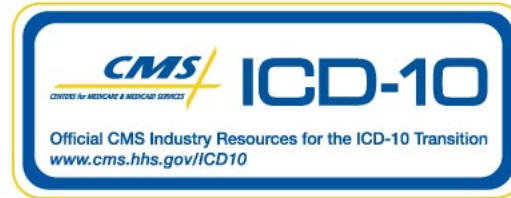


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Modifiable Risk Factors for Vascular Access Site Complications in the IMPACT II Trial of Angioplasty With Versus Without Eptifibatide

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Objectives. This study was designed to identify potential predictors of vascular access site (VAS) complications in the large-scale Integrilin to Minimize Platelet Aggregation and Coronary Thrombosis (IMPACT) II trial, which studied angioplasty with versus without a new glycoprotein (GP) IIb/IIIa receptor inhibitor (eptifibatide).

Background. GP IIb/IIIa receptor inhibition during coronary interventions has been associated with excess VAS complications. If other predictors of VAS complications could be identified, they might be manipulated to reduce complications.

Methods. A total of 4,010 patients undergoing percutaneous transluminal coronary revascularization (PTCR) were randomized into one of three bolus/20- to 24-h infusion arms: placebo bolus/placebo infusion; 135- μ g/kg body weight eptifibatide bolus/0.5- μ g/kg per min eptifibatide infusion; or 135- μ g/kg eptifibatide bolus/0.75- μ g/kg per min eptifibatide infusion. Heparin during the procedure was weight adjusted and stopped 4 h before sheaths were removed. Logistic regression modeling was used to identify independent predictors of VAS complications.

Results. VAS complications were more common in patients treated with eptifibatide (9.9% vs. 5.9% placebo-treated patients, $p < 0.001$). Multivariate analysis identified eptifibatide therapy ($p < 0.0001$), advanced age ($p = 0.0001$), longer time to sheath removal ($p = 0.0002$), stent placement (with intense post-stent anticoagulation) ($p = 0.0004$), female gender ($p = 0.0006$), PTCR within 24 h of thrombolytic therapy ($p = 0.002$), larger heparin doses during PTCR ($p = 0.009$), major coronary dissection ($p = 0.03$) and placement of a venous sheath ($p = 0.04$) as independent predictors of VAS complications.

Conclusions. VAS complications may be reduced by early sheath removal, by avoiding placement of venous sheaths and by limiting heparin dosing to avoid excessive activated clotting times. Early sheath removal during inhibition of platelet aggregation by eptifibatide is feasible.

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Percutaneous transluminal coronary revascularization (PTCR) involves a fundamental dilemma—the need to prevent thrombosis of the target vessel while promoting hemostasis of the

vascular access site (VAS). More robust antithrombotic protocols, designed to minimize abrupt target vessel closure, are associated with higher rates of VAS complications (1-4). Although some devices and drugs may improve short- and long-term outcomes of PTCR, the increased incidence of access site complications may limit the overall benefit of the treatment strategy (2-4).

Patient and procedural characteristics that predict vascular complications of PTCR have been identified in the era before glycoprotein (GP) IIb/IIIa platelet receptor inhibition. To identify predictors of VAS complications in patients undergoing PTCR during GP IIb/IIIa platelet receptor inhibition, we studied the 3,871 patients who received the study drug in the Integrilin to Minimize Platelet Aggregation and Coronary Thrombosis (IMPACT) II trial (5). The size of the IMPACT II trial, its inclusion of a broad spectrum of patients and its

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Abbreviations and Acronyms

ACT	= activated clotting time
EPIC	= Evaluation of c7E3 Fab in Preventing Ischemic Complications of High Risk Angioplasty
EPILOG	= Evaluation in PTCA to Improve Long-Term Outcome with Abciximab Glycoprotein IIb/IIIa Blockade
GP	= glycoprotein
IMPACT	= Integrilin to Minimize Platelet Aggregation and Coronary Thrombosis
OR	= odds ratio
PROLOG	= Precursor to EPILOG Study
PTCR	= percutaneous transluminal coronary revascularization
VAS	= vascular access site

multicenter design provided a unique opportunity to study VAS complications. The present analysis focused on variables that might affect the incidence of VAS complications in future patients.

Methods

Study design. The IMPACT II trial was a multicenter randomized, double-blind efficacy and safety evaluation of eptifibatide, a cyclic heptapeptide inhibitor of the GP IIb/IIIa receptor, for reducing the ischemic complications of coronary angioplasty (5). The study enrolled 4,010 patients scheduled for PTCR with any Food and Drug Administration-approved device between November 1993 and November 1994. Inclusion and exclusion criteria have been published previously (5). The study protocol was approved by the investigational review board of each participating institution, and written informed consent for participation was received from each patient. After randomization, 139 patients did not receive the study drug because of changes in clinical status or withdrawal from the study. This analysis involves the 3,871 patients who received the study drug in one of three bolus/20- to 24-h infusion arms: placebo bolus/placebo infusion; 135- μ g/kg body weight eptifibatide bolus/0.5- μ g/kg per min eptifibatide infusion; or 135- μ g/kg eptifibatide bolus/0.75- μ g/kg per min eptifibatide infusion. At the operator's discretion, heparin therapy was continued 20 to 24 h or discontinued immediately after the procedure. Access site sheaths were removed after heparin was discontinued and when activated partial thromboplastin time (aPTT) measured <45 seconds or activated clotting time (ACT) measured <150 s. The protocol called for hemostasis to be established with commercially available hemostasis clamps with pressure applied for at least 30 min. If clinically indicated, heparin was reinstated 3 to 4 h after hemostasis with a standard bolus of 7.5 U/kg and infusion rate as needed to maintain aPTT at two to three times control values.

Baseline clinical, procedural and postprocedural care characteristics were prospectively recorded using a case report form designed to assess VAS complications. Investigators rated VAS bleeding as mild, moderate (requiring transfusion)

or severe (causing hemodynamic compromise and requiring transfusion or volume replacement) and recorded the incidence of pseudoaneurysms, arteriovenous fistulas and any access site lesion requiring surgical repair. Length of stay in the hospital after the procedure was recorded.

Statistical analysis. Statistical analyses were performed to identify predictors of VAS complications defined as any moderate/severe VAS bleeding or pseudoaneurysm/arteriovenous fistula/surgical VAS repair.

The 135/0.5- and 135/0.75-dose eptifibatide groups were pooled for all analyses, because the IMPACT II trial demonstrated insignificant differences between them in overall efficacy or bleeding complications (5). The eptifibatide and placebo groups were compared with regard to 35 baseline characteristics, 27 procedural characteristics and 12 postprocedural care characteristics using chi-square analysis for discrete variables and Wilcoxon rank sum tests for continuous variables. Each clinical, procedural and postprocedural variable was correlated with the incidence of the combined complication end point. Correlations were evaluated using chi-square analysis for discrete variables and Wilcoxon rank sum tests for continuous variables. Multivariable logistic regression analysis of the univariate predictors was performed to determine which variables were independently associated with access site complications. Separate multivariable logistic models were made, the first using only baseline patient features and the second using all univariate predictors. A p value < 0.05 was considered statistically significant. Postprocedural care characteristics were not included in the multivariable analysis because it was difficult to determine whether they independently contributed to or were dependent on VAS complications.

Results

Moderate to severe VAS bleeding or pseudoaneurysm/arteriovenous fistula/surgical VAS repair occurred in 8.5% of all IMPACT II patients. Of these, 7.1% had moderate VAS bleeding, 0.5% had severe VAS bleeding, and 1.7% had pseudoaneurysm/arteriovenous fistula/surgical VAS repair. Access site bleeding accounted for 71% of all moderate to severe bleeding complications in IMPACT II patients who received the study drug. Table 1 lists the incidence of each of these complications in the three treatment groups.

The treatment groups were similar with regard to baseline patient characteristics. Among procedural variables, eptifibatide prolonged median and interquartile ACT values compared with placebo (high dose eptifibatide 366 s [329 to 416], low dose eptifibatide 362 s [329 to 412] and placebo 349 s [319 to 395]).

There was modest variation in the incidence of any VAS complications across the 82 sites enrolling patients. The median incidence (25th, 75th percentile) of any VAS complications was 5.5% [0, 10.3].

Univariate analysis. Univariate analysis identified 10 baseline characteristics and 12 procedural variables significantly associated with the incidence of any VAS complication (Table

Table 1. Vascular Access Site Complications by Treatment Received in 3,871 Study Patients

	Eptifibatide		Placebo* (n = 1,285)
	135/0.75 Dose (n = 1,286)	135/0.5 Dose (n = 1,300)	
Investigator-rated moderate access site bleed	9.5%	7.1%	4.9%
	p = 0.001	p = 0.02	
Investigator-rated severe access site bleed	0.5%	0.7%	0.5%
	p = 1.0	p = 0.45	
Investigator-rated moderate or severe access site bleed	10.0%	7.8%	5.4%
	p = 0.001	p = 0.01	
Pseudoaneurysm, AVF or surgical repair	1.5%	2.2%	1.3%
	p = 0.74	p = 0.08	
Any investigator-rated moderate or severe bleed, pseudoaneurysm, AVF or surgical repair	10.9%	8.9%	5.9%
	p = 0.001	p = 0.003	

*p value versus placebo. AVF = arteriovenous fistula.

2). The incidence of any VAS complications was higher with PTCR within 24 h of lytic therapy (25.9% vs. 8.4% in all other patients, $p = 0.006$), eptifibatide therapy (9.9% vs. 5.9% in placebo-treated patients, $p < 0.0001$), placement of a venous sheath (9.3% vs. 6.4% without a venous sheath, $p = 0.004$) and placement of a balloon pump (19.3% vs. 9.3% without balloon pump, $p = 0.002$). Among continuous variables, increased incidence of VAS complications was associated with increasing arterial sheath size ($p = 0.05$), maximal in-laboratory ACT ($p = 0.003$), total heparin dose ($p = 0.01$) and time to sheath removal ($p = 0.0002$). Univariate analysis also identified eight postprocedural care characteristics significantly associated with the incidence of any VAS complication (Table 3).

Multivariable analysis. Multivariable analysis using only baseline patient features identified four features that were associated with VAS complications: age, eptifibatide therapy, PTCR within 24 h of lytic therapy and female gender. When multivariable analysis was performed using all the significant univariate determinants, nine of them remained significant independent predictors of risk in multivariable analysis (Table 4). The largest odds ratios were observed for PTCR within 24 h of lytic therapy ($p = 0.002$, odds ratio [OR] 5.2), in-laboratory stent placement ($p = 0.0004$, OR 2.6), eptifibatide therapy ($p < 0.0001$, OR 1.9) and presence of major coronary dissection during PTCR ($p = 0.03$, OR 1.7).

The incidence of pseudoaneurysm/arteriovenous fistula/surgical VAS repair was too low to perform a separate analysis of predictors. There was no trend toward more frequent structural complications with eptifibatide.

Length of stay. Length of stay after the procedure was prolonged in patients with VAS complications. Median length of stay [25th, 75th percentiles] after PTCR was 3 d [2, 6] for patients with VAS complications (vs. 2 days [1, 3] for patients without VAS complications, $p = 0.0001$); 6 days [4, 9] for patients with severe VAS bleeding (vs. 2 days [1, 3] for patients without severe bleeding, $p < 0.0001$); 3 days [2, 5] for patients with moderate or severe bleeding (vs. 2 days [1, 3] for patients

without moderate or severe bleeding, $p < 0.0001$); and 6 days [4, 9] for patients with pseudoaneurysm, arteriovenous fistula or surgical repair (vs. 2 days [1, 3] for patients without these events, $p < 0.0001$).

Discussion

Primary findings. *The most significant finding of this study is that several factors under operator control may affect the incidence of VAS complications of PTCR performed with GP IIb/IIIa receptor inhibition. Because eptifibatide increased the risk of VAS complications twofold, and because VAS bleeding accounted for 71% of all moderate to severe bleeding complications in the IMPACT II trial, the identification of risk factors that can be modified to decrease the incidence of VAS complications is important.*

Potentially modifiable predictors of VAS complications in the present study included PTCR within 24 h of lytic therapy, higher in-laboratory ACT values and heparin doses, the occurrence of PTCR complications treated with more intense anticoagulation (major coronary dissection, rescue stenting), venous sheath placement and late sheath removal.

Baseline patient characteristics. Consistent with previous studies, advanced age (1,6–10) and female gender (6,7,9–11) predicted VAS complications. Patients with thrombolytic therapy in the 24 h before enrollment had a 25.9% incidence of VAS complications compared with 8.4% in patients without thrombolytic therapy in the preceding 24 h ($p = 0.006$). No significant interaction was observed between eptifibatide and recent thrombolytic therapy, suggesting that the increased risk of VAS complications after recent lytic therapy occurs with or without eptifibatide therapy.

Procedural factors. The finding in the present study that total heparin dosing is associated with a higher risk of VAS complications is consistent with other reports. In the Evaluation of c7E3 Fab in Preventing Ischemic Complications of High Risk Angioplasty trial (EPIC), with the GP IIb/IIIa receptor blocker abciximab, all patients received heparin; the maximal in-laboratory ACT was associated with an excess risk of major/minor VAS bleeding (11). The Precursor to EPILOG Study (PROLOG) of low dose (median 5,800 U) versus high dose (median 8,700 U) weight-adjusted heparin during angioplasty with abciximab produced lower ACTs and a two- to threefold reduction in VAS bleeding complications (12). In the Evaluation in PTCA to Improve Long-Term Outcome with Abciximab Glycoprotein IIb/IIIa Blockade (EPILOG) trial, major/minor VAS complications of angioplasty occurred in 2.8% of patients treated with heparin versus 4.0% in patients with abciximab/low dose heparin versus 7.6% in patients with abciximab/high dose heparin (13). Thus, four studies of angioplasty with GP IIb/IIIa receptor inhibition suggest that higher doses of heparin producing higher ACTs are associated with excess VAS complications. Data from the PROLOG and EPILOG trials demonstrate no excess in ischemic complications with lower heparin dosing, and data from IMPACT II (5) suggest this may be true for eptifibatide as well. Recommended

Table 2. Univariable Predictors of Vascular Access Site Complications: Baseline Characteristics and Procedural Characteristics

Characteristic	No VAS Complication	VAS Complication	p Value
Baseline			
Female	858 (24%)	113 (34%)	< 0.0001
Male	2,677 (76%)	217 (66%)	
Age (yr)	60 (52, 68)	63 (54, 72)	0.0001
Smoking history	2,329 (66%)	189 (57%)	0.001
Nonsmoker	1,189 (34%)	141 (43%)	
Height (cm)	173 (167, 180)	172 (165, 178)	0.004
Hemoglobin (g/dl)*	14.0 (13.0, 15.0)	13.9 (12.7, 14.7)	0.004
Lytics in prev 24 h	20 (<1%)	7 (2%)	0.006
No lytics	3,515 (>99%)	323 (98%)	
SBP (mm Hg)	130 (118, 144)	133 (120, 149)	0.01
Hematocrit (%)	41 (38, 44)	41 (37, 43)	0.02
Weight (kg)	84 (75, 95)	81 (72, 95)	0.03
HTN	1,900 (54%)	196 (59%)	0.05
No HTN	1,629 (46%)	134 (41%)	
Procedural			
Eptifibatide	2,328 (66%)	255 (77%)	< 0.0001
No eptifibatide	1,207 (34%)	75 (23%)	
Stent for any indication	119 (3%)	35 (11%)	< 0.0001
No stent	3,416 (97%)	285 (89%)	
Major dissection	204 (6%)	47 (14%)	< 0.0001
No major dissection	3,267 (94%)	279 (86%)	
Length of procedure (min)	29 (16, 49)	36 (21, 59)	0.0001
Time to sheath removal (h)	16 (7, 23)	19 (8, 24)	0.0002
Stent for abrupt closure	23 (<1%)	9 (3%)	0.001
No stent for abrupt closure	3,512 (>99%)	321 (97%)	
IABP used	67 (2%)	16 (5%)	0.002
No IABP	3,467 (98%)	314 (95%)	
Max in-lab ACT (s)	358 (324, 406)	372 (329, 423)	0.003
Venous sheath placed	2,578 (73%)	263 (80%)	0.004
No venous sheath	952 (27%)	65 (20%)	
Total heparin dose (U)	12,000 (9,853, 15,500)	12,721 (10,000, 16,706)	0.01
Arterial sheath size (F)*	8 (8, 9)	8 (8, 9)	0.05
Vessel treated (RCA)	1,277 (36%)	137 (42%)	0.05
Vessel treated (other than RCA)	2,258 (64%)	193 (58%)	

*Tests of significance are based on the entire distribution of the two groups and may not be reflected in the median (25th, 75th percentiles). Data presented are number (%) of patients or (for continuous variables) median (25th, 75th percentiles). ACT = activated clotting time; HTN = hypertension; IABP = intraaortic balloon pump; lab = laboratory; max = maximal; prev = previous; RCA = right coronary artery; SBP = systolic blood pressure; VAS = vascular access site.

ACT thresholds for angioplasty with abciximab have been reduced, and it is possible that similar recommendations will be made for eptifibatide in the future. In the meantime, it would seem prudent to avoid raising the ACT much above 300 s when angioplasty is performed with eptifibatide.

Venous sheaths have been used since the early days of angioplasty to allow temporary transvenous pacemaker placement, infusion of fluid or withdrawal of blood for laboratory testing. However, temporary pacing is rarely necessary (14), and peripheral venous access sites can be used for fluid administration and blood withdrawal. Some interventionists currently use venous sheaths only as needed. In the present study, 74% of patients underwent venous sheath placement, with a 35% increase in the incidence of vascular access complications. Although this may

reflect a population at higher risk of complications, it is also possible that additional needle thrusts aimed at the vein may penetrate the artery or that oozing from venous puncture sites may be a significant source of blood loss. Until further data are available to confirm this observation, it is reasonable to avoid routine venous sheath placement in patients with good peripheral access who are unlikely to need temporary pacing.

Other procedural factors associated with VAS complications in the present study included placement of a coronary stent to rescue an inadequate angioplasty result, and major coronary dissection during angioplasty. The IMPACT II trial was performed in the era of intense post-stent anticoagulation including post-stent heparin and warfarin, which produced excessive VAS complications in previous studies (3,4). Major

Table 3. Univariable Predictors of Vascular Access Site Complications: Postprocedural Characteristics

	No VAS Complication	VAS Complication	p Value*
Postprocedural heparin	2,472 (70%)	52 (16%)	< 0.0001
None	1,061 (30%)	278 (84%)	
Bed rest after sheath removal (h)	14 (8, 19)	18 (10, 28)	0.0001
Nadir platelet count	194 (162, 232)	175 (143, 218)	0.0001
Time to sheath removal (h)	16 (7, 23)	19 (8, 24)	0.0002
VAS compression†			
Femostop	562 (16%)	93 (29%)	< 0.0001
Other	358 (10%)	57 (18%)	< 0.0001
Manual	2,104 (61%)	223 (70%)	0.001
C-clamp	983 (29%)	76 (24%)	0.07
Sandbag	1,446 (42%)	149 (47%)	0.1
Sheath removed by			
MD	789 (23%)	95 (29%)	0.01
Technician	568 (16%)	36 (11%)	0.01
Physician assistant	109 (3%)	3 (<1%)	0.02
LPN	58 (2%)	4 (1%)	0.53
RN	1,925 (55%)	185 (56%)	0.64
Patient positioning*			
Complete bed rest	2,050 (59%)	201 (61%)	0.4
Elevated head of bed	1,764 (51%)	163 (50%)	0.73
Log rolling permitted	986 (28%)	100 (31%)	0.41
Leg restrained	1,267 (37%)	138 (43%)	0.04
VAS hematoma before sheath pull	527 (57%)	164 (69%)	0.001
Oozing before sheath pull	1,555 (91%)	245 (91%)	0.69
Dressing			
Pressure dressing	2,577 (74%)	241 (74%)	
Band-Aid	373 (11%)	28 (9%)	0.06
Op site	230 (7%)	16 (5%)	
Other	290 (8%)	40 (12%)	

*Patients treated versus those not treated with specified method. †Many patients treated with more than one method. Data presented are number (%) of patients or (for continuous variables) median (25th, 75th percentiles). LPN = licensed practical nurse; MD = physician; Op = operative; RN = registered nurse; VAS = vascular access site.

dissection during the IMPACT II trial was treated with postprocedural heparin, which increases VAS bleeding (15–17). Current practice avoids such intense anticoagulation: Major

Table 4. Multivariable Analysis With Baseline Patient Features and Procedural Characteristics

Characteristic	p Value	OR (95% CI per increment in variable)
Eptifibatide therapy (vs. no eptifibatide)	< 0.0001	1.90 (1.45–2.53)
Age (per each 10-yr increase)	0.0001	1.26 (1.13–1.41)
Time to sheath pull (per 1-h increase)	0.0002	1.02 (1.01–1.03)
In-lab stent placement (vs. no stent)	0.0004	2.62 (1.56–4.35)
Female (vs. male)	0.0006	1.59 (1.22–2.06)
PTCR within 24 h of lytic therapy (vs. PTCR not within 24 h of lytic therapy)	0.002	5.17 (1.93–12.48)
Total heparin dose during procedure (per each additional 1,000 U)	0.009	1.04 (1.01–1.08)
Major dissection (vs. no major dissection)	0.03	1.67 (1.05–2.58)
Venous sheath (vs. no venous sheath)	0.04	1.35 (1.01–1.82)

CI = confidence interval; lab = laboratory; OR = odds ratio; PTCR = percutaneous transluminal coronary revascularization.

coronary dissections are now routinely stented, and stents for angioplasty failures are routinely treated only with aspirin and ticlopidine.

Arterial sheath size was a univariate predictor that lost significance in the multivariable model. This weak association of vascular sheath size with VAS complications in the present study reflects discordant results of previous studies. Larger arterial sheath size has been associated with access site complications in several (7–9,18) but not all studies (1,19–22).

Postprocedural factors. Some postprocedural treatment variables associated with VAS complications probably contributed to those complications. Postprocedural heparin administration increases appeared to increase VAS bleeding in this and other (15–17) studies and is probably of no benefit because it does not prevent early occlusion (17). Longer duration of sheath insertion increases VAS complications, probably by increasing oozing around the sheath, sheath kinking or sheath dislodgment. Previous reports also have identified prolonged sheath insertion as a predictor of vascular complications (1,18) and have demonstrated the safety of early sheath removal during infusion of the GP IIb/IIIa receptor blocker abciximab

(12,13). The results of the present study suggest that this strategy should be applied to eptifibatide as well.

Two other postprocedural variables that may have contributed to VAS complications include lower nadir platelet count and the presence of a hematoma before sheath removal. Other variables associated with VAS complications were more likely a reflection of treatment of preexisting VAS complications. These include prolonged bed rest, use of leg restraints, removal of the sheath by a physician and use of a Femostop or clamp (as mandated by the protocol). Because it was unclear whether association of postprocedural variables with VAS complications represented cause or effect, these postprocedural variables with significant univariate associations were not included in the multivariable analysis.

Progress in preventing VAS complications of PTCR with GP IIb/IIIa receptor inhibition. The first study of PTCR during GP IIb/IIIa receptor inhibition was the EPIC trial, which documented a 2.4% incidence of severe VAS bleeding in placebo-group patients, with a threefold increase (7.6%) in abciximab-treated patients. The current study of PTCR during GP IIb/IIIa receptor inhibition with eptifibatide documents a step forward in the prevention of VAS bleeding, with a 0.5% incidence of severe VAS bleeding in placebo-treated patients and only a 0.6% incidence in eptifibatide-treated patients. Data from the EPILOG trial (23) demonstrate similar success in minimizing VAS complications during PTCR with abciximab, with a 0.7% incidence of severe VAS bleeding in placebo-treated patients and a 0.7% incidence in abciximab/low dose heparin-treated patients. The evolution of periprocedural care during these three studies may account for the improvement in VAS bleeding. First, heparin dosing protocols were reduced (10,000 to 12,000 U of heparin in the EPIC trial, 100 U/kg in the IMPACT II trial and 70 U/kg in the low heparin dose arm of the EPILOG trial). The ACT targets also decreased from 300 to 350 s in the EPIC and IMPACT II trials to >200 s in the EPILOG trial. Finally, discontinuation of heparin after the procedure with early removal of sheaths became more frequent during these three studies, occurring rarely in the EPIC trial, more commonly (35% of patients) in the IMPACT II trial and routinely in the EPILOG trial. These changes in intensity of anticoagulation and postprocedural VAS management are likely to have contributed to the dramatic reduction in VAS complications in placebo-treated patients in the IMPACT II and EPILOG trials and the dramatic reduction in excess VAS bleeding associated with GP IIb/IIIa inhibition from threefold in the EPIC trial to negligible in the IMPACT II and EPILOG trials.

Study limitations. The IMPACT II trial was not designed primarily to determine predictors of access site complications. However, the data used in the present analysis were collected prospectively on case report forms designed to carefully assess the incidence and significance of VAS complications. The analyses reported here were anticipated in the IMPACT II study design. Data were not collected prospectively for all VAS problems, such as large hematomas requiring a prolonged hospital stay or arteriovenous fistulas treated conservatively

but eventually needing surgical repair. Statistical analyses were performed with the high and low dose eptifibatide groups pooled. Although this might obscure some differences between these groups, the incidence of any groin complication was not significantly different (10.9% vs. 8.9%, $p = 0.08$) between the two groups. More frequent use of hemostasis clamps might have decreased the incidence of VAS complications in the present study.

The analyses used in the present study identify associations between VAS complications and patient, procedural and postprocedural variables. However, except for the study variable of eptifibatide treatment, which was randomized, association does not prove causality. Some of the variables associated with VAS complications in this study may not be independent predictors; rather, they may be dependent sequelae of the complications or markers for other predictors.

Conclusions. Several factors under the control of the interventionist are associated with VAS complications, including PTCR within 24 h of thrombolytic therapy, use of venous sheaths, stent placement (in the era of intense post-stent anticoagulation), higher doses of heparin during the procedure and later sheath removal. Although the present study does not prove that manipulation of these factors can reduce VAS complications, it would seem prudent to avoid the use of venous sheaths when possible, avoid excessive heparin dosing (aim for an ACT ~300 s) and remove sheaths as soon as possible after the procedure. The wide variation in the incidence of VAS complications among participating sites (25th percentile 0%, 75th percentile 10%) suggests that optimal VAS management practices may minimize VAS complications. Further research is needed to identify optimal management practices.

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Modifiable risk factors for vascular access site complications in the IMPACT II Trial of angioplasty with versus without eptifibatide. Integrilin to Minimize Platelet Aggregation and Coronary Thrombosis

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