Validation of a Risk Score for Target Vessel Revascularization after Coronary Stent Implantation

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**Original Contribution**

**ABSTRACT:** Objective. Our aim was to validate a risk score for new target vessel revascularization (TVR) after bare-metal stent (BMS) implantation. Methods. The risk score was developed in a cohort of patients previously treated with BMS at our institution. This risk score ranges from 0 to 5 points, according to the presence of diabetes mellitus (1 point), reference vessel diameter (> 3.5 mm = 0 points; 3–3.5 mm = 1; < 3 mm = 2) and lesion length (≤ 10 mm = 0 points; 10–20 mm = 1; > 20 mm = 2). Patients included in the validation cohort were treated between January and December 2005. Patient characteristics and 1-year clinical follow-up were prospectively recorded into a dedicated database. A new coronary angiography was performed only when recurrent ischemia was suspected. Results. The mean age of the 491 patients included was 61 ± 10.5 years, and 35% were women. Diabetes mellitus was present in 22%, a previous percutaneous coronary intervention in 12% and previous myocardial infarction in 35%. The mean reference vessel diameter was 2.80 ± 0.56 mm and the mean lesion length was 12.45 ± 6.3 mm. The overall 1-year TVR rate was 13.9%. TVR rates increased with each score level: Score = 0, TVR = 0% (n = 16); Score = 1, TVR = 3.3% (n = 14); Score = 2, TVR = 12% (n = 170); Score = 3, TVR = 14% (n = 146); and Score 4/5, TVR = 25% (n = 54); (p = 0.008). Conclusions. The risk score was significantly associated with TVR rates and can be used as a simple clinical tool to identify those patients at a low risk for a new revascularization procedure.

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The occurrence of restenosis after percutaneous coronary interventions (PCI) is associated with new revascularization procedures, which adversely affect the quality of life of patients.1 Recent reports have also demonstrated an increased risk of acute coronary syndromes in these patients, challenging the view that in-stent restenosis is a benign situation.2–4 Drug-eluting stents (DES) are associated with significantly lower restenosis and target vessel revascularization (TVR) rates than bare-metal stents (BMS).5–7 However, patients with planned non-cardiac surgeries or with a high bleeding risk, and those who do not comply with long-term antiplatelet therapy are poor candidates to receive these new devices.8,9

The current Guidelines state that “a DES should be considered as an alternative to a BMS in those patients for whom clinical trials indicate a favorable effectiveness/safety profile (Class I, Level of Evidence: A”), and that “before implanting a DES, the interventional cardiologist should discuss with the patient the need for and duration of DAT and confirm the patient’s ability to comply with the recommended therapy for DES” (Class I, Level of Evidence: B).10 While application of these criteria results in DES implantation in the majority of patients submitted to PCI, it does not provide support for all situations.11

After three decades of the performance of the first coronary angioplasty by Andreas Gruentzig in 1977, a number of studies have dealt with the problem of identifying predictors of restenosis after PCI. Our group has previously reported an angiographic score to predict restenosis after balloon coronary angioplasty, which identified subgroups of patients with very low (< 5%) or very high (around 80%) restenosis rates.12 Predictive models for restenosis after coronary stenting have also been developed, but the results were not consistent among the reported studies.13–16 Also, these models are generally complicated and cumbersome to use at the bedside or rely on post-procedural characteristics, which preclude its widespread clinical application.

We have recently developed a risk score to assess TVR rates after BMS implantation, which was previously published in this *Journal*.17 This score is based on preprocedural variables: the presence of diabetes mellitus, the reference vessel diameter and the lesion length. However, it was not validated in an independent cohort of patients, which is important to demonstrate the strength of the model and also its potential clinical application.18 In the present study, we sought to validate the score in a contemporary cohort of patients treated with coronary stent implantation.

**Methods**

**Patients.** All patients undergoing PCI with coronary stents as a treatment for symptomatic coronary artery disease at our institution were considered for inclusion in this study. Patients were treated between January and December 2005. Clinical, procedural, and angiographic characteristics and in-hospital follow-up
Validation of Risk Score for TVR after Coronary Stenting

Data regarding the study population were prospectively recorded and entered into a dedicated database.

Excluded from the study were those patients treated with DES, were in cardiogenic shock, had in-stent restenosis or underwent unsuccessful procedures. Unsuccessful procedures were defined as those with significant residual stenosis (>30%) and/or impaired coronary flow (thrombolysis in myocardial infarction [TIMI] 0 to 1) after stent implantation, or when death, myocardial infarction (MI) or urgent revascularization occurred during the in-hospital period. Myocardial infarction was defined as creatine kinase-MB (CK-MB) > 3 times normal and/or development of new pathological Q waves.

The study was approved by the appropriate institutional review board and all patients provided signed informed consent.

**Implantation procedure.** All patients were receiving oral platelet inhibitors: aspirin (100–200 mg daily) and thienopyridines (clopidogrel 75 mg daily or ticlopidine 250 mg twice daily) at the time of PCI. In urgent cases, these drugs were administered during or soon after stenting, and a bolus dose of 300 mg of clopidogrel was given. Intravenous (IV) boluses of heparin were administered during the implantation procedure itself to maintain an activated clotting time of >300 seconds (or 200–300 seconds in those receiving glycoprotein [GP] IIb/IIIa inhibitors). Lesions were treated using standard PCI techniques. Technical aspects like type and number of stents, use of any other devices or GP IIb/IIIa use were left to the discretion of each operator.

**Angiographic analysis.** All angiographic analyses were performed in at least two different views by experienced operators with a previously validated digital caliper system (Siemens Axiom Artis, Munich, Germany), and intracoronary nitroglycerin was routinely given at the dose of 100–200 µg before measurements. Target vessel diameter was defined as the mean diameter of the luminal segments proximal and distal to the lesion, and the severity of stenosis was measured in two orthogonal views. Lesion length was measured “shoulder-to-shoulder,” and longer lesions were considered a single lesion only when a normal segment < 10 mm long lay between them.

**Risk score.** The risk score was developed in a cohort of 848 consecutive patients with long-term follow up, as previously reported. Briefly, predictors of 1-year TVR rates were identified by multivariate analysis, and analysis by means of the Hosmer-Lemeshow goodness-of-fit test identified the model with the best fit to the data. Diabetes mellitus, reference vessel diameter and lesion length were retained in the final model, and points in the score were assigned according to relative risks of each variable: 1) diabetes mellitus: present = 1 point, and absent = 0 points; 2) reference vessel diameter: < 3.0 mm = 2 points, 3.0–3.5 mm = 1 point, and > 3.5 mm = 0 points; and 3) lesion length: > 20 mm = 2 points, 10–20 mm = 1 point, < 10 mm = 0 points. The risk score could range from 0 to 5 points. Patients with score levels 4 or 5 were analyzed together, because few patients had a score of 5/5.

**Follow up and study endpoints.** Patients were followed up for at least 1 year either by clinical evaluation in the outpatient clinic or by telephone contact. Control angiography was performed only when symptoms or signs of recurrent myocardial ischemia were present. The decision to perform a revascularization procedure was taken by the attending physician. Major adverse cardiovascular events (MACE) were defined as death, MI or TVR. The need for a new TVR in the 1-year period after the index stenting procedure (either by PCI or by coronary artery bypass grafting) was registered.

**Statistical analysis.** Categorical variables were expressed as percentiles, continuous variables were expressed as the mean ± standard deviation (SD). All data were analyzed using SPSS software for Windows 13.0 (SPSS, Inc., Chicago, Illinois). A p-value < 0.05 was considered statistically significant for all tests. One-year event rates according to the different score levels were compared by the chi-square test for trend. Accuracy of the score was evaluated by means of the C-statistic.

**Results**

**Patients.** Clinical characteristics are displayed in Table 1. The mean age of the 491 patients included was 61 ± 10.5 years, and 35% were women. A diagnosis of hypertension was present in 81% of the patients and diabetes mellitus in 22%. Regarding medical history, a previous MI was reported by 35% of the patients, and a previous PCI by 12%.

Angiographic characteristics are shown in Table 2. The reference vessel diameter was 2.80 ± 0.56 mm and the stent diameter was 3.02 ± 0.58 mm; the implantation pressure was 13.26 ± 2.79 atmospheres (atm). Lesion length was 12.45 ± 6.3 mm and stent length was 16.10 ± 5.17 mm. The following stents were implanted: Libé (Boston Scientific Corp., Natick, Massachusetts; 222 patients, 45%), BX Sonic (Cardis Corp., Miami Lakes, Florida; 171 patients, 35%) and Lekton Motion (Biotronik Co., Berlin, Germany; 98 patients, 20%).

One-year follow up was complete for 89% of the patients. Figure 1 shows 1-year TVR rates according to each score level. The increase in 1-year TVR rates was significantly associated with the risk score: Score = 0, TVR = 0% (n = 16); Score 1 =

| Table 1. Clinical characteristics of patient population. |
| Age (years) | 61 ± 10.5 |
| Women | 35% |
| Hypertension | 81% |
| DM | 22% |
| Smoker | 46% |
| Dyslipidemia | 60% |
| Medical history |  |
| PCI | 12% |
| MI | 35% |
| CABG | 10% |
| Current MI | 13% |
| DM = diabetes mellitus; PCI = percutaneous coronary intervention; MI = myocardial infarction; CABG = coronary artery bypass grafting |

| Table 2. Angiographic characteristics of the procedures. |
| Reference vessel diameter | 2.80 ± 0.56 mm |
| Lesion length | 12.45 ± 6.3 mm |
| Stent diameter | 3.02 ± 0.58 mm |
| Stent length | 16.10 ± 5.17 mm |
| Implantation pressure | 13.26 ± 2.79 atm |
| atm = atmospheres |
As this score relies on preprocedural characteristics, it can be used to assess the risk of recurrent events before stent implantation, which can aid operators in the decision of whether to implant a BMS or DES in any given patient. The integration of diabetes mellitus, reference vessel diameter and lesion length into a risk score provides physicians with a simple and easy-to-use tool to aid in the clinical decision process of which type of stent to implant. In the development cohort, we identified these variables as strongly and independently associated with 1-year TVR, and were able to integrate this piece of information into the risk score validated in the present study. The validation cohort had patients with smaller vessels and longer lesions, and even in a more diseased population, as that herein reported, the risk score was also statistically associated with outcomes. In the modern cardiology practice, risk scores have gained widespread clinical applicability after the TIMI risk score, and this is deemed a valuable approach when patient care is considered.\cite{19,20} Validation of a risk score in an independent cohort of patients is considered the best method to demonstrate the strength of the model and possible clinical application in a different patient population.\cite{18}

The clinical importance of our risk score relates to the fact that DES are not currently recommended in all PCIs.\cite{10,11,21} Recent reports with large numbers of patients have demonstrated significantly better outcomes with DES when compared with BMS,\cite{22–25} but some subgroups of patients may not experience this clinical benefit. In particular, patients with planned surgical procedures, recent bleeding episodes, or with high bleeding risk due to gastrointestinal diseases or other causes are poor candidates for prolonged dual antiplatelet therapy, which may preclude DES use.\cite{8,9} The long-term treatment adherence to long-term thienopyridines in some subgroups of patients can also be a problem, as demonstrated by previous studies. Spertus and coworkers reported a 13% rate of clopidogrel discontinuation in the first month after the procedure.\cite{26} Finally, economic constraints also compromise the concept of a universal use of DES since these new devices cost significantly more than BMS, and this is associated with an unfavorable cost-effectiveness ratio in those patients at low restenosis risk.\cite{14,27}

The relevance of risk scores in the clinical decision-making process in daily cardiology practice is best demonstrated by the TIMI and GRACE scores.\cite{19,28} The current guidelines recommend that the risk profile of all patients with an ACS should be evaluated by one of those scores.\cite{29} The strategy of risk stratification will guide patient treatment and the choice of an invasive or conservative approach. In the interventional cardiology field, some predictive models have also been described to assess the risk of recurrent events after PCI, but none of them were incorporated into clinical practice.\cite{15–16} The lack of sufficient discriminatory ability and excessive complexity of these models could have played a role. In this regard, the risk score validated in this study has a similar c-statistic than the widespread used TIMI risk score.

The TVR rates described in the present study are similar to those of recent reports of patients treated with BMS.\cite{15,30}
variables included in our score (reference vessel diameter, lesion length and diabetes mellitus) have also been consistently associated with outcomes in several clinical and experimental studies.\textsuperscript{31–37} Greenberg and coworkers described a model to predict clinical restenosis after BMS implantation as a function of the same variables used in our score (lesion length, reference vessel diameter and diabetes mellitus).\textsuperscript{14} However, the format described (a 4 x 4 table) makes it complicated to use in daily practice. Ellis and coworkers reported on their experience with over 5,000 patients treated with BMS at the Cleveland Clinic.\textsuperscript{15} Reference vessel diameter and lesion length, among others, were identified as strong predictors of a new revascularization procedure. In this cohort, the rate of reintervention in patients with lesions shorter than 10 mm located in vessels larger than 3.5 mm was < 3%, a figure similar to our data. Recently, Tu and coworkers reported on a cohort of 3,751 pairs of patients, matched on the basis of a propensity score from a population-based clinical registry of all patients undergoing PCI with BMS or DES implantation in Ontario, Canada.\textsuperscript{22} The 2-year rate of TVR was lower among patients who received DES, but significant reductions in the rate of TVR were observed only among patients with two or three risk factors for restenosis (i.e., presence of diabetes, small vessels [≤ 3 mm in diameter], and long lesions [≥ 20 mm]). On the other hand, recent studies with patients from real-world practice and without routine angiographic follow up have reported very low target lesion revascularization in patients treated with DES, without increasing MI or death.\textsuperscript{25,29} This recent information is the main reason why DES should be used in most eligible patients at risk for restenosis.

Conclusion

In conclusion, the clinical implications of this study relate to the prediction of recurrent cardiac events after BMS based on preprocedural characteristics. This feature of the validated risk score can aid in the decision to implant a DES or a BMS in any given patient, mainly in those with a higher bleeding risk or expected problems with adherence to prolonged dual antiplatelet treatment. Maybe those patients with predicted very low TVR rates based on our score can be treated with BMS, since the absolute incremental clinical benefit of a DES would be small and the systematic use of a DES would be associated with an unfavorable cost-effectiveness disease-specific ratio.\textsuperscript{27} On the other hand, low scores were present in only 15% of all procedures. The complete follow up in only 89% of the patients should also be considered as a limitation, since several recent studies report higher follow-up rates.

References