Percutaneous coronary intervention (PCI) has revolutionized the management of coronary artery disease. Its main goals are to improve the quantity and sometimes the quality of life by reducing mortality and nonfatal outcomes and by improving symptoms. Although these goals were clearly achieved when PCI was applied to the treatment of acute coronary syndromes, there is still uncertainty about the prognostic benefits of PCI in patients with stable coronary artery disease: Whereas PCI clearly improves angina symptoms, its benefits on clinical outcomes remain debated and may occur only if patients are at sufficient risk (because of extensive myocardial ischemia or because the amount of jeopardized myocardium is large enough).

In this issue, Spoon et al report changes in long-term mortality after PCI over nearly 20 years. This study examined 19,077 patients who underwent PCI at the Mayo Clinic in Rochester, MN, and were discharged alive. It spans 3 distinct 6-year periods: the plain old balloon angioplasty era in the early 1990s, the bare metal stent era in the late 1990s, and the drug-eluting stent era in the 2000s. The study records survivors up to 5 years after the procedure, with a detailed description of the patients’ characteristics and indications for PCI, as well as careful analysis and categorization of the causes of death.

In this study, a change in patient characteristics over time was found: PCI was performed in increasingly older patients, with an increasing prevalence of noncardiac comorbidities. In parallel, there was a clear increase in the use of evidence-based therapies for secondary prevention. In-hospital mortality decreased for patients with stable angina but not for patients with acute coronary syndrome. Interestingly, the long-term postdischarge mortality appeared consistently slightly higher in the more recent era compared with older periods, but the most striking observation is a shift in long-term mortality from predominantly cardiac to noncardiac causes as a result of a decrease in cardiac deaths over time (from 9.8% to 7.4% and 6.6% at 5 years; \( P < 0.001 \)) and a parallel increase in noncardiac deaths (from 7.1% to 8.5% and 11.2%; \( P < 0.001 \)). This resulted in the astonishing observation that in the 2000s noncardiac mortality accounted for the majority of postdischarge deaths after PCI. The authors performed detailed sensitivity analyses according to age, geographic location vis-à-vis the institution, major risk factors, indication for PCI, and extent of coronary artery disease and were able to document that these observations are robust and that, after adjustment for baseline risk, there was no change in noncardiac mortality over the 3 time periods but a 50% decline in cardiac mortality, driven largely by a reduction in fatal myocardial infarction/sudden death but without change in heart failure–related deaths.

The authors should be congratulated not only for achieving comprehensive long-term follow-up of this large cohort but also for their astute observations, which have far-ranging implications. Nevertheless, there are a number of potential caveats to this study. First, it was performed in a single center, and replication is important to assess the external validity of the findings. However, the population analyzed is large and reflects the broad indications of PCI performed in “all-comers.” Likewise, although the diagnostic criteria for ST-segment–elevation myocardial infarction have remained stable, the tests and criteria used for defining and identifying patients with non–ST-segment acute coronary syndromes or stable coronary artery disease have evolved over time (with availability of increasingly sensitive tests). This could account for some changes in outcomes over time; the availability of more sensitive diagnostic tests would be expected to identify a population at lower risk of cardiovascular mortality.

It is possible that we have gotten better at selecting patients for coronary angiography and PCI through better screening that incorporates patients’ cardiovascular risk profiles, symptoms, cardiac biomarkers, and noninvasive test results. This could explain the findings of more extensive coronary artery disease and of a higher prevalence of cardiovascular risk factors in patients undergoing invasive procedures in recent periods in this study. The in-hospital mortality for stable angina PCI has fallen, likely reflecting temporal improvement in interventional techniques. However, in-hospital mortality for patients with acute coronary syndrome remained the same. The higher risk of these patients, in addition to their higher comorbidity load, probably negated the positive impact of improved procedural technique and adjuvant therapies.

The decrease in long-term cardiac mortality is likely explained not only by improved procedural techniques and adjunctive therapies but, more important, by the increase in the use of effective evidence-based medical therapy for secondary prevention, relying (in addition to lifestyle...
modifications) on antiplatelet agents, angiotensin-converting enzyme inhibitors, and statins.\textsuperscript{8-11} The impact of these treatments on cardiovascular outcomes is well documented both in stable patients with coronary artery disease\textsuperscript{12} and after acute coronary syndrome.\textsuperscript{13,14} In the present report, the use of angiotensin-converting enzyme inhibitors on discharge increased from 19\% to 63\% and that of lipid-lowering drugs from 25\% to 90\%. This underscores the importance of continued efforts for implementation of evidence-based therapies in patients undergoing PCI. In that respect, it is disturbing that, in recent analyses of patients undergoing PCI in the United States, a substantial proportion of patients fail to receive proper evidence-based medical therapy.\textsuperscript{15}

Although long-term cardiovascular mortality after PCI has decreased steadily over time, this decrease is related mostly to reductions in sudden death and fatal myocardial infarction. In contrast, mortality related to heart failure has remained stable, pointing to the need for improved long-term prevention of congestive heart failure-related mortality as one of the major targets for research in this area. In addition to having more severe coronary disease in the more recent cohorts, patients had a higher burden of noncardiac diseases, and Spoon et al demonstrate, very consistently, a progressive rise in noncardiac deaths over long-term follow-up in recent periods. This is consistent with observations in a recent study of PCI in octogenarians.\textsuperscript{16} The fact that noncardiovascular causes of death have become dominant after PCI is not entirely surprising. Despite success in reducing the short-term risks associated with PCI, we are operating on older patients who are succumbing to cancer and respiratory, liver, and renal failure in the long run rather than to cardiac causes.\textsuperscript{17}

Thus, a new front has opened up in the war against cardiovascular disease, and it has nothing to do with the heart. This observation has several implications. First, from the standpoint of clinical research, although mortality remains the ultimate clinical trial outcome, future clinical trials of cardiovascular outcomes after PCI will need to study outcomes beyond mortality and incorporate nonfatal cardiovascular clinical outcomes and quality of life. Otherwise, trials aiming at mortality reductions would need to be very large. After all, this is to be expected and has been the norm in many other fields in medicine in which mortality reduction is either rare or irrelevant.\textsuperscript{18} Then there are implications for patient care and even for training of cardiologists. It is a reminder that greater attention should be paid to the patient as a whole, including comorbidities, before committing him or her to an invasive procedure. This observation after PCI is a reflection of a broader trend: The prevalence of comorbidities is increasing in the ever-older cardiology patient population. Whereas in the past many patients would die of cardiac disease prematurely before experiencing the many comorbidities that go along with advanced age, progress in prevention and treatment has now decreased the incidence and lethality of cardiac diseases. In turn, patients surviving long term after an initial heart attack have developed an increased prevalence of comorbidities, the treatment of which may pose more problems to cardiologists than the solution to their cardiologic problem. In many coronary care units, the patient with acute myocardial infarction has now become the “simple” patient compared with the patient in whom a cardiac complaint may be associated with a host of severe comorbidities that often require multiple consultations with specialists. This argues for greater integration of cardiology, as a specialty, with internal medicine, not only in the organization of care but even at the stage of training of junior physicians. It is, in some sense, ironic that the successes of cardiology in tackling cardiac mortality now result in the need to reintegrate cardiology and internal medicine when, for many years, cardiology has sought greater specialization and autonomy.

Disclosures

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References


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Death (After Percutaneous Coronary Intervention) Is No Longer What It Used to Be
Phlippe Gabriel Steg and Adrian Piers Cheong

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