.27, respectively, Akaike information criterion change from 8835 to 8839, Table 3).

A significant increase in the risk of cardiovascular events was observed according to one standard deviation (SD) increment of the Sokolow–Lyon voltage and of the BMI-corrected Sokolow–Lyon voltage (HR 1.12, 95% CI 1.02–1.22 and HR 1.16, 95% CI 1.06–1.26, respectively, Akaike information criterion change from 8836 to 8840, Table 4), adjusted for age, sex, cigarette, hypercholesterolemia, diabetes income, education occupational class and physical activity.

The predictive significance of BMI-corrected Sokolow–Lyon and Cornell voltage was assessed in obese subjects; after adjusting for confounders, the hazard ratio of CV events related to 1-SD increment of uncorrected Cornell voltage was not significant and similar to the one conferred by the BMI corrected Cornell voltage (HR 1.05, 95% CI 0.910–1.22 and HR 1.08, 95% CI 0.95–1.23, respectively, Table 3).

Uncorrected Sokolow–Lyon voltage showed a significant association with CV events, that was marginally stronger with BMI-corrected Sokolow–Lyon voltage (HR 1.18, 95% CI 1.02–1.37 and HR 1.17, 95% CI 1.04–1.33 respectively, Akaike information criterion change from 3220 to 3218, Table 4).

In further analyses we also explored interactions between sex (2 levels) and hypertension categories (2 levels because of the low number of events) and ECG LVH voltage criteria uncorrected or BMI corrected on cardiovascular risk and we did not observe a significant improvement in the risk prediction by the use of BMI corrected criteria (Tables 3 and 4).

Table 2 Prevalence of LVH indicators in all population and in BMI categories.

Diagnostic criterium	All	BMI (kg/m^2)			*P*-value[a]
		18.5–24.9	25.0–29.9	≥30.0	
	18,330 (100%)	5088 (27.8%)	7956 (43.4%)	5286 (28.8%)	
Sokolow–Lyon	56 (0.31%)	22 (0.43%)	28 (0.35%)	6 (0.11%)	0.0008
Cornell voltage	176 (0.96%)	34 (0.7%)	70 (0.9%)	72 (1.4%)	0.20

See text for LVH definition according to Sokolow–Lyon and Cornell voltage criteria.
[a] Adjusted for age and sex.

Table 3 Multivariable hazard ratios of fatal and not fatal cardiovascular events related to one-standard deviation increment of Cornell-voltage (mm) or Cornell-voltage × BMI (mm*kg/m^2).

	No. event/No. subjects	Cornell-V uncorrected		Cornell-V × BMI	
		HR (95% CI)	AIC	HR (95% CI)	AIC
All	503/18,330	1.12 (1.03–1.23)	8835	1.17 (1.07–1.27)	8839
Women	198/10,033	1.15 (1.00–1.33)	3231	1.16 (1.02–1.33)	3231
Men	305/8297	1.10 (0.99–1.23)	4964	1.16 (1.04–1.30)	4965
P for interaction		0.37		0.44	
BMI 18.5–24.9 kg/m^2	84/5088	1.20 (0.98–1.46)	1254	1.25 (0.94–1.65)	1253
BMI 25.0–29.9 kg/m^2	212/7956	1.17 (1.02–1.34)	3373	1.20 (1.03–1.40)	3371
BMI ≥30 kg/m^2	207/5286	1.05 (0.91–1.22)	3224	1.08 (0.95–1.23)	3223
P for interaction		0.18		0.20	
Normotensive	79/8363	1.31 (1.03–1.67)	1248	1.50 (1.18–1.91)	1250
Hypertensive	420/9348	1.12 (1.023–1.23)	7098	1.15 (1.05–1.26)	7097
P for interaction		0.066		0.012	

Hazard ratios are adjusted for age, sex, BMI, cigarette, hypertension, hypercholesterolemia, diabetes, income, education, occupational class and physical activity.

Discussion

In the present study we examined the predictive power for cardiovascular events of the correction of Cornell and Sokolow–Lyon voltages for body size among different BMI categories, using data from the Moli-sani study, which enrolled a representative sample of a general population of central-southern Italy.

The main finding is the lack of improvement in the prognostic significance for CV events of Cornell and Sokolow–Lyon voltages corrected for body mass index in obese individuals.

We have previously shown that in normal weight and overweight subjects the Cornell product, but not the Cornell or the Sokolow–Lyon voltage criteria, were associated with an increased risk of CV deaths, after adjusting for numerous confounding factors [26].

The sensitivity of several ECG criteria for LVH, mainly those based on precordial leads voltage amplitude, progressively diminishes from normal-weight to overweight and obese patients. In the Losartan Intervention for Endpoint Reduction in Hypertension (LIFE) study, obese and overweight hypertensive patients had a lower Sokolow–Lyon voltage compared with normal-weight patients and a lower prevalence of ECG LVH by Sokolow–Lyon criterion [34]. In obese subjects the amount of LV mass increase may not correspond to the cardiac electric changes during the hypertrophic response [35] and the increase of epicardial fat may increase the distance between the left ventricle and the skin electrodes on the chest wall, reducing precordial ECG voltages [36].

Despite these evidences, a decrease in QRS voltage has been reported in obese subjects, after weight loss and parallel LVH regression [37,38].

Few studies have suggested that correction of ECG voltages by measures of body size may improve the accuracy of electrocardiography for the diagnosis of LVH, when compared to echocardiography [27–29]. The value of correction for BMI of ECG indexes in improving the prediction of CV events was investigated in only one study, conducted in the Pressioni Arteriose Monitorate E Loro Associazioni (PAMELA) study [30].

Table 4 Multivariable hazard ratios of fatal and non-fatal cardiovascular events related to one-standard deviation increment of Sokolow–Lyon (mm) or Sokolow–Lyon × BMI (mm*kg/m^2).

	No. event/No. subjects	Sokolow–Lyon uncorrected		Sokolow–Lyon × BMI	
		HR (95% CI)	AIC	HR (95% CI)	AIC
All	503/18,330	1.12 (1.02–1.22)	8836	1.16 (1.06–1.26)	8840
Women	198/10,033	1.19 (1.02–1.37)	3230	1.21 (1.06–1.38)	3229
Men	305/8297	1.09 (0.98–1.22)	4965	1.13 (1.01–1.26)	4967
P for interaction		0.26		0.21	
BMI 18.5–24.9 kg/m^2	84/5088	1.05 (0.85–1.30)	1257	1.07 (0.81–1.40)	1255
BMI 25.0–29.9 kg/m^2	212/7956	1.10 (0.97–1.25)	3375	1.10 (0.96–1.27)	3374
BMI ≥30 kg/m^2	207/5286	1.18 (1.02–1.37)	3220	1.17 (1.04–1.33)	3218
P for interaction		0.34		0.087	
Normotensive	79/8363	0.99 (0.76–1.27)	1252	1.10 (0.85–1.42)	1259
Hypertensive	420/9348	1.17 (1.06–1.28)	7093	1.19 (1.09–1.30)	7091
P for interaction		0.10		0.59	

Hazard ratios are adjusted for age, sex, BMI, cigarette, hypertension, hypercholesterolemia, diabetes, income, education, occupational class and physical activity.

Some aspects of our cross-sectional and longitudinal analyses deserve a comment. A lower prevalence of ECG LVH was observed in the Moli-sani study, as compared with other general populations [39–41].

The discrepancy between different criteria ECG–LVH prevalence rates may be explained by demographic factors (age, female sex, etc) and by the concomitant presence of essential hypertension, diabetes mellitus, chronic obstructive lung disease, sleep apnea, thorax anatomic abnormalities, and obesity, all significantly affecting the diagnostic accuracy of some ECG criteria. In fact, an apparent paradoxical finding was observed in this study, i.e. the prevalence of Cornell LVH criteria, adjusted only for age and sex, was twice as high in obese patients compared to those with BMI < 25 kg/m^2, due to the additional effect of hypertension and diabetes mellitus.

Among several cardiovascular and metabolic risk factors, obesity represents a strong biological stimulus for the development of LVH. A comprehensive meta-analysis has recently shown that the likelihood of having anatomic LVH was much higher in obese patients than in their non obese counterparts (odds ratio, 4.19; 95% confidence interval, 2.67–6.53; $P < 0.01$) [42].

As previously performed by Cuspidi et al. in the Pamela cohort [30], we compared the prognostic value of uncorrected and BMI-corrected Sokolow–Lyon and Cornell voltage. In the whole population, both uncorrected Cornell voltage and Sokolow–Lyon index conferred an increased risk of CV events (12% for 1-SD increment for both criteria) after adjusting for traditional risk factors and other confounders. After correction for BMI, a 1-SD increment of the Cornell voltage and of the Sokolow–Lyon voltage remained significantly associated with a 17% and 16% higher risk of CV deaths, respectively. We were not able to confirm the superiority of Cornell voltage over Sokolow–Lyon criterion for risk prediction.

In obese participants of the Moli-sani cohort ($N = 5286$) we did not observe any improvement by the BMI correction of either criteria over the uncorrected value in predicting CV morbidity and mortality.

The large sample size and random allocation into the cohort, minimizing selection bias, and a less than 30% prevalence of obesity, allowing to assess the different value of ECG criteria in predicting CV events across normal weight to overweight and obese subjects, are some strengths of this study. The evaluation of ECG was performed on digital ECG [25]. Moreover, in the Moli-sani study [24,25,31,43] other potential confounders, such as education, income and physical activity were accurately collected and could have been taken into account, in addition to traditional demographic characteristics.

Some limitations of the current analysis need to be mentioned. The number of subjects meeting the criteria for Sokolow–Lyon ECG–LVH is low and the observed event rate indicates the relatively low risk for CV complications in this population. Because of the small number of events observed in the study, the presence and/or absence of differences in risk prediction observed across the 3 categories of body weight might not reflect true differences in predictive power as a function of BMI. Other studies performed in population with a similar overall CV risk, have previously assessed the prognostic value of different ECG abnormalities, but only partially considering BMI categories [30,40].

The participants to the Moli-sani study are all white subjects, and therefore the results cannot be extrapolated to different ethnic groups [44] or populations with prevalent obesity or those at higher CV risk. Office blood pressure values were accurately measured in this study, while a most appropriate effect of blood pressure when assessing LVH may be obtained by 24-h ambulatory blood pressure measurements.

Finally, we have used BMI, but not other more precise markers of obesity, including epicardial fat thickness, or adipose fat and fat-free body mass.

Conclusions

In conclusion, in a large adult Italian population, our observations support the notion that the correction of ECG voltage criteria (Sokolow–Lyon and Cornell) in obese patients does not improve their prognostic information.

We confirm that an easy-to-use and relatively low-cost tool such as ECG can be used to identify LVH using current criteria in normal and overweight subjects, but in obese individuals, belonging to a low cardiovascular risk general population, it does not stratify CV risk.

These findings need to be further evaluated in other populations and in groups of subjects with and without overweight or obesity.

Conflicts of interest

None.

Appendix A

The investigators of the Moli-sani Study are the following:

The enrolment phase of the Moli-sani Study was conducted at the Research Laboratories of the Catholic University in Campobasso (Italy), the follow up of the Moli-sani cohort is being conducted at the Department of Epidemiology and Prevention of the IRCCS Neuromed, Pozzilli, Italy.

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