**Coronary Stenting with MGuard: First-In-Man Trial**

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**ABSTRACT:** MGuard is a bare-metal stent covered by an ultrathin polymer mesh sleeve on its external surface, designed to reduce embolization during coronary, cerebrovascular, and peripheral interventions. **Aim.** To evaluate the feasibility and safety of MGuard-based percutaneous coronary interventions (PCIs) of human native coronary arteries (NCs) and coronary vein grafts (VGs). **Methods.** MGuard-based PCI executed by 2 centers with postprocedural clinical and laboratory monitoring; including creatinine phosphokinase (CPK), troponin, electrocardiography and 6-month angiographic follow-up. The primary endpoint was 30-day major adverse cardiac events (MACE) including cardiac death, myocardial infarction, stent thrombosis and repeat target lesion revascularization. The secondary endpoint was device and procedural success. **Results.** Twenty-nine patients with a mean age of 68.1 ± 12 years were enrolled. The mean VG age (n = 17) was 12.6 years (range 8–19). All patients received heparin, clopidogrel and aspirin, while none received bivalirudin, glycoprotein IIb/IIIa inhibitors (GPIs) or an embolic protection device (EPD). Device and procedural success were 100% and 96.5%, respectively. One patient experienced a procedure-related CPK rise. No MACE were reported at 1 month. **Conclusion.** MGuard-based PCI of NCs and VGs appears encouraging, especially in view of unfavorable patient and lesion characteristics. Both efficacy and safety need to be further established in larger-scale studies with longer follow-up periods.

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The MGuard™ (InspireMD, Tel-Aviv, Israel) is an ultrathin polyethylene theraphthalate (PET or dacron) mesh sleeve fabricated by circular knitting (Figure 1) and is anchored to the external surface of a cobalt-chromium alloy closed-cell stent design (slotted-tube laser cut) with a strut thickness of 80–95 μm (for stent diameters of 3–3.5 and 4–4.5 mm, respectively). During stent deployment, the net stretches and slides over the expanding stent struts, creating custom-designed pores of ≤ 200 microns in diameter (pores created by stent struts have a 5–40-fold larger diameter, translating into 25–1,600-fold larger cross-sectional area).

The microfiber net (string diameter 20 microns) has minimal effects (< 0.1 mm) on the stent’s crossing profile and deliverability. By trapping the thromboembolic debris underneath the fiber net and isolating the prothrombotic subintimal components from the blood stream, MGuard may best suit interventions with high thromboembolic risk. Furthermore, the polymers mesh is biodegradable and can be impregnated with a wide array of drugs, hence serving as a platform for evenly-dispersed drug elution and delivery that is not “strut-based”. Upon conclusion of the coronary porcine trials which showed excellent feasibility and satisfactory safety data, InspireMD decided to engage in human safety trials.

**Methods**

**General.** This was a two-center (Helios Heart Center, Siegburg and Department of Cardiology Krankenhaus der Barmherzigen Brüder Trier) prospective, nonrandomized trial of ≤ 30 patients assessing the feasibility and safety of MGuard stenting in native coronary arteries (NCs) and degenerated coronary vein grafts (VGs).

**Patients. Included** in this study were patients with NC or de novo degenerated VG diameter stenosis > 50%, but < 100%, a reference vessel diameter ≥ 2.5 mm and ≤ 4.5 mm, thrombolysis in myocardial infarction (TIMI) flow grade ≥ 1, and willingness to sign an informed consent. The intention of the study was to assess MGuard deliverability and short-term safety in a high-risk percutaneous coronary intervention (PCI) cohort of patients with diseased NCs (preferably with acute coronary syndromes [ACS]) and degenerated coronary VGs.

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**Figure 1.** MGuard device on an expandable bare-metal stent.
Excluded from the study were patients with suspected or known allergy to aspirin, clopidogrel, contrast agents or heparin; requirement to treat > 1 coronary lesion urgently; left ventricular ejection fraction (LVEF) < 25%; stroke or transient ischemic attack within the past 60 days, baseline creatinine phosphokinase (CPK) values > 3 times the upper limit of normal, creatinine > 2.0 mg/dl; excessive vessel calcification or tortuosity; recent bleeding event.

Procedure. Candidates for the procedure were screened and asked to provide informed consent. Twenty-four hours prior to PCI, the following procedures were performed to secure eligibility: history, physical examination, electrocardiogram (ECG), cardiac isoenzymes (troponin I, CPK and CPK-MB), complete blood count and full chemical profile and pregnancy test, if relevant. The patient was pre-mediated with aspirin (≥ 100 mg, ≥ 24 hours pre-PCI), and clopidogrel (≥ 600 mg ≥ 4 hours pre-PCI). Nitroglycerin (100 µg intracoronary) was administered prior to baseline and final coronary angiograms. PCI was executed using conventional equipment. Employing adjunctive pharmacotherapy and devices (including balloon pre- and post-dilatation) was at the discretion of the investigators. Cardiac isoenzymes were obtained 6–8 hours, 12–16 hours and 24 hours post procedure. ECGs were recorded 6–8 hours and 24 hours post procedure, and at 1- and 6-month follow-up visits. Post-PCI patients received aspirin (100 mg daily indefinitely) and clopidogrel (75 mg daily for ≥ 6 months). Follow-up appointments were scheduled at 1 month and 6 months post PCI. The latter visit included follow-up angiography.

Primary endpoints. The primary endpoints included 30-day major adverse cardiac events (MACE) including cardiac death, myocardial infarction (MI) (defined as chest pain and CPK rise > 3 times the upper limit of normal), stent thrombosis (ARC definition), bypass surgery and repeat target lesion (TLR) or vessel revascularization (TVR).

Secondary endpoints. Secondary endpoints included device success, defined as successful delivery and deployment of the MGuard stent to the target lesion; procedural success, defined as conclusion of the procedure with satisfactory PCI results in the absence of procedural in-hospital MACE; and clinical success, defined as procedural success in the absence of 30-day MACE.

Statistical analysis. Baseline and safety data were summarized descriptively. Baseline characteristics of the study cohort are based on an “intention-to-treat” dataset (n = 29). MACE and other endpoint analyses were based on a “per-protocol set” (n = 28).

Ethical and compliance issues. The study was approved and executed under the supervision of local institutional review boards according to “Good Clinical Practice” guidelines,
as well as the “German Devices Law” (Medizinproduktegesetz MPG), and the international standard IN ISO 14155 on “clinical evaluation of medical devices in humans”. Data were captured on electronic case report forms. Compliance and adherence to the study protocol were monitored by an external monitoring company.

Results
Twenty-nine patients with a mean age of 68.1 ± 12 years were enrolled. Patients' clinical, angiographic and procedural characteristics are summarized in Table 1. The mean VG age (n = 17) was 12.6 years (range 8–19). All patients received heparin, clopidogrel and aspirin, while none received bivalirudin, GPIs or embolic protection devices. One patient was excluded from the study due to safety protocol violation. Twenty-three patients (78%) underwent balloon predilatation with an undersized balloon (2–2.5 mm) prior to MGuard deployment. Seven patients received 2 MGuards, while the rest received a single device. The mean MGuard stented segment length was 23.96 ± 9.0 mm (range 16–50 mm), and the mean MGuard stent diameter was 3.70 ± 0.52 mm (range 3–4.5 mm).

Primary endpoints. One patient experienced a procedure-related CPK rise (> 3 times the upper limit of normal), but 24-hour angiography revealed a patent target vessel and side branches. One patient experienced non-cardiac death 30 days after the procedure (sepsis with multisystem failure after aortic surgery). No other MACE were reported at 30 days.

Secondary endpoints. Device, procedural and clinical success rates were 100%, 96.4% and 96.4%, respectively.

Exploratory endpoints. TIMI flow (Figure 2) in epicardial vessels after the procedure was either unchanged (64%) or improved (36%). There were no events of flow reduction after the procedure, and non-protocol arterial vasodilators (nitroprusside, verapamil and adenosine) were neither required nor used.

Six-month follow-up data revealed no cardiac deaths, MIs or stent thromboses. At 6 months, repeat TLR was 11.1%, while repeat TVR was 11.1%; non-TV R was 7.4%. Some of these interventions were angiographically-driven (performed during 6-month angiography) and not clinically driven. Quantitative coronary angiography conducted by an independent core laboratory demonstrated a mean late loss of 0.372 ± 0.23 mm and a mean percent diameter stenosis of 30.6%. Binary (> 50%) in-segment stent restenosis at 6-month angiographic follow-up was observed in only 1 case.

Discussion
The results of this study suggest that in the particular cohort studied (58.6% of the patients with degenerated VGs and 72.4% with ACS), PCI with the MGuard is feasible and
safe. The incidence of MACE was acceptable, and there were no incidents of PCI-related stent thrombosis, Q-wave MI or cardiovascular death. Although this study is not powered to assess efficacy of the MGuard in reducing embolic events, its results and especially the 17 VG patients (who had no significant rise in CPK or procedure-related morbidity) are very encouraging (Figures 3 and 4 are examples of VG PCIs). The device required no specific training and was handled with ease by operators skilled in coronary stenting while using conventional PCI equipment. The device, procedural and clinical success data were satisfactory.

In order to determine the added value of MGuard use, two questions must be addressed: 1) Is embolization truly a significant clinical problem? 2) Are the currently available EPDs sufficiently effective?

Distal embolization occurs in all PCIs, but tends to occur more frequently during interventions of degenerated VGs and ST-elevation MIs. Embolic debris is showered in nearly all VG interventions and capture of particulate debris varies from 82–98%,2,3 with a median particle area of 4 mm². The reported occurrence of adverse event-related VG interventions is high and includes no-reflow (representing extreme embolization) (9–36.1%), branch occlusion (10%) and CPK rise >20%. Thirty-day MACE of 16.5–20% in the absence of an embolic protection device (EPD), and ~10% in the presence of an EPD is driven mostly by non-Q-wave MI. Thirty-day MACE of individual EPDs are 9.9–10.2%5,14 for the FilterWire device (Boston Scientific Corp., Natick, Massachusetts), 11.2% for Triactive (Kenney-Nash Corp., Exton, Pennsylvania), 9.6–11.6%15 for the GuardWire (Medtronic, Inc., Minneapolis, Minnesota) and 9.2% for the Proxis device16 (St. Jude Medical, St. Paul, Minnesota). Although embolic protection is endorsed by the guidelines during degenerated VG PCI and rendered cost-effective by some, it is used only in 22% of VG interventions in the United States17 (19% of centers reported no use at all and 41% reported < 10% use in VG interventions). This number is probably lower in the rest of the world and can be related to lesion suitability, cost-effectiveness issues and procedure time and complexity. Severe embolization is more likely in de novo lesions presenting as ACS, with either bulky plaques11 or visible thrombus and diffusely diseased old VGs.

Patients with ACS also experience embolization during PCI. In a report of 1,301 patients undergoing primary PCI in acute MI,18 96.1% had normal epicardial flow (TIMI 3), however, myocardial perfusion was defined as normal in 17.4%, reduced in 33.9% and absent in 48.7%. This correlated with a 1-year mortality rate of 1.4%, 4.1% and 6.2%, respectively (p = 0.01). In many of these cases, the microcirculation is compromised prior to PCI, however, a considerable percentage of the patients experience worsening epicardial flow, myocardial perfusion, ischemic symptoms and ECG readings during PCI. Angiographically visible massive embolization and transient reduced flow or no-reflow (which underestimates the true extent of embolization), occurs in at least (conservative estimate) 9–15%,19,20 but could be as high as 17–31.1%17,18 of primary PCI patients. The incidence and severity of embolization depends on infarct age, TIMI flow before PCI, thrombus and plaque volume and characteristics and stent overexpansion. Several studies have confirmed the lack of clinical efficacy of EPDs in the setting of ST-elevation MI.19,20

Magnetic resonance imaging (MRI) studies detect PCI-related downstream myocard necrosis in 23–51%21,22 of patients undergoing elective PCI when optimal technique and aggressive adjunctive therapy are utilized. This may be accompanied by significant perfusion and flow abnormalities,23 as well as ischemic intracoronary ECG changes in 46% of patients.24 The average extent of injury was 5 ± 4.8 % of the myocardial mass.25 Most of these patients had a rise in troponin. Moreover, at a median of 8 months, 28% demonstrated persistent perfusion abnormality on MRI. ACS without ST-elevation reflect an intermediate risk of embolization.

In the authors’ view, PCI-related embolization continues to be a serious and clinically significant problem that is not effectively and completely addressed by current EPDs. Although this “first-in-man” feasibility and safety study was not powered to assess efficacy, it sets the stage for future large-scale studies that will further assess long-term efficacy and safety.
A few procedural issues must be emphasized:
1. **Side branches.** During MGuard PCI of NCs, side branches can potentially be compromised by the presence of the stent struts or polymer mesh. Although in this small series this did not translate into clinical events (Figure 5) during MGuard-based PCR of bifurcation lesions, major side branches should be protected by a second wire and after stenting the major branch could be “unjailed” in a method similar to conventional stenting.
2. **Meab integrity.** The investigators were discouraged from using the device in heavily calcified lesions or extremely tortuous vessels. Passage of the MGuard within other newly-deployed stents was prohibited and considered a protocol violation in this study. Hence, multistenting had to be performed from distal to proximal ends. A protective sleeve could potentially eliminate this problem and render the MGuard more versatile.

**Conclusion**

In this first-in-man trial, MGuard-based PCI of degenerated VGs and high-risk NCs appears encouraging, especially in regard to unfavorable patient and lesion characteristics. Both efficacy and safety need to be further established in larger-scale studies with longer follow-up periods.

**References**


First-in-Man Study of Coronary Stenting with MGuard™