Original Article

Obesity and ECG left ventricular hypertrophy

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Aim: Our aim was to investigate the prevalence and the prognostic significance for fatal and nonfatal cerebrovascular and cardiovascular events of different ECG criteria for left ventricular hypertrophy (LVH) in normal weight, overweight and obese patients in an adult Italian population.

Methods: A total of 18 330 adults (mean age 54 ± 11 years, 55% women, 53% hypertensive patients) were analyzed from the Moli-sani cohort. Obesity was defined using the ATPIII criteria. ECG-LVH was defined according to 2013 ESC-ESH guidelines.

Results: The age and sex adjusted prevalence of ECG-LVH did not differ from normal weight patients to class 1–3 obesity patients, when Cornell-voltage criterion was used. In overweight and obese patients, as compared with normal weight patients, a progressively lower prevalence of ECG-LVH was observed when the Sokolow–Lyon index was used, whereas a higher prevalence was shown by using the aVL R-wave voltage (>11 and >5.7 mm) and the Cornell-voltage-QRS duration product. The incidence of cardiovascular events was significantly greater in patients with ECG LVH diagnosis by the Cornell voltage [hazard ratio 1.89, 95% confidence interval (CI) 1.05–3.39] and the Cornell product (hazard ratio 1.87, 95% CI 1.31–2.67). After adjusting for different confounders (age, sex, cigarette, hypertension, hypercholesterolemia, diabetes, income, education, occupational class and physical activity) and for BMI categories, only the Cornell product remained significantly associated with a higher incidence of cardiovascular events (hazard ratio 1.66; 95% CI 1.16–2.38). The predictive significance of different LVH criteria was assessed across BMI categories; after adjusting for confounders, no LVH criteria were significantly associated with an increased risk of cardiovascular events in obese patients; Cornell-product LVH remained an independent predictor of events in normal weight and overweight individuals (hazard ratio 2.63; 95% CI 1.10–6.28 and hazard ratio 2.72; 95% CI 1.52–4.25, respectively).

Conclusion: Our results confirm that ECG LVH prevalence may differ according to the criteria used across BMI categories *in a low cardiovascular risk cohort*. The use of different LVH criteria according to BMI categories may improve cardiovascular risk stratification in a general population independently of several confounding factors.

Keywords: BMI, cerebrovascular and cardiovascular disease, Cornell product, Cornell voltage, digital ECG, left ventricular hypertrophy, obesity, Sokolow–Lyon

Abbreviations: BP, blood pressure; CV, cardiovascular; LVH, left ventricular hypertrophy

INTRODUCTION

Resting ECG carries important independent prognostic information for future cardiac events [1,2]. In clinical ECG, the detection of left ventricular hypertrophy (LVH) represents a major task, as confirmed by the increasing evidence that LVH is a powerful marker of cardiovascular morbidity/mortality in the general population as well as in different clinical settings [3,4]. Furthermore, regression of ECG LVH induced by treatment results in improved cardiovascular prognosis [5–12].

Cardiac remodeling, characterized by concentric geometry or eccentric geometry and LVH, may be frequently observed in obese patients and is associated with subclinical abnormalities in myocardial function and diastolic filling [13], possibly explaining the increased risk for cardiovascular morbidity, including heart failure. Other comorbidities such as diabetes mellitus, metabolic syndrome and hypertension are usually associated with obesity, carrying a high risk of LVH [14]. Even in the most common genetic heart disease, such as hypertrophic cardiomyopathy, obesity has been shown to influence cardiac phenotype and clinical course [15].

The identification of LVH by ECG, however, may particularly be difficult in obese individuals, although this technique remains a first-line diagnostic tool and the need for more accurate ECG criteria represents a clinical priority in this setting [16]. The accuracy of several ECG criteria for

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LVH (including voltage criteria) has been determined in obese individuals, as compared with echocardiographic [17–20] or MRI left ventricle (LV) mass measurements and calculation [21] with conflicting results. The performance of ECG criteria for LVH based on precordial voltages was 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 [22] have been also shown to be unsatisfactory [23].

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 and cardiovascular diseases (CVD) and cancer and intermediate metabolic phenotypes such as hypertension, dyslipidemia, diabetes, obesity and metabolic syndrome [24–26] in which a computerized ECG acquisition and interpretation was performed.

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

METHODS AND PATIENTS

The Moli-sani study is a large population-based cohort study that recruited patients from the general population of the Molise region, a central-southern area of Italy [27]. 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 patients were recruited by research personnel, accurately trained. The recruitment strategies were carefully defined and standardized; structured digitalized questionnaires were administered to collect personal and clinical information.

Mortality was recorded until December 2011. Overall mortality and cause-specific mortality were assessed by the Italian mortality registry (ReNCaM registry), validated by Italian death certificates (ISTAT form) and coded according to the International Classification of Diseases (ICD-9). Cardiovascular deaths were defined when the underlying cause of death had an ICD-9 code of 390–459 or 745–747, 798 or when diabetes (ICD-9 code 250), as the underlying cause of death associated with an ischemic heart disease (ICD-9 codes 410–414) or a cerebrovascular accident (ICD-9 codes 342, 430–438) as a secondary cause of death, and for cancer deaths an ICD-9 code of 140–208. 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 Moli-sani study complies with the Declaration of Helsinki and was approved by the Catholic University ethical committee. All participants enrolled provided written informed consent.

Anthropometrc, blood pressure measurements and definition of risk factors

Body weight and height were measured on a standard beam balance scale with an attached ruler with patients wearing no shoes and only light indoor clothing. BMI was calculated as kg/m^2. Patients were classified as normal weight (BMI range <25 kg/m^2), overweight (25–30 kg/m^2) and with obesity (class 1–3, i.e. BMI 30–34.9 or >35 kg/m^2) according to WHO definition [28].

Waist circumferences were measured according to the National Institutes of Health Guidelines, heart, lung and blood guidelines [29].

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 [30]. Hypertension was defined as SBP more than 140 mmHg or DBP more than 90 mmHg, or using pharmacological treatment. Diabetes was defined as blood glucose more than 126 mg/dl or using pharmacological treatment. 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). Hypercholesterolemia was considered as cholesterol more than 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.

Patients were classified as nonsmokers 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 ($\leq$10 000 Euros/year), low-medium ($>$10 000 $\leq$ 25 000 Euros/year), medium–high ($>$25 000 $\leq$ 40 000 Euros/year) and high ($>$40 000 Euros/year).

ECG left ventricular hypertrophy

LVH was measured from the standard 12-lead resting ECG. ECG tracings were measured using a Cardiette_ar2100-view ECG storing ECG in standard communication protocol format. QRS duration was calculated by the ECG according to a standardized formula.

The presence of LVH was defined according to different criteria, as suggested by 2013 ESH/ESC guidelines [31]. ECG-LVH was determined using Sokolow–Lyon voltage index ($S_{V1} + R_V$ in V5 or V6, whichever is larger, with a cutoff value of 3.5 mV). The Cornell voltage was calculated as by the sum of R in aVL and S in V3 with cutoff values of

more than 2.8 mV in men and more than 2.0 mV in women. The Cornell-voltage duration product (Cornell product), an approximation of the area under the QRS, was calculated as the Cornell-voltage times QRS duration (milliseconds) [$(R_{aVL} + S_{V3}) \times (\text{QRS duration}) > 2440\,\text{mm} \times \text{ms}$ in men and $(R_{aVL} + S_{V3} + 6\,\text{mm}) \times (\text{QRS duration}) > 2440\,\text{mm} \times \text{ms}$ ms in women]. The voltage of the R wave in lead aVL was also measured and the cutoff value of more than 11 mm was considered for the diagnosis of LVH; an additional cutoff value of 5.7 mm was considered, according to the results of Verdecchia *et al.* [32]. Finally, the presence of strain was evaluated, and strain was defined as the presence in leads V5 and/or V6 of typical-a standard 'strain' pattern with a downsloping ST segment and an asymmetric, inverted T wave without terminal positivity or a T wave with terminal positivity not exceeding its negative component in amplitude or biphasic-downsloping ST segment with an inverted T wave of at least 0.5 mm in amplitude with terminal positivity exceeding the negative component in amplitude.

Statistical analysis

Values for continuous variables are means ± SD or as percentage. Means were compared by 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 sociodemographic variables (age, sex, smoking habit, income, education and occupational class and physical activity), hypertension (as a dichotomic and also by three strata), SBP and DBP, hypercholesterolemia, diabetes and blood glucose. Associations with *P* value less than 0.10 were used in the multivariable model.

The potential predictors tested for association with presence/absence of LVH for each ECG criterion included sociodemographic variables [age, sex, income, education, occupational class, smoking habit, physical activity, hypercholesterolemia, hypertension (as a dichotomic and also by three strata), diabetes and BMI categories]. Hazard ratios with corresponding 95% confidence intervals (CIs) of cardiovascular events (fatal and nonfatal) or all-cause mortality were calculated by the Cox's proportional hazard model to quantify the association of different LVH criteria 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 data analysis was generated using SAS/STAT software, Version 9.1.3 of the SAS SystemforWindows_2009. SAS Institute Inc. and SAS are registered trademarks of SAS Institute Inc., Cary, North Carolina, USA.

RESULTS

For the present analysis, 18 330 patients (10 033 women and 8297 men) were analyzed. Patients with incomplete questionnaire ($n = 235$), history of CVD ($n = 1140$) and with a BMI less than 18 kg/m^2 ($n = 74$) were excluded. Patients underweight (BMI < 18 kg/m^2) showed a greater prevalence of female sex and cancer and were younger. In addition, patients 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 patients ($n = 342$, 1.9%) had class 3 obesity and were considered in a unique group with class 1 and 2 obese patients.

Prevalence of ECG left ventricular hypertrophy

The prevalence of ECG-LVH ranged from 0.31 (identified by the Sokolow–Lyon) to 14.83% (based on the R-wave amplitude in aVL >5.7 mm) in the whole population (Table 2).

In overweight and obese patients, as compared with normal weight patients , a progressively lower age and sex adjusted prevalence of ECG-LVH was observed when the Sokolow–Lyon voltage criterion was used, whereas a higher prevalence was shown by using the aVL R-wave voltage (both >11 and >5.7 mm) and the Cornell product. ECG-LVH prevalence was not statistically different among the different groups when the Cornell-voltage criteria were used. In only 13 patients (0.07%), the presence of strain was identified, and it was slightly, but not significantly, greater in obese individuals (0.13%). Because of such a low prevalence and the limited predictive value in the entire population and across BMI categories, we did not include the strain in further analyses.

We also assessed whether a greater prevalence of ECG LVH was observed in the different groups when LVH was considered present if any of the specified criteria (Sokolow–Lyon, Cornell voltage, Cornell product and R wave in aVL) were abnormal; a progressively greater prevalence of ECG-LVH was observed from normal weight to overweight and obese patients if any of the specified criteria were abnormal.

Cardiovascular events

During the follow-up, there were 503 new cerebrovascular and cardiovascular events ($n = 77$ fatal and $n = 436$ nonfatal; $n = 216$ coronary heart disease, $n = 51$ stroke and $n = 307$ heart failure; some individuals experienced more than one event) (Table 3). The overall event rate was 6.38/

TABLE 1. General characteristics of the study population

Number of patients (%)	18 330 (100%)
Sex (men; *n*, %)	8297 (45.3%)
Age (year, SD)	54 (11)
Smokers (*n*, %)	4309 (23.5%)
Total physical activity (MET-h, SD)	43 (9)
BMI (kg/m^2, SD)	28 (5)
Normotension (*n*, %)	8442 (46.1%)
Grade 1 hypertension (*n*, %)	3690 (20.1%)
Grade 2 hypertension (*n*, %)	5296 (28.9%)
Grade 3 hypertension (*n*, %)	782 (4.3%)
Diabetes (*n*,%)	1459 (8.0%)
HR (bpm, SD)	67 (10)
QRS duration (ms, SD)	89 (8)

HR, heart rate; MET-h, metabolic equivalent task-hours.

TABLE 2. Prevalence of left ventricular hypertrophy indicators in all population and in BMI categories

		BMI (kg/m^2)			
Diagnosis	All 18 330 (100%)	18.5–24.9 5088 (27.8%)	25.0–29.9 7956 (43.4%)	≥30.0 5286 (28.8%)	*P* value*
Sokolow–Lyon	56 (0.31%)	22 (0.43%)	28 (0.35%)	6 (0.11%)	0.0008
Cornell (V)	176 (0.96%)	34 (0.7%)	70 (0.9%)	72 (1.4%)	0.20
R_{aVL} (>11)	271 (1.48%)	19 (0.4%)	113 (1.4%)	139 (2.6%)	<0.0001
Cornell (P)	524 (2.86%)	82 (1.6%)	205 (2.6%)	237 (4.5%)	<0.0001
Any of them	738 (4.03%)	113 (2.2%)	305 (3.8%)	318 (6.02%)	<0.0001
R_{aVL} (>5.7)	2718 (14.8%)	237 (4.7%)	1178 (14.8%)	1303 (24.7%)	<0.0001
Strain	13 (0.07%)	2 (0.04%)	4 (0.05%)	7 (0.13%)	0.22

Cornell (V), Cornell voltage; Cornell (P), Cornell product.
*Adjusted for age and sex.

1000 patients per year, reflecting the low risk for cardiovascular events in this population.

The age and sex-adjusted incidence of events was significantly higher in patients with ECG-LVH according to the Cornell-product and Cornell-voltage criteria (Table 3), but not for the Sokolow–Lyon (hazard ratio 1.67, 95% CI 0.54–5.20) and the R wave in aVL more than 11 mm (hazard ratio 1.31, 95% CI 0.74–2.32) and more than 5.7 mm (hazard ratio 1.10; 95% CI 0.89–1.36). After a further adjustment for cigarette smoking, hypertension grade, hypercholesterolemia, diabetes, income, education, occupational class and physical activity, only the Cornell-product ECG-LVH remained significantly associated with an increased risk of events (hazard ratio 1.69, 95% CI 1.18–2.42).

When BMI categories were additionally included in the statistical analysis model, a statistically significant 1.7-fold increased risk of events was observed in patients with ECG-LVH only according to the Cornell-product criterion (Table 3). When LVH was considered present if any of the specified criteria were abnormal a progressively greater incidence of events was observed from normal weight to overweight and obese patients if any of the specified criteria were abnormal.

In analyses concerning interactions between BMI categories (3 levels), sex (2 levels) and hypertension categories (2 levels because of the low number of events) and ECG LVH criteria on cardiovascular risk, only the Cornell product showed a statistically significant interaction with BMI ($P = 0.027$), whereas the R wave in aVL and the Cornell product showed an interaction with hypertension ($P = 0.0063$ and 0.0011, respectively). When we have analyzed the interaction on the Cornell-product ECG-LVH hazard ratios combining both levels of BMI and of hypertension, we did not observe significant interaction ($P = 0.34$).

The prognostic value of the different criteria for LVH was then assessed in the different categories of BMI, taking into account all confounding variables (Table 4). In the normal weight group and in the overweight groups of individuals, the Cornell-product ECG-LVH was associated with an approximately 2.5-fold increase of events. On the opposite, the incidence of cardiovascular events was not associated with any criteria for LVH in obese patients, nor when LVH was considered present if any of the specified criteria were abnormal.

DISCUSSION

The results of the present study, conducted in a representative sample of the Italian general population, confirm that the prevalence of Cornell and Sokolow–Lyon voltage and Cornell-voltage duration product criteria for ECG-LVH detection is significantly different among BMI categories.

The second, but most relevant, result of the study is the evidence of a different prognostic value of the ECG-LVH criteria across BMI categories. In normal weight and overweight patients, the Cornell product, but not the Cornell or the Sokolow–Lyon voltage criteria, was associated with an increased risk of cardiovascular fatal and nonfatal events, after adjusting for numerous confounding factors.

Some aspects of our cross-sectional and longitudinal analyses deserve comment. The prevalence of ECG LVH,

TABLE 3. Incidence and hazard ratios of cardiovascular events in positive and negative to left ventricular hypertrophy indicators patients

	Positive		Negative		Model 1		Model 2		Model 3	
	N event	%	N event	%	HR	98% CI	HR	98% CI	HR	98% CI
Sokolow–Lyon	3/56	5.4	500/18 274	2.74	1.67	0.54–5.20	1.60	0.51–5.00	1.71	0.54–5.37
Cornell (V)	12/176	6.8	491/18 154	2.70	**1.89**	**1.05–3.39**	1.67	0.93–3.00	1.67	0.93–2.99
R_{aVL} (>11)	12/271	4.4	491/18 059	2.72	1.31	0.74–2.32	1.25	0.70–2.22	1.20	0.68–2.14
Cornell (P)	34/524	6.5	469/17 806	2.63	**1.87**	**1.31–2.67**	**1.69**	**1.18–2.42**	**1.66**	**1.16–2.38**
Any of them	41/733	5.6	463/17 597	**2.63**	**1.61**	**1.16–2.24**	**1.48**	**1.07–2.06**	**1.46**	**1.05–2.03**
R_{aVL} (>5.7)	116/2.715	4.3	387/15 615	2.5	1.10	0.89–1.36	0.98	0.79–1.22	0.95	0.76–1.18

Model 1: adjusted for age and sex. Model 2: adjusted for age, sex, cigarette, hypertension grade 1–3, hypercholesterolemia, diabetes, income, education, occupational class and physical activity. Model 3: as model 2, further adjusted for BMI categories. CI, confidence interval; Cornell (V), Cornell voltage; Cornell (P), Cornell product; HR, hazard ratio. Bold indicates statistical significance.

TABLE 4. Hazard ratios for events, according to BMI categories

	BMI 18.5–24.9 kg/m^2			BMI 25.0–29.9 kg/m^2			BMI ≥ 30.0 kg/m^2			*P* for difference
	N+ (a)	N− (b)	HR[a] (95% CI)	N+ (a)	N− (b)	HR[a] (95% CI)	N+ (a)	N− (b)	HR[a] (95% CI)	
Sokolow–Lyon	1/22 (4.55%)	83/5066 (1.64%)	2.76 (0.37–20.74)	1/28 (3.57%)	211/7928 (2.66%)	0.98 (0.14–7.13)	1/6 (16.67%)	206/5280 (1.64%)	5.18 (0.71–37.94)	0.74
Cornell (V)	2/34 (5.88%)	82/5054 (1.62%)	2.22 (0.52–9.51)	6/70 (8.57%)	206/7886 (2.61%)	2.22 (0.96–5.13)	4/72 (5.56%)	203/5214 (3.89%)	1.15 (0.42–3.17)	0.38
R_{aVL} (>11)	1/19 (5.26%)	83/5069 (1.64%)	0.94 (0.12–7.14)	4/113 (3.54%)	208/7843 (2.65%)	1.17 (0.43–3.17)	7/139 (5.04%)	200/5147 (1.62%)	1.24 (0.57–2.68)	0.87
Cornell (P)	6/82 (7.32%)	78/5006 (1.56%)	**2.63 (1.10–6.28)**	17/205 (8.29%)	195/7751 (2.52%)	**2.55 (1.52–4.25)**	11/237 (4.64%)	196/5049 (3.88%)	0.99 (0.53–1.84)	**0.027**
Any of them	7/111 (6.31%)	77/4977 (1.55%)	2.17 (0.97–4.86)	18/304 (5.92%)	194/7652 (2.54%)	**1.84 (1.12–3.02)**	15/318 (4.72%)	192/4968 (3.86%)	1.08 (0.63–1.85)	0.10

(a) N+ = number of events/total number (%) in patients positive to the corresponding LVH indicator. (b) N− = number of events/total number (%) in patients negative to the corresponding LVH indicator. CI, confidence interval; Cornell (V), Cornell voltage; Cornell (P), Cornell product; HR, hazard ratio; LVH, left ventricular hypertrophy. Bold indicates statistical significance.
[a]Adjusted for age, sex, cigarette, hypertension, hypercholesterolemia, diabetes, income, education, occupational class and physical activity.

as defined by some widely used criteria, suggested by European guidelines, was lower than in other general populations, possibly due to small differences in age, male sex prevalence, BMI and presence of previous CVD. In the PAMELA study, examining an Italian general population sample slightly younger, with a greater prevalence of men and with a lower mean BMI, the prevalence rates of ECG LVH according to Sokolow–Lyon and Cornell voltage index criteria were 0.9 and 7.7%, respectively [33]. In a slightly older general population sample, living in northern Italy (Vobarno study), the prevalence rates for the Sokolow–Lyon and Cornell product criteria were 3.1 and 4.2%, respectively (personal data). In a Finn cohort of 5800 individuals, a significantly higher prevalence of the ECG-LVH by the Sokolow–Lyon and Cornell voltage indexes (10.2 and 7.9%, respectively) was reported [34]. In the Framingham cohort, the prevalence of definite LVH, manifested by repolarization abnormality as well as increased voltage, was 3.7% [35].

Several factors may explain the discrepancy between different criteria ECG-LVH prevalence rates. In addition to demographic factors (age, female sex etc.) [36], some diseases, such as essential hypertension, diabetes mellitus, chronic obstructive lung disease, sleep apnea, thorax anatomic abnormalities and obesity [37], may significantly affect the diagnostic accuracy of some ECG criteria and among them, obesity represents a strong biological stimulus for the development of LVH.

Cuspidi *et al.* [38] have recently performed a comprehensive meta-analysis showing that the likelihood of having anatomic LVH was much higher in obese patients than in their nonobese counterparts (odds ratio, 4.19; 95% CI 2.67–6.53; $P < 0.01$). Even in the most common genetic heart disease, such as hypertrophic cardiomyopathy [15], obesity has been shown to exert an influence on the further increase in LV mass.

The sensitivity of several ECG criteria for LVH, mainly those based on precordial leads voltage amplitude, diminishes from normal weight to overweight and obese patients. In the Losartan Intervention for Endpoint Reduction in Hypertension 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; $P = 0.001$ for all) [37]. In obese patients, the cardioelectric changes during the hypertrophic response may not correspond to the amount of LV mass increase [39], and the distance between the skin electrodes on the chest wall and the LV with an increased epicardial fat may reduce precordial ECG voltages [40], although a decrease in QRS voltage is reported in obese patients after weight loss [41,42] suggesting LVH regression.

The predictive value of several criteria for LVH in nonobese and obese patients has not been extensively evaluated before. Very recently in a cohort of 5800 Finn individuals, no difference in the predictive value of cardiovascular events by the Sokolow–Lyon ECG-LVH was observed between lean and obese patients [34]. Our results provide a new piece of information on the most appropriate

use of the European guidelines ECG criteria in cardiovascular risk stratification.

Some issues in this study are of particular importance. In our study, the prevalence of obesity was less than 30%, allowing one to assess the different values of ECG criteria in predicting cardiovascular events across normal weight to overweight and obese patients. The evaluation of ECG was performed on digital ECG [26] and was not restricted to QRS voltages but considered other variables such as QRS duration, which may have enhanced ECG sensitivity for LVH and ECG value in predicting outcomes. In the Moli-sani study [24], an accurate collection of information on education, income and physical activity is performed and all these potential confounders, in addition to traditional demographic characteristics, could have been taken into account.

We have shown that the Cornell product is related to the incidence of cardiovascular events, independently of all confounders, including BMI in the whole population. When further analysis was conducted in different weight categories, the predictive power of the Cornell product was confirmed in the majority of the groups, that is in those with normal weight or overweight, even after adjusting for several demographic, metabolic and socioeconomic confounders.

The current European guidelines on hypertension proposed an R_{aVL} cutoff more than 1.1 mV for the diagnosis of LVH [31]. We have used two different cutoff values for the R wave in aVL lead and could not confirm in the whole Moli-sani population and in the different classes of body size, the accuracy of any threshold for R_{aVL} in predicting cardiovascular events, previously demonstrated in three different studies including hypertensive patients [32,43,44].

Some authors have suggested that correction of ECG voltages by measures of body size may improve the accuracy of ECG for the diagnosis of LVH [45–47], although the value of adjustment for BMI of ECG indexes in improving the prediction of cardiovascular events still remains poorly investigated [48].

Strengths and limitations

The large sample size and random allocation into the cohort minimizing selection bias are some strengths of the study. Some limitations of the current analysis need to be mentioned.

The number of patients meeting the criteria for Sokolow–Lyon or strain ECG-LVH is low, and the observed event rate indicates the relatively low risk for cardiovascular 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 three categories of body weight might not reflect true differences in predictive power as a function of BMI. Other studies performed in populations with a similar overall cardiovascular risk have previously assessed the prognostic value of different ECG abnormalities, but only partially considering BMI categories [34,48].

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

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

In conclusion, in a large adult Italian population, our observations support the notion that the use of ECG criteria in obese patients may give different prognostic information. BMI is a powerful determinant of LVM, and in the presence of obesity none of the ECG-LVH criteria suggested by European guidelines reached a predictive significance of cardiovascular events.

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

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

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Conflicts of interest

There are no conflicts of interest.

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