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Optimizing the initial 12-lead electrocardiographic diagnosis of acute myocardial infarction

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Aims The optimum definition of ST elevation for diagnosis of acute myocardial infarction, with respect to both the minimum height and the minimum numbers of leads, is unknown. Furthermore, only 50% of patients with acute myocardial infarction present with ST elevation. We thus quantified the sensitivity and specificity of different ST elevation criteria for diagnosis of acute myocardial infarction, and determined whether models incorporating multiple QRST features in addition to ST elevation, could improve detection of acute myocardial infarction.

Methods and Results The study population comprised 1190 subjects: 1041 consecutive patients presenting with chest pain (335 with acute myocardial infarction) and 149 controls without chest pain. Subjects were randomly divided into a training set (587) and a validation set (603). ECG prediction models for acute myocardial infarction incorporating different ST elevation criteria and/or additional QRST features (Q waves, ST depression, T wave inversion, bundle branch block, axes deviations, and left ventricular hypertrophy) were developed in training set patients using forward stepwise multiple logistic regression. Models were then prospectively tested in the validation set patients. The optimum ST elevation model (based on ≥ 1 mm ST elevation in ≥ 1 inferior/lateral leads, or ≥ 2 mm ST elevation in ≥ 1 anteroseptal leads) correctly classified 83·1% of subjects (55·8% sensitivity, 94·0% specificity). The choice of ST elevation definition had marked influence on the sensitivity (45·4–68·6%) and specificity (81·2–98·1%) for diagnosis of acute myocardial infarction. The addition of multiple QRST variables only marginally improved overall classification but did result in high specificity (92·6–96·1%).

Conclusion Different definitions of 'significant' ST elevation led to marked variations in sensitivity and specificity for diagnosis of acute myocardial infarction. Multiple QRST features in addition to ST elevation only marginally improved overall classification.
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Key Words: Electrocardiography, diagnosis, myocardial infarction, modelling.

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Introduction

The electrocardiogram (ECG) is established as the cornerstone for early diagnosis of acute myocardial infarction[1–3], particularly in the era of fibrinolytic therapy, where the earliest possible diagnosis is essential[4–7]. Initial ST elevation as part of the classic evolutionary pattern of acute myocardial infarction was first described by Pardee in 1920[8], and the experimental foundation for use of ST elevation as a marker of myocardial injury was established in the 1970s by epicardial and praecordial ECG mapping[9–11].

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However, the definition of 'significant' ST elevation varies considerably with respect to both the required minimum height (mm) of ST elevation, and the numbers of leads with ST elevation. The Minnesota code 9-2[12] requires ≥ 1 mm ST elevation in one or more of leads I, II, III, aVL, aVF, V_5, V_6, or ≥ 2 mm ST elevation in one or more of leads V_1–V_4. This and similar definitions have been incorporated in several diagnostic computer algorithms[13–15]. In contrast, recent clinical trials of fibrinolytic agents have required ST elevation ≥ 1 mm in two or more anatomically contiguous leads[16,17].

Irrespective of which definition is used, ST elevation has poor sensitivity for acute myocardial infarction with up to 50% of patients reported as exhibiting 'atypical' changes at presentation[2] including isolated ST depression, T inversion, or even a normal ECG[18–20]. Furthermore, ST elevation is not specific with potential false

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Table 1 Definitions of abnormal 12-lead ECG features

Pathological Q waves
duration $\geq$0·03 s
amplitude Q:R ratio $\geq$25%
ST elevation (corresponding to Minnesota code 9-2)
PR segment taken as the isoelectric reference
$\geq$1·0 mm (0·1 mV) in leads I, II, III, aVL, aVF, V_5, V_6
$\geq$2·0 mm (0·2 mV) in leads V_1–V_4
'Non-Minnesota' ST elevation
$\geq$1·0 mm but <2·0 mm in V_1–V_4
ST depression
$\geq$1·0 mm depression at 80 ms following the J point
T inversion
T inv $\geq$1·0 mm
Biphasic T wave (in the absence of coexistent ST depression), with a negative component $\geq$1·0 mm
Complete left bundle branch block minimum criteria:
QRS duration $\geq$120 ms
QS or rS in V_1 and broad slurred R waves in lead I, V_5 and V_6
Complete right bundle branch block minimum criteria:
QRS duration $\geq$120 ms
rSR′ in V_1 and V_2 and S waves in lead I and V_5 or V_6
Left axis deviation (LAD) $< -30°$
Right axis deviation (RAD) $\geq$90°
Left ventricular hypertrophy (LVH) minimum voltage criteria:
R in aVL $\geq$11 mm or,
R in V_5 or V_6 $\geq$27 mm or,
S in V_1+R in V_5 or V_6 $\geq$35 mm

positives including pericarditis, left bundle branch block, left ventricular hypertrophy, early repolarization syndrome and raised intracranial pressure[21]. Thus some investigators have considered additional ECG features including reciprocal ST depression, isolated ST depression, T inversion or Q waves[13–15,22,23]. However, data for development of such ECG criteria have often been obtained from clinical drug trials[1,24,25] or those with suspected acute myocardial infarction[18,22,26], thereby introducing possible selection bias.

The aims of this study were twofold: (a) to quantify the sensitivity and specificity of different ST elevation criteria for the diagnosis of acute myocardial infarction in an unselected consecutively recruited population and (b) to determine, in this population, whether the development of mathematical models incorporating multiple morphological QRST features in addition to ST elevation, could improve detection of acute myocardial infarction.

Methods

Patients were recruited consecutively over a 17 month period as they presented with ischaemic type chest pain to a 24 h physician-manned mobile coronary care unit (cardiac ambulance), an accident and emergency department, or to a medical ward. In addition, over the same time period, patients without chest pain (controls) were recruited opportunistically from healthy participants of a World Health Organisation epidemiological screening program, non-cardiac inpatients, and outpatients.

A 12-lead ECG was recorded at presentation by a physician or ECG technician. All ECG machines were maintained by a single electronics laboratory, precalibrated at 1 mV=10 mm and recorded at a paper speed of 25 mm . s^{-1}. A single, independent investigator, blinded to patient outcome (thereby minimizing intra-observer bias, and eliminating inter-observer variability) measured key elements of QRST morphology with respect to ECG interpretation in ischaemic heart disease. All measurements were made using a Minnesota approved measuring loupe (6 × EDSCORP pocket comparator) which has been shown to reduce intra-observer error[12]. Abnormal ECG features were defined as listed in Table 1. Each feature was coded as a categorical variable (e.g. ST elevation in a given lead — present/absent). Minimum criteria to define regional site involvement (inferior, anteroseptal, anterolateral, lateral) were defined as listed in Table 2. Exceptions to minimum site criteria were defined for inferior Q waves, inferior T inversion, and anteroseptal T inversion, to account for normal variation.

Acute myocardial infarction was defined by the presence of chest pain $\geq$20 min duration, elevation of creatine kinase $\geq$2 × the upper laboratory normal reference level (creatine kinase-MB activity $\geq$7% if the aetiology of the total creatine kinase was equivocal), and/or elevation of creatine kinase <2 × the upper laboratory normal reference level accompanied by serial ECG changes consistent with new myocardial infarction (new Q waves $\geq$0·03 s duration, and/or new persistent T wave inversion in $\geq$2 contiguous leads). Clinical and ECG data were entered into an SPSS (v 8.0) file for analysis.

Table 2 Regional site definitions for the 12 lead ECG

Minimum requirements	
inferior	—one or more of II,III, aVF
anteroseptal	—one or more of V_1–V_4
lateral	—one or more of V_5,V_6, I, aVL
anterolateral	—one or more anteroseptal, and one or more lateral, and V_5
Exceptions	
inferior Q wave	—one or more of II, aVF, or III and one or more of II, aVF
inferior T inversion	—one or more of II, aVF, or III and one or more of II, aVF
anteroseptal T inversion	—one or more of V_2–V_4, or VI and one or more of V_2–V_4

Patients were randomly divided into two groups; a training set in which prediction models were developed, and a validation set in which the models were prospectively tested. Prediction models were developed using a multiple logistic regression technique to model the relationship between the binary clinical outcome variable (acute myocardial infarction=1, not-acute myocardial infarction=0) and single or multiple ECG features.

Where multiple ECG features were modelled, a stepwise forward (likelihood ratio) regression method was used to select ECG variables which best contributed to the prediction of acute myocardial infarction. An inclusion probability of $P<0{\cdot}05$ was used in order to select only those feature components with high discriminatory power. Multivariate modelling allocated a unique coefficient to each variable, thus weighting its contribution to the overall model.

ST elevation variables were tested by both univariate analysis e.g. the presence or absence of ST elevation in any of the 12 leads, or any of the four regional sites, and multivariate analysis e.g. the presence or absence of ST elevation in specific leads (12 variables), or specific regional sites (four variables). Models incorporating QRST features, in addition to ST elevation, were by definition, multivariate. However, each model was tested simply (the presence or absence of a particular QRST feature in any lead or any regional site), and in more detail (a particular QRST feature in a specific lead or regional site).

Between-group comparisons of baseline variables and clinical outcomes were performed using a 2-tailed ANOVA for continuous variables and chi-square analysis for categorical variables, with $P<0{\cdot}05$ taken as significant.

Results

During the course of the study, 1190 patients were recruited; 1041 with chest pain and 149 without chest pain. Three hundred and thirty-five (28·2%) had a final diagnosis of acute myocardial infarction (201 with ST elevation, 134 without ST elevation), 706 (59·3%) had chest pain but not-acute myocardial infarction (495 abnormal ECG, 211 normal ECG), and 149 (12·6%) were patients without chest pain (121 abnormal ECG, 28 normal ECG). Males comprised 70·4% of the study population and were more likely (by regression analysis) to have had a history of previous myocardial infarction (40·7% vs 28·5% [$P=0{\cdot}001$]); or to be smokers (50·5% vs 35·4% [$P<0{\cdot}001$]). Females were older (age $\geq$75 in 21·3% vs 10·9% [$P<0{\cdot}001$]) and were more likely to have had a history of hypertension (44·0% vs 29·2% [$P<0{\cdot}001$]).

Baseline characteristics in the training set (587 patients) and the validation set (603 patients) are listed in Table 3. The sets were comparable with no significant differences apart from fewer patients who were smokers ($P=0{\cdot}05$) or were hypertensive ($P=0{\cdot}029$) in the validation set. Final diagnoses, incidence of new acute myocardial infarction, and sites of acute myocardial infarction were not significantly different between the training and validation sets (Table 4). A final diagnosis of acute myocardial infarction with an initially normal ECG occurred in only two patients, one in each set. The incidence of false-positive ST elevation (significant ST elevation in a patient without acute myocardial infarction) was not significantly different between sets, occurring in 72 (12·3%) patients in the training set and 81 (13·4%) patients in the validation set. Left bundle branch block occurred in 28 patients in the training set and 41 patients in the validation set ($P=0{\cdot}139$).

Results of acute myocardial infarction classification by different ECG models are shown in Table 5. Unless otherwise stated, figures quoted for sensitivity, specificity and overall classification refer to the performance of the model when tested prospectively in the validation set patients. The choice of ST elevation definition had a marked influence on the sensitivity (45·4–68·6%) and specificity (81·2–98·1%) for diagnosis of acute myocardial infarction. Simple univariate models based on the presence or absence of a particular ECG feature performed almost as well as more complex multivariate models. Model 1, for example, (the presence or absence of ST elevation in any of the 12 leads) had the highest sensitivity for acute myocardial infarction of all models tested (68·6%), although the lowest specificity. Multivariate models tended to significantly improve specificity, albeit with some loss in sensitivity leading to an improvement in overall classification. Model 5 for example, based on four variables (the presence or absence of ST elevation in inferior, anteroseptal, anterolateral, or lateral leads), resulted in high specificity (94·0%), which despite lower sensitivity (55·8%), improved overall classification to 83·1%. Definitions requiring ST elevation in $\geq$2 anatomically contiguous

Table 3 Baseline characteristics

	Training set (n=587)	Validation set (n=603)	Overall (n=1190)
Males	70·6%	70·2%	70·4%
Mean age (± SD)	60·6 ± 13·1	60·0 ± 13·5	60·3 ± 13·3
Age ≥75 years	75 (12·8%)	62 (10·3%)	137 (11·5%)
Family history of ischaemic heart disease	295 (50·3%)	301 (49·9%)	596 (50·1%)
Current smokers*	239 (40·7%)	213 (35·3%)	452 (38·0%)
Diabetes	59 (10·0%)	46 (7·6%)	105 (8·8%)
Hypertension**	184 (31·3%)	146 (24·2%)	330 (27·7%)
Hyperlipidaemia	147 (25·0%)	145 (24·0%)	292 (24·5%)
Previous myocardial infarction	187 (31·9%)	177 (29·4%)	364 (30·6%)
Where applicable			
Mean (± SE) time of pain to ECG (hours)	6·28 ± 1·25	5·06 ± 0·74	5·60 ± 0·69
Use of fibrinolytic therapy if acute myocardial infarction	77/163 (47·2%)	94/172 (54·6%)	171/335 (51·0%)
Median time from onset of pain to fibrinolytic therapy (h)	3·0	2·8	2·9

*P=0·05; **P=0·029.

Table 4 Final diagnosis and presentation ECG

Final diagnosis	Training set (n=587)	Validation set (n=603)	Overall (n=1190)
Acute myocardial infarction with ST elevation			
Inferior	54	66	120
Anteroseptal	17	8	25
Anterolateral	19	29	48
Lateral	4	4	8
Total acute myocardial infarction with ST elevation	94 (16%)	107 (17·7%)	201 (16·9%)
Acute myocardial infarction with atypical ECG			
Inferior	21	25	46
Anteroseptal	4	5	9
Anterolateral	9	7	16
Lateral	11	3	14
Site unknown	24	25	49
Total acute myocardial infarction with atypical ECG	69 (11·8%)	65 (10·8%)	134 (11·3%)
Chest pain with abnormal ECG	239 (40·7%)	256 (42·5%)	495 (41·6%)
Chest pain with normal ECG	116 (19·8%)	95 (15·8%)	211 (17·7%)
Control with abnormal ECG	54 (9·2%)	67 (11·1%)	121 (10·2%)
Control with normal ECG	15 (2·6%)	13 (2·2%)	28 (2·4%)

leads or reciprocal ST depression improved specificity only at the expense of sensitivity and thus did not improve overall classification. Use of a lower anteroseptal threshold (ST elevation ≥1 mm in V_1–V_4) resulted in a small improvement in sensitivity (but fall in specificity) for models based on individual lead measurements (e.g. model 12 compared with model 3). A lower anteroseptal threshold did not improve models based on specific regional site measurements as neither ≥2 mm, nor ≥1 mm anteroseptal ST elevation, were of independent predictive value in multivariate models. Of note, univariate analysis showed that ≥2 mm anteroseptal elevation may be a preferable threshold as it correctly classified a higher proportion of patients (68·7%) compared with ≥1 mm anteroseptal elevation (53·1%).

The addition of multiple QRST variables (models 15–18) resulted in high specificity for acute myocardial infarction (92·6–96·1%) but little improvement in sensitivity (53·5–61·0%), thus giving only a small improvement in overall classification (up to 84·1%). Of interest, QRST variables of independent additional value to ST elevation typically included variables which may be used by cardiologists as part of a decision making process. For example, model 18 included the variables — anteroseptal ST depression, anterolateral ST depression, lateral T inversion, left ventricular hypertrophy and left bundle branch block, in addition to ST elevation. The structure of model 18 is shown in Table 6.

The inclusion of baseline demographic or risk factor variables in ECG models was not found to be of additional benefit.

If patients with left bundle branch block were excluded from the study population, diagnostic performance was improved further (Table 7).

Of the patients with acute myocardial infarction, 40% presented with atypical ECG changes i.e. without ST elevation. In this subgroup, the best models used weighted contributions from specific leads or regional

Table 5 Results of univariate and multivariate ECG feature modelling

ECG Feature Models (Nos 1–18)	Training set			Validation set		
	% sensitivity for AMI	% specificity for AMI	% overall classification	% sensitivity for AMI	% specificity for AMI	% overall classification
ST elevation (Minnesota 9-2)						
1. any lead including aVR*	64·4	83·0	77·8	68·6	81·2	77·6
2. any lead excluding aVR*	57·1	85·8	77·8	65·7	84·0	78·8
3. in a specific lead	34·4	97·2	79·7	45·9	95·4	81·3
4. any regional site*	57·1	85·8	77·8	65·7	84·0	78·8
5. in a specific regional site	42·9	95·0	80·6	55·8	94·0	83·1
ST elevation and reciprocal ST depression						
6. any regional site*	38·0	89·9	75·5	53·5	91·2	80·4
7. in a specific regional site	34·4	95·5	78·5	46·5	96·3	82·1
ST elevation in $\geq$2 leads						
8. any 2 leads*	49·1	93·2	80·9	59·3	90·0	81·3
9. any 3 leads*	31·3	96·0	78·0	48·3	92·8	80·1
10. any regional site*	44·8	93·6	80·1	57·0	90·7	81·1
11. in a specific regional site	30·7	99·3	80·2	45·4	98·1	83·1
ST elevation $\geq$1 mm only						
12. in a specific lead	38·0	97·6	81·1	51·2	94·7	82·3
13. in a specific regional site	42·9	95·0	80·6	55·8	94·0	83·1
14. $\geq$2 leads in a specific regional site	30·7	99·3	80·2	45·4	98·1	83·1
Any abnormal QRST feature						
15. any lead	48·5	92·9	80·6	53·5	95·8	83·8
16. in a specific lead	55·8	95·8	84·7	61·0	92·6	83·6
17. any regional site	42·3	92·9	78·9	54·1	96·1	84·1
18. in a specific regional site	48·5	93·9	81·3	57·0	94·0	83·4

*univariate models.
AMI=acute myocardial infarction.

Table 6 ECG prediction model based on presence of abnormal QRST features in a specific site (model 18)

Variable	Regression coefficient	SE	significance
Inferior ST elevation	1·9819	0·3438	<0·0001
Anteroseptal ST elevation	1·1636	0·3250	0·0003
Anterolateral ST elevation	3·1030	1·1209	0·0056
Lateral ST elevation	3·0881	0·8329	0·0002
Anteroseptal ST depression	2·0958	0·4732	<0·0001
Anterolateral ST depression	1·8115	0·3342	<0·0001
Lateral T wave inversion	0·6081	0·2530	0·0162
Left bundle branch block	− 1·9235	0·6265	0·0021
Left ventricular hypertrophy	− 0·5801	0·2890	0·0447
Constant	− 1·9147	0·1653	n/a

sites. These models resulted in good overall classification with high specificity although low sensitivity (Table 8). The structure of the model based on specific lead features (model 25) is shown in Table 9.

Primary ST depression (ST depression without coexistent ST elevation) occurred in 130 patients (45 acute myocardial infarction, 85 not acute myocardial infarction) equally distributed in training and validation sets. Modelling in this subgroup tended to be more unstable due to the smaller numbers. There was no difference in mean numbers of leads with ST depression between those with or without acute myocardial infarction ($3{\cdot}11 \pm 0{\cdot}27$ vs $2{\cdot}64 \pm 0{\cdot}16$ respectively), however determination of the numbers of leads with ST depression (Table 10) showed that the presence of $\geq$5 or $\geq$6 leads with ST depression was associated with high specificities for acute myocardial infarction of 81% and 96% respectively.

Discussion

The marked variation in sensitivity and specificity between different ST elevation definitions has important implications for use of fibrinolytic therapy. Sensitivity and thus patients correctly predicted as 'eligible for treatment' increased from 45·4% in the least sensitive models (models 11 and 14) to 68·6% in the most sensitive

Table 7 Results of ECG feature modelling following exclusion of left bundle branch block

ECG Feature Model (Nos 19–24)	Training set			Validation set		
	% sensitivity for AMI	% specificity for AMI	% overall classification	% sensitivity for AMI	% specificity for AMI	% overall classification
19. ST elevation in a specific lead	48·7	96·8	83·2	56·6	95·7	84·2
20. ST elevation in a specific regional site	44·3	96·8	81·9	55·4	96·2	84·2
21. ST elevation and reciprocal ST depression	35·4	97·0	79·6	45·8	98·0	82·6
22. ST elevation $\geq$2 leads in a specific regional site	45·6	96·0	81·8	56·0	96·0	84·2
23. Any abnormal QRST feature in a specific lead	60·1	96·0	85·9	61·4	94·2	84·5
24. Any abnormal QRST feature in a specific regional site	49·4	94·0	81·4	58·4	94·7	84·0

AMI=acute myocardial infarction.

Table 8 Results of ECG feature modelling in patients without ST elevation

ECG Feature Model (Nos 25, 26)	Training set			Validation set		
	% sensitivity for AMI	% specificity for AMI	% overall classification	% sensitivity for AMI	% specificity for AMI	% overall classification
Any abnormal QRST feature						
25. in a specific lead	20·7	98·0	87·1	11·1	96·0	84·6
26. in a specific regional site	13·8	98·6	86·6	9·3	97·1	85·4

AMI=acute myocardial infarction.

Table 9 ECG prediction model based on presence of abnormal lead specific features in the absence of ST elevation (model 25)

Variable	Regression coefficient	SE	Significance
Q wave V_1	1·5661	0·4922	0·0015
Q wave V_2	− 1·6995	0·8772	0·0527
Q wave V_5	2·0418	0·8254	0·0134
ST depression aVF	2·0946	1·0703	0·0504
ST depression V_3	1·6603	0·6631	0·0123
ST depression V_5	1·5582	0·4279	0·0003
Left axis deviation	1·008	0·4739	0·0334
Constant	− 2·4574	0·2093	n/a

model (model 1), although specificity tended to fall with increasing sensitivity. However, as administration of fibrinolytic therapy is not without risk, the choice of ST elevation definition may be guided by the sensitivity/specificity ratio required. Thus if using an established fibrinolytic agent with a known favourable benefit–risk ratio, a high sensitivity definition may be appropriate, for example the Minnesota code ST elevation definition, as incorporated in the optimum ST elevation model (model 5). In contrast, if conducting a clinical trial of a new fibrinolytic with an unknown benefit–risk ratio, use of a higher specificity, although lower sensitivity definition may be more appropriate, for example the 'TIMI' group criteria ($\geq$1 mm in two or more contiguous leads) or the 'GUSTO' group criteria ($\geq$1 mm in two or more limb leads, or $\geq$2 mm in two or more contiguous praecordial leads).

Table 10 Sensitivity and specificity of primary ST depression (without ST elevation) for the diagnosis of acute myocardial infarction

No. of leads with ST depression	% Sensitivity for AMI	% Specificity for AMI	% Overall classification
$\geq$2 leads	80·0	24·7	43·8
$\geq$3 leads	55·6	60·0	58·5
$\geq$4 leads	35·6	75·3	61·5
$\geq$5 leads	20·0	81·2	60·0
$\geq$6 leads	13·3	96·5	67·7

AMI=acute myocardial infarction.

We had hypothesized that incorporation of QRST features other than ST elevation might improve classification. New Q waves and T wave inversion, for example, may be seen within 4–6 h of acute myocardial infarction evolution. Pre-existing abnormalities of QRST morphology may be associated with prior ischaemic heart disease or old myocardial infarction, and thus with an increased likelihood of new acute myocardial infarction. In patients with ST elevation, incorporation of these additional QRST features into our models only marginally improved overall classification. However, in patients without ST elevation, although QRST models had poor sensitivity, their high specificity may usefully identify some patients in whom further investigation, and/or management is warranted (Table 8). Whilst the value of fibrinolytic therapy in this subgroup remains unproven[17], use of IIb/IIIa receptor antagonists or low molecular weight heparin may be of benefit.

The significance of primary ST depression (ST depression without coexistent ST elevation) is an area of particular interest in the literature[17,18]. Lee *et al.*[18] in a study of 136 patients with primary ST depression reported specificity of $\geq$89% if ST depression was present in $\geq$7 leads. Their study population was, however, pre-selected on the basis of clinically suspected acute myocardial infarction. In our study, the presence of greater numbers of leads with ST depression resulted in higher specificity for acute myocardial infarction (Table 10). This finding was notable, particularly as our population was unselected. It could be argued that it would have been useful to incorporate the depth of ST depression as well as the number of leads with ST depression in our models. However, the Lee data[18]

showed that specificity of $\geq 89\%$ was only achieved with ≥ 7 leads, irrespective of the depth of ST depression.

Unlike the MILIS study group[25], we did not find baseline characteristics to be of additional benefit to simple ECG models.

Use of QRST features in addition to ST elevation to improve acute myocardial infarction classification is not a new concept. However some previous studies have been small[22,23], thus limiting the potential to determine minor classifiers. Those studies with adequate numbers have tended to recruit from clinical drug trials[1,24,25], or from those with suspected acute myocardial infarction[25,26], thereby introducing selection bias. The MILIS study, a model using Q waves and ST depression in addition to ST elevation, resulted in good sensitivity (81%), but low specificity (69%)[25]. Some studies have restricted recruitment to either pre-hospital or in-hospital patients only. In our study, it was thought important to recruit from both pre-hospital and in-hospital patients. Pre-hospital patients may present at an earlier stage of acute myocardial infarction evolution with more subtle ECG changes[23] and thus represent an important sub-population for model training. Our study did not formally stratify diagnosis by admission route, but the large numbers and consecutive recruitment make a representative sample likely.

The inclusion of a control population was important because some patients, even with 'typical' chest pain, may not have experienced cardiac ischaemia, but rather 'non-cardiac' pain. Our control population was not formally proven 'healthy' by angiography, and indeed it is likely that some, particularly those with left ventricular hypertrophy or bundle branch block, did have significant underlying disease. However, in developing a model for use in patients with chest pain, this may be an advantage rather than disadvantage.

In almost all patients, the diagnosis of acute myocardial infarction was made on the basis of a creatine kinase rise $\geq 2\times$ upper laboratory normal ($\pm$ creatine kinase-MB $\geq 7\%$ if the aetiology of the total creatine kinase was equivocal). This definition is known to have suboptimal sensitivity and specificity for acute myocardial infarction compared with cardiac specific troponin which may rise following episodes of micro-necrosis (minor myocardial damage) undetected by creatine kinase or creatine kinase-MB[27]. However, as most clinicians and clinical trials still define a formal biochemical diagnosis of acute myocardial infarction based on a cut-off level of creatine kinase or creatine kinase-MB elevation, it was felt useful to define acute myocardial infarction in this conventional manner. In the small number of patients with a creatine kinase rise $<2\times$ the upper laboratory normal the diagnosis of acute myocardial infarction was only made if accompanied by serial ECG changes consistent with new myocardial infarction (new Q waves $\geq 0{\cdot}03$ s duration, and/or new persistent T wave inversion in ≥ 2 contiguous leads). Thus the initial ECG findings were independent of the gold standard final diagnosis of acute myocardial infarction.

Performance of ECG models is often expressed in terms of positive and negative predictive values[23]. As these values vary depending on the prevalence of disease, we prefer to use sensitivity and specificity to compare models derived from different populations. Some argue that models should be standardized, with specificity fixed at $\geq 90\%$ allowing more direct comparisons of sensitivities. However, it may be helpful to alter the balance of sensitivity and specificity in a model depending on the clinical purpose. In populations where the prevalence of ischaemic heart disease is high, maximizing sensitivity may be appropriate for evaluation of patients with chest pain, whereas in an ostensibly healthy population, high specificity may be more important[28].

In recent years, the use of digitally acquired ECG data has facilitated research in much larger populations[15,29]. The acquisition of data in a digital format may also reduce measurement error[28], although despite sophisticated methods to filter noise and correct baseline wander[29], beats presented for automated analysis may still be imperfect. Complex measures of ST slope, global ECG interrogation, and weighting of site specific data, have been used successfully in automated ECG diagnosis with up to 65% sensitivity and >90% specificity[13–15]. Of interest though, in several studies, a physician's ECG diagnosis was still more sensitive than the computer interpretation[22,28,30]. This perhaps justifies the preference among some cardiologists for continuing to use more familiar diagnostic ECG criteria.

It would appear that even with the help of optimal data acquisition and analysis, multivariate modelling, or application of self adaptive neural networks[31], there are limits to the diagnostic information contained in the initial 12-lead ECG. Perhaps, in the process of praecordial lead standardization, the reduction of data points was over-ambitious and the addition of spatial information from additional sites by 15-lead[32], 18-lead[33], 22-lead[34], or multi-lead body surface mapping[35] may be required, particularly in patients with atypical ECG changes.

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