The variable Jung as a predictor of mortality in patients with pulmonary edema


*Institute of Cardiovascular Diseases of Vojvodina, Sremska Kamenica, Serbia; †Institute for Pulmonary Diseases of Vojvodina, Sremska Kamenica, Serbia; ‡“Dr Baškot Clinic”, Belgrade, Serbia

Abstract

Background/Aim. In our Intensive Coronary Care Unit (CCU) a specific scoring system named the AMIS_NS was developed both for prediction of mortality in patients with acute myocardial infarction and for evaluation of the quality of work. One of the most important variables of the AMIS_NS system is the variable Jung which stands for the interrelationship unified mortality predictors. The variable includes all the values of systolic blood pressure, heart rate and age, without limiting values for any of these. The cut-off value is 2.08. The patients with the lower variable value account for a significantly higher mortality. Data on the actual infarction are not necessitated now for this variable. The aim of this study was to assess the significance of the variable Jung as a predictor of mortality in patients with pulmonary edema. Methods. In a 24-month period out of 2,223 patients there were 1,087 and 1,136 patients with and without acute myocardial infarction, respectively. There was the subgroup without myocardial infarction of 312 (84.1%) patients admitted with the diagnosis of pulmonary edema. The subgroup with myocardial infarction consisted of 59 (15.9%) patients who were admitted for acute myocardial infarction and pulmonary edema which developed immediately after admission or during hospitalization in the CCU. For all the patients a uniform questionnaire was fulfilled on admission. Data were put into the personal computer. The variable “Jung” was used: (systolic blood pressure/heart rate × age) × 100. Results. Regarding sex, there was no difference in mortality, so that males and females were regarded as a whole. Previous myocardial infarction was equally registered in both groups. The investigated persons had less percent of mortality and a significantly higher systemic pressure as well as higher value of the variable Jung. There was no statistically significant difference in the heart rate between the two groups. In both groups of deceased patients the variable Jung (1.5 ± 1.6) was significantly lower in respect to the survived patients (2.3 ± 2.1). Conclusion. The variable Jung is simple, highly reliable and can absolutely be used as a significant indicator of clinical status also in non-infarction patients with the acute pulmonary edema, no matter if it is caused by acute myocardial infarction or not.

Key words: pulmonary edema; mortality; heart rate; age groups; blood pressure; prognosis.

Apstrakt

Uvod/Cilj. U koronarnoj jedinici Instituta za kardiovaskularne bolesti urađen je sopstveni sistem ocenjivanja nazvan AMIS_NS, za predviđanje mortaliteta bolesnika sa akutnim infarktom miokarda i procenu kvaliteteta rada. Taj sistem je primenjiv u svim koronarnim jedinicama. Jedna od najvažnijih varijabli AMIS_NS sistema je varijabla Jung koja predstavlja međusobnu odnos sistemskog sistolnog krvišta i proizvoda srčane frekvencije i životnog doba. Granična vrednost varijable Jung je 2.08. Bolesnici sa nižom vrednošću varijabile imaju značajno viši mortalitet. Za ovu varijablu nisu nužni podaci o aktuelnom infarktu. Cilj rada bio je da se proveri značajnost varijable Jung kod neinfarktnih bolesnika sa akutnim plućnim edemom. Metode. U periodu ispitivanja od 24 meseca, od ukupno 2 223 bolesnika bilo je 1 087 bolesnika sa, a 1 136 bez akutnog infarkta miokarda. Grupu ispitanika činilo je 312 (84.1%) bolesnika sa dijagnozom plućnog edema na prijemu. Kontrolnu grupu predstavljalo je 59 (15.9%) bolesnika sa akutnim infarktom i plućnim edemom koji se razvio neposredno po prijemu ili tokom hospitalizacije u koronarnoj jedinici. Za sve bolesnike pri prijemu popunjavao se jednoobimni upitnik. Podaci su se unosili u personalni račun. Varijabla Jung je izračunavana prema formuli: (sistolni krvišni pritisak/srčana frekvencija × životno doba) × 100. Rezultati. U odnosu na pol, nije bilo razlike u mortalitetu tako da su muškarci i žene bili posmatrani kao celina. Pret-
hodni infarkt miokarda podjednako je bio zastupljen u obe grupe. Ispitanici su imali manji mortalitet i značajno viši sistemski krvni pritisak, kao i veću vrednost varijable Jung. Nije bilo statistički značajne razlike u srčanoj frekvenciji između dve grupe. U obe grupe kod umrlih bolesnika varijabla Jung (1.5 vs 1.6) bila je značajno niža nego kod preživelih (2.3 vs 2.1). 

Zaključak. Varijabla Jung se, apsolutno, može primeniti kao značajan prediktor mortaliteta kod bolesnika bez akutnog infarkta miokarda koji imaju plućni edem.

Ključne reči: pluća, edem; mortalitet; srcu, frekvencija; životno doba; grupe; krvni pritisak; prognoza.

Introduction

Out of the necessity for accurate evaluation of the patient’s current clinical state, necessary diagnostic procedures, rational treatment, assessment of the final outcome and financial costs – numerous mathematically derived scoring systems have been developed worldwide.

Practically, so far all scoring systems refer to the intensive care units (ICUs), and not to the coronary care units (CCUs). Literature indicates that there were attempts of applying various scoring systems also in CCUs for patients with acute myocardial infarction (AMI).

The most famous ICU scoring systems were: APACHE III and SAPS II. Comparison of these two scoring systems (APACHE III vs SAPSII) shows that their characteristics were: specificity 75.9% vs 72.2%, sensitivity – 39% vs.75.9% and total prediction – 84.0% vs 75.4%, respectively. Area under the ROC curve for SAPS II was 0.908. There was no data about the Hosmer and Lemeshow goodness off-life test. They proved their applicability, but they were very complicated and unpractical.

Precisely, because of the fact that there is no specific score system for CCUs, a unique scoring system was created in the CCUs of the Institute of Cardiovascular Disease of Vojvodina in Sremska Kamenica, Serbia. The scoring system was developed on 505 patients with AMI. It was used for the evaluation of outcomes in patients with AMI immediately after the admission to the CCU. We named this scoring system the AMIS_NS score – acronym for acute myocardial infarction score, Novi Sad. All mathematical models in creation of AMIS_NS have specificity of over 95%, sensitivity of over 40% and overall accurate prediction of over 90%. These mathematical results show that the presented models rank in the top of prediction models. The area under the ROC curve was 0.85. This scoring system is simple, but highly reliable from the aspect of mathematics and statistics (Hosmer and Lemeshow goodness off-life test = 0.78).

The first use of the mathematical models AMIS_NS score gave only relatively acceptable results. The number of patients with the lower score coefficient was noticed, who according to the mathematical model, were supposed to survive but they did not. The sensitivity and specificity were low. Separate analysis of the deceased patients’ records showed certain patterns among them. All the patients were elder, with low systemic blood pressure (SBP) (but not less than 80 mmHg), and higher heart rate (HR) (but not over 140/min). We found data in the literature that confirm a correlation between lower blood pressure (< 120 mm Hg) and higher heart rate (> or = 90/min) which appear to be predictors of mortality not only in cardiac patients, but also in non-cardiac patients. A combination of heart rate, blood pressure and age was not found as a single variable. We combined these variables (SBP, age and heart rate) together to form a single variable. It includes all the values of age, heart rate and SBP. We named the new variable “the variable Jung”.

Univariate and multifactorial analysis proved the variable Jung to be an important predictor of mortality in the AMIS_NS score system with the referential value of 2.08 for patients with AMI. It also gives the best proportion between sensitivity and specificity for mortality prediction. Therefore, it is one of the most significant variables of the AMIS NS scoring system.

The Variable

Jung = \frac{\text{Systolic systemic pressure}}{\text{Heart rate} \times \text{Age}} \times 100

The lower value of the variable, the greater mortality risk, while the higher value means higher survival rate. Logically, the variable as a predictor of mortality is not enough by itself. It is necessary to combine it with other risk factors.

The use of this variable significantly improves the possibility of predicting mortality with the increase of sensitivity, specificity and surface under the ROC curve.

The aim of this paper was to examine the applicability and significance of the variable Jung in the prediction of mortality among the patients who were hospitalized for the life-threatening condition – acute pulmonary edema whether or not they had AMI, as well as to prove its applicability for patients without AMI, based on sensitivity, specificity and the surface under the ROC curve.

Methods

In a 24-month period out of 2,223 admitted patients hospitalized at the CCU, 1,087 (48%) patients were treated for AMI. There were 1,136 (52%) non-infarction patients.

Out of 1,087 (48.9%) patients with AMI, 59 (5.43%) patients also had pulmonary edema.

Out of 1,136 patients without myocardial infarction 312 (27.5%) were diagnosed with acute pulmonary edema.

The target group of 371 patients with pulmonary edema were divided into two subgroups. The subgroup I without AMI consisted of 312 (84.1%) non-infarction patients with the diagnosis of pulmonary edema. The subgroup II with AMI consisted of 59 (15.9%) patients who were admitted for the AMI, and the pulmonary edema which developed immediately after the admission or during the hospitalization at the CCU. Clinical characteristics of study participants are shown in Table 1.

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As measures of central tendency the arithmetic mean was calculated as well as the standard deviation and the range of dispersion of parameters (measurements). The relations were analyzed by the suitable parametric and non-parametric tests. In order to find cut-point values, and sensitivity and specificity, ROC analyses were performed.

The basis and data processing were done using the EPI 5 and SPSS statistical program.

Results

The subgroup of patients without AMI included 312 patients with the confirmed pulmonary edema. Ischemic edema was the most frequent one (43.0%), followed by edema as a part of hypertensive crisis (38.2%), dilated cardiomyopathy (8.5%), valvular diseases (6.9%) and edema with undefined etiology (3.4%).

The subgroup of patients with AMI contained all edemas that were solely of ischemic origin.

Previous myocardial infarction was equally represented in both groups. In the group without AMI it was 106 (37.2%) and in the group with AMI 20 (37.3%).

The main characteristics of patients and components of the variable Jung in all groups and in cohorts with pulmonary edema with and without AMI, are shown in Table 1.

In all the patients without AMI, and in those with AMI there was no difference in age between the survivors and deceased patients ($p = 0.746$).

There was no statistically significant difference in age in deceased patients between two subgroups without AMI, and with AMI (70.15 years vs 67.28 years, respectively; $p = 0.267$). In the group without AMI, according to age, deceased patients were significantly older (70.3 years vs 67.1 years; $p = 0.013$). In the group with AMI the deceased patients were older (67.28 years vs 66.23 years; $p = 0.623$), but the difference was not significant.

In deceased patients according gender there was no difference in age in the group with edema ($p = 0.08$) without AMI ($p = 0.209$) and with AMI ($p = 0.209$).

In all the patients without AMI and with AMI, admission SBP was significantly lower in deceased patients ($p < 0.001$).

The subgroup without AMI had a statistically significantly higher SBP than the patients from the group with AMI (161.6 mmHg vs 140.4 mmHg; $p = 0.001$). In both subgroups the admission SBP in deceased patients was significantly lower than in the survivors ($p = 0.0001$ and $p = 0.00245$, respectively).

In all the patients without AMI and with AMI, the heart rate is significantly lower in deceased patients ($p = 0.004$).

There was no significant difference in heart rate on admission in deceased patients between the two subgroups (97.89 beat/min vs 104.54 beat/min; $p = 0.370$). In the group without AMI of heart rate deceased patients was significantly lower ($p = 0.037$). In the group with AMI it was not statistically different ($p = 0.0817$).

The value of the variable Jung in all the patients without AMI, and with AMI was statistically significantly ($p < 0.001$) higher in the survived patients than in the deceased patients (2.28 vs 1.53, respectively).

Table 1

<table>
<thead>
<tr>
<th>Parameters</th>
<th>All the patients</th>
<th>The patients with pulmonary edema and without AMI</th>
<th>The patients with pulmonary edema and AMI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years), $\bar{X}$ ± SD</td>
<td>$67 ± 9$</td>
<td>$65 ± 9$</td>
<td>$67 ± 9$</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>152 (52.4)</td>
<td>35 (43.2)</td>
<td>140 (54.7)</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>138 (47.6)</td>
<td>46 (56.8)</td>
<td>116 (45.3)</td>
</tr>
<tr>
<td>Systolic arterial pressure at admission (mmHg)</td>
<td>$161 (45.4)$</td>
<td>$140 (45.3)$</td>
<td>$162 (45.3)$</td>
</tr>
<tr>
<td>Heart rate (beats/minute)</td>
<td>$111 (31.6)$</td>
<td>$108 (31.6)$</td>
<td>$108 (31.2)$</td>
</tr>
<tr>
<td>Jung’s variable, $\bar{X}$ ± SD</td>
<td>$2.28 ± 0.91$</td>
<td>$2.31 ± 0.95$</td>
<td>$2.31 ± 0.95$</td>
</tr>
</tbody>
</table>

Statistically, in the survived patients, there was no significant difference in the numeric value of the variable Jung (without AMI 2.31 and with AMI group 2.09; $p = 0.201$).

Statistically, in the deceased patients, there was no significant difference in the numeric value of the variable Jung (the group without AMI 1.49 and the group with AMI 1.63; $p = 0.383$).

Out of patients with pulmonary edema 16.6% died. Mortality was frequently higher in the group with edema and myocardial infarction (39.2% vs 12.3%).

In order to evaluate values of the created variable Jung, standard statistics indicators were used: specificity, sensitivity and surface under the ROC curve (Figures 1–3).

For ST-elevation myocardial infarction (STEMI) patients in AMIS_NS scoring system the cut-off value was: alive > 2.08 > deceased.

In this research for pulmonary edema patients the cut-off value was: alive > 1.58 > deceased.

**Discussion**

Acute cardiogenic pulmonary edema is a common medical emergency with high early mortality. Initial clinical assessment would benefit from accurate mortality prediction.

Fifty percent of patients admitted with acute heart failure syndromes will present with acute cardiogenic pulmonary edema as the principal finding. Clinical management pathways may be improved by rapid and accurate estimation of early mortality.

Results in the incidents of death vary in the literature. Data from 3CPO score are from 1.069 patients (78 ± 10 years; 43% men; 7-day mortality 9.6%) 7.

In PEPS score, 276 consecutive patients hospitalized with acute pulmonary edema from 1998 to 2000 were retrospectively studied. During the initial hospitalization, 58 (21%) patients died and 218 (79%) patients were discharged 8.

In our study mortality rate in patients who died of pulmonary edema was 16.6%. Mortality was frequently higher in the subgroup with edema and AMI (39.2%) vs 12.3% without AMI.

Of particular interest is the strong independent predictive value of systolic blood pressure, which has been described in numerous trial data 9–13.

Lee et al. 9 developed a risk score for 30-day and 1-year mortality rate in community-based patients presenting with heart failure and found that age and systolic blood pressure were independent predictors, alongside respiratory rate, blood urea nitrogen level, hyponatremia, and a number of comorbidities.

Gray et al. 7 developed a simple risk score, 3CPO, to predict early outcome in severe acute cardiogenic pulmonary edema. Patients were elderly (78 ± 10 years), predominantly women (57%), and unwell with a marked tachycardia (112 ± 22 beats per minute), tachypnoea (32 ± 7 respiratory rate per minute), hypertension (SBP 161 ± 36 mm Hg), acidosis (pH 7.22 ± 0.09), and hypercapnia (pCO2, 7 ± 2.3 kPa) 7.

Fiutowski et al. 8 in their score system (PEPS) for pulmonary edema used calculation of common clinical diagnostic tests (electrocardiogram, blood pressure, heart rate, and white cell count) to determine in-hospital mortality risk in patients with an acute episode of cardiogenic pulmonary edema. Statistical analyses revealed that the most significant predictors of in-hospital mortality were acute myocardial infarction, heart rate greater than 115/beats/min, SBP of 130 mmHg or less, and white blood cell count greater than 11,500/mm³ on presentation 8.

Fonarow et al. 10 reported that blood pressure above 115 mmHg was the best cut-point to indicate lower risk.

The literature proves the significance of low SBP, especially when followed with high heart rate. This combination was proved by multifactorial analysis to be an independent
mortality predictor, both for intra-hospital and long term follow-up. In our study, SBP was less than 110 mmHg within all the groups of deceased patients, while heart rate was over 100 beat/min. These facts correlate with the literature. Measurement of SBP, apart of heart rate, is one of the basic examinations of each patient, especially a life threatening patient. SBP gives information about left myocardial pump function. This is of vital essence for patients not only with AMI but also with heart failure. Together with heart rate it is one of the key elements that determine: level of urgency, type of required intervention and adequate medication. SBP lower than 80 mmHg leads to cardiac shock with all its fatal implications.

In almost all studies, predictors of mortality are: SBP (overall accepted as the most important), age and heart rate. In the literature all data confirms the importance of age as risk factor of both morbidity and mortality. Old age is a significant risk factor of atherosclerosis and its complications.

In 1989 Assmann and Schulte stated: “With today’s level of knowledge, we have to treat the age as an independent and unchanged variable, but as we learn more about impact of genetic on risk of early appearance of atherosclerosis, maybe it will be proved that significance of age actually varies depending on genetic constitution”.

Although it is accessed as an independent risk factor, age of life is in correlation with other risk factors, including hyperlipoproteinemia, hypertension and diabetes which prevalence increase with aging.

Univariate analysis results in AMIS_NS score system prove age to be an important and reliable predictor of mortality. Multivariate analysis results in AMIS_NS score system prove age to be an important and reliable predictor of mortality. In this research, evaluation of only heart rate did not confirm it as a predictor of mortality, opposite to data from the literature.

Predictors of mortality: SBP, age of life and heart rate are quoted as sole or in combination of two factors of prediction. However, until this day these factors have not been unified together as mortality predictor.

We unified the mentioned predictors, not limiting values for any of these. The formula includes all the values of age, heart rate and SBP. Age of life represents not only mathematical but also biological age of patient. In this way it includes not only genetic predispositions but also social and health changes gained through time. SBP represents pump function of the left ventricle – the ability of the heart muscle to sustain the volume of strike. Together with heart rate, it represents the compensatory mechanism.

Applying the variable Jung also in the patients with pulmonary edema gives acceptable values of sensitivity 62.1%, specificity 83.2% and surface under the ROC curve 0.727, the positive prediction value = 47% and negative prediction value = 90%; cut-off is 1.58.

The presented statistical parameters prove applicability of the variable Jung as a valid indicator of clinical status of patients with pulmonary edema and without AMI, immediately after admission.

Within the AMIS_NS score the cut-off variable Jung was 2.08. The patients with lower variable value had higher risk of mortality, while the patients with a higher variable value were more likely to survive.

In this research the cut-off value was 1.58, which precisely shows its limitations. One cut-off cannot be considered as universal – its value will most likely be different for each disease. Therefore it is necessary to calculate the benchmark cut-off for a specific disease and after that it can be used in routine practice. The variable is not a score for a specific disease, but rather an important parameter of patient’s clinical state in the given moment in time.

The variable alone is not enough to be used as an exact and independent mortality predictor. In order to be used for prediction of mortality it should be combined with other risk factors or predictors of mortality.

This variable can be used to provide an immediate assessment of the patients’ risk for mortality and guide initial management.

**Conclusion**

The variable Jung is simple, highly reliable and can absolutely be used as a significant indicator of clinical status also in non-infarction patients with acute pulmonary edema, no matter if it is caused by AMI or not.
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