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Multivariate analysis in the prediction of death in hospital after acute myocardial infarction

Yongyuth Sahasakul, Suphachai Chaithiraphan, Pradit Panchavinnin, Payonk Jootar, Vichian Thongtang, Naris Srivanasont, Narumol Charoenchob, Charuwan Kangkagate

Abstract

Prognostic factors in patients with acute myocardial infarction based on clinical and investigative data on admission were evaluated prospectively in 111 consecutive patients. Seventeen patients (15·3%) died during hospital stay. Age, a previous infarct, high Killip class, cardiomegaly, high serum concentrations of cardiac enzymes, a low ejection fraction, and a high wall motion score index correlated significantly with in-hospital mortality; whereas sex, risk factors, and pericardial effusion did not. Multivariate analysis showed that age and the wall motion score index were the best predictors of death in hospital. Wall motion detected by cross sectional echocardiography may reflect the extent of myocardial involvement. Age and wall motion score index predicted in-hospital mortality with a sensitivity of 76·5%, a specificity of 91·5%, and a predictive accuracy of 89·2%. Age and the wall motion score index can be determined on admission and are useful for identifying patients at high risk of cardiac death who might benefit from early intervention.

It is clinically useful to identify high risk patients reliably after acute myocardial infarction. Studies showed that clinical assessment to identify high risk patients could be performed within the first day of admission.[1-4] The most powerful predictor of prognosis was the degree of left ventricular pump dysfunction caused by infarction, which the clinical and investigative variables indirectly reflect.[5-7] However, the ambiguity of the clinical findings and the lack of the sensitivity and specificity of these data to assess the function of the left ventricle hamper the prediction of death in hospital in patients with acute myocardial infarction.[1-4]

We attempted to identify the prognostic factors that are associated with outcome (survival or death). To do this we applied a binary logistic regression model to the clinical and investigative data obtained on the first day of admission.

Patients and methods

PATIENTS

From October 1986 to September 1987 we studied 111 consecutive patients with definite acute myocardial infarction—as defined by typical chest pain, electrocardiographic changes, and serial enzyme changes—who were admitted to the coronary care unit of Siriraj Hospital within 48 hours of the onset of chest pain. Seventeen patients (15·3%) died in hospital within 2 weeks of admission.

CLINICAL DATA

We studied 78 men and 33 women (mean age 62·22 (12·60) years (range 33 to 87)). Twenty two patients had a clinical history or electrocardiographic findings of a previous myocardial infarction or both. On admission, 24 (21·6%) patients were in Killip class II, seven (6·3%) patients were class III, and 17 (15·3%) were class IV (table 1).

We noted the following risk factors for coronary heart disease: family history of coronary artery disease, cigarette smoking, hypertension, hyperlipidaemia, diabetes mellitus, alcohol consumption, sedentary work, gout, obesity, contraceptive pills, and personality type (table 2). Cigarette smoking was defined as consumption of $\geq 0 \cdot 5$ pack/day for ≥ 6 months before the myocardial infarction.[8] Hypertension was diagnosed if the initial value recorded showed a systolic pressure > 150 mm Hg or a diastolic pressure > 90 mm Hg or if there was a previous history of hypertension with associated treatment.[8] Glucose intolerance was defined as a history of diabetes mellitus or the use of oral hypoglycaemic agents or insulin. Obesity (body-mass index) was defined as the value of equal or more than 30 (weight divided by the square root of height).[8]

INVESTIGATIVE DATA

Table 3 shows data obtained within 24 hours of admission. Q wave myocardial infarction was found in 88 patients (57 anterior and 31 inferior) and non-Q wave myocardial infarction in 23 patients. We examined anteroposterior chest *x* rays of each patient (upright or sitting) taken at a distance of 6 feet for evidence of pulmonary oedema and diversion of blood to

Table 1 Characteristics of survivors and non-survivors of acute myocardial infarction

Characteristic	*Survivors (94)*	*Non-survivors (17)*	*p value*
Age (yr) (SD)	60·84 (12·16)	70·18 (12·51)	< 0·005
Sex:			NS
Male	64	11	
Female	27	6	
Old MI	15	7	<0·01
Killip class (SD)	1·6 (1·0)	2·9 (1·1)	<0·005

MI, myocardial infarction.

Division of Cardiology, Department of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand
Y Sahasakul
S Chaithiraphan
P Panchavinnin
P Jootar
V Thongtang
N Srivanasont
N Charoenchob

Cardiac Center, Siriraj Hospital, Mahidol University, Bangkok, Thailand
C Kangkagate

Correspondence to Dr Yongyuth Sahasakul, Division of Cardiology, Department of Medicine, Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand.

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Table 2 Risk factors in survivors and non-survivors

Risk factors	*Overall No (%)*	*Survivors (94)*	*Non-survivors (17)*	*p value*
Family history	9 (8·1)	9	—	—
Cholesterol*	23 (20·7)	19	4	NS
Triglyceride*	25 (22·5)	21	4	NS
Hypertension	47 (42·3)	38	9	NS
Smoking	69 (62·2)	60	9	NS
Alcohol†	11 (9·9)	10	1	NS
Sedentary work	58 (52·3)	50	8	NS
Gout‡	9 (8·1)	9	—	—
Diabetes mellitus	21 (18·9)	19	2	NS
Obesity	9 (8·1)	8	1	NS
Contraceptive pills§	2/27	2/27	—	—
Personality:				NS
Type A	78 (70·3)	67	11	
Type B	33 (29·7)	27	6	

*Cholesterol ⩾ 6·5 mmol/l; triglyceride ⩾ 1·7 mmol/l.
†Regular heavy drinker for > 10 years.
‡Symptomatic hyperuricaemia.
§Treatment for > 5 years.

the upper lobe and to calculate the cardiothoracic ratio. We also noted the increase in cardiac enzymes on the first day of admission.

Cross sectional echocardiography was performed within 24 hours of admission with an Aloka mechanical scanner Model SSD-118 and 3·0 MHz transducer. The images were recorded on 1/2 inch videotape for real time and slow motion playback. We obtained parasternal long and short axis views and apical four chamber and two chamber views. The short axis view was recorded at three levels: mitral (basal), papillary muscle (mid), and apical. A 14 segment model of the left ventricle was used.[5 6 9] The site and severity of the regional myocardial dysfunction were visually evaluated by review of each echocardiographic study and graded by the Herman and Gorlin scoring system for ventricular wall motion[10]: normal = 1, mild or moderate hypokinesia = 2, severe hypokinesia or akinesia = 3, dyskinesia = 4, and aneurysmal = 5. The values determined for each segment were added to give a total score. Thus in patients with normal scores in all 14 segments the wall motion score index was (14 × 1)/14 = 1. Each study was reviewed by two observers who arrived at a wall motion score index by consensus. The ejection fraction (EF) was determined by a modified Quinones' equation[11 12].

$$EF = ((Ded^2 - Des^2)/Ded^2) + ((Des^2/Ded^2)(\triangle L)),$$

where Ded and Des are the internal dimension at end diastole and end systole respectively level with the tip of papillary muscle in the parasternal short axis view and $\triangle L$ is the fractional shortening of the long axis. Because the shortening of the long axis contributes only slightly to the global ejection fraction and because this axis is frequently foreshortened by the apical views, we decided to estimate this component of the ejection fraction equation from a subjective assessment of the wall motion at the apex. Thus $\triangle L = 0·15$ with normal motion, 0·05 with apical hypokinesia, 0 with akinesia, −0·05 with dyskinesia, and −0·10 with aneurysm.[9 11] We took the mean of at least three values of the ejection fraction in each patient.[6 9] We used echocardiography to detect pericardial effusion.[13]

STATISTICAL ANALYSIS

All continuous variables were analysed by Student's *t* test for unpaired data. Frequency data were tested by the Z test for proportion or the χ^2 test (tables 1–3).

MULTIVARIATE ANALYSIS

We used multifactorial analysis to identify factors that independently predicted the outcome in our study group and we applied a binary logistic regression model to the data.[14–16]

Y denoted survival and Y = 1 death. If $\underset{\sim}{X}$ is a vector of prognostic factors where $\underset{\sim}{X} = (X_1, X_2, \ldots)$ the logistic regression model specifies that the outcome or non-survival probability, P (Y), is related to the prognostic factors $\underset{\sim}{X}$ by the following equation: $P(Y = 1\underset{\sim}{X}) = 1/1 + \exp(-a - b\underset{\sim}{X})$, where a is a constant term in the equation and b is a column vector of regression coefficients corresponding to the numerically coded factors, and $\exp(K) = (2·7182)^k$.

The data (nine factors) from 111 patients were fitted to this statistical model. These factors were the patient's age in years (X_1); the wall motion score index of the left ventricle (X_2); ejection fraction in percentage (X_3); concentrations of creatine kinase (X_4), lactic dehydrogenase (X_5), and aspartate aminotransferase (X_6); the cardiothoracic ratio (X_7), Killip class (X_8), and history of old myocardial infarction (X_9). For the first seven factors (X_1–X_7) actual values were used. The Killip class was 0 if the patient was in class I or class II and 1 if

Table 3 Results of investigation data in survivors and non-survivors (mean (SD))

Investigation	*Survivors (94)*	*Non-survivors (17)*	*p value*
Electrocardiogram:			NS
Anterior	47	10	
Inferior	26	5	
Non-Q MI	21	2	
LVH	5	1	
Chest *x* ray:			<0·025
Ratio	0·57 (0·07)	0·62 (0·06)	<0·025
Upper lobe venous diversion	18	6	NS
Pulmonary oedema	5	2	NS
Cardiac enzymes (U/l)			
CK	975·77 (1109·50)	2420·24 (1895·40)	<0·0005
AST	107·33 (118·04)	492·65 (674·82)	<0·025
LDH	483·67 (437·80)	1214·29 (1200·46)	<0·025
Echocardiogram:			
Ejection fraction (%)	45·23 (12·61)	33·24 (13·47)	<0·0005
WMSI	1·69 (0·38)	2·37 (0·38)	<0·0005
Pericardial effusion	14	3	NS

AST, aspartate aminotransferase; CK, creatine kinase; LDH, lactic dehydrogenase; LVH, left ventricular hypertrophy; WMSI, wall motion score index.

Table 4 Maximum likelihood of fit of logistic regression model in 111 patients with acute myocardial infarction

Variable	Logistic coefficient	Standard error	Z value
Age	0·0897	0·0322	2·79 (p = 0·0052)
WMSI	4·4961	1·0516	4·28 (p < 0·0001)
Constant	−16·7414	3·7651	·

WMSI, wall motion score index.

the patient was in class III or class IV. The history of old myocardial infarction scored zero if the patient had no history of previous myocardial infarction and one if he/she did. Data were calculated through the program LOGRESS[17] on the IBM PC/XT computer (table 4).

We applied the binary logistic regression model to age and the wall motion score index as the predictive factors to calculate the probability of death P (Y) in each patient. The sensitivity, specificity, positive predictive value, negative predictive value, and predictive accuracy of the model were calculated in a two-by-two table (table 5). A non-survival probability of $\geq 0·3$ was regarded as predicting death in hospital.

Results

CLINICAL AND INVESTIGATIVE DATA

There were significant correlations between death in hospital and the following variables: age ($p < 0·005$); previous myocardial infarction ($p < 0·01$); Killip class ($p < 0·005$); presence of cardiomegaly on the chest *x* ray ($p < 0·025$); serum concentrations of creatine kinase ($p < 0·0005$), aspartate transaminase ($p < 0·025$), and lactic dehydrogenase ($p < 0·025$); ejection fraction ($p < 0·0005$); and wall motion score index ($p < 0·0005$) (tables 1–3).

MULTIVARIATE ANALYSIS

All the above nine factors were used for multivariate analysis. The maximum likelihood estimate of the coefficient, its standard error, and the corresponding Z value were also calculated. An absolute value of $Z > 2·57$ indicates a significant association ($p < 0·01$) between the factors and the patient's survival (table 4). Only age and the wall motion score index were significantly associated with outcome ($p < 0·01$). The positive sign of the coefficients indicated that the estimated probability of death in hospital rose with age and the wall motion score index. Table 5 shows the sensitivity, specificity, predictive value, and accuracy of age and wall motion score index determined in the binary logistic regression model.

Table 5 Sensitivity, specificity, and predictive accuracy of age and wall motion score index determined by the logistic regression model

Predicted outcome	Outcome: Non-survivors	Outcome: Survivors	Total
Non-survivors	13	8	21
Survivors	4	86	90
Total	17	94	111

Sensitivity = 13/17 (76·5%), specificity = 86/94 (91·5%), positive predictive value = 13/21 (61·9%), negative predictive value = 86/90 (95·56%), predictive accuracy = 99/111 (89·2%).

Discussion

In an earlier study we combined clinical characteristics and investigative data to identify a subgroup of patients with acute myocardial infarction.[5] The variables previously shown to be useful in the risk stratification of patients with acute myocardial infarction include clinical assessment, initial chest *x* ray, electrocardiographic ST segment mapping, peak serum concentration of creatine kinase, and cross sectional echocardiography.[1–6] The most powerful prognostic factor is the degree of left ventricular pump dysfunction caused by infarction, which these variables indirectly reflect.[5–6 18–20]

PROGNOSTIC FACTORS

The following nine variables, measured on the first day of admission within 48 hours of the onset of chest pain, correlated significantly with an increased risk of death in hospital: old age, a previous infarct, high Killip class, cardiomegaly, high concentration of cardiac enzymes (creatine kinase, aspartate aminotransferase, lactic dehydrogenase), low ejection fraction, and high wall motion score index.

MULTIVARIATE ANALYSIS

Multivariate analysis of these nine variables in patients with acute myocardial infarction showed that age and the wall motion score index were the best prognostic factors. Left ventricular function decreases with age, as the incidence of multivessel coronary artery disease increases.[21] In elderly patients with acute myocardial infarction not only was the myocardium more severely damaged but also the amount of myocardium at risk was high because critical multivessel disease of the coronary arteries was more common.[21] Cross sectional echocardiography allows non-invasive determination of both global left ventricular function and segmental wall motion abnormalities. The extent of myocardial involvement was one of the most useful indices for predicting the outcome of myocardial infarction.[5–7 22] Wall motion score index was a useful predictor of death in hospital after acute myocardial infarction (sensitivity 71%, specificity 90%, and predictive accuracy 87%).[23] Combination of age and wall motion score index in the present study increased the predictive power further (sensitivity 76·5%, specificity 91·5%, and predictive accuracy 89·2%).

Multivariate analysis enabled us to identify the two most important prognostic factors in the prediction of death in hospital.

CLINICAL IMPLICATIONS

Both age and the wall motion score index can easily be obtained on the first day of

hospital admission. These two variables can be used rapidly to identify high risk patients who will benefit most from thrombolytic treatment, immediate percutaneous transluminal coronary angioplasty, or coronary bypass grafting.[24–26]

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