JACC: CARDIOVASCULAR INTERVENTIONS
VOL. 8, NO. 2, 2015

ISSN 1936-8798/$36.00
PUBLISHED BY ELSEVIER INC.
http://dx.doi.org/10.1016/j.jcin.2014.07.032

PERIPHERAL

Early Experimental and Clinical Experience With a Focal Implant for Lower Extremity Post-Angioplasty Dissection

Peter A. Schneider, MD,* Robert Giasolli, MS,† Adrian Ebner, MD,‡ Renu Virmani, MD,§ Juan F. Granada, MD‖

ABSTRACT

OBJECTIVES This study provides preliminary data on the safety and feasibility of the use of a novel focal implant for managing post-percutaneous transluminal balloon angioplasty (post-PTA) dissection.

BACKGROUND Post-PTA dissection of the lower extremity arteries is managed with stent placement. This provides an acceptable post-intervention result but has long-term disadvantages, such as in-stent restenosis. Focal treatment of post-PTA dissection and avoidance of stents are the objectives of the Tack-It (Intact Vascular, Inc., Wayne, Pennsylvania) device.

METHODS A preclinical study and first-in-human data are presented. Seven swine underwent superficial femoral artery device placement, with a self-expanding nitinol stent on 1 side and a series of 4 Tack-It devices on the other side. Specimens were harvested at 28 days. The clinical study included 15 limbs that underwent revascularization for critical limb ischemia (n = 9) or claudication (n = 6). Twenty-five lesions were treated in the superficial femoral (n = 8), popliteal (n = 7), and tibial (n = 10) arteries.

RESULTS The preclinical study demonstrated a reduction in stenosis with the Tack-It (16.8 ± 2.6%) compared with stents (46.4 ± 9.8%). Neointimal thickness and injury score decreased with the Tack-It. Clinically, Tack-It placement resulted in acute technical success with resolution of the post-PTA dissection in 100% of lesions. There were no device-related complications or major amputations. Eighteen of the 25 lesions were available for angiographic follow-up at 1-year, and patency was 83.3%.

CONCLUSIONS Preclinical data suggest that the Tack-It device causes minimal vessel injury. Clinical use of the Tack-It to manage post-PTA dissection was safe and feasible in this early study and resulted in apposition of dissection flaps without stent placement. (J Am Coll Cardiol Intv 2015;8:347–54) © 2015 by the American College of Cardiology Foundation.

The existing paradigm for managing lower extremity occlusive lesions is severely limited by currently available tools. Balloon angioplasty (percutaneous transluminal balloon angioplasty [PTA]) functions by inducing dissection and causes excessive acute vascular injury (1–4). Post-PTA results are often suboptimal, and stents are the only practical solution available to manage this problem. Challenging morphologies such as longer lesions and occlusions are more likely to

From the *Kaiser Foundation Hospital, Honolulu, Hawaii; †Intact Vascular, Inc., Wayne, Pennsylvania; ‡The Italian Hospital, Asuncion, Paraguay; §CV Path, Gaithersburg, Maryland; and the ‖Skirball Research Center, Cardiovascular Research Foundation, Orangeburg, New York. Both the pre-clinical and clinical studies were supported by Intact Vascular, Inc. Work on this project was contracted to and performed by both CV Path and Cardiovascular Research Foundation. Mr. Giasolli is a cofounder of Intact Vascular. Dr. Virmani has financial relationships with Abbott Vascular, Atrium 3, Biosensors International, Biotronik, Boston Scientific, CeloNova, Cordis J&J, GlaxoSmithKline, Kona Medical, Medtronic, MicroPort Medical, Mitralign, OrbusNeich, ReCor Medical, SINO Medical, Terumo, 480 Biomedical, and W.L. Gore. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

Manuscript received July 8, 2014; accepted July 31, 2014.

ABBREVIATIONS AND ACRONYMS

MAE = major adverse event

PTA = percutaneous transluminal balloon angioplasty

SFA = superficial femoral artery

require mechanical support with stent placement. Unfortunately, stents induce chronic injury and underlying inflammation, leading to intimal hyperplasia formation and in-stent restenosis (5–7). Stent fracture is the consequence of implanting relatively rigid metal scaffolds in areas exposed to complex biomechanical forces, leading to the continuous and unrelenting deformation of the stent within the vessel (8,9).

These untoward clinical outcomes have motivated investigators to seek alternative solutions that provide the benefits of scaffolding but aim to induce low levels of inflammation and neointimal hyperplasia. It has been proposed that treatment with a minimal implant aimed at providing focal tissue apposition and fixation of dissection flaps would provide a smooth arterial flow surface without the long-term disadvantages imposed by a stent. The Tack-It device (Intact Vascular, Inc., Wayne, Pennsylvania) provides focal mechanical support only where needed after PTA. This is an opportunity to achieve an acute stentlike angiographic result without a stent. The technology functions on the basis of less metal, less outward force, minimal scaffolding, spot treatment, and an opportunity for more natural remodeling of the treated lesion while maintaining arterial flexibility.

METHODS

EXPERIMENTAL PROTOCOL. A total of 7 healthy swine received bilateral superficial femoral artery (SFA) implants and were kept alive for 28 days. At the time of the implantation, 1 SFA underwent deployment of a series of 4 (each 6 mm in length) nitinol self-expanding Tack-It devices. The contralateral artery received a self-expanding nitinol stent (40 mm long SMART stent [Cordis Corporation, Fremont, California) as a control. Fourteen vessels were explanted at 28 days and submitted for light microscopy and morphometric analysis. Animal investigation included animal care and use by qualified individuals, supervised by veterinarians, and facilities and transportation complying with legal requirements and guidelines; anesthesia was used for all interventions, and animal facilities met the standards of the American Association for Accreditation of Laboratory Animal Care.

LIGHT MICROSCOPY PROTOCOL. Explanted vessels were dehydrated in a graded series of ethanol solutions and embedded in methyl methacrylate plastic. After polymerization, each Tack-It device was sawed at 3 levels, and each stent was sawed at 4 levels. All segments were glued onto plastic slides and ground to a thickness of 17 to 70 μm using Exakt Linear Grinding technology (EXAKT Technologies, Inc., Oklahoma City, Oklahoma). All sections were examined by light microscopy for the presence of inflammation, thrombus, neointimal formation, and vessel wall injury. Histologic sections were analyzed using digital planimetry with a calibrated microscope system (IP Lab Software, Rockville, Maryland). Cross-sectional areas of the vessel, stent, and lumen were analyzed using conventional and previously published formulas. In addition, vessel healing was analyzed by quantifying strut apposition, fibrin deposition, granuloma and giant cell reactions, hemorrhage around the device struts, and total number of uncovered struts.

PATIENT POPULATION AND STUDY DESIGN. The clinical study was a prospective, nonrandomized, first-in-human safety and feasibility study with 1-year follow-up, registered at ClinicalTrials.gov (NCT02044003). Patients were treated at 2 sites in Asunción, Paraguay (Santa Clara Hospital and The Italian Hospital). Eleven patients were enrolled (15 lower extremities treated). Seven patients underwent treatment of 1 lower extremity, and 4 patients underwent treatment in both legs. The protocol was approved by the Human Subjects and Ethics Committee of each hospital. Major adverse events (MAEs) were reviewed by an independent clinical events committee. The subjects' written informed consent was obtained. Baseline clinical data were collected on case report forms by a clinical research coordinator at the study sites. A database of patients and dissections was maintained. Data management was performed by Northwest Clinical Research Group, Inc. (Woodinville, Washington). The database was built on Microsoft Excel, and the data were audited by Databent (Seattle, Washington). The safety endpoint was the MAE rate, defined as the composite of death, device embolization, the occurrence of surgery related to the device, device-related occlusion of the artery, or major unplanned amputation of the ipsilateral lower extremity at 30 days. The feasibility endpoint was the ability to secure vascular dissection flaps with the device at the time of implantation. The technical success endpoint was defined as acute luminal patency at the conclusion of the revascularization procedure, with angiography demonstrating that the lumen of the artery at the location of implant remains patent. Patients were followed at 1 month, 6 months, and 12 months with clinical examination. One-year angiographic follow-up was obtained. Restenosis was defined as ≥50% by angiography.

TACK-IT DEVICE AND PLACEMENT PROCEDURE. Each patient underwent angiography to assess lower