Journal of the American College of Cardiology
© 2005 by the American College of Cardiology Foundation
Published by Elsevier Inc.

Vol. 46, No. 9, 2005
ISSN 0735-1097/05/$30.00
doi:10.1016/j.jacc.2005.06.073

Randomized Evaluation of the TriActiv Balloon-Protection Flush and Extraction System for the Treatment of Saphenous Vein Graft Disease

Joseph P. Carrozza, JR, MD, FACC,* Michael Mumma, MD, FACC,†
Jeffrey A. Breall, MD, PHD, FACC,‡ Aland Fernandez, MD, FACC,§ Eugene Heyman, PHD,‖
Christopher Metzger, MD, FACC,¶ for the PRIDE Study Investigators

Boston, Massachusetts; Sarasota and Clearwater, Florida; Indianapolis, Indiana; Montgomery Village, Maryland; and Kingsport, Tennessee

OBJECTIVES The Protection During Saphenous Vein Graft Intervention to Prevent Distal Embolization (PRIDE) study compared outcomes with the TriActiv System (Kensey Nash Corp., Exton, Pennsylvania), a balloon-protection flush and extraction device, with an embolic protection group during treatment of saphenous venous grafts (SVGs).

BACKGROUND Treatment of SVGs with embolic protection reduces adverse cardiac events.

METHODS We conducted a prospective trial randomizing 631 patients with coronary ischemia and lesions in SVGs to embolic protection with the TriActiv System or control group (Guardwire System [Medtronic AVE, Santa Rosa, California] or Filterwire EX [Boston Scientific Corp., Maple Grove, Minnesota]).

RESULTS The incidence of major adverse cardiac events at 30 days was 11.2% for the TriActiv group and 10.1% for the control group (relative risk = 1.1%; 95% confidence interval 0.67 to 1.76; p = 0.65; p = 0.02 for non-inferiority). Safety and efficacy end points were similar between groups except that patients randomized to the TriActiv System had more hemorrhagic complications (10.9% vs. 5.4%; p = 0.01).

CONCLUSIONS The TriActiv System was not inferior to approved embolic protection devices for the treatment of diseased SVGs. (J Am Coll Cardiol 2005;46:1677–83) © 2005 by the American College of Cardiology Foundation

Percutaneous catheter intervention (PCI) for saphenous vein graft (SVG) disease is associated with significant myonecrosis, increasing the risk of late mortality (1). The pathophysiology of embolization is multifactorial, involving liberation of thrombus and atheromatous debris and soluble mediators of vasoconstriction (2,3). The Saphenous Vein Graft Angioplasty Free of Emboli, Randomized (SAFER) trial demonstrated that PCI performed with embolic protection was associated with a lower incidence of no-reflow, peri-procedural myocardial infarction and adverse events (4). The FilterWire EX Randomized Evaluation (FIRE) trial reported that use of the Filterwire EX (Boston Scientific Corp., Maple Grove, Minnesota) offered protection against distal embolization similar to the balloon-occlusion Guardwire System (Medtronic AVE, Santa Rosa, California) (5).

The SAFER and FIRE studies established that embolic protection with either balloon-occlusion or a filter was the first approach to improve outcome during SVG PCI. These devices were difficult to use, however, and did not prevent adverse events in 8% to 10% of patients. These limitations led to the development of a number of newer balloon-occlusion and filter devices. The multicenter, randomized Protection During Saphenous Vein Graft Intervention to Prevent Distal Embolization (PRIDE) study compared PCI of SVGs with a novel embolic protection system, TriActiv (Kensey Nash Corp., Exton, Pennsylvania), to the Guardwire (Medtronic AVE) and Filterwire EX (Boston Scientific Corp.) devices.

METHODS

TriActiv balloon protected flush extraction system. The components of the TriActiv System have been described previously (6). The lesion is crossed with the 0.014-inch Shieldwire temporary occlusion balloon guidewire and the balloon (expansion range 3 to 5 mm) inflated via CO_2-filled syringe. After intervention, the FlushCath catheter is attached side-to-side to the Shieldwire and advanced to the occlusion balloon. Saline is infused at 50 cc/min through the FlushCath catheter by a sterile unit (autostream flow control [n = 70]). This replaced a free standing, drive console used in the early part of the PRIDE study (n = 273). The effluent is extracted through the guiding catheter (200 cc/min through 8-F guiding catheters or 125 cc/min with 7-F guiding catheters). The balloon is deflated, and flow restored.

The PRIDE study. The PRIDE study was a "hybrid" investigation (Fig. 1). At the commencement of the study,

From the *Section of Interventional Cardiology-Beth Israel Deaconess Medical Center, Boston, Massachusetts; †Sarasota Memorial Hospital, Sarasota, Florida; ‡Krannert Institute of Cardiology, Indiana University of Medicine, Indianapolis, Indiana; §Morton Plant Hospital, Clearwater Cardiovascular & Interventional Consultants, Clearwater, Florida; ‖Montgomery Village, Maryland; and the ¶Wellmont Holston Valley Medical Center, Kingsport, Tennessee. Drs. Carrozza, Mumma, and Metzger served as members of the Scientific Advisory Board for the Kensey Nash Corp., the sponsor of this study.

Manuscript received February 28, 2005; revised manuscript received June 17, 2005, accepted June 21, 2005.

Abbreviations and Acronyms

FIRE = FilterWire EX Randomized Evaluation
MACE = major adverse cardiac events
MI = myocardial infarction
PCI = percutaneous coronary intervention
PRIDE = Protection During Saphenous Vein Graft Intervention to Prevent Distal Embolization trial
SAFER = Saphenous Vein Graft Angioplasty Free of Emboli, Randomized study
SVG = saphenous vein/venous graft
TIMI = Thrombolysis In Myocardial Infarction
TLR = target lesion revascularization
TVR = target vessel revascularization

one embolic protection device was approved in the U.S. Investigators randomized patients to protection with the TriActiv System versus PCI without embolic protection ("Cohort I"), to demonstrate superiority of the TriActiv System compared with an "unprotected" group. To demonstrate non-inferiority of the TriActiv System compared with a "protected" control group, investigators randomized patients to protection with TriActiv or another protection system approved for use in SVGs ("Cohort II"). Once a site enrolled a patient in Cohort II, future enrollment was limited to Cohort II. Each site enrolled a minimum of two to six "roll-in" patients. The PRIDE study was approved by the institutional review board at each site; all patients provided written informed consent to participate.

Entry criteria. Criteria for inclusion were age ≥21 years, angina or objective evidence of ischemia, lesion in a SVG (≥3.0 mm and ≤5.0 mm), Thrombolysis In Myocardial Infarction (TIMI) flow grade ≥0, and ability to provide informed consent. Patients were excluded if any of the following were present: pregnancy, lesion in a native artery or internal mammary graft, distal shoulder of the lesion within 2.0 cm of the distal anastomosis, left ventricular ejection fraction <25%, sequential grafts unless the lesion was >2 cm proximal to the branch point, myocardial infarction (creatine kinase [CK] and CK-MB more than twice the upper limit of normal within 24 h), allergy to aspirin or both clopidogrel and ticlopidine, treatment of ≥2 SVGs, and co-morbidities limiting life-expectancy to ≤6 months.

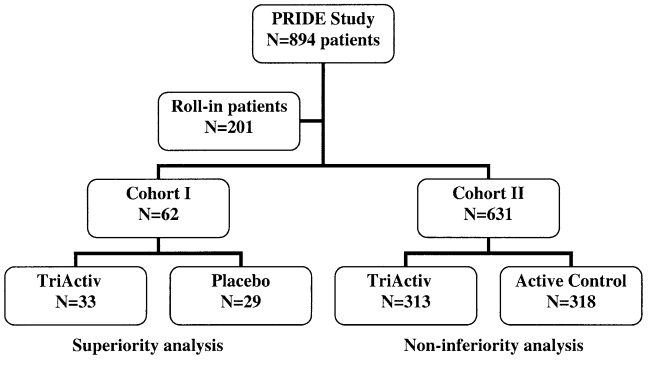

Figure 1. Enrollment in the PRIDE study.

Table 1. Baseline Demographics

	Cohort II		
	TriActiv (n = 313)	Active Control (n = 318)	p Value*
Female gender, n (%)	51 (16.3)	64 (20.1)	0.21
Age (yrs), mean ± SD	68.5 ± 9.9	68.5 ± 10.3	0.98
Range	39–99	41–93	
Hypertension, n (%)	269 (85.9)	264 (83.0)	0.31
Diabetes mellitus, n (%)	129 (41.2)	133 (41.8)	0.88
Dyslipidemia†, n (%)	266 (85.0)	278 (87.4)	0.37
Cigarette smoking, n (%)	54 (17.3)	54 (17.0)	0.93
Family history of CAD, n (%)	92 (29.4)	107 (33.7)	0.25
Prior MI, n (%)	201 (64.2)	200 (62.9)	0.73
Peripheral vascular disease, n (%)	81 (25.9)	82 (25.8)	0.98
Stroke or TIA, n (%)	44 (14.1)	37 (11.6)	0.36
Canadian cardiovascular class			
I	38 (12.2)	45 (14.3)	0.39
II	75 (24.1)	84 (26.8)	
III	98 (31.5)	87 (27.7)	
IV	100 (32.2)	99 (31.5)	
LVEF (%), mean ± SD	48.7 ± 11.5	48.7 ± 11.9	0.97
Range	25–75	25–88	

*TriActiv Cohort II versus Active Control. †Requiring treatment.
CAD = coronary artery disease; LVEF = left ventricular ejection fraction; MI = myocardial infarction; TIA = transient ischemic attack.

Randomization was stratified by intention to administer a glycoprotein IIb/IIIa receptor antagonist before intervention. Patients received aspirin before the procedure and either heparin or bivalirudin during the procedure. After the procedure, aspirin and either clopidogrel or ticlopidine were administered for a minimum of one month. Cardiac enzymes were assessed every 8 h for 24 h. Patients were assessed clinically at 30 days.

Prespecified study end points. Device success was defined as delivery of the device to the target location with successful operation and removal of the device. Lesion success was defined as the attainment of <50% residual stenosis at the end of the procedure. Procedure success was defined as device success without a major adverse cardiac event (MACE). The primary end point was MACE (either cardiac death, myocardial infarction [any post-procedure CK-MB level ≥3 × the upper limit of normal], or target lesion revascularization) at 30 days. Pre-specified efficacy and safety end points were device success and final TIMI flow grade, myocardial infarction, in-hospital MACE, stroke at 30 days, and major vascular complications (perforation, hematoma at access site >5 cm, false aneurysm, arteriovenous fistula, retroperitoneal hemorrhage, peripheral ischemia/nerve injury, vascular repair, ultrasound compression, and transfusion).

Study organization (Appendix). Electrocardiograms and angiograms were analyzed by core laboratories blinded to treatment assignment. A blinded events committee adjudicated all events. The overall performance of the study was reviewed by the Data Safety Monitoring Board.