

Intracoronary Abciximab Use in Patients Undergoing PCI at a Community Hospital: A Single Operator Experience

Sandeep S. Patel, MD, Hiralal Rana, MD, and
Daniel A. N. Mascarenhas, MD, FACC, FSCAI

Objective: To evaluate the safety of intracoronary (IC) abciximab during percutaneous coronary intervention (PCI). **Background:** Adjunctive treatment with glycoprotein IIb/IIIa inhibitors, especially abciximab, during PCI has been shown to improve clinical and procedural outcomes in numerous studies. However, significant bleeding complications exist with its use and this has limited its standard use. Interest has grown in local (IC) use with studies showing safety and long-term effectiveness, especially in patients with high thrombus loads. **Methods:** A retrospective review of records in a database of patients

who had PCI by a single operator at the Easton Hospital. **Results:** 611 patients received IC abciximab, and there were no complications in 610 (98.3%) patients; only 1 had an allergic reaction. **Conclusions:** IC abciximab is safe and has a unique role in the catheterization lab and in patients at high risk of bleeding complications who would benefit from its limited use.

Keywords: percutaneous coronary intervention (PCI); glycoprotein IIb/IIIa inhibitors; abciximab; acute coronary syndrome

Introduction

Since the advent of percutaneous coronary interventions (PCI) and stenting, patients with acute coronary syndromes (ACSs) have had better coronary reperfusion with fewer adverse effects like bleeding and stroke, when compared with fibrinolytic therapy.¹ Subsequent development and use of glycoprotein IIb/IIIa inhibitors (GpIs), particularly abciximab, as adjunctive treatment during PCI has resulted in improved survival and reinfarction rates as reported in major studies.²⁻⁵ There have been reports of up to 40% reductions in ischemic

events after PCI in a 1-year follow-up.^{6,7} Abciximab has been preferred because it has been studied extensively in large clinical trials, and more data exist showing its benefits. It is usually administered via the intravenous (IV) route, but during the past 5 years, interest has grown in its intracoronary (IC) use during stenting. The rationale for this is based on an increased (concentration-dependent) dethrombotic effect and on its non-IIb/IIIa properties.⁸ Wohrle and colleagues⁹ showed in a landmark study that IC abciximab reduced major adverse cardiac events (ie, death, myocardial infarction, urgent revascularization) by 50% at 30 days post-PCI. Recent studies have shown greater effectiveness of the IC route, given during PCI, over IV abciximab,⁹⁻¹¹ with better outcomes relating to increased antegrade flow in culprit vessels, need for revascularization, recurrent myocardial infarction, and lower mean levels of postprocedural cardiac enzymes.¹² In light of these studies, we retrospectively reviewed our database of consecutive patients who had received the IC route of abciximab to evaluate the safety of its use by a single operator during PCI.

From the Department of Cardiology, Mt. Sinai Medical Center/Bronx VA, Bronx, New York (SSP); the Department of Medicine (HR, DANM) and the Division of Cardiology (DANM), Easton Hospital, Easton, Pennsylvania; and Drexel University, Philadelphia, Pennsylvania (DANM).

There are no disclosures.

Address correspondence to: Daniel A. N. Mascarenhas, MD, FACC, Drexel University, 175 South 21st Street, Easton, PA 18042; e-mail: danmasc@rcn.com.

Methods

We retrospectively reviewed the records of 611 patients who underwent PCI at the Easton Hospital by a single operator between January 2001 and June 2006. Prior to undergoing PCI, all patients received aspirin at a dose of 325 mg and clopidogrel of 75 mg. During PCI, the patients were given a standard bolus dose of IC abciximab at 0.25 mg/kg over 1 minute, prior to stent deployment, and all patients received a stent. Post-PCI, patients did not receive heparin or abciximab but were continued on aspirin at 162 mg and clopidogrel 75 mg daily. Patients who had been referred for ACS from outside centers for PCI had received either enoxaparin or heparin as a bolus dose. A small number of referred patients who did not receive enoxaparin or heparin were given weight-based IV bivalirudin during the procedure. 87 of the 611 patients who were previously stented were on concurrent thienopyridine therapy. Descriptive statistics, including means and percentages, were used for tables.

Results

During the 6-year period, we reviewed the records of 611 patients. The patient characteristics are summarized in Table 1. The cohort included patients who underwent PCI for 1 of 4 indications: acute ST-elevation myocardial infarction (STEMI), non-ST-elevation MI (NSTEMI), unstable angina, or stable angina undergoing an elective procedure. Most of the patients (76%) had PCI for stable angina—half of them for a positive stress test and the other half for worsening symptoms, including shortness of breath and chest pain. Almost two thirds of the patients were male, and a similar number were under 75 years of age. The mean age of the group was 66.7 years (± 13.2 years), and 37% of the patients had diabetes. A little more than half of the group had previously documented coronary artery disease by angiography. Details of the target lesions are given in Table 2. Most of the lesions were in native vessels: single vessel, 80%, and 2 or 3 vessels, 20%.

Clinical outcomes at the completion of the intervention are summarized in Table 2. The thrombolysis in MI (TIMI) flow described in the table refers to the following: 0, no-flow or complete occlusion; 1, some penetration but without perfusion distally; 2, perfusion but with slow flow; and 3, full perfusion or normal flow. Most of the patients with stable angina had complex lesions at angiography and were associated with significant dissection and haziness post-PCI (though not flow limiting) and, therefore, received IC abciximab.

Table 1. Patient Characteristics at Admission for PCI

Characteristics	Number (%)
Total number of patients	611 (100)
Age (years)	
<75	409 (67)
>75	202 (33)
Sex	
Male	398 (65)
Female	213 (35)
Comorbidities	
Hypertension	449 (74)
Diabetes	226 (37)
Preexisting coronary artery disease	325 (53)
Dyslipidemia	378 (62)
Smoking	212 (35)
Indication for PCI	
STEMI	68 (11)
NSTEMI	60 (10)
Unstable angina	21 (3)
Stable angina	462 (76)

Abbreviations: PCI, percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction; NSTEMI, non-ST-elevation MI.

Table 2. Details During PCI

Procedural Characteristics	Number (%)
Target vessel	
Single vessel	487 (80)
Multiple vessel (2 or 3)	124 (20)
Flow	
Pre-PCI	
TIMI 0	51 (8)
TIMI 1	98 (16)
TIMI 2	462 (76)
Post-PCI	
TIMI 2	12 (2)
TIMI 3	599 (98)
Degree of stenosis	
>90%	554 (91)
70%-90%	57 (9)

Abbreviations: PCI, percutaneous coronary intervention; TIMI, thrombolysis in myocardial infarction.

Eight patients had an idioventricular rhythm, and 1 patient had ventricular tachycardia/fibrillation (VT/VF) related to STEMI and PCI of the right coronary artery (RCA), necessitating cardioversion. None of the patients had complications during the procedure related to IC administration of abciximab. Only 1 case of allergic reaction occurred in a patient 2 minutes post-IC abciximab, manifesting with hypotension, bronchospasm, and tachycardia, which

Table 3. Bleeding Complications Post-PCI

Bleeding Complications	Number (%)
None	594 (97.2)
Minor	15 (2.5)
Major	2 (0.3)

Abbreviations: PCI, percutaneous coronary intervention.

responded to subcutaneous epinephrine in the catheterization lab.

Table 3 describes the bleeding complications in the catheterization lab, holding area, and prior to discharge. Minor bleeding complications were seen in 15 patients (2.5%) and included bleeding at the groin site that required only a compression device; major bleeding occurred in 2 (0.3%) patients, which needed immediate vascular surgery at the groin site and blood transfusion. They were both women and above 80 years of age. There were no other sites of bleeding reported.

Discussion

The ACC Practice guidelines indicate that GpIs have reduced the frequency of ischemic complications after coronary angioplasty.¹³ The IC route of administration was preferred by the operator based on the following principles. During PCI, the greatest platelet activation occurs at the site of injury, that is, during plaque rupture, balloon deployment, and at the stent placement site. Thus, the highest concentrations of IC abciximab are achieved in the culprit vessel providing optimal clot lysis. It would also help prevent further clot aggregation and maintain the stability of the microvasculature post-stenting,¹⁴ after a procedure that is definitely traumatic. It would avoid clot dissolution at the groin entry site and theoretically prevent major bleeding locally. Also, IV abciximab may not reach the culprit lesion or its distal coronary vessel until good TIMI flow has been achieved or during no-reflow phenomenon. Marciniak et al¹⁵ showed a dose-dependent disaggregation of platelets that was maximal or complete at 6.25 µg/mL in vitro. This dose is unlikely to be achieved by the IV route as demonstrated by Kleiman and colleagues,¹⁶ who showed that a standard bolus dose of abciximab achieved a maximum of about 1.2 µg/mL of concentration at administration. The COMPARE investigators¹⁷ demonstrated that the greatest inhibition of platelet aggregation with abciximab occurs within the

first 15 minutes of administration, and with continued infusion, there is some recovery and variability of platelet aggregation.¹⁵ Furthermore, a non-IIb/IIIa effect has also been demonstrated, including anti-inflammatory actions via interactions with leukocyte integrin and inhibition of the vitronectin receptor in the endothelial cells of the culprit vessels.⁸ An immediate improvement of myocardial blood flow and vasodilator reserve via reduction of coronary microvascular resistance was also shown.¹⁸ Thus, the unique properties attributed to abciximab include the ability to cause dethrombosis (by partial displacement of platelet-bound fibrinogen), dispersion of platelet aggregation, impeding the formation and reducing the stability of clot structures and allowing penetration of endogenous fibrinolytic agents into the clot, thus promoting spontaneous thrombolysis, and a potent non-IIb/IIIa effect described above.^{8,15,19,20}

A very recent study analyzing the use of IC abciximab in high-risk patients with probable high embolic loads showed safety and procedural success in all cases, especially where abrupt closure was imminent during PCI.²¹ This may be related to the fact that abciximab is a large monoclonal antibody that has a prolonged half-life with significant action at the site of vascular injury or plaque rupture and that also reduces distal embolization by influencing adhesion of platelets with endothelial cells, leukocytes, and other platelets as well as platelet products that may damage the microcirculation.²² Romagnoli and colleagues¹⁰ showed that IC abciximab administration acutely decreased the corrected TIMI frame count in culprit vessels of patients with ACS undergoing PCI. Another study looked at local delivery before percutaneous saphenous venous graft intervention with significantly reduced thrombus burden, improved percent diameter stenosis, and excellent acute procedural results.²³ Most of the published data conclude that downstream (or IC) abciximab shows improved coronary blood flow, and its anecdotal use as a “clot-buster” during high-risk, or urgent, PCI threatened with abrupt closure is an added benefit.^{10,21,24,25} Thus, a unique role of IC abciximab may be for rescue clot disintegration during PCI.

Safety studies have shown that Octogenarians and women generally have higher bleeding complication rates with GpIs, including IV abciximab, mostly related to comorbidities like renal insufficiency and peripheral vascular disease and arterial calcification, and may be particularly related to standard IV dosing regimens.²⁶⁻²⁹ Indeed, in our study, the 2 (0.3%) patients who had

major bleeding were elderly women. Reported rates of major bleeding in the EPIC,⁵ EPISTENT,²⁸ and EPILOG³⁰ trials were 14%, 1.5%, and 2.0% to 3.5%, respectively. Minor bleeding rates in all these major studies ranged from 2.9% to 14% depending on the dose of heparin used, and it was generally higher when standard dose heparin was administered at PCI. In our study, the minor bleeding rate was 2.5% and limited to the groin site. A Mayo study³¹ reported greater frequency of major and minor bleeding when abciximab was used during PCI and particularly frequent in patients treated in the setting of acute MI. These patients had heparin continued post-PCI as well. The authors concluded by saying that new strategies were needed to reduce the frequency of bleeding in such patients. The AQUIITY Timing trial³² recently concluded that selective administration of GpI₂ in the catheterization lab during PCI led to no significant increase in composite ischemia (death from any cause, MI, or unplanned revascularization for ischemia). However, they did observe a significant reduction in major bleeding, minor bleeding, and blood transfusions. There was a 0.7% rate of access-site bleeding requiring intervention or surgery, almost similar to our findings. The patient characteristics in this study were very similar to ours in terms of the comorbid conditions. One patient who had VT/VF had PCI of the RCA for STEMI. The PAMI investigators showed that there was a high incidence of VT/VF associated with PCI of the RCA.³³

The authors feel that based on these observations, the local administration of abciximab prevents the dispersion of the drug to nontarget sites that may lead to these bleeding episodes and hence to longer hospital stays and increased morbidity and mortality.

Conclusion

Abciximab is a unique GpI and may have a unique role especially when used IC in the catheterization lab during PCI. It has been shown to be safe and effective. One of these roles is its effectiveness as a clot dissolver during inadvertent thrombus formation while stenting. Another could be its use in high-risk patients, that is, the very elderly, those with diabetes, women, and patients with renal insufficiency, where there is a high risk for bleeding complications if used as an infusion but with an associated benefit with local use.

References

1. Gibson CM. Primary angioplasty compared with thrombolysis: new issues in the era of glycoprotein IIb/IIIa inhibition and intracoronary stenting. *Ann Intern Med.* 1999;130:841-847.
2. Antoniucci D, Migliorini A, Parodi G, et al. Abciximab-supported infarct artery stent implantation for acute myocardial infarction and long-term survival: a prospective, multicenter, randomized trial comparing infarct artery stenting plus abciximab with stenting alone. *Circulation.* 2004;109:1704-1706.
3. Antoniucci D, Rodriguez A, Hempel A, et al. A randomized trial comparing primary infarct artery stenting with or without abciximab in acute myocardial infarction. *J Am Coll Cardiol.* 2003;42:1879-1885.
4. Montalescot G, Barragan P, Wittenberg O, et al. Platelet glycoprotein IIb/IIIa inhibition with coronary stenting for acute myocardial infarction. *N Engl J Med.* 2001;344:1895-1903.
5. The EPIC Investigators. Use of monoclonal antibody directed against the platelet glycoprotein IIb/IIIa receptor in high risk coronary angioplasty. *N Engl J Med.* 1994;330:956-961.
6. Lincoff AM, Tcheng JE, Califf RM, et al. Sustained suppression of ischemic complications of coronary intervention by platelet GP IIb/IIIa blockade with abciximab: one-year outcome in the EPILOG trial. Evaluation in PTCA to Improve Long-term Outcome with abciximab GP IIb/IIIa blockade. *Circulation.* 1999;99:1951-1958.
7. Islam MA, Blankenship JC, Balog C, et al. EPISTENT investigators. Effect of abciximab on angiographic complications during percutaneous coronary stenting in the Evaluation of Platelet IIb/IIIa Inhibition in Stenting Trial (EPISTENT). *Am J Cardiol.* 2002;90:916-921.
8. Romagnoli E, Burzotta F, Trani C, et al. Rationale for intracoronary administration of abciximab. *J Thromb Thrombolysis.* 2007;23:57-63.
9. Wohrle J, Grebe OC, Nusser T, et al. Reduction of major adverse cardiac events with intracoronary compared with intravenous bolus application of abciximab in patients with acute myocardial infarction or unstable angina undergoing coronary angioplasty. *Circulation.* 2003;107:1840-1843.
10. Romagnoli E, Burzotta F, Trani C, et al. Angiographic evaluation of the effect of intracoronary abciximab administration in patients undergoing urgent PCI. *Int J Cardiol.* 2005;105:250-255.
11. Kakkar AK, Moustapha A, Hanley HG, et al. Comparison of intracoronary vs. intravenous administration of abciximab in coronary stenting. *Catheter Cardiovasc Interv.* 2004;61:31-34.

12. Bellandi F, Maioli M, Gallopin M, et al. Increase of myocardial salvage and left ventricular function recovery with intracoronary abciximab downstream of the coronary occlusion in patients with acute myocardial infarction treated with primary coronary intervention. *Catheter Cardiovasc Interv.* 2004;62:186-192.
13. Smith SC Jr, Feldman TE, Hirshfeld JW Jr, et al; American College of Cardiology/American Heart Association Task Force on Practice Guidelines; ACC/AHA/SCAI Writing Committee to Update 2001 Guidelines for Percutaneous Coronary Intervention. ACC/AHA/SCAI 2005 guideline update for percutaneous coronary intervention: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (ACC/AHA/SCAI Writing Committee to Update 2001 Guidelines for Percutaneous Coronary Intervention). *Circulation.* 2006;113:e166-e286.
14. Aymong ED, Curtis MJ, Youssef M, et al. Abciximab attenuates coronary microvascular endothelial dysfunction after coronary stenting. *Circulation.* 2002;105:2981-2985.
15. Marciniak SJ Jr, Mascelli MA, Furman MI, et al. An additional mechanism of action of abciximab: dispersal of newly formed platelet aggregates. *Thromb Haemost.* 2002;87:1020-1025.
16. Kleiman NS, Raizner AE, Jordan R, et al. Differential inhibition of platelet aggregation induced by adenosine diphosphate or a thrombin receptor-activating peptide in patients treated with bolus chimeric 7E3 Fab: implications for inhibition of the internal pool of GPIIb/IIIa receptors. *J Am Coll Cardiol.* 1995;26:1665-1671.
17. Batchelor WB, Tolleson TR, Huang Y, et al. Randomized COMparison of platelet inhibition with Abciximab, TiRoFiban and Eptifibatide during PCI in ACS. The COMPARE trial. *Circulation.* 2002;106:1470-1476.
18. Marzilli M, Sambucetti G, Testa R, Fedele S. Platelet glycoprotein IIB/IIIa receptor blockade and coronary resistance in unstable angina. *J Am Coll Cardiol.* 2002;40:2102-2109.
19. Collet JP, Montalescot G, Lesty C, et al. Effects of abciximab on the architecture of platelet-rich clots in patients with acute myocardial infarction undergoing primary coronary intervention. *Circulation.* 2001;103:2328-2331.
20. Collet JP, Montalescot G, Lesty C, et al. Disaggregation of in vitro preformed platelet-rich clots by abciximab increases fibrin exposure and promotes fibrinolysis. *Arterioscler Thromb Vasc Biol.* 2001;21:142-148.
21. Sharma S, Makkar R, Lardizabal J. Intracoronary administration of abciximab during percutaneous coronary interventions: should this be the routine and preferred approach? *J Cardiovasc Pharmacol Ther.* 2006;11:136-141.
22. Waldmann TA, Levy R, Collier BS. Emerging Therapies: Spectrum of Applications of Monoclonal Antibody Therapy. *Hematology Am Soc Hematol Educ Program.* 2000:394-408.
23. Barsness GW, Buller C, Ohman EM, et al. Reduced thrombus burden with abciximab delivered locally before percutaneous intervention in saphenous vein grafts. *Am Heart J.* 2000;139:824-829.
24. Lee CH, Ho KT, Tan HC. Instant dissolution of intracoronary thrombus by abciximab. *Int J Cardiol.* 2005;104:102-103.
25. Muhlestein JB, Karagounis LA, Treehan S, Anderson JL. "Rescue" utilization of abciximab for the dissolution of coronary thrombus developing as a complication of coronary angioplasty. *J Am Coll Cardiol.* 1997;30:1729-1734.
26. Alexander KP, Chen AY, Newby LK, et al. Sex differences in major bleeding with glycoprotein IIb/IIIa inhibitors: results from the CRUSADE (Can Rapid risk stratification of Unstable angina patients Suppress ADverse outcomes with Early implementation of the ACC/AHA guidelines) initiative. *Circulation.* 2006;114:1380-1387.
27. Sadeghi HM, Grines CL, Chandra HR, et al. Percutaneous coronary interventions in octogenarians: glycoprotein IIb/IIIa receptor inhibitors' safety profile. *J Am Coll Cardiol.* 2003;42:428-432.
28. Randomized placebo-controlled and balloon-angioplasty-controlled trial to assess safety of coronary stenting with use of platelet glycoprotein- IIb/IIIa blockade: the EPIS-TENT investigators. Evaluation of Platelet IIb/IIIa inhibitor for stenting. *Lancet.* 1998;352:87-92.
29. Guagliumi G, Stone GW, Cox DA, et al. Outcome in elderly patients undergoing primary coronary intervention for acute myocardial infarction: results from the Controlled Abciximab and Device Investigation to Lower Late Angioplasty Complications (CADILLAC) trial. *Circulation.* 2004;110:1598-1604.
30. The EPILOG investigators. Platelet glycoprotein IIb/IIIa receptor blockade and low-dose heparin during percutaneous coronary revascularization. *N Engl J Med.* 1997;336:1689-1696.
31. Cote AV, Berger PB, Holmes DR Jr, et al. Hemorrhagic and vascular complications after percutaneous coronary intervention with adjunctive abciximab. *Mayo Clin Proc.* 2001;76:890-896.
32. Stone GW, Bertrand ME, Moses JW, et al; ACUTY Investigators. Routine upstream initiation vs deferred selective use of glycoprotein IIb/IIIa inhibitors in acute coronary syndromes: the ACUTY Timing trial. *JAMA.* 2007;297:591-602.
33. Mehta RH, Harjai KH, Grines L, et al. Sustained ventricular tachycardia or fibrillation in the cardiac catheterization laboratory among patients receiving primary percutaneous coronary intervention: incidence, predictors, and outcomes. Primary Angioplasty in Myocardial Infarction (PAMI) Investigators. *J Am Coll Cardiol.* 2004;43:1765-1772.