ST-segment depression in non–ST elevation acute coronary syndromes: Quantitative analysis may not provide incremental prognostic value beyond comprehensive risk stratification

Andrew T. Yan, MD,[a] Raymond T. Yan, MD, Mary Tan, BSc, Chi-Ming Chow, MDCM, MSc, David H. Fitchett, MD, Alina A. Georgescu, MD, Quamrul Hassan, MD, Janna Luchansky, MD, Anatoly Langer, MD, MSc, and Shaun G. Goodman, MD, MSc, for the Canadian ACS Registry Investigators ***Toronto, Ontario, Canada***

Background It is unclear whether quantitative ST-segment assessment can improve risk stratification of unselected acute coronary syndrome (ACS) patients using the validated Global Registry of Acute Cardiac Events (GRACE) risk model.

Methods In the prospective, multicenter, Canadian ACS Registry, the admission electrocardiogram was evaluated centrally at a blinded core laboratory. Patients with ST-elevation myocardial infarction and other electrocardiogram confounders were excluded. ST depression (ST↓) was measured and summed in all leads except aVR. Patients with ST↓ were divided into 3 groups based on tertiles of cumulative ST↓. A multivariable model was developed to examine the independent prognostic value of ST↓ severity after adjusting for other known prognosticators in the GRACE risk model.

Results Among 2590 patients with non–ST-elevation ACS, more severe ST↓ was associated with advanced age, higher heart rate and Killip class, elevated creatinine, abnormal biomarkers, higher GRACE risk score, and higher 1-year mortality (all $P < .001$). After adjusting for these confounding prognosticators, the presence of any ST↓ remained independently associated with higher 1-year mortality (odds ratio 1.78, 95% CI 1.21-2.63, $P = .004$). However, the gradient of risk with increasing magnitude of ST↓ was no longer evident (adjusted odds ratios 1.77, 1.77, 1.81, for ascending tertiles of cumulative ST↓, respectively). Moreover, quantitative ST↓ did not improve the model discrimination for 1-year mortality. The results were similar when the number of leads with ST↓ or the maximum magnitude of ST↓ was analyzed, after adjusting for tertiles of GRACE risk score or inhospital revascularization, or using the composite end point of death or myocardial (re)infarction at 1 year.

Conclusions Greater ST↓ is associated with other adverse prognosticators across the broad spectrum of non–ST-elevation ACS. Although the presence of any ST↓ is an independent predictor of 1-year mortality, its quantitative assessment is not as important as its mere presence when studied on the background of comprehensive clinical and biomarker evaluation in a nonclinical trial–based ACS population. (Am Heart J 2006;152:270-6.)

The admission electrocardiogram (ECG) is a well-established tool in the early risk stratification of non–ST-elevation (NSTE) acute coronary syndromes (ACS), which represent a heterogeneous condition with a variable prognosis.[1] The presence of even minor ST depression (ST↓) is independently associated with a worse outcome [2,3] and identifies high-risk patients who benefit from more aggressive medical and interventional therapies.[4,5] Although the prognostic significance of the magnitude of ST↓ has been demonstrated in several clinical trials,[6-8] there are limited data among less-selected, nonclinical trial ACS populations, especially in the long term. Furthermore, although the presence of ST↓ has been incorporated as a dichotomous independent prognosticator in various risk models,[9-11] the additional utility of quantitative ST-segment assessment has not been studied.

Accordingly, we sought to determine (1) the relationship between the magnitude of ST↓ and 1-year mortality across the broad spectrum of NSTE ACS and

From the Canadian Heart Research Centre and Terrence Donnelly Heart Centre, Division of Cardiology, St. Michael's Hospital, University of Toronto, Toronto, Ontario, Canada.
[a]Dr Andrew Yan is supported by the Canadian Institutes of Health Research, the Canadian Heart Research Centre Fellowship Awards, and the Detweiler Travelling Fellowship.
Submitted August 8, 2005; accepted December 6, 2005.
Reprint requests: Shaun G. Goodman, MD, MSc, Division of Cardiology, St. Michael's Hospital, 30 Bond Street, Room 6-034 Queen, Toronto, Ontario, Canada M5B 1W8.
E-mail: goodmans@smh.toronto.on.ca
0002-8703/$ - see front matter

doi:10.1016/j.ahj.2005.12.003

(2) whether quantitative ST-segment evaluation would provide incremental prognostic information beyond that of a validated risk model based on clinical variables on admission.

Methods

Study population

The rationale and study design of the Canadian ACS Registry have been described elsewhere.[12] In brief, patients were eligible for enrollment in this prospective observational study if they were (1) ≥18 years old on presentation, (2) admitted to hospital with a suspected ACS (defined by symptoms consistent with acute cardiac ischemia within 24 hours of onset), and (3) the qualifying ACS was not precipitated by a serious concurrent event such as trauma or gastrointestinal bleeding. There were no other specific exclusion criteria, and consecutive patient enrollment was encouraged in all 51 participating academic and community hospitals across Canada. At each site, the designated physician or study coordinator collected data on patient demographics, clinical and laboratory findings, inhospital treatment, outcome, and discharge diagnosis and medications using standardized case report forms, which were then centrally scanned into an electronic database. Standardized definitions of adverse events and outcomes were used. A copy of the admission 12-lead ECG was forwarded to the coordinating center (Canadian Heart Research Centre). Central data checks were performed and queries were sent for correction. The local institutional review boards approved study protocol, and all patients followed up after discharge gave informed consent.

All admission ECGs were analyzed centrally at the ECG core laboratory at the Canadian Heart Research Centre, with blinding to clinical data and outcome. The core laboratory ECG interpretation had been validated previously.[13] The 12-lead ECGs were recorded at the standard paper speed of 25 mm/s and calibrated at 1 mm = 0.1 mV. ST deviation was measured to the nearest 0.5 mm at 0.08 seconds after the J point in all leads except aVR. Left ventricular hypertrophy was diagnosed based on the Cornell or Sokolow-Lyon criteria. ST elevation was defined as any ST elevation ≥1 mm in 2 contiguous leads. ST depression was considered to be present if ST-segment depression was ≥0.5 mm in any lead because it has been previously shown to be an adverse prognosticator.[2,3] Cumulative ST↓ was calculated by the summation of the magnitude of ST↓ in all leads except aVR. The number of leads with ST↓ ≥0.5 mm and the maximum amount of ST↓ in any lead except aVR were also recorded.

Between September 1999 and June 2001, 4627 patients with ACS were recruited. Patients with potential confounders of ST-segment interpretation, including incomplete or technically inadequate ECG data (n = 69), ventricular paced rhythm (n = 64), left bundle branch block (n = 211), and left ventricular hypertrophy (n = 227) were excluded from the analysis. Thus, 4056 patients with ACS (94.7%) had interpretable ST segments: 1466 (36.1%) had ST elevation as defined above and the remaining 2590 patients (63.9%) without ST elevation constituted the study cohort. For each patient, we calculated the Global Registry of Acute Cardiac Events (GRACE) risk score according to the published risk model.[9]

The primary outcome was all-cause mortality at 1 year. Inhospital vital status was available for all patients. At 1 year after index hospitalization, patients were contacted via standardized telephone interview to ascertain the vital status. Survival status was unknown for 163 patients (6.3%) who were lost to follow-up at 1 year. These patients did not differ significantly from the remaining cohort in baseline characteristics and the extent of ST↓.

Statistical analysis

Categorical variables are summarized as frequencies or percentages and continuous variables as medians with interquartile ranges (IQR). For comparisons between groups, χ^2 and Kruskal-Wallis tests were used for categorical and continuous data, respectively. We examined trends by the Kendall's τ-b test. The receiver-operating characteristic curve was generated to evaluate the predictive value of summed ST↓ (as an ordinal continuous variable) for 1-year mortality, and the area under the curve (*c* statistic) was calculated. For the main analyses, the study population was categorized into 4 groups: no ST↓ and tertiles of cumulative ST↓. To verify the results, the severity of ST↓ was also examined as categorical variables (with no ST↓ as the referent group), according to (1) tertiles of the total number of leads with ST↓ and (2) maximum ST↓ in any lead <1.5 mm or ≥1.5 mm. In bivariate analysis, logistic regression was used to calculate unadjusted odds ratios (ORs) with 95% CIs. A multivariable logistic regression model to predict 1-year mortality was also developed (backward stepwise with $P < .05$ for entry and $P > .10$ for removal) by including age, heart rate, systolic blood pressure, Killip class, creatinine, and cardiac biomarker status on admission. Abnormal biomarker was defined as elevated creatine kinase, creatine kinase-MB, or troponin level above the upper limit of normal according to the local hospital laboratory. These covariates were chosen based on the GRACE risk model, which had been validated in the Canadian ACS Registry.[14] The presence of ST↓ (as a dichotomous variable) and severity of ST↓ (as a categorical variable defined above) were then entered into separate multivariable models. Model discrimination was evaluated by the *c* statistic and calibration by the Hosmer-Lemeshow goodness-of-fit test, for which a low *P* value indicates lack of fit. The discriminatory performances of the models (*c* statistics) that incorporated the presence of any ST↓ versus the severity of ST↓ were compared using the method described by Hanley and McNeil.[15] We also investigated the prognostic significance of the distribution of ST↓ by categorizing the lead with maximum ST↓ into the following regions: anteroseptal (leads V_1 through V_3), apical (lead V_4 through V_6), lateral (leads I and aVL), and inferior (leads II, III, and aVF). Finally, the impact of inhospital revascularization and biomarker status on the prognostic value of cumulative ST↓ were also considered by including interaction terms in the model. Statistical significance was set at 2-sided *P* values <.05. Data processing and statistical analyses were conducted using SPSS version 12.0.0 (SPSS Inc, Chicago, IL).

Results

Among the 2590 patients with NSTE ACS, ST↓ was present in 1349 (52.1%). Of these patients, 957 (70.9%) and 392 (29.1%) had maximum ST↓ <1.5 and ≥1.5 mm

Table I. Patient demographic and clinical data

	No ST↓ (n = 1241)	Cumulative ST↓ <2 mm (n = 544)	Cumulative ST↓ 2-4 mm (n = 418)	Cumulative ST↓ >4 mm (n = 387)
Age*	63 (54, 72)	68 (58, 75)	69 (59, 76)	71 (63, 77)
Men (%)	66.6	65.4	65.1	65.4
Hypertension (%)	48.5	50.5	47.8	57.3
Diabetes (%)	23.0	26.9	26.1	33.3
Previous angina (%)	58.1	58.2	57.2	59.4
Previous MI (%)	34.5	33.5	34.8	35.0
Previous heart failure (%)	6.9	9.2	10.4	14.8
Previous PCI (%)	18.0	13.9	12.7	13.5
Previous CABG (%)	11.7	16.2	17.3	13.4
Heart rate (beat/min)*	68 (60, 79)	72 (61, 84)	73 (63, 87)	86 (71, 100)
Systolic BP (mm Hg)*	145 (130, 161)	149 (128, 170)	148 (130, 170)	150 (133, 172)
Diastolic BP (mm Hg)*	80 (72, 90)	81 (70, 93)	80 (70, 91)	86 (70, 96)
Killip class (%):				
I	90.0	83.7	83.8	73.9
II	8.9	13.4	13.2	22.3
III/IV	1.1	2.9	3.1	3.8
Serum creatinine (μmol/L)*	87 (75, 102)	89 (77, 105)	90 (78, 110)	93 (80, 117)
Abnormal cardiac biomarker (%)†	51.3	63.2	68.7	75.7

CABG, Coronary artery bypass graft; *PCI*, percutaneous coronary intervention; *BP*, blood pressure.
*Median (25th, 75th percentiles).
†On admission or serial measurements within the first 24 hours.

Table II. Severity of ST depression and 1-year mortality

Severity of ST↓	n	1-y mortality (%)	*P* for trend	Unadjusted OR (95% CI)	*P*
Cumulative ST↓*					
0 mm	1160	3.8	<.001		
<2 mm	505	8.3		2.30 (1.49-3.56)	<.001
2-4 mm	396	11.4		3.25 (2.11-5.01)	<.001
>4 mm	366	15.8		4.78 (3.17-7.21)	<.001
No. of leads with ST↓*					
0	1160	3.8	<.001		
1-2	474	8.2		2.27 (1.46-3.55)	<.001
3-4	377	12.5		3.61 (2.35-5.55)	<.001
≥5	416	14.2		4.19 (2.79-6.31)	<.001
Maximum ST↓ in any lead*					
0 mm	1160	3.8	<.001		
<1.5 mm	897	9.1		2.55 (1.75-3.72)	<.001
≥1.5 mm	370	17.0		5.21 (3.47-7.81)	<.001

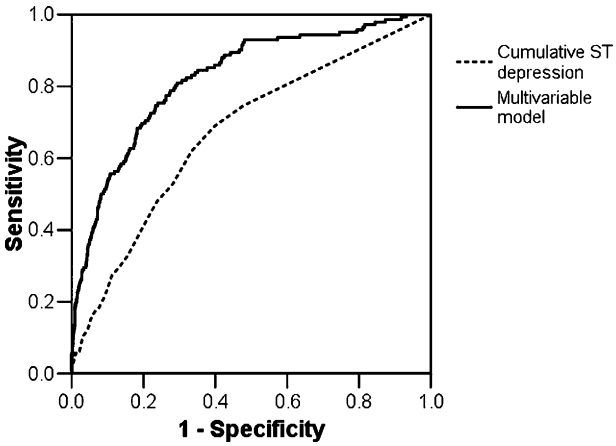
*Except aVR.

in any one lead, respectively. The median number of leads showing ST↓ was 3 (IQR 3-5); the median cumulative ST↓ and median GRACE risk score were 2.5 mm (IQR 1-5 mm) and 111 (IQR 92-135), respectively. There was a strong positive correlation between the maximum amount of ST↓ in any lead and the number of leads with ST↓ (Kendall's τ-b coefficient = 0.87, $P < .001$).

The baseline demographic and clinical characteristics of the 4 groups of patients are shown in Table I. Across the strata of greater ST↓, patients were more likely to have advanced age, diabetes, and history of heart failure (all *P* for trend <.001). They also more frequently presented with higher heart rate, worse Killip class, higher serum creatinine, and elevated cardiac biomarker (all *P* for trend <.001). Cumulative ST↓ was positively correlated with the GRACE risk score (Kendall's τ-b coefficient = 0.31, $P < .001$).

Overall, the 1-year mortality rate was 7.8%. Patients with any ST↓ had a higher mortality than those without ST↓ (3.8% vs 11.4%, $P < .001$). There was a significant gradient of higher risk of death with more severe ST↓, as reflected by cumulative ST↓, the number of leads with ST↓, or the maximum degree of ST↓ (Table II). When analyzed as a continuous variable, cumulative ST↓ had

Figure 1



Receiver operating characteristic curves to predict 1-year mortality. *c* statistic (area under curve) = 0.67 and 0.83 for cumulative ST depression and the multivariable model, respectively (*P* for difference <.001).

moderate ability in predicting death at 1 year, with a *c* statistic of 0.67 (95% CI 0.63-0.71) (Figure 1).

In multivariable analysis, advanced age, higher heart rate, worse Killip class, elevated creatinine, and abnormal cardiac biomarker were all independently associated with increased 1-year mortality (Table III). Although ST↓ remained an independent predictor of mortality, the gradient of risk with worsening ST↓ was not observed after adjusting for other prognosticators, as evidenced by the almost identical ORs across the tertiles of cumulative ST↓. The model *c* statistic was 0.83 (95% CI 0.79-0.86) and Hosmer-Lemeshow goodness-of-fit *P* value was .29, which indicate very good discrimination and adequate calibration, respectively. Compared with cumulative ST↓ alone as a predictor of death, the multivariable model provided superior discrimination (*c* statistic 0.67 vs 0.83, $P < .001$) (Figure 1). When the presence of ST↓ was incorporated into the model instead of ST↓ severity, it was also an independent adverse prognosticator (adjusted OR 1.78, 95% CI 1.21-2.63, $P = .004$), whereas the model *c* statistic remained unchanged at 0.83. Therefore, once the presence of ST↓ had been considered, more detailed quantitative evaluation did not further improve the discriminatory performance of the multivariable model (*P* for difference in *c* statistics = 0.99). After adjusting for tertiles of the GRACE risk score, the odds ratios for cumulative ST↓ were also similar (adjusted OR 1.83, 1.88, and 1.98 for increasing tertiles of cumulative ST↓). Using the composite end point of death or myocardial (re)infarction at 1 year also did not alter the results (adjusted OR 1.47, 1.61, and 1.80 for increasing tertiles of cumulative ST↓). When the number of leads with ST↓ and maximum ST↓ were analyzed, the results were similar (data not shown). The regional distribution of the lead with maximum ST↓ was not an independent predictor of outcome ($P = .71$).

Table III. Multivariable logistic regression model for 1-year mortality

Independent predictors	Adjusted ORs	95% CIs	*P*
Age*	2.37	1.96-2.87	<.001
Heart rate†	1.10	1.01-1.19	.021
Killip class‡			.002
II	1.90	1.28-2.82	.001
III/IV	2.10	0.97-4.53	.06
Serum creatinine§	1.07	1.04-1.09	<.001
Abnormal cardiac biomarker	1.52	1.05-2.21	.028
Cumulative ST↓			.036
<2 mm	1.77	1.11-2.83	.017
2-4 mm	1.77	1.09-2.88	.021
>4 mm	1.81	1.12-2.94	.016

*Per-decade increase.
†Per 10-beat/min increase.
‡Referent to Killip class I.
§Per 10 μmol/L increase.

The rates of revascularization in hospital and medication use at discharge are presented in Table IV. Similar proportions of patients underwent percutaneous coronary intervention, coronary bypass surgery, or any revascularization during index hospitalization (*P* = NS for all). The use of aspirin, β-blockers, and lipid-lowering therapies were also similar at discharge, although angiotensin-converting enzyme inhibitors were more frequently prescribed for patients with the most severe ST↓ ($P = .008$ for group comparison). After controlling for all the prognosticators in the multivariable model, there was a nonsignificant association between inhospital revascularization and lower 1-year mortality (adjusted OR 0.69, $P = .13$). However, there was no significant interaction between revascularization and the severity of ST↓ ($P = .78$). This implies that the similar adjusted ORs for death across the extent of ST↓ were not influenced by treatment with revascularization. The prognostic impact of the severity of ST↓ was also similar irrespective of cardiac biomarker status ($P = .91$ for interaction).

Discussion

To the best of our knowledge, this study is among the first to examine the incremental prognostic value of quantitative ST-segment evaluation beyond that of a validated risk model in a large, nonclinical trial patient population presenting with a wide range of NSTE ACS. Furthermore, by incorporating qualitative versus quantitative ST-segment deviation separately into a validated risk model[9,14] and comparing their overall discriminatory abilities (*c* statistics),[15] the true additional

Table IV. Inhospital treatment and discharge medication use

%	No ST↓ (n = 1241)	Cumulative ST↓ <2 mm (n = 544)	Cumulative ST↓ 2-4 mm (n = 418)	Cumulative ST↓ >4 mm (n = 387)
Inhospital				
PCI	17.1	18.7	15.5	13.0
CABG	4.5	3.4	3.2	6.0
PCI or CABG	21.4	21.7	18.4	18.9
Discharge medication use*				
Aspirin	88.0	89.0	86.9	88.6
β-blockers	76.1	77.7	78.0	74.9
ACE inhibitors	48.3	50.4	45.7	57.2
Lipid lowering agents	59.1	55.1	52.7	57.0

ACE, Angiotensin-converting enzyme.
*Discharge medication use available for 2534 hospital survivors.

predictive value of quantitative ST-segment analysis can be rigorously assessed. Our results show that severe ST↓ is correlated with increasing age, higher heart rate and Killip class, renal insufficiency, elevated cardiac biomarkers, and overall higher GRACE risk score. The presence of ST↓, but not its degree, is an independent predictor of 1-year mortality when these potent prognosticators are also considered.

The ECG is critical in the initial risk assessment of patients with NSTE ACS. Even 0.5 mm of ST↓ has been shown to be a powerful predictor of unfavorable outcome.[2,3] However, because other clinical characteristics on presentation also carry important prognostic information, the current American College of Cardiology/American Heart Association guidelines adopt a more integrated approach to early risk assessment.[1] Over the past decade, several risk models developed to objectively predict patient outcome have been published. The TIMI risk score, for example, may guide physicians' clinical decision making in the selection of an early invasive versus conservative strategy.[16] Although various risk models have incorporated the presence of ST↓ as a predictor of adverse outcome,[9-11] thereby confirming its independent prognostic value, it is unclear whether its quantitative assessment would substantially enhance model performance. Because ST↓ is readily measurable and may represent a surrogate marker of the ischemic burden, this question is clinically relevant with profound implications. Nevertheless, there are only limited data on the quantitative evaluation of ST↓ in nonselected ACS populations.

Early single-center studies suggested that more severe ST↓ was associated with worse outcome.[2,17] In the TIMI III Registry ECG Ancillary study, which enrolled 1416 patients with unstable angina or non–Q-wave myocardial infarction (MI), those with 0.5-mm ST deviation had the highest rate of death or MI at 1 year.[3] Furthermore, ≥0.5 mm ST↓ was a better independent predictor of poor outcome, with a higher adjusted hazard ratio than ≥1 mm ST↓. Using data from 1588 patients in the PARAGON-A study, Kaul et al[6] derived a risk model that examined the prognostic significance of the magnitude and extent of ST↓ in predicting 1-year mortality. In multivariable analysis, 1 mm ST↓ (OR 3.65, 95%CI 1.89-7.06) and ≥2 mm ST↓ (OR 5.73, 95%CI 2.82-11.64) both independently predicted mortality. However, cardiac biomarker status was not a predictor, and the relatively wide CIs could not definitively establish the increasing gradient of risk with more severe ST↓. In the PARAGON-B troponin T substudy involving 959 patients, after controlling for troponin measurements, ST↓ became less powerful predictors of death/MI at 6 months.[7] The difference in the adjusted ORs for 1 mm ST↓ (1.34, 95% CI 0.86-2.09) and ≥2 mm ST↓ (1.91, 95% CI 1.10-3.32) also diminished with overlapping CIs. In the FRISC II ECG substudy of 2201 patients, Holmvang et al[18] demonstrated that more extensive ST↓ identified patients who obtained the greatest benefit from an invasive treatment strategy. Although these patients were at higher risk compared with those with only minor ST↓, the independent prognostic value of ST↓ was not specifically assessed. In the largest study to date, the extent of ST↓ was an independent predictor of 30-day mortality among 5192 patients enrolled in the GUSTO-IIb trial (OR 1.07 per 1-mm increase in cumulative ST↓),[8] but its long-term prognostic significance has not been determined. Importantly, ST↓ itself was an entry criterion in these clinical trials, and the impact of inhospital revascularization was not adjusted for. Therefore, despite these original studies, uncertainties about the utility of quantitative ST evaluation persist, particularly in a less-selected, nonclinical trial setting.

The present study provides further insights in several aspects. In addition to confirming the independent prognostic importance of ST↓, our study corroborates previous investigations demonstrating the relationship between ST↓ severity and worse outcome. Of note, severe ST↓ may be a surrogate marker of the underlying

atherosclerotic or ischemic burden—it is associated with other adverse prognosticators, such as advanced age, higher heart rate and Killip class, renal dysfunction, and abnormal cardiac biomarkers. After adjusting for these confounders, only the presence of ST↓, but not its severity, remains an independent predictor in a comprehensive risk model that comprises renal function and Killip class. Several large studies from both clinical trials and registries have consistently shown that renal dysfunction is an independent predictor of mortality.[19,20] Khot et al[21] pooled the data from 26 090 patients with NSTE ACS enrolled in GUSTO-IIb, PURSUIT, PARAGON-A and PARAGON-B and found that age, Killip class, heart rate, systolic blood pressure, and ST↓ accounted for most of the prognostic information. Because the selection of covariates in our multivariable analysis was based on the validated GRACE risk model,[9] which also includes creatinine and biomarker status in addition to these powerful predictors, our findings should be more robust. Indeed, this is reflected by the good model discrimination (*c* statistic = 0.83) and calibration that lend credence to the results. The lack of mortality risk gradient with increasing ST↓ demonstrated only after adjustment of other prognosticators, together with the CIs that exclude a several-fold increase in mortality, suggests that inadequate power is less plausible. Furthermore, similar results were obtained from additional analyses using the number of leads with ST↓ or the maximum magnitude of ST↓ and controlling for the effects of revascularization. This should confirm the robustness of our conclusion. Finally, because the Canadian ACS Registry recruited less selected patients across the broad spectrum of ACS, our findings are more generalizable than similar analyses of clinical trials, in which ST↓ itself was often used as an inclusion criterion. It should be underscored that more extensive ST depression does portend a worse outcome and, therefore, must not be ignored; although by itself, the predictive accuracy (*c* statistic = 0.67) is significantly less than that of the comprehensive GRACE risk model (*c* statistic = 0.83).

Several study limitations should be recognized. First, the observed low inhospital mortality rate (1.6%) suggests nonconsecutive patient enrollment with the exclusion of early deaths, which could introduce an unknown bias. However, risk stratification would be least relevant for these evidently high-risk patients. Because quantitative results of biomarker assays were not available, their comparative prognostic significance could not be determined, although they would likely further reduce the prognostic implications of quantitative ST↓ evaluation. Because the Canadian ACS Registry was initiated before the efficacy of early invasive management was established, revascularization rates during index hospitalization were low. Because high-risk patients benefit more from the invasive strategy, which is currently more widely accepted, the gap in outcome is expected to narrow. A small proportion of patients in the ACS Registry were lost to follow-up at 1 year. However, examination of their baseline characteristics and ECGs did not reveal any systematic differences compared with the rest of the study cohort. It must be emphasized that in addition to differences in the study populations, the prognostic significance of quantitative ST↓ evaluation hinges specifically on what other prognosticators have already been considered, which together probably explain the discrepancy with other investigations.[6-8] Thus, it remains to be elucidated whether quantitative ST assessment would refine risk stratification based on other clinical predictors not examined in the present study.

Conclusions

Across the broad spectrum of NSTE ACS, more severe ST↓ is associated with other adverse clinical characteristics and higher 1-year mortality. Although the presence of any ST↓ is a potent independent predictor of unfavorable outcome, its quantitative evaluation does not confer significant incremental prognostic information beyond that of a comprehensive risk model that incorporates age, hemodynamic variables, creatinine, and biomarker status. Because quantitative ST-segment analysis does not substantially improve the prognostic performance of the validated GRACE risk model, its routine inclusion beyond the simple presence of ST↓ does not appear warranted.

We thank Sue Francis for her secretarial assistance. We also thank all the study investigators, coordinators, and patients who made invaluable contributions to the Canadian ACS Registry.

References

1. Braunwald E, Antman EM, Beasley JW, et al. ACC/AHA 2002 guideline update for the management of patients with unstable angina and non–ST-segment elevation myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on the Management of Patients with Unstable Angina). Circulation 2002;106:1883-90.
2. Hyde TA, French JK, Wong CK, et al. Four-year survival of patients with acute coronary syndromes without ST-segment elevation and prognostic significance of 0.5-mm ST-segment depression. Am J Cardiol 1999;84:379-85.
3. Cannon CP, McCabe CH, Stone PH, et al. The electrocardiogram predicts one-year outcome of patients with unstable angina and non–Q wave myocardial infarction: results of the TIMI III Registry ECG ancillary substudy. J Am Coll Cardiol 1997;30:133-40.
4. Sabatine MS, Januzzi JL, Snapinn S, et al. A risk score system for predicting adverse outcomes and magnitude of benefit with glycoprotein IIb/IIIa inhibitor therapy in patients with unstable angina pectoris. Am J Cardiol 2001;88:488-92.

5. Diderholm E, Andrén B, Frostfeldt G, et al. ST depression in ECG at entry indicates severe coronary lesions and large benefits of an early invasive treatment strategy in unstable coronary artery disease. Eur Heart J 2002;23:41-9.
6. Kaul P, Fu Y, Chang WC, et al. Prognostic value of ST segment depression in acute coronary syndromes: insights from PARAGON-A applied to GUSTO-IIb. J Am Coll Cardiol 2001;38:64-71.
7. Kaul P, Newby LK, Fu Y, et al. Troponin T and quantitative ST-segment depression offer complementary prognostic information in the risk stratification of acute coronary syndrome patients. J Am Coll Cardiol 2003;41:371-80.
8. Savonitto S, Cohen MG, Politi A, et al. Extent of ST-segment depression and cardiac events in non–ST-segment elevation acute coronary syndromes. Eur Heart J 2005 [published online June 29].
9. Granger CB, Goldberg RJ, Dabbous O, et al. Predictors of hospital mortality in the Global Registry of Acute Coronary Events. Arch Intern Med 2003;163:2345-53.
10. Boersma E, Pieper KS, Steyerberg EW, et al. Predictors of outcome in patients with acute coronary syndromes without persistent ST-segment elevation. Results from an international trial of 9461 patients. Circulation 2000;101:2557-67.
11. Antman EM, Cohen M, Bernink PJ, et al. The TIMI risk score for unstable angina/non–ST elevation MI: a method for prognostication and therapeutic decision making. JAMA 2000;284:835-42.
12. Yan AT, Tan M, Fitchett D, et al. One-year outcome of patients after acute coronary syndromes (from the Canadian Acute Coronary Syndromes Registry). Am J Cardiol 2004;94:25-9.
13. Fu Y, Goodman S, Chang W-C, et al. Time to treatment influences the impact of ST segment resolution on one-year prognosis: insights from ASSENT 2. Circulation 2001;104:2653-9.
14. Yan AT, Jong P, Yan RT, et al. Clinical trial–derived risk model may not generalize to real world acute coronary syndrome patients. Am Heart J 2004;148:1020-7.
15. Hanley JA, McNeil BJ. A method of comparing the areas under receiver operating characteristic curves derived from the same cases. Radiology 1983;148:839-43.
16. Cannon CP, Weintraub WS, Demopoulos LA, et al. Comparison of early and conservative strategies in patients with unstable coronary syndromes treated with the glycoprotein IIb/IIIa inhibitor tirofiban. N Engl J Med 2001;344:1879-87.
17. Lee HS, Cross SJ, Rawles JM, et al. Patients with suspected myocardial infarction who present with ST depression. Lancet 1993;342:1204-7.
18. Holmvang L, Clemmensen P, Lindahl B, et al. Quantitative analysis of the admission electrocardiogram identifies patients with unstable coronary disease who benefit the most from early invasive treatment. J Am Coll Cardiol 2003;41:905-15.
19. Gibson CM, Dumaine RL, Gelfand EV, et al. Association of glomerular filtration rate on presentation with subsequent mortality in non–ST-segment elevation acute coronary syndrome; observations in 13,307 patients in five TIMI trials. Eur Heart J 2004;25:1998-2005.
20. Santopinto JJ, Fox KA, Goldberg RJ, et al. Creatinine clearance and adverse hospital outcomes in patients with acute coronary syndromes: findings from the global registry of acute coronary events (GRACE). Heart 2003;89:1003-8.
21. Khot UN, Jia G, Moliterno DJ, et al. Prognostic importance of physical examination for heart failure in non–ST-elevation acute coronary syndromes. The enduring value of Killip classification. JAMA 2003;290:2174-81.