

# Comparative Assessment of the Prognostic Value of Four Biochemical Markers of Myocardial Damage After Percutaneous Coronary Stenting

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## Objective

To assess the prognostic effect of the changes in the levels of 4 biochemical markers of myocardial damage (CK-MB activity/mass and troponins T and I) after stent implantation in regard to the occurrence of death, infarction, and new myocardial revascularization procedures in a one-year period. The study also aimed at determining the incidence of their elevations and the existence of predictive variables.

## Methods

Those 4 markers were measured in 199 patients treated with stent implantation in native arteries in the following 3 periods: before the procedure, 6-8 hours after the procedure, and 14-18 hours after the procedure. Survival curves and Cox logistic regression were used to determine the prognostic impact of the changes on the occurrence of cardiac events in one year.

## Results

Changes in the levels of the 4 markers after stent implantation are relatively frequent (6.1% to 32.8%), are associated with the degree of complexity of the lesions treated (long lesions and angulations > 45°) and with the development of problems during the procedure (occlusion of the secondary branches, presence of angina, and electrocardiographic changes). The infarction-free survival rate and the need for a new revascularization were significantly lower only in the patients with an elevation in the CK-MB activity after the procedure as compared with those in patients without that alteration (60% x 85.08%;  $P=0.025$ ). The following variables influenced the event-free survival rate: diabetes mellitus (OR: 2.27;  $P=0.0256$ ), balloon predilation (OR: 3.16;  $P=0.0082$ ), and an elevation in the CK-MB activity after the procedure (OR: 3.64;  $P=0.0162$ ).

## Conclusion

Systematic monitoring of CK-MB activity after coronary stenting is justified due to its clinical and laboratory behavior reported in studies relating its elevation after the procedure to a worse late outcome, and due to its low cost.

## Keywords

stent, biochemical markers, prognosis

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Received for publication: 02/03/2004  
Accepted for publication: 09/29/2004  
English version by Stela Maris Costalonga

The systematic assessment of total creatine kinase (total CK) and its MB subfraction (CK-MB) after percutaneous coronary intervention shows that 5% to 40% of the patients successfully treated have an elevation in the serum level of those enzymes, which may represent a certain degree of myocardial necrosis<sup>1-3</sup>. Recently, the analysis of other very sensitive biochemical markers specific for identifying myocardial damage (CK-MB mass, troponins T and I) has intensified the detection of that phenomenon, which has been much more frequently observed with the implantation of coronary stents<sup>4,5</sup>.

This study aimed at establishing the clinical meaning of those alterations and their impact on the occurrence of adverse cardiac events. It also had the following objectives: 1) to assess the incidence of the elevations in the CK-MB activity and mass and in the levels of troponins T and I after elective coronary stenting; 2) to analyze the association between the elevation of the markers and clinical, angiographic, and technical variables, and periprocedure problems; 3) to determine the prognostic effect of the elevation of the 4 markers after intervention on the occurrence of death, myocardial infarction, and need for new revascularization procedures in a one-year period.

## Methods

This prospective study comprised 199 consecutive patients from the coronary angioplasty unit at the Instituto Dante Pazzanese de Cardiologia. They underwent elective coronary stent implantation for the treatment of stenoses located in native coronary arteries from August 2001 to January 2002. The patients met the following inclusion criteria: both genders; no restriction regarding age; normal levels of CK-MB activity in the 24 hours preceding the intervention; patients with clinically controlled stable or unstable angina (no recurrence of pain in the 2 weeks preceding the percutaneous treatment, to reduce the chances of an elevation in the troponins before the procedure); asymptomatic patients with ischemia detected on functional tests; presence of luminal obstruction > 50% in one or more vessels, with primary lesions anatomically favorable to stent implantation; absence of severe left ventricular dysfunction (EF > 0.30); elective treatment with angiographic success at the end of the procedure.

The exclusion criteria were as follows: renal failure (creatinine > 2.0 mg/dL); presence of comorbidities that could affect late

survival; recent (< 3 months) history of myocardial revascularization (percutaneous or surgical) or myocardial infarction; contraindication to the use of aspirin and thienopyridine; lesions > 50% in the nonprotected left main coronary artery; ablation or brachytherapy procedures associated with stent implantation; drug-eluting stents; and treatment of saphenous vein grafts.

The protocol preceding the intervention was as follows: 24 hours before the procedure the patients underwent blood sample collection for measuring the 4 markers (CK-MB activity, CK-MB mass, and troponins T and I) and received aspirin (200 mg/day) in association with a thienopyridinic agent (ticlopidine, 500 mg/day, or clopidogrel, attack dosage of 300 mg followed by 75 mg/day). The routine techniques for optimal stent implantation (predilation, if required, endoprosthesis deployment, and later dilation with high pressure) were adopted, and the relevant technical data of the intervention (number, diameter, and extension of the stent; balloon predilation; number, time, and maximal pressure of the inflations) were recorded, as were the periprocedure problems (angina, changes in the ST segment, rhythm disorder, occlusion of the branches, presence of dissections and thrombi, incarcerated branch, coronary spasm, changes in arterial flow, and distal embolization) that could have any relation with an elevation in the markers.

In-hospital assessment: after the procedure, the patients underwent clinical and electrocardiographic assessment, in addition to blood collection for measuring the markers performed twice as follows: 6 to 8 hours after the procedure (sample 1); and the next morning, on average, 14 to 18 hours after intervention (sample 2). Only the result of the CK-MB activity before and after the procedure, routinely used in our hospital, was available for immediate assessment. Hospital discharge occurred on the following morning, after clinical and electrocardiographic assessment, and the result of the CK-MB activity. The results of the other 3 markers (CK-MB mass, and troponins T and I) were not available before and after the intervention, and did not interfere with the decision about hospital discharge.

The laboratory methods for measuring the biochemical markers were as follows: 1) CK-MB activity: was determined by the colorimetric immunoenzymatic method using the Starter reactive (Roche Diagnostics Corp, Mannheim, Germany) in the BM/Hitachi 912 device (Roche – Switzerland), and values between 0 and 10 U/L were considered normal; 2) CK-MB mass: measured through the immunometric method (quantitative determination) using the Immulite Analyser (Diagnostic Products Corporation, Los Angeles, USA), with mono- and polyclonal antibodies associated with chemoluminescence reactions. The maximum normal reference value was 4.45 ng/mL; 3) troponin T: measured through the electrochemoluminescence immunoassay method, using the Elecsys (Roche Diagnostics Corp, Mannheim, Germany). Values  $\geq 0.1$  ng/mL are clinically relevant; 4) troponin I: determined through the immunometric method using the Immulite Analyser (DPC - Diagnostic Products Corporation, Los Angeles, USA), with anti-troponin I antibodies and chemoluminescence reactions. Values below 1.0 ng/mL are considered normal.

The patients were followed up in the coronary angioplasty unit with 5 programmed visits as follows: after 15 and 30 days (clinical and hematological assessment); and after 3, 6, and 12 months (clinical assessment and functional tests).

The following terms were defined: angiographic success - re-

sidual lesion < 30%, absence of thrombi and dissections in the margins of the stent, and normal flow (TIMI 3); clinical success - angiographic success and lack of death, infarction, and emergency surgery; periprocedure infarction - an elevation in the CK-MB activity greater than 3 times the normal value, associated with new Q waves or not; emergency surgery - the revascularization surgery performed within the 24 hours following the procedure in a situation of acute ischemia related to the vessel treated; angiographic restenosis - target-lesion stenosis equal to or greater than 50%; target-vessel revascularization - new percutaneous or surgical procedure due to restenosis or progression of the coronary artery disease; nontarget-vessel revascularization - new percutaneous or surgical procedure in another vessel for the treatment of stenoses > 50%; cardiac death - any cardiac cause of death; major events - cardiac death, myocardial infarction, and new revascularization procedures in the first year after stent implantation.

Statistical analysis - The results of quantitative variables were expressed as mean and standard deviation, and the qualitative variables were expressed as absolute and relative frequencies (percentages). The associations between the categorical variables were assessed by using the chi-square test or the Fisher exact test. Logistic regression was performed to determine the independent factors associated with the elevation in each of the 4 markers after stent implantation. The accumulated probabilities of adverse events (death, infarction, and new revascularization procedures) were estimated by use of the Kaplan-Meier curves and the presence of differences by the log-rank test. Cox regression was used to determine the variables with independent prognostic value for the occurrence of events. The significance level of  $P < 0.05$  was adopted.

## Results

From August 2001 to January 2002, 202 patients were selected, 3 of whom were excluded due to elevated CK-MB activity 24 hours before the intervention. Therefore, this study assessed 199 patients undergoing stent implantation, whose clinical characteristics are shown in table I. All patients studied had normal CK-MB activity 24 hours before stent implantation (according to protocol requirement); on later assessment of the other markers 24 hours before the procedure, most patients were observed to

Table I – Clinical data

Variables	
Age (mean and standard deviation) – (years)	60.3 (SD 10.16)
Elderly (> 70 years)	36 (18%)
Female sex	72 (36.2%)
Risk factors	
Diabetes mellitus	66 (33.2%)
Diabetic patients using insulin	17 (8.5%)
Arterial hypertension	139 (69.8%)
Hypercholesterolemia	124 (62.3%)
Current smoking	47 (23.6%)
Cardiovascular antecedents	
Myocardial infarction	119 (59.8%)
Percutaneous intervention	42 (21.1%)
Revascularization surgery	15 (7.5%)
Clinical findings pre-intervention	
Asymptomatic/Silent ischemia	72 (36.1%)
Stable angina	65 (32.7%)
Unstable angina	62 (31.2%)



have them within the normal range. The percentage elevation of those markers before stenting ranged from 4.5% (troponin I) to 9.5% (CK-MB mass). The angiographic characteristics before the intervention and the technical characteristics of the procedure are shown in table II. It is worth emphasizing that 216 stents (1.1/patient) were used, and, in 15 (7.6%) patients, 2 or more prostheses were used.

During stent implantation, 49 (24.6%) patients had angina related to the following facts: branch occlusion in 14 (28.5%) patients, spasm in 7 (14.3%) patients, and the rest related to balloon inflation. In 41 (20%) patients, transient changes in the ST segment or disorders in cardiac rhythm were observed. Other problems included the presence of dissection in 22 (11%) patients and coronary spasm in 21 (10.5%). Regarding the 148 branches incarcerated by the prosthesis, 43 (23%) showed occlusion, evolving with angina in 14 (32.5%) or electrocardiographic changes in 10 (23.3%), or both. Thrombus formation occurred in 5 (2.5%) patients, requiring additional inflations or the use of IIb-IIIa glycoprotein inhibitors, or both. Of the 6 (3%) patients with flow alterations, 4 (67%) did not show its normalization until the end of the intervention.

In regard to in-hospital results, the success rate of stent implantation with no clinical or angiographic complication was elevated (193/199 = 97%). The procedures in the 6 (3%) remaining patients were not considered successful as follows: in 2 patients, the target lesion could not be overcome; 3 patients had, at the end of stent implantation, TIMI-2 flow; and in the last patient CK-MB elevation was 3 times greater than the normal value, with no electrocardiographic changes (non-Q-wave infarction). Therefore, the major complications in the in-hospital phase were limited to a periprocedure infarction (0.5%). No cases of acute or subacute thrombosis occurred. The mean length of hospitalization was 1.1 days (SD = 0.5).

**Table II - Angiographic characteristics before intervention and technical characteristics of the procedure**

Variables	
Extension of the coronary artery disease	
Multivessel	76 (38.2%)
Vessel treated	
Anterior descending/Diagonal artery	87 (43.7%)
Right coronary artery	64 (32.2%)
Circumflex artery	47 (23.6%)
Protected left main coronary artery	1 (0.5%)
Location of the target lesion	
Ostial / Proximal	90 (45.2%)
Middle/distal third	109 (54.8%)
Extension > 20 mm	34 (17.1%)
Important morphologic characteristics	
Calcification	59 (29.6%)
Angulation > 45°	21 (10.5%)
Irregular margin	54 (27.1%)
Presence of thrombus	15 (7.5%)
Branches involved	145 (72.8%)
TIMI flow < 3	23 (11.5%)
Type B <sub>2</sub> / C	158 (79.4%)
Balloon predilation	108 (54.8%)
Total time of inflation (sec)	
≤120	173 (87.4%)
≥ 120 e ≤ 180	25 (12.6%)
Mean	87.86s
Maximum pressure of inflation (atm)	
≤ 16	139 (70.2%)
> 16 e ≤ 20	59 (29.8%)
Mean	15.2 atm

In regard to late outcomes, 100% of the patients successfully treated were assessed (193 of 199 patients). Four patients ceased to provide information 6 months after the procedure, but until then, no major event was reported. The follow-up of the 193 patients revealed the following findings: 1) cardiac death in 2 (1%) patients: one, 2 months after percutaneous revascularization (sudden death), and the other, 10 months after stent implantation, due to myocardial infarction; none of the patients had any elevation in the markers right after the procedure; 2) Q-wave myocardial infarction in one (0.5%) patient; 3) target-lesion revascularizations in 25 (13%) patients, 22 of which were percutaneous and 3 surgical. Therefore, in the one-year period, 28 (14.5%) patients had major cardiac events. Two deaths of noncardiac origin occurred related to liver neoplasia and septicemia secondary to acute cholecystitis; 4 (2.1%) patients had stroke (ischemic); and, in 7 (3.6%) other patients, the coronary disease progressed and new revascularization procedures were performed in the nontarget vessel (3 percutaneous and 4 surgical).

In regard to the behavior of the biochemical markers, figure 1 shows the percentages of patients with changes in the markers after the procedure, and the most frequent elevation occurred in the second sample. The CK-MB activity (MBa) increased in 12 (6.1%) patients, of whom 11 had mild increases, ranging from one to three times the normal value. The other patient had an elevation of 5 times the normal value. In regard to the CK-MB mass (MBm), it was increased in 65 (32.8%) patients and was categorized as follows: > 1x and < 3x the normal value, 74% of the patients; ≥ 3x and < 5x the normal value, 9% of the patients; ≥ 5x, 17% of the patients. In 22 (34%) patients, the elevation occurred in an isolated form, with no concomitant alteration in the other 3 markers. The troponins T and I (respectively, TnT and TnI) had a similar behavior, increasing in 23% and 20.2% of the patients, respectively, in the second sample.

To assess the association between the biochemical markers and the clinical, angiographic, and technical variables and the problems of the procedure, univariate analysis was performed. In regard to the clinical variables analyzed (tab. I), they did not relate to the alterations in the markers after stent implantation. In regard to the angiographic characteristics of the lesion, the presence of angles > 45° (TnI + 22% x TnI - 6.7%; P = 0.002), lesion length greater than 20 mm (MBa + 42% x MBa - 15.5%; P = 0.009; and MBm + 27% x MBm - 12%; P = 0.017), and type B<sub>2</sub>/C lesions (MBm + 87% x MBm - 75%; P = 0.027) were associated with a significant elevation in at least one of the markers

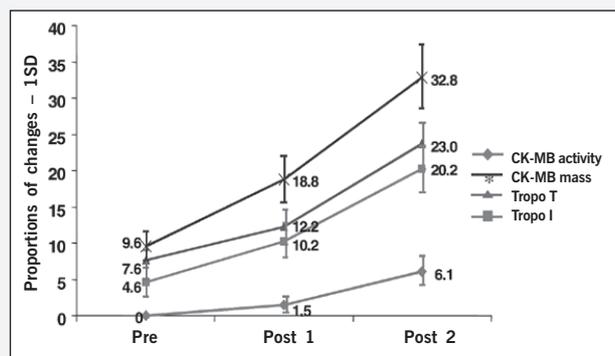


Fig. 1 - Graph comparing the percentage of patients with elevated levels of biochemical markers in the 3 periods analyzed: before intervention = Pre, first sample = Post 1 (6 – 8 hours), and second sample = Post 2 (following morning).

after intervention (univariate analysis). In regard to the technical variables of the procedure (balloon predilation, time of balloon inflation > 120 seconds, pressure > 16 atmospheres, number of stents implanted per patient > 1, and stent diameter < 3 mm) none of them was associated with an elevation in any of the 4 markers analyzed. On the other hand, the problems occurring during the intervention were frequently associated with alterations in the markers. On univariate analysis, the presence of angina, the electrocardiographic alterations, and the occlusion of the branches were the variables related to the elevation of at least 2 markers after stent implantation.

Logistic regression identified the factors independently associated with an alteration in each marker, and concluded that branch occlusion was the only variable with an independent prognostic value for the elevation of all 4 markers analyzed in this study (MBa: OR = 7.0, 95% CI = 2.0-24.4, P = 0.002; MBm: OR = 3.0, 95% CI = 1.37-6.6, P = 0.005; TnT: OR = 3.25; 95% CI = 1.45-7.26, P = 0.004; TnI: OR = 4.29, 95% CI = 1.92-9.6, P = 0.0004). On the other hand, the presence of angina during the procedure was independently related to an elevation in MBa (OR = 4.27; 95% CI = 1.22-14.9, P = 0.022) and in TnI (OR = 2.53, 95% CI = 1.19-5.39, P = 0.015), but the transient electrocardiographic changes were independently associated with an elevation in MBm (OR = 2.40, 95% CI = 1.15-4.99, P = 0.019) and in TnT (OR = 2.21, 95% CI = 1.0-4.85, P = 0.047).

In the one-year follow-up, the major event-free survival was 83.77% in 193 patients. The Kaplan Meier curves for survival free from infarction and new revascularization procedures in the patients with and without alteration in the markers are shown in figures 2, 3, 4, and 5. Cox regression identified the following variables that influenced survival free from adverse events: the elevation in the CK-MB activity after stent implantation (OR = 3.64, 95% CI = 1.27-10.4, P = 0.016), balloon predilation (OR = 3.16, 95% CI = 1.34-7.41, P = 0.0082), and the presence of diabetes mellitus (OR = 2.27, 95% CI = 1.10-4.67, P = 0.025).

## Discussion

Our results have shown that markers of myocardial damage frequently increase after elective stent implantation, ranging from 6.1% to 32.8% of the patients. We also observed that in elective pro-

cedures, the presence of more complex lesions (extension and angulation), and mainly, the complications during the procedure (branch occlusion and presence of angina and electrocardiographic changes) are strongly associated with an elevation in those markers. At the end of one year, the event-free survival was significantly lower only in patients who had an elevation in the CK-MB activity after stent implantation. The independent variables that negatively influenced the clinical outcome were diabetes mellitus, balloon predilation, and the elevation in the CK-MB activity after stent implantation.

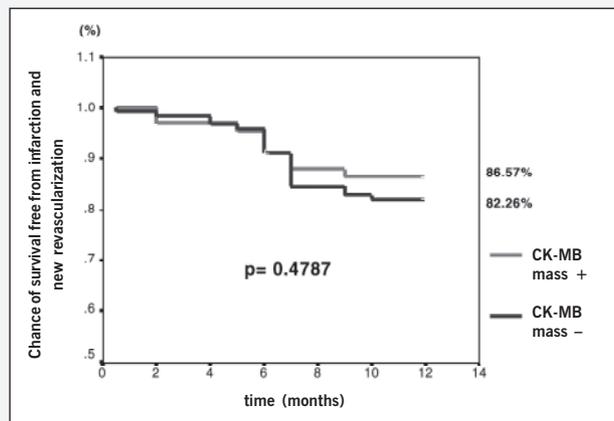


Fig. 3 - Event free survival curves in patients with and without CK-MB mass elevation.

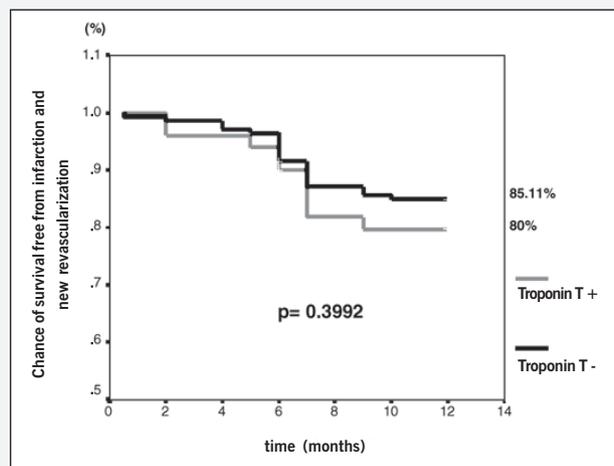


Fig. 4 - Event free survival curves in patients with and without troponin T elevation.

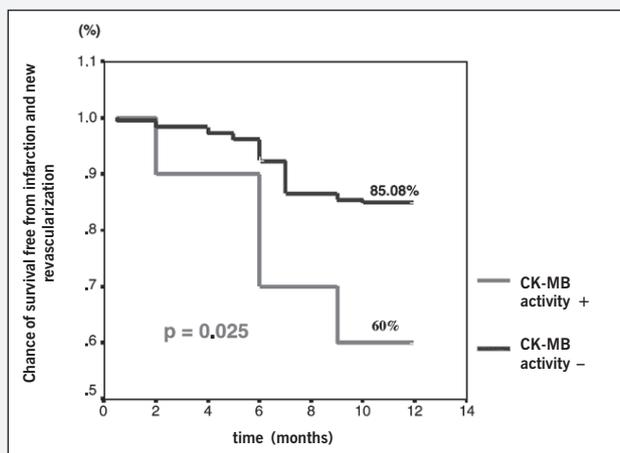


Fig. 2 - Event free survival curves in patients with and without CK-MB activity elevation.

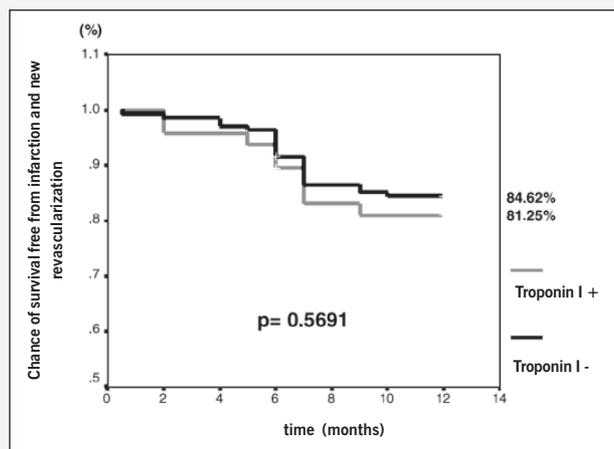


Fig. 5 - Event free survival curves in patients with and without troponin I elevation.



We observed that the CK-MB activity increased in 12 (6.1%) patients after stent implantation. In most patients (92%), it did not exceed 3 times the normal value. In only one patient, that value was exceeded, characterizing periprocedure infarction. The percentage of elevations in CK-MB activity in our study are lower than those reported in the literature, usually occurring in 15 to 25% of the patients<sup>2,6,7</sup>. This may be attributed to the exclusion of patients more prone to enzyme release (patients with lesions in the saphenous vein graft and those with recent acute coronary syndrome)<sup>8,9</sup>, and also to the influence of the technical characteristics and controlled invasiveness strategy that characterized our interventions (total time of balloon inflation < 120 seconds in 87% of the patients, maximum pressure of stent deployment  $\leq$  16 atmospheres in 70%, direct implantation of the prosthesis in 45% of the patients).

The CK-MB mass was the marker that most frequently increased after stent implantation (32.8%), but, in more than two thirds of the patients (74%), it did not exceed 3 times the normal value. On the other hand, the troponins I and T, considered a pattern for detecting myonecrosis, had a similar behavior, with 20 and 23% elevations in the second sample after stent implantation. Researchers have reported that the elevation of these 3 markers after intervention ranges from 20 to 40%<sup>10-12</sup>, usually exceeding the percentages of the cardiac enzymes, particularly the CK-MB activity, in concordance with our findings. We also observed that all 4 markers had increased more frequently in the second sample after the procedure. Therefore, if we decide to perform only one measurement of the markers, the ideal period would be between 12 and 18 hours after stent implantation, the equivalent to the second sample, due to the possibility of adding all the possible temporal repercussions of dilation.

When the patients are analyzed according to the elevation of each one of the 4 markers, we observed that event-free survival was significantly lower only in patients with an elevation in CK-MB activity after stent implantation, which occurred in only 12 patients, 92% of whom (11) had levels 1 to 3 times the normal value. Nevertheless, these alterations were related to worse clinical outcome, which makes us believe that this is the marker that identifies which is clinically relevant, with a negative impact on late outcome. The pathophysiology involved in this process has not yet been completely clarified. Ishikawa et al<sup>13</sup>, however, in experimental studies with dogs, reported that coronary occlusion longer than 20 minutes was associated with enzyme release (total CK and CK-MB) and produced histopathologic evidence of myocardial necrosis (ie, irreversible damage), an observation with relevant diagnostic and therapeutic implications<sup>14-16</sup>. In addition, when the combined events were decomposed, we observed that the patients with an elevation in the CK-MB activity after stent implantation had a greater tendency towards mortality (10.6% x 0.6%;  $P = 0.10$ ) and additional revascularization procedures (30% x 12%;  $P = 0.14$ ) in one year. This could be related to microembolizations of the collaterals during the intervention, which increased the risks of the events, intensifying the ischemic effects of a subsequent coronary occlusion at the same site. Enzyme release could also identify patients susceptible to future events in the same area, identifying a high-risk population with a tendency towards developing myonecrosis in response to minor stimuli (Leaker syndrome)<sup>17,18</sup>.

In regard to the other 3 markers, we observed that, despite

the greater incidence of their alterations after stent implantation, this did not negatively influence late outcomes. Some studies have analyzed the impact of troponin elevation on the occurrence of major cardiac events in patients treated percutaneously, and no significant differences were found in patients with and without an elevation in those markers<sup>19</sup>. These results indicate that the troponins are very sensitive and specific for identifying myocardial damage, which is particularly desirable in critical situations, such as acute coronary syndrome<sup>20,21</sup>. However, one does not know the cutoff value above which the diagnosis of infarction after percutaneous intervention is made, which is the outcome with a negative prognostic impact.

It is worth noting the influence of the anatomical aspects of complex coronary obstructions, represented by long lesions (> 20 mm), located in angulations, and of the B<sub>2</sub>/C type (involvement of lateral branches, excessive calcification, presence of thrombus, and abnormal coronary flow), and which were associated with an elevation in biochemical markers. Those characteristics offer greater difficulty to the passage and action of the device, leading to the embolization of plaque fragments and platelet aggregates, and occlusion of the branches, causing myonecrosis detected by the markers<sup>22,23</sup>.

In regard to the technique itself, approximately half of the patients underwent direct stent implantation, with no need for balloon predilation, whose major advantage was to cause less damage to the vascular wall<sup>24</sup>. Recent studies assessing those 2 techniques have shown an equivalence in regard to immediate and late results<sup>25,26</sup>. In our study, the laboratory findings showed that the incidence of predilation among the patients with and without alteration in the markers was similar; this variable, however, had an independent negative prognostic influence on the occurrence of major events. It is worth emphasizing that other technical aspects, such as time of balloon inflation and the pressure of stent deployment, did not relate to the elevation in the biochemical markers analyzed.

The problems occurring during the procedure may interfere with the laboratory behavior of biochemical markers. In terms of laboratory repercussion, the worst finding of the 3 mentioned was occlusion of the side branches identified as the only variable independently associated with the elevation in all markers after stent implantation; however, its negative prognostic impact on the occurrence of major events was not confirmed on Cox regression. Since the initial investigations by Abdelmeguid et al<sup>1,27</sup>, later confirmed by other researchers<sup>11,28</sup>, the occlusion of secondary branches is one of the most frequent factors related to postintervention myonecrosis.

Predilation performed in approximately 50% of our patients is desirable in more complex lesions (calcification, ostial location, tortuous segments, and occluded vessels). In those cases, the technique provides necessary conditions for safe stent deployment and implantation, avoiding the risk of embolization or incomplete expansion of the prosthesis<sup>24</sup>. In our study, the negative influence of that variable on event-free survival at the end of one year draws attention to the possibility of damage to the vascular wall and microembolizations in the approach of complex lesions, which could have a greater tendency to require new revascularization and to have a higher rate of major events.

The prevalence of diabetic patients in our group was high (33%) and did not relate to the alterations in markers after stent implan-

tation, but the presence of this risk factor confirms which is reported in the literature: the negative influence of diabetes on the late prognosis of the patients with coronary atherosclerosis, elevating the risks of death, infarction, and other cardiac events<sup>29,30</sup>. Regarding to percutaneous interventions, the presence of diabetes does not impair clinical success; however, the rate of restenosis, even with the use of stents, is high, being attributed to exacerbated intimal hyperplasia. In addition, the disease tends to progression, particularly in insulin-dependent patients, generating the frequent need for new revascularization<sup>31</sup>. Of the 193 patients in this study, 64 were diabetics who have twice as many adverse cardiac events (28% x 12.5%;  $p = 0.015$ ), particularly related to the need for new revascularization procedures (25% x 11%;  $p = 0.019$ ), as compared with nondiabetic. A tendency towards a lower event-free survival in diabetic patients (76.5% x 87.4%;  $p = 0.065$ ) was observed, even in a relatively small sample (in which it was not previously intended to analyze that subgroup in particular), corroborating the results of several studies that showed the negative impact of diabetes on coronary artery disease and in the outcomes after percutaneous and surgical revascularization.

The routine use of multiple markers for identifying myonecrosis after stent implantation, particularly troponins, does not seem necessary, because no difference was observed in the event-free survival rate in one year in patients with and without changes in

these markers. Yet, CK-MB mass did not add any advantages, because it may increase in situations not related to myocardial damage (manipulation of the skeletal muscle).

In conclusion, we suggest the use of systematic monitoring of CK-MB activity after coronary stent implantation. The arguments that justify that suggestion are based on the clinical and laboratory behavior of CK-MB, on the knowledge acquired through studies relating its elevation after the procedure to a worse late outcome, and its low cost. It is worth stressing that even small elevations in this marker levels (1 to 3 times the normal value) should be valued, because its presence has a negative prognostic impact and determines a lower event-free survival rate at one-year.

Ideally, the accurate assessment of the prognostic impact of the elevations of different biochemical markers of myocardial damage after percutaneous intervention should include a larger population and a prolonged clinical follow-up (> 5 years). In cohort observational studies, such as ours, that analyze stable patients undergoing elective procedures, the occurrence of events, such as death, infarction, and new revascularization is less frequent. Therefore, an exceptionally large number of individuals is required for assessing those events, which, however, would make the research impossible due to the high costs involved and the impracticality of performing an adequate clinical follow-up in the medium- and long-term period.

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