New Prognostic Score for Stable Coronary Disease Evaluation

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Abstract

Background: The need to improve the exercise testing accuracy, pushed the development of scores, whose applicability was already broadly recognized.

Objective: Prognostic evaluation of stable coronary disease through a new simplified score.

Methods: A new score was applied in 372 multivessel coronary patients with preserved ventricular function, 71.8% male, age: 59.5 (± 9.07) years old, randomized to medical treatment, surgery (CABG) or angioplasty (PTCA), with 5 years of follow-up. Cardiovascular death was considered the primary endpoint. Non-fatal myocardial infarction, death and re-intervention were considered for a combined secondary endpoint. The score was based on an equation previously validated, resulting from a sum of one point for: male gender, infarction history, angina, diabetes, insulin use and one point for each decade of life after 40 years old. Positive exercise testing summed one additional point.

Results: Thirty six deaths was observed (10 in group PTCA, 15 in CABG and 11 in the clinical group), p = 0.61. We observed 93 combined events: 37 in PTCA group, 23 in CABG and 33 in the clinical group (p = 0.058). 247 patients presented clinical score ≥ 5 points and 216 ≥ 6 points. The cutoff point ≥ 5 or ≥ 6 points identified higher risk, p = 0.015 and p = 0.012, respectively. The survival curve showed a different death incidence after the randomization when score reached 06 points or more (p = 0.07), and a distinct incidence of combined events between the patients with score < 6 and ≥ 6 points (p = 0.02).

Conclusion: The new score was consistent for multiarterial stable coronary disease risk stratification. (Arq Bras Cardiol 2011;96(5):411-419)

Keywords: Exercise test; coronary disease; angina *pectoris*; prognosis.

Introduction

Even with advances in medicine, exercise testing (ET) with its low cost, security and easy applicability is recommended by the American guideline[1] as the first procedure to be performed in patients with coronary artery disease (CAD). Thus, maximizing the information obtained in the ET is of paramount importance and the need to improve its accuracy, determined the development of scores, widely recognized in the scientific literature[2-9].

For a more didactic approach of CAD, these scores were classified as: pretest, posttest, simplified, multivariate, diagnostic or prognostic. In a pre-test score, only clinical variables are analyzed, incorporating parameters of ET is defined as a post-test score[6].

The pre-test scores include: Diamond-Forrester[2], Morise and Jalisi[3], Froelicher et al[4] and Hubbard et al[10], among others.

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This preliminary probabilistic analysis is recommended by the American guideline[1] on ET.

The major post-test scores include: Mark et al[7], Raxwal et al[8], Morrow et al[11], Froelicher et al[4], Morise et al[3], Do et al[9], Morise et al[6], Detrano et al[12], Lu et al[13], Villella et al (GISSI 2)[14], Koide et al[15], Hollenberg et al[16].

Scores based on multivariate equations have complex formulas, which derive simplified scores whose calculations involve the simple sum of points.

Diagnostic scores are intended to estimate the probability of CAD and may have predictive value when performing the estimation of severe disease (triple vessel or pattern or left coronary artery lesion). Prognostic scores are well suited for risk assessment, especially of cardiovascular death or nonfatal myocardial infarction.

The prognostic score most widely used is the one by Mark et al (Duke)[17], and although it is widely validated, it does not sort properly asymptomatic, elderly patients, patients after coronary artery bypass surgery (recent) and recent post-myocardial infarction. Moreover, it is composed exclusively of ET data, its results and classification into risk categories are complex and difficult to memorize.

A simplified clinical scoring system was devised by Hubbard et al[10] with diagnostic purposes, and subsequently validated[18] for prognostic analysis of CAD. However, this score does not include documentary evidence of ischemia in its composition, since it impacts the prognosis of patients with coronary artery disease.

Aiming to provide a more complete and objective risk stratification of patients with stable coronary artery disease, we propose a new post-test score, which includes the result of ET with the score parameters of Hubbard et al[10].

Methods

The study was based on a retrospective analysis of data prospectively collected from the study (MASS-II) Hueb et al[19] with 05 years of follow up. MASS refers to the initials of Medicine, Angioplasty or Surgery Study, whose aim was to make a random evaluation of the treatment of patients with stable multivessel coronary artery disease and preserved ventricular function. The study design, selection criteria and randomization procedures were previously published[20]. The study was approved by the scientific and ethics committee, and all the patients signed an informed consent. All ET were performed on a treadmill Fukuda Denshi STAR ML- 8000, with 15 simultaneous leads and Bruce[21] protocol.

Initially, we selected 611 patients, of which 18 patients did not undergo ET for social reasons, 58 had an inconclusive ET (presence of left bundle branch block, atrial fibrillation and left ventricular hypertrophy) and in 163 patients, the examination was considered ineffective for failing to achieve submaximal heart rate.

Thus, the final sample included 372 patients, all with coronary angiographic confirmation of double or triple vessel disease and preserved left ventricular function, with 267 men (71.8%), with a mean age of 59.5 (± 9.07) years, distributed into three groups: transluminal coronary angioplasty (PTCA) 34.4%, coronary artery bypass grafting (CABG) 34.9%, and clinical treatment (CT) 30.6%.

The study design allowed patients to shift between the different treatment groups based on the occurrence of symptoms at any time of the study. There was no difference in the types of drugs among the three groups.

The selection criteria were:

1. Stable angina.

2. Normal left ventricular ejection fraction (LVEF), as assessed by Doppler echocardiography using the area-length method.

3. Angiographic confirmation of double or triple vessel CAD, with documentation of luminal obstruction of at least 70%, considering only the main coronary branches.

Non-inclusion criteria:

1. Valvular Heart Diseases.

2. Left ventricular aneurysm.

3. Left ventricular dysfunction.

4. Previous cerebrovascular accident.

5. Limitation of morphological analysis for definition of myocardial ischemia on electrocardiogram: syndrome of ventricular pre-excitation, left bundle branch block and other intraventricular conduction abnormalities, left ventricular hypertrophy, cardiac pacing, etc.

6. Physical disability of any kind.

Simplified clinical score or Hubbard score

The score of Hubbard et al[10] was validated retrospectively in a consecutive and symptomatic population investigated for coronary artery disease through myocardial scintigraphy and coronary angiography within 6 months. Through logistic regression analysis, we selected five variables composing a score of 5 points that provided estimates of severe coronary artery disease, demonstrating that disease severity increases with the score.

This score results from the sum of 1 point for each parameter: male gender, history of myocardial infarction and/or Q waves on ECG, typical angina, diabetes, insulin use and scores according to age. Up to 39 years, points are not added, from 40 to 49, 1 point is added, 50 to 59 years, 2 points, 60 to 69 years, 3 points, 70 to 79 years, 4 points and ≥ 80 years, 5 points.

The score ranges from zero to 10 points, estimating the probability of coronary artery disease in 3 groups: high (> 5 points), intermediate (equal to 5 points) and low (< 5 points).

Development of the new score

The new score was based on the simple sum of the variables of Hubbard et al[10] score, also incorporating the results of the ET. When the ET was positive, 1 point was added. Negative ET did not determine additional score. Thus, the total score of the new score ranged from 0 to 11 points as illustrated in Table 1. The cutoff value for high-risk events and death was 6 points, after examining the survival curve.

A positive test was considered the presence of ST segment depression ≥ 1 mm, horizontal or downward morphology, during or after exercise, and the magnitude of the gap was measured at 80 ms from J point; or presence of ST segment elevation ≥ 1.0 mm in leads without pathological Q waves, following the recommendations of the guidelines on ET[1,22].

The positive result was taken as documentary evidence of myocardial ischemia, adding a new point on the prognostic score. The negative result was defined as absence of documented myocardial ischemia and no additional prognostic value in the score.

Statistical analysis

The association between the new score and each of the outcomes was analyzed by the Cox regression[23], to identify high-risk subgroups. The cardiovascular survival curve was generated according to the Kaplan-Meier method[24] and the Log-Rank test was used to compare these survival curves. For all the analyses, a $p < 0.05$ was considered statistically significant.

Results

Out of the 372 patients studied, 156 patients had a history of myocardial infarction, 334 had angina class II, 137 (36.8%) were diabetic, and 16 (0.11%) using regular insulin.

Table 1 - Variables of the new score with the corresponding scores

Variables	Score
Sex	
Female	0
Male	1
History of myocardial infarction	
No	0
Yes	1
Angina *pectoris*	
Atypical	0
Typical	1
Diabetes mellitus	
Absent	0
Non-insulin-dependent	1
Insulin-dependent	2
Age group	
< 40 years	0
40 to 49 years	1
50 to 59 years	2
60 to 69 years	3
70 to 79 years	4
At or older than 80 years	5
Stress test	
Negative	0
Positive	1

During the total follow-up, there were 29 episodes of non-fatal myocardial infarction, of which 11 in the PCI group, 6 in the CABG group and 12 in the CT group; this difference between the groups was not significant (p = 0.21).

Regarding the need for CABG after randomization, there were 06 cases in the PCI group, 2 cases in the CABG group and 16 cases in the CT group, this difference between groups was statistically significant (p = 0.001).

The need for CABG after randomization, there were 18 cases in the PCI group, 03 cases in the MR group and 04 cases in the CT group, this difference between groups was statistically significant (p = 0.001).

We observed 36 deaths during follow-up, 10 in the PTCA group, 15 in the CABG group and 11 cases in the CT group (p = 0.61). The death rate after randomization occurred in 10 patients with score < 6 points and in 26 patients with score ≥ 6 (p = 0.07).

Total combined events was 93, with the following distribution between the groups: 37 in the PTCA group, 23 in the CABG group and 33 in the CT group, with a marginally significant difference (p = 0.058). The incidence of combined events after randomization was observed in 34 patients with score < 6 points and in 59 patients with score ≥ 6 (p = 0.22).

When assessing age for different groups, there was no significant difference (p = 0.73), with a mean age of 59.75 ± 9.5 years for the PCI group (127 patients), 59.97 ± 8.4 years for the CABG group (130 patients), 59.08 ± 9.3 years for the CT group (115 patients).

With regard to sex, a score below 06 points was observed in 97 men and 59 women. Score ≥ 06 points was observed in 169 men and 47 women.

The need for CABG after randomization occurred in 8 patients with score < 6 points and in 26 patients with score > 6 (p = 0.37).

The need for PTCA after randomization occurred in 12 patients with score < 6 points and in 13 patients with score ≥ 6 (p = 0.52).

The analysis for survival curve showed that there was a marginally significant difference in the incidence of combined events for patients with a score of Hubbard < 5 or ≥ 5 points (p = 0.062) (Figure 1).

When we assessed the incidence of combined events for the new score, there was a statistically significant difference (p = 0.02) among patients with scores < 6 and ≥ 6 points, as shown by their comparative survival curves of Figure 2.

The incidence of cardiovascular death was higher in patients with scores ≥ 5 points by the Hubbard's score (p = 0.015), figure 3. The difference in the incidence of death was more significant among patients with scores < 6 and ≥ 6, p = 0.004, Figure 4.

Comparing the two scores, it was observed that 31 patients were classified as high risk by the Hubbard's score, but considered with low risk by the new scoring system. No individual at low risk by the Hubbard's score was classified as high risk in the new scoring system, as illustrated in Table 2. The difference between the risk rating between scores was considered statistically significant (p = 0.001). Out of all patients analyzed, 247 (66.4%) had a score of Hubbard ≥ 5 and 216 points (58%) ≥ 6 points, as shown in Table 2. The cutoff ≥ 5 or ≥ 6 points identified individuals of higher death risk with p = 0.015 and p = 0.004, respectively.

Regarding the primary outcome, the survival curve analysis showed no difference among the three treatment groups, Figure 5.

Regarding the incidence of death and Hubbard scores ≥ 5, there were 15 deaths in the PCI group, 12 in the CABG group and 10 in the CT group (p = 0.59), while using a score < 5 points, we observed 1 death in the PTCA group, 5 in the CABG group and 3 in the TC group (p = 0.176).

Regarding the incidence of death and new score ≥ 5, there were 11 deaths in the PTCA group, 7 in the CABG group and 6 in the CT group (p = 0.4), while using the new score < 6 points, we observed 1 death in the PTCA group, 6 in the CABG group and 3 in the TC group (p = 0.163).

As for the combined events in patients with Hubbard scores ≥ 5 points, there were 33 events in the PTCA group, 13 in the CABG group and 23 in the CT group, with a significantly reduced incidence of events in the CABG group (p < 0.001). Analysis of combined events in the patients with Hubbard

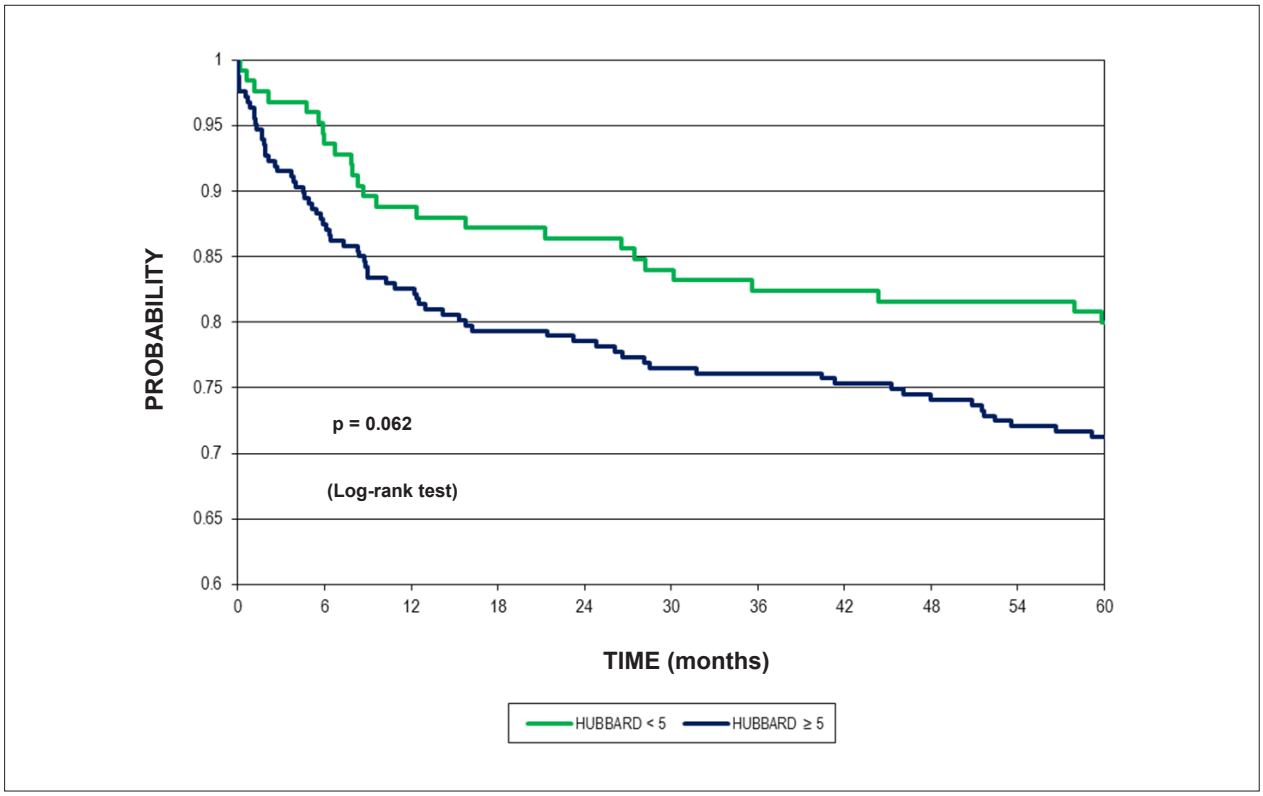

Figure 1 - Comparison of the combined event rate among patients with Hubbard score < 5 and ≥ 5 points.

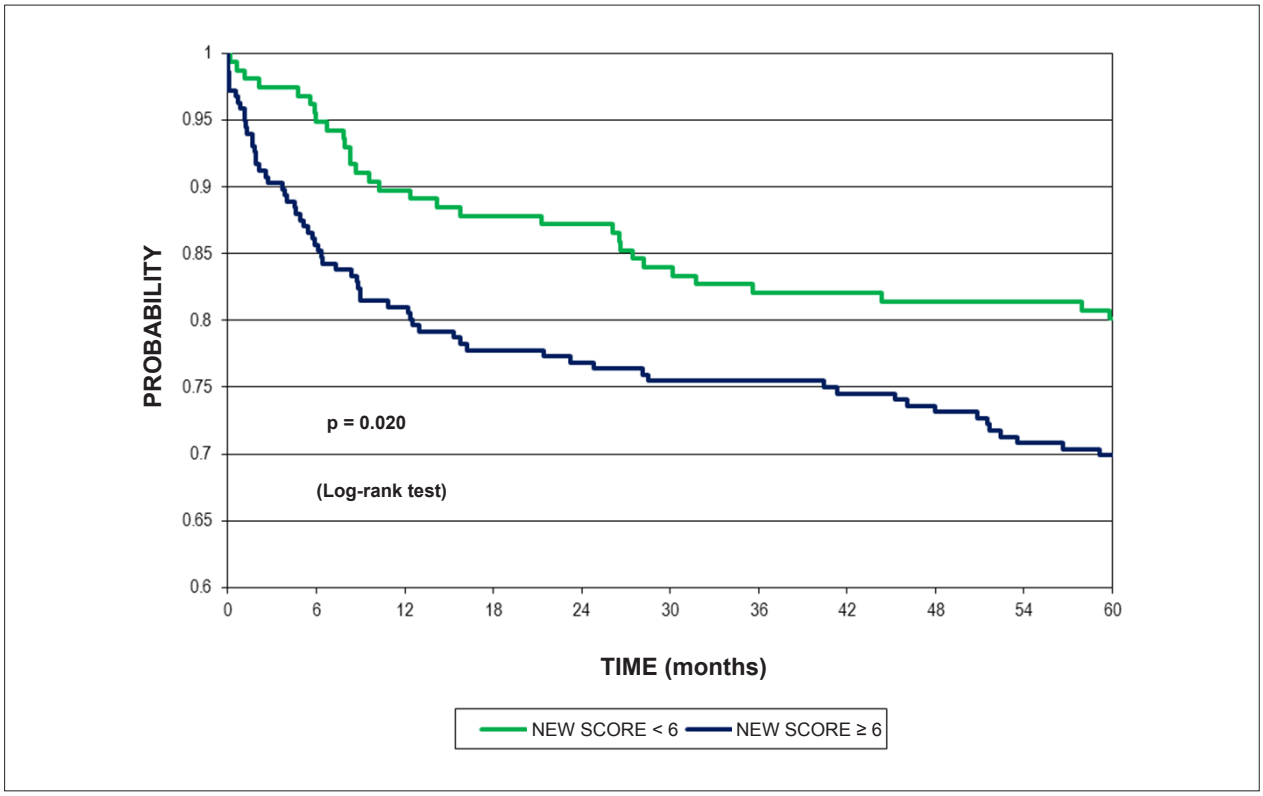

Figure 2 - Comparison of the combined event rate among patients with the new score < 6 and ≥ 6 points.

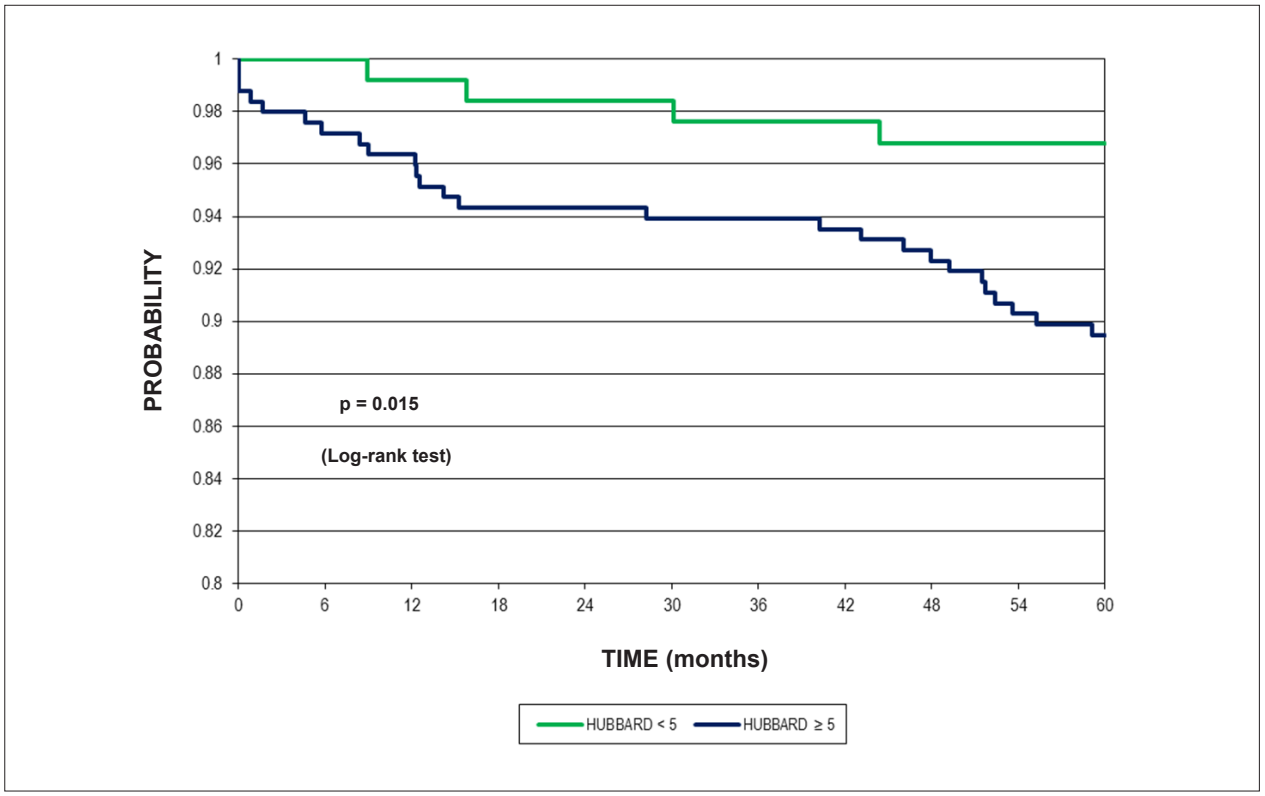

Figure 3 - Comparison between cardiovascular death rate in patients with Hubbard score < 5 and ≥ 5 points.

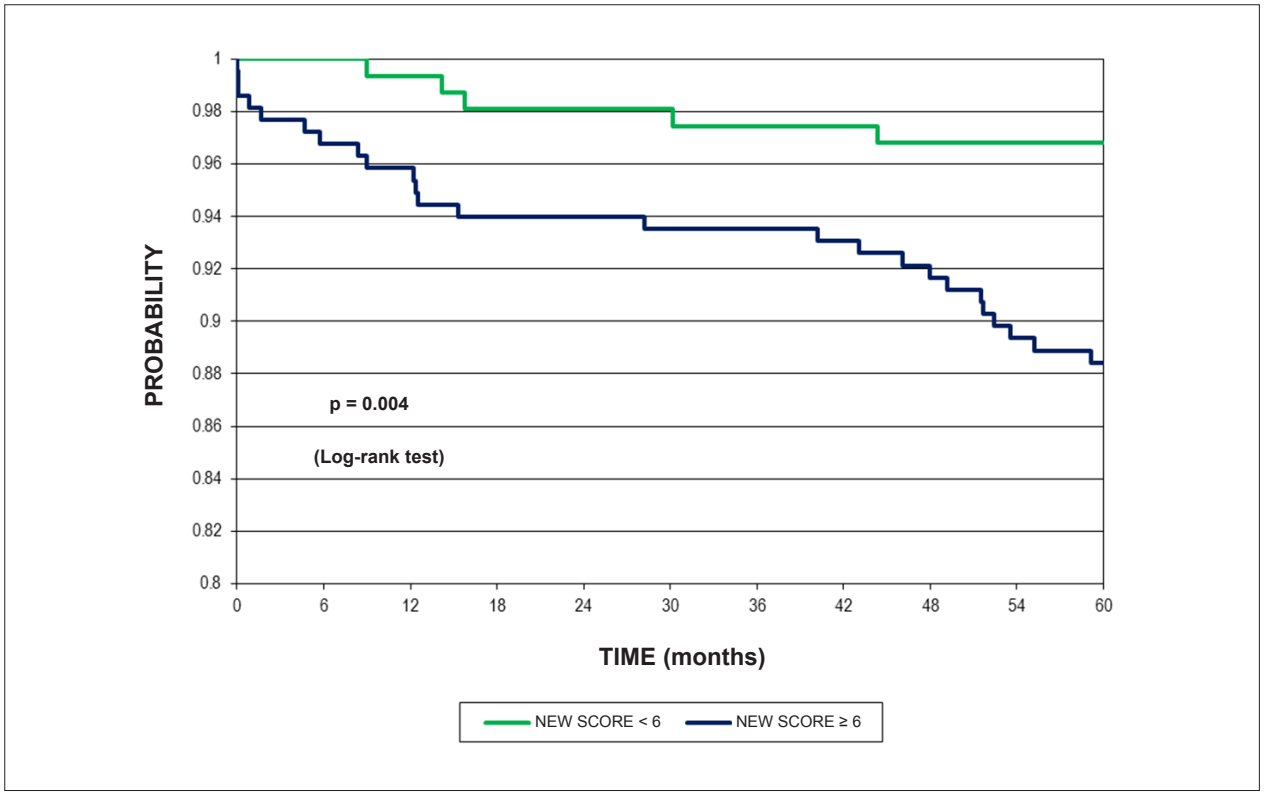

Figure 4 - Comparison between cardiovascular death rate in patients with the new score < 6 and ≥ 6 points.

Table 2 - Comparison between the scores. Distribution of patients according to scores on both scores

Score	< 5 points	≤ 5 points
< 6 points	125	31
≥ 6 points	0	216
Total	125	247

score < 5 points showed 1 event in the PTCA group, 5 events in the CABG group and 3 in the CT group (p = 0.24).

By analyzing the incidence of combined events in patients with the new score ≥ 6, we observed 24 events in the PTCA group, 8 in the CABG group and 12 in the CT group (p = 0.001). In patients with a score < 6 points, we observed 9 events in the PTCA group, 5 in the CABG group and 9 in the CT group (p = 0.334).

Discussion

The prognostic evaluation is a crucial component of clinical evaluation of CAD. Although patients with stable angina have low mortality rate[25-27], the risk of myocardial infarction, the need for interventions and the symptoms impact the clinical evolution in a representative manner.

Several scores were developed for stratification of CAD adopting the clinical parameters and ET or combined parameters[28,29]. However, prognostic scores in patients with stable angina are scarce[30].

The objective of this study was to develop an index for risk stratification of stable multivessel coronary artery disease through a simple and affordable method, in contrast to the wide range of high-cost procedures available.

In our series, the average age of 59.5 years determined a higher baseline score. Our sample was represented by individuals with a higher age range, therefore with a higher risk profile. The male predominance in our sample did not impact the interpretation of results due to the documentation of multivessel CAD in both sexes.

Most men (63.29%) had a score ≥ 6 points, while in most women there was a score < 6 points. The higher score for men may be related to the fact that the male sex already defines an additional score. In addition to that, myocardial infarction is more common in men, but women have a worse prognosis, due to higher rates of death and re-infarction[31]. As for chest pain, although it is more frequent in women, the prevalence of significant CAD is lower, causing a lower predictive value for non-invasivetesting[32,33].

The prognostic analysis did not consider the difference between double or triple vessel coronary angiographic patterns due to a low number of outcomes during follow-up.

The mortality rate (10.33%) in our study was higher than the overall mortality of patients with stable angina, which is around 1% per year according to the guideline on stable angina[33]. This can be explained by the presence of a greater number of high-risk patients in our study, with higher prevalence of multivessel disease and diabetes, despite preserved left ventricular function.

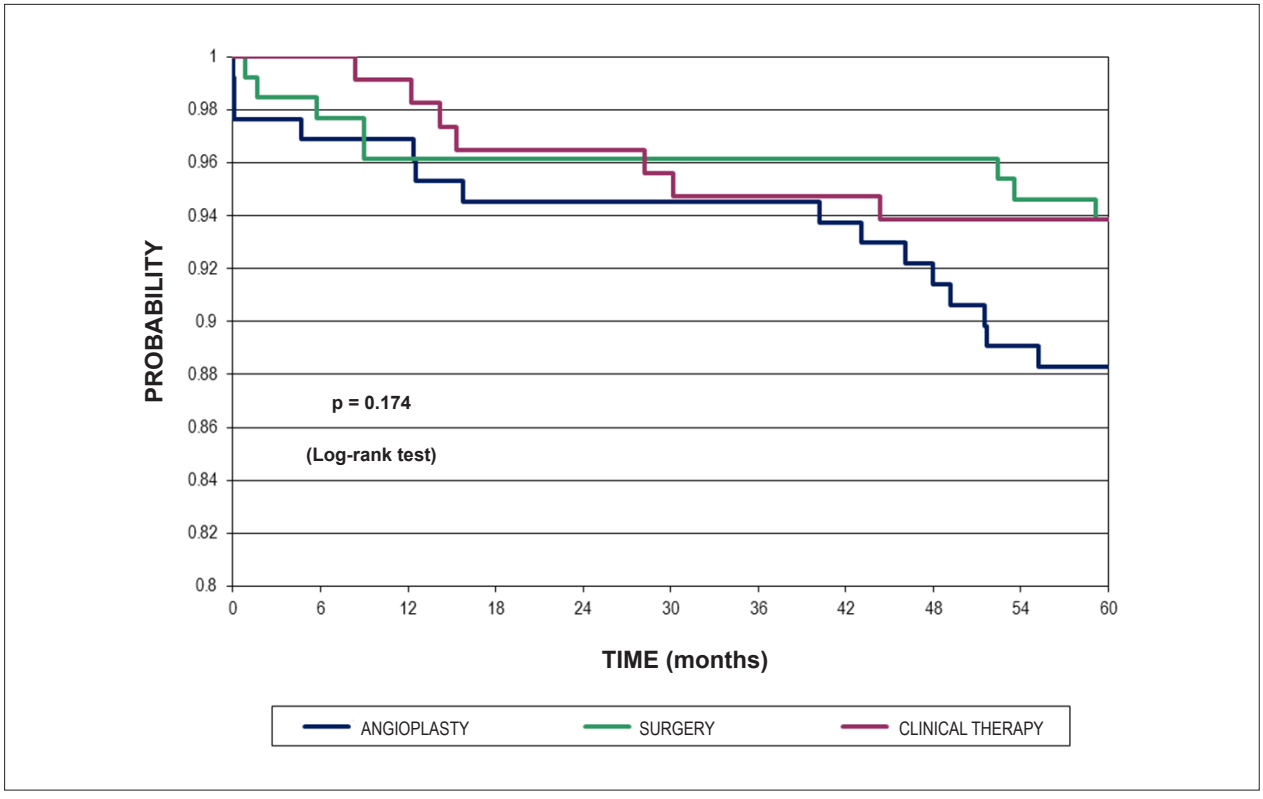

Figure 5 - Analysis of survival curve regarding the primary outcome comparing the three treatment groups.

The incidence of combined events and the need for re-intervention with angioplasty after randomization was higher in the PTCA group. This is probably related to a higher rate of restenosis, as a representative portion of our sample has diabetes. Higher rates of restenosis are commonly found in patients with diabetes[34].

The high rate of diabetes (36.8%) also determined a higher baseline scoring. This is compatible with the fact that patients with diabetes have a higher incidence of severe coronary artery disease. It is well established that diabetes is a major risk factor for coronary events[35]. Type 2 diabetes is of particular importance because it is more common and often occurs in the elderly when multiple risk factors coexist.

With respect to ET, patients with diabetes represent a particularized group: there is a higher incidence of hypertension, peripheral vascular disease, peripheral neuropathy, obesity and lower functional capacity. Moreover, they are more exposed to the use of drugs that limit heart rate. Thus, when multiple risk factors coexist, there are limitations to the achievement of a low risk in the Duke score. Additionally, the level of work achieved may not be sufficient for the documentation of myocardial ischemia, even with a significant CAD.

The score of Hubbard was initially selected to compose the new score, as it contains variables that are easy to evaluate. The number of variables is small, the sum of points is simple and easy to interpret, having a linear correlation between the outcome and prognosis. Moreover, it can identify individuals at high risk, even when classified as low risk by the Duke score[36]. However, it has limitations, such as the exclusive analysis of clinical variables, not considering documentary evidence of myocardial ischemia which confirmedly provides additional prognostic information[37].

By adding this variable in the analysis, 31 patients were classified as low risk by the new scoring system, because they had a negative exercise testing. Thus, the Hubbard score may have overestimated the highest risk group in the population studied.

In the ET, although other variables such as functional capacity, arrhythmias, inotropic and chronotropic responses, are thought to have higher predictive value than the ST-segment depression, there are flaws in the interpretation of several studies. It was not considered that in clinical practice a positive ET eventually influences the indication of cineangiocardiography and, consequently, pharmacological treatment or coronary artery bypass grafting (either surgical or percutaneous). Such therapeutic interventions determine a change in the natural history of coronary artery disease that impacts the prognostic value of electrocardiographic marker for myocardial ischemia.

The prognostic analysis of the new score did not incorporate these specific variables of the ET, adopting only the presence of electrocardiographic documentation of myocardial ischemia, because the goal was to apply a practical system that was easy to remember and interpret, so it is more widely accepted by both the clinicians and experts.

With the use of simplified prognostic scores used in combination with the ET, we can stratify more accurately the patients with stable coronary artery disease, reducing the rate of requests of high-complexity procedures.

Scores improve the prognostic accuracy of the ET, reduce bias in interpretation and organize the various clinical information, determining a reduction in the subjectivity and variability in risk stratification. Particularly, the score proposed by this study demonstrated its prognostic value in a comprehensive manner through a simple and organized system.

Conclusions

This new score is a simple and objective method for risk stratification of stable coronary artery disease.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Sources of Funding

There were no external funding sources for this study.

Study Association

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