The majority of interventional cardiologists spend considerable time reviewing the angiograms before performing a percutaneous coronary intervention (PCI). Over the years, considerable experience has been gained from both clinical observations and investigations that guide the assessment of the risk-to-benefit ratio that leads to the decision of when and how to proceed with coronary revascularization in individual patients. During the early years of balloon angioplasty, the majority of interventional cardiologists spent considerable time reviewing the angiogram, because it largely predicted whether the procedure would be successful, but the consistency of such a review among cardiologists was not always present. In that era, angiographic variables by and large predicted outcomes and investigations that guide the assessment of the risk-to-benefit ratio that leads to the decision of when and how to proceed with coronary revascularization in individual patients.

During the early years of balloon angioplasty, the majority of interventional cardiologists spend considerable time reviewing the angiograms before performing a PCI. Over the years, considerable experience has been gained from both clinical observations and investigations that guide the assessment of the risk-to-benefit ratio that leads to the decision of when and how to proceed with coronary revascularization in individual patients. During the early years of balloon angioplasty, the majority of interventional cardiologists spent considerable time reviewing the angiogram, because it largely predicted whether the procedure would be successful, but the consistency of such a review among cardiologists was not always present. In that era, angiographic variables by and large predicted outcomes, because abrupt vessel closure and peri-procedural myocardial infarction (MI) were relatively common and also predicted later long-term mortality. However, it was also recognized that the nonangiographic variables were more important in predicting the long-term outcomes. Over time, improved techniques and better understanding of antithrombotic and antiplatelet therapies have reduced both the need for emergent coronary artery bypass grafting (CABG) and the mortality rate despite the increased use of PCI in high-risk populations. Given the technical successes in interventional cardiology, focus has now moved from the feasibility of PCI to the optimal use of existing techniques to improve survival and reduce symptomatic heart disease.

In order to optimize care, the interventional cardiologist needs to be able to predict the outcomes, including long-term mortality, so that he or she can best define the risks and benefits of PCI for the patient. Multivariable analyses from multiple registries and clinical trials have helped to define the risk factors for the development of adverse outcomes in patients undergoing PCI. In the current era of PCI, long-term mortality is now by and large only predicted by clinical variables such as symptom status (acute MI versus elective PCI) and baseline clinical variables such as age and congestive heart failure. (See Table 1–7) These variables have been combined into risk scores, such as those from the Mayo Clinic and the American College of Cardiology-National Cardiovascular Data Registry (ACC-NCDR) PCI registries that have been developed by interventional cardiologists to better define and predict outcomes in PCI. Some risk scores have also been validated in a broad population, including both high-risk and low-risk populations.

None of these risk scores have directly included preprocedural biomarkers, with the exception of renal function defined by either creatinine or creatinine clearance. Renal dysfunction is a well-recognized marker of both adverse events after PCI, not only of contrast-induced renal dysfunction but also long-term mortality. Until now, biomarkers have not been incorporated into the assessment of risk for elective PCI.

Cardiac troponins are now universally used for diagnosing acute MI and have been known for some time to be associated with a higher risk of mortality in a broad array of clinical conditions. It has also been recognized that the troponins may be able to detect ongoing myocardial necrosis in the absence of the clinical diagnosis of acute MI in patients with cardiomyopathy or heart failure. Therefore, the troponins can be regarded as universal markers of risk in cardiac disease. There have been many studies carried out to explore the prognostic implications of post-PCI troponin elevations. However, few of these have investigated preprocedural cardiac marker elevations, and if these elevations have been explored, they have been linked to the higher risk of PCI in an acute MI population, compared with PCI in a non-MI population.

In this issue of Circulation, Jeremias et al11 used the Evaluation of Drug Eluting Stents and Ischemic Events (EVENT) registry to show that stable angina and elevated troponin levels in a patient before PCI is an independent prognostic indicator of death or MI at hospital discharge and 1 year. The EVENT registry was initially designed to evaluate both periprocedural and late events associated with the “real world” implantation of drug-eluting stents. The registry is populated with patients who have had no revascularization within 4 weeks of enrollment undergoing PCI at 47 different clinical sites. Although patients with acute coronary syndromes are included in the registry, they were excluded from the current analysis. This theoretically results in only patients with stable angina or a positive stress test being used in the current analysis. Patients in whom preprocedural creatine kinase myocardial band isoenzyme (CK-MB) and troponin were not measured were excluded from the analysis; however, the routine measurement of cardiac biomarkers was not performed. The decision to check cardiac biomarkers appears to have been left to the discretion of the treating physician given that 36% of the eligible patient population was excluded because of the lack of preprocedural biomarkers.

In the included population of 2382 patients, 6% were found to have positive biomarkers. Of these 142 patients, only 5...
were on renal replacement therapy and 12 had known congestive heart failure. The vast majority of patients (70%) had biomarkers that were only slightly elevated; however, a surprising 30% had an elevation that was greater than 3 times the upper limit of normal. The frequency of death or MI during the index hospitalization was significantly greater (13.4% versus 5.6%, P<0.001) in the group with a preprocedural troponin elevation; however, this combined end point was driven almost entirely by periprocedural MI (determined by CK or CK-MB 3 times the upper limit of normal or persistent ST-segment elevation) because only 1 in-hospital death occurred. Given that the population with elevations in troponin before undergoing PCI had more complex anatomy and was more likely to receive bifurcation stenting, periprocedural MI after high-risk PCI seems to be driving the short-term differences in outcomes that are seen. This conclusion is supported by the increased rate of procedural complications and need for urgent repeat PCI seen in the cohort with troponin elevation before PCI. Almost identical information has also recently been observed by investigators at the Mayo Clinic,12 thus strengthening these observations.

These data provide support for the role of cardiac troponin as a preprocedural marker of in-hospital MI and a higher risk of mortality. This may be through the association of complex coronary anatomy, difficult-to-treat lesions, and high-risk interventions with long-term outcomes associated with this preprocedure elevation. This study does provide indirect support for the prognostic implications of periprocedural MI more common in patients undergoing complex coronary interventions. Previous studies have demonstrated that an elevation in cardiac biomarkers after undergoing PCI is frequent and associated with a significant increase in both the short- and long-term risk of death or MI.13 This work should serve to refocus efforts to determine implications of periprocedural MI on the treatment of patients. Despite these unanswered questions, the 2% increase in the 1-year absolute mortality rate (2.4% versus 0.4%, P=0.03) in the cohort with preprocedural troponin elevation does make cardiac troponin an important marker for long-term outcomes. Whether troponin elevations are a direct result of a mechanism that results in increased long-term mortality or a marker for higher risk or more severe coronary disease remains unclear.

There are significant confounders present in this study which could be influencing the results seen. These confounders are expected to be in any study that is observational in nature. For example, 36% of the eligible population was excluded because preprocedural biomarkers were lacking. The evaluation of cardiac markers before elective PCI is not routine in most clinical settings. Thus, this could signify that a portion of the troponin-positive population was either mislabeled or misdiagnosed and actually represented a population of patients with acute coronary syndrome. However, patients with positive troponin received pretreatment with clopidogrel in only 44% of cases despite their high-risk anatomy, suggesting possibly that the troponin elevation was a harbinger of “silent” problems to come. Finally, multivariable logistic modeling did not account for the presence of heart failure. Given the known prognostic implications of troponin elevation in patients with heart failure, would the association between troponin elevation and increased mortality at 1 year still have been seen if the presence of heart failure had been taken into account?

Despite these limitations, the associations shown in Jeremias et al11 and in the article by Prasad et al in Circulation: Cardiovascular Interventions12 have significant implications that will lay the foundation for further investigational study and clinical application. The measurement of troponin has once again been shown to be effective in the risk stratification of patients, even in a population of patients undergoing elective PCI that is historically at low risk of complications. These data provide additional evidence that the presence of troponin before coronary angiography predicts a higher likelihood of high-risk lesions known to be associated with worse long-term outcomes.

We therefore have entered into a new era of PCI, where preprocedure biomarkers have an important role to play in predicting the outcomes of PCI. With many new combinations of antithrombin and antiplatelet therapies available for

### Table. Previously-Associated Predictors of Adverse Events From PCI From Selected Registries

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<td>Renal disease</td>
<td>Female</td>
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<tr>
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<td>Chronic lung disease</td>
<td>CHF (NYHA Class III–IV)</td>
<td>Peripheral vascular disease</td>
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<td>Nonelective PCI</td>
<td>Acute MI</td>
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<tr>
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<td>Intraaortic balloon pump</td>
<td>Acute MI</td>
<td>Acute MI</td>
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<td>Decreased LVEF</td>
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<td>SCAI lesion class</td>
<td>Left main disease</td>
<td>Left main disease</td>
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<tr>
<td>characteristics</td>
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<td></td>
<td>Multivessel disease</td>
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<td>Renal failure</td>
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CHF indicates congestive heart failure; LVEF, left ventricular ejection fraction.
use with PCI, one can imagine that some of the therapies that are associated with a higher risk for use, such as the risk for bleeding complications, could be reserved for the patients with a substantially higher long-term risk of mortality, where the risk-to-benefit ratio would favor a higher-risk therapy. On the other hand, for patients with a lower risk of long-term mortality, the optimal peri- and post-PCI pharmacotherapies would be those that are associated with a lower risk for the patient. The same argument could also be made for the appropriate device use in PCI.

An important next step will be to appropriately make the right match between therapeutic risk and preprocedural risk. It is our hope that the many registries that are ongoing or are being planned can collect the most appropriate data on patient risk (from the models discussed) and the use of therapies during and after PCI, so that we can start analyzing these important trade-off decisions in PCI. For this to be possible, we need to recognize that the best approach will come when academic entities oversee this process to make sure that we have the ultimate goal of improving PCI outcomes irrespective of drug or device used.14.15

The challenge for the interventional cardiologist will be that performing this risk calculation is not easy, although a simplified “bedside” version of the Mayo risk score is available.16.17 However, we believe that it is now time for the interventional cardiologist to adopt a strategy similar to what has been recommended for the risk assessment of non–ST-elevation acute coronary syndrome. Recent guidelines recommend the use of risk stratification tools, such as the Global Registry of Acute Coronary Events (GRACE) risk score,18 which can accurately predict long-term mortality in the early assessment of patients with acute coronary syndrome in order to better guide the use of therapies.19 Of note, most of these acute coronary syndrome risk scores include positive biomarkers in the models that predict long-term risk. This predictive practice of medicine has now come to interventional cardiology, with biomarkers now likely to be as important as the review of the angiogram. Let us get ready with the calculator!

Acknowledgments

We dedicate this Editorial to Dr Richard Stack and Dr Robert Califf, as it reflects 20 years of stimulating academic discussion over PCI and outcomes. We also appreciate the editorial assistance of Betty Summers.

Disclosures

None.

References


Key Words: Editorials ▪ angioplasty ▪ myocardial infarction ▪ registries ▪ risk score
What Do You Need to Know Before Performing a Percutaneous Coronary Intervention?
Matthew A. Cavender and E. Magnus Ohman

Circulation. 2008;118:609-611
doi: 10.1161/CIRCULATIONAHA.108.791848
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2008 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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