Advances in Interventional Cardiology I: Case Studies

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Cover Illustration by Scott Holladay
I. INTRODUCTION

Coronary atherosclerotic heart disease (CASHD) is currently the single largest cause of mortality in the United States, resulting in approximately 500,000 deaths each year. Estimates for the United States indicate that more than 12 million people may have a history of heart attack, angina, or both and that roughly 1 million people will have a new or recurrent heart attack this year alone. As of 1997 (the most recent data available), this enormous disease burden led to more than 1 million diagnostic heart catheterizations and an almost equal number of revascularization procedures each year. Nearly 50% of these revascularizations are performed by means of percutaneous transluminal coronary angioplasty (PTCA), and this percentage has continued to increase.1

PTCA was developed more than 20 years ago from the pioneering efforts of Andreas Gruentzig. Building on the work of Dotter2 Zeitler,3 and Porstmann,4 Gruentzig envisioned that atherosclerotic arterial lesions could be treated endovascularly with expandable balloon-tipped catheters; he subsequently designed, constructed, tested, and first used this therapy clinically.5–8 Since that time, increases in our understanding of the biology of atherosclerotic disease and its responses to treatment, vast improvements in the equipment available, and use of adjunctive therapies have led physicians to perform PTCA for an expanding spectrum of disease, with steadily improving results.

This is the first part of a 2-part review on interventional cardiology. The first part emphasizes diagnosis and treatment of multivessel coronary artery disease (CAD) as well as coronary thrombosis. Two case patients are presented to highlight features of the management of these conditions. The second part presents one case patient and discusses intravascular radiation for the prevention of restenosis after angioplasty. A complete review of interventional cardiology is beyond the scope of this article; however, major advances in the field are described as are trials supporting the use of current interventions.

II. CASE PATIENT 1

PRESENTATION

Patient 1 is an active 52-year-old man who presents to a cardiologist with a 1-year history of exertional chest discomfort. He describes the discomfort as a pressure sensation across his left chest, accompanied by shortness of breath that is relieved with rest. The discomfort had initially occurred only with strenuous exercise but has progressively been occurring with less activity. He was seen 3 months earlier by his primary care physician for these symptoms and was started on a mononitrate. This therapy improved his symptoms somewhat, but they have continued to progress. His medical history is significant for hypertension and hypercholesterolemia, for which he is receiving treatment. He has a strong family history of early atherosclerotic disease, and he quit smoking 8 months ago after a 60 pack-year history of cigarette use. On physical examination, his heart rate is 72 bpm and his blood pressure is 132/76 mm Hg. The remainder of the physical examination is within normal limits. The electrocardiogram also shows normal findings.

Patient 1’s physician obtains an exercise stress test, which is positive for ischemia by stage III of a Bruce protocol. Patient 1 subsequently undergoes a cardiac catheterization, revealing normal left ventricular function and pressures with an ejection fraction of 55%. Selective angiography shows significant lesions in the mid-left anterior descending artery (LAD) and the proximal right coronary artery (RCA) (Figures 1 and 2).

• What is the most appropriate treatment for patient 1’s multivessel coronary artery disease?
A) Continued medical therapy and risk factor modification  
B) PTCA of both the LAD and RCA lesions in staged procedures  
C) Referral to a cardiothoracic surgeon for a coronary artery bypass graft surgery (CABG)  
D) Testing via stress-nuclear imaging to identify the more significant lesion and then treating it with PTCA

Discussion

The correct answer is B. Patient 1 had a slowly progressing pattern of angina, which had become lifestyle limiting despite medical therapy, but had no acute events suggesting an unstable atherosclerotic plaque. Noninvasive testing confirmed inducible ischemia, and catheterization revealed multivessel coronary artery disease with preserved left ventricular function. Based on the available clinical trials, patient 1 is an ideal candidate for elective revascularization by PTCA for relief of his angina. Although CABG would be beneficial, concerns about periprocedural complications and long-term graft patency would favor an initial therapeutic approach with PTCA.

Patient 1 underwent angioplasty of both lesions, with excellent angiographic and long-term results.

GENERAL PRINCIPLES

PTCA versus Medical Therapy

The ACME (Angioplasty Compared to Medicine) study was the first randomized trial to compare PTCA with medical therapy.\(^9\) Conducted at Veterans’ Affairs Medical Centers, this prospective study randomly assigned 212 patients with stable angina and single-vessel CASHD either to medical therapy or PTCA; the primary endpoints were change in exercise tolerance and angina symptoms. After 6 months, PTCA was found to be superior to medical therapy in improving exercise performance and relieving angina symptoms. Subsequent analysis also showed PTCA to be better at improving quality-of-life measures compared with medical therapy alone.\(^10\) No difference was seen, however, in the incidence of myocardial infarction (MI) or death between the 2 groups. A smaller study administered as part of the ACME trial, which enrolled patients in parallel, failed to demonstrate a similar benefit for PTCA in patients with 2-vessel disease.\(^11\) This study has been criticized because of its small size and the low levels of complete revascularization achieved in patients randomly assigned to PTCA.

The largest trial comparing medical therapy with PTCA is the RITA-2 (Second Randomized Intervention Treatment of Angina) trial.\(^12\) In this study, 1018 patients with angina and 1-, 2-, or 3-vessel CASHD were randomly assigned to PTCA or medical therapy. As was found in the ACME trial, PTCA provided a small but significant improvement in exercise tolerance at 3 months’ follow-up; however, PTCA was not significant at 1 year. The reduction in grade 2 or greater angina symptoms seen with PTCA remained significant through 2 years (Figure 3). However, PTCA patients had a significantly higher rate of MI chiefly related to periprocedural events.

PTCA versus CABG

Multiple studies\(^13\text{–}16\) have demonstrated the superiority of CABG versus medical therapy as initial treatment procedures.
of multivessel CASHD in patients with high-risk characteristics (e.g., left main disease, 3-vessel disease with reduced left ventricular function). However, the highly invasive nature of CABG and the limitations on long-term durability of venous bypass grafts have led to direct comparisons of PTCA and CABG as initial therapy in CASHD. Five major trials have compared these treatment strategies in patients with angina and multivessel coronary disease (Table 1). Each study enrolled patients with multivessel disease believed to be treatable with either PTCA or CABG and excluded patients with high-risk disease, although the criteria for the latter varied from study to study.

The RITA (Randomized Intervention Treatment of Angina) trial\(^1\), randomly assigned 1011 patients with 1-vessel (45%), 2-vessel (43%) or 3-vessel (12%) disease to either PTCA or CABG as an initial strategy. The patients were considered equally suitable for either treatment, although complete revascularization was not mandated as part of therapy. By 2.5 years of follow-up, no significant difference was noted in the combined endpoint of death or nonfatal MI between PTCA or CABG (9.8% versus 8.6%, respectively). However, patients initially assigned to PTCA had a significantly greater need for repeat revascularization (38%) compared with CABG patients (11%, \(P < 0.001\)) and experienced more angina symptoms. The lack of difference in the primary endpoint was seen despite the fact that only 81% of patients with 2-vessel disease and 63% of patients with 3-vessel disease had complete revascularization in the PTCA-assigned group, compared with 97% and 87% of the CABG-assigned group.

The GABI (German Angioplasty Bypass Surgery Investigation) trial\(^1\) randomly assigned 358 patients (80% with 2-vessel, 20% with 3-vessel disease) to either PTCA or CABG, with a primary endpoint of freedom from class II or greater angina. At 1-year follow-up, the primary endpoint did not differ between the 2 groups, although the need for repeat revascularization was more common in the PTCA group (44%) than in the CABG group (6%), as was the use of antianginal medications. Interestingly, the surgical group had a significantly higher rate of death or nonfatal MI than did the angioplasty group (13.6% versus 6.0%); this finding appears to be related to perioperative infarctions, reflecting the higher up-front risk of surgery.

The EAST (Emory Angioplasty Surgery Trial) study\(^1\) randomly assigned 392 patients (60% with 2-vessel disease, 40% with 3-vessel disease) to PTCA or CABG. Equivalence of revascularization was not a requirement of enrollment, and only 61% of PTCA patients had complete revascularization, compared with 98% of surgical patients. Despite this lack of equivalence, no significant difference was noted in the primary 3-year composite endpoint of death, Q-wave MI, or large thallium defect between the groups (27.3% for PTCA versus 26.8% for CABG). As with the other trials, need for repeat revascularization was more common with PTCA (54%) than with CABG (13%), as was persistent angina. The equivalence of the 2 treatment modalities with regard to the primary endpoint was confirmed in 8-year follow-up.\(^2\)

The CABRI (Coronary Angioplasty versus Bypass Revascularization Investigation) trial\(^1\) randomly assigned
1154 patients with 2- or 3-vessel disease to either PTCA or CABG. One-year data showed no significant difference in the rates of death or MI between the groups, but PTCA patients required more revascularization procedures and experienced more angina.

The largest study to compare these 2 treatment modalities is the BARI (Bypass Angioplasty Revascularization Investigation) trial, which randomly assigned 1829 patients with 2-vessel (58%) or 3-vessel (41%) disease amenable to treatment with either PTCA or CABG. The primary endpoint of the study was 5-year mortality in all patients, with additional multiple pre-defined subgroup analyses. After 5 years, no significant difference was seen in the primary endpoint between the 2 groups; cumulative survival was 86.3% for the PTCA group and 89.3% for the CABG group. In addition, surviving patients in both groups were equally free of Q-wave MI. Once again, PTCA patients (54%) required more repeat revascularizations than did CABG patients (8%) during the course of the study; however, 60% of the PTCA group achieved an equivalent survival benefit without ever requiring CABG.

**CASE PATIENT 1: ALTERNATE PRESENTATION**

- If patient 1 also had diabetes that required insulin, what would be the most appropriate treatment for his multivessel coronary artery disease?

**Discussion**

- A) Continued medical therapy for risk factor modification
- B) PTCA of both the LAD and RCA lesions in staged procedures
- C) Referral for a CABG
- D) Testing via stress-nuclear imaging to identify the more significant lesion and then treating with PTCA

The correct answer is C. In the patient with multivessel CAD, diabetes would significantly increase his long-term risk for complications from CAD and would dramatically worsen his prognosis. In a predefined subgroup analysis in the BARI trial, patients with diabetes who underwent PTCA as initial therapy had significantly decreased survival compared with those receiving CABG (65.5% versus 80.6%, \( P = 0.003 \)). At 7-year follow-up, this difference in survival persisted (55.7% for PTCA versus 76.4% for CABG, \( P = 0.043 \)), although no difference was noted in patients without diabetes. In light of this data, CABG would be the preferred treatment for patient 1 if he also had diabetes.

The applicability of all of these studies to current practice is sometimes questioned because much of the therapy (both medical and invasive) would not be considered standard care by today’s criteria. Although this
is a limitation, these studies currently remain the best evidence to guide therapy. Multiple ongoing or recently completed trials are evaluating these same questions using more current therapies, and the results of these trials are eagerly anticipated.

III. CASE PATIENT 2

PRESENTATION

Patient 2 is a 67-year-old woman who presents to the emergency department with 4 to 5 hours of intermittent chest discomfort occurring at rest, accompanied by mild shortness of breath. The longest episode lasted for more than 20 minutes and prompted her to come to the hospital. She has never had chest pain before this episode. Her medical history is significant for hypertension, which is treated with a calcium channel blocker. On route to the hospital, she took 2 of her husband’s nitroglycerin tablets, with resolution of her symptoms.

On physical examination, patient 2 is a moderately obese woman in no distress with a heart rate of 84 bpm, a blood pressure of 155/85 mm Hg, and a respiratory rate of 14 breaths/min. Her chest is clear, and there is no jugular venous distention. The cardiac examination is remarkable for a soft S4 heart sound and a II/VI systolic ejection murmur at the base. The remainder of her physical examination is within normal limits. An electrocardiogram shows a normal sinus rhythm with nonspecific ST and T wave changes in the lateral leads.

Patient 2 is treated with aspirin, low-molecular-weight heparin, nitroglycerin, and a β-blocker. She remains hemodynamically stable and has no further episodes of chest pain. Although an initial set of cardiac enzyme levels was negative on arrival, a subsequent set obtained 8 hours later shows a small but positive elevation in troponin-I. The following day, patient 2 undergoes cardiac catheterization, which reveals a total occlusion of her distal RCA with extensive collateral filling of the posterior descending artery and left ventricular branches from the LAD (Figure 4). The LAD and left circumflex coronary artery system have moderate luminal irregularities, and left ventricular function is normal. Closer examination suggests a substantial amount of fresh thrombus is present in the distal RCA.

• What is the best treatment option for total occlusion of the distal RCA?
  A) Referral for a CABG
  B) Immediate balloon angioplasty of the lesion, with provisional stenting for treatment of acute or threatened closure
  C) Immediate primary stenting of the lesion with high-pressure stent deployment
  D) Treatment with a glycoprotein (GP) IIb/IIIa receptor inhibitor and continued heparin for 24 hours, followed by repeated diagnostic catheterization and possible PTCA

Discussion

The correct answer is D. Patient 2 presented with an acute coronary syndrome that was stabilized rapidly with medical therapy. Her cardiac catheterization revealed a thrombus-laden occlusion of the distal RCA, but she had relatively little evidence of myocardial injury, presumably because of substantial collateral filling of the vessels distal to the occlusion. Although often difficult to identify by angiography, the presence of visualized thrombus has been associated with an increased rate of ischemic complications during angioplasty. These increased complications are presumably the result of distal embolization of thrombus with vessel occlusion. Because patient 2 is clinically stable and without evidence of ongoing myocardial injury, the thrombus burden should be reduced in the lesion before intervention. Several therapies, both mechanical and pharmacologic, are available for treating intracoronary thrombus, but only one was provided as an answer to this question.

Patient 2 receives a bolus and subsequent infusion of a GP IIb/IIIa receptor inhibitor and has a repeated

Figure 4. Angiogram from patient 2 of the right coronary artery showing total occlusion (arrow) in the distal segment.
catheterization the following day. Angiography of the RCA reveals that the intracoronary thrombus is gone, leaving a patent vessel with a high-grade lesion (Figure 5). This lesion is subsequently angioplastied and stented without complications. The decision to use a GP IIb/IIIa receptor inhibitor is based on the fact that platelet activation and aggregation play a major role in the formation of intracoronary thrombus. Although patient 2’s treatment is a dramatic demonstration of the effect of GP IIb/IIIa receptor inhibitors, extensive studies have shown benefit across a wide spectrum of interventional cases with multiple agents.

GLYCOPROTEIN IIb/IIIa RECEPTOR INHIBITORS

The platelet membrane GP IIb/IIIa receptor is one of several membrane integrins found on the surface of platelets. After platelets are activated, the GP IIb/IIIa receptor undergoes a conformational change allowing it to bind circulating fibrinogen and to form cross-links to other platelets. As this process continues, a mass of cross-linked platelets in combination with circulating coagulation proteins can form a thrombotic occlusion in an artery. Because it is the final common pathway for platelet aggregation, the GP IIb/IIIa receptor is an ideal site for pharmacologic intervention.

Three GP IIb/IIIa receptor inhibitors are currently approved for use in the United States (Table 2). Tirofiban (Aggrastat, Merck, White House Station, NJ) and eptifibatide (Integrilin, COR Therapeutics, South San Francisco, CA) are small molecules that are competitive inhibitors of the GP IIb/IIIa receptor, whereas abciximab (Reopro, Centocor, Malvern, PA) is a human-murine chimeric antibody fragment directed against the GP IIb/IIIa receptor. Although both types of agents are very effective at inhibiting platelet aggregation, their pharmacologic profiles differ significantly. The small molecules have relatively short half-lives, allowing rapid recovery of platelet function after discontinuation of the drug. These agents are also highly specific for the GP IIb/IIIa receptor. On the other hand, abciximab demonstrates prolonged platelet binding and inhibition (up to 3 weeks) and can also inhibit the αβ3 integrin, a vitronectin receptor.

In addition to their clear indications for the medical management of acute coronary syndromes, GP IIb/IIIa receptor inhibitors have been extensively evaluated as adjunctive therapy for coronary interventions (Table 3).

Small Molecules

The RESTORE (Randomized Efficacy Study of Tirofiban for Outcomes and Restenosis) trial randomly assigned 2139 patients undergoing PTCA or directional atherectomy within 72 hours of presentation with an acute coronary syndrome to receive either placebo or tirofiban in addition to heparin and aspirin therapy. After the guidewire had crossed the coronary lesion, the tirofiban was given as a 10 µg/kg bolus over 3 minutes followed by a 36-hour infusion of 0.15 µg/kg/min. The primary endpoint—evaluated at 2, 7, and 30 days—was a composite of death, MI, CABG or repeat PTCA, or stent placement for recurrent ischemia or abrupt closure. This endpoint was significantly reduced in the tirofiban group at 2 and 7 days (relative reduction, 38% and 27%, respectively) but became nonsignificant at 30 days. Major bleeding was not different between the 2 groups.

Eptifibatide has been evaluated as adjunctive therapy for coronary interventions in 2 large trials, IMPACT-II (Integrilin to Minimize Platelet Aggregation and Coronary Thrombosis-II) and ESPRIT (Enhanced Suppression of the Platelet Receptor GP IIb/IIIa using Integrilin Therapy). IMPACT-II randomly assigned 4010 patients undergoing elective, urgent, or emergent coronary interventions to receive either placebo or 1 of 2 doses of eptifibatide for 20 to 24 hours in addition to procedural heparin. The primary endpoint was death, MI, placement of a stent to treat abrupt closure, or need for urgent revascularization. At the early time-point of 24 hours, there was a significant reduction of events in both treatment groups compared with placebo. As was seen in RESTORE, this difference became nonsignificant.
by the 30-day time-point using intention-to-treat analysis. However, in those who received any amount of allocated treatment, a significant reduction in events at 30 days was noted in the low-dose eptifibatide group compared with placebo \((P = 0.035)\). Although eptifibatide was clearly effective, no dose-response effect was observed.

The ESPRIT trial evaluated eptifibatide in the much broader spectrum of patients undergoing elective PTCA with stent placement for a native coronary artery lesion.\(^5\) In addition, a new dosing regimen (two 180-µg/kg boluses 10 minutes apart followed by a 2 µg/kg per min infusion) was used in an attempt to overcome some limitations seen in IMPACT-II. Originally, ESPRIT randomly assigned 2400 patients to either eptifibatide or placebo in addition to weight-based heparin, aspirin, and a thienopyridine. However, this trial was terminated early after 2064 patients were enrolled because of clear efficacy in the treatment group. The 48-hour primary endpoint of death, MI, or urgent revascularization was seen in 6.6% of the treatment group compared with 10.5% of the placebo group \((P = 0.0015)\). Most of this difference stemmed from a reduction in the number of moderately sized infarctions, defined as a myocardial-bound creatine kinase (creatine kinase MB fraction [CK-mb]) isoenzyme level greater than 3 times normal; however, no significant difference was seen for the individual endpoints of death or large MI \((P = 0.0015)\). The composite endpoint of death, MI, or urgent revascularization remained significantly reduced in the treatment group \((6.8\%)\) versus placebo \((10.5\%)\) through 30 days \((P = 0.0003)\), with a very small absolute further increase in events.

**Abciximab**

Three major trials have evaluated the use of abciximab during coronary interventions. The EPIC (Evaluation of 7E3 for the Prevention of Ischemic Complications) study\(^\text{54}\) randomly assigned 2099 patients undergoing coronary angioplasty or atherectomy to receive—in addition to aspirin and non-weight-based heparin—a placebo, a bolus of abciximab, or a bolus of abciximab plus a 12-hour infusion of the agent. The patients were all considered at high risk for cardiac ischemia because of an unstable clinical presentation or because of high-risk angiographic characteristics. The 30-day composite endpoint of death, MI, or need for urgent revascularization was reduced by 35% \((P = 0.009)\) in the group receiving a bolus plus infusion of abciximab when compared with placebo. This benefit was also significant for the individual endpoints of MI and need for emergent repeated PTCA. No benefit beyond placebo was seen in the group receiving only a bolus of abciximab but no infusion. The benefit derived from bolus and infusion therapy was preserved at 6 months\(^\text{55}\) and 3 years.\(^\text{56}\) This treatment strategy, however, was associated with a significant increase in both major bleeding and need for transfusion, which was most likely caused by the relatively high doses of heparin used.

In an effort to evaluate abciximab use in a broader interventional patient population and to determine if altered heparin dosing could reduce hemorrhagic complications, the EPILOG (Evaluation in PTCA to Improve Long-term Outcome with Abciximab GPIIb/IIIa Blockade) trial\(^\text{57}\) enrolled 2792 patients undergoing elective or urgent PTCA. Patients with an acute MI or those with unstable angina and electrocardiographic changes within 24 hours were excluded. Study patients were randomly assigned to receive abciximab bolus and infusion with standard-dose heparin (100 U/kg bolus), abciximab bolus and infusion with low-dose heparin (70 U/kg bolus), or placebo with standard-dose heparin. Again, the primary endpoint was the composite of death, MI, or urgent revascularization at 30 days. In both treatment groups, the use of abciximab was associated with an

<table>
<thead>
<tr>
<th>Agent</th>
<th>Molecule</th>
<th>Half-Life</th>
<th>Elimination</th>
<th>Specificity</th>
<th>Reversible with Platelets</th>
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<tbody>
<tr>
<td>Abciximab (Reopro)</td>
<td>Chimeric antibody fragment</td>
<td>Long</td>
<td>Plasma</td>
<td>High (also binds (\alpha_v\beta_3) integrin)</td>
<td>Yes</td>
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<tr>
<td>Tirofiban (Aggrastat)</td>
<td>Nonpeptide, small molecule</td>
<td>Short</td>
<td>Renal</td>
<td>High</td>
<td>No</td>
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<tr>
<td>Eptifibatide (Integrin)</td>
<td>Heptapeptide, small molecule</td>
<td>Short</td>
<td>Renal</td>
<td>High</td>
<td>No</td>
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</tbody>
</table>
### Table 3. Clinical Trials Evaluating Glycoprotein IIb/IIIa Receptor Inhibitors as Adjunctive Therapy for Angioplasty

<table>
<thead>
<tr>
<th>Trial (Reference)</th>
<th>Composite Endpoint (Death, MI, Revascularization)</th>
</tr>
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<tbody>
<tr>
<td>Name</td>
<td>Intervention*</td>
</tr>
<tr>
<td>RESTORE (51)</td>
<td></td>
</tr>
<tr>
<td>2 day</td>
<td>Tirofiban</td>
</tr>
<tr>
<td>7 day</td>
<td>Tirofiban</td>
</tr>
<tr>
<td>30 day</td>
<td>Tirofiban</td>
</tr>
<tr>
<td>IMPACT-II (52)</td>
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<td>Low-dose eptifibatide</td>
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<td>30 day</td>
<td>Low-dose eptifibatide</td>
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<tr>
<td>ESPRIT (53)</td>
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<td>2 day</td>
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<td>30 day</td>
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<tr>
<td>EPIC</td>
<td></td>
</tr>
<tr>
<td>30 day (54)</td>
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<td>6 mo‡</td>
<td>Abciximab</td>
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<tr>
<td>3 yr (56)‡</td>
<td>Abciximab</td>
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<tr>
<td>EPILOG (57)</td>
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</tr>
<tr>
<td>30 day</td>
<td>Abciximab &amp; low-dose heparin</td>
</tr>
<tr>
<td></td>
<td>Abciximab &amp; standard-dose heparin</td>
</tr>
<tr>
<td>6 mo</td>
<td>Abciximab &amp; low-dose heparin</td>
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<tr>
<td></td>
<td>Abciximab &amp; standard-dose heparin</td>
</tr>
<tr>
<td>EPISTENT‡§</td>
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<tr>
<td>30 day (58)</td>
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<td></td>
<td>Abciximab &amp; angioplasty</td>
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<td>6 mo (59)</td>
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<tr>
<td></td>
<td>Abciximab &amp; angioplasty</td>
</tr>
<tr>
<td>1 yr (60)‡</td>
<td>Abciximab &amp; stent</td>
</tr>
<tr>
<td></td>
<td>Abciximab &amp; angioplasty</td>
</tr>
</tbody>
</table>

EPIC = Evaluation of 7E3 for the Prevention of Ischemic Complications; EPILOG = Evaluation in PTCA to Improve Long-term Outcome with Abciximab GP IIb/IIIa Blockade; EPISTENT = Evaluation of Platelet IIb/IIIa Inhibitor for Stenting; ESPRIT = Enhanced Suppression of the Platelet Receptor GP IIb/IIIa using Integrilin Therapy; GP = glycoprotein; IMPACT-II = Integrilin to Minimize Platelet Aggregation and Coronary Thrombosis–II; MI = myocardial infarction; NS = not significant; PTCA = percutaneous transluminal coronary angioplasty; RESTORE = Randomized Efficacy Study of Tirofiban for Outcomes and Restenosis.

*See text for complete discussion of therapeutic interventions.

†The placebo group was standard-dose heparin for the EPILOG trial. The placebo group was stent alone in the EPISTENT trial.

‡The composite endpoint for these trials included any revascularization, whereas the composite endpoint for all the other trials included urgent revascularization.

§EPISTENT is the only study to show a reduction in mortality.
approximately 50% reduction in the primary endpoint at 30 days; this reduction was maintained at 6 months. This benefit was seen across the prespecified subgroups, including the lower-risk patients. In addition, the abciximab plus low-dose heparin group had no significant increase in major or minor bleeding events compared with placebo, thereby confirming the safety of this combination.

Like the ESPRIT study, the EPISTENT (Evaluation of Platelet IIb/IIIa Inhibitor for Stenting) trial58 was designed to evaluate abciximab use as part of contemporary patterns of coronary interventions, which increasingly use elective coronary stenting. In this study, 2399 patients with ischemic heart disease were randomly assigned to coronary stenting plus abciximab, balloon angioplasty plus abciximab, or coronary stenting plus placebo and then were evaluated for the primary endpoint of death, MI, or urgent revascularization. All patients received aspirin and low-dose weight-adjusted heparin, and patients receiving stents were treated with ticlopidine for 4 weeks.

At 30 days, the group treated with stenting plus abciximab had a significant reduction in the primary endpoint compared with those undergoing stenting plus placebo. Indeed, the balloon angioplasty plus abciximab group also had a significant reduction in the primary endpoint compared with the stent plus placebo group. This benefit was seen for the secondary endpoints of death and large MI and was seen across subgroups. With the low-dose heparin use, no difference was noted in the rates of hemorrhagic complications among the groups. After 6 months, a continued reduction was observed in the composite endpoint in the abciximab groups.29 Most strikingly, at 1-year follow-up, the stent plus abciximab group had a significant reduction in mortality compared with the placebo group.40 EPISTENT is the only study to show a reduction in mortality in a comparison of interventional techniques.

IV. SUMMARY POINTS

MULTIVESSEL DISEASE
• In patients with coronary atherosclerosis, PTCA improves symptom relief without a difference in mortality when compared with medical therapy.
• In specific high-risk subgroups of patients with CASHD, CABG provides a mortality benefit when compared with medical therapy.
• For the treatment of multivessel CASHD amenable to either PTCA or CABG, mortality or recurrent MI are similar with either treatment modality in the general population; however, PTCA is associated with a more frequent need for repeat revascularization.
• In diabetic patients, a mortality benefit occurs after treatment with CABG when compared with PTCA.
• Whether the most recent advances in adjunctive therapy alter the previous results further in favor of PTCA is yet to be determined.

GLYCOPROTEIN IIb/IIIa INHIBITORS
• Coronary thrombosis is chiefly the result of deposition, activation, and aggregation of platelets at the site of atherosclerotic plaque disruption.
• Glycoprotein (GP) IIb/IIIa inhibitors affect the final common pathway of platelet aggregation and profoundly inhibit platelet function.
• The use of GP IIb/IIIa inhibitors has markedly reduced complication rates associated with PTCA, particularly in situations with high levels of platelet activity and thrombus formation.

REFERENCES


