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Late ventricular potentials can be predicted from twelve-lead ECG in post-infarction heart failure

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ABSTRACT

Introduction: Late ventricular potentials (LVP), recorded using signal averaged ECG (SA-ECG), are low-amplitude, high-frequency waveforms, appearing in the terminal part of the QRS complex, and are considered predictors of ventricular arrhythmia and sudden cardiac death.

Hypothesis: SA-ECG parameters can be predicted from 12-lead ECG variables in post-infarction heart failure patients.

Methods: Thirty post infarction heart failure patients were enrolled in our study, and they underwent: 12-lead ECG and SA-ECG.

Results: Among patients with LVP, 75% had a prolonged QTmax (maximal QT interval), 85% a prolonged QTc (heart rate corrected QTmax), 55% QTm (mean QT) ≥ 400ms, 100% QRS (QRS duration) ≥ 100ms, 95% T0e (T wave duration) > 270 ms, 95% Tpe (Tpeak-Tend interval) > 120 ms, 90% Tampl (T wave amplitude) > 0.35 mV. A significant correlation was found between SA-QRS (signal averaged ECG QRS duration) and: QT parameters ($p < 0.05$), QRS ($r = 0.78$; $p < 0.01$), T wave variables ($p < 0.01$); between RMS40 (the root mean square of the terminal 40 ms of the filtered QRS) and: QTm ($p = 0.049$), QRS, Toe and between LAS40 (the duration of the low-amplitude signal) and: QTc, Tampl. LVP were significant associated only with QRS ($p = 0.034$). QRS ≥ 110 ms and T0e ≥ 270 ms are the most sensitive predictors' of late ventricular potentials and QTm ≥ 400 ms is the most specific.

Conclusion: SA-ECG parameters and the presence of LVP can be predicted from 12-lead ECG variables in post-infarction heart failure patients.

Keywords: Signal averaged electrocardiogram, ventricular late potentials, myocardial infarction, heart failure, QT interval, Tpeak-Tend interval

Introduction

The prevalence of congestive heart failure (CHF) is increasing, and more than half of the CHF-related deaths are sudden, due to ventricular arrhythmias (1). The high electrical instability in patients with post-infarction heart failure is due to structural inhomogeneities: patchy areas of fibrous tissue interdigitating with viable myocardium (2, 3). Ventricular arrhythmia risk can be assessed using signal averaged electrocardiography (SAECG) and 12-lead ECG.

Late ventricular potentials (LVP), recorded using SA-ECG, are low-amplitude, high-frequency waveforms, appearing in the terminal part of the QRS complex, due to fragmented depolarization, and are considered predictors of ventricular arrhythmia and sudden cardiac death. LVP are thought to originate from slow-conducting areas of the myocardium, the surface signals which correspond to delayed, fractionated electrograms (2-5).
Twelve-lead ECG still continues to be the most frequently recorded noninvasive test in medicine. The QT interval and Tpeak-Tend interval are also known to predict ventricular arrhythmia risk (6).
The hypothesis was that SA-ECG parameters can be predicted from 12-lead ECG variables in post-infarction heart failure patients.

Materials and methods

Study population

Thirty consecutive post infarction heart failure patients, stage B and C, were enrolled in our study. The patients underwent: standard 12-lead ECG and SA-ECG in the Functional Exploration Laboratory of the Pathophysiology department of the "Victor Babes" University of Medicine and Pharmacy, using a Siemens Megacart electrocardiograph. The clinical characteristics of the study population are included in table 1.
The investigations conform to the principles outlined in the Declaration of Helsinki (Cardiovascular Research 1997; 35:2-4) and were approved by the Ethics Committee of the University.
The most important inclusion criteria were: chronic myocardial infarction, diagnosed considering the criteria of the Joint European Society of Cardiology 2007 (7); heart failure, diagnosed considering the ESC Guidelines for the diagnosis and treatment of Acute and Chronic Heart Failure 2008 and the ACC/AHA Guidelines for the Diagnosis and Management of Heart failure in Adults 2009 (8) and a written informed consent of the patient.
The most important exclusion criteria were: atrial flutter, atrial fibrillation, electrolyte imbalances, systemic inflammatory processes, active infections and trauma. Patients with ventricular pacemaker were also excluded.

ECG

Standard 12-lead ECG was assessed at a paper speed of 25 mm/sec. QT interval (QTmax), heart rate corrected QT interval (QTc), mean QT interval (QTm), QRS duration (QRS), T wave duration (T0e), Tpeak-Tend interval (Tpe) and T wave amplitude (Tampl) were manually measured in all 12 ECG leads. The measurement of each parameter in each lead was obtained by averaging two consecutive beats (2).
QTmax was corrected for rate using using the Bazett formula (9): $QTc = QT/\sqrt{RR}$, where RR represents the R-R distance. The Bazett's formula is the most popular heart rate correction used in clinical practice.
The end of the T wave was defined as the intersection of a tangent to the steepest slope of the last limb of the T wave and the baseline (10). The leads in which the end of the T wave couldn't be determined exactly, or in which the T wave had low amplitude or was isoelectric, were eliminated (2). If the U wave was present, the QT interval was measured to the nadir of the curve between the T and U wave (11).
Twelve-lead ECGs were examined by two independent observers, who were blinded to clinical data. The methodology was previously described (2).

SA-ECG was used to assess: SA-QRS (signal averaged ECG QRS duration), the duration of the low-amplitude signal (LAS40) and the root mean square of the terminal 40 ms of the filtered QRS (RMS40) (2, 12). LVP were considered as present if two of the following

time-domain criteria were positive: SA-QRS >120 ms, LAS40 ("low amplitude signal"<40 μV) >38 ms and RMS40<20 μV in in the absence of bundle branch block, and SA-QRS ≥145 ms, LAS40 ≥55 ms and RMS40≤17 μV in presence of bundle branch block (12). SA-ECG methodology was also previously described (2).

Statistical methods

The Bravais-Pearson correlation, linear and multiple regression analysis, sensitivity and specificity were used. A $p < 0.05$ was considered statistical significant.

Results

The values obtained for the ECG and SAECG parameters are included in table 2.

LVP were found in 67% of the patients. Among patients with LVP, 75% had QTmax > 450ms, 85% QTc > 450ms, 55% QTm ≥ 400ms, 100% QRS ≥ 100ms, 95% T0e > 270 ms, 95% Tpe > 120 ms, 90% Tampl > 0.35 mV (figure 1).

A significant correlation was found between SA-QRS and: QTmax ($r = 0.50$, $p = 0.004$), QTc ($r = 0.52$, $p = 0.023$), QTm ($r = 0.60$, $p < 0.01$), QRS ($r = 0.78$, $p < 0.01$), T0e ($r = 0.65$, $p < 0.01$) (figure 2), Tpe ($r = 0.62$, $p < 0.01$), Tampl ($r = 0.50$, $p < 0.01$), between RMS40 and: QTm ($r = -0.47$, $p = 0.007$), QRS ($r = -0.66$, $p < 0.01$), Toe ($r = -0.40$, $p = 0.027$) and between LAS40 and: QTc ($r = 0.5$, $p = 0.019$), Tampl ($r = 0.50$, $p = 0.0042$) (figure 3).

Multiple regression analysis revealed a significant association between SA-QRS and QTm ($p = 0.049$), QRS ($p < 0.01$), Tpe ($p = 0.026$) and Tampl ($p < 0.01$). RMS40 was significant associated with QRS ($p = 0.016$). LVP were significant associated with QRS ($p = 0.034$).

The most sensitive 12-lead ECG criteria for the diagnosis of late ventricular potentials (figure 4) were: QRS ≥ 110 ms and T0e ≥ 270 ms (table 3). The highest specificity was obtained for QTm ≥ 400 ms.

Discussion

The most important finding in this study is that LVP can be predicted using a simple test: standard 12-lead ECG. The most important economical and technical advantages of standard 12-lead ECG are its accessibility and simplicity.

Several studies have already mentioned correlations between surface standard 12-lead ECG and SA-ECG parameters. The relation between LVP and QT dispersion (QTd) (13, 14), suggested that the existence of some slow conducting myocardial areas, related to positive LVP, is associated with a higher inhomogeneity of ventricular repolarisation, expressed as a higher QTd.

Breithardt et al. (15) showed that the presence of late potentials was positively correlated with an ECG score based on R and Q wave duration and R/S ratio in 211 myocardial infarction patients with or without a history of sustained ventricular tachycardia.

Signal averaging is an effective de-noising method (15). LVP occur at the end of the QRS complex and usually extend into the S-T segment enhancing the QRS energy beyond its normal length (16). The significant association between SA-QRS and Tpe and Tampl, respectively, could be due to the extension of LVP into the ST segment.

The study correlates for the first time both QT parameters and T wave variables with SAECG and LVP. The best and most correlations were found for SA-QRS, but RMS40 and LAS40, correlated, as well with 12-lead ECG parameters. A high prevalence of prolonged QT and Tpe intervals was found in patients with LVP. QRS ≥ 110 ms and T0e ≥ 270 ms were the most sensitive predictors of late

ventricular potentials and QTm ≥ 400 ms the most specific.

SAECG is useful for risk stratification of patients at risk of developing life-threatening ventricular arrhythmias (5) and has some advantages compared to 12-lead ECG, improving the signal-to-noise ratio of a surface ECG, permitting the identification of low-amplitude (microvolt level) signals at the end of the QRS complex referred to as "late potentials" (5). Bauer et al. (17) suggested that LVP are of limited use for risk stratification in post infarction patients who received reperfusion/revascularization therapy. Our patients did not receive reperfusion/revascularization therapy, but up-to-date pharmacological treatment (aspirin, beta-blockers and ACE-inhibitors).

Limitations

It is known that late potentials are seen more frequently in post MI patients that have spontaneous or induced sustained ventricular tachycardia. In this study, late potentials were seen in 67% of patients. We have no information if these patients experienced any spontaneous or induced ventricular arrhythmias and no history of syncope is known. Only premature ventricular contractions were mentioned in 4 patients (13%) and nonsustained ventricular arrhythmias in 3 patients (10%). Another limitation of our study was the low number of patients. The results need to be confirmed in larger groups and in longitudinal studies. Many factors are associated with QT prolongation and shortening and it is difficult to control for all the possible confounding factors. Some of the drugs prolong the QT interval: class III antiarrhythmic drugs, diuretics, calcium channel blockers and beta blockers (18 - 21). Other causes of QT interval elongation are: heart failure, hypertension, left ventricular hypertrophy and obesity (18, 20-22). A shorter QT interval was observed in diabetics and current smokers (18). Unfortunately, there is no SAECG parameter known to be useful in predicting drug efficacy (23). Amiodarone prolongs the total QRS duration and LAS40 and significantly reduces RMS40 (24). No SAECG recordings are available for patients on amiodarone before therapy, and non-responders to amiodarone could not be identified. The current study only evaluated patients with post-infarction heart failure. Hence, our results cannot be extrapolated to patients with other conditions or healthy controls. Behavioral and lifestyle practices are known as major determinants in health (25). Alcohol consumption, physical inactivity and unhealthy diets were not considered. But smoking and obesity were mentioned as cardiovascular risk factors.

The results of our study, if confirmed in larger groups, can be valuable in clinical management of post-infarction patients who do not receive reperfusion/revascularization therapy, using a very simple and accessible method: 12-lead ECG. Considering the high negative predictive value of LVP, our study may be also useful for the identification of patients at low risk for ventricular arrhythmia.

Conclusion

The presence of LVP and SA-ECG parameters can be predicted from 12-lead ECG variables in post-infarction heart failure patients.

List of abbreviations

LAS40 = "low amplitude signal"<40 μV
LVP = late ventricular potential
QRS = QRS duration
QTmax = maximal QT interval
QTc = heart rate corrected QTmax
QTm = mean QT

r = Bravais-Pearson correlation coefficient
RMS40 = the root mean square of the terminal 40 ms of the filtered QRS
SA-ECG = signal averaged electrocardiogram
SA-QRS = signal averaged ECG QRS duration
T0e = T wave duration
Tpe = Tpeak-Tend interval
Tampl = T wave amplitude

Authors' contributions

The work presented here was carried out in collaboration between all authors. Ioana Mozos defined the research theme and designed methods. Ioana Mozos and Mircea Hancu performed the investigations and co-worked on data collection. Anca Tudor analysed and interpreted the results. Ioana Mozos, Corina Serban and Lelia Susan wrote the paper.

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Table 1: Characteristics of the patients Characteristics of the patients

Age (Mean±SD)	62±3 years
Sex: M/F	5/1
Myocardial infarction (MI) survival	1–9 years
MI location	18 (60%): anterior; 10 (33%): inferior; 2 (7%): anterior and inferior
Ejection fraction	46±3%: only 2 patients (7%) with an EF<30%
Heart rate	77±4 beats/minute
Cardiovascular risk factors	diabetes mellitus: 9 (30%), obesity: 10 (33%), hypertension: 5 (17%), smoking: 3 (10%)
Associated pathology	left ventricular aneurism: 2 (7%), chronic bronchitis: 4 (13%), chronic kidney disease 10 (33%)
Arrhythmia history	atrial fibrillation: 2 (7%), premature ventricular contractions: 4 (13%), nonsustained ventricular arrhythmias: 3 (10%)
Therapy	angiotensin conversion enzyme inhibitors: 15 (50%), calcium blockers: 4 (13%), nitrates: 27 (90%), beta-blockers: 20 (67%), digitalis: 4 (13%), class III antiarrhythmics: 7 (23%).

Table 2: Results

Parameter	Mean±SD
QTmax	500±40 ms
QTc	560±63 ms
QTm	377±52 ms
QRS	140±27 ms
SA-QRS	128±18 ms
LAS40	61±24 ms
RMS40	21±8 μV
T0e	330±38 ms
Tpe	150±19 ms
Tampl	0.47± 0.15 mV

QTmax = maximal QT interval duration, QTc = heart rate corrected QTmax, QTm = the mean QT interval duration in all leads, QRS = maximal QRS duration, SA-QRS = signal averaged ECG QRS duration, LAS40 = the duration of the low-amplitude signal, RMS40 = the root mean square of the terminal 40 ms of the filtered QRS, T0e = T wave duration, Tpe = Tpeak-Tend interval, Tampl = T wave amplitude.

Table 3: Sensitivity and specificity of 12-lead ECG parameters as predictors of late ventricular potentials

ECG parameter	Sensitivity (95% CI)	Specificity (95% CI)
QTmax ≥ 450 ms	0.9 (0.699 to 0.972)	0.5 (0.237 to 0.763)
QTc ≥ 450 ms	0.85 (0.64 to 0.948)	0.5 (0.237 to 0.763)
QTm ≥ 350 ms	0.682 (0.473 to 0.836)	0.875 (0.529 to 0.978)
QTm ≥ 400 ms	0.55 (0.342 to 0.742)	0.9 (0.598 to 0.982)
QRS ≥ 110 ms	0.95 (0.764 to 0.991)	0.2 (0.057 to 0.51)
QRS ≥ 120 m	0.92 (0.773 to 0.992)	0.889 (0.565 to 0.98)
T0e ≥ 270 ms	0.95 (0.764 to 0.991)	0.2 (0.057 to 0.51)
Tpe > 120 ms	0.895 (0.686 to 0.971)	0.182 (0.051 to 0.477)
Tampl ≥ 0.35 mV	0.905 (0.711 to 0.973)	0.667 (0.354 to 0.879)

CI=confidence interval, QTmax = maximal QT interval duration, QTc = heart rate corrected QTmax, QTm = the mean QT interval duration in all leads, QRS = maximal QRS duration, T0e = T wave duration, Tpe = Tpeak-Tend interval, Tampl = T wave amplitude.

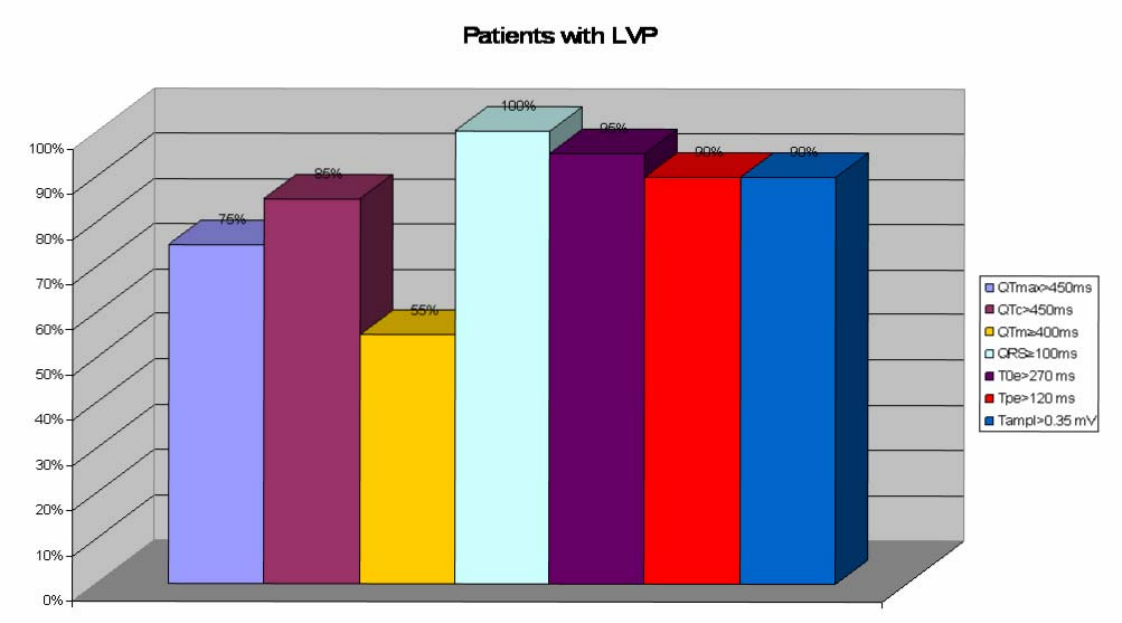


Figure 1: The prevalence of prolonged QTmax, QTc, QTm, QRS, T0e, Tpe and increased Tampl in patients with late ventricular potentials

QTmax = maximal QT interval duration, QTc = heart rate corrected QTmax, QTm = the mean QT interval duration, QRS = maximal QRS duration, T0e = T wave duration, Tpe = Tpeak-Tend interval, Tampl = T wave amplitude, LVP = late ventricular potentials

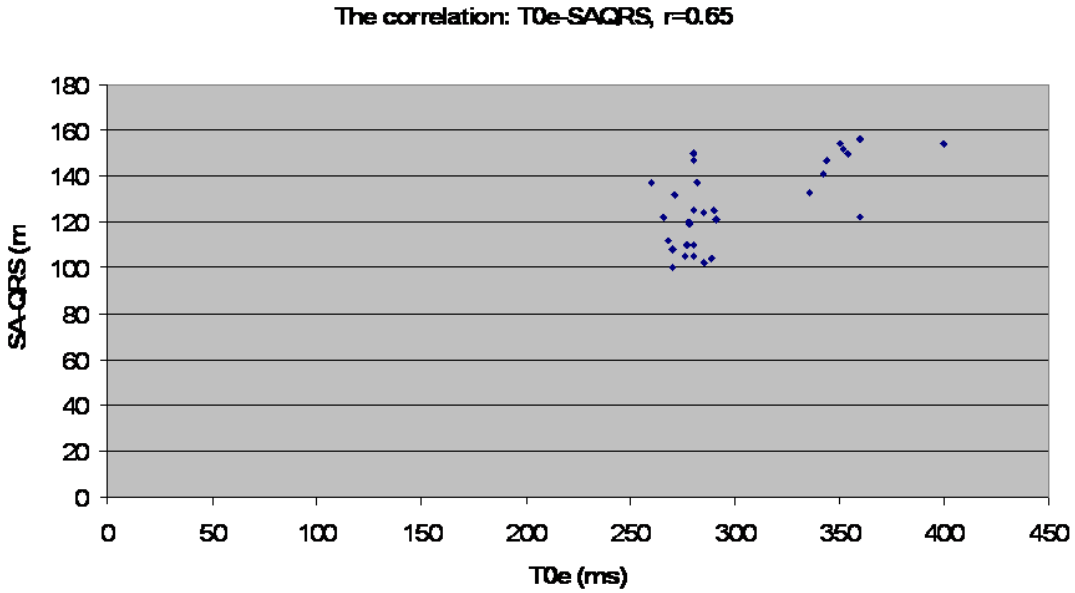


Figure 2: The correlation between T wave duration and signal averaged ECG QRS duration in post-infarction heart failure patients

SA-QRS = signal averaged ECG QRS duration, T0e = T wave duration, r = the Bravais-Pearson correlation coefficient

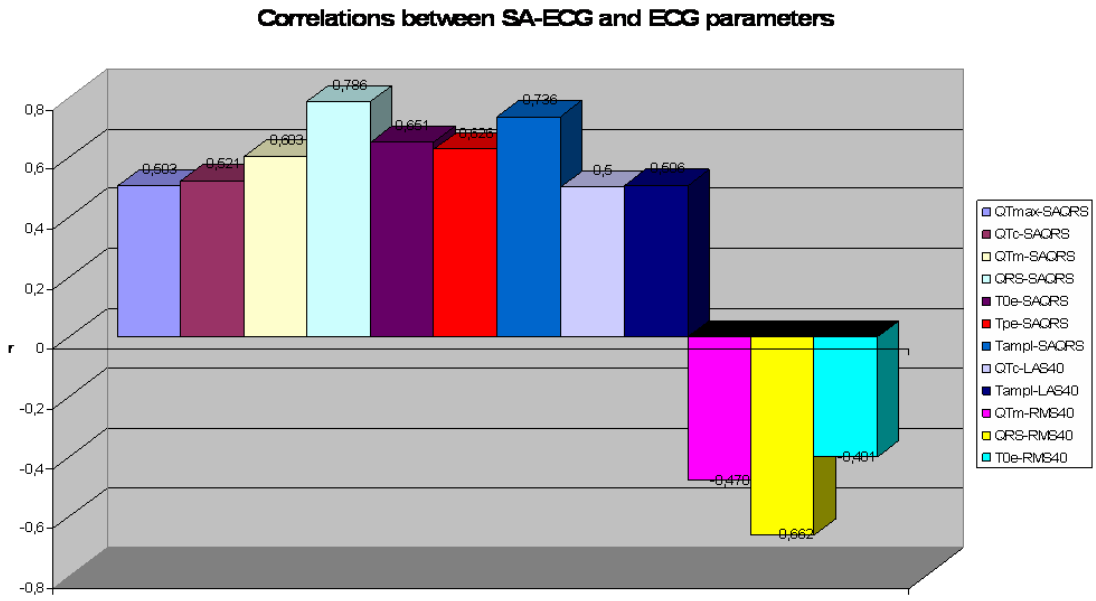
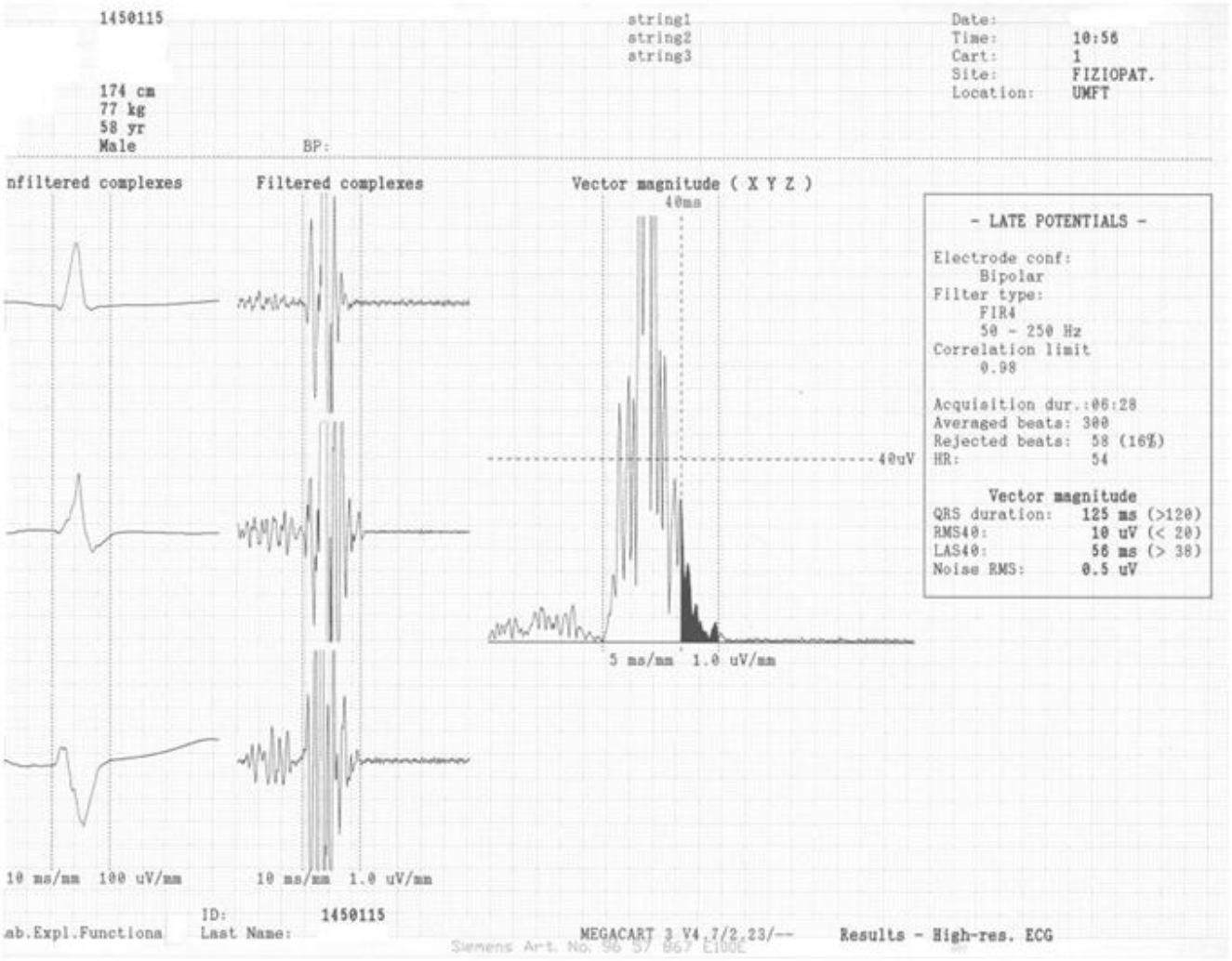


Figure 3: Correlations between Signal averaged ECG and 12-lead ECG parameters.

QTmax = maximal QT interval duration, QTc = heart rate corrected QTmax, QTm = the mean QT interval duration in all ECG leads, QRS = maximal QRS duration, SA-QRS = signal averaged ECG QRS duration, LAS40 = the duration of the low-amplitude signal, RMS40 = the root mean square of the terminal 40 ms of the filtered QRS, T0e = T wave duration, Tpe = Tpeak-Tend interval, Tampl = T wave amplitude.



Figurs 4: Late ventricular potentials in a patient with post-infarction heart failure

QRS duration = signal averaged ECG QRS duration, LAS40 = the duration of the low-amplitude signal, RMS40 = the root mean square of the terminal 40 ms of the filtered QRS