The Influence of Abciximab 
Use on Clinical Outcome After 
Aortocoronary Vein Graft Interventions

Verghese Mathew, MD, Diane E. Grill, MS, Christopher G. Scott, BS, J. Aaron Grantham, MD, Henry H. Ting, MD, Kirk N. Garratt, MD, FACC, David R. Holmes, Jr., MD, FACC

Rochester, Minnesota

OBJECTIVES
The purpose of this study was to evaluate the effect of abciximab use on clinical outcome in aortocoronary vein graft interventions.

BACKGROUND
Although large randomized trials have demonstrated a significant benefit of abciximab use in the setting of percutaneous coronary interventions, there is relatively little data with respect to the use of this agent in percutaneous vein graft interventions.

METHODS
Three hundred and forty-three patients were identified; 210 undergoing vein graft intervention without abciximab and 133 patients with abciximab.

RESULTS
There were differences in baseline clinical and angiographic characteristics between the two groups; advanced age, unstable angina, older vein grafts and thrombus containing lesions were relatively common in both groups. Angiographic and procedural success rates were similar with or without the use of abciximab (89% vs. 92%, p = 0.15, and 85% vs. 91%, p = 0.12, respectively). The in-hospital composite end point of death/Q-wave myocardial infarction (QWMI)/repeat revascularization was similar between the two groups. Utilizing statistical modeling to adjust for baseline differences between the groups, abciximab use did not influence the cumulative long-term composite end point of death/MI/repeat revascularization.

CONCLUSIONS
This study demonstrates that in this relatively high-risk population undergoing aortocoronary vein graft interventions, the administration of abciximab periprocedurally does not appear to reduce major adverse clinical events. (J Am Coll Cardiol 1999;34:1163–9) © 1999 by the American College of Cardiology

Aortocoronary vein graft failure is relatively frequent during the course of long-term follow-up after coronary artery bypass graft surgery (CABG) (1–4). Repeat CABG in such patients is associated with an increased rate of periprocedural death and myocardial infarction (MI) (5–7), reduced graft patency (5) and decreased event-free survival (8,9). Therefore, an increasing number of patients with vein graft disease with recurrent ischemia are referred for percutaneous intervention. Percutaneous vein graft intervention can be performed with a relatively high rate of angiographic success, although distal embolization and poor reflow culminating in MI occurs more commonly than with native coronary interventions (10–12). In addition, restenosis after percutaneous transluminal coronary angioplasty (PTCA) of vein graft disease is substantial (13,14), although it may be improved by the use of stents (15,16).

Whether other adjunctive therapies may reduce the relatively high short- and long-term adverse event rates in patients undergoing vein graft interventions remains to be seen. The platelet glycoprotein IIb-IIIa receptor antagonist, abciximab, has been shown to reduce adverse events in patients undergoing percutaneous revascularization, initially in high-risk subsets (17,18) and later in a broader spectrum of patients (19). However, bypass graft interventions were performed on a minority of cases in the randomized trials of this agent. Therefore, the question remains as to whether abciximab may offer a benefit in the high-risk lesion subset of vein graft interventions.

The purpose of this study was to evaluate our recent experience with vein graft interventions and to evaluate the influence of abciximab use on clinical outcome in such procedures.

METHODS
The study protocol was approved by the Mayo Clinic Institutional Review Board. We reviewed our institutional
coronary interventional database from January 1, 1995 through December 31, 1997 and identified all patients undergoing percutaneous intervention involving at least one aortocoronary venous bypass graft and subdivided these into patients receiving abciximab periprocedurally and those who did not. Follow-up information in this database is obtained in a prospective fashion. For all patients, baseline demographic information, procedural, lesional and angiographic data acquired during the case were reviewed.

**Definitions.** Acute myocardial infarction was considered to have occurred when at least two of the following three criteria were met: 1) chest pain >30 min, 2) persistent electrocardiographic changes suggestive of ischemia or 3) characteristic elevations in serum creatine kinase levels with a corresponding rise in the MB isoform within 24 h of the procedure. Multivessel disease was defined as the presence of ≥70% stenosis of the luminal diameter in a major epicardial coronary artery with ≥50% stenosis in a second major epicardial vessel (2 vessel disease) or both of the other epicardial vessels (3 vessel disease). Angiographic success was defined as a ≥20% improvement in diameter stenosis with a ≤50% residual diameter stenosis. Procedural success was defined as an angiographically successful procedure without in-hospital, death, Q-wave MI or CABG. Procedural risk as assessed by the operator in our database was categorized as low, intermediate or high and incorporated clinical and angiographic characteristics including patient age, multivessel disease, left ventricular function, presence or absence of unstable angina, lesion length, presence or absence of intraluminal thrombus and age of the vein graft treated. Comorbid conditions including significance pulmonary disease, renal insufficiency and significant vascular disease were also considered.

**Statistical analysis.** Baseline characteristics are presented as mean values with standard deviation or as a percentage of total patients with available data in each group. Pearson’s chi-square test for discrete variables and Student t test for continuous variables were used for comparisons. A logistic regression model utilizing a forward stepwise variable selection process was developed to determine which clinical and angiographic variables were associated with abciximab use for vein graft interventions in our database. Logistic regression models and Cox proportional hazard models were developed to assess the relationship between abciximab use and in-hospital and follow-up events, respectively. These models were developed in two different ways. First, a propensity score was calculated from the coefficients of the logistic regression model that utilized abciximab use and in-hospital and follow-up events, respectively. These models were used to calculate odds ratios (ORs)
for abciximab use for the in-hospital composite end point of death/Q-wave MI/repeat revascularization (repeat PTCA of the target lesion or CABG) and risk ratios for the cumulative long-term end point of death/MI/repeat revascularization from the time of procedure onward, which included in-hospital events as well. Adjusted survivals were calculated from the Cox models fixing the coefficients for the other covariates at their means and varying the coefficient for abciximab.

Results of these analyses were similar utilizing either the propensity score model or the forward stepwise regression model; therefore, data are presented from the latter.

RESULTS

Baseline and clinical characteristics. During the specified study period, 343 patients undergoing aortocoronary vein graft interventions were identified; 210 without abciximab and 133 with abciximab administered periprocedurally. Baseline clinical characteristics are shown in Table 1. Patients receiving abciximab were slightly older (70 ± 9 yr vs. 68 ± 9 yr, p = 0.03), had older vein grafts (9.6 ± 4.4 yr vs. 7.9 ± 4.9 yr, p = 0.001) and a higher incidence of prior MI (77.1% vs. 66.7%, p = 0.04), although the rates of acute MI on presentation were similar between the two groups (12.8% vs. 9.0%, p = 0.27). Patients receiving abciximab were less likely to present with unstable angina (70.7% vs. 81.4%, p = 0.02).

Of the patients receiving abciximab periprocedurally, the agent was initiated before the first balloon inflation (or before beginning the intervention in non-PTCA cases) in 85 (63.9%), whereas in 48 patients (36.1%), abciximab was initiated during the procedure sometime after the initiation of the intervention. Additionally, patients receiving abciximab were more likely to be considered a high-risk procedure by the operator performing the procedure (48.9% vs. 33.3%, p = 0.004).

Lesion/procedural characteristics. Lesion and procedural characteristics of the two groups are shown in Table 2. The patients receiving abciximab were more likely to have received a stent during the course of their procedure (84% vs. 75%, p = 0.04). The frequency of concomitant native vessel interventions, coronary territory supplied by the treated graft and treatment site within the graft were similar between the two groups. Patients receiving abciximab were more likely to have angiographic evidence of intragraft thrombus (66% vs. 40%, p < 0.001) and were more likely to
have American College of Cardiology/American Heart Association (ACC/AHA) type C lesions (82% vs. 67%, p < 0.001). Abciximab patients were also more likely to have Thrombolysis in Myocardial Infarction (TIMI) 0 flow before the intervention (21% vs. 8%, p < 0.001) and were less likely to have TIMI 3 flow at the end of the procedure (79% vs. 93%, p < 0.001).

Of note, newer technologies including directional atherectomy, extractional atherectomy and rotational atherectomy were relatively uncommon in both groups.

Postprocedural anticoagulation. Patients receiving abciximab were less likely to receive warfarin upon dismissal (11.5% vs. 23.4%, p = 0.006) and were more likely to receive low molecular heparin upon dismissal (13.1% vs. 6.3%, p = 0.03).

In-hospital events. Table 3 displays the in-hospital events of the two groups. Angiographic success was similar with or without the use of abciximab (89% vs. 92%, p = 0.15), as was procedural success (85% vs. 91%, p = 0.12). The rates of in-hospital death, Q-wave MI, bypass surgery and repeat PTCA were similar between the two groups. The in-hospital composite end point of death/Q-wave MI/repeat revascularization was also similar between the two groups.

Table 4 displays other in-hospital end points, which were not included in the prespecified in-hospital composite end point. Patients receiving abciximab had higher rates of distal embolization (17% vs. 7%, p = 0.004), and non-Q-wave MI (NQWMI) (21.1% vs. 6.7%, p < 0.001). In addition, patients receiving abciximab were more likely to have a cerebrovascular event (2% vs. 0%, p = 0.03) as well as major bleeding (19% vs. 8%, p = 0.002), although this series included our early experience with abciximab, which utilized standard dose periprocedural heparin therapy.

In patients sustaining an MI, mean creatine phosphokinase (CPK) values were somewhat higher in patients receiving abciximab (1,454 ± 865 IU/L vs. 1,118 ± 1,045 IU/L, p = 0.051).

Correlates of abciximab use. Table 5 shows the univariate correlates of periprocedural abciximab use. Patient age as a continuous variable, prior MI, graft age as a continuous variable, graft age >5 years, intragraft thrombus, type C lesion and high-risk procedure were all associated with a greater likelihood of abciximab use. Other variables including diabetes mellitus, multivessel disease, unstable angina, acute MI, reduced ejection fraction and reduced TIMI flow preprocedure were not correlated with the utilization of abciximab.

Multivariate analysis demonstrated that the presence of intragraft thrombus and type C lesions were correlated with abciximab use. Graft age >5 years and high-risk procedures were weakly correlated with the use of abciximab (Table 6). These variables were incorporated into the propensity score.

Correlates of in-hospital death/Q-wave MI/repeat revascularization. After adjustment for differences in baseline variables, the variable of high-risk procedure was most strongly correlated with the occurrence of the prespecified in-hospital composite end point (OR 3.11, confidence interval [CI] 1.01–9.55, p = 0.047). Patient age was weakly correlated with the occurrence of in-hospital adverse events (OR 1.06, CI 0.99–1.12, p = 0.06). The use of periprocedural abciximab did not affect in-hospital adverse events (OR 1.21, CI 0.48–3.04, p = 0.68) (Table 7).
Correlates of death/MI/repeat revascularization from the time of procedure onward. Table 8 demonstrates the variables associated with the cumulative long-term end point of death/MI/repeat revascularization from the time of procedure onward. After adjustment for differences in baseline characteristics, it appeared that the occurrence of death/MI/repeat revascularization was correlated with reduced TIMI flow pre- or postprocedure (OR 1.96, CI 1.35 to 2.84, \( p = 0.0004 \)), multivessel disease (OR 1.57, CI 1.02 to 2.42, \( p = 0.04 \)) and was weakly correlated with patient age (OR 1.02, CI 1.0 to 1.04, \( p = 0.063 \)). The use of abciximab periprocedurally was also weakly correlated with a greater relative risk of this composite end point during the course of a long-term follow-up period (OR 1.42, CI 0.97 to 1.59, \( p = 0.077 \)) (Fig. 1).

Influence of timing of abciximab administration. In the current series, 63.9% of patients receiving abciximab had the agent initiated before the onset of the intervention. Baseline clinical characteristics were similar in patients receiving abciximab before the intervention when compared with those receiving the agent after the intervention began, except that those receiving abciximab before the procedure were more likely to present with unstable angina (78.8% vs. 56.3%, \( p < 0.006 \)) and less likely to present with acute MI (4.7% vs. 27.1%, \( p = 0.002 \)). Procedural success and in-hospital events of death, Q-wave MI, NQWMI, repeat PTCA and CABG were similar between the two groups (Table 9). Distal embolization occurred more commonly in patients receiving abciximab after the intervention began, although this difference was not statistically significant (22.9% vs. 14.1%, \( p = 0.20 \)).

To determine the influence of the timing of abciximab administration on the occurrence of adverse events, multivariate analysis was performed incorporating this as a variable. In this analysis, administration of abciximab before the intervention was associated with a nonsignificant relative risk reduction as compared with patients receiving abciximab sometime after the initiation of the intervention (adjusted relative risk 0.70, CI 0.41 to 1.20, \( p = 0.19 \)). However, patients receiving abciximab before the initiation of the intervention had a similar risk of adverse events when compared with patients not receiving abciximab (adjusted relative risk 1.05, CI 0.67 to 1.66, \( p = 0.83 \)). Because it was plausible that provisional abciximab (administered after the balloon inflation) occurred because of unsatisfactory angiographic appearance after initiation of the intervention, we constructed Kaplan-Meier survival curves for freedom from death/MI/revascularization from the time of procedure for patients receiving abciximab before the intervention compared with patients not receiving abciximab at all, adjusting for differences in baseline clinical and angiographic variables. In this analysis, there was no difference between

**Table 7. Multivariate Model for In-Hospital Death/QWMI/Repeat Revascularization**

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR</th>
<th>CI</th>
<th>( p ) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>High-risk procedure</td>
<td>3.11</td>
<td>(1.01–9.55)</td>
<td>0.047</td>
</tr>
<tr>
<td>Age</td>
<td>1.06</td>
<td>(0.99–1.12)</td>
<td>0.06</td>
</tr>
<tr>
<td>Abciximab</td>
<td>1.21</td>
<td>(0.48–3.04)</td>
<td>0.68</td>
</tr>
</tbody>
</table>

CI = confidence interval; QWMI = Q-wave myocardial infarction; OR = odds ratio; TIMI = thrombolysis in myocardial infarction.

**Table 8. Correlates of Death/MI/Repeat Revascularization From Time of Procedure**

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR</th>
<th>CI</th>
<th>( p ) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TIMI &lt;3 pre- or postoperation</td>
<td>1.96</td>
<td>(1.33–2.82)</td>
<td>0.0004</td>
</tr>
<tr>
<td>Age</td>
<td>1.02</td>
<td>(1.0–1.04)</td>
<td>0.063</td>
</tr>
<tr>
<td>Multivessel disease</td>
<td>1.57</td>
<td>(1.02–2.41)</td>
<td>0.043</td>
</tr>
<tr>
<td>Abciximab</td>
<td>1.42</td>
<td>(0.97–1.59)</td>
<td>0.077</td>
</tr>
</tbody>
</table>

CI = confidence interval; MI = myocardial infarction; OR = odds ratio; TIMI = thrombolysis in myocardial infarction.

**Figure 1. Adjusted survival estimates of freedom from death/MI/repeat revascularization from the time of procedure onwards with abciximab versus without abciximab. MI = myocardial infarction.**

**Table 9. In-Hospital Events for Patients Receiving Abciximab Prior to Initiation of Intervention Versus Those Receiving Abciximab After Initiation of Intervention**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Abciximab Prior to Initiation of Intervention</th>
<th>Abciximab After Initiation of Intervention</th>
<th>( p ) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>85</td>
<td>48</td>
<td>0.54</td>
</tr>
<tr>
<td>Procedural success</td>
<td>83.5%</td>
<td>87.5%</td>
<td>0.86</td>
</tr>
<tr>
<td>Death</td>
<td>6 (7.1)</td>
<td>3 (6.3)</td>
<td>0.97</td>
</tr>
<tr>
<td>Q-Wave MI</td>
<td>1 (1.2)</td>
<td>1 (2.1)</td>
<td>0.68</td>
</tr>
<tr>
<td>NQWMI</td>
<td>19 (22)</td>
<td>9 (19)</td>
<td>0.62</td>
</tr>
<tr>
<td>CABG</td>
<td>0</td>
<td>0</td>
<td>—</td>
</tr>
<tr>
<td>Repeat PTCA</td>
<td>1</td>
<td>0</td>
<td>0.45</td>
</tr>
<tr>
<td>Distal embolization</td>
<td>12 (14.1)</td>
<td>11 (22.9)</td>
<td>0.20</td>
</tr>
</tbody>
</table>

Numbers in parentheses are percentages of total in each group.

CABG = coronary artery bypass grafting; MI = myocardial infarction; NQWMI = non-Q-wave myocardial infarction; PTCA = percutaneous transluminal coronary angioplasty.
patients receiving abciximab versus those who did not (Fig. 2).

DISCUSSION

This study represents a recent single-center experience of aortocoronary vein graft interventions and comprises a relatively high-risk cohort: advanced age, unstable angina on presentation, diabetes mellitus, multivessel disease and older vein grafts with thrombus were frequent in this group. In this group, utilization of periprocedural abciximab did not improve the in-hospital composite end point of death/Q-wave MI/repeat revascularization or the cumulative long-term end point of death/Q-wave MI/repeat revascularization.

In the Evaluation of c7E3 in Preventing Ischemic Complications (EPIC) and Chimeric 7E3 Antiplatelet in Unstable Angina Refractory to Standard Treatment (CAPTURE) trials, it has been demonstrated that abciximab use was associated with improved clinical outcome after percutaneous and coronary interventions in high-risk patients (17,18). Later, the Evaluation of PTCA to Improve Long Term Outcomes by c7E3 Glycoprotein IIb/IIIa Receptor Blockade (EPILOG) study confirmed that the benefit of abciximab in percutaneous coronary interventions was not necessarily limited to high-risk patients (19). Furthermore, it has been demonstrated that the benefit of abciximab was apparent even in the absence of angiographically apparent thrombus (21).

However, these randomized trials primarily included patients undergoing native coronary interventions, with a relatively small proportion of patients with aortocoronary vein graft interventions; for example, in the EPIC study, only 4% of patients underwent vein graft interventions. It has been previously reported that the prophylactic administration of abciximab before vein graft interventions reduces the occurrence of distal embolization and NQWMI periprocedurally (22). Nevertheless, this study is in accord with recently reported data from the EPIC and EPILOG trials, which failed to demonstrate a relative risk reduction with abciximab use in patients undergoing percutaneous intervention of degenerated saphenous vein grafts (23).

Of note is that there was a greater incidence of distal embolization and NQWMI in the abciximab group in this study. However, because 36.3% of patients in this study receiving abciximab received the agent provisionally (after the intervention had begun), it is likely that the increase in distal embolization and NQWMI in this group was due to adverse angiographic events that had occurred, prompting administration of abciximab, rather than being the result of abciximab use. Such “rescue” administration of abciximab has been demonstrated in an observational study to be beneficial in patients in whom intracoronary thrombus developed after PTCA, with no instances of distal embolization or no reflow in a series of 29 patients (24), although no vein graft interventions were reported. However, in our study, even when excluding patients receiving provisional abciximab, there was no apparent risk reduction in the composite end points.

Because routine CPK assessment was not performed in this series, it is possible that “enzyme MI” without apparent ECG changes or symptoms may have been missed, thereby underestimating the incidence of NQWMI. Therefore, an advantage of abciximab use in preventing asymptomatic enzyme rises cannot be addressed in the current series; however, recent data suggest that abciximab use is not protective in preventing CPK elevation after vein graft intervention (25).

Although atherosclerotic plaques in vein grafts are histologically similar to those found in native coronary atherosclerosis, the rates of progression of disease appears to be accelerated (26). In general, the absolute volume of plaque and thrombus within a vein graft is greater than that observed in the native coronary artery; this is particularly true in older, aneurysmal vein grafts (27,28). This, combined with the fact that a significant component of intraluminal filling defects visualized on angiography of vein grafts may actually represent atherosclerotic debris and organized thrombus as opposed to acute thrombus, may in part explain the limited efficacy of abciximab in vein graft disease demonstrated in this series. It is also notable that the use of abciximab was associated with a slightly higher risk of major bleeding and cerebrovascular accident, although this included our early experience with concomitant high-dose heparin use.

Study limitations. These data are part of a retrospective analysis of a single-center database. Because the study is nonrandomized, it is impossible to determine with certainty the objective patient and procedural characteristics that prompted the operator’s decision whether to use abciximab during the course of the procedure. In addition, patients receiving abciximab received abciximab at variable times relative to the beginning of the intervention; however, even the administration of abciximab prior to the intervention...
did not afford a risk reduction in this series. Furthermore, asymptomatic CPK rises would have been missed in this series, although the significance of such increases is a subject of ongoing debate.

Conclusions. This study demonstrates that, in a relatively high-risk population undergoing saphenous vein graft interventions with a high preponderance of advanced age, unstable angina, older vein grafts and thrombus containing lesions, the administration of abciximab periprocedurally does not appear to reduce major adverse clinical events. Given the demonstrated benefits of this agent in other subsets, this issue may be definitively addressed with a prospective randomized trial.

Reprint requests and correspondence: Dr. Vergheese Mathew, Division of Cardiovascular Diseases, Mayo Clinic, 200 First St. SW, Rochester, Minnesota 55905. E-mail: mathew.verghese@mayo.edu.

REFERENCES


