# Electrocardiographic damage scores and cardiovascular mortality

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**Background** A number of electrocardiogram (ECG) classification systems have been developed to estimate cardiac injury, infarct size, and left ventricular function. Although many studies have documented an association between clinical, imaging, and autopsy data, few have evaluated their prognostic value.

**Methods and Results** ECGs from 46933 patients were analyzed using computerized measurements and algorithms. The Simplified Selvester Score, the Cardiac Infarction Injury Score (CIIS), and a Q-wave score were calculated. Other ECG characteristics such as left ventricular hypertrophy and bundle-branch blocks were also evaluated. The main outcome was cardiovascular (CV) mortality. During a mean follow-up of 6 years, the CIIS outperformed all other ECG classifications in determining prognosis. Going from lowest to highest tertile of CIIS, each step had a hazard ratio of 1.39 (CI 1.32-1.45) or a 39% increase in risk per tertile. Using clinically based thresholds, the annual mortality for high-risk CIIS was 4.5% (CI 4.0-4.6) versus 0.3% (CI 0.0-1.3) for those in the low-risk group.

**Conclusions** A low-risk damage score was associated with a <1% annual CV mortality and a high-risk damage score with annual CV mortality of >4%. A damage score should be calculated as part of all computerized ECG interpretations. (Am Heart J 2005;149:458-63.)

Electrocardiography remains the most commonly used noninvasive tool for diagnosing and evaluating cardiac disease. Certain electrocardiogram (ECG) features are associated with myocardial damage such as bundle branch block and Q waves.<sup>1</sup> When an ECG is completely normal, the probability of normal ventricular function is very high. However, when ECG abnormalities exist, it is more difficult to evaluate the patient. To improve on the electrocardiographic classification of myocardial damage, ECG classification systems were contrived.<sup>2,3</sup> Also known as damage scores, these classification systems were initially designed to assess cardiac injury, infarct size, and left ventricular function.<sup>2,4</sup> Given the strong association between myocardial damage and death, these classification systems were later assessed for their ability to predict prognosis.<sup>5-10</sup> The most investigated damage scores are the Cardiac Infarction Injury Score (CIIS) and the Simplified Sylvester score (SSS).

Starting in March 1987, the Palo Alto Veterans Administration Medical Center has maintained a data-

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base with at least one computerized ECG from 46933 veterans. These ECGs were obtained both from inpatients and outpatients and represent findings from a very broad population.

There are few studies that have used computerized ECG to compare and evaluate the prognostic ability of the damage scores and compare them with other abnormalities of the ECG. With this in mind, we used our large database of computerized ECGs and information on cardiovascular (CV) mortality to evaluate the damage scores.

## **Methods**

All ECGs obtained in the Palo Alto Veterans Administration Medical Center from March 1987 to December 1999 were digitally recorded and stored. When a patient had >1 ECG in the database, only the first ECG was considered. Both the Social Security death index and the California Health Department Service were used to ascertain vital status as of December 31, 2000. Cardiovascular death was defined as a death for a reason other than accidents or oncologic, hematologic, renal, pulmonary, or any other clearly defined noncardiac cause. Electrocardiograms obtained in an inpatient medical or surgical setting or in the emergency room were identified because they could be associated with acute clinical events. Electronically paced rhythms (n = 309) and Wolff-Parkinson-White syndrome (n = 44) were excluded from the analysis.

Standardized computerized ECG criteria as described by the Marquette/GE 12-lead ECG analysis program were used for ECG analysis (www.gemedicalsystems.com). All of the ECGs

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acteristics

Characteristic	Total (n = 46,580)	Patients with CV death (n = 4128)	Patients without CV death (n = 42,452)	P
Age	57 + 15	68 + 11	56 + 15	<.0001
Men	41,980 (90.1)	3926 (95.1)	38.054 (89.6)	<.0001
Women	4600 (9.9)	202 (4.9)	4398 (10.4)	<.0001
Body weight (kg)	82.9 ± 18.3	80.9 ± 17.3	83.1 ± 18.3	<.0001
Height (m)	1.75 ± 0.09	1.74 ± 0.09	1.74 ± 0.09	.05
BMI	27.2 ± 5.5	26.8 ± 5.3	$\textbf{27.3} \pm \textbf{5.5}$	<.0001
Outpatient	30,193 (64.8)	2165 (55.9)	28,028 (66.0)	<.0001
Heart rate	74 ± 17	<b>78</b> ± 17	74 ± 16	<.0001

Men, women, and outpatients are listed as number (%), and other data are listed as mean  $\pm$  SD. BMI, Body mass index.

#### Table II. ECG characteristics

	Total	Patients with CV death	Patients without CV death	
	(n = 46,580)	(n = 4126)	(n = 42,452)	P
Characteristic				
Atrial fibrillation	1332 (2.9)	357 (8.6)	975 (2.3)	<.0001
LVH	2083 (4.5)	464 (11.2)	1619 (3.8)	<.0001
PVC	1840 (4.0)	378 (9.2)	1462 (3.4)	<.0001
lad	4469 (9.6)	767 (18.6)	3702 (8.7)	<.0001
RAD	1101 (2.4)	150 (3.6)	951 (2.2)	<.0001
RBBB	1675 (3.6)	307 (7.4)	1368 (3.2)	<.0001
LBBB	625 (1.3)	162 (3.9)	463 (1.1)	<.0001
IVCD	1478 (3.2)	262 (6.3)	1216 (2.9)	<.0001
Negative T	5657 (12.1)	1256 (30.4)	3374 (7.9)	<.0001
ST depression	7657 (16.4)	1382 (33.5)	4746 (11.2)	<.0001
Q waves				
Q wave	5789 (12.4)	1038 (25.1)	4754 (11.2)	<.0001
present				
Number				
0	40,791 (87.6)	3090 (74.9)	37701 (88.8)	<.0001
1	5177 (11.1)	872 (21.1)	4305 (10.1)	<.0001
2	532 (1.1)	134 (3.2)	398 (0.9)	<.0001
3	79 (0.2)	32 (0.8)	47 (0.1)	<.0001
Q-wave				
score 1				
Anterior	818 (15.8)	164 (18.8)	654 (15.2)	.008
Inferior	3476 (67.1)	553 (63.4)	2923 (67.9)	.63
Septal	736 (14.2)	119 (13.6)	617 (14.3)	.014
Lateral	147 (2.8)	36 (4.1)	111 (2.6)	.011
Scores				
Q-wave	0.14 ± 0.39	0.30 ± 0.57	$0.12\pm0.37$	<.0001
CIIS	$13.7 \pm 10.5$	$20.1 \pm 11.1$	$13.1 \pm 10.2$	< 0001
	$3.7 \pm 10.3$ $2.4 \pm 2.0$	$20.1 \pm 11.1$	$3.1 \pm 10.2$ $21 \pm 27$	< 0001
555	$2.0 \pm 2.7$	4.Z ± 3.0	Z.4 ± Z./	~.0001

Electrocardiogram characteristics are listed as number (%), and scores are listed as mean  $\pm$  SD. *RBBB*, Right bundle branch block; *LBBB*, left bundle branch block; *PVC*, premature ventricular contraction; *LAD*, left axis deviation; *RAD*, right axis deviation; *IVCD*, intraventricular conduction delay.

were overread initially by a single cardiologist. Electrocardiograms were reread by a separate cardiologist to confirm QRS duration >120 milliseconds, PVCs, and atrial fibrillation. The

Table III. Annual Cy monality based on admage score	Table III	<ul> <li>Annual</li> </ul>	CV	mortality	based	on	damage score
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	Annual mortality (%)
Q-wave score	
0	1.3
1	2.8
2	4.8
3	7.0
CIIS	
Low	0.4
Medium	1.2
High	4.4
SSS	
Low	0.6
Medium	1.3
High	3.9

Using practical clinical utility thresholds, the CIIS and SSS were also divided as high, low, and intermediate risk. These thresholds were 0 for low risk and 30 for high risk for the CIIS, and 0 for low risk and 5 for high risk for the SSS.

CIIS and the SSS were calculated using computerized algorithms developed by our group and implemented using macros in EXCEL and ACCESS (Microsoft, Redmond, Wash), and a subset was validated manually. The Q-wave score was calculated using diagnostic Q waves defined as  $\geq$ 40 milliseconds and 25% of the amplitude of the following R wave in 2 adjacent leads. A Q wave in each of 4 ECG areas (inferior, anterior, lateral, and septal) was assigned a value of 1 with a total Q-wave score from 0 to 3 (only 2 patients had a total of 4 and were included under the score of 3).

#### Statistical analysis

Statistical analysis was performed using Number Cruncher Statistical System (Kaysville, Utah) software. Descriptive statistics were used to find mean values for continuous variables and to test for normality. Associations between the survivors and those who had CV death were tested by using  $\chi^2$  tests for categorical data and t tests for continuous variables. P < .05 were considered significant. Cox Hazard Proportional testing was performed to assess the significance and independence of predictors of CV mortality. The models were age-, sex-, and heart rate-adjusted; variables evaluated included left bundle branch block, right bundle branch block, left ventricular hypertrophy (LVH), Q-wave score, the SSS, and the CIIS. Because the CIIS and SSS scoring systems have different distributions, the scores were divided into tertiles to better compare them (ie, to have equal numbers within any group). Hazard ratios with confidence limits were calculated using log ranking. The analysis was repeated in outpatients only to remove all possible ECGs associated with acute myocardial infarctions.

Kaplan-Meier survival curves were then generated for individual variables and annual CV mortality calculated to assess the clinical utility of these variables and scores in a similar population. Kaplan-Meier survival curves were also generated for the Q wave, CIIS, and SSS. Using practical clinical utility thresholds, the CIIS and SSS were also divided as high, low, and intermediate risk. These thresholds were 0 for low risk and 30 for high risk for the CIIS, and 0 for low risk and 5 for high risk for the SSS. The Kaplan-Meier survival



Kaplan-Meier survival plot for CV death using the Q-wave area sum score. Numbers refer to patients evaluated at each time point for each survival curve; numbers in parentheses are cumulative numbers of deaths.

curves were replotted using the CIIS and SSS in patients without Q waves.

Receiver operating curves (ROCs) with CV death as the outcome variable were plotted to compare the prognostic characteristics of the 3 damage scores as well as the sensitivity and specificity at a range of cut points.

## Results

## Patient demographics

Electrocardiogram data from 41980 male and 4600 female veterans were included for analysis (46580 total after excluding those with paced rhythms and Wolff-Parkinson-White syndrome). The mean age of the male patients was 57  $\pm$  14 years; the mean age of the female patients was 57  $\pm$  17 years. Sixty-five percent of the ECGs were obtained in an outpatient setting. There were 4145 CV deaths during a mean follow-up of 6.0  $\pm$  3.8 years. Baseline characteristics of the patients are in Table I.

### Electrocardiogram characteristics

The prevalence of all ECG abnormalities was significantly higher in patients with CV deaths (Table II). Of the total population, diagnostic Q waves were found in 12.4%. Diagnostic Q waves were found in only 1 area in 89% of the patients, and 67% of those were in the inferior territory. The CIIS score ranged from -15 to 60 with a gaussian distribution, and the SSS ranged from 0



Kaplan-Meier survival plot for CV death using the CIIS. Numbers refer to patients evaluated at each time point for each survival curve; numbers in parentheses are cumulative numbers of deaths.

to 15 with a skewed distribution because 20% of the population had a score of 0. Those who had a CV death had significantly higher damage scores compared to those that survived.

#### Survival analysis

Cardiovascular mortality is higher at each level of all of the damage scores (Table III). The annual mortality increased from 1.3% in those with no Q waves to 7% in those with Q waves in 3 areas. Using clinical cut points to separate the CIIS and SSS into low-, medium- and highrisk groups, CV mortality increases from 0.4% and 0.6% for low risk to 4.4% and 3.9% for high risk, respectively.

Kaplan-Meier survival curves were plotted for each of the damage scores. The Q-wave score demonstrated a wide separation in survival (Figure 1). The CIIS shows a separation between the survival curves for the low- and intermediate-risk group and a larger separation between the intermediate- and high-risk groups (Figure 2). The survival curves for the low- and intermediate-risk SSS have less separation, but the difference in survival between the intermediate- and high-risk groups is more notable (Figure 3).

An age-, heart rate-, and sex-adjusted Cox hazard analysis was performed in the total population. The results are listed in Table IV. The CIIS was chosen first by the Cox regression analysis as the best predictor of CV mortality. Left ventricular hypertrophy had the next best predictive ability with the SSS, Q-wave score, and left bundle branch block following in order. Coded as tertiles of CIIS, each step had a hazard ratio of 1.39



Kaplan-Meier survival plot for CV death using the SSS. Numbers refer to patients evaluated at each time point for each survival curve; numbers in parentheses are cumulative numbers of deaths.

Table IV.         Cox proportional hazard analysis						
	Hazards (95% CI)	Р				
Variable						
CIIS	1.39 (1.32-1.45)	<.0001				
LVH	2.00 (1.82-2.21)	<.0001				
SSS	1.23 (1.19-1.29)	<.0001				
Q-wave score	1.24 (1.19-1.30)	<.0001				
Left bundle-branch block	1.53 (1.31-1.81)	<.0001				

Adjusted for age, heart rate, and sex. The variables are listed in order of their predictive ability as determined by the Cox regression analysis. The CIIS is the best predictor based on this hazard model. The categorical variables CIIS and SSS are divided into tertiles, and the Q-wave score is 0, 1, 2, or 3. Left ventricular hypertrophy and left bundle-branch blocks are dichotomous variables. RBBB was also evaluated but is not listed above because the result was not significant.

(CI 1.32-1.45) or a 39% increase in risk per tertile or 78% from the lowest risk group to the highest. Coded similarly, each tertile of the SSS had a hazard ratio of 1.23 (CI 1.19-1.29) or a 23% increase in risk per tertile or 46% from the lowest risk group to the highest. The Q-wave score had a hazard ratio of 1.24 (CI 1.19-1.30) or a 72% risk increase from no Q-wave area to 3 areas. This same statistical analysis was performed in outpatients to avoid any acute myocardial infarctions, and similar results were obtained. The analysis was also performed in patients without Q waves, and similar results were obtained.

Using a receiver operating curve, the scores were evaluated and compared (Figure 4). As only 12.4% of the total population had Q waves and only 1.3% had Q waves in >1 area, the Q-wave score has a limited sensitivity. The Q-wave score ROC curve is severely



Receiver operating curves. The ROC curve for CIIS falls to the left of the curve for SSS at all values, and the area under the curve is higher for the CIIS score, supporting superior performance of the CIIS score.

truncated and cannot be compared with the CIIS and SSS ROC curves. Each point along the curves represents a cut point at which different sensitivities and specificities would be achieved. The ROC curve for CIIS falls to the left of the curve for SSS at all values, and the area under the curve is higher for the CIIS score, supporting superior performance of the CIIS score.

# Discussion

The resting ECG is readily available, noninvasive, and inexpensive, making it one of the most widely used CV diagnostic tests. It is beneficial not only as a diagnostic tool, but also as a prognostic tool. The presence of Q waves which represent myocardial damage is known to portend a poor prognosis. Although Q waves have a limited ability to predict myocardial infarction size and location because of the prevalence of non-Q-wave myocardial infarction as well as Q-wave regression, there have been studies showing Q-wave correlation with ejection fraction.<sup>11,12</sup> Depending on the area of myocardium, except true posterior, correlation has been up to 80%.<sup>13</sup> Previous studies have shown that in asymptomatic populations, Q and QS patterns are associated with significant excess mortality from coronary heart disease, CV mortality, and all-cause mortality.<sup>1</sup> Q waves in multiple regions are associated with a higher 3-year mortality.12 When followed over time, the presence of Q waves, whether recognized and/or associated with known myocardial infarction, was just as likely to predict stroke, congestive heart failure, or death.<sup>14,15</sup>

Despite Q-wave regression, the increased risk remains. We replicated these findings and confirmed that as the number of Q waves increases, the CV risk increases.

Although the Q-wave score is simple to calculate and highly predictive of risk, it has limited sensitivity because of the low prevalence of Q waves in the general population. Even among the 12.4% of the population with Q waves in our study, high-risk patients with Q waves in multiple areas are exceedingly rare. Therefore, other damage scores such as the CIIS and SSS are needed to increase the sensitivity of classification and improve the predictive power of the ECG by considering more than Q waves.

The SSS was initially developed for estimating myocardial infarction and is based on the duration of the Q and R waves and on the ratios of the R/Q amplitude and R/S amplitude in each of the 10 leads (I, II, aVL, aVF, and V1-V6).<sup>3,16</sup> It achieved a 95% specificity for estimating myocardial infarction, was shown to be highly predictive of acute anterior myocardial infarction size, and based on autopsy data, was able to predict anterior, inferior, and posterolateral myocardial infarctions.<sup>17-20</sup> Using radionuclide ventriculography, it is proportional to wall motion abnormalities and inversely proportional to ejection fraction.<sup>4</sup> Similar to our findings, other studies have shown that the higher the SSS, the lower the survival rates.<sup>8,10</sup>

Rataharju et al<sup>2</sup> developed the CIIS to improve the diagnosis of myocardial infarction. The criteria for the coding system were developed by comparing ECGs from patients with and without myocardial infarction. Two thirds of the ECGs were randomly assigned to develop the code and one third to test the accuracy. The sensitivity and specificity of the CIIS for detecting myocardial infarction were 85% and 95%, respectively. It was also later shown to be independently and significantly associated with total and cardiac mortality.<sup>5-7</sup> Other studies in both healthy populations and patients after myocardial infarction followed over many years have shown that the higher the CIIS, the higher the risk of CV death. Similarly, we found increased CV mortality with higher CIIS scores.

Cox hazard analysis showed both the CIIS and SSS to be independent predictors of mortality. There is a 78% increased risk of CV death when the CIIS score increases from the low-risk third to the high-risk third, and similarly, a 46% increase in the SSS, supporting the usefulness of the CIIS and SSS as predictors of CV mortality. Although we refer to these as "damage" scores, the term is problematic because the ECG findings reflect both permanent infarctions and the temporary ischemia; a clearer term is not available.

### Study limitations

As is typical of data from Veterans Administration systems, our data represent a predominantly male

population (only 10% of the patients are women). The ECGs represent a broad sample from inpatients and outpatients, but the specific reasons why the ECGs were obtained are not available. This limitation may actually be a strength in evaluating scores that are applied to a general population. We do not have results of diagnostic testing such as echocardiogram or cardiac catheterization and are therefore unable to evaluate prognostication for such events as myocardial infarction, heart failure, and coronary heart disease. Incorporating other tests or using test results as surrogate end points would very much bias our results because these tests are performed for specific clinical indications in a subset of our population. Our study uses CV death as the primary end point as it is a more suitable end point than total mortality to study CV tests. However, our reliance on the death certificate for the cause of death raises some potential for error.

A prior study indicated that although automated scoring can be developed, accurate duplication of expert manual application is difficult and requires multiple iterative steps.<sup>21</sup> However, to make these scores practical, they must be automated. Our study used relatively simple automated tools to calculate the scores, and it should not be difficult to duplicate this process.

#### Conclusion

We propose that these scores should be used in general practice to aid in the risk stratification of patients. A CIIS a score of  $\geq$ 30 or an SSS score of  $\geq$ 5 should be considered high risk. In addition, a score of 0 in all 3 damage scores is associated with an annual mortality of  $\leq$ 0.7% and is a very reassuring finding. Survival curves demonstrate an increased mortality in those with a higher number of Q waves, higher CIIS score, or higher SSS. The statistical analysis shows that the CIIS is superior to the SSS, yet both could be used in clinical practice.

Although the damage scores were developed initially to assist in diagnosis of myocardial infarction or assessment of left ventricular function, they are essentially markers of damage to the myocardium and have prognostic value. These scores are additional useful data that can be obtained from a simple ECG and provide information that should not be wasted. They are easily programmable into ECG machines, and a CIIS or SSS score should be included as part of all standard ECG reports.

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