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Risk of perioperative death and sudden cardiac arrest: a study of 113 456 cases from the National Registry of Invasive Cardiology Procedures (ORPKI) for estimation of the perioperative prognosis

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WHAT'S NEW?

A large number of studies have identified numerous predictors of short-term mortality in patients with STEMI. The present investigation, relying on a large and verifiable national database, describes the most significant factors affecting periprocedural mortality and sudden cardiac arrest in STEMI patients comparing two statistical models (based on comorbidities as well as pre-hospital and pharmacological factors). A better understanding of these factors facilitates the preparation of the team for optimal patient care.

ABSTRACT

Background: Despite optimizing treatment of ST-segment elevation myocardial infarction (STEMI) a lot of patients die during the invasive procedure or experience sudden cardiac arrest (SCA) that complicates further hospitalization.

Aims: The aim of the study was to identify the most important risk factors leading to SCA and death in the cath lab among STEMI patients.

Methods: We used the National Registry of Invasive Cardiology Procedures (ORPKI) between 2014 and 2019. The study population consisted of 113 465 patients. Descriptive statistics,

univariate and multiple logistic regression analysis of factors affecting perioperative mortality (PM) and SCA in the cath lab were performed.

Results: Death and SCA occurred in 1549 (1.4%) and 945 (0.8%) patients, respectively. Diabetes (odds ratio [OR] 1.76; $P < 0.0001$), previous brain stroke (OR 2.26; $P < 0.0001$), prior myocardial infarction (OR 1.81; $P < 0.0001$), psoriasis (OR 1.79; $P = 0.04$) and chronic renal failure (OR 2.79; $P < 0.0001$) were the strongest predictors of PM. The occurrence of SCA was dependent mainly on diabetes (OR 1.37; $P = 0.0001$), previous brain stroke (OR 2.23; $P < 0.0001$), prior myocardial infarction (OR 1.73; $P < 0.0001$), psoriasis (OR 2.03; $P = 0.04$), chronic renal failure (OR 2.79; $P < 0.0001$). Of the pre-hospital factors, the Killip–Kimball class showed the strongest relationship with the two endpoints (OR 3.53; $P < 0.0001$ and OR 2.65; $P < 0.0001$).

Conclusions: Diabetes, previous brain stroke and myocardial infarction, psoriasis, chronic renal failure and the Killip–Kimball class were the strongest predictors of PM and SCA in the cath lab.

Key words: periprocedural mortality, risk factors, STEMI

INTRODUCTION

Out-of-hospital cardiac arrest (OHCA) remains a major clinical challenge. According to various studies survival after an OHCA ranges from 5.7 to 8.3% [1, 2].

OHCA is an acute event that can potentially affect any hospitalized patient. For the purposes of clinical care, research and practice guideline development, in-hospital cardiac arrest is most commonly defined as the loss of circulation prompting resuscitation with chest compression, defibrillation or both [3]. In-hospital cardiac arrest occurs in over 290 000 adults each year in the United States. The mean age of these patients is 66 years, 58% are men [4, 5]. The causes of the arrest are most commonly cardiac (50%–60%), whereas respiratory insufficiency accounts for 15%–40% of cases. The basic elements of treatment during in-hospital cardiac arrest include external cardiac massage, ventilation, early defibrillation, and correction of hypokalemia and hypoxia [6].

Perioperative cardiac arrest is a separate entity with its own incidence, diagnosis and treatment. The incidence of OHCA associated with ST-segment elevation myocardial infarction (STEMI) oscillates between 8 and 10% [7, 8]. In recent years, outcomes in such patients have generally improved. However, patients after an OHCA and with cardiac arrest in the catheterization

laboratory (cath lab) are at high risk of mortality despite treatment with emergent coronary revascularization and other aggressive options [9, 10].

Sweden has the most complete STEMI registry in Europe. According to the 2015 report the incidence rate for STEMI was 58 cases/100 000 per year [11]. Other European countries report the incidence rate around 43–144 cases/100 000 per year [12].

Cardiac arrest in the cath lab among STEMI patients has not been studied extensively in Poland so far. The purpose of the present study is to describe patients experiencing cardiac arrest in the cath lab based on the data from the National Registry of Invasive Cardiology Procedures (ORPKI).

PATIENTS AND METHODS

The aim of the study is to identify the risk factors that can lead to cardiac arrest and death in the cath lab among patients with STEMI in the era of the increased availability of cardiac catheterization facilities in Poland and reduced perioperative mortality (PM) rates.

Data in the ORPKI have been collected since 2004. The electronic ORPKI was launched on 1 January 2014. The database was created by the Association of Cardiovascular Interventions of the Polish Cardiac Society. At the moment the registry is coordinated by the Jagiellonian University Medical College in Krakow, collecting data from 161 catheterization labs in Poland. For purposes of analysis data from 2014 to 2019 were extracted from the database. The study population consisted of patients admitted to hospital in compliance with the guidelines of the Polish Cardiac Society and selected for invasive treatment of acute coronary syndromes with persistent ST-segment elevation. Finally, after exclusion of cases with missing data, the study group consisted of 113 465 participants. Of them, patients who died or experienced cardiac arrest in the cath lab were identified. We conducted a pooled analysis of comorbidities in patients with STEMI, predisposing factors and the medications used to treat STEMI. Initial aspirin doses were skipped in patients already taking chronic ASA therapy.

Chronic renal failure was defined in compliance with the recommendations as the presence of epidermal growth factor receptor less than 60 ml/min/1.73 m². The ORPKI registry accumulated information on cardiac arrest and sudden cardiac death, but not on their mechanism (VT/VF, asystole and pulseless electrical activity). Cardiac arrest occurred either prior to hospitalization (out-of-hospital cardiac arrest) thus qualifying the patient for invasive therapy, or during hospitalization in the cath lab. Univariate and multiple logistic regression analysis of clinical, pre-hospital and pharmacological factors affecting perioperative mortality and cardiac arrest in the cath lab was also performed. The study was carried out in accordance

with the ethical standards of the 1964 Declaration of Helsinki. All conscious patients had been informed about the invasive procedure and gave their consent before treatment. If the patient was unconscious, the decision was made by two specialists in compliance with the current recommendations in emergency situations to prevent death. The study was exempt from the bioethics committee approval as it used anonymous data from the ORPKI Registry.

Statistical analysis

Quantitative variables were expressed as median (interquartile range). Categorical variables were presented as numbers and percentages. The normality of data distribution was tested with the Kolmogorov–Smirnov test. The χ^2 test was used to test the interdependence between pairs of variables for double classifications. The Mann–Whitney test for non-normally distributed variables was used to assess within-group differences. The univariate and multiple logistic regression models were used to estimate odds ratios with 95% confidence intervals and *P*-values. The FORWARD (enter significant variables sequentially) option was used to select variables for the model. The receiver operating characteristic analysis was used to estimate the fit of a multivariable logistic regression models based on predicted probabilities of logistic models. The comparisons of Areas Under Curves (AUC) are presented in graphical form. A *Z* statistic was used for comparing AUCs. A *P*-value less than 0.05 was considered significant. Statistical analysis was performed using the Med-Calc Statistical Software 20, version 19.7 (MedCalc Software, Ostend, Belgium) [13].

RESULTS

We analyzed the ORPKI data from 2014 to 2019 and a total of 113 456 patients with STEMI selected for invasive treatment. In this group periprocedural death occurred in 1549 (1.4%) patients. Cardiac arrest during the procedure occurred in 0.8% patients. The remaining 0.6% deaths occurred in patients during the agonal state when all treatment options were exhausted. *Table S1* (Supplementary material) summarizes the prevalence of comorbidities in STEMI patients who died in the cath lab and experienced periprocedural cardiac arrest. *Table S2* (Supplementary material) shows the use of antiplatelet agents and the distribution of selected pre-hospital and pharmacological factors. PM/sudden cardiac arrest was most strongly related to a history of diabetes, prior myocardial infarction and stroke, psoriasis and a history of renal failure (Table 1). Among the pre-hospital and pharmacological factors the most significant relationship was seen when comparing perioperative mortality between patients with higher Killip–Kimball classes in whom time from onset of pain to first medical contact, time from

onset of pain to angiogram and time from first medical contact to angiogram was prolonged (Table 2). Of the pre-hospital and pharmacological factors, patients with heart failure in higher Killip–Kimball class were at increased risk of PM/cardiac arrest in the cath lab (Table 3). Analysis of two groups of factors i.e. clinical/pharmacological and procedural factors revealed higher sensitivity and specificity of the model based on the clinical factors for prediction of both perioperative mortality and cardiac arrest. Results are shown in Figure 1 and Figure 2.

DISCUSSION

Before the COVID-19 pandemic several national registries were available to explore the effect of various factors on the management of STEMI. One such example is ORPKI.

Previous research similar to ours usually estimated medium- and long-term risk [14, 15]. However, it is equally important to determine perioperative risk, especially in studies involving larger groups of patients, and lasting for many years. For instance, Siudak et al. [16] and Tokarek et al. [17] evaluated a number of factors that could affect the management of acute coronary syndromes within the context of the perioperative environment. Diabetes, chronic renal failure, prior myocardial infarction and psoriasis were the factors that were found to significantly influence perioperative outcomes.

The effect of diabetes on prognosis in STEMI patients has been very well documented in the Thrombus Aspiration in ST-Elevations myocardial infarction in Scandinavia (TASTE) trial. This randomized study had 7244 patients with STEMI. Of them, 901 subjects were diabetic. The study showed a significantly higher all-cause and one-year mortality [18]. Recently, Kim et al. [19] evaluated 4097 patients with STEMI and multi-vessel disease, diabetes, prediabetes and normoglycemia. They revealed a significantly higher mortality among patients with diabetes as compared to those with prediabetes and normoglycemia. In the present study of 113 456 STEMI patients selected for invasive treatment there was a significant relationship between diabetes and death in the cath lab and cardiac arrest during the procedure.

Chronic renal failure is a well-known factor which worsens the prognosis of STEMI. Brown et al. evaluated a total of 24 405 veterans between 2005 and 2010. In that study chronic renal failure was associated with more common myocardial infarction and higher risk of death [20]. Between 2007 and 2014 Ismail et al. [21] investigated 6563 patients from the Malaysian National Cardiovascular Disease Database — Percutaneous Coronary Intervention (NCVD-PCI). The study showed a higher cardiovascular risk in patients with diabetes (54.6%), hypertension (79.2%) and dyslipidemia (68.8%). In these groups risk of death among patients with chronic renal failure and STEMI was also higher. The present study revealed a

significantly higher risk of death in the cath lab and cardiac arrest during the procedure in patients with chronic renal failure.

Other cardiovascular events are associated with progression of atherosclerosis. Myocardial reinfarction in patients with prior STEMI is the manifestation of such progression. Fraticelli et al. [22] investigated a group of patients with STEMI in the OSCAR trial carried out between 2013 and 2017. The study population consisted of 6306 participants, including 5423 first-presentation STEMI patients and 883 individuals with previous myocardial infarction. There were no significant differences in in-hospital mortality between groups. The Feedback Intervention and Treatment Times in ST-Elevation Myocardial Infarction trial (FITT-STEMI) is another large study in STEMI patients with reinfarction. The study population consisted of 12 676 subjects. They were subdivided into four groups with accompanying cardiogenic shock and with or without out-of-hospital cardiac arrest. The reinfarction group consisted of 1378 patients. The study showed the lowest mortality in hemodynamically stable patients, and the highest death rate in patients with cardiogenic shock but without OHCA. As compared to the two groups with cardiogenic shock mortality was lower in patients with OHCA and without cardiogenic shock [23].

Another manifestation of the progression of atherosclerosis is acute ischemic stroke complicated by STEMI. Pana et al. studied 9840 patients with myocardial infarction after stroke between 2003 and 2016. Survival was measured at 1 year, between 1 and 5 years and between 5 and 10 years. The highest mortality rate was observed at one year. The prognosis of post-stroke myocardial infarction was generally poor [24]. In a large group of patients with STEMI and a history of stroke studied by Hariri et al. [25] risk of death during hospitalization was significantly higher than in patients without stroke. Similarly in a large study by Liao et al. [26], 211 (2.3%) of 9180 patients with stroke experienced myocardial infarction in hospital. Of these, 64.9% died as compared to 35.8% in the entire study group. Mortality at 1 year after stroke was 56.4% in patients with myocardial infarction as compared to 21.9% in the entire study group. In the present study of almost 113 500 patients with STEMI there was a significant relationship between periprocedural death and cardiac arrest in the cath lab in patients with a history of stroke.

Periprocedural prognosis, in this study based on the occurrence of death in the cath lab or cardiac arrest, is determined not only by conventional risk factors such as diabetes, chronic renal failure, previous myocardial infarction and stroke. New evidence shows that risk of perioperative death depends also on a history of psoriasis in patients with STEMI, however these observations are ambiguous. Siudak et al. [27] carried out a large study in 405 078 patients

who underwent coronary angiography due to acute coronary syndrome. Psoriasis was diagnosed in 1507 (0.4%) patients. In that study psoriasis was an independent predictor of increased allergic reaction. There were no differences in perioperative mortality in patients with and without psoriasis. Between 2005 and 2016 Karbach et al. [28] in a study in 3 307 703 patients with myocardial infarction of whom 9028 (0.3%) had psoriasis showed lower in-hospital mortality rates in psoriatic patients. However, these patients were on average 5 years younger than the remaining subjects. The present study carried out between 2014 and 2019 exclusively in patients with STEMI showed a significantly higher risk of perioperative death and cardiac arrest in the cath lab.

Another very important factor affecting survival and perioperative mortality is the Killip–Kimball class on admission. The index of heart failure severity in patients with acute myocardial infarction was proposed by Killip and Kimball in the 1960s [29]. Now the Killip–Kimball classification is widely used in clinical practice. Oliveira et al. analyzed 5-year mortality data for 1906 patients admitted to hospital between 1995 and 2011. The results showed a significant relationship between mortality at 5 years and the Killip–Kimball class [30]. The present study in 113456 patients confirms the significant association between PM/sudden cardiac arrest in the cath lab and the Killip–Kimball class on admission.

Some studies describe the paradoxically protective effects of smoking. It is a very interesting phenomenon. Cigarette smoking is a well-known risk factor for STEMI, however, smokers' paradox has been described in the literature. Redfors et al. [31] analyzed 10 randomized studies with STEMI patients undergoing primary PCI (n = 2564). Smokers had a lower in-hospital mortality and shorter hospital stay. The investigators ascribed this paradox to younger age of the patients and fewer comorbidities. Other investigators confirmed the smokers' paradox [32]. Diabetes is a well-known risk factor of poor outcome in patients with STEMI. A large study based on the Polish Registry of Acute Coronary Syndromes shows that diabetes increases the prevalence of pulmonary edema, cardiogenic shock, cardiac arrest, major bleeding and in-hospital mortality but has no impact on stroke or transient ischemic attack [33]. The National Emergency Medical Services Management Support System, a unique information and communication technology system, was developed to reduce the burden of ST-segment elevation myocardial infarction (STEMI) in Poland. A recent study shows that there are many differences in pre-hospital STEMI treatment between provinces in Poland [34]. These 2 studies and the ORPKI registry may provide helpful insights to improve treatment of patients with STEMI.

Summing up, the study carried out in a large group of STEMI patients selected for invasive treatment shows a significant relationship between conventional and less common (psoriasis) risk factors and PM.

CONCLUSIONS

1. Of all factors, diabetes, renal failure, previous myocardial infarction, previous stroke, psoriasis and Killip-Kimball class had the strongest influence on perioperative mortality and sudden cardiac arrest.
2. Models of logistic regression based on pre-hospital and pharmacological factors fit better than models based on comorbidities i.e. better distinguish between positive and negative cases.
3. Risk stratification based on the above mentioned most important risk factors facilitates preparation of the team for the procedure.

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Study based on retrospective registry.

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Table 1. Clinical factors affecting the occurrence of periprocedural death

Variable	Univariate (Unadjusted)		Multivariable (Adjusted) ^a	
	OR (95% CI)	P-value	OR (95% CI)	P-value
Age, years	1.05 (1.04–1.05)	<0.001	1.04 (1.03–1.04)	<0.001
Sex (male)	0.61 (0.55–0.68)	<0.001	0.83 (0.75–0.93)	0.01
Diabetes	1.76 (1.57–1.97)	<0.001	1.55 (1.37–1.75)	<0.001
Previous stroke	2.26 (1.86–2.76)	<0.001	1.58 (1.29–1.94)	<0.001
Previous MI	1.81 (1.60–2.05)	<0.001	1.88 (1.59–2.23)	<0.001
Previous PCI	1.30 (1.13–1.50)	<0.001	0.81 (0.67–0.97)	0.03
Previous CABG	1.54 (1.13–2.09)	0.01	NI	

Smoking status	0.45 (0.39–0.51)	<0.001	0.68 (0.59–0.78)	<0.001
Psoriasis	1.79 (1.03–3.11)	0.04	2.07 (1.19–3.63)	0.01
Hypertension	0.71 (0.65–0.79)	<0.001	0.52 (0.47–0.58)	<0.001
Kidney disease	2.79 (2.34–3.33)	<0.001	1.67 (1.39–2.01)	<0.001
COPD	1.33 (0.95–1.86)	0.09	NI	

^aMultivariable logistic regression, adjusting for other factors shown in the table; Significant variables entered sequentially (Forward option).

Abbreviations: CABG, coronary artery bypass grafting; CI, confidence interval; COPD, chronic obstructive pulmonary disease; MI, myocardial infarction; NI, not included; OR, odds ratio; PCI, percutaneous coronary intervention

Table 2. Clinical factors affecting the occurrence of cardiac arrest

Variable	Univariate (Unadjusted)		Multivariable (Adjusted) ^a	
	OR (95% CI)	<i>P</i> -value	OR (95% CI)	<i>P</i> -value
Age, year	1.02 (1.02–1.03)	<0.001	1.02 (1.01–1.02)	<0.001
Sex (male)	0.74 (0.65–0.85)	<0.001	0.83 (0.73–0.96)	0.01
Diabetes	1.37 (1.17–1.60)	<0.001	1.26 (1.07–1.48)	0.01
Previous stroke	2.23 (1.73–2.87)	<0.001	1.85 (1.44–2.40)	<0.001
Previous MI	1.73 (1.48–2.04)	<0.001	2.04 (1.64–2.54)	<0.001
Previous PCI	1.24 (1.03–1.49)	0.03	0.73 (0.57–0.94)	0.02
Previous CABG	1.34 (0.88–2.03)	0.17	NI	
Smoking status	0.76 (0.65–0.88)	<0.001	NI	
Psoriasis	2.03 (1.05–3.93)	0.04	2.13 (1.10–4.14)	0.03
Hypertension	0.85 (0.75–0.97)	0.01	0.71 (0.62–0.81)	<0.001
Kidney disease	1.80 (1.38–2.36)	<0.001	NI	
COPD	1.33 (0.87–2.04)	0.19	NI	

^aMultivariable logistic regression, adjusting for other factors shown in the table; Significant variables entered sequentially (Forward option).

Abbreviations: see Table 1

Table 3. Pre-hospital and pharmacological risk factors affecting the occurrence of cardiac arrest and perioperative death

Variable	Death during procedure				Cardiac arrest during procedure			
	Univariate (Unadjusted)		Multivariable (Adjusted) ^a		Univariate (Unadjusted)		Multivariable (Adjusted) ^a	
	OR (95% CI)	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value
ASA	0.57 (0.51– 0.64)	<0.001	1.19 (1.03– 1.38)	0.02	0.71 (0.61– 0.82)	<0.001	NI	
Heparin	0.80 (0.70– 0.91)	<0.001	NI		1.06 (0.88– 1.27)	0.56	1.29 (1.07– 1.57)	<0.001
P2Y12 inhibitor	0.37 (0.34– 0.41)	<0.001	0.40 (0.35– 0.46)	<0.001	0.57 (0.49– 0.65)	<0.001	0.62 (0.53– 0.72)	<0.001
GP IIb/IIIa inhibitor	1.06 (0.95– 1.18)	0.28	0.83 (0.74– 0.93)	0.01	1.23 (1.08– 1.41)	0.01	NI	
Time from pain to first contact, hours (≤12; 12–48; >48)	1.33 (1.23– 1.45)	<0.001	1.37 (1.25– 1.50)	<0.001	0.83 (0.72– 0.96)	0.01	0.85 (0.74– 0.98)	0.03
Time from pain to inflation or angiogram, hours (≤12; 12–48; >48)	1.32 (1.13– 1.54)	<0.001	NI		0.95 (0.74– 1.23)	0.70	NI	
Time from first contact to inflation or angiogram,	1.31 (1.19– 1.44)	<0.001	NI		0.83 (0.70– 0.98)	0.03	NI	

hours (≤12; 12–48; >48)								
Direct transport to cath lab	1.32 (1.18– 1.47)	<0.001	1.22 (1.09– 1.37)	0.01	1.83 (1.60– 2.08)	<0.001	1.65 (1.45– 1.89)	<0.001
Killip–Kimball Class (I–IV)	3.53 (3.39– 3.68)	<0.001	3.47 (3.33– 3.61)	<0.001	2.65 (2.52– 2.78)	<0.001	2.57 (2.44– 2.70)	<0.001

^aMultivariable logistic regression, adjusting for other factors shown in the table; Significant variables entered sequentially (Forward option).

Abbreviations: ASA, acetylosalicylic acid; GPI glycoprotein inhibitor. Other — see Table 1

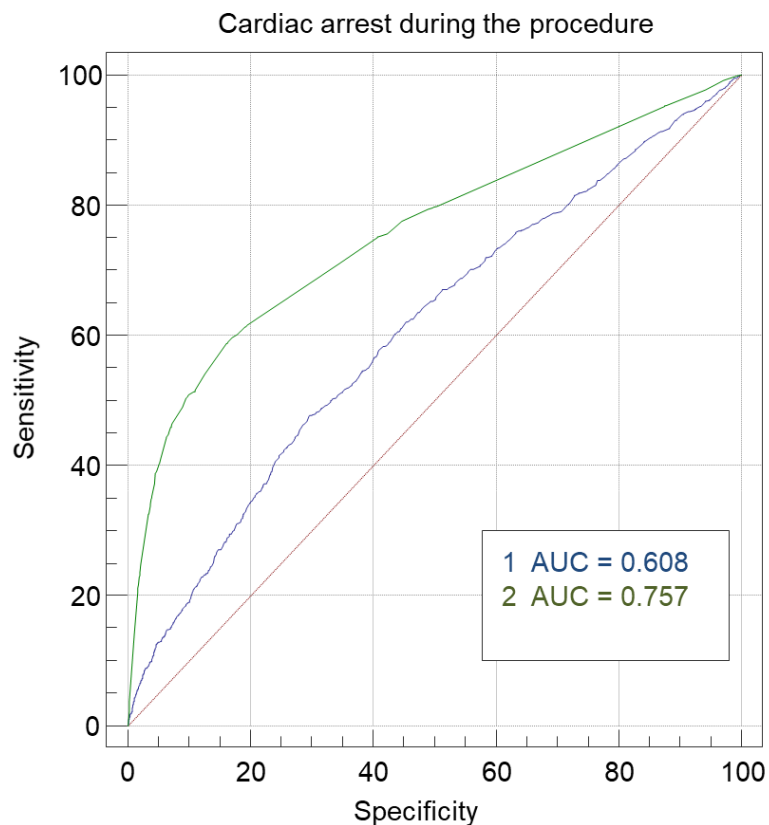


Figure 1. Pairwise comparison of ROC curves for multivariable logistic regression model for cardiac arrest during procedure based on (1) clinical factors and (2) pre-hospital and pharmacological factors.

Abbreviations: AUC, area under the curve; ROC, receiver operating characteristic

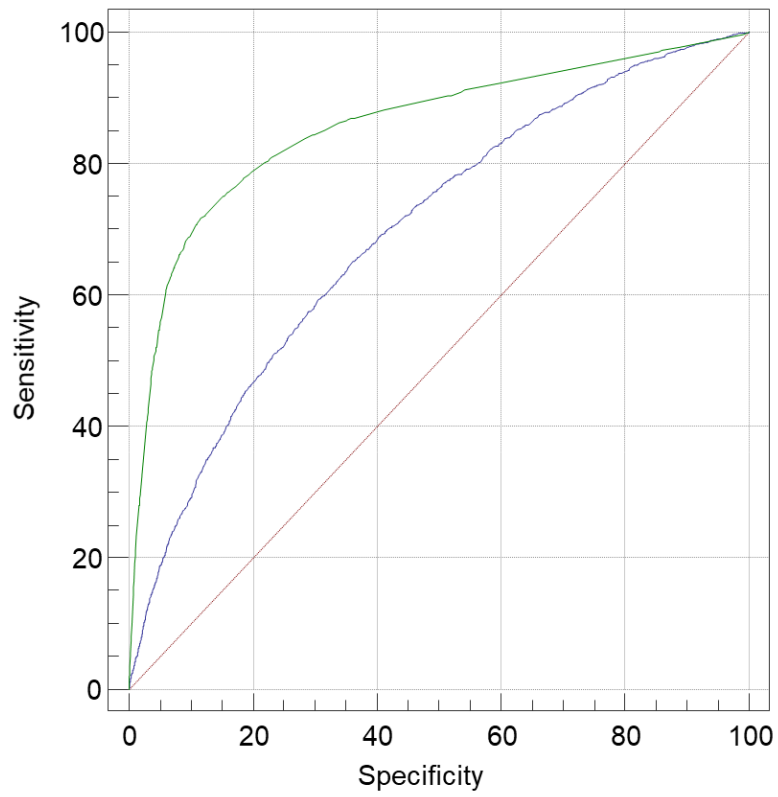


Figure 2. Pairwise comparison of ROC curves for multivariable logistic regression model for death during procedure based on (1) clinical factors and (2) pre-hospital and pharmacological factors.

Abbreviations: see Figure 1