Interventional Cardiology

Predicting the Restenosis Benefit of Drug-Eluting Versus Bare Metal Stents in Percutaneous Coronary Intervention

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Background—Drug-eluting stents (DES) for percutaneous coronary intervention decrease the risk of restenosis compared with bare metal stents. However, they are costlier, require prolonged dual antiplatelet therapy, and provide the most benefit in patients at highest risk for restenosis. To assist physicians in targeting DES use in patients at the highest risk for target vessel revascularization (TVR), we developed and validated a model to predict TVR.

Methods and Results—Preprocedural clinical and angiographic data from 27,107 percutaneous coronary intervention hospitalizations between October 1, 2004, and September 30, 2007, in Massachusetts were used to develop prediction models for TVR at 1 year. Models were developed from a two-thirds random sample and validated in the remaining third. The overall rate of TVR was 7.6% (6.7% with DES, 11% with bare metal stents). Significant predictors of TVR included prior percutaneous coronary intervention, emergency or salvage percutaneous coronary intervention, prior coronary bypass surgery, peripheral vascular disease, diabetes mellitus, and angiographic characteristics. The model was superior to a 3-variable model of diabetes mellitus, stent diameter, and stent length (c statistic, 0.66 versus 0.60; P<0.001) and was well calibrated. The predicted number needed to treat with DES to prevent 1 TVR compared with bare metal stents ranged from 6 (95% confidence interval, 5.4–7.6) to 80 (95% confidence interval, 62.7–116.3), depending on patients’ clinical and angiographic factors.

Conclusions—A predictive model using commonly collected variables can identify patients who may derive the greatest benefit in TVR reduction from DES. Whether use of the model improves the safety and cost-effectiveness of DES use should be tested prospectively. (Circulation. 2011;124:1557–1564.)

Key Words: coronary intervention ■ outcome assessment ■ predictors ■ restenosis ■ stents

Prospectively defining patients’ risks before invasive procedures is critical for the rational application of technologies to improve outcomes.1,2 This principle is of particular importance when potential alternative treatment strategies are associated with a competing, but distinct, set of risks. The characterization of potential risks and benefits is also essential to improve the transparency and accuracy of informed consent.

Clinical Perspective on p 1564

For patients undergoing percutaneous coronary intervention (PCI), drug-eluting stents (DES) significantly reduce the rate of restenosis of the target vessel compared with bare metal stents (BMS).3–5 However, they require the prolonged use of thienopyridines to avoid the rare but potentially fatal complication of stent thrombosis and may have higher rates of very late stent thrombosis than BMS.6–8 In addition, DES are significantly more expensive than BMS, so the cost-effectiveness of their use is dependent on the expected absolute reduction in restenosis for a given patient.9 Collectively, these data support the preferential use of DES in patients at highest risk for restenosis. Although a number of prior studies have identified predictors of target vessel revascularization (TVR), they have a number of limitations that limit their use in guiding stent selection in routine practice, including derivation from restricted clinical trial

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patient populations. Incorporation of post-PCI data that can be obtained only after a stent has already been implanted, or use of predictors that are not typically or easily assessed. To improve the prospective stratification of patients’ risks for TVR, predictive models that are limited to preprocedural clinical and angiographic data are required. By providing this information at the point of care, it may be possible to support the optimal use of DES and to engage patients in the decision-making process. Engaging patients in selecting stent type is particularly important because they will need to comply with long-term dual antiplatelet therapy if DES is used.

The goal of this study was to develop and validate a model to predict the likelihood of TVR after PCI with either DES or BMS within a large real-world population using variables commonly collected as part of the National Cardiovascular Disease Registry (NCDR) CathPCI data collection instrument. This prediction model could then be used to derive the anticipated absolute risk reduction in TVR associated with DES use compared with BMS use and prospectively support clinical decision making.

Methods

Study Population

Since 2003, the Massachusetts Department of Public Health has systematically collected data on all PCI procedures performed at all acute care, nonfederal Massachusetts hospitals. The data are collected by trained hospital personnel using the NCDR CathPCI data collection instrument and are submitted electronically to the Massachusetts Data Analysis Center at Harvard Medical School. Selected covariates and outcomes are audited and adjudicated as previously described. To obtain subsequent TVR rates, we linked the index PCI to data on all subsequent revascularization procedures longitudinally from the Massachusetts Data Analysis Center and to hospital discharge billing data collected by the Massachusetts Division of Health Care Finance and Policy.

We initially identified all PCI admissions between October 1, 2004, and September 30, 2007. For admissions in which multiple PCI procedures were performed, we included only the first PCI in the analysis. We subsequently excluded PCI admissions for the following reasons: no stent deployed (n=3054), both DES and BMS stents used (n=1648), inability to link data or patient was not a Massachusetts resident (n=4394), and missing data (n=98). We additionally excluded those patients who received devices <2.25 and >4 mm in diameter, for which DES were not available (n=708). We next developed a propensity score model to predict the log odds of DES (versus BMS) use, conditioned on 46 demographic and clinical variables, and plotted the frequency distribution of propensity scores by stent type. To identify a sample of patients who were eligible for both stent types, we excluded procedures falling into regions of nonoverlap in propensity scores, identified by having a logit of the predicted probability of receiving DES <0.0 or >3 (n=96 BMS and 769 DES patients). The remaining 27107 PCI admissions were included in the analysis and represent a group for whom either stent type might be reasonably considered.

Definitions

The primary outcome of interest was the occurrence of TVR within 12 months of the index procedure. We defined TVR as PCI performed in a vessel treated during the index procedure or any coronary artery bypass graft surgery performed after the index procedure. Definitions for the data elements for version 3.04 of the CathPCI registry are available at http://www.ncdr.com/WebNCDR/Elements.aspx, and definitions for all variables retained in final risk prediction models can be found in Table I of the online-only Data Supplement.

We identified a list of variables to be included in the initial multivariable model to predict TVR based on clinical relevance. These included sociodemographic information (age, sex, race/ethnicity, insurance status, and smoking status), medical history (body mass index, hypertension, diabetes mellitus, glomerular filtration rate, hemodialysis), cardiovascular history (prior myocardial infarction, cerebrovascular disease, peripheral vascular disease, prior PCI, prior coronary artery bypass graft, prior congestive heart failure, and Canadian Cardiovascular Society/New York Heart Association classification), and clinical status variables at admission (disease presentation [ST-segment–elevation myocardial infarction, non–ST-segment–elevation myocardial infarction, unstable angina, stable angina or atypical chest pain, no chest pain] and PCI status [elective, urgent, emergent, salvage]). Estimated glomerular filtration rate was calculated from the abbreviated Modification of Diet in Renal Disease formula based on creatinine assessed at the time of admission.

We additionally identified a list of relevant angiographic variables, including minimum stent diameter (<3 versus ≥3 mm), total stent length (<30 versus ≥30 mm), bifurcation lesion, previously treated lesion, lesion within saphenous vein graft, treated lesion within left anterior descending artery, multivessel disease (≥2 vessels with ≥70% stenosis), and number of treated lesions. Dichotomization for stent length was selected after inclusion of a categorical variable revealed a cutoff value (30 mm) at which the multivariable adjusted odds of TVR increased substantially. Stent diameter was dichotomized to retain meaningful numbers of patients above and below the cutoff value and to improve the ease of subsequent implementation of the model. Stent diameter and length were included as estimates of lesion length and reference diameter because these values were not available. In addition, these stent characteristics can be readily predicted from the preprocedural angiogram and used to inform stent selection.

Statistical Analysis

We first examined bivariate associations of TVR with variables identified on the basis of their clinical relevance. Next, multivariable logistic regression was performed in a randomly selected two-thirds sample (developmental cohort) to identify predictors of TVR. In the first model, we considered only clinical variables, without inclusion of angiographic variables, to support preprocedural discussions with patients regarding the benefits of alternative stent types. Forward elimination of variables was performed until the adjusted R² of the model reached 95% of that of the full model. We then generated a similar model including angiographic variables (the full model). For all models, an indicator variable for DES versus BMS was used. Although recent data suggest potential differences in outcomes among DES types, these differences are small in magnitude relative to differences in TVR between DES and BMS. Because the purpose of our model was to help inform the DES versus BMS decision, we elected to group all DES together instead of analyzing each DES type separately. A number of interaction terms were considered to evaluate the possibility that the strength of the association of clinical and angiographic characteristics with TVR might differ for BMS- and DES-treated patients, including interactions of stent type with age, diabetes mellitus, renal function, clinical presentation, saphenous vein graft intervention, vessel location, stent length, and stent diameter. However, none of these interactions were found to be significant and thus were not included in the models.

For validation, we applied coefficients of the models to the remaining one-third sample (validation cohort). Model discrimination was assessed with the c index, and model calibration was assessed by examining predicted versus observed rates of TVR within deciles of predicted TVR risk and testing the difference with the Hosmer-Lemeshow χ² test. Overfitting statistics were estimated as described by Harrell. After the models were found to perform similarly in the developmental and validation cohorts, final nonangiographic and angiographic models using the entire study sample (merged developmental and validation cohorts) were generated. We calculated the integrated discrimination improvement (IDI) to assess...
the improvement in discrimination of the full model including angiographic characteristics compared with the nonangiographic model. The IDI provides a quantitative summary that measures the average absolute improvement in individual risk predictions that results from the inclusion of additional variables to a prediction model. Prior studies have advocated using as few as 3 variables to predict restenosis: diabetes mellitus, lesion/stent length, and vessel/stent diameter. We therefore also compared the improvement in discrimination of the full model compared with a more parsimonious model accounting for stent type and these 3 variables as measured by the c statistic and IDI.

To assess the distribution of predicted reduction in TVR associated with DES use, we generated predicted probabilities of TVR using PCI with either DES or BMS by individually applying the clinical and angiographic profile of each patient in the study population to the models. We then subtracted the predicted probability of TVR with DES from that with BMS to derive the predicted TVR reduction associated with DES for each patient in the sample and calculated the estimated number needed to treat (NNT). To quantify our uncertainty with both the predicted TVR reduction and the NNT estimates, we used resampling procedures implemented through bootstrapping. Specifically, we sampled all admissions with replacement, re-estimated the logistic regression model, and computed summaries of both the predicted reduction in TVR with DES and the NNT. These summaries included the minimum, maximum, mean, and median benefit (and corresponding NNT). We repeated this 1000 times and computed the mean of the various summaries over the 1000 samples. We also constructed bootstrap 95% confidence intervals (CIs) for these selected summaries by determining the 2.5th and the 97.5th percentiles of the empirical distribution. All analyses were conducted with SAS version 9.2.

Results

Of the 27 107 PCI admissions examined, 21 933 (80.9%) underwent PCI with DES, and the remaining 5174 (19.1%) received BMS. Baseline clinical and angiographic characteristics, stratified by the occurrence of TVR by 1 year, are shown in Tables 1 and 2. By 1 year after the index PCI, TVR occurred in 7.6% of patients overall (6.7% of DES patients and 11.0% of BMS patients). Bivariate analyses suggested that patients who had TVR were younger, were more often diabetic, and had higher rates of prior myocardial infarction, peripheral vascular disease, prior PCI, and prior coronary artery bypass graft. Patients with TVR more often had multivessel disease and had received stents with smaller diameters and longer lengths at the index procedure. The mortality rates at 1 year for patients with and without TVR were similar (5.3% versus 5.2%; P = 0.78).

Model Development and Validation

The nonangiographic and full models had c statistics of 0.61 and 0.66, respectively, in the developmental models. Model discrimination when applied to the validation sample was similar (c statistic, 0.64 and 0.65 for the nonangiographic and angiographic models, respectively). A comparison of observed TVR rates at 1 year in the validation sample and the predicted risk of TVR demonstrated good calibration of both the nonangiographic (Hosmer-Lemeshow P = 0.65) and angiographic (Hosmer-Lemeshow P = 0.90) models without evidence of overfitting (Figure 1).

Final Nonangiographic and Full Models

Because models showed similar discrimination and similar calibration in both the developmental and validation samples, the improvement in discrimination of the full model including angiographic characteristics compared with the nonangiographic model. The IDI provides a quantitative summary that measures the average absolute improvement in individual risk predictions that results from the inclusion of additional variables to a prediction model. Prior studies have advocated using as few as 3 variables to predict restenosis: diabetes mellitus, lesion/stent length, and vessel/stent diameter. We therefore also compared the improvement in discrimination of the full model compared with a more parsimonious model accounting for stent type and these 3 variables as measured by the c statistic and IDI.

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Because models showed similar discrimination and similar calibration in both the developmental and validation samples,
Table 2. Angiographic Characteristics

<table>
<thead>
<tr>
<th>Angiographic Variables</th>
<th>Target Vessel Revascularization (n=2047)</th>
<th>No Target Vessel Revascularization (n=25 060)</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vessels with &gt;70% stenosis (mean±SD), n</td>
<td>1.3±0.7</td>
<td>1.2±0.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Lesions treated (mean±SD), n</td>
<td>1.5±0.8</td>
<td>1.4±0.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LAD treated, %</td>
<td>43.5</td>
<td>42.9</td>
<td>0.60</td>
</tr>
<tr>
<td>Previously treated lesion, %</td>
<td>5.6</td>
<td>3.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Bifurcation lesion, %</td>
<td>14.7</td>
<td>13.7</td>
<td>0.22</td>
</tr>
<tr>
<td>Saphenous vein graft intervention, %</td>
<td>8.0</td>
<td>4.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Minimum stent diameter (mean±SD), mm</td>
<td>2.98±0.42</td>
<td>3.04±0.42</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total stent length (mean±SD), mm</td>
<td>32.2±21.2</td>
<td>29.0±19.0</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

LAD indicates left anterior descending artery.

final models were generated with the entire study sample. Beta weights and standard errors for models are included in Table II of the online-only Data Supplement, and a Web-based calculator that enables the clinical use of this model is available at http://www.massdac.org/riskcalc_revasc. Within the nonangiographic model, DES was associated with a significant decrease in 1-year TVR compared with BMS (odds ratio, 0.57; 95% CI, 0.52–0.64). The variables retained in the nonangiographic model were the use of DES, age, diabetes mellitus, peripheral vascular disease, hypertension, prior PCI, prior coronary artery bypass graft, admission symptoms, Canadian Cardiovascular Society/New York Heart Association class, and PCI indication (Figure 2).

Angiographic variables retained in the full model included having ≥2 vessels with ≥70% stenosis, the number of lesions treated, stent diameter ≥3.0 mm, and total stent length ≥30 mm. All nonangiographic variables except prior coronary artery bypass graft were also retained in the full model. The addition of angiographic variables further improved model discrimination (c statistic, 0.62 for nonangiographic model in the complete cohort compared with 0.66 for the full model; IDI, 0.010; \( P<0.001 \)). This IDI value means that the percent of variation in TVR risk explained by the model increased by 1.0% in absolute terms in the full model compared with the nonangiographic model. Treatment with DES continued to be associated with a significant reduction in 1-year TVR (odds ratio, 0.53; 95% CI, 0.47–0.59). There were no statistically significant interactions in either model.

Comparison of Final Model With Usual Practice

Given that current practice emphasizes 3 factors, diabetes mellitus, lesion/stent length, and vessel/stent diameter, in considering TVR risk, we compared the full model with the discrimination of these 3 variables alone (in addition to stent type). We found that model discrimination improved significantly (c statistic, 0.60 versus 0.66; IDI, 0.013; \( P<0.001 \)), supporting the potential for the new model to improve clinicians’ estimates of TVR risk compared with the prevailing standard.

Predicted Target Vessel Revascularization and Restenosis Benefit With Drug-Eluting Stents

The distribution of predicted rates of TVR from the full model assuming use of BMS varied broadly, from 2.7% to 57.4% (Figure 3). These values corresponded to absolute TVR reductions associated with DES use ranging from 1.2% (95% CI, 0.9–1.6) to 15.9% (95% CI, 13.0–18.4), with an interquartile range of 3.5% to 6.3%. Similarly, the predicted NNT to prevent 1 TVR with DES compared with BMS ranged from as few as 6 patients (95% CI, 5.4–7.6) to as high as 80 patients (95% CI, 62.7–116.3), depending on clinical and angiographic characteristics. Similar results were observed for the nonangiographic model, with the NNT ranging from 8 (95% CI, 6.6–10.3) to 61 (95% CI, 46.2–86.4).

Discussion

In a large statewide registry of patients undergoing PCI, we found that TVR at 1 year occurred in 6.7% of patients undergoing PCI with DES and 11.0% of patients undergoing PCI with BMS. Using variables routinely collected as part of the NCDR CathPCI instrument, we developed and validated parsimonious models to predict TVR using both clinical and angiographic variables. We found that the predicted reduction...
in TVR for DES compared with BMS varied broadly, depending on patient characteristics.

The factors associated with TVR in our study were similar to those found in previous studies examining predictors of TVR, including prior PCI, diabetes mellitus, longer stent length, and smaller stent diameter, although we identified other important variables that further improved risk stratification.\textsuperscript{21–23} The addition of angiographic variables significantly improved overall discrimination of the models. Although prior studies have found strong associations of angiographic variables with restenosis, they have typically not assessed the incremental improvement in discrimination that resulted from the addition of these variables to nonangiographic clinical characteristics, as we have done in this study.\textsuperscript{12,24–26} Moreover, we found a significant improvement in discrimination of TVR risk compared with the current clinical practice of relying solely on patients’ diabetes status, lesion/stent length, and vessel/stent diameter, underscoring the potential clinical utility of our model.

Our study differs from prior work in a number of important ways. First, because all nonfederal hospitals in Massachusetts are required to participate in the registry, the results are generated from a population-based sample of patients undergoing PCI in routine clinical practice without being subjected to the selection biases that occur with clinical trials or volunteer registries. In addition, the model is built on various predictors of TVR.
ables commonly collected as part of the NCDR CathPCI instrument, which is currently used in >1000 hospitals across all 50 US states, making it widely applicable and potentially easily integrated into routine care at these facilities.27–29 Finally, our analysis was performed during a time period that included a large number of both BMS and DES patients, allowing the precise estimation of expected TVR reduction with DES across the entire spectrum of clinical profiles.

As expected, the use of DES was associated with a significant decrease in the occurrence of TVR compared with BMS. None of the interaction terms we explored to examine whether the benefit of DES was modified by clinical factors were found to be significant, so the relative risk reduction in TVR (≈45%) was constant for all patients in the study. However, the absolute risk reduction differed substantially between patients on the basis of their clinical profiles, with the NNT to prevent 1 TVR ranging from 6 to 80, depending on patient characteristics.

Such differences in absolute risk reduction create the opportunity to prospectively identify and use DES in patients who stand to derive the greatest benefit from DES while considering BMS in patients with low anticipated benefit, given the added bleeding risk and costs associated with DES and its requirement for prolonged dual antiplatelet therapy. In fact, when the risk of restenosis with BMS is <10%, the NNT exceeds 25, meaning that >25 patients would need to be treated with DES to avoid a single repeat PCI procedure for restenosis (Figure 4). Prior economic analyses have suggested that a TVR rate with BMS of <11% is associated with an increase in society-based costs of more than $10 000 to prevent 1 repeat procedure and would not be considered a cost-effective use of DES.9 In our sample, >45% of patients undergoing PCI had a predicted rate of restenosis with BMS that was less than this threshold, 78.6% of whom received DES. Because our model specifically used variables obtainable before stent implantation, it could be used prospectively to help guide physicians in stent selection and to apprise patients more accurately of the risks and benefits of the different stent choices. Such a use of the model would enable greater and more informed patient participation in clinical decisions, a priority for the Institute of Medicine’s goals for improving the quality of care.30 In fact, our group is currently testing the impact of prospective risk stratification, through individualized informed consent documents imbedded with this risk model, on patient and physician decision making and long-term compliance with dual antiplatelet therapy.27

Our analyses should be interpreted in the context of several potential limitations. Although we included a large number of clinically relevant variables in our models, the discrimination of the models was modest. Whereas our model discrimination compares favorably with other reported models,23 including those that incorporate post-PCI variables,31 there may be unobserved procedural (eg, quality of stent deployment), biological (eg, genetic predisposition), or social (eg, access to

![Figure 3. Distribution of predicted rate of 1-year target vessel revascularization (TVR) assuming treatment with bare metal stents (BMS) within the study sample. Results are based on the full model that includes angiographic variables.](http://circ.ahajournals.org/)

![Figure 4. Relationship between predicted 1-year target vessel revascularization (TVR) with bare metal stents (BMS) and number needed to treat (NNT) with drug-eluting stents to prevent a single occurrence of TVR. The dashed line shows the threshold of predicted 1-year TVR risk below which the NNT is >25. CI indicates confidence interval.](http://circ.ahajournals.org/)
care, compliance with therapy) factors that are associated with TVR and not accounted for in these models. In addition, because the goal of our study was to produce a model that could be prospectively used to guide decisions during PCI, we did not incorporate variables that could be ascertained only after completion of the procedure such as adequate stent deployment, apposition, or coronary dissection that might further improve model discrimination. Because inherent uncertainty exists for the application of prediction models to any individual patient, estimates of predicted TVR risk are meant to enhance but not replace clinical judgment. To highlight this uncertainty, results of predicted TVR risk are presented with associated 95% CIs when the publicly available Web-based calculator is used, an advantage over using common risk scores, which do not account for imprecision in estimates. Next, our results are based on prospectively collected observational data, and thus are vulnerable to the omission of unobserved risk factors that may confound the choice of stent type with patient illness. Although the model was found to be well calibrated in both the DES- and BMS-treated patients, regression estimates were generated primarily from a DES population, and may therefore be optimized for this subgroup. Because we found no significant interactions between stent type and other covariates for the TVR outcome, we derived estimates of absolute risk reduction in TVR for DES that are based on this assumption. Next, we captured only data on PCI that occurred within nonfederal Massachusetts hospitals, which may limit some of the generalizability of our findings. In addition, there might be circumstances in which one stent choice over another was clearly clinically indicated, although we restricted the sample to patients who were apparently eligible for both types of stents. In using TVR as our primary outcome, we were not able to determine whether revascularization of the target vessel was due to restenosis of the index lesion or to new coronary lesions within the same vessel. This outcome may also depend on a variety of factors, including patient and physician perception of benefit. However, we believe that TVR is an appropriate patient-oriented outcome compared with angiographically defined restenosis, which may not be functionally significant.

**Conclusions**

We developed and validated a predictive model to predict the occurrence of TVR after PCI that allows the quantification of the anticipated benefit of PCI with DES compared with BMS in a large community-based population. The prospective use of individualized assessments of patient benefits may support the safer and more cost-effective application of this technology. Moreover, prospectively informing patients of the benefits of a DES may support shared medical decision making and improve patients’ understanding of the need for long-term dual antiplatelet therapy within the context of their reduced risk for TVR after DES.

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**Disclosures**

Dr Yeh is an investigator for the Harvard Clinical Research Institute and a consultant for the Kaiser Permanente Division of Research. Dr Normand is director of the Massachusetts Data Analysis Center, contracted by the Massachusetts Department of Public Health, and is funded to collect, validate, analyze, and disseminate evidence of quality of cardiovascular care at acute care nonfederal hospitals in Massachusetts. R.E. Wolf is senior programmer for the Massachusetts Data Analysis Center and is funded to support biostatistical and programming aspects of the Center. Dr Cohen receives grant support from Boston Scientific, Medtronic, and Abbott Vascular and has served as a consultant to Medtronic, Abbott Vascular, and Cordis. Dr Mauri receives institutional research support from Abbott, Boston Scientific, Cordis, Medtronic, Eli Lilly, Daiichi Sankyo, Bristol Myers Squibb, and Sanoﬁ-aventis and has consulted for Cordis and Medtronic. Dr Spertus has received research grants from the National Heart, Lung, and Blood Institute (HL096624) and the American Heart Association (0875149N) to study the impact of prospective risk estimation on the use of DES as a function of patients’ risks for restenosis. Within the past 2 years, he has also received research grant support from Lilly, Sanoﬁ, Amgen, and Evahart and has consulted for United Healthcare, Gilead, Quest Diagnostics, and St. Jude Medical. He has patents and an equity position in Health Outcomes Sciences, which supports the technology to deliver individualized estimates of patients’ outcomes based on multivariable models. The other authors report no conflicts.

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http://circ.ahajournals.org/content/suppl/2013/10/14/CIRCULATIONAHA.111.045229.DC2

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Supplemental Table 1. Model Coefficients and Standard Errors

<table>
<thead>
<tr>
<th>Label</th>
<th>Estimated ß (Excluding Angiographic Characteristics)</th>
<th>Standard Error</th>
<th>P-value</th>
<th>Estimated ß (Including Angiographic Characteristics)</th>
<th>Standard Error</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>-2.6444</td>
<td>0.1136</td>
<td>&lt; 0.001</td>
<td>-2.8867</td>
<td>0.1264</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Drug-Eluting Stent</td>
<td>-0.5588</td>
<td>0.0536</td>
<td>&lt; 0.001</td>
<td>-0.6418</td>
<td>0.0546</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 50</td>
<td>0.2380</td>
<td>0.0662</td>
<td>&lt; 0.001</td>
<td>0.2913</td>
<td>0.0665</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>50 - 80</td>
<td>Reference</td>
<td></td>
<td></td>
<td>Reference</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 80</td>
<td>-0.3062</td>
<td>0.0745</td>
<td>&lt; 0.001</td>
<td>-0.3942</td>
<td>0.0752</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Diabetes</td>
<td>0.1848</td>
<td>0.0506</td>
<td>&lt; 0.001</td>
<td>0.1443</td>
<td>0.0509</td>
<td>0.005</td>
</tr>
<tr>
<td>Peripheral Vascular Disease</td>
<td>0.2878</td>
<td>0.0654</td>
<td>&lt; 0.001</td>
<td>0.2683</td>
<td>0.0649</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0.1759</td>
<td>0.0603</td>
<td>0.004</td>
<td>0.1471</td>
<td>0.0604</td>
<td>0.015</td>
</tr>
<tr>
<td>Previous PCI</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>Reference</td>
<td></td>
<td></td>
<td>Reference</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 1 year</td>
<td>0.7720</td>
<td>0.1391</td>
<td>&lt; 0.001</td>
<td>0.9331</td>
<td>0.1402</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>&gt; 1 year or timing</td>
<td>0.2265</td>
<td>0.0572</td>
<td>&lt; 0.001</td>
<td>0.2597</td>
<td>0.0571</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Unknown</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NYHA Class</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>Reference</td>
<td></td>
<td></td>
<td>Reference</td>
<td></td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>-0.0941</td>
<td>0.0777</td>
<td>0.23</td>
<td>-0.1061</td>
<td>0.0782</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>III</td>
<td>-0.0845</td>
<td>0.0742</td>
<td>0.26</td>
<td>-0.1073</td>
<td>0.0749</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>IV</td>
<td>-0.1853</td>
<td>0.0760</td>
<td>0.02</td>
<td>-0.2120</td>
<td>0.0767</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>
The predicted risk is computed as $(\exp(z)/(1 + \exp(z)) \times 100$, where $z = \text{intercept} + \text{sum of the } \beta \text{ coefficients} \times \text{risk factor values}$. A model calculator is available at www.massdac.org/riskcalc_revasc
### Supplemental Table 2. Definitions of Variables Included in Models, Adapted from the NCDR Version 3.04 Data Definitions

<table>
<thead>
<tr>
<th>Variable</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Non-Angiographic Variables</strong></td>
<td></td>
</tr>
<tr>
<td>Drug-Eluting Stent</td>
<td>Placement of a drug-eluting stent in the target vessel for the index procedure.</td>
</tr>
<tr>
<td>Age</td>
<td>Age of patient at time of index PCI.</td>
</tr>
</tbody>
</table>
| Diabetes                        | A history of diabetes, regardless of duration of disease, or need for antidiabetic agents. This includes diagnosis on admission or pre-procedure. It does not include gestational diabetes. A history of peripheral vascular disease, including:  
   1. Claudication either with exertion or at rest.  
   2. Amputation for arterial vascular insufficiency.  
   3. Aorto-iliac occlusive disease reconstruction, peripheral vascular bypass surgery, angioplasty or stent; or percutaneous intervention to the extremities.  
   4. Documented AAA repair or stent.  
   5. Positive non-invasive/invasive test.  
   This does not include procedures such as vein stripping, carotid disease, or procedures originating above the diaphragm.  
   A history of hypertension, as documented by one of the following:  
   1. History of hypertension diagnosed and treated with medication, diet and/or exercise.  
   2. Blood pressure greater than 140 systolic or 90 diastolic on at least 2 occasions.  
   3. Currently on antihypertensive pharmacologic therapy.  
| Peripheral Vascular Disease     | Previous percutaneous coronary intervention (even if unsuccessful) of any type (balloon angioplasty, stent or other), performed prior to the current admission.                                                 |
| Hypertension                    |                                                                                                                                                                                                 |
| Previous PCI                    |                                                                                                                                                                                                 |
| CCS/NYHA Class                  | Patient has cardiac disease but without resulting limitations of ordinary physical activity. Ordinary physical activity (e.g., walking several blocks or climbing stairs) does not cause undue fatigue, palpitation, dyspnea, or anginal pain. Limiting symptoms may occur with marked exertion. Patient has cardiac disease resulting in slight limitation of ordinary physician activity. Patient is comfortable at rest. Ordinary physical activity such as walking more than two blocks or climbing more than one flight of stairs results in limiting symptoms (e.g., fatigue, palpitation, dyspnea, or anginal pain). Patient has cardiac disease resulting in marked limitation of physical activity. Patient is comfortable at rest. Less than ordinary physical activity (e.g., walking one to two level blocks or climbing one flight of stairs) causes fatigue, palpitation, dyspnea, or anginal pain. Patient has dyspnea at rest that increases with any physical activity. Patient has cardiac disease resulting in inability to perform any physical activity without discomfort. Symptoms may be present even at rest. If any |
physical activity is undertaken, discomfort is increased.

Admissions
Symptoms

None
No anginal symptoms

Atypical Chest Pain
Pain, pressure or discomfort in the chest, neck or arms not clearly exertional or not otherwise consistent with pain or discomfort of myocardial ischemic origin.

Stable Angina
Angina without a change in frequency or pattern for the six weeks prior to this cath lab visit. Angina is controlled by rest and/or oral or transcutaneous medications.

The patient was hospitalized for unstable angina documented in the medical record with serial ECG’s and biochemical profiles. One of the following criteria are necessary:

1. Angina at rest (usually prolonged >20 minutes).
2. New onset angina (<2 months) exertional angina of at least Canadian Cardiovascular Society Classification (CCSC) Class III.
3. Increasing angina - previously diagnosed angina that has become distinctly more frequent, longer in duration, or lower in threshold (i.e., increased by greater than or equal to 1 CCS class to at least CCS Class III severity).

The patient was hospitalized for a myocardial infarction documented in the medical record.

AT LEAST ONE OF THE FOLLOWING BIOCHEMICAL INDICATORS for detecting myocardial necrosis must be present:

1. Troponin T or I:
   a. Maximal concentration of troponin T or I > the MI decision limit on at least one occasion during the first 24 hours after the index clinical event.
2. CK-MB:
   a. Maximal value of CK-MB > 2 x the upper limit of normal on one occasion during the first hours after the index clinical event. OR
   b. Maximal value of CK-MB, preferable CK-MB mass, > upper limit of normal on two successive samples.
3. Total CK:
   a. In the absence of availability of a troponin or CK-MB assay, total CK > 2 x the upper limit of normal, or the B fraction of CK may be employed, but these last two biomarkers are considerably less satisfactory than CK-MB.

AND ONE OF THE FOLLOWING:

1. Either ST segment depression or T wave abnormalities; or
2. Ischemic symptoms in the presence or absence of chest discomfort. Ischemic symptoms may include:
   a. unexplained nausea and vomiting; or
   b. persistent shortness of breath secondary to left ventricular failure; or
   c. unexplained weakness, dizziness, lightheadedness, or syncope.

The patient was hospitalized for an ST Elevation Myocardial Infarction (STEMI) documented in the medical record.

STEMI
AT LEAST ONE OF THE FOLLOWING BIOCHEMICAL INDICATORS for detecting myocardial necrosis must be present (see below for a definition of Reference Control Limits):
1. Troponin T or I:
   a. Maximal concentration of troponin T or I > the MI decision limit on at least one occasion during the first 24 hours after the index clinical event.

2. CK-MB:
   a. Maximal value of CK-MB > 2 x the upper limit of normal on one occasion during the first hours after the index clinical event; OR
   b. Maximal value of CK-MB, preferable CK-MB mass, > upper limit of normal on two successive samples.

3. Total CK
   a. In the absence of availability of a troponin or CK-MB assay, total CK > 2 x the upper limit of normal, or the B fraction of CK may be employed, but these last two biomarkers are considerably less satisfactory than CK-MB.

AND ONE OF THE FOLLOWING ECG CHANGES:

1. ST-segment elevation: New or presumed new ST segment elevation at the J point in two or more contiguous leads with the cut-off points >=0.2 mV in leads V1, V2, or V3, or >=0.1 mV in other leads; OR

2. Development of any Q wave in leads V1 through V3, or the development of a Q-wave > or = to 30 ms (0.03s) in leads I, II, aVL, aVF, V4, V5, or V6. (Q wave changes PCI Indication

Elective

The patient's cardiac function has been stable in the days or weeks prior to the procedure. The procedure could be deferred without increased risk of compromised cardiac outcome.

ALL of the following conditions are met:

1. Not elective status.
2. Not emergency status.
3. Procedure required during same hospitalization in order to minimize chance of further clinical deterioration.

Urgent

4. Worsening, sudden chest pain, CHF, acute myocardial infarction (AMI), anatomy, IABP, unstable angina (USA) with intravenous (IV) nitroglycerin (TNG) or rest angina (but stabilized patient) may be included.

The patient’s clinical status includes any of the following:

1. Ischemic dysfunction (any of the following):
   a. Ongoing ischemia including rest angina despite maximal medical therapy (medical and/or IABP));
   b. Acute Evolving Myocardial Infarction within 24 hours before Cardiac Cath Lab Procedure; or
   c. pulmonary edema requiring intubation.

Emergency

2. Mechanical dysfunction (either of the following):
   a. shock with circulatory support; or
   b. shock without circulatory support.

Salvage

The patient is undergoing CPR en route to the Cardiac Cath Lab or prior to procedure.

Prior CABG

Previous coronary artery bypass surgery by any approach.
## Angiographic Variables

<table>
<thead>
<tr>
<th>Variable</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 2 vessels with ≥ 70% stenosis</td>
<td>Two more vessels with ≥ 70% stenosis. Stenosis represents the percentage diameter reduction, from 0 to 100, associated with the identified vessel systems. Percent stenosis at its maximal point is estimated to be the amount of reduction in the diameter of the &quot;normal&quot; reference vessel proximal to the lesion. In instances where multiple lesions are present, enter the single highest percentage stenosis noted. The LM, LAD, RCA/PDA, CIRC and Ramus are the systems of interest and should include major branch vessels of &gt; 2.0 mm in diameter.</td>
</tr>
<tr>
<td>Number of Lesions Treated</td>
<td>Number of distinct coronary lesions undergoing PCI by any technique.</td>
</tr>
<tr>
<td>Stent Diameter ≥ 3.0 mm</td>
<td>Maximum stent diameter implanted in the target vessel is ≥ 3.0 mm</td>
</tr>
<tr>
<td>Total Stent Length ≥ 30 mm</td>
<td>Combined total length of stent implanted in the target vessel is ≥ 30 mm</td>
</tr>
</tbody>
</table>
Figures

Supplemental Figure 1. Predicted vs. Observed Rates of Target Vessel Revascularization, By Stent Type, in the Validation Sample. Groups are approximately evenly sized, ordered by predicted TVR risk at 1-year.

A. Full Model, Bare-Metal Stent Patients

Hosmer-Lemeshow Chi-square = 0.81

B. Full Model, Drug-Eluting Stent Patients

Hosmer-Lemeshow Chi-square = 0.80
약물방출스텐트 시술로 더 큰 도움을 받을 수 있는 환자를 예측할 수 있다

강 현 재 교수 서울대학교병원 순환기내과

Summary

배경
약물방출스텐트는 일반금속스텐트에 비해 관동맥중재술에 따른 재협착의 위험도를 낮춘다. 그러나 약물방출스텐트는 더 비싸고, 더 장기간의 두 가지 항혈소판제의 투약을 필요로 하고, 재협착의 고위험군에서 가장 큰 효과를 보인다. 재치료의 위험도가 높은 환자군에서 약물방출스텐트의 시술을 고려하는 진료의를 돕기 위해 목표혈관 재치료율을 예측하는 검증된 모델을 개발하였다.

방법 및 결과
2004년 10월 1일에서 2007년 9월 30일 사이에 27,107명의 관동맥중재술을 위해 메사추세츠 주에 입원한 환자들의 시술 전 임상 및 관동맥조영술 자료를 이용하여 1년 관동맥목표혈관 재치료율을 예측하는 모델을 만들었다. 모델은 2/3의 환자를 무작위로 뽑아서 만들어진 후, 나머지 1/3의 환자를 이용하여 검증하였다. 전체 관동맥목표혈관 재치료율은 7.6%였고, 약물방출스텐트는 6.7%, 일반금속스텐트는 11%였다. 목표혈관 재치료율의 유의한 예측인자는 과거의 중재시술 여부, 응급 중재시술 여부, 관동맥우회로술의 병력, 말초혈관질환, 당뇨병, 그리고 혈관조영술상의 특성이었다. 이번에 개발된 모델은 당뇨병, 스텐트의 직경 및 길이 등 3가지 변수만을 이용하는 모델에 비해 유의하게 우월한 결과를 보였다(c statistic, 0.66 vs. 0.60; P<0.001). 약물방출스텐트를 이용하였을 때 목표혈관 재치료율을 예방하는 데 필요한 환자는 임상적 특성 및 혈관조영술 소견에 따라 6(95% CI, 5.4–7.6)-80(95% CI, 62.7–116.3)명이었다.

결론
일반적으로 수집 가능한 임상변수들로 이루어진 모델이 약물방출스텐트로 가장 큰 도움을 받을 수 있는 환자군을 예측할 수 있음을 보였다. 이 모델의 사용이 약물방출스텐트 사용의 안전성과 효과를 증진할 수 있을지는 추후 전향적 연구를 통한 평가가 필요하다.
약물방출스텐트의 효과 및 안전성 개선에도 불구하고 지속적인 장기간의 항혈소판제 사용이 필수적이라는 점은 약물방출스텐트 사용의 가장 큰 제한점이 되고 있다. 국내 약물방출스텐트의 사용 비율이 외국에 비해 매우 낮은 현실임에도 불구하고, 임상적인 변수나 혈관조영술상의 특성에 따라 일반금속스텐트 혹은 약물방출스텐트의 사용 여부를 임상적으로 판단하는 것은 중재시술을 시행하는 심장내과의에게는 매일의 일상이 되고 있다. 그럼에도 불구하고 어떤 기준으로 일반금속스텐트와 약물방출스텐트의 임상적 혹은 경제적 효능을 비교하고 선택할 것인지 정확한 기준이 합의되어 있지 않고, 논의가 지속되고 있다.

이 모델은 비교적 손쉽고 빨리 계산할 수 있으며, 그 계산기는 웹사이트(www.massdac.org/riskcalc_revasc)에서 내려받을 수 있다. 간단히 그 구성요소를 살펴보면, 연령, 당뇨병, 말초혈관질환, 고혈압, 1년 이내의 중재시술 여부, Canadian angina class, 허혈성 심질환의 임상진단, 응급 관동맥중재술 여부, 다혈관질환여부, 스텐트의 직경 및 길이 그리고 약물방출스텐트 혹은 일반금속스텐트 여부에 대한 정보만 있으며, 위험도의 산출이 가능하다. 이 모델에서 산출된 일반금속스텐트의 목표혈관재치료율은 2.7-57.4%의 범위에 있고, 이에 대하여 약물방출스텐트를 사용하였을 때 예상되는 목표혈관 재치료의 목표혈관재치료율은 1.2-15.5%였다. 모델에서 예측되는 약물방출스텐트의 일반금속스텐트에 비교한 상대적인 재치료율을 감소 효과는 비교적 넓은 범위에서 균일하게 45% 정도로 관찰되었다. 이 모델이 가지고 있는 많은 제한점에 대해 논의하자면 많은 시간이 필요할 것이지만, 우선 좀 더 근본적인 문제, 즉 이 같은 모델을 어떻게 임상현장에 적용할 것인지에 대한 논의가 되지 않아야 할 것으로 생각된다. 이 모델에서 어느 정도의 재치료율 감소가 예상되면 약물방출스텐트를 사용하는 것이 일반금속스텐트의 사용에 비해 상대적으로 이익이 될 수 있을 것인지에 대한 결정이 필요하다. 저자들은 논의에서 일반금속스텐트 시술시 재협착이 11%이하이면 경제적 측면에서 이득이 없을 것이라고 제안하고 있다. 즉, 10,000 달러의 경제적인 비용 증가를 약물방출스텐트의 사용이 일반금속스텐트 시술에 비해 경제적으로 이득이 되는 분기점으로 제시하고 있다. 물론 의료비용 및 소득이 미국에 비해 낮은 우리나라에서 같은 기준을 적용하기는 어려울 것으로 예상된다. 본 연구의 대상군에서는 이와 같은 기준을 받아들였을 때 전체 모집단의 약 45%가 약물방출스텐트 사용이 이 기준이하의 효과를 보이고 있어, 약물방출스텐트의 사용이 경제적인 측면에서 정당화할 수 없는 경우라고 추정하였다. 두 스텐트 간의 효능을 임상적인 결과 측면에서 비교하기는 더욱 어려운데 실제 본 연구의 모집단에서는 1년 목표혈관재치료 여부와 관계없이 환자의 1년 생존율이 동일함을 보고하고 있다.

비슷한 조건으로 선택 가능한 두 가지 치료법 중 한 가지를 선택하도록 결정하기 위해서는 매우 신중하고 객관적으로 자료의 축적 및 비교 평가가 필요하다. 이 같은 모델 개발을 통해 치료법을 가이드하려는 대표적인 예가 SYNTAX score라고 할 수 있다. SYNTAX score는 상대적으로 고위험 환자들을 무작위 배정 임상연구를 통해 모집한 후, 선별기준에 의해 모집된 환자를 대상으로 산출된 변수들로서 임상적 예후의 차이를 판단의 지표로 사용하여 본 연구에서 제시된 모델에 비해서는 좀 더 임상적 타당성을 가질 수 있다. 하지만 선별된 고위험환 자를 대상으로 제한된 치료방침을
적용토록 하였다는 점에서는 일반화에 약점을 지닌다고 할 수 있겠다. 이처럼 현재 개발되고 있는 질병의 위험도 예측모델들을 기반으로 치료의 선택을 객관화, 최적화하려고 노력이 진행되고 있으나, 아직은 이 모델들이나 알고리즘이 임상적 가치를 지니는지 여부에 대한 평가조차도 충분치 않은 상태이다. 그러나 이 같은 체계적인 분석과 자료의 축적을 통해 좀 더 현재의 임상 현장의 진료가 개선 발전되어가는 데 기여할 수 있을 것으로 기대한다.

Reference
Predicting the Restenosis Benefit of Drug-Eluting Versus Bare Metal Stents in Percutaneous Coronary Intervention


Background—Drug-eluting stents (DES) for percutaneous coronary intervention decrease the risk of restenosis compared with bare metal stents. However, they are costlier, require prolonged dual antiplatelet therapy, and provide the most benefit in patients at highest risk for restenosis. To assist physicians in targeting DES use in patients at the highest risk for target vessel revascularization (TVR), we developed and validated a model to predict TVR.

Methods and Results—Preprocedural clinical and angiographic data from 27,107 percutaneous coronary intervention hospitalizations between October 1, 2004, and September 30, 2007, in Massachusetts were used to develop prediction models for TVR at 1 year. Models were developed from a two-thirds random sample and validated in the remaining third. The overall rate of TVR was 7.6% (6.7% with DES, 11% with bare metal stents). Significant predictors of TVR included prior percutaneous coronary intervention, emergency or salvage percutaneous coronary intervention, prior coronary bypass surgery, peripheral vascular disease, diabetes mellitus, and angiographic characteristics. The model was superior to a 3-variable model of diabetes mellitus, stent diameter, and stent length (c statistic, 0.66 versus 0.60; P<0.001) and was well calibrated. The predicted number needed to treat with DES to prevent 1 TVR compared with bare metal stents ranged from 6 (95% confidence interval, 5.4–7.6) to 80 (95% confidence interval, 62.7–116.3), depending on patients’ clinical and angiographic factors.

Conclusions—A predictive model using commonly collected variables can identify patients who may derive the greatest benefit in TVR reduction from DES. Whether use of the model improves the safety and cost-effectiveness of DES use should be tested prospectively. (Circulation. 2011;124:1557-1564.)

Key Words: coronary intervention □ outcome assessment □ predictors □ restenosis □ stents

Prospectively defining patients’ risks before invasive procedures is critical for the rational application of technologies to improve outcomes.1-2 This principle is of particular importance when potential alternative treatment strategies are associated with a competing, but distinct, set of risks. The characterization of potential risks and benefits is also essential to improve the transparency and accuracy of informed consent.

Clinical Perspective on p 64

For patients undergoing percutaneous coronary intervention (PCI), drug-eluting stents (DES) significantly reduce the rate of restenosis of the target vessel compared with bare metal stents (BMS).3-5 However, they require the prolonged use of thienopyridines to avoid the rare but potentially fatal complication of stent thrombosis and may have higher rates of very late stent thrombosis than BMS.6-8 In addition, DES are significantly more expensive than BMS, so the cost-effectiveness of their use is dependent on the expected absolute reduction in restenosis for a given patient.9 Collectively, these data support the preferential use of DES in patients at highest risk for restenosis. Although a number of prior studies have identified predictors of target vessel revascularization (TVR), they have a number of limitations that limit their use in guiding stent selection in routine practice, including derivation from restricted clinical trial data.
patient populations, incorporation of post-PCI data that can be obtained only after a stent has already been implanted, or use of predictors that are not typically or easily assessed. To improve the prospective stratification of patients’ risks for TVR, predictive models that are limited to preprocedural clinical and angiographic data are required. Providing this information at the point of care, it may be possible to support the optimal use of DES and to engage patients in the decision-making process. Engaging patients in selecting stent type is particularly important because they will need to comply with long-term dual antiplatelet therapy if DES is used.

The goal of this study was to develop and validate a model to predict the likelihood of TVR after PCI with either DES or BMS within a large real-world population using variables commonly collected as part of the National Cardiovascular Data Registry (NCNR) CathPCI data collection instrument. This prediction model could then be used to derive the anticipated absolute risk reduction in TVR associated with DES use compared with BMS use and prospectively support clinical decision making.

Methods

Study Population

Since 2003, the Massachusetts Department of Public Health has systematically collected data on all PCI procedures performed at all acute care, nonfederal Massachusetts hospitals. The data are collected by trained hospital personnel using the NCNR CathPCI data collection instrument and are submitted electronically to the Massachusetts Data Analysis Center at Harvard Medical School. Selected covariates and outcomes are audited and adjudicated as previously described. To obtain subsequent TVR rates, we linked the index PCI to data on all subsequent revascularization procedures longitudinally from the Massachusetts Data Analysis Center and to hospital-discharge billing data collected by the Massachusetts Division of Health Care Finance and Policy.

We initially identified all PCI admissions between October 1, 2004, and September 30, 2007. For admissions in which multiple PCIs were performed, we included only the first PCI in the analysis. We subsequently excluded PCI admissions for the following reasons: no stent deployed (n=2794), both DES and BMS stents used (n=1648), inability to link data or patient was not a Massachusetts resident (n=4394), and missing data (n=98). We additionally excluded those patients who received devices <2.25 and >4 mm in diameter, for which DES were not available (n=708).

We next developed a propensity score model to predict the log odds of DES (versus BMS) use, conditioned on 46 demographic and clinical variables, and plotted the frequency distribution of propensity scores by stent type. To identify a sample of patients who were considered to evaluate the possibility that the strength of the association of clinical and angiographic characteristics with TVR might differ for BMS- and DES-treated patients, including interactions of stent type with age, diabetes mellitus, renal function, clinical presentation, saphenous vein graft intervention, vessel location, stent length, and stent diameter. However, none of these interactions were found to be significant and thus were not included in the models.

For validation, we applied coefficients of the models to the remaining one-third sample (validation cohort). Model discrimination was assessed with the c index, and model calibration was assessed by examining predicted versus observed rates of TVR within deciles of predicted TVR risk and testing the difference with the Hosmer-Lemeshow \( \chi^2 \) test. Overfitting statistics were estimated as described by Harrell. After the models were found to perform similarly in the developmental and validation cohorts, final nonangiographic and angiographic models using the entire study sample (merged developmental and validation cohorts) were generated. We calculated the integrated discrimination improvement (IDI) to assess

Definitions

The primary outcome of interest was the occurrence of TVR within 12 months of the index procedure. We defined TVR as PCI performed in a vessel treated during the index procedure or any coronary artery bypass graft surgery performed after the index procedure.

Definitions for the data elements for version 3.04 of the CathPCI registry are available at http://www.ncdr.com/WebsNCDR/Elements.aspx, and definitions for all variables retained in final risk prediction models can be found in Table I of the online-only Data Supplement.
the improvement in discrimination of the full model including angiographic characteristics compared with the nonangiographic model.20 The IDI provides a quantitative summary that measures the average absolute improvement in individual risk predictions that results from the inclusion of additional variables to a prediction model.

Prior studies have advocated using as few as 3 variables to predict restenosis: diabetes mellitus, lesion/stent length, and vessel/stent diameter.4,10 We therefore also compared the improvement in discrimination of the full model compared with a more parsimonious model accounting for stent type and these 3 variables as measured by the c statistic and IDI.

To assess the distribution of predicted reduction in TVR associated with DES use, we generated predicted probabilities of TVR assuming PCI with either DES or BMS by individually applying the clinical and angiographic profile of each patient in the study population to the models. We then subtracted the predicted probability of TVR with DES from that with BMS to derive the predicted TVR reduction associated with DES for each patient in the sample and calculated the estimated number needed to treat (NNT). We repeated this 1000 times and computed the mean of the various summaries and the NNT estimates, we used resampling procedures implemented through bootstrapping. Specifically, we sampled all admissions with replacement, re-estimated the logistic regression model, and computed summaries of both the predicted reduction in TVR with DES and the NNT. These summaries included the minimum, maximum, mean, and median benefit (and corresponding NNT). We repeated this 1000 times and computed the mean of the various summaries over the 1000 samples. We also constructed bootstrap 95% confidence intervals (CIs) for these selected summaries by determining over the 1000 samples.

To quantify our uncertainty with both the predicted TVR reduction and the NNT estimates, we used resampling procedures implemented through bootstrapping. Specifically, we sampled all admissions with replacement, re-estimated the logistic regression model, and computed summaries of both the predicted reduction in TVR with DES and the NNT. These summaries included the minimum, maximum, mean, and median benefit (and corresponding NNT). We repeated this 1000 times and computed the mean of the various summaries over the 1000 samples. We also constructed bootstrap 95% confidence intervals (CIs) for these selected summaries by determining over the 1000 samples. All analyses were conducted with SAS version 9.2.

Results
Of the 27,107 PCI admissions examined, 21,933 (80.9%) underwent PCI with DES, and the remaining 5174 (19.1%) received BMS. Baseline clinical and angiographic characteristics, stratified by the occurrence of TVR by 1 year, are shown in Tables 1 and 2. By 1 year after the index PCI, TVR occurred in 7.6% of patients overall (6.7% of DES patients and 11.0% of BMS patients). Bivariate analyses suggested that patients who had TVR were younger, were more often diabetic, and had higher rates of prior myocardial infarction, peripheral vascular disease, prior PCI, and prior coronary artery bypass graft. Patients with TVR more often had multivessel disease and had received stents with smaller diameters and longer lengths at the index procedure. The mortality rates at 1 year for patients with and without TVR were similar (5.3% versus 5.2%; P=0.78).

Model Development and Validation
The nonangiographic and full models had c statistics of 0.61 and 0.66, respectively, in the developmental models. Model discrimination when applied to the validation sample was similar (c statistic, 0.64 and 0.65 for the nonangiographic and angiographic models, respectively). A comparison of observed TVR rates at 1 year in the validation sample and the predicted risk of TVR demonstrated good calibration of both the nonangiographic (Hosmer-Lemeshow P=0.65) and angiographic (Hosmer-Lemeshow P=0.90) models without evidence of overfitting (Figure 1).

Final Nonangiographic and Full Models
Because models showed similar discrimination and similar calibration in both the developmental and validation samples,
Table 2. Angiographic Characteristics

<table>
<thead>
<tr>
<th>Angiographic Variables</th>
<th>Target Vessel Revascularization</th>
<th>No Target Vessel Revascularization</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vessels with &gt;70% stenosis (mean±SD), n</td>
<td>1.3±0.7</td>
<td>1.2±0.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Lesions treated (mean±SD), n</td>
<td>1.5±0.8</td>
<td>1.4±0.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LAD treated, %</td>
<td>43.5</td>
<td>42.9</td>
<td>0.60</td>
</tr>
<tr>
<td>Previously treated lesion, %</td>
<td>5.6</td>
<td>3.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Bifurcation lesion, %</td>
<td>14.7</td>
<td>13.7</td>
<td>0.22</td>
</tr>
<tr>
<td>Saphenous vein graft intervention, %</td>
<td>8.0</td>
<td>4.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Minimum stent diameter (mean±SD), mm</td>
<td>2.98±0.42</td>
<td>3.04±0.42</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total stent length (mean±SD), mm</td>
<td>32.2±21.2</td>
<td>29.0±19.0</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

LAD indicates left anterior descending artery.

final models were generated with the entire study sample. Beta weights and standard errors for models are included in Table II of the online-only Data Supplement, and a Web-based calculator that enables the clinical use of this model is available at http://www.massdac.org/riskcalc_revasc. Within the nonangiographic model, DES was associated with a significant decrease in 1-year TVR compared with BMS (odds ratio, 0.57; 95% CI, 0.52–0.64). The variables retained in the nonangiographic model were the use of DES, age, diabetes mellitus, peripheral vascular disease, hypertension, prior PCI, prior coronary artery bypass graft, admission symptoms, Canadian Cardiovascular Society/New York Heart Association class, and PCI indication (Figure 2).

Angiographic variables retained in the full model included having ≥2 vessels with ≥70% stenosis, the number of lesions treated, stent diameter ≥3.0 mm, and total stent length ≥30 mm. All nonangiographic variables except prior coronary artery bypass graft were also retained in the full model. The addition of angiographic variables further improved model discrimination (c statistic, 0.62 for nonangiographic model in the complete cohort compared with 0.66 for the full model; IDI, 0.010; P<0.001). This IDI value means that the percent of variation in TVR risk explained by the model increased by 1.0% in absolute terms in the full model compared with the nonangiographic model. Treatment with DES continued to be associated with a significant reduction in 1-year TVR (odds ratio, 0.53; 95% CI, 0.47–0.59). There were no statistically significant interactions in either model.

Comparison of Final Model With Usual Practice
Given that current practice emphasizes 3 factors, diabetes mellitus, lesion/stent length, and vessel/stent diameter,4,10 in considering TVR risk, we compared the full model with the discrimination of these 3 variables alone (in addition to stent type). We found that model discrimination improved significantly (c statistic, 0.60 versus 0.66; IDI, 0.013; P<0.001), supporting the potential for the new model to improve clinicians’ estimates of TVR risk compared with the prevailing standard.

Predicted Target Vessel Revascularization and Restenosis Benefit With Drug-Eluting Stents
The distribution of predicted rates of TVR from the full model assuming use of BMS varied broadly, from 2.7% to 57.4% (Figure 3). These values corresponded to absolute TVR reductions associated with DES use ranging from 1.2% (95% CI, 0.9–1.6) to 15.9% (95% CI, 13.0–18.4), with an interquartile range of 3.5% to 6.3%. Similarly, the predicted NNT to prevent 1 TVR with DES compared with BMS ranged from as few as 6 patients (95% CI, 5.4–7.6) to as high as 80 patients (95% CI, 62.7–116.3), depending on clinical and angiographic characteristics. Similar results were observed for the nonangiographic model, with the NNT ranging from 8 (95% CI, 6.6–10.3) to 61 (95% CI, 46.2–86.4).

Discussion
In a large statewide registry of patients undergoing PCI, we found that TVR at 1 year occurred in 6.7% of patients undergoing PCI with DES and 11.0% of patients undergoing PCI with BMS. Using variables routinely collected as part of the NCDR CathPCI instrument, we developed and validated parsimonious models to predict TVR using both clinical and angiographic variables. We found that the predicted reduction...
in TVR for DES compared with BMS varied broadly, depending on patient characteristics.

The factors associated with TVR in our study were similar to those found in previous studies examining predictors of TVR, including prior PCI, diabetes mellitus, longer stent length, and smaller stent diameter, although we identified other important variables that further improved risk stratification.21–23 The addition of angiographic variables significantly improved overall discrimination of the models. Although prior studies have found strong associations of angiographic variables with restenosis, they have typically not assessed the incremental improvement in discrimination that resulted from the addition of these variables to nonangiographic clinical characteristics, as we have done in this study.12,24–26 Moreover, we found a significant improvement in discrimination of TVR risk compared with the current clinical practice of relying solely on patients’ diabetes status, lesion/stent length, and vessel/stent diameter, underscoring the potential clinical utility of our model.

Our study differs from prior work in a number of important ways. First, because all nonfederal hospitals in Massachusetts are required to participate in the registry, the results are generated from a population-based sample of patients undergoing PCI in routine clinical practice without being subjected to the selection biases that occur with clinical trials or volunteer registries. In addition, the model is built on vari-

<table>
<thead>
<tr>
<th>Without Angiographic Variables</th>
<th>With Angiographic Variables</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug-eluting vs. bare metal stent</td>
<td>0.57 (0.52, 0.64)</td>
</tr>
<tr>
<td>Age</td>
<td>1.27 (1.11, 1.45)</td>
</tr>
<tr>
<td>&lt;50</td>
<td>1.00</td>
</tr>
<tr>
<td>≥80</td>
<td>0.74 (0.64, 0.85)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.20 (1.09, 1.33)</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>1.33 (1.17, 1.52)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.19 (1.06, 1.34)</td>
</tr>
<tr>
<td>Previous PCI ≤ 1 year</td>
<td>2.16 (1.65, 2.84)</td>
</tr>
<tr>
<td>Previous PCI &gt; 1 year (or timing unknown)</td>
<td>1.25 (1.12, 1.40)</td>
</tr>
<tr>
<td>Previous CABG</td>
<td>1.45 (1.27, 1.64)</td>
</tr>
<tr>
<td>NYHA class</td>
<td></td>
</tr>
<tr>
<td>Class I (reference)</td>
<td>1.00</td>
</tr>
<tr>
<td>Class II</td>
<td>0.91 (0.78, 1.06)</td>
</tr>
<tr>
<td>Class III</td>
<td>0.92 (0.80, 1.06)</td>
</tr>
<tr>
<td>Class IV</td>
<td>0.83 (0.72, 0.96)</td>
</tr>
<tr>
<td>Presenting symptoms</td>
<td></td>
</tr>
<tr>
<td>No symptoms/no angina (reference)</td>
<td>1.00</td>
</tr>
<tr>
<td>Typical chest pain</td>
<td>0.94 (0.70, 1.26)</td>
</tr>
<tr>
<td>Stable angina</td>
<td>1.33 (1.09, 1.62)</td>
</tr>
<tr>
<td>ACS: Unstable angina</td>
<td>1.24 (1.02, 1.51)</td>
</tr>
<tr>
<td>ACS: Non-STEMI</td>
<td>1.09 (0.86, 1.34)</td>
</tr>
<tr>
<td>ACS: STEMI</td>
<td>0.90 (0.69, 1.18)</td>
</tr>
<tr>
<td>PCI status</td>
<td></td>
</tr>
<tr>
<td>Elective (reference)</td>
<td>1.00</td>
</tr>
<tr>
<td>Urgent</td>
<td>1.16 (1.02, 1.33)</td>
</tr>
<tr>
<td>Emergency or salvage</td>
<td>1.88 (1.48, 2.34)</td>
</tr>
<tr>
<td>Angiographic characteristics</td>
<td></td>
</tr>
<tr>
<td>2 or more vessels with ≥ 70% stenosis</td>
<td>1.61 (1.46, 1.78)</td>
</tr>
<tr>
<td>Number of lesions treated (per lesion)</td>
<td>0.68 (0.61, 0.75)</td>
</tr>
<tr>
<td>Device diameter ≥ 3mm</td>
<td>1.32 (1.19, 1.47)</td>
</tr>
</tbody>
</table>

Figure 2. Predictors of 1-year target vessel revascularization, excluding and including angiographic variables. PCI indicates percutaneous coronary intervention; CABG, coronary artery bypass graft surgery; NYHA, New York Heart Association; ACS, acute coronary syndrome; and STEMI, ST-segment–elevation myocardial infarction.
ables commonly collected as part of the NCDR CathPCI instrument, which is currently used in >1000 hospitals across all 50 US states, making it widely applicable and potentially easily integrated into routine care at these facilities.\textsuperscript{27–29} Finally, our analysis was performed during a time period that included a large number of both BMS and DES patients, allowing the precise estimation of expected TVR reduction with DES across the entire spectrum of clinical profiles.

As expected, the use of DES was associated with a significant decrease in the occurrence of TVR compared with BMS. None of the interaction terms we explored to examine whether the benefit of DES was modified by clinical factors were found to be significant, so the relative risk reduction in TVR (\(\approx 45\%\)) was constant for all patients in the study. However, the absolute risk reduction differed substantially between patients on the basis of their clinical profiles, with the NNT to prevent 1 TVR ranging from 6 to 80, depending on patient characteristics.

Such differences in absolute risk reduction create the opportunity to prospectively identify and use DES in patients who stand to derive the greatest benefit from DES while considering BMS in patients with low anticipated benefit, given the added bleeding risk and costs associated with DES and its requirement for prolonged dual antiplatelet therapy. In fact, when the risk of restenosis with BMS is \(\leq 10\%\), the NNT exceeds 25, meaning that >25 patients would need to be treated with DES to avoid a single repeat PCI procedure for restenosis (Figure 4). Prior economic analyses have suggested that a TVR rate with BMS of \(< 11\%\) is associated with an increase in society-based costs of more than $10 000 to prevent 1 repeat procedure and would not be considered a cost-effective use of DES.\textsuperscript{9} In our sample, >45% of patients undergoing PCI had a predicted rate of restenosis with BMS that was less than this threshold, 78.6% of whom received DES. Because our model specifically used variables obtainable before stent implantation, it could be used prospectively to help guide physicians in stent selection and to apprise patients more accurately of the risks and benefits of the different stent choices. Such a use of the model would enable greater and more informed patient participation in clinical decisions, an explicit priority for the Institute of Medicine’s goals for improving the quality of care.\textsuperscript{30} In fact, our group is currently testing the impact of prospective risk stratification, through individualized informed consent documents imbedded with this risk model, on patient and physician decision making and long-term compliance with dual antiplatelet therapy.\textsuperscript{27}

Our analyses should be interpreted in the context of several potential limitations. Although we included a large number of clinically relevant variables in our models, the discrimination of the models was modest. Whereas our model discrimination compares favorably with other reported models,\textsuperscript{23} including those that incorporate post-PCI variables,\textsuperscript{31} there may be unobserved procedural (eg, quality of stent deployment), biological (eg, genetic predisposition), or social (eg, access to

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure3.png}
\caption{Distribution of predicted rate of 1-year target vessel revascularization (TVR) assuming treatment with bare metal stents (BMS) within the study sample. Results are based on the full model that includes angiographic variables.}
\end{figure}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure4.png}
\caption{Relationship between predicted 1-year target vessel revascularization (TVR) with bare metal stents (BMS) and number needed to treat (NNT) with drug-eluting stents to prevent a single occurrence of TVR. The dashed line shows the threshold of predicted 1-year TVR risk below which the NNT is >25. CI indicates confidence interval.}
\end{figure}
care, compliance with therapy) factors that are associated with TVR and not accounted for in these models. In addition, because the goal of our study was to produce a model that could be prospectively used to guide decisions during PCI, we did not incorporate variables that could be ascertained only after completion of the procedure such as adequate stent deployment, apposition, or coronary dissection that might further improve model discrimination. Because inherent uncertainty exists for the application of prediction models to any individual patient, estimates of predicted TVR risk are meant to enhance but not replace clinical judgment. To highlight this uncertainty, results of predicted TVR risk are presented with associated 95% CIs when the publicly available Web-based calculator is used, an advantage over using common risk scores, which do not account for imprecision in estimates. Next, our results are based on prospectively collected observational data, and thus are vulnerable to the omission of unobserved risk factors that may confound the choice of stent type with patient illness. Although the model was found to be well calibrated in both the DES- and BMS-treated patients, regression estimates were generated primarily from a DES population, and may therefore be optimized for this subgroup. Because we found no significant interactions between stent type and other covariates for the TVR outcome, we derived estimates of absolute risk reduction in TVR for DES that are based on this assumption. Next, we captured only data on PCI that occurred within nonfederal Massachusetts hospitals, which may limit some of the generalizability of our findings. In addition, there might be circumstances in which one stent choice over another was clearly clinically indicated, although we restricted the sample to patients who were apparently eligible for both types of stents. In using TVR as our primary outcome, we were not able to determine whether revascularization of the target vessel was due to restenosis of the index lesion or to new coronary lesions within the same vessel. This outcome may also depend on a variety of factors, including patient and physician perception of benefit. However, we believe that TVR is an appropriate patient-oriented outcome compared with angiographically defined restenosis, which may not be functionally significant.

Conclusions

We developed and validated a predictive model to predict the occurrence of TVR after PCI that allows the quantification of the anticipated benefit of PCI with DES compared with BMS in a large community-based population. The prospective use of individualized assessments of patient benefits may support the safer and more cost-effective application of this technology. Moreover, prospectively informing patients of the benefits of a DES may support shared medical decision making and improve patients’ understanding of the need for long-term dual antiplatelet therapy within the context of their reduced risk for TVR after DES.

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References


Drug-eluting stents for percutaneous coronary intervention decrease the risk of restenosis compared with bare metal stents. However, they are costlier, require prolonged dual antiplatelet therapy, and provide the most benefit in patients at highest risk for restenosis. To assist physicians in targeting drug-eluting stent use in patients at the highest risk for target vessel revascularization, we developed and validated a model to predict target vessel revascularization from a contemporary population-based registry in Massachusetts based on commonly collected clinical and angiographic variables that are obtainable before percutaneous coronary intervention. The ability of the model to discriminate 1-year target vessel revascularization risk among percutaneous coronary intervention patients was significantly better than a simpler model obtainable before percutaneous coronary intervention: the development of a clinical risk algorithm from the National Cardiovascular Data Registry. J Am Coll Cardiol. 2010:55:1923–1932.

