ORIGINAL ARTICLE

# RISK INDEX TO PREDICT IMMEDIATE MORTALITY IN MYOCARDIAL REVASCULARIZATION SURGERY


## ABSTRACT

**Introduction:** The current trend is to improve the quality of life of patients treated by coronary surgery and reduce complications and resources. **Objectives:** To construct and validate a risk index to predict immediate mortality in myocardial revascularization surgery. **Method:** Development research was carried out in the Cardiovascular Surgery service of the Cardiology Center of Hospital "Hermanos Ameijeiras", from March 2012 to 2017, the sample included 340 patients. The investigation work was divided into two phases, the first one for the construction of the instrument and the second for its validation. **Results:** The logistic regression model had a good calibration given by the Hosmer and Lemeshow analysis (p = 0.914). The final score resulted from multiplying the value of each variable by its weight. The area under the ROC curve for the probability of dying was 0.902 (95% CI: 0.852-0.952). By dividing the calculated probability into three zones, it was observed that the majority of patients with immediate mortality were grouped into high risk. The area under the ROC curve for the quantitative index was 0.869 (95% CI: 0.825–0.913), showing good discrimination. The intraclass correlation coefficient for the probability-based index was 0.966 (95% CI: 0.955-0.975) and for the quantitative index it was 0.935 (95% CI: 0.913-0.952). Conclusions: The index for the prediction of immediate mortality in myocardial revascularization surgery demonstrates validity and reliability that make it a feasible and useful instrument to be applied.



***Keywords***: *Predictive mortality index, myocardial revascularization surgery, coronary surgery, mortality, risk scale, risk score.*



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## INTRODUCTION

Coronary artery disease (CAD) is the first cause of death for cardiovascular diseases worldwide[1]. In the Middle East, Latin America and the Far East, the prevalence of risk factors increases at the same rate of coronary events[2]. In 2019, 16,397 individuals died in Cuba as a result of ischemic cardiopathy[3]. Myocardial revascularization surgery (MRS) is the most common treatment option for ischemic cardiopathy, being the most frequent cardiothoracic intervention[4,5,6]. The Hospital Clínico Quirúrgico Hermanos Ameijeiras has over 50 years of experience in MRS, with over 150 interventions a year[3]. Coronary surgery implies risks, which requires planning to improve quality of life. Creating algorithms to support decision-making seeks the purpose of identifying the populations that can benefit the most[7]. Cardiologists and cardiovascular surgeons can thus predict potential adverse events and mortality related to the surgery. In the past, this risk was estimated in an intuitive and inaccurate way. At present, there are different risk indexes, including: EuroSCORE, SYNTAX, Mayo Clinic Risk Score, Parsonnet, STS and ACEF[8,9,10,11]. The most broadly used indexes are EuroSCORE II and STS, the usefulness of both has been proven in cohorts of patients treated with MRS[12].

Said risk models were not developed in Latin American populations and their application in different populations may lead to less efficiency due to regional differences, with a negative effect in decision-making and in the results of surgical procedures. In 1999 a risk model was developed in Argentina for intrahospital mortality in cardiac surgery, the Argentinean System for Cardiac Operative Risk Evaluation (ArgenSCORE), recalibrated in 2007 and later in 2009. Its application in populations with similar geographic and demographic characteristics as those for which it was developed has shown better performance than the EuroSCORE[13].

All models developed to predict mortality in cardiac surgery have limitations resulting from the specific definitions, the methodology applied, the feasibility of the calculation, the impossibility to reflect all relevant variables in morbidity and mortality or an insufficient external validation. These have been elaborated with specific populations and in different periods of time, with variables selected in contexts that differ from Cuba. Each territory and hospital should determine what scale or index is more appropriate for each specific "reality", which has led to conducting this study with the purpose of elaborating a risk index for the prediction of immediate mortality in myocardial revascularization surgery and validating it.

## METHODS

This work has been considered as development research as it consists in the elaboration and validation of a measurement instrument by the Cardiovascular Surgery Department of Hospital Clínico Quirúrgico Hermanos Ameijeiras. Patient data was collected from March 2012 to March 2017; based on such data a score was elaborated from 2019 to January 2021.

Scope: all patients with a diagnosis of ischemic cardiopathy that required surgery and were treated in this hospital, taking into consideration the indications established by the protocol and clinical practice guidelines[14].

Exclusion criteria: patients that could not be followed-up, were not willing to collaborate with the study or required combined surgery.

Sample: 340 patients treated with MRS from March 2012 to March 2017.

The study was conducted in two phases: the first consisted in the elaboration of the instrument, during which two indexes were created, and the second phase consisted in the validation of said indexes.

### Phase I: Elaboration of both quantitative indexes

Selection of variables: up-to-date literature was reviewed, including articles in books and specialized journals, Internet and PubMed, Scielo and Hinari data bases. Based on this review an instrument was elaborated with proposed variables that were submitted to the consideration of experts who were to contribute new variables for the proposed index.

A search was conducted in Hinari, Medline and Lilacs in July 2020 to identify authors with experience in cardiovascular surgery, more specifically in MRS, and investigations on prognosis, elaboration, application or validation or risk scores to predict mortality in this group. Contacts were made with expert cardiologists and surgeons of the Cardiology and Cardiovascular Surgery Institute in Havana, the Hospital Clínico Quirúrgico Hermanos Ameijeiras and other cardiology centers in other provinces, all with over 10 years of experience as specialists and researchers. As a result, 45 professionals were identified, including cardiovascular surgeons and cardiologists who, based on published studies and investigations could be rated as experts. Finally, 20 experts accepted to participate in the investigation. There was no discrepancy in the individual criterium of specialists, for which reason it was necessary to reach a consensus through a group discussion.

Upon analyzing the surveys sent to experts, the variables to be considered for the elaboration of the proposed index were the following: age over 70,

sex, hypertension, diabetes Mellitus, recent acute myocardial infarction, angina functional class IV, chronic obstructive pulmonary disease (COPD), extracardiac arteriopathy, low and moderate glomerular filtration rate (GF), left ventricular ejection fraction (LVEF) lower than 50%, incomplete revascularization, body mass index (BMI), complications during the immediate postoperative period, perioperative AMI, urgency surgery and prolonged surgical time.

Variables to predict immediate mortality for cardiac causes: death of cardiovascular etiology or related to surgery occurred after MRS up to 30 days following surgery.

### Data collection

At first the data obtained were: informed consent, general data, preoperative, intraoperative and postoperative variables and immediate mortality. Follow-up was implemented 30 days after the MRS, immediate mortality was documented by means of an interview with the attending physicians, a review of the clinical record and death certificates. This information was collected in an individual file elaborated by the authors and these data were used to create an Excel spreadsheet with items that were later used for the elaboration of the index and statistical processing in SPSS version 20.

The sample was randomly divided into two equal groups (estimation and validation), with approximately 50% of patients in each group, in such a way that the sample comprised 179 patients for the elaboration of the index and another with 161 patients for validation.

Elaboration of the index based on the probability of dying immediately: the multivariate logistic regression function with dichotomic response was used to calculate the probability of immediate mortality after myocardial revascularization surgery.

Determination of the final score: in the investigation sample and using the formula obtained, the probability of each patient dying immediately was calculated *(See Results)*.

Index and probability-of-dying zones: with the idea of the index having a more practical value, three zones were established for values limited by empirical percentiles 33.3 and 66.6 in order to divide the possible range of values into three equal zones. In this way three zones would be established, the first, from the lowest value to percentile 33.3 a zone with a very low risk of dying (<0,01), an intermediate zone between percentile 33.3 and 66.6, that would imply the intermediate risk of dying and could be called a doubtful zone or "grey area", or medium intermediate (0.01-0.04), and above percentile 66.6 high risk (>0.04), would be the zone with the highest risk of dying. By way of validation (conceptual) of these divisions, the percentage of immediate deaths was calculated for each zone and an evaluation was made to determine whether there were differences between these percentages. It was expected to find the highest frequency of deaths in the high score zone and the lowest frequency in the low score zone.

Construction of the quantitative index: the same variables used for the construction of the probability-based index were used for the construction of this index, perhaps more practical, to be used by attending physicians in the regular practice given the ease of calculation.

Scale for each variable: these variables, with the exception of BMI, were classified into dichotomic categories, a value of 1 was assigned if it was present and 0 if it was absent. Then, odds ratio (OR) results, estimated by means of the logistic regression function and rounded to whole numbers and in some cases to a decimal number, and the weights for each variable, were estimated on the basis of the importance assigned to each one.

Determination of the final score: it was found to be the summation of all values reached by each variable after having multiplied by the corresponding weight based on the importance assigned *(See Results)*.

Scales and zones for the quantitative index: the same as with the probability value, the score was calculated for each patient, and this empirical distribution was divided into three parts (terciles) by means of percentiles 33.6 and 66.7 to classify into three risk groups for each patient, low (37), medium (37-45) and high (>45).

### Phase II: Validation of both indexes

Since a truth criterion is applied (immediate mortality), the validation of indexes was elaborated with the values of both indexes, two ROC curves to assess discrimination (capacity to discriminate between immediate deaths or non-deaths). Calibration (the measure by which the estimated probability reflects the true death risk) of the logistic regression model was determined applying the Hosmer and Lemeshow statistical test. Contingency tables were built for the different risk stratifications according to the values of the two scores (risk zones) and the presence of immediate mortality variable (yes or no) and using the Bartholomew $\chi^2$ test the existence of a correlation between these two variables was determined.

Reliability: since the variables were evaluated by specialists, the most useful reliability measure is the one that measures inter-observer variability.

The reliability coefficient was obtained (intraclass correlation coefficient) based on the repeated measures ANOVA, which is useful to assess the concordance among observers for quantitative variables. This coefficient was obtained for the proposed index. The score was calculated independently by two specialists.

Ethical considerations: the results of the study will be used for scientific purposes without disclosing data that would affect the patient´s privacy. The Helsinki declaration for research involving human subjects was observed[15].

## RESULTS

### Phase I: Construction of both quantitative indexes

#### Index based on the probability of immediate death calculated by the logistic regression model

The estimated logistic regression model had a good calibration (the predicted probability of dying matched the observations) given by the results of the Hosmer and Lemeshow statistical analysis (p= 0.914).

The probability of dying immediately calculated for each patient for said function was an indicator to predict said event and therefore is be given a value from 0 to 1. (Estimated logistic regression equation).

**Estimated logistic regression equation**

P (y=immediate mortality) 1/1+ exp-(4.230+2.021× age+0.682× gender-0.077× HTA+1.065× DM-0.751× recent IMA-0.395× functional class IV with angina+0.939× EPOC+0.317× extracardiac arteriopathy-1.6592× low to moderate GF +1.057× LVEF >50 %-0.639× type of myocardial revascularization+2.147× postoperative complications +2.264×perioperative AMI+0.017× BMI-1.221× prolonged surgical time+1.115× emergency surgery.

#### Quantitative index

It was created with the same variables described in the previous index, weighted by their respective odds ratios (OR), estimated by the logistic regression function and rounded to whole numbers and in

**TABLE 1.** Variables according to their coefficient of variation, categories and weight

| VARIABLES | CATEGORIES | VALUE | WEIGHT ($W_i$) |
|---|---|---|---|
| Age >70 years | Yes | 1 | 8 |
| | No | 0 | |
| Sex | Male | 0 | 2 |
| | Female | 1 | |
| Hypertension | Yes | 1 | 1 |
| | No | 0 | |
| DM | Yes | 1 | 3 |
| | No | 0 | |
| Recent AMI | Yes | 1 | 1 |
| | No | 0 | |
| Functional class IV angina | Yes | 1 | 1 |
| | No | 0 | |
| COPD | Yes | 1 | 3 |
| | No | 0 | |
| Peripheral arteriopathy | Yes | 1 | 1 |
| | No | 0 | |
| Low to moderate GFR | Yes | 1 | 0.2 |
| | No | 0 | |
| LVEF <50 | Yes | 1 | 3 |
| | No | 0 | |
| Incomplete revascularization | Yes | 1 | 1 |
| | No | 0 | |
| BMI | Quantitative | | 1 |
| Complications in the immediate postop | Yes | 1 | 9 |
| | No | 0 | |
| Perioperative AMI | Yes | 1 | 10 |
| | No | 0 | |
| Emergency surgery | Yes | 1 | 3 |
| | No | 0 | |
| Prolonged surgical time | Yes | 1 | 0.3 |
| | No | 0 | |

AMI: acute myocardial infarction, LVEF: left ventricle ejection fraction, FC: functional class, GF: glomerular filtration, DM: diabetes mellitus, HTA: hypertension, BMI: body mass index, ST: surgical time.

some cases to a decimal number. The final score was the result of multiplying the value of each variable by the number corresponding to its weight, as shown in *Table 1*.

## Phase II: Validation of both indexes

### Index based on the probability of immediate death calculated by the logistic regression model

The area under the ROC curve for the probability of dying immediately after myocardial revascularization was 0.889 (95 % CI: 0.835-0.944), *(Graphic 1)*.

### Division into three zones according to the immediate death probability, calculated by the logistic regression model

When dividing the probability, calculated by the logistic regression model in three zones according to percentiles 33.6 and 66.7, it was observed that most immediate mortality patients were in the high-risk group, represented by 89.3%, and none had been classified as low risk. These differences were significant (89.3 % vs 28.2 %) p<0.001 *(Table 2)*.

The area under the ROC curve for the quantitative index was 0.856 (95 % CI: 0.801-0.911) which shows good discrimination between patients that die immediately and those who do not *(Graphic 2)*.

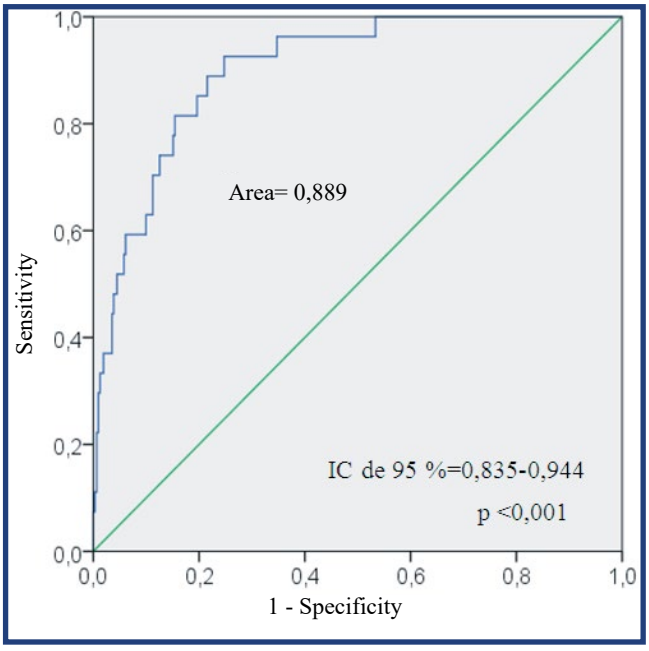
When dividing the quantitative index score into three zones based on percentiles 33.6 and 66.7, it was observed that most of the patients that died immediately had been classified as high-risk, represented by 82.1% and none had been classified as low risk. These differences were highly significant, 82.1% vs 25.3 %), *(Table 3)*.

### Reliability

As can be observed in *Table 4*, the intraclass correlation coefficient for the index based on probability was 0.966 (95% CI: 0.955-0.975) and for the quantitative index it was 0.935 (95% CI: 0.913-0.952).

## DISCUSSION

The impact of cardiovascular risk factors vary according to age[16]. This is compatible with the results of this investigation, in which the weight of the different variables is presented in individuals older than 70 years old. Rocha *et al.*[17] described higher mortality and complication rates in patients older than 70 years old treated by MRS.




**GRAPHIC 1.** Area under the ROC curve according to the probability of immediate death index calculated by the logistic regression model

**TABLE 2.** Distribution of patients by category of index risk for the probability of immediate death calculated by the logistic regression model

| RISK | IMMEDIATE MORTALITY | | | | TOTAL | |
|---|---|---|---|---|---|---|
| | Yes | | No | | | |
| | Number | % | Number | % | Number | % |
| Low (<0.01) | 0 | 0.0 | 110 | 35.3 | 110 | 32.4 |
| Medium (0.01-0.04) | 3 | 10.7 | 114 | 36.5 | 117 | 34.4 |
| High (>0.04) | 25 | 89.3 | 88 | 28.2 | 113 | 33.2 |
| Total | 28 | 100 | 312 | 100 | 340 | 100 |

Bartholomew Chi-Square test p<0.001.

**GRAPHIC 2.** Area under the ROC curve according to the quantitative index for immediate mortality

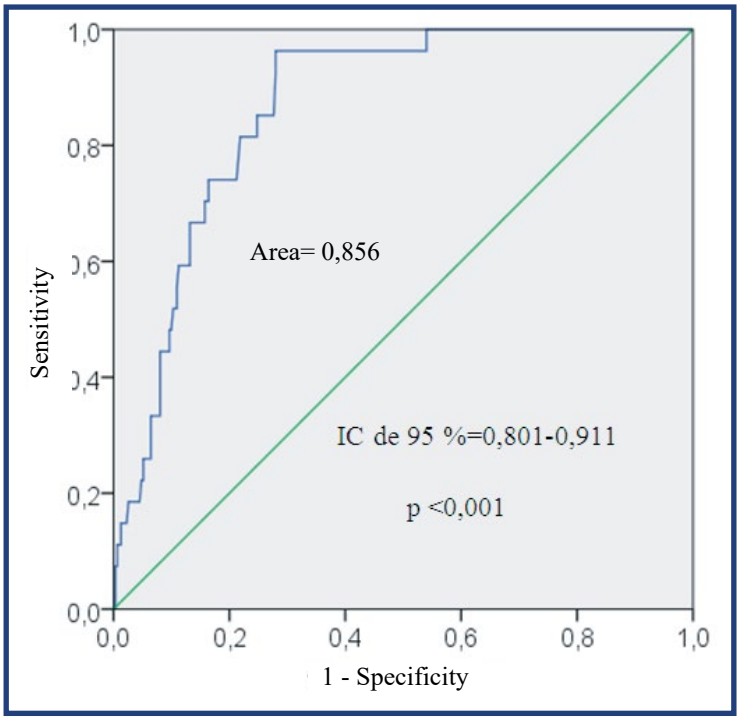



**TABLE 3.** Distribution of patients by risk category of the quantitative index for immediate mortality

| RISK | IMMEDIATE MORTALITY | | | | TOTAL | |
|---|---|---|---|---|---|---|
| | Yes | | No | | | |
| | Number | % | Number | % | Number | % |
| Low (<37) | 0 | 0.0 | 103 | 33.0 | 103 | 30.3 |
| Medium (37-45) | 5 | 17.9 | 130 | 41.7 | 135 | 39.7 |
| High (>45) | 23 | 82.1 | 79 | 25.3 | 102 | 30.0 |
| Total | 28 | 100 | 312 | 100 | 340 | 100 |

Source: clinical record, Bartholomew Chi-Square test : p<0.001.

**TABLE 4.** Intraclass correlation coefficient for the two scores or indexes

| INTRACLASS CORRELATION COEFFICIENT | POINT ESTIMATION | IC DE 95 % | P |
|---|---|---|---|
| Index (probability) | 0.966 | 0.955-0.975 | <0.001 |
| Quantitative index | 0.935 | 0.913-0.952 | <0.001 |

Prolonged ECC time may contribute to hemolysis, blood loss and need for transfusion[17]. Perioperative myocardial infarction (pAMI) after an isolated MRS is associated with poor prognosis[18]. Rao *et al.*[19], identified in the MRS postoperative period, LVEF <20%, female sex, diabetes, age > 70 years, recent AMI and multivessel disease as independent predictors of mortality, similar findings as this study. Postoperative infection and renal lesion were associated to higher mortality in the Brazil study[20]. The results were equivalent to those of this investigation, where complications presented a high weigh. Dessotte *et al.*[21] found that mortality in MRS was closely related to age, sex and comorbidities, similar variables as that of the score created in the investigation. In turn, Lopez *et al.*[22] in the Hermanos Ameijeiras study, concluded that the variables that kept an independent relation with immediate mortality were: longer surgery time, low glomerular filtration and complications, where the possibility of dying increased by approximately 16 times. These results match with the variables that had the greatest weight to predict mortality in this study and greater importance in the created score.

### Validity

The ROC curve is used to assess the prognostic (or diagnostic) capacity of a quantitative indicator[23]. For the scale proposed in its two variants (reduced and extended), the criterium of truth is death. The validity of the index may be considered highly acceptable

given the results of the ROC curve elaborated with the application of immediate mortality as a criterium of truth, since areas between 0.7 and 0.8 are considered acceptable for indexes of this type. In the case of the two indexes created in this research, the areas under the curve were significant p<0,001and are very good. One area with good capacity to discriminate between living and dead individuals must be 0.80 or higher, it is to be noted that the lower limits of the 95% CI of the two areas are very distant from 0.5, that is the value of said curve for non-discrimination[22,24,25,26]. Thus, the discrimination capacity of both indexes to predict immediate mortality in this study was very high. The ArgenSCORE presents good discrimination power for mortality and capacity to assign risk by showing an excellent relation between observed and predicted mortality[13]. Similar characteristics as for the indexes created in this study that are only applicable to patients treated by MRS. Studies[14,27] indicate that the EuroSCORE II has shown good general capacity to differentiate between dead and live patients with an area under the curve greater than 0.792 (95% CI, 0.773-0.811). In the indexes created as part of this investigation for MRS, the area under the curve is much greater, which indicates that its discriminatory and predictive capacity is higher.

### Reliability

When there are scales that give rise to continuous variables (or that may be considered as such), the appropriate index to measure concordance among observers is the intraclass correlation coefficient (ICC). This coefficient indicates which part of the total variance of the index observations obtained is due to the sample; when it is high (close to 1 or 100%), it is assumed that the variation among observers is low, since there are only two sources of variation: among subjects and among observers[28,29]. The values obtained for the intraclass correlation coefficient, both in the estimation sample as in the validation, may be considered highly satisfactory in terms of the concordance between the two specialists, as values above 0.75 have been rated as excellent by authors like Casado *et al.*[30], Fleiss *et al.*[31] and Rosner[32]. Other experts on the topic have published that values above ICCI are considered adequate[33]. In this way, according to this criterium, the value obtained in this study is highly acceptable.

## CONCLUSIONS

An instrument is built with two variants: an index based on the probability of dying immediately and another, quantitative and practical and applicable in the context of coronary surgery. Both indexes are valid and reliable for the prediction of immediate mortality after myocardial revascularization surgery, which means that they are feasible and useful when applied.

**Conflicts of interest**
The authors have no disclosures to declare.

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