

Identification of predictors of inhospital postreperfusion mode of death in patients with acute ST-elevation myocardial infarction

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Key words: percutaneous coronary interventions; myocardial reperfusion therapy; postreperfusion inhospital death; risk stratification of postreperfusion complications.

Summary. Objectives. The aim of this study was to identify the predictors of the postreperfusion mode of death using the distinctions in clinical characteristics of patients who died and survived after reperfusion therapy, treated due to ST-elevation myocardial infarction (STEMI).

Material and methods. This consecutive study has involved 36 patients: 18 patients who died from progressive heart failure (PHF) (group 1, n=13) or from cardiac rupture (CR) (group 2, n=5) after primary coronary intervention. The control group consisted of 18 randomly selected patients who survived inhospital period (group 3). The initial and postreperfusion heart rate (HR), systolic and diastolic arterial pressures (SAP and DAP), maximal ST elevation (max ST \uparrow) and depression (max ST \downarrow), ST score, TIMI flow grade, coronary score (CS), and their perireperfusion changes were assessed for each patient. The complex prognostic predictors – TIMI Risk Score and TIMI Risk Index – were also assessed. The data analysis was performed by standard statistical and machine learning approach methods.

Results. The comparison of three patients' groups according to simple ECG or circulatory characteristics showed that more significant differences were seen in postreperfusion characteristics or their perireperfusion changes. Herewith, the major part of significantly different characteristics (baseline SAP, DAP, and HR, postreperfusion SAP, DAP, ST score, and TIMI flow grade, resolution of ST score) was observed comparing both the groups of dead patients with survivors (control group). The differences in the complex predictors (TIMI Risk Score and TIMI Risk Index) were similar. However, the smallest number of significantly different characteristics was seen comparing both the groups of dead patients. The baseline DAP ($P=0.045$), postreperfusion SAP ($P=0.04$) and DAP ($P=0.03$), and ST score ($P=0.0025$) were higher in the patients who died from CR. The postreperfusion ST score and SAP were also identified as necessary components in the assessment of informative prognostic sets according to feature selection methods used in data mining field.

Conclusion. The postreperfusion ST score, SAP, and DAP could be useful for the prediction of inhospital postreperfusion mode of death in patients with STEMI; evidently more clinical predictors could be useful for the prediction of general occurrence of postreperfusion deaths.

Introduction

Recent clinical trials suggest that the increased 30-day mortality in patients with ST-elevation myocardial infarction (STEMI) can be significantly reduced with the use of early reperfusion therapy (RT) (1–3). However, it seems likely that the current use of RT has a minimal causal impact on hospital mortality rates principally because sometimes technically

successful RT is associated with more acute cardiac and vascular complications (4, 5). The increased paradoxical risk of death has been reported in patients during the first 24 hours after RT (6–8). The real mechanism of this phenomenon, excluding the mechanism of recurrent myocardial ischemia (4, 9), is not exactly known (10). Additionally, the mechanisms of postreperfusion deaths may be different and

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manifested as the sudden death from life-threatening arrhythmia, death from cardiac rupture (CR), and death from progressive heart failure (PHF) (6, 11, 12). The prediction of postreperfusion mode of death is consequently underestimated clinical problem (12–14). The lack of an adequate or consistent classification of modes of deaths contributes to the current confusion in analyzing the causes of postreperfusion mortality also.

The rationale usage of different methods of statistical data analysis may be valuable in identification of clinical predictors (15, 16). The main objective of feature selection is obtaining a feature space with 1) low dimensionality, 2) retention of sufficient information, and 3) enhancement of separability in feature space, for example, in different categories by removing effects due to noisy features.

The aim of this study was to identify the possible predictors and sets of predictors of the postreperfusion mode of death using the distinctions in clinical characteristics of dead patients and survivors, treated by primary percutaneous coronary interventions (PCI) due to STEMI.

Material and methods

Study design

In this consecutive study, we tried to identify the informative clinical characteristics suitable for prediction of postreperfusion mode of death using the discrepancies in simple and complex clinical characteristics of 36 patients with STEMI, who died or survived in-hospital period and underwent primary PCI in the Department of Cardiology of Kaunas University of Medicine during 2003. The patients' circulatory status (heart rate, systolic and diastolic arterial blood pressure), electrocardiography data (QRS score, maximal ST-segment elevation and depression, and total ST dislocation [ST score]), angiography data (postreperfusion TIMI flow, coronary score), and popular complex prognostic characteristics – the TIMI risk score (17–19) and the TIMI risk index (20) – were assessed for each patient and compared between survivors and dead patients. The autopsy patients (n=18) were divided into 2 groups: those who died from PHF (group 1, n=13) and who died from CR (group 2, n=5). The control group consisted of the randomly selected survivors (group 3, n=18). The mode of death was verified by autopsy data in all the cases.

Patients' selection criteria

The inclusion criteria for all dead patients and survivors were as follows: 1) typical chest pain longer than 30 min in duration; 2) ST-segment elevation of

≥1 mm (at the J point) in two or more contiguous leads on 12-lead ECG at admission. Treatment assignment was not randomized, and patients were treated with PCI by the judgment of the attending cardiologist based on availability of the catheterization team, presenting characteristics, and duration of symptoms. Exclusion criteria were as follows: concomitant valvular or myopathic heart disease, intraventricular conduction defects, and previous coronary artery bypass graft surgery. The written informed consent was obtained from all the cases before treatment.

Electrocardiogram evaluation

The serial 12-lead ECG, recorded at admission and after PCI, were analyzed using the following criteria: 1) a Selvester QRS score; 2) maximal ST-segment elevation and depression in mm in the target lead; and 3) a total ST dislocation (ST score).

The QRS score proposed and modified by Wagner and others (21–23) was calculated manually by two observers for each electrocardiogram.

The maximal ST-segment elevation and depression in mm were measured at the J point of ECG leads with maximal ST-segment elevation and depression. The total ST score was calculated as the arithmetic sum of ST-segment elevation and depression in each lead and taken as an average value for one of three standard LV regions (regional ST score). The relevant leads for the anterior region were V1 to V4; for lateral, I, aVL, V5, and V6; and for inferior, II and aVF. The sum of averaged ST-segment dislocations in all LV regions was defined as total ST score.

Technique of percutaneous coronary interventions

The primary PCI were performed using the brachial or femoral approach and the Judkins' technique. Multiple-view coronary angiography was performed in all the patients. The degree of “culprit lesion” and coronary artery stenosis were defined as the greatest percentage reduction of luminal diameter in any view compared with the nearest normal segment (percent diameter stenosis) and was determined using the DSA computerized technique. The coronary score was calculated as the number of coronary artery segments with >50% stenosis. All patients undergoing balloon angioplasty were supplemented with stenting in cases of suboptimal PTCA results, which included dissection and/or residual “culprit lesion” stenosis of >30%.

Antegrade blood flow in the infarct artery was graded using the Thrombolysis in Myocardial Infarction (TIMI) scale (24).

Assessment of complex predictors

The TIMI risk score (19) based upon 10 various clinical risk indicators (age, diabetes mellitus, history of hypertension and angina pectoris, systolic blood pressure of <100 mm Hg, Killip class, heart rate, body weight of <67 kg, anterior ST elevation or left bundle branch block, time to reperfusion of >4 h) and TIMI risk index based on combination of a patient's age, heart rate and systolic blood pressure at admission (20) were used for prediction of short-term mortality also.

Evaluation of autopsy data

Each autopsy report was reviewed for the following: 1) the premortem coronary thrombus, and 2) the presence of significant stenosis (25). The different cardiovascular causes and modes of deaths were defined according to autopsy findings. PHF was considered as the cause of death in cases of occluded or patent infarct-related artery and typical changes of circulatory congestion in the lungs and other organs. PHF was defined as the death from pump failure even if the terminal event was associated with an arrhythmia. CR was assessed as the cause of death by detection and localizing of a rupture, and by estimation of its length and the amount of blood in the pericardial sac.

Data analysis

A. Statistical analysis approach

Data were expressed as mean \pm SD. Differences

of values between patients' groups were assessed with the one-way ANOVA followed by a post hoc Bonferroni *t* test analysis. Parameters before and after PCI were tested using the *t* test for paired samples. $P < 0.05$ was considered significant.

B. Machine learning approach

In our study, we decided not to limit to one approach in selection of informative features but to look at four of them. For selection of predictor subset, we used the method described in the book by Hall (1998) (26). In this book, the value of a subset of features is evaluated by considering the individual predictive ability of each feature along with the degree of redundancy among them. The features that are highly correlated with the outcome while having low intercorrelation were preferred. The best subset among others was selected by using two methods: genetic algorithm and backward greedy search. Also we used random decision trees (27) and linear support vector machines (15). A bootstrap procedure was used to stabilize the variable selection methods.

Results

Differences in baseline clinical characteristics

The baseline clinical characteristics are shown in Table 1. No significant differences in the initial ECG data were observed comparing all groups. More significant differences were recorded comparing circulatory characteristics among the groups. The initial

Table 1. The baseline characteristics of patients' groups

Clinical characteristic	Group 1 patients dead from PHF, n=13	Group 2 patients dead from CR, n=5	Group 3 survivors n=18	P value
Circulatory characteristics				
SAP, mm Hg	102.7 \pm 35.59	117.4 \pm 20.09	144.6 \pm 30.02	1 vs. 3, $P=0.0007$ 2 vs. 3, $P=0.035$
DAP, mm Hg	61.4 \pm 23.99	82.2 \pm 14.28	88.4 \pm 16.16	1 vs. 3, $P=0.0004$ 1 vs. 2, $P=0.045$
HR, beats per min	89.8 \pm 32.18	86.8 \pm 34.33	79.9 \pm 12.84	
ECG characteristics				
QRS score	3.84 \pm 2.91	4.0 \pm 3.24	2.64 \pm 1.96	NS
Total ST score	5.07 \pm 2.25	7.0 \pm 2.82	5.94 \pm 1.95	NS
Maximal ST \uparrow , mm	3.7 \pm 2.46	5.4 \pm 3.28	3.5 \pm 1.76	NS
Maximal ST \downarrow , mm	2.1 \pm 2.01	2.8 \pm 2.16	4.6 \pm 3.05	NS
Coronary angiography characteristics				
TIMI flow grade	0.0 \pm 0.0	0.2 \pm 0.44	0.55 \pm 0.92	NS
Coronary score	4.38 \pm 1.38	3.0 \pm 2.91	3.0 \pm 1.60	1 vs. 3, $P=0.009$

Data presented are mean value \pm SD. CR, cardiac rupture; DAP, diastolic arterial pressure; HR, heart rate; Max ST \uparrow , maximal ST elevation in mm; Max ST \downarrow , maximal ST depression in mm; PHF, progressive heart failure; SAP, systolic arterial pressure; TIMI, Thrombolysis in Myocardial Infarction; NS, not significant.

systolic arterial pressure (SAP) in the survivors was higher than in the patients who died from PHF and CR ($P=0.0007$ and $P=0.035$). The initial diastolic arterial pressure (DAP) in the survivors and patients who died from CR was the similar; however, it was higher in the survivors than in the patients who died from PHF ($P=0.0004$). There was no difference in the coronary score (CS) between the survivors and patients dead from CR, but it was greater in the patients who died from PHF than survivors ($P=0.009$). There was no difference in the TIMI flow grade and HR comparing all the patients' groups.

Differences in postreperfusion characteristics

The postreperfusion clinical characteristics are shown in Table 2. Evidently, postreperfusion characteristics showed more significant differences. Postreperfusion systolic and diastolic arterial pressures remained the lowest in the patients who died from PHF (group 1 vs. group 3, $P=0.00001$; group 2 vs. group 3, $P=0.0051$; and group 1 vs. group 2, $P=0.04$ and group 1 vs. group 3, $P=0.00001$; group 2 vs. group 3, $P=0.027$; and group 1 vs. group 2, $P=0.039$, respectively). Coronary reperfusion by TIMI flow grade was better in survivors than in patients who died from PHF or CR (group 1 vs. group

3, $P=0.0014$; group 2 vs. group 3, $P=0.0009$). The postreperfusion ECG characteristics, contrary to baseline ECG characteristics, revealed a significant difference in ST score between both the groups of dead patients. The postreperfusion ST score in the patients dead from CR (5.8 ± 3.11) was higher as compared with patients dead from PHF (3.46 ± 1.66 ; $P=0.0025$) and control patients (1.61 ± 1.09 ; $P=0.0001$). However, no changes in maximal ST \uparrow or ST \downarrow were seen between both the groups of dead patients; the maximal ST \uparrow and ST \downarrow were significantly higher in the patients who died from PHF and CR, respectively, than in survivors ($P=0.0041$ and $P=0.0002$, respectively). No more differences in other parameters were seen comparing both the groups of dead patients.

Perireperfusion clinical characteristics in different patients groups

The periprocedural changes in the circulatory characteristics (heart rate, systolic and diastolic arterial pressure), TIMI flow grade, and data of ECG were expressed by quantitative difference in the baseline and postreperfusion clinical characteristics. The circulatory characteristics showed no significant changes in all the groups during PCI. The significant changes in TIMI flow grades were equally expressed in all

Table 2. Postreperfusion clinical characteristics of patients' groups

Clinical characteristic	Group 1 patients dead from PHF, n=13	Group 2 patients dead from CR, n=5	Group 3 survivors n=18	P value
Circulatory characteristics				
SAP, mm Hg	85.5 \pm 20.63	106.8 \pm 26.21	131.0 \pm 13.89	1 vs. 2, $P=0.04$ 1 vs. 3, $P=0.00001$ 2 vs. 3, $P=0.0051$
DAP, mm Hg	53.8 \pm 18.83	72.8 \pm 20.47	85.1 \pm 8.79	1 vs. 2, $P=0.039$ 1 vs. 3, $P=0.00001$ 2 vs. 3, $P=0.027$
HR, beats per min	116.8 \pm 38.17	100.4 \pm 37.95	79.5 \pm 14.21	1 vs. 3, $P=0.0003$ 2 vs. 3, $P=0.03$
ECG characteristics				
QRS score	5.46 \pm 3.04	5.6 \pm 3.64	4.77 \pm 2.23	NS
ST score	3.46 \pm 1.66	5.8 \pm 3.11	1.61 \pm 1.09	1 vs. 2, $P=0.0025$ 1 vs. 3, $P=0.0004$ 2 vs. 3, $P=0.0001$
Max ST \uparrow , mm	2.9 \pm 1.97	4.0 \pm 2.73	1.22 \pm 1.0	1 vs. 3, $P=0.0041$
Max ST \downarrow , mm	1.15 \pm 1.28	2.6 \pm 2.3	0.61 \pm 0.6	2 vs. 3, $P=0.0002$
Postreperfusion flow in infarct related artery				
TIMI flow grade	2.0 \pm 1.22	2.2 \pm 0.83	2.94 \pm 0.24	1 vs. 3, $P=0.0014$ 2 vs. 3, $P=0.0009$

Data presented are mean value \pm SD. CR, cardiac rupture; DAP, diastolic arterial pressure; HR, heart rate; Max ST \uparrow , maximal ST elevation in mm; Max ST \downarrow , maximal ST depression in mm; PHF, progressive heart failure; SAP, systolic arterial pressure; TIMI, Thrombolysis in Myocardial Infarction; NS, not significant.

the groups ($P<0.0001$); however, a periprocedural resolution of ST score was mostly expressed in survivors ($P<0.00001$), less expressed in the group 1 ($P=0.024$), and in the patients who died from CR, there was no significant resolution at all. A statistically significant resolution of max ST \uparrow ($P<0.0001$) and max ST \downarrow ($P<0.0001$) was achieved in survivors only.

Table 3 shows significant perireperfusion changes in Δ ST-segment comparing different groups. The difference in the total ST score was the highest in the control group, as the differences in max ST \uparrow and max ST \downarrow were the lowest in the patients who died from PHF and CR, respectively.

The complex characteristics in different patients' groups

The substantial difference in the complex predictors – the TIMI risk score and the TIMI risk index –

was detected between both the groups of dead patients and survivors (Table 4); however, there were no differences in these parameters comparing both the groups of patients with different mode of death.

The identification of prognostic sets of characteristics (features) using different data mining methods of feature selection

The sets of prognostic characteristics (features) obtained by different data-mining methods are shown in Table 5. The comparison of the sets of characteristics showed that the total ST score, SAP after RT, and TIMI risk index felt into all the sets selected by different methods.

Discussion

Previous trials have showed that the myocardial infarct size (28, 29), female gender, elder age,

Table 3. Perireperfusion changes in Δ ST-segment dislocation in all patients' groups

Clinical characteristic	Group 1 patients dead from PHF, n=13	Group 2 patients dead from CR, n=5	Group 3 survivors n=18	P value
Total Δ ST score, mm	1.6 \pm 1.8	1.2 \pm 1.3	4.2 \pm 2.3	1 vs. 3, $P=0.0021$ 2 vs. 3, $P=0.01$
Max Δ ST \uparrow , mm	0.7 \pm 1.43	1.4 \pm 1.14	2.3 \pm 1.8	1 vs. 3, $P=0.025$
Max Δ ST \downarrow , mm	0.9 \pm 1.4	0.2 \pm 1.3	1.77 \pm 1.36	2 vs. 3, $P=0.04$

Data presented are mean value \pm SD. Only the statistically significant differences are shown in this table. CR, cardiac rupture; PHF, progressive heart failure.

Table 4. TIMI risk score and TIMI risk index in dead patients and survivors

Risk stratification method	Group 1 patients dead from PHF, n=13	Group 2 patients dead from CR, n=5	Group 3 survivors n=18	P value
TIMI Risk Score	9.76 \pm 2.35	9.0 \pm 2.44	5.0 \pm 2.05	1 vs. 3, $P=0.00001$ 2 vs. 3, $P=0.0006$
TIMI Risk Index	48.61 \pm 26.7	43.76 \pm 25.92	21.31 \pm 8.68	1 vs. 3, $P=0.0002$ 2 vs. 3, $P=0.002$

Data presented are mean value \pm SD. Only the statistically significant differences are shown in this table. TIMI, Thrombolysis in Myocardial Infarction.

Table 5. The most informative sets of characteristics (features) suitable for prognosis of in-hospital mode of death obtained using four different methods of feature selection (feature are presented in order of importance)

Genetic algorithm	Greedy backward search	Random decision tree	Linear SVM
SAP initial	SAP initial	<u>SAP postreperfusion</u>	<u>SAP postreperfusion</u>
<u>SAP postreperfusion</u>	<u>SAP postreperfusion</u>	DAP postreperfusion	<u>ST score postreperfusion</u>
DAP initial	DAP initial	TIMI Risk Score	SAP initial
<u>TIMI Risk Index</u>	TIMI Risk Score	DAP initial	TIMI SAP
Max ST depression initial	<u>TIMI Risk Index</u>	Total ST score initial	TIMI Risk Score
<u>ST score postreperfusion</u>	Max ST depression initial	<u>TIMI Risk Index</u>	DAP postreperfusion
Coronary score	<u>ST score postreperfusion</u>	<u>ST score postreperfusion</u>	<u>TIMI Risk Index</u>

DAP, diastolic arterial pressure; SAP, systolic arterial pressure; SVM, support vector machine.

hypertension with LV hypertrophy (1, 2, 9, 30), increased coronary injury score (10, 30, 31) are associated with increased general intrahospital mortality after RT. The circulatory disorders such as hypotension, sinus tachycardia, and left ventricle failure (7, 9, 10, 32) have been mentioned by other authors as more important predictors of early postreperfusion death. The present study dedicated for identification of clinical characteristics for the prediction of postreperfusion death is important in identification of the predictors of life-threatening complications, which determine the occurrence of death due to PHF, CR, or arrhythmia. Therefore, the specific distinctions in clinical characteristics of patients who died due to different pathologic mechanism and survivors could be informative. The prediction of a postreperfusion mode of death is underestimated, and it is an important clinical problem especially due to the existing opinion that early obtained and appreciated predictors usually enable to prevent of life-threatening complications and postreperfusion deaths (19, 20, 33, 34).

The possibilities for prediction of imminent CR in postinfarction patients have been studied by many authors previously (35–37). CR most commonly presents in elderly women with anterior STEMI and patients with the first STEMI, not preceded by angina. The primary PCI had a striking impact on reducing the incidence of ventricular septal rupture after AMI compared to elective PCI in patients who did not receive thrombolytic therapy. Advanced age, female gender, anterior infarction, and low body mass index had potentially increased the risk of this catastrophic complication after AMI in large population. However, the predictors of postreperfusion CR are not clear. Our experience confirms the opinion that successful coronary reopening of infarct-related artery assessed by TIMI flow grade is not so important for occurrence of CR as the insufficient adequacy of myocardial reperfusion expressed by ST resolution (35, 36). So, early and successful RT may be the most powerful determinant of the avoidance of this catastrophic complication after STEMI (38). The increased postreperfusion systolic and diastolic arterial pressure may be valuable for the occurrence of CR also. In our material, an increased coronary score was more common among patients who died from PHF (39).

According to our data, the complex risk predictors – the TIMI risk score and TIMI risk index – were less significant in the prediction of mode of death. The TIMI risk score derived from 10 initial clinical indicators (age, weight, heart rate, systolic blood

pressure, Killip class, diabetes mellitus, hypertension, time to RT, ST \uparrow) could be informative for the prediction of general early postreperfusion mortality after STEMI. The TIMI risk index had approximately the same prognostic value based on combination of three indicators (age, heart rate, and systolic arterial pressure). Other complex predictors used in the PURSUIT, PREDICT, and other trials (31) were not adequately tested for prediction of the postreperfusion mode of death.

The lack of an adequate or consistent classification of how patients die contributes to the current confusion over the predicting of the mode of death. A demand and propositions for more accurate classification are evident, because the postmortem examination is generally accepted as the gold standard for determining the real causes and mechanisms of death (40). A framework for the classification of the mode of death has been developed in two mortality studies: AIRE and NETWORK (25). Simon et al. (41) developed a new scheme for classifying cardiac death that defines 3 categories of underlying mechanism: primary arrhythmia, acute myocardial ischemia/infarction, and myocardial pump failure. It is possible, using these data, to classify the cardiac deaths not only based on death timing, but based on its mechanism (arrhythmia, ischemia, CR, PHF) (13, 14). In our study, we followed the classification, which provides a useful algorithm for classifying deaths by underlying mechanism. However, the correct assessment of death mechanism is dependent on the bias of the investigator, and we had difficulties with differentiation of modes of death also (14). After RT, the residual myocardial stunning, functional myocardial insufficiency, and PHF dominated in our study; however, by other authors, about 47% of deaths were classified as arrhythmic, 43% as ischemic, and 8% as due to PHF. Different interpretation of mode and cause of death worsens the identification of specific predictors of different modes of deaths. The optimized classification will minimize inconsistencies, but it does not solve the problem that the mechanism of death is difficult sometimes to assign (14), although diagnosis of death in many situations (reocclusions, reinfarctions, CR) is unchallenged.

The usage of different statistic approaches may be valuable for identification of predictors also. The machine learning methods in the evaluation of the most informative features sets were used in this study. Selection of informative features (characteristics) has been an active research area in statistics, machine learning and data mining communities. Feature selection

is the problem of choosing a small subset of features that ideally is necessary and sufficient to describe the target concept. There are several reasons for selecting only a subset of the features (characteristics):

1. It is cheaper to measure only a subset of variables;
2. Prediction accuracy might be improved through exclusion of irrelevant variables;
3. The predictor to be built is usually simpler and potentially faster when less input variables are used;
4. Knowing which variables are relevant can give insight into the nature of the prediction problem at hand (16).

When a number of features are comparatively high to a number of observations, the prognostic models and the informative feature subsets are very unstable. To reduce the number of features, we used not rough features but integrated indices (QRS score, ST score, TIMI risk index, TIMI risk score).

Simply the selection of the top-ranked features is not a good approach. A limitation of this approach is that the features could be correlated among themselves and does not form a good feature set. This suggests that redundancy of predictor set is one of the critical issues to consider.

The approaches for feature selection are very diverse and motivated by various theoretical arguments. In our study, we decided not to limit to one approach in selection of informative features but to look at four of them. For evaluation of feature subset, we used method described by Hall (26), where the value of a subset of attributes is evaluated by considering the individual predictive ability of each feature along with the degree of redundancy between them. The features that are highly correlated with the outcome while having low intercorrelation are preferred. The *backward greedy search* and *genetic algorithm* (42) show good results comparable to exhaustive search but requires significantly less computation resources. The

recent developments in feature selection revealed that classification algorithms like *random decision trees* (27) and *linear support vector machines* (15) are also efficient methods of feature search.

To stabilize variable selection, we used a bootstrap procedure. The variable selection process was repeated with subsamples of the training data, and the union of the subsets of variables selected in the various bootstraps was taken as the final stable feature subset. This joint feature subset is at least as predictive as the best bootstrap subset.

Limitations

We had no possibility to include more patients and more clinical characteristics such as angiographic TIMI count or myocardial blush grade, angiographic perfusion score, and others. In many circumstances, it may be desirable to utilize more complex risk stratification systems. However, we have shown that sometimes simple predictors may be more effective in prediction of mode of death after RT than more complex risk assessment tools.

Conclusions

1. The popular complex prognostic criteria – TIMI risk score and TIMI risk index as postreperfusion TIMI flow grade – are informative for prediction of early general mortality, but not informative for prediction of the postreperfusion inhospital mode of death.

2. The high total ST score expressed in mm and absence of adequate ST resolution during reperfusion therapy could be used as a possible predictor for occurrence of inhospital cardiac rupture.

3. Low postreperfusion systolic and diastolic arterial pressures, which remained the same or decreased after reperfusion especially in combination with high coronary score, could be predictive for occurrence of death from progressive heart failure.

Poreperfuzinių mirčių stacionariu laikotarpiu patomechanizmo prognostinių kriterijų paieška sergantiesiems ūminiu miokardo infarktu su ST pakilimu

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Raktažodžiai: perkutaninės koronarinės intervencijos, reperfuzinė miokardo infarkto terapija, poreperfuzinės mirtys stacionariu laikotarpiu, poreperfuzinių komplikacijų prognozavimas.

Santrauka. *Tyrimo tikslas.* Remiantis mirusiųjų ir išgyvenusiųjų poreperfuzinį stacionarinį laikotarpį klinikinių charakteristikų skirtumais, rasti tinkamus klinikinius kriterijus poreperfuzinių mirčių stacionare patomechanizmui prognozuoti sergantiesiems ūminiu ST elevaciniu miokardo infarktu (STEMI).

Tyrimo medžiaga ir metodai. Šios nuoseklios imties tyrimas apima 36 ligonius, iš kurių 18 mirė nuo progresuojančio širdies nepakankamumo (1 grupė, n=13) arba širdies plyšimo (2 grupė, n=5) po skubios koronarinės intervencijos, atliktos dėl ūminio STEMI. Kontrolinę grupę sudarė 18 atsitiktinai atrinktų pointerfuzinių stacionarinį laikotarpį išgyvenusių ligonių (3 grupė). Pradinis ir porekanalizacinis širdies susitraukimų dažnis (ŠSD), arterinis sistolinis ir diastolinis spaudimai (ASS ir ADS), maksimalus ST pakilimas (maks. ST \uparrow) ir nusileidimas (maks. ST \downarrow), suminis ST rodmuo balais (ST score), TIMI tėkmė ir suminis vainikinių arterijų pažeidimo laipsnis kartu su perireperfuziniais šių rodmenų skirtumais – nustatyti kiekvienam tiriamajam. Papildomai apskaičiuoti ir kompleksiniai prognostiniai kriterijai, t. y. TIMI rizikos balai (TRB) ir TIMI rizikos indeksas (TRI). Duomenų analizė atlikta naudojant įprastinę statistinę analizę ir informatyvių kriterinių kompleksų atrinkimo metodiką, pagrįstą charakteristikų (požymių) atrinkimo metodais.

Rezultatai. Palyginus trijų ligonių grupių elektrokardiografinius ir hemodinaminis kriterijus, nustatyta, kad ryškiausi skirtumai tarp grupių išryškėjo po reperfuzijos ir pagal jų perireperfuzinio pokyčio laipsnius. Kartu didžioji dalis požymių (priešreperfuziniai: ASS, ADS ir ŠSD; poreperfuziniai: ASS, ADS, ST rodmuo ir TIMI tėkmė bei perireperfuzinis ST rodmuo) patikimai skyrėsi, palyginus abi mirusiųjų grupes su išgyvenusiais (kontrolinė grupė). Kompleksinių prognostinių kriterijų (TRB ir TRI) skirtumai buvo panašūs. Mažiausiai patikimų skirtumų nustatyta palyginus abi mirusiųjų grupes. Priešreperfuzinis ADS (p=0,045), poreperfuzinis suminis ST rodmuo (p=0,0025), ASS (p=0,04), ADS (p=0,03) buvo aukštesni mirusiųjų nuo širdies plyšimo. Poreperfuzinis ST balų rodmuo ir ASS taip pat pakliuvo į informatyviausių prognostinių kriterijų rinkinius, apskaičiuotus naudojant kelis skaičiavimo mašinos apmokymo variantus.

Išvada. Remiantis poreperfuziniu suminiu ST rodmeniu ir arteriniu sistoliniu kraujo spaudimu, galima prognozuoti ankstyvosios poreperfuzinės mirties pobūdį arba patomechanizmą; pagal daugelį klinikinių požymių galima prognozuoti mirštamumą poreperfuziniu laikotarpiu stacionare.

References

1. Kubota I, Ito H, Yokoyama K, Yasumura S, Tomoike H. Early mortality after acute myocardial infarction: observational study in Yamagata, 1993-1995. *Jpn Circ J* 1998;62:414-8.
2. Stone GW, Grines CL, Browne KF, Marco J, Rothbaum D, O'Keefe J, et al. Predictors of in-hospital and 6-month outcome after acute myocardial infarction in the reperfusion era: the Primary Angioplasty in Myocardial Infarction (PAMI) trial. *J Am Coll Cardiol* 1995;25:370-7.
3. Yip HK, Fang CY, Tsai KT, Chang HW, Yeh KH, Fu M, et al. The potential impact of primary percutaneous coronary intervention on ventricular septal rupture complicating acute myocardial infarction. *Chest* 2004;125:1622-8.
4. Maynard C, Weaver WD, Litwin PE, Martin JS, Kudenchuk PJ, Dewhurst TA, et al. Hospital mortality in acute myocardial infarction in the era of reperfusion therapy (the Myocardial Infarction Triage and Intervention Project). *Am J Cardiol* 1993;72:877-82.
5. Jacobi JA, Parikh SV, McGuire DK, Delemos JA, Murphy SA, Keeley EC. Racial disparity in clinical outcomes following primary percutaneous coronary intervention for ST elevation myocardial infarction: influence of process of care. *J Interv Cardiol* 2007;20:182-7.
6. Brodie BR, Stuckey TD, Hansen CJ, Muncy DB, Weintraub RA, Kelly TA, et al. Timing and mechanism of death determined clinically after primary angioplasty for acute myocardial infarction. *Am J Cardiol* 1997;79:1586-91.
7. Krikorian RK, Vacek JL, Beauchamp GD. Timing, mode, and predictors of death after direct angioplasty for acute myocardial infarction. *Cathet Cardiovasc Diagn* 1995;35:192-6.
8. Ohman EM, Topol EJ, Califf RM, Bates ER, Ellis SG, Kereiakes DJ, et al. An analysis of the cause of early mortality after administration of thrombolytic therapy. The Thrombolysis Angioplasty in Myocardial Infarction Study Group. *Coron Artery Dis* 1993;4:957-64.
9. Mahon NG, O'Rourke C, Codd MB, McCann HA, McGarry K, Sugrue DD. Hospital mortality of acute myocardial infarction in the thrombolytic era. *Heart* 1999;81:478-82.
10. Bedotto JB, Kahn JK, Rutherford BD, McConahay DR, Giorgi LV, Johnson WL, et al. Failed direct coronary angioplasty for acute myocardial infarction: in-hospital outcome and predictors of death. *J Am Coll Cardiol* 1993;22:690-4.
11. Buxton AE, Lee KL, Hafley GE, Wyse DG, Fisher JD, Lehmann MH, et al. Relation of ejection fraction and inducible ventricular tachycardia to mode of death in patients with coronary artery disease: an analysis of patients enrolled in the multicenter unsustained tachycardia trial. *Circulation* 2002;106:2466-72.
12. Goldman S, Johnson G, Cohn JN, Cintron G, Smith R, Francis G. Mechanism of death in heart failure. The Vasodilator-Heart Failure Trials. The V-HeFT VA Cooperative Studies Group. *Circulation* 1993;87(6 Suppl):VI24-31.
13. Narang R, Cleland JG, Erhardt L, Ball SG, Coats AJ, Cowley AJ, et al. Mode of death in chronic heart failure. A request and proposition for more accurate classification. *Eur Heart J* 1996;17:1390-403.
14. Ziesche S, Rector TS, Cohn JN. Interobserver discordance in the classification of mechanisms of death in studies of heart failure. *J Card Fail* 1995;1:127-32.

15. Weston J, Elisseff A, Schoelkopf B, Tipping M. Use of the zero-norm with linear models and kernel methods. *J Mach Learn Research* 2003;3:1439-61.
16. Reunanen J. Overfitting in making comparisons between variable selection methods. *Journal of Machine Learning Research* 2003;3:1371-82.
17. Karpaliotis D, Turakhia MP, Kirtane AJ, Murphy SA, Kosmidou I, Morrow DA, et al. Sequential risk stratification using TIMI risk score and TIMI flow grade among patients treated with fibrinolytic therapy for ST-segment elevation acute myocardial infarction. *Am J Cardiol* 2004;94:1113-7.
18. Thune JJ, Hoefsten DE, Lindholm MG, Mortensen LS, Andersen HR, Nielsen TT, et al. Simple risk stratification at admission to identify patients with reduced mortality from primary angioplasty. *Circulation* 2005;112:2017-21.
19. Morrow DA, Antman EM, Charlesworth A, Cairns R, Murphy SA, de Lemos JA, et al. TIMI risk score for ST-elevation myocardial infarction: a convenient, bedside, clinical score for risk assessment at presentation: an intravenous nPA for treatment of infarcting myocardium early II trial substudy. *Circulation* 2000;102:2031-7.
20. Rathore SS, Weinfurt KP, Gross CP, Krumholz HM. Validity of a simple ST-elevation acute myocardial infarction risk index: are randomized trial prognostic estimates generalizable to elderly patients? *Circulation* 2003;107:811-6.
21. Wagner GS, Freye CJ, Palmeri ST, Roark SF, Stack NC, Ideker RE, et al. Evaluation of a QRS scoring system for estimating myocardial infarct size. I. Specificity and observer agreement. *Circulation* 1982;65:342-7.
22. Bounous EP Jr, Califf RM, Harrell FE Jr, Hinohara T, Mark DB, Ideker RE, et al. Prognostic value of the simplified Selvester QRS score in patients with coronary artery disease. *J Am Coll Cardiol* 1988;11:35-41.
23. Vaicekavičius E, Kalinauskienė E, Anužytė I, Ramanauskaitė V. Quantitative assessment of acute myocardial infarction size. Impact of early mechanical recanalization of infarct related artery. *Medicina (Kaunas)* 2002;38:990-5.
24. The Thrombolysis in Myocardial Infarction (TIMI) trial. Phase I findings. TIMI Study Group. *N Engl J Med* 1985;312:932-6.
25. Cleland JG, Erhardt L, Hall AS, Winter C, Ball SG. Validation of primary and secondary outcomes and classification of mode of death among patients with clinical evidence of heart failure after a myocardial infarction: a report from the Acute Infarction Ramipril Efficacy (AIRE) Study Investigators. *J Cardiovasc Pharmacol* 1993;22(9):S22-7.
26. Hall MA. Correlation-based feature subset selection for machine learning. New Zealand: Hamilton; 1998.
27. Breiman L. Random forests. *Machine Learning* 2001;45:5-32.
28. Miller TD, Christian TF, Hopfenspirger MR, Hodge DO, Gersh BJ, Gibbons RJ. Infarct size after acute myocardial infarction measured by quantitative tomographic 99mTc sestamibi imaging predicts subsequent mortality. *Circulation* 1995;92:334-41.
29. Henriques JP, Zijlstra F, van't Hof AW, de Boer MJ, Dambrink JH, Gosselink M, et al. Angiographic assessment of reperfusion in acute myocardial infarction by myocardial blush grade. *Circulation* 2003;107:2115-9.
30. Dzavik V, Sleeper LA, Cocke TP, Moscucci M, Saucedo J, Hosat S, et al. Early revascularization is associated with improved survival in elderly patients with acute myocardial infarction complicated by cardiogenic shock: a report from the SHOCK Trial Registry. *Eur Heart J* 2003;24:828-37.
31. Brilakis ES, Wright RS, Kopecky SL, Mavrogiorgos NC, Reeder GS, Rihal CS, et al. Association of the PURSUIT risk score with predischARGE ejection fraction, angiographic severity of coronary artery disease, and mortality in a non-selected, community-based population with non-ST-elevation acute myocardial infarction. *Am Heart J* 2003;146:811-8.
32. Wiviott SD, Morrow DA, Frederick PD, Giugliano RP, Gibson CM, McCabe CH, et al. Performance of the thrombolysis in myocardial infarction risk index in the National Registry of Myocardial Infarction-3 and -4: a simple index that predicts mortality in ST-segment elevation myocardial infarction. *J Am Coll Cardiol* 2004;44:783-9.
33. De Luca G, Ernst N, Zijlstra F, van't Hof AW, Hoorntje JC, Dambrink JH, et al. Preprocedural TIMI flow and mortality in patients with acute myocardial infarction treated by primary angioplasty. *J Am Coll Cardiol* 2004;43:1363-7.
34. Gulati M, Patel S, Jaffe AS, Joseph AJ, Calvin JE Jr. Impact of contemporary guideline compliance on risk stratification models for acute coronary syndromes in The Registry of Acute Coronary Syndromes. *Am J Cardiol* 2004;94:873-8.
35. Becker RC, Gore JM, Lambrew C, Weaver WD, Rubison RM, French WJ, et al. A composite view of cardiac rupture in the United States National Registry of Myocardial Infarction. *J Am Coll Cardiol* 1996;27:1321-6.
36. Cheriex EC, de Swart H, Dijkman LW, Havenith MG, Maessen JG, Engelen DJ, et al. Myocardial rupture after myocardial infarction is related to the perfusion status of the infarct-related coronary artery. *Am Heart J* 1995;129:644-50.
37. Yip HK, Wu CJ, Chang HW, Wang CP, Cheng CI, Chua S, et al. Cardiac rupture complicating acute myocardial infarction in the direct percutaneous coronary intervention reperfusion era. *Chest* 2003;124:565-71.
38. Keeley EC, Grines CL. Primary percutaneous coronary intervention for every patient with ST-segment elevation myocardial infarction: what stands in the way? *Ann Intern Med* 2004;141:298-304.
39. Garcia S, Canoniero M, Peter A, de Marchena E, Ferreira A. Correlation of TIMI risk score with angiographic severity and extent of coronary artery disease in patients with non-ST-elevation acute coronary syndromes. *Am J Cardiol* 2004;93:813-6.
40. Uretsky BF, Thygesen K, Armstrong PW, Cleland JG, Horowitz JD, Massie BM, et al. Acute coronary findings at autopsy in heart failure patients with sudden death: results from the assessment of treatment with lisinopril and survival (ATLAS) trial. *Circulation* 2000;102:611-6.
41. Simon SR, Powell LH, Bartzokis TC, Hoch DH. A new system for classification of cardiac death as arrhythmic, ischemic, or due to myocardial pump failure. *Am J Cardiol* 1995;76:896-8.
42. Haupt RL. Practical genetic algorithms. USA: Wiley; 2004.

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