ORIGINAL ARTICLE

Novel Sign of Frontal Plane Ventricular Repolarization to Predict Left Ventricular Systolic Dysfunction

Nuevo signo de la repolarización ventricular en el plano frontal para predecir disfunción sistólica ventricular izquierda

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ABSTRACT

Background: Different electrocardiographic abnormalities have been associated with left ventricular systolic dysfunction (LVSD), although the association with standard electrocardiographic frontal plane ST-segment depression (STD) has not been established.
Objective: The aim of this study was to evaluate whether lead I STD (STD-I) allows predicting the presence of LVSD.
Methods: Patients with risk factors or stable chronic heart disease, and baseline electrocardiogram (ECG) and echocardiogram that provided evaluation of left ventricular ejection fraction (LVEF), left ventricular wall motility, and dichotomous evaluation of left ventricular hypertrophy (LVH), were prospectively included in the study. ST-segment morphology in leads I and V6 was evaluated, defining horizontal (≥1mm at 80 ms from the J point) or downsloping STD as abnormal STD-I and STD-6.
Results: A total of 691 patients; with mean age of 69.8±12 years and 61.6% men, were prospectively analyzed. STD-I and STD-6 were identified in 250 (36.2%) and 199 (28.8%) cases, respectively. Presence of STD-I and STD-6 was associated with a significantly lower LVEF compared with the absence of this finding: 44.8±13.9% vs. 55.6±8.9% (p <0.0001) and 45.8±14.1% vs. 54.1±10.4% (p <0.0001), respectively. Both were associated with the presence of LVSD, defined as LVEF <50%, although STD-I showed better diagnostic performance than STD-6 [area under the ROC curve 0.72 (95% CI 0.69-0.76) vs. 0.64 (95% CI 0.61-0.68), p=0.0001].
Conclusions: This study showed that STD-I predicts the presence of LVSD better than STD-6. The potential relevance of these findings should be placed in the current context of the emerging use of wearable devices that analyze electrocardiographic information through a single lead.

Keywords: ST depression - Lead I – Lead V6 - Frontal Plane - Left ventricular systolic dysfunction

RESUMEN

Objetivo: Distintas alteraciones del electrocardiograma (ECG) han sido asociadas a disfunción sistólica ventricular izquierda (DSVI), si bien la asociación con el infra-desnivel del segmento ST (IST) del plano frontal del ECG estándar no se encuentra establecida. El objetivo del presente trabajo fue evaluar si el IST de la derivación DI (IST-I) permite predecir la presencia de DSVI.
Material y métodos: Se incluyeron de forma prospectiva pacientes portadores factores de riesgo o cardiopatías crónicas estables, con ECG basal y ecocardiograma que aportara evaluación de la fracción de eyección (FEVI), motilidad ventricular izquierda y evaluación dicotómica sobre la presencia de hipertrofia ventricular izquierda (HVI). Evaluamos la morfología del segmento ST en derivaciones DI y V6, definiéndose como anormal (IST-I; IST-6) al ST infradesnivelado (≥1mm a 80mseg del punto J) o descendente.
Resultados: Se analizaron en forma prospectiva 691 pacientes, edad media 69,8±12 años, 61,6% hombres. Se identificó IST-I y IST-6 en 250 (36,2%) y 199 (28,8%) casos, respectivamente. La presencia de IST-I y IST-6 se asoció a una FEVI significativamente menor comparado con la ausencia de dicho hallazgo: 44,8±13,9% vs. 55,6±8,9%, (p<0,0001) y 45,8±14,1% vs. 54,1±10,4 % (p<0,0001) respectivamente. Ambos se asociaron a la presencia de DSVI, definida como FEVI<50%, aunque el IST-I mostró mejor rendimiento diagnóstico que el IST-6 [área bajo la curva 0,72 (IC 95% 0,69-0,76) vs. 0,64 (IC 95% 0,61-0,68), p=0,0001].
Conclusiones: Este estudio mostró que la depresión del segmento ST de la derivación DI permite predecir la presencia de DSVI mejor que IST-6. La potencial relevancia de dichos hallazgos debería situarse en el contexto actual de la emergente utilización de dispositivos wearables que analizan la información electrocardiográfica mediante una única derivación.

Palabras clave: Infradesnivel ST – Derivación DI – Derivación V6 – Plano Frontal – Disfunción sistólica ventricular izquierda

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INTRODUCTION

Some electrocardiographic abnormalities, such as duration of the QRS complex, pathological Q waves, classic ST-segment depression in left precordial leads, and T wave inversion, have been associated with left ventricular dysfunction and/or myocardial necrosis. (1-4) Other markers of ventricular repolarization, such as corrected QT interval or QT interval dispersion, and some measurements and combinations between peak T wave and QT interval, have been associated with malignant arrhythmias and sudden death. (5) There are also studies that correlate the pattern of left ventricular overload present in left precordial leads V5-V6 with left ventricular remodeling. (6, 7) This electrocardiographic pattern is associated with concentric left ventricular hypertrophy (LVH), mainly in individuals with hypertension and aortic valve stenosis. (6, 8) The same electrocardiographic ST-segment depression pattern described for leads V5-V6 may appear in frontal plane leads, although reports in this regard are very limited.

At present, most studies involve complex images, and few clinicians are trained to evaluate certain advanced electrocardiographic characteristics. Therefore, the simple estimation of a single frontal plane lead can be useful, particularly with the emergence of wearable devices capable of remote analysis, as well as the eventual evaluation using machine learning tools that allow the automatic detection of certain forms of heart disease, as the ones currently revealing atrial fibrillation. (9)

Therefore, the objective of the present study was to evaluate whether the presence of ST-depression in lead I (STD-I) allows predicting the presence of left ventricular systolic dysfunction (LVSD).

METHODS

Study design

Investigators from different Latin American institutions (Argentina, Bolivia, Colombia, Ecuador and the Dominican Republic) related to the Postgraduate Degree in Cardiology at Universidad del Salvador (Argentina) were summoned to participate in this research. Each institution obtained the approval of the local Ethics Committee and all enrolled patients gave their informed consent.

The study included stable patients attending the outpatient cardiology clinic due to cardiovascular risk factors (RF) or with chronic heart diseases. All patients had a baseline electrocardiogram (ECG) (with 10 mm/mV calibration and a speed of 25 mm/s) and transthoracic echocardiogram (TTE), obtained with less than 30 days difference between studies. The TTE was performed by an accredited operator according to each investigator's opinion and provided the following data: left ventricular ejection fraction (LVEF); left ventricular wall motility; presence or absence of LVH; and final echocardiographic diagnosis of the eventual underlying heart disease present. Patients with acute cardiac or clinical pathologies, treatment with drugs that prolong the QT interval or alter ventricular repolarization (VR), or electrolyte alterations that modify VR were excluded from the study.

The study investigators used a smartphone WhatsApp application to anonymously submit the information of each patient, having previously obtained informed consent to use the data. The following information was sent: standard ECG; demographic variables; diagnosis of underlying heart disease; and final TTE report. The data was sent through high-quality smartphone photographs.

The investigators were randomly divided into two groups to send each patient's information to two researchers in Argentina (CAS and JAJG).

Electrocardiographic study

In each patient, baseline ECG was analyzed by an investigator (CAI) with experience in advanced ECG evaluation, blinded to the rest of the clinical-echocardiographic information. The parameters included in the analysis were: 1. ST-segment morphology in lead I, defining the ascending or isoelectric ST as normal, and horizontal (≥1mm at 80 ms from the J point) or downsloping ST-segment depression (STD-I) as abnormal; 2. ST-segment morphology in lead V6 (STD-6) was defined as established for STD-I; 3. T wave polarity in leads I and V6: a positive T wave was defined as normal and a negative or bipolar T wave as abnormal; 4. T wave electrical axis in the frontal plane; 5. QRS intrinsicoid deflection duration in lead I; 6. QRS complex duration; 7. QRS electrical axis in the frontal plane; 8. Presence of branch blocks or hemiblocks; 9. Presence of LVH according to Cornell's (QRS duration × R in aVL + S in V6, + 6 mm in women) >2400 mm × ms, and Sokolow-Lyon (S in Vi + R in V5 or V6) >38 mm criteria; 10. Presence of pathological Q waves according to the Minnesota code. Only the results of the comparison between STD-I and STD-6 are reported in the present investigation.

Transthoracic echocardiogram

A simplified echocardiographic protocol was used evaluating the presence of LVH (interventricular septum >12 mm), the status of left ventricular systolic function (LVSF) according to the modified Simpson method, and left ventricular wall motion abnormalities according to regional comparisons, data which are simple to determine and with demonstrated predictive prognosis. (10)

Statistical analysis

Discrete variables were expressed as counts and percentages. Continuous variables had normal distribution and were expressed as mean ± standard deviation (SD). Comparisons between groups were performed using Student's t test for independent samples. Diagnostic yield was calculated using sensitivity, specificity, positive and negative predictive value, and positive and negative likelihood ratio to detect abnormal TTE data (LVEF <50%, LVH and motility abnormalities) and history of heart disease (defined by presence of coronary heart disease, non-ischemic cardiomyopathy, moderate or severe valve disease, or combined pathology).

ROC curve analysis to predict the endpoints mentioned and paired comparisons between areas under the ROC curve using the De Long et al. method (11) were also performed. A two-tailed $p < 0.05$ was considered statistically significant. SPSS 22.0 (IBM SPSS Statistics for Windows, Armonk NY) and Medcalc (Ostende, Belgium) software packages were used for data analysis.

RESULTS

A total of 783 patients were analyzed. Ninety-two cases presented not analyzable or missing data, reducing the study population to 691 patients. The distribution

by country was: Argentina, 55%, Bolivia, 8%, Colombia, 24%, Ecuador, 9% and Dominican Republic, 4%. Table 1 summarizes demographic data and the reasons for consultation with the diagnosis for each patient. Most were elderly patients of male gender. In 189 cases (27.4%) the cause of consultation was the presence of RF, while 455 patients (65.8%) presented some type of heart disease (coronary, valvular, cardiomyopathy or combined). A small percentage (5.2%) presented vascular disease (peripheral, aortic or cerebral) or another disease (1.6%), without conclusive evidence of associated heart disease, though they had RF.

STD-I and STD-6 was identified in 250 (26.2%) and 199 (28.8%) cases, respectively, in both cases associated with the presence of LVEF impairment (Table 2). STD-I showed better diagnostic yield both for the detection of TEE findings (LVEF impairment, presence of LVH or left ventricular wall motion abnormalities) as for the presence of heart disease (Table 3). Particularly, STD-I presented an acceptable diagnostic yield for detecting LVEF <50%, with an area under the ROC curve of 0.72 (95% CI 0.69-0.76), significantly greater than that shown by STD-6 [area under the curve of 0.64 (95% CI 0.61-0.68), p=0.0001]. Table 4 shows the result comparing STD-I and STD-6 areas under the curve for detecting LVEF <50%, LVH, left ventricular wall motion abnormalities and heart disease.

Figures 1 and 2 illustrate electrocardiographic examples. Both figures, with different pathologies (left bundle branch block and LVH, respectively), clearly show that lead I presents downsloping ST depression, which is not recorded in V6. Figure 3 schematically represents the frontal plane vector description of normal VR, which explains its electrocardiographic recording, as shown in leads I and II: In normal conditions the three VR vectors have the same vector direction (inferior and left), so the J point will be recorded as positive, the ST-segment will be ascending and the T wave will be positive in both leads.

Among the remaining electrocardiographic parameters analyzed, it is worth highlighting that left anterior block or hemiblock was present in 178 patients (26%), prevailing in the STD-I group (75 patients, 30%) with respect to the STD-6 group (42 patients,

Table 1. Demographic characteristics and associated disease in the 691 patients included in the study

Age – years	69.8±12.0
Men – n (%)	426 (61.6%)
Hypertension – n (%)	537 (77.7%)
Hypercholesterolemia – n (%)	429 (62.1%)
Diabetes – n (%)	199 (28.8%)
Smoking – n (%)	194 (28.1%)
Heart disease # – n (%)	455 (65.8%)
Coronary heart disease – n (%)	207 (30.0%)
Valve diseases – n (%)	116 (16.8%)
Cardiomyopathies – n (%)	106 (15.3%)
Combined heart diseases – n (%)	26 (3.8%)
Peripheral vascular disease – n (%)	36 (5.2%)
Other – n (%)	11 (1.6%)

Heart disease includes patients with diagnosis of: coronary heart disease, valve diseases, cardiomyopathies (also including patients with atrial fibrillation and/or heart failure), and combined heart diseases. Other: includes kidney failure, pulmonary disease, etc.

Table 2. Relationship between STD-I and STD-6 and left ventricular ejection fraction (LVEF)

STD-I	LVEF (%)	STD-6	LVEF (%)
Presence (n=250)	44.8±13.9	Presence (n=199)	45.8±14.1
Absence (n=441)	55.6±8.9	Absence (n=492)	54.1±10.4
p value	<0.0001	p value	<0.0001

STD-I: ST-segment depression in lead I. STD-6: ST-segment depression in lead V6

Table 3. STD-I and STD-6 sensitivity (Sen), specificity (Sp), positive (PPV) and negative (NPV) predictive value, and positive (LR+) and negative (LR-) likelihood ratio for detecting left ventricular ejection fraction (LVEF) <50%, abnormal motility (Ab. mot), left ventricular hypertrophy (LVH) and heart diseases (Heart dis.) observed by transthoracic echocardiography.

STD-I	Sen (%)	Sp (%)	PPV (%)	NPV (%)	LR+	LR-
LVEF <50%	68 (61-74)	77 (73-81)	55 (49-61)	85 (81-88)	2.9 (2.4-3.6)	0.4 (0.3-0.5)
Ab. mot	59 (52-65)	74 (70-78)	51 (44-57)	80 (76-83)	2.3 (1.9-2.7	0.6 (0.5-0.7)
LVH	50 (43-57)	69 (65-73)	40 (33-46)	78 (73-81)	1.6 (1.4-2.0	0.7 (0.6-0.8)
Heart dis.	49 (44-53)	88 (83-92)	88 (84-92)	47 (42-52)	4.0 (2.8-5.6)	0.6 (0.5-0.7)
STD-6	**Sen (%)**	**Sp (%)**	**PPV (%)**	**NPV (%)**	**LR+**	**LR-**
LVEF <50%	49 (42-56)	80 (76-83)	50 (43-57)	79 (75-82)	2.4 (1.9-3.0)	0.6 (0.6-0.7)
Ab. mot	4 (38-51)	78 (74-82)	48 (41-55)	75 (71-79)	2.0 (1.6-2.6)	0.7 (0.6-0.8)
LVH	39 (32-46)	75 (71-78)	39 (32-46)	75 (71-79)	1.6 (1.3-2.0)	0.8 (0.7-0.9)
Heart dis.	37 (33-41)	87 (85-91)	85 (79-90)	42 (37-46)	2.9 (2.1-4.2)	0.7 (0.7-0.8)

Table 4. Comparison of diagnostic yield evaluated through ROC curves between STD-I and STD-6 to predict left ventricular hypertrophy (LVH), left ventricular ejection fraction (LVEF) <50%, abnormal motility and heart disease

	Area under the ROC curve (95% CI)		
	STD-I	STD-6	p
LVEF <50%	0.72 (0.69-0.76)	0.64 (0.61-0.68)	0.0001
LVH	0.60 (0.56-0.63)	0.57 (0.53-0.61)	<0.0001
Abnormal motility	0.66 (0.63-0.70)	0.61 (0.58-0.65)	0.009
Associated heart disease	0.68 (0.65-0.72)	0.62 (0.59-0.66)	0.0001

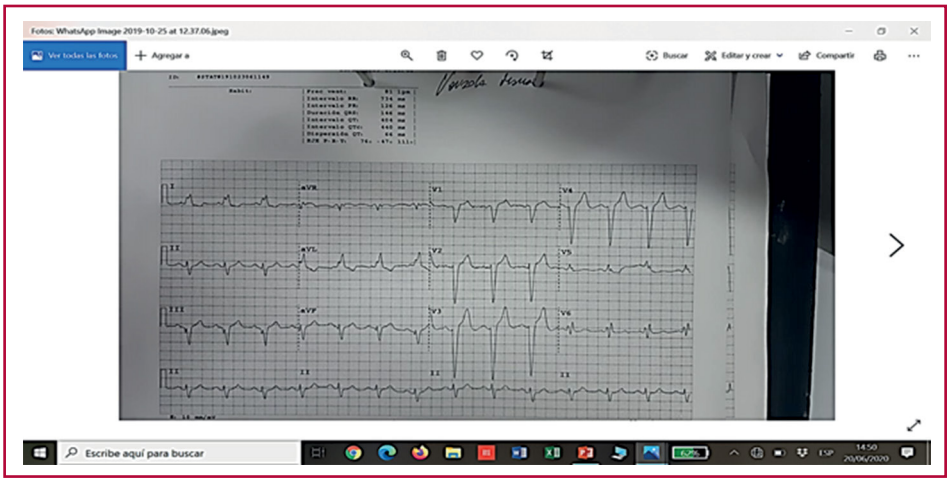

Fig. 1. Example of an ECG sent via WhatsApp. Patient with complete left bundle branch block: Lead I shows downsloping ST-segment depression, while V6 shows an ascending ST-segment with positive T wave.

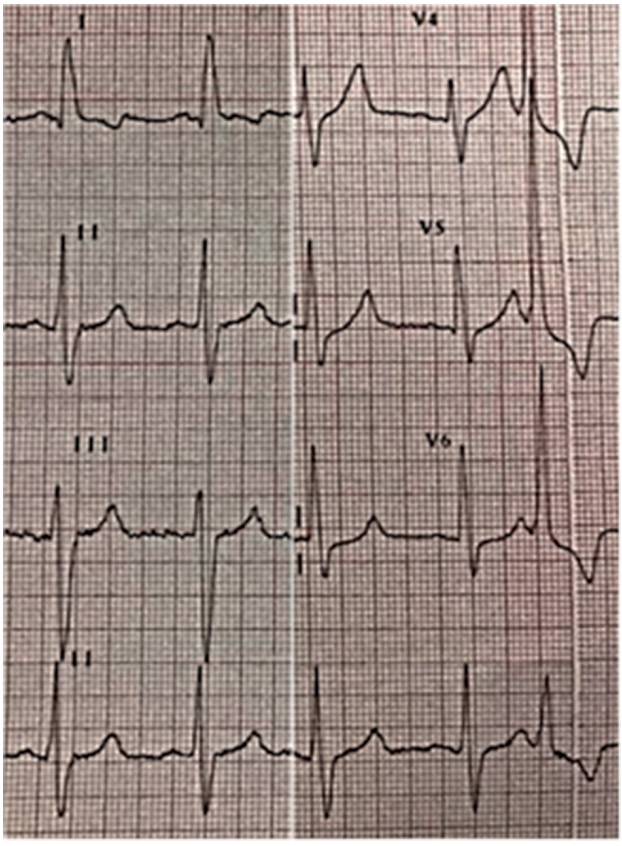

Fig. 2. Example of an ECG sent via WhatsApp. Only leads I, II, III, V4, V5 and V6 are shown. Downsloping ST-segment depression in lead I and ascending in V6 with frontal axis markedly deviated to the left in a patient with left ventricular hypertrophy both by ECG and transthoracic echocardiography

21%) (p=0.00007). Similarly, the electrocardiographic diagnosis of LVH was obtained in 179 patients (25.9%), 118 (65.9%) of which were associated with STD-I vs. 97 (94.2%) with STD-6 (p=0.011).

Also, in this group with LVH, the QRS frontal axis markedly deviated to the left occurred in STD-I vs. STD-6 (41 vs. 29 cases, respectively, p=0.024) and in accordance, 82% of anterior hemiblocks were present in patients who had some type of heart disease.

DISCUSSION

The main finding of this investigation is that STD in lead I is associated with electrocardiographic patterns of LVSD. Furthermore, STD-I presented better diagnostic performance than the classic STD-6. According to our best knowledge, this is the first observation of the usefulness of VR lead I abnormalities to predict LVSD. It is worth noting that it is a simple electrocardiographic sign that only requires the observation of repolarization in lead I, with acceptable sensitivity and specificity. Therefore, considering the simplicity of the test, it could result clinically useful. Moreover, a single lead similar to lead I is currently used to detect atrial fibrillation in certain smart wearable devices with single lead electrocardiographic recording capacity, highlighting the potential utility of the finding.

Previous findings demonstrated that the spatial QRS vector-T wave angle (QRS-T) is an independent marker of mortality in different groups of cardiac patients. (12-15) This angle reflects the abnormal opposition between depolarization and VR due the increase in action potential duration and the modification of the recovery sequency in certain myocardial regions.

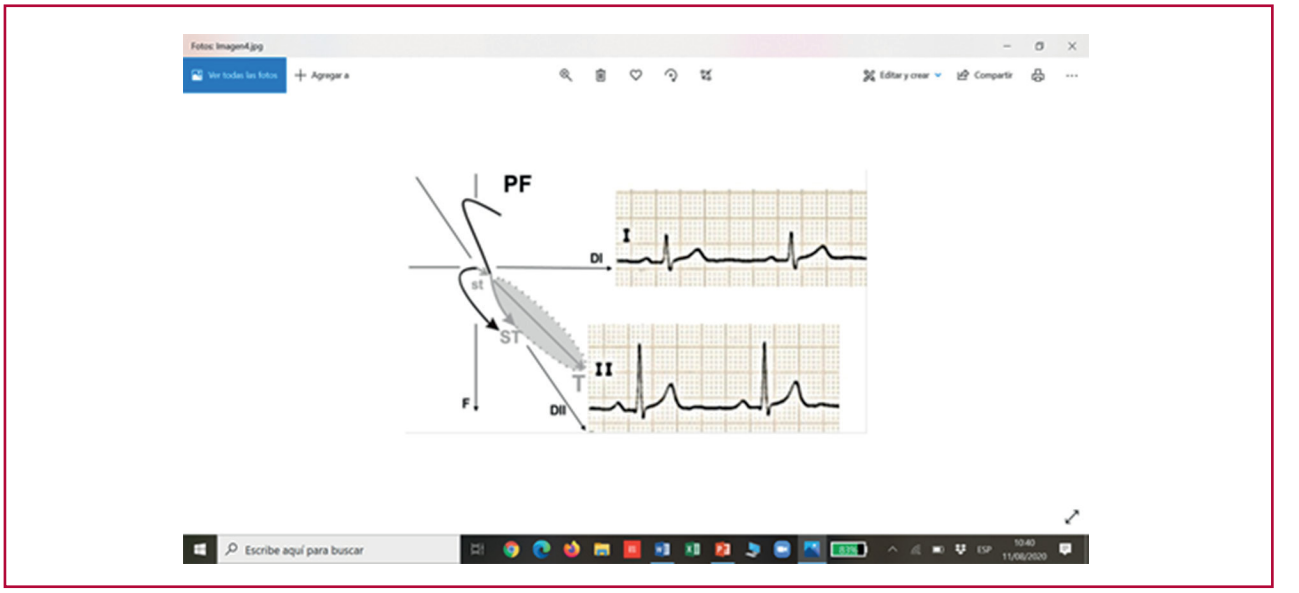

Fig. 3. Vector recording diagram of frontal plane ventricular repolarization and electrocardiographic leads I and II. Leads I, II and aVF axes were included, whose positive half was marked by an arrowhead. The vector diagram of ventricular repolarization was drawn in gray: st means st vector (vector equivalent of the ECG J point), that joins the start and indicates the end of the QRS vector; ST represents the ST-segment (gray solid line that follows the QRS and ends in an arrowhead) and continues with the T wave vector (indicated as T and marked with a dotted gray line; the inside arrow represents the maximum T vector). The QRS start and end was drawn in solid black lines (its complete inclusion was not considered necessary for the purpose of this investigation): the start was interrupted with an arrowhead and the end is indicated by the st vector, The examples of electrocardiographic leads I and II show normal repolarization characteristics: minimum J point elevation, ascending ST-segment and normal positive T wave (slow initial ascending ramp and faster descending ramp). From the vector viewpoint, the key data is that the three elements of VR (J point, ST-segment and T wave) are recorded with concordant polarity in normal conditions, given the coincident direction and sense explained in the vector diagram. Modified from Ingino et al. (21)

This can be detected in the increased spatial QRS vector-T wave angle. (16) Nevertheless, the spatial angle has normally limited use in clinical practice, in addition to requiring a special calculation.

A simplification of the spatial angle is the measurement of the angle formed by the QRS vector and the T wave in the frontal plane. In normal conditions, this angle is usually <45° and explains why in frontal electrocardiographic leads, the QRS polarity and the T wave coincide in the absence of heart disease. (17) Conversely, an angle > 90° was predictor of adverse events in different populations, and was associated with myocardial ischemia, LVH and branch block. (18)

Recently, Whang et al. reported, in a population without heart disease (NHANES III), that a frontal QRS-T angle was a marker of increased cardiovascular risk and mortality. (19) On the other hand, in the Multiethnic Study of Atherosclerosis (MESA), although the frontal QRS-T angle resulted predictor of events, this was mainly attributed to T wave abnormalities. (20) However, this conclusion seems to separate the ST-segment from the T wave as if they were different events (see Figure 2), when, in fact, it is the continuous electrocardiographic recording of the same process.

Based on previous publications, our investigation used the ST-segment as an equivalent of the frontal QRS-T angle. (21, 22) In normal conditions, the QRS, the ST-segment and the T wave frontal vectors coincide, so we believe that it is possible to replace T wave polarity by that of the ST-segment, with some advantages:

a. The first abnormal sign of VR can be detected in the ST-segment, generally including the accompanying displacement of the J point. In this way, the beginning of opposition between the QRS axes and VR would be recorded as ST depression, while the abnormal angle between the QRS and the T wave would correspond to a later or more advanced stage in the development of the VR disorder.
b. In some cases of myocardial ischemia or LVH, the T wave may develop a bipolar pattern (6) in many ECG leads. From a vector viewpoint, this finding corresponds to a rounded T wave that facilitates its bimodal electrocardiographic recording and explains the difficulty in determining a single vector to represent it.

A similar pattern has been reported for horizontal plane V5-V6 leads, particularly in patients with hypertensive heart disease. The classic description (ST-segment depression and inverted T wave) has been associated with LVSD, (6) heart failure (23) and poor prognosis. (4, 24-26) Therefore, the finding of a similar correlation in our population with STD-I deserves to be emphasized.

Left ventricular anterior hemiblock generates,

in addition to a marked frontal plane QRS electrical axis deviation to the left, certain changes in the QRS recording and VR in precordial leads, as it displaces the electrical axis due to the asynchronous activation of both left ventricular anterolateral and inferoposterior walls. Presence of this conduction disorder prevailed in the STD-I group. Moreover, this leftward deviation was also associated with the electrocardiographic presence of LVH, with similar implication in the greater prevalence observed in STD-I. Therefore, the abnormal change of the frontal electrical axis to the left of the QRS could potentially explain our findings, as it would facilitate the opposition between QRS vectors and repolarization, especially in the presence of a heart disease generating deviation.

Our study has certain limitations. Firstly, the VR abnormal findings in frontal plane leads studied in our population should be corroborated in future investigations. Similarly, the low proportion of VR abnormalities observed limits the sensitivity of results. However, a similar prevalence occurs with the electrocardiographic diagnosis of LVH, which also has adequate specificity, (6) a fact that does not hinder the clinical utility of the finding.

CONCLUSIONS

In this hypothesis-generating study we demonstrated that ST-segment depression in lead I allows the prediction of LV dysfunction, with moderate sensitivity and specificity. The potential relevance of this finding should be placed in the current context of the emerging use of wearable devices that employ a single electrocardiographic lead.

Conflicts of interest

None declared.

(See authors' conflict of interests forms on the web/Additional material.)

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