Computerized ST Depression Analysis Improves Prediction of All-Cause and Cardiovascular Mortality: *The Strong Heart Study*

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Background: Nonspecific ST depression assessed by standard visual Minnesota coding (MC) has been demonstrated to predict risk. Although computer analysis has been applied to digital ECGs for MC, the prognostic value of computerized MC and computerized ST depression analyses have not been examined in relation to standard visual MC.

Methods: The predictive value of nonspecific ST depression as determined by visual and computerized MC codes 4.2 or 4.3 was compared with computer-measured ST depression $\geq$ 50 μV in 2,127 American Indian participants in the first Strong Heart Study examination. Computerized MC and ST depression were determined using separate computerized-ECG analysis programs and visual MC was performed by an experienced ECG core laboratory.

Results: The prevalence of MC 4.2 or 4.3 by computer was higher than by visual analysis (6.4 vs 4.4%, $P < 0.001$). After mean follow-up of 3.7 $\pm$ 0.9 years, there were 73 cardiovascular deaths and 227 deaths from all causes. In univariate Cox analyses, visual MC (relative risk [RR] 4.8, 95% confidence interval [CI] 2.6-9.1), computerized MC (RR 6.0, 95% CI 3.5-10.3), and computer-measured ST depression (RR 7.6, 95% CI 4.5-12.9) were all significant predictors of cardiovascular death. In separate multivariate Cox regression analyses that included age, sex, diabetes, HDL and LDL cholesterol, body mass index, systolic and diastolic blood pressure, microalbuminuria, smoking, and the presence of coronary heart disease, computerized MC (RR 3.0, 95% CI 1.6-5.6) and computer-measured ST depression (RR 3.1, 95% CI 1.7-5.7), but not visual MC, remained significant predictors of cardiovascular mortality. When both computerized MC and computer-measured ST depression were entered into the multivariate Cox regression, each variable provided independent risk stratification (RR 2.1, 95% CI 1.0-4.4, and RR 2.1, 95% CI 1.0-4.4, respectively). Similarly, computerized MC and computer-measured ST depression, but not visual MC, were independent predictors of all-cause mortality after controlling for standard risk factors.

Conclusions: Computer analysis of the ECG, using computerized MC and computer-measured ST depression, provides independent and additive risk stratification for cardiovascular and all-cause mortality, and improves risk stratification compared with visual MC. These findings support the use of routine computer analysis of ST depression on the rest ECG for assessment of risk and suggest that computerized MC can replace visual MC for this purpose. **A.N.E. 2001;6(2):107–116**

electrocardiogram; computerized; Minnesota code; ST depression

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The standard resting ECG remains the most widely used clinical tool to detect the presence of coronary heart disease and for assessing risk in population-based studies. Minnesota coding (MC) of the ECG,[1] originally developed as a classification system by Blackburn et al.,[2] has become the standard for evaluating the resting ECG in clinical trials and epidemiologic studies over the past 30 years.[3-15] Indeed, nonspecific ST segment changes on the ECG as determined by the MC have been established as an important ECG predictor of increased coronary heart disease incidence and mortality.[4-16] However, use of the MC for assessing ST segment depression has intrinsic limitations based on the categorical nature of the specific criteria and the decision-tree structure used in assigning codes.[1,2,16-21] As a consequence of these issues and the time-consuming nature and complexity of the multiple measurements and comparisons required for accurate assignment of codes, MC has not become a routine component of clinical ECG interpretation.

Computer-assisted interpretation of the ECG has become wide-spread in clinical use with the development of digital ECG recording equipment and numerous computer programs for interpretation of the ECG.[21-23] Moreover, computer programs for analyzing ECGs on the basis of the MC have been available for several years[17,19,20] and the diagnostic accuracy of computerized MC has been found to be similar to standard visual MC in limited testing to date.[19,20] However, the relative prognostic value of standard visual and computerized MC of ST segment depression have not been compared and the role of computer-measured ST depression alone, independent of hierarchical MC criteria, for the prediction of mortality has not been examined. Therefore, the present study was undertaken to compare ST segment changes on the rest ECG as defined by MC 4.2 and 4.3 using standard visual analysis by an established MC core laboratory to both MC performed by the MEANS program of Erasmus University[18,20,24] and to computer-measured ST depression for the prediction of cardiovascular and all-cause mortality.

METHODS

Study Population

The Strong Heart Study is a community-based study of cardiovascular disease and its risk factors in American Indians.[25] American Indians aged 45—74 years during the period July 1989 to January 1992, who were resident members of the following 13 tribes, were eligible for participation in the first Strong Heart Study examination: the Akimel O'odham/PecPosh/Johona O'odham tribes of central Arizona who live in the Gila River, Salt River, and Ak-Chin communities; the seven tribes of southwestern Oklahoma (the Apache, Caddo, Comanche, Delaware, Fort Sill Apache, Kiowa, and Wichita); and the Oglala and Cheyenne River Sioux in South Dakota and the Spirit Lake community in the Fort Totten area of North Dakota. Enrollment by previously published procedures (n = 4,549)[25] achieved a 62% participation rate. Participants and nonparticipants were similar with respect to tobacco use and diabetes prevalence, but nonparticipants were more likely to be male (54 vs 41%), were slightly older (59 vs 57 years), and less likely to be hypertensive (30 vs 42%) than participants.[26]

Electrocardiography

Standard 12-lead ECGs were performed using MAC-PC or MAC-12 digital ECG systems (GE-Marquette Medical Systems) as previously described.[3,26] For each ECG, 10 seconds of data were digitally recorded at a 250 Hz sampling frequency to a resolution of 5 μV and stored in a Marquette MUSE system for computer measurements. ST depression was measured on median complexes from the 10 second tracings by the MUSE at the midpoint of the ST segment between the J-point and the end of the ST segment, defined as 1/8 the average R-R interval from the J-point. ST depression of $\geq$ 50 μV in any lead (excluding aVR) was considered abnormal, a value that corresponded to the 95th percentile of ST depression findings in the current population and parallels use of this threshold for detection of ST depression by MC.[1,2] Digital ECG records were available on 2,140 of the 4,549 (47.0%) eligible participants in the first Strong Heart Study examination; the remainder of digital ECGs had been lost in a catastrophic computer disk crash at the Fitzsimons Army Medical Center, where the ECGs were originally stored. Participants with digital ECGs were similar in age (56.1 $\pm$ 8.2 vs 56.5 $\pm$ 8.0 years) but were slightly more likely to be male (42.1 vs 39.1%, P = 0.04) than those without digital ECGs. Thirteen participants

with digital ECGs (0.5%) were excluded because of nonsinus rhythm or bundle branch block.

Minnesota Coding

All ECGs were sent to the University of Minnesota ECG Coding Center for standard visual MC as previously reported.[3] Minor ST depression was defined by the presence of MC 4.2 or 4.3, according to standard definitions and exceptions.[1,2] MC 4.2 was coded in the presence of J-point ST depression ≥ 50 μV and < 100 μV with the ST segment horizontal or downsloping in any of leads I, II, aVL, aVF, or V_1 through V_6. MC 4.3 was coded in the presence of < 50 μV of J-point ST depression with the ST segment downsloping and the segment or T-wave nadir ≥ 50 μV below P-R segment baseline in leads I, II, aVL, or V_2-V_6. Of note, MC 4.1, identifying more marked ST depression (≥ 100 μV), was not present in the study population.

Computer MC was performed by the MEANS program of Erasmus University, Rotterdam,[24] as previously described in detail.[20] For the purposes of MC, measurements and morphologic analyses are performed on averaged complexes derived from representative beats over the entire 10 seconds of the tracing, which is intrinsically different from the majority rule or other rules for beat selection used for standard visual MC.[1,2,20] Based on these measurements and determinations, the presence or absence of MC 4.2 or 4.3 were determined and output by the program. Accuracy of the MEANS MC program for ST depression codes has been compared with standard visual MC in 300 patients using visual coding by a highly experienced investigator and a reference standard derived from a consensus approach,[20] with slightly better agreement of the computer coding than the visual coding with the reference standard (98.3 vs 96.7%, P = ns).

Clinical Evaluation

All participants underwent a personal interview including the Rose questionnaire,[27] physical examination, and fasting blood and urine sampling, as previously reported.[3,25] Participants were categorized as having definite or possible coronary heart disease based on clinical and ECG evidence of coronary disease or myocardial infarction and were classified as diabetic as previously reported.[28]

Definition and Determination of Clinical Endpoints

For survival analyses, observation began on the date of the ECG recording. Deaths were identified in an ongoing manner from sources in each community and through annual follow-up of each participant, and were verified using death certificates and medical records. Deaths were classified as cardiovascular if due to myocardial infarction, stroke, sudden death due to coronary heart disease, or congestive heart failure, according to standardized criteria as previously defined,[29,30] by an independent review panel of physicians who were unaware of ST depression or MC findings on the baseline ECG.

Data Analysis and Statistical Methods

Data were stored and analyzed using SPSS, Release 9.0 (SPSS Inc.). Mean values were compared between groups using two-way analysis of variance to adjust for possible differences between study centers (Arizona, Oklahoma, North/South Dakota). Proportions were compared using chi-square tests. Mortality rates were calculated by the product-limit method and were plotted according to the Kaplan-Meier method,[31] with comparisons of death rates between groups performed with the log-rank test. Mortality analyses were performed for both continuous and discrete variables by fitting Cox proportional-hazards models to the data after stratification by center.[32] With the proportional-hazards models, the estimated relative risk of the incidence of death for positive compared with negative test outcomes was computed as the antilog of the estimated coefficient corresponding to the dichotomous variable.[33] When ST depression was considered as a continuous variable, the comparison in relative risk was computed for a 10 μV increase in ST depression, as the antilog of the estimated coefficient multiplied by 10. The 95% CIs of each relative risk were calculated from estimated coefficients and their standard errors[34] and Wald χ^2 statistics and P values were calculated. To test the independence of variables as predictors of mortality, multivariate Cox models were performed including age, sex, body mass index, diabetes, diastolic and systolic blood pressure, HDL and LDL cholesterol, albuminuria, alcohol use, history of smoking or prevalent coronary heart dis-

Table 1. Clinical Characteristics and ST Depression in Participants According to Survival Status*

Variable	Survivors (n = 1900)	All-Cause Death (n = 227)	P Value	Survivors and NonCVD Death (n = 2054)	CVD Death (n = 73)	P Value
Age (years)	55 ± 8	59 ± 9	< 0.001	56 ± 8	61 ± 9	< 0.001
Sex (% male)	41	49	0.015	41	58	0.007
BMI (kg/m^2)	30.9 ± 6.2	29.6 ± 6.9	0.006	30.8 ± 6.3	29.8 ± 5.3	0.133
Diastolic BP (mm Hg)	78 ± 11	76 ± 12	0.023	77 ± 11	79 ± 11	0.473
Systolic BP (mm Hg)	127 ± 19	130 ± 23	0.017	127 ± 19	135 ± 25	0.004
HDL cholesterol (mg/dL)	45 ± 13	45 ± 17	0.434	45 ± 13	41 ± 13	0.008
LDL cholesterol (mg/dL)	117 ± 32	110 ± 41	0.006	116 ± 33	128 ± 47	0.002
Triglycerides (mg/dL)	148 ± 129	158 ± 164	0.345	148 ± 128	182 ± 231	0.061
Albuminuria (mg/g)	2.7 ± 2.0	4.1 ± 2.6	< 0.001	2.8 ± 2.1	4.7 ± 2.6	< 0.001
Diabetes or IGT (%)	61	78	< 0.001	62	82	< 0.001
Prevalent CHD			< 0.001			< 0.001
None (%)	82	65		81	56	
Possible (%)	16	27		17	32	
Definite (%)	2	8		2	12	
Smoking			0.902			0.143
Never (%)	30	30		30	26	
Previous (%)	35	36		35	34	
Current (%)	35	34		35	40	
ST depression (μV)	−14 ± 18	−18 ± 23	0.003	−14 ± 18	−24 ± 28	< 0.001

* Adjusted for differences between tribal centers using two-way analysis of variance; BMI = body mass index; BP = blood pressure; CHD = coronary heart disease; CVD = cardiovascular disease; IGT = impaired glucose tolerance .

ease, and study center as covariates. For all tests, a two-tailed $P < 0.05$ was required.

RESULTS

Participant Characteristics

After a mean follow-up of 3.7 ± 0.9 years there were 227 deaths from all causes and 73 cardiovascular deaths. Clinical characteristics of survivors and those who died from any cause and in participants with and without cardiovascular death are compared in Table 1. The 227 participants who died were older, more likely to be male, had higher systolic and lower diastolic blood pressures, more albuminuria, a higher prevalence of diabetes and possible or definite prevalent coronary heart disease, lower body mass indexes and LDL cholesterol levels, but did not differ in HDL or triglyceride levels or in smoking status compared to those who survived. The 73 participants who suffered cardiovascular death were similarly older, more likely to be male, with higher systolic blood pressures, greater albuminuria, and higher prevalences of diabetes and possible or definite coronary heart disease, but also had lower HDL and higher LDL cholesterol levels than those who had not died from a cardiovascular cause. The relation of ST depression to clinical outcome is also shown in Table 1. Participants who died had greater ST depression than those who survived, with the greatest ST depression in those who suffered cardiovascular death. Overall, 6.4% of participants had MC 4.2 or 4.3 by computer, significantly greater than the 4.4% prevalence by standard visual coding ($P < 0.001$) and the 4.9% prevalence of computer-measured ST depression ≥50 μV ($P = 0.013$).

Prediction of Cardiovascular Mortality

The univariate predictive values of visual and computer MC and computer-measured ST depression for cardiovascular mortality are compared in Table 2. In Cox analyses adjusting for possible differences between study centers, standard visual MC assessment of ST depression was a significant predictor of cardiovascular mortality ($\chi^2 = 24.1$, $P < 0.0001$), associated with a 4.8-fold increased risk of cardiovascular death. Compared with standard visual coding, computerized MC was more strongly associated with cardiovascular death ($\chi^2 = 43.8$, $P < 0.0001$) with a 6.0-fold increased risk. However, in univariate analyses, computer-mea-

Table 2. Univariate Cox Proportional Hazards Models for Prediction of Cardiovascular Disease and All-Cause Mortality Examining Visual and Computerized Minnesota Codes 4.2 and 4.3 and ST Segment Depression of ≥50 μV*

Variable	Hazard Ratio	95% CI	χ^2	P Value
Prediction of Cardiovascular Disease Mortality				
Visual MC	4.83	2.57–9.05	24.1	< 0.0001
Computerized MC	6.02	3.54–10.25	43.8	< 0.0001
ST depression ≥ 50 μV	7.58	4.46–12.89	55.9	< 0.0001
Prediction of All-Cause Mortality				
Visual MC	3.98	2.72–5.83	50.1	< 0.0001
Computerized MC	3.68	2.60–5.19	54.7	< 0.0001
ST depression ≥ 50 μV	3.81	2.63–5.53	49.6	< 0.0001

* Stratified for possible center effects.
MC = Minnesota codes 4.2 or 4.3.

sured ST depression ≥50 μV was the strongest predictor of cardiovascular mortality (χ^2 = 55.9, P < 0.0001) with a 7.6-fold increased risk of cardiovascular death. When the relation of cardiovascular mortality to ECG findings was examined using Kaplan-Meier survival analyses (Fig. 1), computerized MC more accurately stratified risk of cardiovascular death than standard visual MC, and computer-measured ST depression had the highest log rank score due to earlier separation of the mortality curves because of higher early cardiovascular mortality in participants with ST depression ≥50 μV (Fig. 1). Five-year cardiovascular mortality was 30% in participants with ≥ 50 μV of ST depression and only 5% among those with more normal ST segments. When ST depression was examined as a continuous variable it remained associated with a significant risk of cardiovascular mortality (χ^2 =

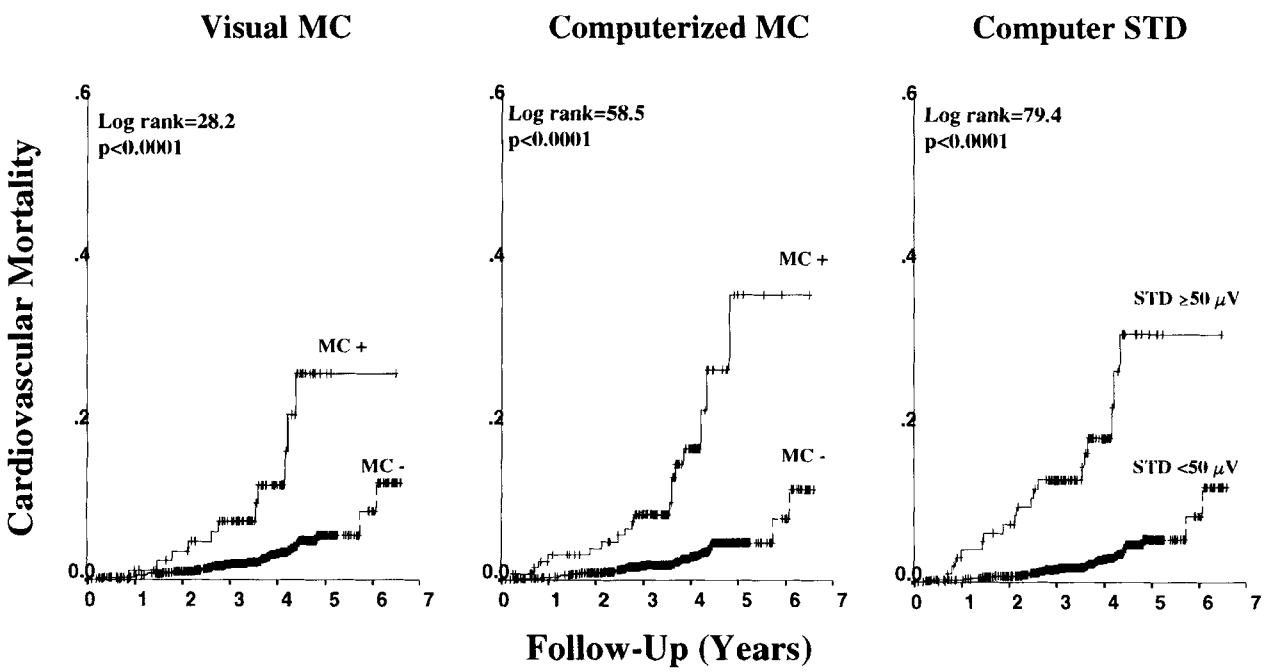

Figure 1. Kaplan-Meier plots of cardiovascular mortality in relation to the presence or absence of Minnesota codes (MC) 4.2 or 4.3 by visual and computerized criteria and according to the presence or absence of computer-measured ST depression (STD) ≥ 50 μV. (MC+, MC present; MC-, MC absent).

Table 3. Multivariate Cox Proportional Hazards Models for Prediction of All-Cause and Cardiovascular Disease Mortality Examining Visual and Computerized Minnesota Codes 4.2 and 4.3 and ST Segment Depression of ≥50 μV*

Variable	Hazard Ratio	95% CI	χ^2	P Value
Prediction of Cardiovascular Disease Mortality				
Visual MC	1.01	0.46–2.23	0.1	0.8027
Computerized MC	3.03	1.65–5.56	12.7	0.0004
ST depression ≥ 50 μV	3.07	1.66–5.70	12.7	0.0004
Prediction of All-Cause Mortality				
Visual MC	0.90	0.52–1.57	0.01	0.9262
Computerized MC	1.65	1.06–2.56	4.9	0.0352
ST depression ≥ 50 μV	1.62	1.01–2.60	4.0	0.0455

* Adjusted for age, sex, body mass index, diabetes, diastolic and systolic blood pressure, HDL and LDL cholesterol, triglycerides, albuminuria, alcohol use, a history of smoking or prevalent coronary heart disease, and stratified by study center.
MC = Minnesota codes 4.2 or 4.3.

33.86, $P < 0.0001$) with a hazard ratio of 1.25 (95% CI 1.16-1.34) for each 10 μV of additional ST depression. In this model, 100 μV (1 mm) of ST depression on the resting ECG would be associated with a greater than 9-fold increased risk of cardiovascular death (hazard ratio 9.1, 95% CI 4.3-19.2).

After multivariate adjustment for age, sex, body mass index, diabetes, diastolic and systolic blood pressure, HDL and LDL cholesterol, triglycerides, albuminuria, history of smoking and prevalent coronary heart disease (Table 3), computerized MC and computer-measured ST depression ≥ 50 μV, but not visual MC, remained significant predictors of cardiovascular mortality. After controlling for these risk factors, computerized MC and computer-measured ST depression were both associated with approximately 3.0-fold increased risk of cardiovascular death. When both computerized MC and computer-measured ST depression were entered into the Cox multivariate regression, each variable remained associated with cardiovascular death (computerized MC $\chi^2 = 4.3$, $P = 0.037$, hazard ratio 2.1, 95% CI 1.0-4.4 and computer-measured ST depression $\chi^2 = 4.1$, $P = 0.044$, hazard ratio 2.1, 95% CI 1.0-4.4).

Because both computerized MC and computer-measured ST depression were independent predictors of cardiovascular death, their combined value for prediction of cardiovascular mortality was examined (Table 4 and Fig. 2). In univariate Cox analyses, compared to the risk associated with the absence of both computerized MC 4.2 or 4.3 and ≥ 50 μV of ST depression, the finding of either abnormality was associated with a greater than 4.5-fold increased risk of cardiovascular death while the presence of both an abnormal computerized MC and abnormal computer-measured ST depression was associated with a greater than 12-fold increased risk of cardiovascular death (Table 4). Five-year cardiovascular mortality in this population was only 4% when both tests were negative, 21% when either test was positive, and 56% when both computerized MC and computer-measured ST depression were abnormal (Fig. 2). After controlling for other potential risk factors, risk of cardiovascular mortality was increased by > 250% when either ECG measure was present and by nearly 400% when both MC and 50 μV of ST depression were present (Table 4).

Prediction of All-Cause Mortality

The univariate predictive values of visual and computer MC and computer-measured ST depression for all-cause mortality are shown in Table 2. The presence of ST changes by standard visual MC was a significant predictor of all-cause mortality ($\chi^2 = 50.1$, $P < 0.0001$) with a fourfold increased risk of death. Compared with visual coding, computerized MC ($\chi^2 = 54.7$, $P < 0.0001$) and computer-measured ST depression ≥ 50 μV ($\chi^2 = 49.6$, $P < 0.0001$) provided similar risk stratification with hazard ratios of 3.7 and 3.8, respectively. When the relation of all-cause mortality to ECG findings was examined using Kaplan-Meier analyses (Fig. 3), computerized MC appeared to stratify mortality risk most accurately, and was associated with a 5-year total mortality of 46% compared to 17% in

Table 4. Center-Adjusted and Multivariate Cox Proportional Hazards Models for Prediction of All-Cause and Cardiovascular Disease Mortality According to Combined Computerized Minnesota Code and ST Segment Depression Criteria

	Univariate		Multivariate*	
Variable	Hazard Ratio	95% CI	Hazard Ratio	95% CI
Prediction of Cardiovascular Disease Mortality†				
MC− and STD−	1	—	1	—
MC+ or STD+	4.47	2.46–8.14	2.66	1.36–5.19
MC+ and STD+	12.59	6.58–24.09	3.85	1.79–8.26
Prediction of All-Cause Mortality‡				
MC− and STD−	1	—	1	—
MC+ or STD+	2.80	1.93–4.07	1.40	0.88–2.22
MC+ and STD+	5.61	3.51–8.97	1.85	1.00–3.44

† Univariate $\chi^2 = 70.3$, $P < 0.0001$; Multivariate $\chi^2 = 17.0$, $P = 0.0007$.
‡ Univariate $\chi^2 = 72.9$, $P < 0.0001$; Multivariate $\chi^2 = 5.15$, $P = 0.0760$.
MC = Minnesota codes 4.2 or 4.3; STD = ST depression ≥ 50 μV.
* Adjusted for age, sex, body mass index, diabetes, diastolic and systolic blood pressure, HDL and LDL cholesterol, triglycerides, albuminuria, alcohol use, a history of smoking or prevalent coronary heart disease, and stratified by study center.

participants without the ECG finding. When ST depression was analyzed as a continuous variable, it remained a significant predictor of all-cause mortality ($\chi^2 = 30.39$, $P < 0.0001$) with a hazard ratio of 1.15 (95% CI 1.10-1.22) for each 10 μV of additional ST depression. Thus, in this model, 100 μV of STD on the resting ECG would be associated with a greater than fourfold increased risk of all-cause mortality (hazard ratio 4.22, 95% CI 2.54-7.03). After multivariate adjustment for age, sex, and other potential predictors of mortality (Table 3), computerized MC and computer-measured ST depression ≥ 50 μV, but not visual MC, remained significant predictors of all-cause mortality, associated with greater than 60% increases in the risk of death after controlling for these confounders.

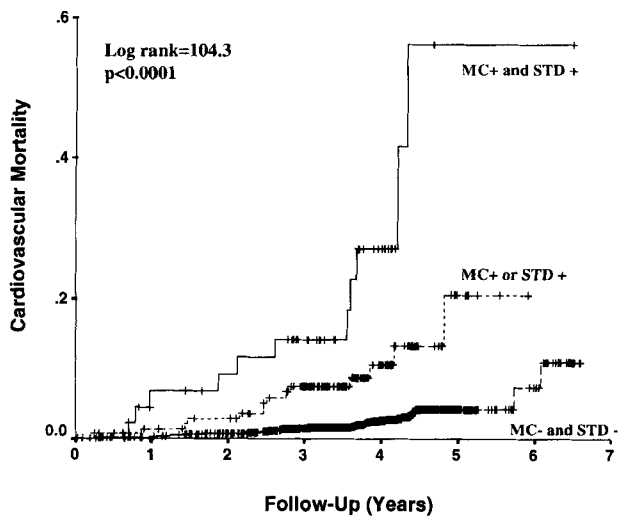

Figure 2. Kaplan-Meier plots of cardiovascular mortality according to combined computerized Minnesota code (MC) and ST depression (STD) criteria.

The value of the combination of computerized MC and computer-measured ST depression for prediction of all-cause mortality is illustrated in Table 4 and Figure 4. Compared to the absence of both findings on computerized ECG analyses, the presence of either MC abnormality or ≥ 50 μV of ST depression was associated with a 2.8-fold increased risk of death and the presence of both ECG abnormalities was associated with a 5.6-fold higher mortality risk. Five—year all-cause mortality in this population was 17% when both tests were negative, 32% when either test was positive, and 65% when both computerized MC and computer-measured ST depression were abnormal (Fig. 4). After controlling for other potential risk factors, the rate of all—cause mortality was increased by 40% when either ECG measure was present and by 85% when both MC and ST depression ≥ 50 μV were present (Table 4), although this association did not quite achieve statistical significance ($P = 0.076$).

DISCUSSION

This study demonstrates the strong prognostic value of computerized interpretation of minor (≥

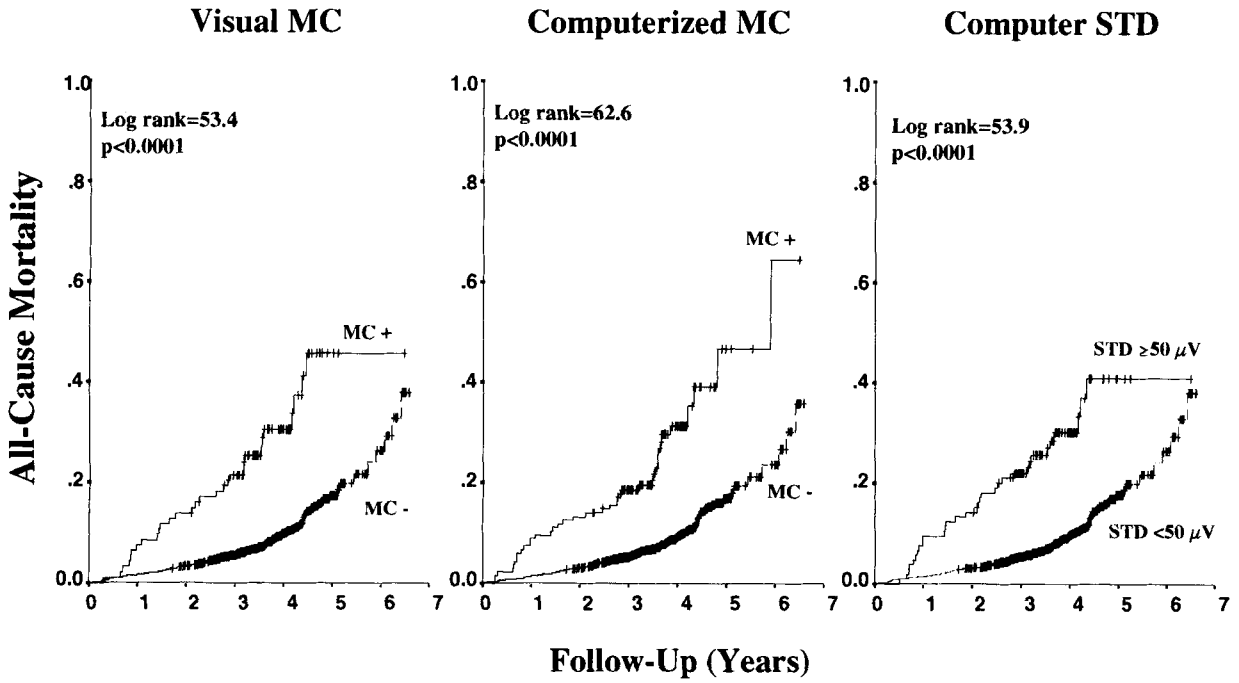

Figure 3. Kaplan-Meier plots of all-cause mortality in relation to the presence or absence of Minnesota codes (MC) 4.2 or 4.3 by visual and computerized criteria and according to the presence or absence of computer-measured ST depression (STD) ≥ 50 μV. (MC+, MC present; MC-, MC absent).

50 μV) ST depression on digitally-acquired 12-lead ECGs and shows that this is stronger than visual MC abnormalities–the reference standard for nearly four decades–in a large, population—based study of cardiovascular disease and its risk factors.

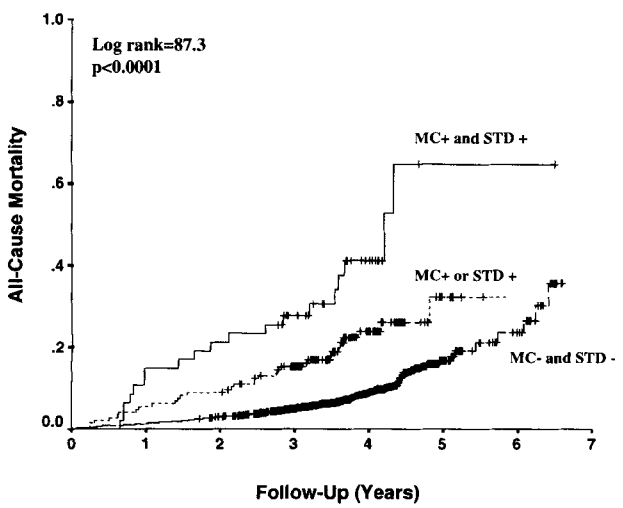

Figure 4. Kaplan-Meier plots of all-cause mortality according to combined computerized Minnesota code (MC) and ST depression (STD) criteria.

The presence of computer—determined MC 4.2 or 4.3 or computer-measured ST depression ≥ 50 μV was associated with 6- to 7.5-fold increased risk of cardiovascular mortality and with nearly 4-fold increased risk of all—cause mortality in univariate analyses and each method remained strongly predictive of both cardiovascular and all-cause mortality after adjustment for other factors known to predict death. These findings additionally highlight the potential of combining MC and standard approaches to ST depression measurement and analysis to further improve risk stratification, with the greatest mortality risk associated with the presence of both ECG abnormalities.

Although computer-assisted interpretation of the rest ECG has been in clinical use for many years,[21-23] and computerized MC has also been available for some time,[17-20] to the best of our knowledge, this is the first study to compare the prognostic value of computerized analysis of the rest ECG to that of standard visual analysis. Most previous studies of computerized ECG and MC have focused on comparing coding algorithms with other programs or with a consensus interpretation of expert readers,[17-23] and have demonstrated rea-

sonably good accuracy for most, if not all, computerized analysis systems, including the two used in the present study. Indeed, in a previous study that examined 300 ECGs there was a 98.3% agreement between computerized MC of ST depression using the MEANS program and a reference standard derived from a consensus approach.[20] The present results are supported by findings from The West of Scotland Coronary Prevention Study which utilized computerized MC for risk stratification and found an increased 5-year risk of death associated with minor ST and T-wave abnormalities coded for by MC 4.2, 4.3, 5.2, or 5.3.[15,17] However, those studies grouped ST depression and T-wave repolarization abnormalities together, did not compare computer MC with standard visual assessment, and did not adjust for baseline differences in risk factors.[15]

The improved risk stratification found for computerized MC and computer-measured ST depression may well reflect the tendency of visual determination to underestimate the magnitude of primarily upsloping ST depression associated with these MC compared with computer measurements, as has been demonstrated for exercise testing.[35] The higher prevalences of computerized MC and ST depression than visual MC findings in the present population supports this hypothesis. Differences in prevalence and performance between computer and visual MC may also reflect use of measurements from computer-averaged beats for computerized MC, whereas standard visual MC uses coding of individual beats and then applies a majority rule to assign the final code.[1,2,20] Indeed, repeat analysis of visually-coded ECGs in the Zutphen Study [12] resulted in identical reclassification in only 75% of patients, illustrating the potential for misclassification of ST depression by visual analyses.

The additive value of combining computerized MC and quantification of ST depression to identify people at highest risk of both cardiovascular and all-cause mortality indicates that these different approaches to analysis of ST segment abnormalities on the rest ECG provide complementary information. This may be in part related to differences in the algorithms used to measure ST depression and/or may reflect a true increased utility provided by simple ST depression measurements without the requirements for ST slope used in MC 4.2 or 4.3.[1,2] Moreover, use of computer-measured ST depression as a continuous as opposed to discrete variable allows assessment of levels of risk associated with increasing magnitude of ST depression.

Stronger association of MC and ST depression findings with cardiovascular mortality than with all-cause mortality is not unexpected given the known association between ST depression and both ischemic heart disease and left ventricular hypertrophy. However, given the potential difficulties with accurate ascertainment of cause of death even in prospective studies which utilize physician review panels to assign a cause of death,[36] the association of computerized MC and ST depression findings with all-cause mortality further highlights the value of these methods. Of note, the absence of information on the use of medications which could effect the ST segment is a limitation of the current study.

These findings further suggest that computerized interpretation and analysis of the ECG, at least with respect to these MC and ST depression measurements, may finally be achieving the accuracy and clinical utility that has been sought for many years.[21-23] These results and previous findings documenting the accuracy of these computer programs,[18,20,23] support the use of computer analysis of the ST segment on the rest ECG for risk assessment.

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