Effects of Coronary Stents on Cardiovascular Outcomes in Broad-Based Clinical Practice

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Background: Although stents have been shown to reduce the need for repeated percutaneous coronary intervention (PCI) in randomized trials, the effects of stents in broad-based, diverse clinical practice have not been well studied, nor has their effect on subsequent myocardial infarction or cardiac death.

Methods: A retrospective cohort study was performed that included all 43 hospitals performing PCI in Pennsylvania in the last quarter of 1995, with the use of the Pennsylvania Health Care Cost Containment Council database. All 5258 patients who underwent PCI, excluding those with previous PCI within the preceding 6 months, were included. The primary outcomes were in-hospital events (death or coronary bypass), 6-month revascularization rates, and 6-month rates of cardiac death or myocardial infarction.

Results: A total of 1240 patients (24%) had a stent procedure. Compared with nonstent procedures, stents reduced the risk of in-hospital events (multivariable odds ratio adjusted for patient and hospital level differences, 0.63; 95% confidence interval, 0.41-0.97), primarily because of a 52% reduction in the need for coronary bypass. Stents also reduced the need for follow-up revascularization procedures (multivariable hazard ratio, 0.72; 95% confidence interval, 0.59-0.87), primarily because of a 31% reduction in repeated PCI. However, stents had no effect on 6-month rate of myocardial infarction or cardiac death (multivariable hazard ratio, 0.97; 95% confidence interval, 0.71-1.33).

Conclusions: Using stents decreases the need for repeated PCI in broad-based clinical practice, confirming results from randomized trials. However, this study did not detect any effect on subsequent myocardial infarction or cardiac death.

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PATIENTS AND METHODS

STUDY DESIGN AND DATA SOURCE

This population-based cohort study used data from the Pennsylvania Health Care Cost Containment Council (PHC4). The PHC4 is a state agency created by the Pennsylvania General Assembly in 1986 that collects demographic, billing, and clinical outcomes data on every inpatient at nonfederal hospitals in the state, as required by law. Information collected includes patient and hospital demographics; 1 principal and up to 8 additional discharge diagnoses, coded with the use of the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM); 1 principal and up to 5 additional procedure codes; and discharge disposition, including mortality. In addition, an admission severity group (ASG) score (from 0 to 4) as defined by the MedisGroup System is included for all patients as the method of case-mix adjustment, relating clinical variables at admission to the risk of death. A regular audit of data consisting of logic checks and evaluation for completeness is performed by PHC4. In addition, several more detailed internal audits of the data on a sample of large (>100 beds) general acute care hospitals are performed by PHC4 to ensure accuracy of the data before they are released in public reports. These audits include computerized logic edits, manual data verification checks, and data auditing.

PATIENT POPULATION

All residents of Pennsylvania at least 21 years old undergoing a PCI from October 1, 1995, through December 31, 1995, made up the inception cohort. This period was selected because it was the first time that the ICD-9-CM coding procedure included a separate code for coronary stenting and the period for which there were at least 6-month follow-up data on all subjects (PHC4 data were available through June 30, 1996). The data were limited to Pennsylvanians residents to minimize loss to follow-up of patients returning to neighboring states after their PCI. The first procedure performed on any subject within this time frame was considered the “index PCI.” Because of concerns of selection bias among patients undergoing a second PCI for restenosis, subjects in the cohort who had PCIs within 6 months before their index PCI were excluded from the cohort. Each subject had a unique, encrypted patient identifier (available in 99.5% of subjects), allowing for identification of readmissions on virtually all subjects across all hospitals.

According to ICD-9-CM procedure codes, 2 hospitals had a total of 2 PCIs recorded and 9 hospitals had only 1. This exceedingly small number of procedures raised the likely possibility of miscoding of procedures in these institutions, and they were therefore excluded.

STUDY VARIABLES

Outcomes

The primary outcomes for this study were the 6-month rates of follow-up hospitalization for either (1) revascularization, defined as a PCI or coronary artery bypass grafting (CABG) procedure, or (2) a nonrevascularization cardiac event (referred to as “cardiac event”), defined as either an MI (ICD-9-CM codes 410.xx, excluding a fifth digit of 2) or any cardiac condition that resulted in death (“cardiac death,” defined as ICD-9-CM codes 410, MI; 411, other acute/subacute ischemic heart disease; 413, angina; 426, conduction disorders; 427, dysrhythmias; 428, heart failure; and 429, ill-defined descriptions and complications of heart disease [with all fourth and fifth digits included], and a discharge status coded as death). The latter codes were chosen to replicate, as closely as possible, the definition of cardiac death used in the National Heart, Lung, and Blood Institute 1985-1986 prospective angioplasty registry. Secondary outcomes included in-hospital death or CABG during the admission for the index PCI. All events, including those occurring at another hospital to which the patient was transferred, were included.

It is recognized that follow-up PCIs do not necessarily represent repeated procedures for restenosis on target lesions and that, therefore, the term follow-up PCI includes a proportion of procedures performed on new vessels. To determine the proportion of follow-up PCIs that were performed for new lesions vs restenotic lesions, data were collected from the medical records of patients...
undergoing PCI at 3 hospitals (the Hospital of the University of Pennsylvania, a tertiary care teaching hospital; Presbyterian Hospital, at the time of the study a community-based but higher-volume academic center; and Pennsylvania Hospital, at the time a lower-volume, private-practice setting), all in Philadelphia.

To examine the specificity of ICD-9-CM code 410 for MI in Pennsylvania, we analyzed participants in a separate ongoing study of MI who were identified by ICD-9-CM code 410. Of 374 participants, 334 (89%) met criteria for definite or probable MI by Minnesota Heart Survey criteria.

Potential Confounders

The variables available in the database that identify potential subgroups at increased or decreased risk of events are shown in Table 1. Previous PCI was identified if a previous angioplasty was found by searching backward in the database through 1990 or if the patient had an ICD-9-CM V-code (V45.82) for previous PCI. Medical record review at the 3 hospitals discussed above was also performed for patients undergoing PCI from October 1, 1994, through December 31, 1995, to assess the validity of several PHC4 variables.

ANALYSIS

The demographic characteristics of subjects undergoing stent vs other procedures were compared by χ² statistics. For the primary outcomes, the unadjusted association between stent use and the outcomes were determined with Kaplan-Meier plots and univariable Cox proportional hazards models. For these analyses, subjects were excluded if they died or had a CABG during their PCI admission. Separate sub-analyses included these subjects. For the secondary outcomes, odds ratios and χ² statistics were used.

To control for not only confounding by patient-level factors but also the potential for confounding by hospital (because of enormous variation in the rates of use of stents across the participating hospitals), a 2-stage procedure was used. First, a propensity score model was adopted to predict the use of stents across hospitals. Propensity scores allow for adjustment for multiple confounders simultaneously without resulting in multivariable model overfitting (as would occur if each hospital were included in a multivariable regression model) and reduce the potential for selection bias. In this initial model, the outcome was stent (vs nonstent) procedures, and the predictors included hospital, age, sex, race, previous PCI, ASG score, insurance, and principal diagnosis of MI. We did not use other ICD-9-CM diagnosis codes because of potential lack of validity. Length of stay was not included in the propensity score because it was likely to be a result, rather than a predictor, of stent use. Similarly, multivessel vs single-vessel PCI was not included because the use of stents for abrupt vessel closure after PCI could lead to aborting of a planned multivessel PCI and would make single-vessel PCI appear to predict stent use when, in fact, the stent use (for abrupt closure) was the reason for performing only a single-vessel PCI.

In the second stage, the patients were grouped into quintiles of propensity to receive a stent. These quintiles were then used as a stratification variable in a Cox proportional hazards model that included the device variable as an independent variable. This method provides for adjustment for all variables included in the initial propensity score model (discussed above). In addition, the length of stay and multivessel PCI variables were included in this model. For the secondary outcomes of in-hospital events, logistic regression models were used and included only the propensity score and the device variable as independent variables. Length of stay was not included because it is a result, rather than a predictor, of the in-hospital outcomes; multivessel PCI was not included because patients having an acute complication after the first of a planned multivessel PCI do not undergo multivessel PCI, so the number of vessels dilated can be affected by the outcome and therefore should not be included. The Hosmer-Lemeshow goodness-of-fit statistic for all logistic models was nonsignificant (P > .20), demonstrating good fit. All analyses accounted for clustering of patients within hospitals. Multiple imputation also was performed with the use of 5 datasets, with imputations generated by the Markov Chain Monte Carlo method for missing values for ASG (n = 270) and race (n = 225), and did not change the results of the study. Analyses were performed with SAS version 6.12 (SAS Institute Inc, Cary, NC) and Stata version 5 (Stata Corp, College Station, Tex) statistical software.

SIX-MONTH CARDIAC EVENTS AND MORTALITY

Despite the benefit of stents in reducing CABG and follow-up PCI rates, they were not associated with a statistically significant reduction in readmission for MI or cardiac death (Table 3, Figure 2). Adjustment for all variables described in the “Patients and Methods” section did not affect the results (Table 3). Inclusion of subjects who had CABG during their index admission also did not alter the results (odds ratio, 1.01; 95% CI, 0.70-1.47), nor did excluding patients with events within 2 weeks of their PCI, the time frame during which subacute thrombosis is most likely to occur (hazard ratio, 0.98; 95% CI, 0.68-1.40).

Overall mortality at 6 months was similar for stent (1.1%) and nonstent (0.9%) procedures (Table 3). Including in-hospital deaths during the index procedure
Consistent with results from randomized trials in se-
however, support the efficacy of stenting for preventing
EFFECTS OF STENTS ON REVASCULARIZATION
and cardiac outcomes.
In contrast, stents had no detectable effect on sub-
CLINICAL IMPLICATIONS
The fact that stents offer an advantage compared with
other interventional procedures vis à vis both acute com-
ferences, does not reduce the risk of nonrevascularization,
TABLE 1. CLINICAL CHARACTERISTICS OF PATIENTS
BY PROCEDURE TYPE

<table>
<thead>
<tr>
<th>Procedure Type, No. (%)</th>
<th>Stent</th>
<th>Nonstent</th>
<th>P†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stent (n = 1240)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nonstent (n = 4018)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age &gt;65 y</td>
<td>663 (53.5)</td>
<td>1976 (49.2)</td>
<td>.008</td>
</tr>
<tr>
<td>Mi†</td>
<td>931 (75.1)</td>
<td>2505 (62.3)</td>
<td>&lt;.001‡</td>
</tr>
<tr>
<td>None</td>
<td>174 (14.0)</td>
<td>1094 (27.2)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Post-MI PCI</td>
<td>135 (10.9)</td>
<td>419 (10.4)</td>
<td>.18</td>
</tr>
<tr>
<td>ASG</td>
<td>568 (47.6)</td>
<td>1789 (47.3)</td>
<td>NA</td>
</tr>
<tr>
<td>0-1</td>
<td>2566 (47.4)</td>
<td>1723 (45.6)</td>
<td>.62</td>
</tr>
<tr>
<td>2</td>
<td>60 (5.0)</td>
<td>267 (7.1)</td>
<td>.02</td>
</tr>
<tr>
<td>Female sex</td>
<td>402 (32.4)</td>
<td>1419 (35.3)</td>
<td>.06</td>
</tr>
<tr>
<td>Insurance</td>
<td>590 (47.6)</td>
<td>1942 (48.3)</td>
<td>NA</td>
</tr>
<tr>
<td>Commercial</td>
<td>31 (2.5)</td>
<td>241 (6.0)</td>
<td>&lt;.001§</td>
</tr>
<tr>
<td>Medicare</td>
<td>617 (49.8)</td>
<td>1828 (45.5)</td>
<td>.11</td>
</tr>
<tr>
<td>Length of stay during index PCI, d</td>
<td>60-3</td>
<td>339 (27.3)</td>
<td>1884 (46.9)</td>
</tr>
<tr>
<td>0-3</td>
<td>595 (48.0)</td>
<td>1441 (35.9)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>2</td>
<td>0.71 (20.2)</td>
<td>0.565 (14.1)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>4-14</td>
<td>55 (4.4)</td>
<td>128 (32.3)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Multivessel PCI code</td>
<td>110 (8.9)</td>
<td>341 (8.5)</td>
<td>.67</td>
</tr>
<tr>
<td>PCI &gt;6 mo earlier</td>
<td>174 (14.0)</td>
<td>541 (13.5)</td>
<td>.61</td>
</tr>
<tr>
<td>Race</td>
<td>23 (1.9)</td>
<td>53 (1.4)</td>
<td>.18</td>
</tr>
<tr>
<td>White</td>
<td>1116 (94.0)</td>
<td>2597 (93.6)</td>
<td>NA</td>
</tr>
<tr>
<td>Black</td>
<td>48 (4.0)</td>
<td>191 (5.0)</td>
<td>.20</td>
</tr>
<tr>
<td>Other</td>
<td>23 (1.9)</td>
<td>53 (1.4)</td>
<td>.18</td>
</tr>
</tbody>
</table>

*Numbers may not add up to total because of missing data. PCI indicates percutaneous transluminal coronary revascularization; ASG, admission severity group as defined by the MedisGroup System; Mi, myocardial infarction; and NA, not applicable.
†P values for tests for overall association between variable and stent use.
‡Early MI PCI indicates PCI within 1 day of admission with MI diagnosis; post-MI PCI, PCI more than 1 day after admission with MI diagnosis.
§P values for tests for overall association between variable and stent use.

In contrast, stents had no detectable effect on subsequent hospitalizations for MI or cardiac death. Unlike results from some previous studies,3,4,6 the results of this study also exclude a substantial increase in risk of these end points, as evidenced by the upper limit of the 95% CIs. Despite the limitations of this study (discussed below), the results also provide confirmatory evidence that coronary stenting, at least in the absence of adjuvant therapies, does not reduce the risk of nonrevascularization, intermediate-term cardiac events.

CLINICAL IMPLICATIONS
The fact that stents offer an advantage compared with other interventional procedures vis à vis both acute complications and the need for repeated revascularization procedures supports the increased use of coronary stent procedures. However, the lack of an effect of stents on intermediate-term, nonrevascularization cardiac events in this or any other study to date (in the absence of adjuvant glycoprotein Iib/IIa inhibitor therapy) has potentially important implications for the rational selection of interventional procedures for patients with coronary artery disease and use of platelet inhibition in those undergoing percutaneous revascularization.

The Evaluation of Platelet Iib/IIa Inhibitor for Stenting (EPISTENT) recently showed that patients receiving a coronary stent plus the glycoprotein Iib/IIa receptor blocker abciximab had a 53% reduction in the primary 6-month end point of death or MI when compared with
patients receiving only a coronary stent. The primary effect of abciximab was to prevent Q-wave and large non–Q-wave MI. The addition of coronary stenting to abciximab (ie, vs balloon PCI plus abciximab) significantly reduced the need for repeated target vessel revascularization. Thus, the combination of stenting and abciximab was associated with a significant reduction in the composite end point of death, MI, or repeated target vessel revascularization. Lincoff et al have advocated the use of glycoprotein IIb/IIIa receptor blockers along with coronary stenting as the standard of care for patients requiring PCI. The present study’s results provide some support for these recommendations. Coronary stenting alone reduces the need for revascularization but, without the use of glycoprotein IIb/IIIa inhibitors, does not appear to reduce nonrevascularization 6-month cardiac events. Of course, the cost-effectiveness and generalizability of this approach must be further determined.

**LIMITATIONS**

The main strength of this study was its use of a broad-based population, reflecting clinical practice at the time of the study. Also, although limited by inclusion of patients treated mostly in the era before glycoprotein IIb/IIIa blockers, this limitation has the advantage of permitting the study to examine the effects of stents independent of the effects of glycoprotein IIb/IIIa blockers. However, because this study was not a randomized trial and because of the time frame studied, the effects of possible uncontrolled confounding and bias must be considered.

**In-Hospital Events**

It is possible that patients with smaller, more complex lesions were less likely to receive a stent and more likely to be referred for CABG if the PCI was unsuccessful. However, it is more likely that the stent group had a higher risk of in-hospital complications (including CABG) because of the inclusion of stent use as unplanned therapy, which is associated with an approximately 4-fold increased risk for emergent CABG. Although a recent study demonstrated a reduction in in-hospital mortality after stenting, and although our study also was associated with fewer in-hospital deaths, the results were not statistically significant and the 95% CIs were wide.

**Table 3. Association of Stent Use With Outcomes**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Risk of Event, %</th>
<th>Univariable OR or HR (95% CI)†</th>
<th>Multivariable OR or HR (95% CI)†</th>
<th>Multivariable P</th>
</tr>
</thead>
<tbody>
<tr>
<td>In-hospital CABG or death</td>
<td>3.1</td>
<td>0.56 (0.39-0.79)</td>
<td>0.63 (0.41-0.97)</td>
<td>.04</td>
</tr>
<tr>
<td>In-hospital CABG</td>
<td>1.6</td>
<td>0.44 (0.28-0.71)</td>
<td>0.48 (0.29-0.82)</td>
<td>.007</td>
</tr>
<tr>
<td>In-hospital death</td>
<td>1.4</td>
<td>0.72 (0.43-1.21)</td>
<td>0.88 (0.46-1.67)</td>
<td>.69</td>
</tr>
<tr>
<td>6-mo PCI or CABG</td>
<td>12.5</td>
<td>0.69 (0.57-0.82)</td>
<td>0.72 (0.58-0.89)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>6-mo PCI</td>
<td>9.9</td>
<td>0.67 (0.55-0.82)</td>
<td>0.69 (0.56-0.86)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>6-mo CABG</td>
<td>3.4</td>
<td>0.74 (0.53-1.04)</td>
<td>0.87 (0.61-1.24)</td>
<td>.45</td>
</tr>
<tr>
<td>6-mo MI or cardiac death</td>
<td>3.7</td>
<td>1.00 (0.72-1.41)</td>
<td>0.97 (0.71-1.33)</td>
<td>.86</td>
</tr>
<tr>
<td>6-mo MI</td>
<td>3.2</td>
<td>0.99 (0.69-1.42)</td>
<td>0.97 (0.69-1.37)</td>
<td>.89</td>
</tr>
<tr>
<td>6-mo Cardiac death</td>
<td>0.8</td>
<td>1.13 (0.55-2.32)</td>
<td>0.89 (0.47-1.67)</td>
<td>.77</td>
</tr>
<tr>
<td>6-mo Overall mortality</td>
<td>1.1</td>
<td>1.21 (0.64-2.29)</td>
<td>0.98 (0.55-1.74)</td>
<td>.97</td>
</tr>
</tbody>
</table>

†Odds ratio used for in-hospital events; hazard ratio used for 6-month events.

\*OR indicates odds ratio; HR, hazard ratio; CI, confidence interval; CABG, coronary artery bypass graft; PCI, percutaneous transluminal coronary revascularization; and MI, myocardial infarction.

**Figure 1. Survival curves for 6-month revascularization outcome (percutaneous coronary intervention or coronary artery bypass grafting).**

**Figure 2. Survival curves for 6-month cardiac events (myocardial infarction or cardiac death).**
Six-Month Revascularization

The reduction observed in follow-up PCIs was probably not caused by confounding or bias because most factors likely biased the results against showing a benefit of stents. First, in 1995, dual antiplatelet therapy (aspirin plus ticlopidine hydrochloride) was not yet used routinely after stent procedures. Current use of antiplatelet agents might yield even lower rates of repeated PCI after stenting. Similarly, high-pressure balloon inflation was not routinely performed. Second, stents used as bailout therapy for abrupt vessel closure (not discernible from the administrative dataset) might increase the risk of target lesion revascularization in the stent group, independent of the use of stents. Third, not all repeated revascularizations were for restenosis of the initially treated vessel; if, as is likely, the proportion of these revascularizations was not different between stent and nonstent procedures, the results would be biased toward the null. Therefore, all of these factors would bias the results of this study toward showing either no effect of stents or an increased risk of follow-up revascularization from stents. Despite these potential biases, the results favored stent procedures. It is possible that the use of stents in larger-diameter coronary vessels relative to nonstent procedures or the limited use of stents in vein grafts could have spuriously inflated the protective effect of stents on repeated procedures; however, given the currently available data on stenting in vein grafts and the other biases against stents listed above, it is unlikely that the protective effect from stents in this study were due solely to these factors.

Six-Month Nonrevascularization Cardiac Events

Several sources of error must be considered in examining the lack of a finding of a beneficial relationship between stents and 6-month nonrevascularization cardiac events. First, it is possible that patients receiving stents were at higher risk of cardiac events, therefore masking a truly beneficial effect of stenting. However, stents were used less frequently in higher-risk patients (those with an MI and those with a higher ASG score, both of which were accounted for by the multivariable analyses), and stents may have been used primarily in patients with larger-diameter, less complex vessels. Therefore, uncontrolled confounding is unlikely to explain the results.

Second, bias could have resulted because administrative data rely on ICD-9-CM codes to detect cardiac outcomes, and the study was limited to follow-up events that required hospital admission in Pennsylvania. However, the use of ICD-9-CM code 410 for identifying definite MI in our and other studies has been shown to have good sensitivity and specificity, and it is unlikely that a substantial number of patients had cardiac events that occurred in the absence of admission to a hospital. In addition, limiting the population to Pennsylvania residents should have minimized the loss to follow-up. The agreement found between PHC4 data and medical record review for repeated PCI rates also suggests that follow-up admissions were comprehensively identified in the database. The readmission rate for MI estimated in this study also was consistent with expected rates after PCI: higher than that in the more stable, selected population of the Stent Restenosis Study and similar to that of the more diverse population of Benestent II. Finally, the review of medical records showed that the proportion of procedures done for MI was almost identical to that derived from ICD-9-CM codes for MI in the PHC4 data.

Third, because of lesion size and complexity, the members of the nonstent group were probably more likely than the stent group to be treated with nonballoon devices. However, there is no evidence that any of these other devices alter the risk of subsequent events when compared with balloon angioplasty, and they may, in fact, increase complications. Therefore, inclusion of these devices should, if anything, have biased the results toward showing a beneficial effect of stents on cardiac events, which was not observed.

Fourth, type II error could result in a failure to detect a reduction in risk from stents. However, on the basis of the 95% confidence intervals of the hazard ratio for cardiac events, the study can reasonably exclude a relative risk reduction from stents of at least 30%, corresponding to an absolute difference in risk for cardiac events from stents vs nonstents of 1.1%.

Fifth, greater use of abciximab in the nonstent group could have reduced the apparent benefit of coronary stenting. However, use of abciximab during this period has been estimated to be only about 3% and therefore was unlikely to have biased the results. The current use of dual antiplatelet therapy after stenting would be expected to reduce early cardiac events relative to anticoagulation therapy. However, the effect of ticlopidine on cardiac (nonrevascularization) outcomes is primarily on early events (subacute thrombosis), and analyses excluding events that occurred within 2 weeks of the PCI did not change the results.

CONCLUSIONS

This study provides evidence that coronary stenting, when used outside of the strict control and limited populations of randomized trials, still reduces the need for in-hospital CABG and repeated PCI at 6 months. However, with data from populations treated in randomized trials, stents do not appear to reduce the risk of subsequent cardiac events (MI or cardiac death), outcomes that may be best minimized with use of platelet glycoprotein IIb/IIIa blockers, at least in high-risk subsets of patients.

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