Prediction of Severe Complications and Mortality in Patients Admitted to a Coronary Care Unit

R.L. Kennedy, R.F. Harrison, H.S. Fraser, S. Fletcher, A.M. Burton, L.N. McStay, and K.L. Woods

R.L. Kennedy	Professor in Medicine, The University of Sunderland
R.F. Harrison	Senior Lecturer, Department of Automatic Control and Systems Engineering, The University of Sheffield
H.S. Fraser	Registrar in Cardiology
S. Fletcher	Audit Assistant, Leicester Royal Infirmary
A.M. Burton	Research Nurse, The University of Edinburgh
L.N. McStay	Research Nurse, The University of Edinburgh
K.L. Woods	Senior Lecturer in Therapeutics, The University of Leicester

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Abstract

The aim of this study was to design a statistical model which will predict death or life-threatening complications in patients admitted to Coronary Care Unit using data which is available at the time of presentation. The study included 3721 consecutive admissions over a four year period. Predictive models were developed using logistic regression analysis (with data from 1000 patients) and their performance was assessed using receiver operating characteristic (ROC) curve analysis. The most useful model included nine data items and was tested on data from 2721 patients. These could be divided into four groups according to their calculated probability of developing a serious complication. The lowest risk group had a mortality of 0.05%, compared with 3.5%, 6.4% and 18.1% respectively in the higher risk groups ($p < 0.001$). The proportion of patients developing large infarctions (CK > 1000 U/l) in the four groups was 14.1%, 21.2%, 46.9% and 51.5% respectively ($p < 0.001$). The overall complication rates were 16.9%, 35.4%, 75.4% and 71.8% respectively ($p < 0.001$).

Introduction

A method to predict prognosis of patients admitted to coronary care units with unstable cardiac disease would not only help to improve the care of these patients, but may also assist with planning and management of facilities. In this study, we have used logistic regression to develop predictive models using clinical and electrocardiographic data which is routinely collected at the time of admission. Logistic regression is a non-linear classification technique which uses suitably coded input date to yield a series of coefficients which, when applied to unseen input vectors yield a probability of the event under consideration (e.g. death in a CCU patient). The method has previously been used to develop predictive models for the early diagnosis of acute myocardial infarction (AMI).[1-5] Two recent studies have used logistic regression models to quantify risk in patients with ischaemic heart disease.[6,7] Parsons et al.[7] identified a group of patients at low risk of death in the 28 days following AMI. Karlson et al.[6] identified high and low risk groups of patients from a large cohort of patients presenting with acute chest pain. The admission ECG is itself predictive of prognosis in patients with suspected AMI[8,9] and has been combined with clinical data by a number of other authors in smaller studies to produce models to predict prognosis. In this study we have used data from a large cohort of CCU admissions to derive a model which identifies groups which are at low, or high, risk during their admission.

Patients and Methods

Patients

The study included 3721 consecutive patients admitted to the Coronary Care Unit (CCU) of Leicester Royal Infirmary, Leicester, U.K. between August 1988 and August 1992. The patients were 2636 men and 1085 women with a mean age of 62.5 years (SD 12.3, range 17 - 96). Information on symptoms, risk factors, therapy and complications was recorded on a proforma during the patient's admission. This data was subsequently stored on a purpose-designed computer database. The final diagnosis was assigned independently by the senior clinician involved in the care of the patient. This was Q wave MI in 1642 cases, non-Q wave MI in 323 cases, unstable angina in 898 cases and other diagnoses (pericarditis, arrhythmias, cardiac failure etc.) in 858 cases. Analyses of cardiac enzymes were carried out using standard methods in the Department of Clinical Biochemistry, Leicester Royal Infirmary. The upper limit of normal for the creatine kinase (CK) assay was 160 U/l. The admission ECG for each of the 3721 patients was reviewed independently by one of the authors (RLK).

Of the 3721 patients, 295 died in the CCU while a total of 1712 patients developed complications. These were cardiac arrest in 184 cases, cardiac failure requiring treatment with loop diuretics in 1285 cases, ventricular arrhythmias in 514 cases and cardiogenic shock in 341 cases. A CK value of 1000 U/l or above was taken to indicate the presence of a large myocardial infarction, and was found in 1302 cases.

Approval for the study was obtained from the Local Ethical Committee.

Logistic Regression Models

These were derived using the maximum likelihood method to calculate coefficients on the Advanced Statistics Module of the SPSS for Windows Program (SPSS Inc., Chicago, Illinois, USA). The final probability of AMI was calculated as described previously [3] using the equation:-

$$\text{Probability (\%)} = 100 \times (1-1/(1 + \exp(b_0 + \Sigma b_r x_i))$$

where b_0 is the constant term, b_r is the coefficient for any given input and x_i is the numerical value for that input.

Logistic regression models were derived using 1000 training cases selected at random from the 3721 patients. Data items were coded as either 1 (if present) or 0 (if absent), with the exception of age and time for which symptoms had been present both of which were entered as the actual numbers (in years and hours respectively). For sex, males were coded as 1 and females as zero. The remaining 2721 cases were used as an independent test set.

Data Analysis

Logistic regression models were evaluated using the receiver operating characteristic (ROC) curve. For a full review of the use of this tool see Zweig & Cambell [10]. Basically, as used here, the plots were of sensitivity versus 100 - specificity at different diagnostic thresholds. The plots allowed us to estimate the optimum diagnostic thresholds for the models. The area under each of the curves, and their standard error was calculated according to the method described by Hanley and McNeill. [11] This area gives a measure of the ability of each test to correctly rank normal and abnormal cases. It is related to, but not equivalent to, the diagnostic accuracy of the test and can be used to statistically compare two curves. Such comparison was achieved using the method described in a further paper by Hanley and McNeill. [12] Kendall Tau correlation of the paired ratings for this calculation was performed using the SPSS program. Other statistical comparisons were made using one-way analysis of variance (ANOVA) and the Chi square test on 2 x 2 contingency tables, as appropriate.

Results

A: Logistic Regression Models

These were derived using a training set of 1000 patients (660 men and 340 women, mean age 63.2 years (SD 12.6, range 18-93)). In all, eight logistic regression models were derived. The coefficients and constants for these models are shown in Table 1. Models 2, 4, 6 and 8 were produced by eliminating data items which did not contribute significantly to the final decision from models 1, 3, 5 and 7 respectively. The output for models 1 and 2 was death, for models 3 and 4 death or CK > 1000 U/l, for models 5 and 6 development of cardiac failure, life-threatening arrhythmia, cardiogenic shock or death, and for models 7 and 8 the development of these complications or CK > 1000 U/l. The ROC curves for these eight models are shown in Figure 1 and the areas under these curves, along with the standard errors and optimum diagnostic thresholds are shown in Table 2. Since the models which contained fewer data items performed as well as those which included all data items in each case, only models 2, 4, 6 and 8 were used for further analysis.

B: Performance of Models on Training Data

The performance of Model 2 on the 1000 training cases is shown in Table 3. For the 674 patients with a calculated probability of death of less than 5.0% (the optimal threshold), the mortality was 1.7%, compared with 7.4% for those with a score of between 5.0% and 10.0%, 13.8% for those with a score of between 10.% and 20.0% and 31.9% for those with a calculated score of greater than or equal to 20.0% ($p < 0.001$). There was also a good relationship between a high score on this model and the development of other complications: For example, 62/69 (89.9%) of the group with a calculated score of 20.0% or above either died or developed a severe complication and 66/69 (95.7%) either had a large MI, died or developed a complication.

Model 4 was designed to identify patients with either a large MI or a high risk of death and who should, therefore, definitely be admitted to CCU. The performance of this model on the 1000 training cases is shown in Table 4 (percentage values are omitted from Tables 3 - 6 for the sake of simplicity). The proportion of patients who either died or developed a large MI in the four groups was 5.1%, 18.8%, 44.6% and 77.7% respectively ($p < 0.001$). Again, there was a relationship between group membership and the development of life-threatening complications such as cardiac arrest and cardiogenic shock. Model 6 was trained to identify patients who developed severe complications. Its performance is shown in Table 5. As with other models, the patients were divided into four groups according to their calculated probability of developing complications. The incidence of complications in the four groups was 11.3%, 29.0%, 54.4% and 88.8% respectively ($p < 0.001$). None of the 222 patients in the low risk group died compared with 38 of the 251 (15.1%) patients in the high risk group ($p < 0.001$). Only one patient developed cardiogenic shock and one suffered cardiac arrest in the low risk group compared with 52 and 26 patients respectively in the high risk group (both $p < 0.001$).

Of the four models which were assessed in detail on the training data, Model 8 appeared to be the most useful (see Table 6). Thus, none of the patients in the two groups with low calculated scores died compared with 12 and 48 in both of the two higher risk groups respectively (both $p < 0.001$). Similarly, the incidence of cardiogenic shock and cardiac arrest was very low in the groups with lower scores compared with the higher risk groups. The incidence of large MI/severe complication in the four groups was 20.0%, 43.4%, 71.0% and 91.2% respectively ($p < 0.001$). Since this model showed greater potential than the other models described to predict large MI, death or life-threatening complication, only the results of the performance of this model on test data are reported.

C: Performance of Model 8 on Test Data

The model was tested on an independent set of 2721 cases comprising 1976 men and 745 women with a mean age of 61.7 years (SD 12.5, range 17 - 96). The performance of the model on these cases is shown in Table 7. The incidence of large MI, death or life-threatening complication (cardiac arrest, CCF, ventricular dysrhythmia or cardiogenic shock) in the four groups was 28.9%, 48.9%, 75.4% and 91.7% respectively ($p < 0.001$). CCF is not always immediately life-threatening. When this was excluded from the analysis, the incidence of death or life-threatening complication (cardiac arrest, ventricular dysrhythmia or cardiogenic shock) in the four groups was 8.0%, 15.9%, 23.1% and 40.9% respectively ($p < 0.001$). Mortalilty in the low-scoring group was 0.05% compared with 18.1% in the high-scoring group ($p < 0.001$).

Discussion

In this study, we describe the development and testing of logistic regression models to predict the prognosis of patients admitted to CCU. The models described make use of clinical and ECG information available at the time of admission. One cohort of patients (1000 cases) was used to derive the models, while a further cohort (2721 cases) was used for testing as in previous studies. [7,13] In all, eight logistic regression models were produced - four with all of the available data items included and four with only those items which made a statistically significant contribution to the models. In each case, the models with fewer data items performed as well as models which included a more extensive set of inputs. In a separate study (unpublished) using logistic regression models for early diagnosis of AMI, we have found that models which incorporate a larger number of input items can perform better, even if some of the individual data appear not to have discriminatory power. In the present study, the most effective model was one trained to identify patients who either died, suffered a life-threatening complication or a large AMI. The model which is described in detail identified. from the test set of 2721 patients, a group of 939 patients of which 91.7% fulfilled one of the above criteria. By contrast, a low-risk group (516 patients) had a mortality of only 0.05% and a complication rate (including death) of 16.9%.

This study differs substantially from two other recent studies which have used logistic regression models to predict prognosis in patients with confirmed [7] or suspected [6] AMI: The study of Parsons et al. [7] was designed to predict 28 day mortality and identified a group, comprising about one third of the patients, who had a very high (99.2%) chance of survival. The study, like the present one made use of ROC curve analysis. Predictors of survival included a pulse rate of less than 100 beats/minute on admission, age under 60 years, presence of typical symptoms, no previous history of AMI or diabetes and absence of Q waves on the

admission ECG. We have attempted to predict both in-hospital mortality and complications in all patients admitted to a coronary care unit. It is well recognised that death and complications are common in patients admitted to CCU, even when they do not appear to have suffered AMI. [14] Parsons et al. restricted their study to patients who were under 65 years of age, while the present study included patients of all ages. We have identified both high- and low-risk groups of patients. The proposed model may thus be useful for identifying patients who can be discharged to a lower level of care at an early stage (say after 12-24 hours), while the high risk group may require continued intensive monitoring and aggressive therapy. The model by Karlson et al. [6] was derived and tested using data from 7157 patients presenting to Accident and Emergency with suspected AMI. The study included patients who were discharged directly home, those who were admitted to medical wards, and those admitted to CCU. As with the present study, logistic regression analysis was used to select the variable for inclusion in the model. The predictive variables in the study of Karlson et al. were age, clinical suspicion of AMI, ECG changes of AMI, diabetes, cardiac failure, syncope and ventricular dysrhythmias. The model identified a group (64% of the total patient population) with a mortality of just over 1%. Unlike the present study population, the patients in Karlson's study were at relatively low risk overall - the incidence of death or severe complication was 6.7% and only 20% of those admitted to hospital developed AMI. In this very mixed patient population, the ECG was highly predictive of severe complications. Patients with a normal ECG were at very low risk, as described previously. [8,9,15]

A number of other studies have described the development of simple models using clinical and ECG data from presentation to predict risk in patients admitted with suspected AMI. [13,16,17] The major differences between these studies and the present one or those of Parsons et al. [7] or Karlson et al. [6] is that they are smaller and were conducted before the use of thrombolytic agents became widespread. Nevertheless, these earlier studies did successfully combine clinical and electrocardiographic variables to produce models which divided the patient populations into high and low risk groups. For example, Dubois et al. [13] in their study of 536 acute admissions identified a group (62% of the total) whose risk of death was 4% compared with 24% in the rest of the study population. In a more extensive study, Lee et al. [18] used a previously developed model [19,20] in a Bayesian system to identify a group of patients who were at low risk and, therefore, suitable to be transferred from the CCU after only twelve hours. As with this study, Lee et al. focused on predicting short-term prognosis in unselected acute admissions to the CCU. Two recent studies have described statistical models for medium- to long-term risk stratification in patients with ischaemic heart disease: Steurer et al. [21] were able to predict prognosis over twelve months in patients with sustained ventricular tachycardia, while Silver et al. [22] used a logistic regression model to identify a cohort of AMI patients with well-preserved left ventricular function.

The variables we used were dictated to an extent by what was available on the CCU database. However, the significant variables are very similar to those used in the other prognostic models described above. As with other authors [8,9,23,24], we found the most powerful predictive data to be that available from the admission ECG. We did not include the site of ECG changes in our model. Previously, patients with anterior ischaemic changes have been shown to have a worse prognosis [13,25,26], although Parsons et al. [7] did not find this factor to be significant. Although the presence of ST segment changes on the admission ECG is highly predictive of evolving AMI and poorer prognosis in chest pain patients, modest ST segment elevation or depression does not always indicate that the patient belongs to a high risk group [27], particularly in the hour or two after symptoms begin. The ECG may also be misleading in patients who have suffered previous ischaemic damage [24], making combination of ECG data with clinical data highly desirable. The simple combination of a doctor's estimate of the probability that the patient is developing AMI with the ECG data has been found to predict AMI with a high degree of accuracy. [24] Our aim was only to use data which could be obtained at presentation. Clearly, the clinical situation in most patients is evolving and a model which takes account of this may well provide a more accurate scoring system. We did not take account of the influence of treatments such as aspirin or thrombolytic agents which favourably influence mortality. Other data available after admission which would almost certainly add to a model include cardiac enzymes (to give an indication of the size of infarcts) and measures of left ventricular function. The persistence of chest pain 24 hours or more after admission has been said to indicate a poorer prognosis in the longer term, [16,28] although this effect was recently found to be less marked in patients who had been thrombolysed.

Logistic regression models for the early diagnosis of myocardial infarction have been described previously. [1-3,5] The model described by Selker et al. [3] is a very simple one and is similar to the one described in this paper. This model performed well when applied to retrospective data gathered from patients' case notes. Other techniques which have been used for early diagnosis of AMI include Bayesian systems [29,30] and classification trees developed using recursive partition analysis[19,20]. A recent study by Long et al. [4] demonstrates that logistic regression offers superior classification to the classification tree approach. Currently, logistic regression is the most widely used method for developing predictive models from clinical data. We have not, to date, attempted to apply the model described here to data collected from different centres. Lack of portability has been one of the problems with algorithms designed to predict early diagnosis of AMI. [31,32]

Apart from the potential to streamline clinical care for patients presenting with acute cardiac disease, application of predictive models may also improve the usage of facilities. [8,20,33] This application of clinical algorithms as an aid to maximising the use of high-dependency facilities has not been explored in practice. They could also be used in health care planning - for example, in deciding how many coronary care beds are required in a given hospital. It has been estimated, in the United States, that reliable identification of low-risk cardiac patients and their admission to lower dependency units could lead to an annual saving of many millions of dollars. [33] Clinical scoring systems which incorporate a means of quantifying the proportions of low and high-risk patients admitted to different hospitals could also form part of a methodology for measuring case-mix and performance of different centres.

In conclusion, we describe the development of a simple model to predict death or severe complications in patients admitted to coronary care unit. The model described is easy to apply and makes use of a few items of clinical and electrocardiographic data which are available at the time of presentation. The use of such a model may improve clinical care of patients by identifying individuals who are at high-risk. The model could also be valuable in planning and management of facilities.

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Table 1: Coefficients and Constants for Logistic Regression Models

	Model 1	Model 2	Model 3	Model 4	Model 5	Model 6	Model 7	Model 8
Atrial Fibrillation	0.66	-	0.12	-	0.66	0.64	0.35	-
Age (years)	0.04	0.05	0.007	-	0.04	0.03	0.03	0.02
Bundle Branch Block	1.59	1.63	0.61	0.72	1.62	1.63	1.44	1.58
Diabetes	0.80	0.87	1.00	1.03	0.94	0.97	0.97	0.97
Ex-Smoker	-0.21	-	-0.47	-0.50	-0.13	-	-0.20	-
Family History of IHD	-0.67	-	-0.06	-	0.05	-	0.05	-
Nausea	-0.31	-	0.18	-	-0.12	-	-0.002	-
Chest pain	-0.12	-	0.47	0.52	-0.87	-0.96	-0.48	-
Palpitations	-1.04	-	-1.60	-1.59	0.02	-	-0.33	-
Previous CCU	-0.59	-	-0.96	-1.00	0.71	0.68	0.20	-
Pulmonary Oedema	1.30	1.10	0.39	0.33	2.40	2.36	2.77	2.81
Q waves	-0.07	-	0.08	-	0.53	0.51	0.48	0.49
Sex	-0.23	-	0.68	0.67	-0.08	-	0.22	-
Smoker	-0.46	-	0.17	-	0.14	-	0.19	-
Breathless	-0.31	-	-0.57	-0.53	0.56	0.55	0.02	-
ST Depression	1.30	1.37	0.98	1.01	0.25	0.27	0.75	0.79
ST Elevation	0.98	0.92	2.08	2.17	0.49	0.49	1.65	1.66
SVT	-4.65	-	0.06	-	0.81	-	0.18	-
Sweating	-0.02	-	0.13	-	-0.51	-0.49	-0.39	-0.39
Syncope	0.75	0.95	-0.64	-0.61	0.26	-	-0.32	-
Time (Hours)	-0.002	-	-0.002	-	-0.004	-	-0.007	-
T Wave Inversion	0.66	0.56	-0.20	-	0.21	0.22	-0.06	-
Ventricular Rhythm	2.29	2.05	1.92	1.97	1.28	1.18	1.34	1.51
Constant	-6.92	-8.63	-2.88	-2.40	-3.13	-3.01	-1.99	-2.06

Models 1 and 2 were used to predict death, 3 and 4 to predict death or high CK, 5 and 6 to predict life-threatening complication or death, 7 and 8 to predict complications, death or high CK. Data items were coded as 1 when present and 0 when absent. For sex, males were coded as 1 and females as 0. The ECG data items were taken from the admission ECG.

Table 2: Areas under ROC curves and Optimum Diagnostic Thresholds

	Area	SE	Threshold
Model 1	82.5	3.1	5%
Model 2	79.9	3.3	5%
Model 3	85.2	1.2	30%
Model 4	85.1	1.2	30%
Model 5	83.6	1.3	45%
Model 6	83.1	1.3	35%
Model 7	84.2	1.2	65%
Model 8	84.0	1.2	55%

The areas under the curves and ther standard errors were calculated as described in the Methods section. The thresholds are quoted to the nearest 5% and indicate the value at which the logistic regression equation can best separate positive from negative cases.

Table 3: Performance of Model 2 on Training Data

Calculated Probability	< 5.0	5.0 - 9.9	10.0 - 19.9	> 20.0
High CK	181	62	45	33
Death	12	11	15	22
HighCK/Death	189	71	56	46
CCF	173	76	56	42
Arrhythmia	65	20	21	15
Cardiogenic Shock	22	12	25	21
Cardiac Arrest	20	5	14	8
All Complications	216	95	77	62
Complication/High CK	332	123	95	66
Number	674	149	108	69

Table 4: Performance of Model 4 on Training Data

Calculated Probability	≤ 10.0	10.0 - 29.9	30.0 - 59.9	≥ 60.0
High CK	11	55	64	191
Death	0	13	14	33
HighCK/Death	11	65	74	212
CCF	65	118	72	92
Arrhythmia	31	27	22	41
Cardiogenic Shock	2	16	24	38
Cardiac Arrest	3	9	10	25
All Complications	80	136	91	143
Complication/High CK	86	167	121	242
Number	215	346	166	273

Table 5: Performance of Model 6 on Training Data

Calculated Probability	< 15.0	15.0 - 34.9	35.0 - 59.9	> 60.0
High CK	47	115	76	83
Death	0	7	15	38
HighCK/Death	47	122	86	107
CCF	16	72	72	187
Arrhythmia	10	27	25	59
Cardiogenic Shock	1	7	20	52
Cardiac Arrest	1	7	13	26
All Complications	25	97	105	223
Complication/High CK	62	185	135	234
Number	22	334	193	251

Table 6: Performance of Model 8 on Training Data

Calculated Probability	≤ 30.0	30.0 - 54.9	55.0 - 79.9	≥ 80.0
High CK	16	38	87	180
Death	0	0	12	48
HighCK/Death	16	38	98	210
CCF	22	54	77	194
Arrhythmia	7	18	38	58
Cardiogenic Shock	0	4	13	63
Cardiac Arrest	2	3	7	35
All Complications	28	66	106	250
Complication/High CK	41	95	159	321
Number	205	219	224	352

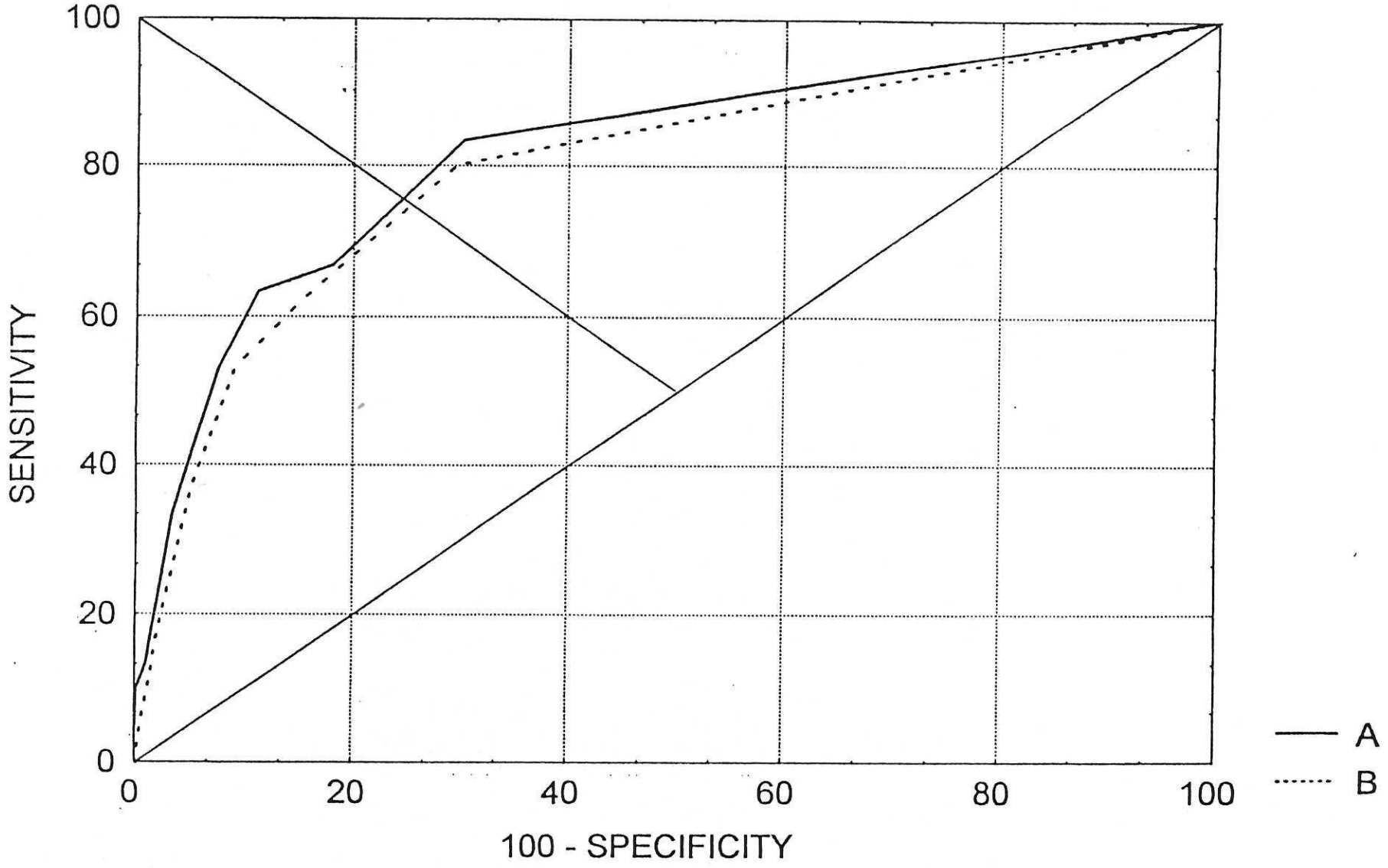
Table 7: Performance of Model 8 on Test Data

Calculated Probability	< 30.0	30.0 - 54.9	55.0 - 79.9	> 80.0
High CK	73 (14.1)	132 (21.2)	292 (46.9)	484 (51.5)
Death	3 (0.05)	22 (3.5)	40 (6.4)	170 (18.1)
HighCK/Death	76 (14.7)	149 (24.0)	322 (51.8)	595 (63.4)
CCF	53 (10.3)	156 (25.1)	200 (32.2)	529 (56.3)
Arrhythmia	29 (5.6)	65 (10.5)	101 (16.2)	198 (21.1)
Cardiogenic Shock	6 (1.2)	27 (4.3)	38 (6.1)	190 (20.2)
Cardiac Arrest	7 (1.4)	14 (2.3)	34 (5.5)	82 (8.7)
All Complications	87 (16.9)	220 (35.4)	281 (45.2)	674 (71.8)
Complication/High CK	149 (28.9)	304 (48.9)	469 (75.4)	861 (91.7)
Number	516	622	644	939

The model was tested on data from 2721 patients. Percentages for each prediction are given in parentheses.

Legends to Figures

Figures 1 to 4 show ROC curves for the eight logistic regression models described in the text. In each case the solid line (A) represents the model which includes all of the available data inputs while the dotted line (B) represents the model which makes use of the lesser number of data points.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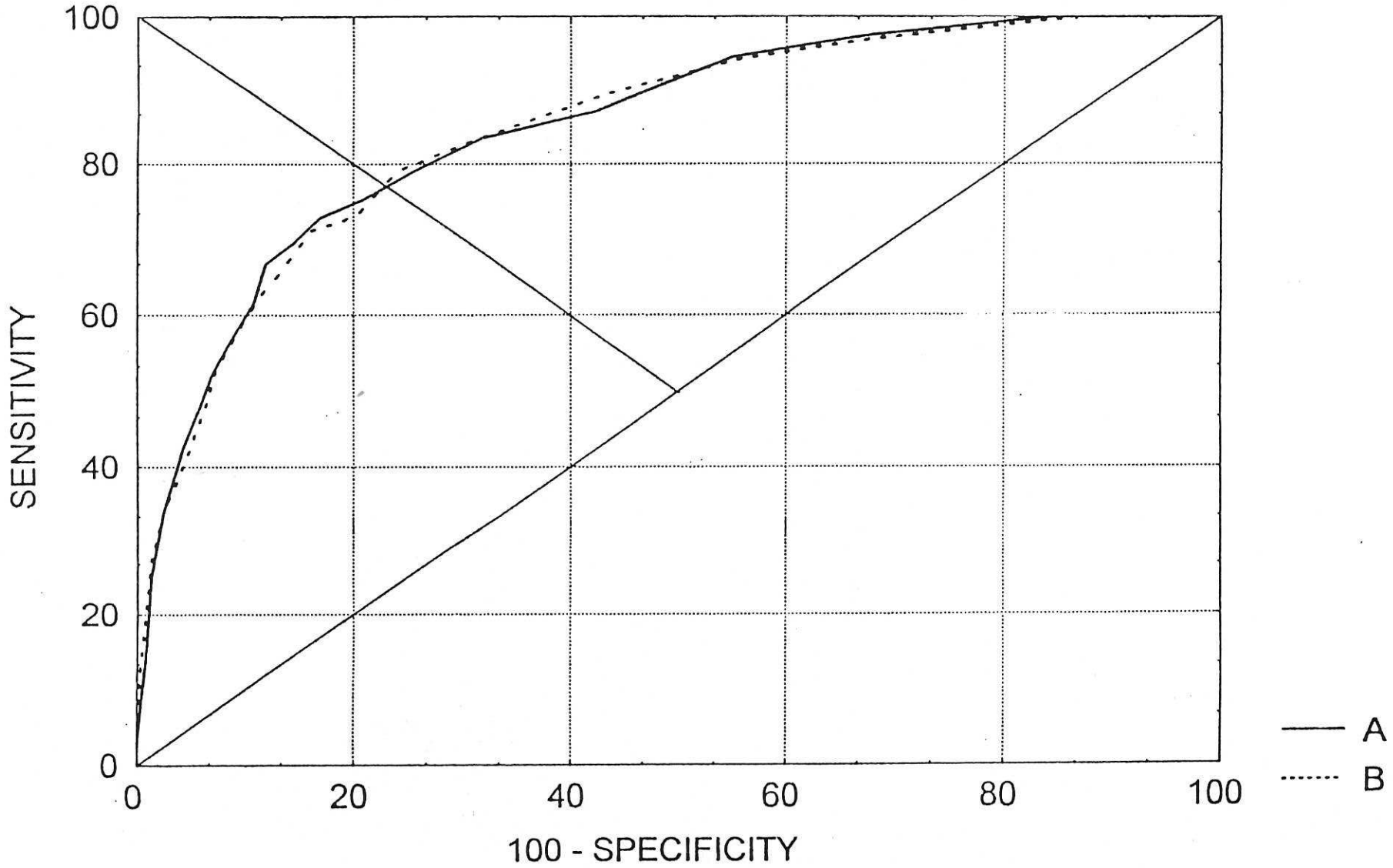
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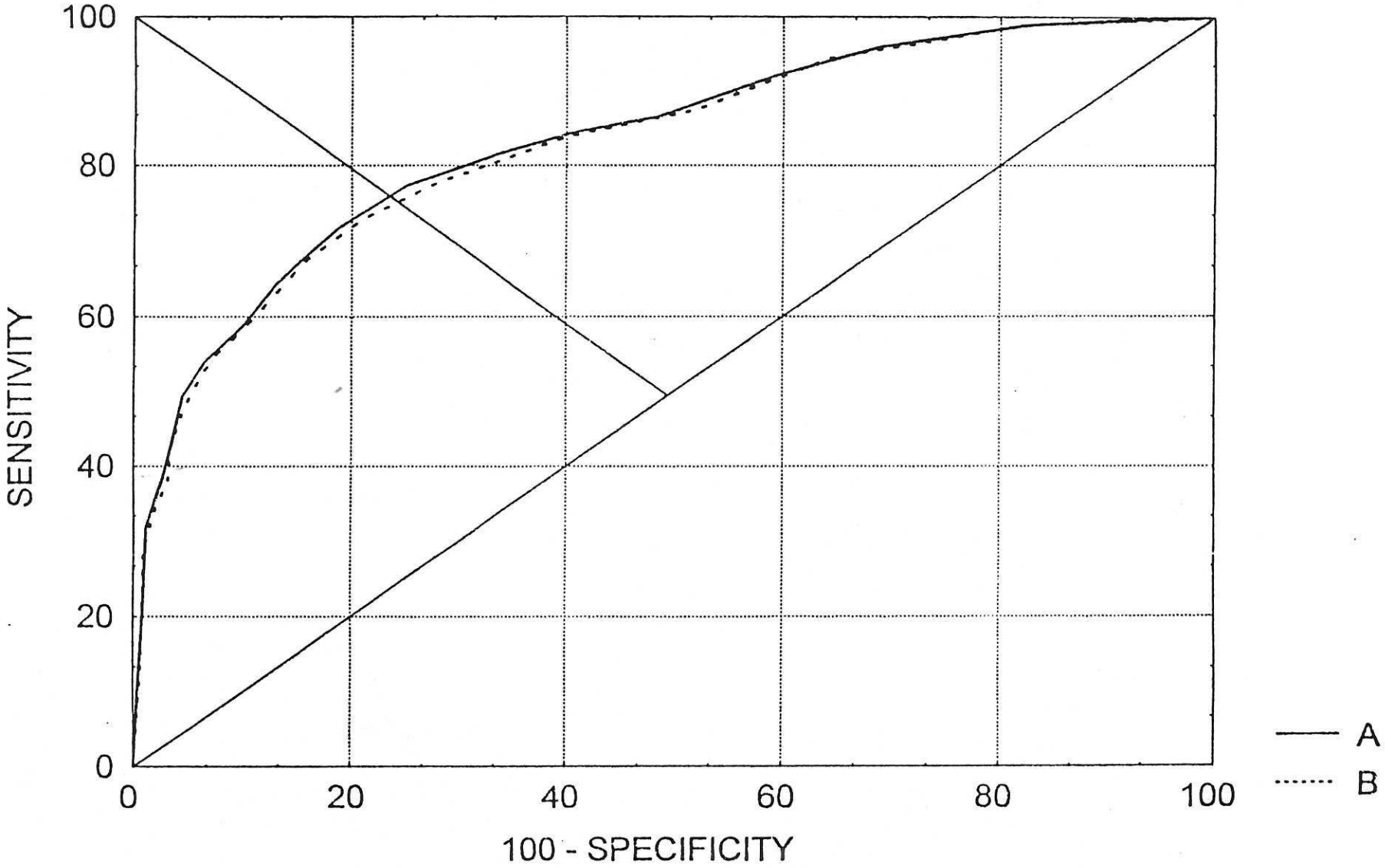
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