The Dueling Hazards of Incomplete Revascularization and Incomplete Data

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Although the survival benefit of complete revascularization after bypass surgery is well documented, the importance of opening all stenotic or occluded vessels during percutaneous coronary intervention (PCI) is less certain. On the contrary, much data support targeting only the culprit vessel during PCI. A strategy of “ischemic-driven revascularization” is often the standard of care. Through a potpourri of noninvasive imaging (eg, nuclear imaging, positron emission tomography, stress echocardiography), as well as invasive techniques (eg, fractional flow reserve, intravascular ultrasound measurements, quantitative angiography), much effort has gone into identifying the functional importance of coronary blockages and confining intervention to diseased vessels that significantly limit blood flow to viable myocardium.1,2 Indeed, the phrase oculostenotic reflex was invented to describe the indiscriminate interventionalist, bent on opening any suspicious angiographic blockage. This subcortical reflex has long been considered a liability, and interventionalists are taught to be more cerebral in their decision making. In this issue of Circulation, Hannan et al, in a provocative report, use data from the New York State reporting system to turn decades of teaching on its ear.3 Using a database created from a State of New York reporting registry, procedural information was collected on 21,945 patients with 2-vessel coronary artery disease undergoing PCI. Then, using patient’s Social Security numbers, these in-hospital data were correlated with the New York State Vital Statistics Death File to capture mortality events over a follow-up period of ≈3 years. The study found that patients with incomplete revascularization (after adjustment for baseline differences) were 15% more likely to die at follow-up than patients with complete revascularization. This mortality risk increased with the degree of incomplete revascularization. Patients with 1 unopened total occlusion were 35% more likely to die. If ≥2 vessels were incompletely revascularized, and at least 1 of them was totally occluded, the risk of death was 36% higher. A finding of only 1 incompletely revascularized vessel without a total occlusion did not increase the risk of subsequent mortality. The authors conclude that in patients receiving stents, incomplete revascularization results in increased mortality, and therefore cardiologists should consider either “achieving complete revascularization, opting for surgery, or monitoring PCI patients with incomplete revascularization more closely after discharge.”

If the authors are correct, their conclusions should have profound effects on how cardiologists treat patients. But are the authors correct?

How Strong Is the Case Against Incomplete Revascularization in PCI Patients?

Before we throw away the concept of ischemic-driven revascularization, it is worth obtaining a perspective on the data. The New York State Percutaneous Coronary Intervention Reporting System (PCIRS) is not free from controversy. This state-mandated system for data collection and analysis certainly serves an important purpose in tracking hospital outcomes, disclosing complication rates to the public, and identifying outlier physicians and hospitals in need of remedial education. It may even identify physicians and/or hospitals that should not be performing PCI. As a vehicle for population-based research, however, this database has its limitations. Unfortunately, because of its magnitude (>55,000 patients entered per year) and the fact that it is coordinated by individuals with significant statistical expertise, these limitations are often overlooked. The PCIRS is an unfunded New York State mandate. Every New York hospital is required to complete a data form containing >100 fields for each patient undergoing a PCI procedure. Because it is unfunded, most hospitals employ 1 person to collect data for every 1000 to 2000 patients undergoing PCI per year. Only in-hospital data are entered. There is no outcome data collection. For the present study, follow-up was obtained by querying the New York State Vital Statistics Death File with the use of the patient’s Social Security number. This death file is a completely different database with its own set of limitations, the most relevant being absence of accurate reporting about the cause of death. The major end point of the present study was death, yet we do not know whether the deaths reported were cardiac in nature. The PCIRS also suffers from an absence of “monitoring.” Instead, there is “auditing” of the data, which consists only of spot checks on a small fraction of the data forms. There is also the potential for bias. Data collection is under the direction of each individual hospital, and conflict of interest may play a role. Competition in New York State between hospitals and physicians seeking the lowest risk-adjusted mortality is fierce. Although competition to reduce mortality is laudable, it provides significant incentive to document every patient
risk factor possible, so that after risk adjustment, a given hospital’s data may appear more favorable. How can we be sure that documentation of patient risk is performed in a similar manner among different hospitals and patients in this study?

Contrast this with the quality of evidence-based medicine we have come to rely on when making major decisions in cardiology. A typical government- or industry-sponsored FDA-approved study has 1 study coordinator for ~50 to 100 patients enrolled per year. An independent monitor from outside the institution is physically present every 4 to 6 weeks, not to “audit” the case report forms but to match each and every data entry against a source document. Patient follow-up is obtained at regular intervals, and monitoring persists throughout the study.

This is not an indictment of the PCIRS. The PCIRS serves a valuable function. However, a longitudinal study based on the combination of the PCIRS database and a statewide death file, with no cause of death reported, does not promote confidence in the data. Therefore, although the data presented might, in fact, be accurate, many questions about its validity are raised.

Beyond the accuracy of the data, one must also be skeptical of the data analysis. Much of the impact of this study is based on the science of risk adjustment. Although this science is elegant, even the authors admit it is imperfect. Hazard models cannot identify all confounders, and propensity analysis cannot account for selection bias related to unmeasured characteristics. Some examples of risk factors that might influence late mortality not collected by the New York State database include cancer, anemia, home oxygen use, dementia, and pre- or post-PCI noncardiac surgery. Of note, in this study we learn that as a patient’s left ventricular ejection fraction diminishes, the finding of incomplete revascularization increases, and, as incomplete revascularization increases, so does late mortality. Is it really surprising to find increased mortality among patients with reduced ejection fraction? The correlation of low ejection fraction and increased mortality is one of the most basic, universal associations in cardiology. Similarly, patients with renal failure and congestive heart failure were found to more likely have incomplete revascularization. Again, it is no surprise to find increased mortality in these patient subgroups. This study even includes a small number of patients with hemodynamic instability, shock, and cardiopulmonary resuscitation (CPR). Not surprisingly, nearly 100% of these patients had incomplete revascularization. The study uses Cox proportional hazards regression and propensity analysis to “adjust” for this increased risk of death, but can statistical science reliably adjust for such significant risk? You do not need a PhD in statistics to know that patients requiring CPR before PCI will have an increased risk of death. The cause of death in that circumstance is unlikely to be incomplete revascularization, and it is hard to imagine a statistical technique capable of adjusting for that degree of risk.

Even if the data are correct and complete revascularization does improve survival, there are probably some glaring exceptions. For example, opening a totally occluded vessel that supplies akinetic, nonviable myocardium is unlikely to provide benefit. In addition, opening an occluded right coronary artery, even if it feeds viable myocardium, may be of only marginal benefit. Surprisingly, in the present study the authors do not distinguish between nonrevascularization of a totally occluded right coronary artery versus an occluded left anterior descending artery. Most cardiologists will refer patients with a totally occluded left anterior descending artery not amenable to PCI to bypass surgery, but many are comfortable leaving an occluded right coronary artery closed. It would be worth learning whether an occluded right coronary artery, not revascularized, conveys a significant mortality risk. Because these data are available within the New York PCI registry, yet not mentioned in the article, one assumes that leaving a right coronary artery occluded is not an independent risk factor for death, but this is not specifically addressed.

Assuming That Incomplete Revascularization Is Associated With Increased Late Mortality, What’s a Cardiologist to Do?

Let us assume that patients in whom complete revascularization cannot be obtained have worse outcomes. Does this mean, as the authors indicate, that they should be considered for bypass surgery? The authors suggest this but offer no evidence to support it. There was no surgical arm in this study. There is no evidence that, given the increased risk profile of patients with incomplete revascularization, a surgical revascularization would have provided a better outcome. To take it to the extreme, do the authors really think the 21 patients in shock or 15 patients receiving CPR in this study would have had better outcomes with bypass surgery?

A better way to answer this question, of course, is through a randomized trial comparing PCI with bypass surgery in patients with both complete and incomplete revascularization. In fact, the randomized trials reported to date support just the opposite conclusion. For example, the Bypass Angioplasty Revascularization Investigation (BARI) found that nondiabetic patients randomized to balloon angioplasty with intended incomplete revascularization had similar long-term survival compared with patients randomized to surgery. In the Arterial Revascularization Therapies Study (ARTS), randomization to stenting in patients with incomplete revascularization, including diabetics, did not influence late mortality. Although an increased need for subsequent revascularization in incompletely revascularized PCI patients is a consistent finding of randomized trials, mortality is not increased.

The authors of the present study criticize these randomized trials as being too selected and too controlled. They argue that patients in randomized trials are more carefully selected for improved revascularization outcomes (ie, fewer total occlusions) and monitored more closely than patients in everyday, real practice. The authors suggest that closer follow-up of patients (who are also better suited for revascularization) results in such a decrease in mortality that differences in survival between patients with complete and incomplete revascularization are masked. Although no trial is perfect, and this explanation is creative, it is hard to see how the limitations of a randomized trial will be overcome by a
registry, no matter how large the database. It is much more likely that the aforementioned flaws in the data collection and analysis result in the discrepancy between the findings of the present study and those reported in randomized trials.

A Call to Action

Despite criticisms of the present study, the author’s central message, that incomplete revascularization adversely affects outcomes, may be accurate. If so, these findings have implications for patient care, albeit implications that are different from those suggested by the authors. These data imply that interventionalists must make a commitment, within the limits of safety, to attempt complete recanalization on each patient undergoing PCI. This may require changes in practice. For example, it may necessitate increased staging of procedures. To limit risk, many patients with complex 2- and 3-vessel disease will require staging because of excessive contrast load, x-ray exposure, myocardium at risk, patient fatigue, and even physician fatigue. This requires a “buy in” from the patient and third-party payors for multiple procedures, and this should be part of the consenting process. In addition, a logical extension of complete revascularization is the universal use of drug-eluting stents. If achieving complete recanalization at the time of the procedure is important, presumably it is important to maintain complete revascularization. To this end, the benefit of drug-eluting stents is undisputable.

Finally, this article is a call to action for interventionalists to commit to improving their skills at opening totally occluded coronary arteries. The total occlusion is one of the final frontiers in interventional cardiology, and recently many have focused on increasing success rates within this challenging lesion subset.6,7 Interestingly, over the past decade several novel, high-tech devices designed to open totally occluded coronaries have failed to improve outcomes. Surprisingly, success rates have been improved more by the age-old operator attributes of patience and experience than by expensive technology. A cadre of interventionalists has recently focused on the total occlusion as a distinct acquired skill set. These physicians exchange technical pearls at unique conferences and working groups specializing in total occlusions. Over the past 2 years, in some centers, new approaches such as “the parallel wire technique,” ultrasound-guided recanalization, and even retrograde recanalization via septal collaterals have improved total occlusion success rates from the historical 50% to 70%, to almost 90%. A spectrum of new guidewires with variable stiffness, lubricity, and torque, coupled with a patient, skilful operator, is proving increasingly effective at conquering the recalcitrant occlusion. The present study lends legitimacy to the time and energy currently focused on total occlusions by the interventional community.

To summarize, the results of this study can be used to stimulate more aggressive pursuit of complete revascularization during PCI. This means working hard to open all blockages even if it requires multiple procedures (staging). It also means near-universal use of drug-eluting stents. Additionally, these data should inspire more interventionalists to hone their skills in crossing total occlusions. Finally, this study can also be used to highlight some of the hazards of drawing conclusions on the basis of patient registries. It is important that the large number of patients within the New York State reporting system and the sophisticated statistical analysis not overshadow the limitations inherent in its method of data collection, verification, and lack of follow-up. We will all do better when both the recanalization and the data are more complete.

Disclosures

Dr Teirstein reports having received research grants and honoraria from Cordis and Boston Scientific, having an ownership interest in Cordis and Boston Scientific, and having served as a consultant and/or on the advisory board of Cordis and Boston Scientific.

References


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