Impact of Introducer Sheath Coating on Endothelial Function in Humans After Transradial Coronary Procedures

Ellen A. Dawson, PhD*; Sudhir Rathore, MD*; N. Timothy Cable, PhD; D. Jay Wright, MD; John L. Morris, MD; Daniel J. Green, PhD

Background—The aim of this study was to compare the impact of transradial catheterization with hydrophilic-coated catheter sheaths versus uncoated sheaths on NO-mediated endothelial-dependent and -independent vasodilator function.

Methods and Results—Thirty-five subjects undergoing transradial catheterization were recruited and assessed before and the day after catheterization. A subgroup was also assessed 3 to 4 months after catheterization. Subjects received hydrophilic-coated sheaths (n = 15) or uncoated sheaths (n = 20). Radial artery flow-mediated dilatation and endothelium- and NO-dependent arterial dilatation were assessed within the region of sheath placement. Glyceryl trinitrate endothelium-independent NO-mediated function was also assessed. The noncatheterized arm provided an internal control. Flow-mediated dilatation in the catheterized arm decreased from 10.3 ± 3.8% to 5.3 ± 3.3% and 8.1 ± 2.4% to 5.2 ± 3.7% in the coated and uncoated groups, respectively (P < 0.01). These values returned toward baseline levels 3 months later (coated, 6.4 ± 1.4%; uncoated, 9.4 ± 4.1%; P < 0.05) versus postprocedure. Glyceryl trinitrate decreased from 14.8 ± 7.2% to 9.5 ± 4.1% (P < 0.05) in the coated group and from 12.2 ± 4.6% to 7.5 ± 4.2% (P < 0.01) in the uncoated group. Values returned to baseline at 3 months (coated, 16.6 ± 5.6%; uncoated, 12.1 ± 3.9%; P < 0.05). There was no difference in the magnitude of decrease in flow-mediated dilatation or glyceryl trinitrate between coated and uncoated groups. No changes in function occurred in the noncatheterized arm.

Conclusions—Placement of a catheter sheath inside the radial artery disrupts vasodilator function, which recovers after 3 months. No differences were evident between hydrophilic-coated and uncoated sheaths. (Circ Cardiovasc Interv. 2010;3:148-156.)

Key Words: flow-mediated dilatation ■ radial artery catheter ■ endothelium

Since its introduction in 1989, transradial catheterization has gained popularity as an approach for diagnostic and coronary interventional procedures. This approach has been associated with lower vascular complication rates, reduced procedural costs, comparable procedural success rates, earlier patient mobilization, improved quality of life, and reduced hospitalization costs. However, it is probable that insertion of the catheter sheath into the relatively small radial artery has a direct physical impact on the endothelial lining of the vessel wall, a squamous monolayer that is easily damaged as a consequence of mechanical disruption. Removal or damage of the endothelial lining impairs arterial relaxation by decreasing NO bioavailability. It may also promote intimal hyperplasia, thrombus formation, and the development of atherosclerotic plaques, which could have implications for the use of the artery as a donor graft for coronary artery bypass surgery because graft longevity is partly related to the capacity to remodel and dilate in response to changes in metabolic demand and blood flow.

Clinical Perspective on p 156

Recent advances in the development of catheter sheaths include the development of hydrophilic coatings that aim to reduce frictional resistances during sheath placement and removal. Although hydrophilic-coated sheaths have been reported to result in a reduction in the occurrences of discomfort and clinical spasm, no previous study has addressed the questions of whether sheath coating results in less endothelial dysfunction. The aim of this study, therefore, was to measure endothelium-dependent and -independent vasodilator function in patients undergoing transradial catheterization with either a hydrophilic-coated or an uncoated sheath.

Methods

Informed written consent was obtained from 35 subjects (32 men) recruited from the list of patients requiring radial artery catheterization for coronary angiography or angioplasty. The exclusion criteria were as follows: previous coronary artery bypass graft or coronary

Received September 25, 2009; accepted February 22, 2010.
From the Research Institute for Sport and Exercise Sciences (E.A.D., N.T.C., D.J.G.), Liverpool John Moores University, and Liverpool Heart and Chest Hospital (S.R., D.J.W., J.L.M.), Liverpool, England, and School of Sport Science, Exercise and Health (D.J.G.), University of Western Australia, Western Australia, Australia.
*The first 2 authors contributed equally to this work.
Correspondence to Ellen Dawson, PhD, Research Institute for Sport and Exercise Sciences, Liverpool John Moores University, Liverpool L32ET, UK.
E-mail e.dawson@ljmu.ac.uk
© 2010 American Heart Association, Inc.

Circ Cardiovasc Interv is available at http://circinterventions.ahajournals.org

DOI: 10.1161/CIRCINTERVENTIONS.109.912022
intervention through the radial route or myocardial infarction during the previous 3 months, valvular heart disease, left ventricular ejection fraction <40%, chronic obstructive lung disease, and renal or hepatic dysfunction. The study conformed to the Declaration of Helsinki, and ethical approval was obtained from the Liverpool Local Regional Ethics Committee.

Study Design
In this prospective randomized study, patients were assigned to 1 of the 2 different introducer sheath groups: hydrophilic-coated sheath (coated group), sheath without coating (uncoated group). Patients were tested on 3 occasions: the day of the transradial procedure (before catheterization [pre]), the day after catheterization (post), and ∼3 months after catheterization (reconv).

Radial Artery Access and Procedural Details
The radial artery was approached with the arm extended and supported with the wrist in mild hyperextension. Local anesthesia was achieved with 2% lignocaine after disinfection at the puncture site. The radial artery was punctured with a 21-gauge arterial needle through which a 0.118-inch platinum-tipped nitinol guide wire was introduced. Next, the needle was withdrawn, and a small skin incision was made. A 6F introducer sheath (length, 13 or 23 cm; external diameter, 2.6 mm) with a dilator tip length of 2.5 cm was inserted. Routine use of vasodilator cocktail (nitroglycerine, verapamil, or diltiazem) was avoided if possible, and a weight-adjusted dose of heparin was introduced into the central circulation after the introduction of the first catheter. All introducer sheaths were removed at the end of the procedure and hemostasis achieved in the catheterization laboratory through a compression device. The patients were mobilized immediately, and the compression device removed after 2 to 4 hours.

Experimental Procedures
Patients were requested to abstain from alcohol, caffeine, and cigarettes for 12 hours before each session. Assessments were taken in a quiet, temperature-controlled room. Patients rested in the supine position for ∼20 min to ensure that all hemodynamic variables stabilized. The radial artery was imaged with the arm extended and supported at 80° from the torso. A rapid inflation/deflation pneumatic cuff was positioned on the imaged arm around the wrist. A standard catheter sheath was used to mark the length of the catheter on the surface of the arm from the scaphoid process. Care was taken to image the same section of the artery during repeat measurements. We assessed both arms to determine whether changes as a consequence of catheterization were specific or more generalized throughout the vascular system. On each occasion, endothelial-dependent function (flow-mediated dilatation [FMD]) was assessed over a distal section of the radial artery, within the zone containing the sheath, and above the cuff. Endothelium-independent function was assessed as the vascular response to a sublingual dose of glyceryl trinitrate (GTN). A minimum of 30 min was given between repeat doses of GTN. The sonographer was blinded to the catheter sheath type during scanning and analysis.

Ultrasound Assessment of Conduit Artery Function
Heart rate and mean arterial pressure (MAP) were determined from an automated sphygmomanometer on the contralateral arm. A 12-MHz multifrequency linear array probe attached to a high-resolution ultrasound machine was used to image the radial artery.

Flow-Mediated Dilatation (Endothelium-Dependent, NO-Mediated Function)
Baseline scans assessing resting vessel diameter and flow were recorded in the final minute of the initial rest period. The occluding cuff then was inflated to >200 mm Hg for 5 min. Diameter and flow recordings resumed 30 sec before cuff deflation and continued for 5 min thereafter. MAP and heart rate were recorded during the resting period and after cuff release.

Glyceryl Trinitrate Dilatation (Endothelial-Independent, NO-Mediated Function)
Vessel diameter was recorded 1 min before and continuously for 10 min after sublingual administration of GTN (400 μg). Heart rate and MAP were recorded at rest and 5 min after GTN administration. Posttest analysis was carried out using custom-designed edge detection and wall-tracking software. Our previous detailed analysis of power requirements using this software indicated that at an alpha level of 0.05, 7 subjects were required to ensure 90% power to detect a 2% improvement in FMD. FMD and GTN were calculated as the percentage rise from preceding baseline diameters. Time to peak diameter was calculated from the point of cuff deflation to the time of peak postdilation diameter. Postdilation shear rate area under the curve was calculated for data up to the point of maximal postdilation diameter (FMD) using the Riemann sum technique for each patient. Shear rate area under the curve represents the stimulus for FMD. Further detailed methods are available elsewhere.

Data Analysis
The responses initially were assessed using 3-way ANOVAs with linear mixed models. We followed-up with 2-way repeated-measures ANOVAs on the coated or uncoated groups compared over time and between arms. Further post hoc analysis was carried out using paired t tests. The effects of the FMD test or GTN administration on MAP were assessed using a 1-way ANOVA. Baseline characteristic

Table 1. Clinical Characteristics and Outcomes of the Study Patients (n=35)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Coated (n=15)</th>
<th>Uncoated (n=20)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>62.7±9.7</td>
<td>62.0±10.5</td>
<td>0.82</td>
</tr>
<tr>
<td>Male</td>
<td>13 (86)</td>
<td>19 (95.0)</td>
<td>1.00</td>
</tr>
<tr>
<td>MAP, mm Hg</td>
<td>95±11</td>
<td>93±13</td>
<td>0.89</td>
</tr>
<tr>
<td>Heart rate, bpm</td>
<td>62±13</td>
<td>62±13</td>
<td>0.95</td>
</tr>
<tr>
<td>Hypertension</td>
<td>11 (73)</td>
<td>16 (80)</td>
<td>0.71</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>13 (87)</td>
<td>19 (95)</td>
<td>0.57</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>3 (20)</td>
<td>5 (25)</td>
<td>1.00</td>
</tr>
<tr>
<td>Height, cm</td>
<td>153.5±9.2</td>
<td>165.3±8.1</td>
<td>0.38</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>76.8±9.7</td>
<td>86.5±19.3</td>
<td>0.23</td>
</tr>
<tr>
<td>Wrist circumference, cm</td>
<td>16.3±3.9</td>
<td>17.1±1.0</td>
<td>0.37</td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current</td>
<td>2 (13)</td>
<td>3 (15)</td>
<td></td>
</tr>
<tr>
<td>Former</td>
<td>10 (67)</td>
<td>14 (70)</td>
<td>0.26</td>
</tr>
<tr>
<td>Stable angina</td>
<td>15 (100)</td>
<td>20 (100)</td>
<td>1.00</td>
</tr>
<tr>
<td>Time sheath in situ, min</td>
<td>70.4±30.3</td>
<td>64.2±24.0</td>
<td>0.54</td>
</tr>
<tr>
<td>Vascular complications</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ecchymosis</td>
<td>2 (13)</td>
<td>3 (15)</td>
<td></td>
</tr>
<tr>
<td>Oozing</td>
<td>4 (27)</td>
<td>1 (5)</td>
<td>0.18</td>
</tr>
<tr>
<td>Radial artery occlusion</td>
<td>1 (7)</td>
<td>0 (0)</td>
<td>0.43</td>
</tr>
<tr>
<td>Late local infection</td>
<td>1 (7)</td>
<td>0 (0)</td>
<td>0.43</td>
</tr>
<tr>
<td>Radial artery occlusion follow-up</td>
<td>1 (7)</td>
<td>0 (0)</td>
<td>0.43</td>
</tr>
</tbody>
</table>

Data are presented as n (%) or mean±SD. Hypertension is defined as systolic blood pressure >140 or diastolic blood pressure >90 mm Hg. Hyperlipidemia was considered apparent on treatment for total serum cholesterol >5.0 mmol/L. Diabetes mellitus was determined on treatment. Radial artery spasm is defined as discomfort felt by patient or resistance felt during removal of introducer sheath.
differences were determined using t tests or \( \chi^2 \) tests. Results are expressed as mean±SD, and \( P<0.05 \) was considered significant.

**Results**

**Study Patients**

The clinical characteristics of the patients are described in Table 1. The majority of the patients were taking aspirin, clopidogrel, a statin, an angiotensin-converting enzyme inhibitor, and a \( \beta \)-blocker, and there were no systematic differences between the groups in terms of medication use. Efforts were made to avoid changes to the patients’ drug regimens throughout the study. In any event, the within-subject design, with contemporaneous contralateral limb measures at each time point, provided an important experimental control. All patients had successful transradial coronary procedures. Coronary artery angioplasty and stenting was performed in 33 patients, and 2 patients had only coronary angiography. The mean procedure time was 67±27 minutes. Three patients needed intraarterial isosorbide dinitrate to treat radial artery spasm during the procedure (2 in uncoated group and 1 in coated group). One patient in the coated sheath group had an occluded artery postprocedure that remained occluded at 3 months. Occlusion was confirmed by a reverse Allen’s test, and the existence of impaired shear rate after ischemia. The data for this patient were removed from subsequent analysis. The other 14 subjects in the coated sheath group had FMD data collected before and after catheterization, and 12 of these had GTN before and after catheterization. A subgroup of 6 patients from the coated sheath group was retested 3 months after procedure. Twenty patients were recruited to the uncoated group of whom all had pre- and post-FMDs, whereas 19 completed pre- and post-GTN testing. From this group, 13 patients were retested for FMD and 12 for GTN 3 months later. The difference in group size was due to patient drop-out or poor ultrasound images.

**Baseline Characteristics and Clinical End Points**

The baseline clinical characteristics are shown in Table 1 and were similar in both groups. The incidence of minor access site complications was low in both groups. There was no significant difference in MAP between arms or between catheter sheath coatings.

The 3-way ANOVA produced a significant effect of arm (\( P=0.003 \)); time (\( P=0.000 \)); interaction of arm and time; and coating, arm, and time for the FMD percent. For the GTN percent, there was a significant effect of coating, time, and arm and time. These data were followed up by a simple main effects model using 2-way ANOVAs.

**Impact of Sheath Placement on Endothelium-Dependent and -Independent Vasodilation**

In the coated group, there was a significant effect of time (\( P=0.046 \)), arm (\( P=0.002 \)), and interaction between arm and
time ($P=0.003$) on FMD. There was a reduction in FMD in the catheterized arm pre to post ($P=0.01$), with no change in the noncatheterized arm ($P=0.18$) (Figure 1).

In the uncoated group, there was a significant effect of time ($P=0.005$), arm ($P=0.001$), and interaction between arm and time ($P<0.001$) on FMD. There was also a significant reduction in FMD in the catheterized arm ($P<0.05$), with no change in the noncatheterized arm (Figure 1).

In the coated group, ANOVA revealed no significant effect of time ($P=0.089$), but there was a significant effect of arm ($P=0.029$) and interaction between arm and time for GTN data ($P=0.012$). There was a reduction in the GTN response in the catheterized arm pre to post ($P<0.05$), with no change in the noncatheterized arm ($P=0.32$) (Figure 2).

In the uncoated group, there was no significant effect of time ($P=0.11$), but there was a significant effect of arm ($P=0.017$) and interaction between arm and time for GTN data ($P<0.001$) (Figure 2). There was a reduction in GTN in the catheterized arm pre to post ($P<0.01$), with no change in the noncatheterized arm ($P=0.65$).

Although there was a significant interaction among arm, time, and coating with the 3-way ANOVA, there was no significant difference in the magnitude of change in FMD between the coated and uncoated conditions in the catheterized arm, with a 2-way ANOVA demonstrating a significant effect of time ($P<0.001$) but no interaction of time and coating ($P=0.085$). Likewise, an ANOVA on GTN data comparing the effect of time and coating in the catheterized arm showed a significant effect of time ($P<0.001$) but no interaction between time and coating ($P=0.63$). Baseline arterial diameters, time to peak, and shear rate area under the curve are presented in Table 2.

Figure 2. Changes in GTN (%) in the catheterized and noncatheterized control arms before and after procedure. Top panel shows coated sheath, and bottom shows uncoated sheath. Data are presented as mean±SD. *Significantly different from pre $P<0.05$.

Impact of Sheath Placement on the Recovery of Endothelium-Dependent and -Independent Vasodilation

In the subjects who participated in the 3-month follow-up, matched data revealed that FMD decreased nonsignificantly ($P=0.063$) as a result of catheterization and then returned toward baseline at 3 months ($P<0.05$ post to recov) in the coated group (n=6) (Figure 3). In the contralateral control limb, FMD was unchanged. ANOVA on the post versus recov data comparing time and arm revealed no significant effect of time ($P=0.21$), a significant effect of arm ($P=0.004$), but no significant interaction ($P=0.14$). In the uncoated group (n=13), the FMD decreased from pre to post ($P<0.01$) and returned toward baseline post to recov ($P<0.05$). In the contralateral control limb, FMD was unchanged. ANOVA on the post versus recov data comparing time and arm revealed no significant effect of time ($P=0.38$), a near significant effect of arm ($P=0.05$), and a significant interaction ($P=0.020$) (Figure 3).
The GTN data in the coated group (n=6) decreased from pre to post (P<0.05) and then returned toward baseline post to recov (P<0.05). In the contralateral control limb, GTN was unchanged. ANOVA on the post versus recov data comparing time and arm revealed no significant effect of time (P=0.39) or arm (P=0.18) but a significant interaction between arm and time (P=0.014). In the uncoated group (n=12), GTN decreased from pre to post and returned toward baseline levels at 3 months post to recov (P<0.05). In the contralateral control limb, GTN was unchanged. ANOVA on the post versus recov data comparing time and arm showed a significant effect of time (P=0.036), an almost significant effect of arm (P=0.052), and a significant interaction between arm and time (P=0.001) (Figure 4).

There was no significant difference in the recovery of FMD post versus recov between the coated and uncoated conditions in the catheterized arm, with a 2-way ANOVA demonstrating a significant effect of time (P=0.005) but no interaction of time and coating (P=0.52). There was also no significant difference in the recovery of the GTN post versus recov between the coated and the uncoated conditions in the catheterized arm, with 2-way ANOVA demonstrating a significant effect of time (P=0.000) but no interaction between time and coating (P=0.58). Baseline arterial diameters, time to peak, and shear rate area under the curve are presented in Table 3.

### Discussion

The aim of this study was to determine the impact of coating of sheaths used during radial artery catheterization on vascular function in vivo. Catheterization may have implications for long-term artery health, as endothelial damage leads to the

![Table 2. Baseline Diameter, Time to Peak, and Shear Rate Area Under the Curve Preprocedure and the Day After the Procedure in the Catheterized and Noncathetherized Arms](http://circinterventions.ahajournals.org/)

<table>
<thead>
<tr>
<th>Protocol</th>
<th>Baseline Diameter, mm</th>
<th>Time to Peak</th>
<th>SR&lt;sub&gt;AUC&lt;/sub&gt;, s&lt;sup&gt;-1&lt;/sup&gt;×10&lt;sup&gt;3&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre</td>
<td>Post</td>
<td>Pre</td>
</tr>
<tr>
<td><strong>FMD protocol</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cath</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coated</td>
<td>2.7±0.5</td>
<td>3.0±0.4*</td>
<td>97±42</td>
</tr>
<tr>
<td>Uncoated</td>
<td>2.9±0.4</td>
<td>3.1±0.4*</td>
<td>106±48</td>
</tr>
<tr>
<td>Contr</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coated</td>
<td>2.6±0.5</td>
<td>2.5±0.4</td>
<td>91±50</td>
</tr>
<tr>
<td>Uncoated</td>
<td>2.6±0.4</td>
<td>2.9±0.4*</td>
<td>86±28</td>
</tr>
<tr>
<td><strong>GTN protocol</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cath</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coated</td>
<td>2.6±0.5</td>
<td>2.9±0.5</td>
<td>316±87</td>
</tr>
<tr>
<td>Uncoated</td>
<td>2.9±0.4</td>
<td>3.3±0.3*</td>
<td>345±83</td>
</tr>
<tr>
<td>Contr</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coated</td>
<td>2.7±0.5</td>
<td>2.7±0.3</td>
<td>354±125</td>
</tr>
<tr>
<td>Uncoated</td>
<td>3.0±0.3</td>
<td>2.9±0.3</td>
<td>276±108</td>
</tr>
</tbody>
</table>

Data are presented as mean±SD. Coated group, n=14 for FMD and n=12 for GTN. Uncoated group, n=20 for FMD and n=19 for GTN. Endothelium-dependent (FMD) and endothelial-independent function (GTN) in groups. Cath indicates catheterized arm; Contr, noncatheterized control arm, SR<sub>AUC</sub>, shear rate area under the curve.

*Significantly different from pre P<0.05.
impaired FMD and GTN function nonetheless allows for the possibility that both endothelial and smooth muscle function were affected. We favor the latter interpretation because we believe that impairment in the function of the middle layer of the wall as a result of the introduction of a sheath, which is of similar outer diameter to that of the artery lumen, is likely to have resulted in endothelial denudation or dysfunction. Although we have no direct evidence of endothelial denudation or damage, it is important to consider that animal studies that established a role for the endothelial function in FMD did so by placing a balloon inside an artery to denude the inner layer. We would contend that sheath placement in this study represents a similar, or perhaps even more robust, intervention, which is supported by the significantly larger diameter postprocedure in the catheterized but not in the noncatheterized arm. Therefore, it seems likely that both endothelial and smooth muscle function were affected by sheath placement.

The recovery of endothelial-dependent and -independent function in the catheterized arm indicates that transradial catheterization should not be considered an absolute contraindication to subsequent use of the radial artery as a donor graft. Some caution is warranted; however, as cannulation of the radial artery has been shown to reduce arterial lumen size and result in intima-medial thickening. Damage of the smooth muscle also may be associated with intimal hyperplasia, cell proliferation, collagen synthesis, and inward remodeling. Furthermore, transradial catheterization has been shown to induce intimal hyperplasia, medial inflammation, and tissue necrosis at the puncture site. Despite good clinical outcomes, caution in using the radial artery as a graft is advocated by several groups due to its propensity to spasm, an increased likelihood of development of atherosclerosis, and damage induced by catheterization.

A unique aspect of this study was examination of the impact of sheath coating on vascular function. The development of hydrophilic coating purportedly leads to reduction in the force required to remove the sheath and the likelihood of damage during removal. There is some evidence that sheath coating has beneficial clinical effects, including reduced spasm and pain. We therefore hypothesized that sheath coating would limit impacts on vessel function and that diminished impact on the endothelium may preserve its well-established antiatherogenic properties. However, our data show that there was no difference between hydrophilic-coated and uncoated sheaths in terms of endothelium-dependent or -independent function after sheath placement. Furthermore, we observed no evidence of a beneficial effect of sheath coating on the recovery of the artery after sheath removal. These data indicate that if clinical and outcome benefits from coating sheaths do exist, then the mechanisms

**Figure 3.** Changes in FMD (%) in the catheterized and noncatheterized arms post and recov. Top panel shows coated sheath data, and bottom shows uncoated sheath data. Data are presented as mean±SD. *Significantly different from pre P<0.05.
responsible are unlikely to be attributable to preserved endothelial or vascular smooth muscle function. In addition, several recent articles have suggested that patients can develop a granulomatous inflammation due to shedding of some of the hydrophilic coating into the artery. These findings, in combination with our data, support the suggestion of Tharmaratnam et al. that the increased cost of hydrophilic sheaths, the cost of treatment of inflammation, and the apparent lack of difference in spasm and depressed function need to be carefully balanced against the putative benefits of reduced spasm and pain on removal.

This study had a number of limitations. There were a relatively small number of patients in each group, and we could not get all to return at 3 months. This limitation is somewhat mitigated by our within-subject design and analysis. We did not control for age, preexisting vascular disease, history of smoking, or drug treatment; however, the use of the contralateral arm as an internal control negated this limitation, and our data set has the advantage of representing responses in typical unselected patients. Finally, sheath insertion increased baseline artery diameter before our postprocedural measures of FMD and GTN. It has been suggested that baseline diameter is an important determinant of the dilator response magnitude, at least between individuals or between arteries, when large differences can exist in the resting diameter. However, the change in diameter we observed is unlikely to explain the magnitude of impairment in FMD. For example, on the basis of our recent article, an FMD difference of 0.2% to 1.5% would be expected for a 0.3-mm change in baseline radial artery diameter. In addition, FMD data collected 3 months after catheterization (Table 3) remained impaired, despite return of the resting diameter to values below that observed before catheterization. Of course, the impact of baseline diameter change per se on FMD and GTN responses is not relevant to the issue of sheath coating because both types of sheath have similar effects on baseline artery diameter. Although our findings are clear and consistent, with a large number of tests, we cannot rule out the possibility of a type I error.

In conclusion, transradial catheterization results in reversible depression in NO-mediated vasodilator function in the catheterized arm. This effect is not mitigated in patients who received a hydrophilic-coated sheath. The purported benefits of hydrophilic-sheath coating need to be weighed against the increased cost, possible increased risk of inflammation, and lack of reduction in arterial function. Future research and technological development should seek to minimize the effects of the catheter and the sheath on the vasculature. It is also possible that optimizing the function and size of the artery before its cannulation may improve the outcome and recovery of the artery and reduce the chance of graft failure if the artery is removed for coronary artery bypass. To this end, exercise training has been shown to improve arterial function and induce outward remodeling, both of which might improve the health and recovery of the artery after the procedure.

Figure 4. Changes in GTN (%) in the catheterized and noncatheterized arms post to recov. Top panel shows coated sheath data, and bottom shows uncoated sheath. Data are presented as mean±SD. *Significantly different from pre P<0.05.
Table 3. Baseline Diameter, Time to Peak, and Shear Rate Area Under the Curve Preprocedure, the Day After the Procedure, and ~3 Months After Procedure in the Catheterized and Noncatheterized Arms

<table>
<thead>
<tr>
<th></th>
<th>Baseline Diameter, mm</th>
<th>Time to Peak, s</th>
<th>SR_AUC, $s^{-1} \times 10^3$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre</td>
<td>Post</td>
<td>Recov</td>
</tr>
<tr>
<td><strong>FMD protocol</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cath Coated</td>
<td>2.6±0.5</td>
<td>2.9±0.4</td>
<td>2.7±0.6</td>
</tr>
<tr>
<td>Uncoated Coated</td>
<td>2.9±0.4</td>
<td>3.2±0.4</td>
<td>2.7±0.4†</td>
</tr>
<tr>
<td>Contr Coated</td>
<td>2.6±0.5</td>
<td>2.4±0.4</td>
<td>2.6±0.5</td>
</tr>
<tr>
<td>Uncoated Coated</td>
<td>2.6±0.4</td>
<td>2.9±0.4†</td>
<td>2.8±0.4†</td>
</tr>
<tr>
<td><strong>GTN Protocol</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cath Coated</td>
<td>2.7±0.5</td>
<td>2.9±0.5</td>
<td>2.5±0.3</td>
</tr>
<tr>
<td>Uncoated Coated</td>
<td>3.0±0.5</td>
<td>3.2±0.2</td>
<td>2.7±0.3†</td>
</tr>
<tr>
<td>Contr Coated</td>
<td>2.7±0.2</td>
<td>2.9±0.5</td>
<td>2.8±0.3</td>
</tr>
<tr>
<td>Uncoated Coated</td>
<td>2.9±0.3</td>
<td>2.9±0.3</td>
<td>3.1±0.4†</td>
</tr>
</tbody>
</table>

Data are presented as mean±SD. Coated group, n=6 for FMD and GTN. Uncoated group, n=13 for FMD and n=12 for GTN. Endothelium-dependent (FMD) and endothelial-independent function (GTN) was assessed in both groups. Cath indicates catheterized arm; Contr, noncatheterized control arm; SR_AUC, shear rate area under the curve.

*Significantly different from pre P<0.05.
†Significantly different from post.

Acknowledgments
We thank Chris Reed for his assistance with development of the edge detection and wall tracking software.

Sources of Funding
Dr Green received funding from the National Heart Foundation of Australia and the Australian Research Council.

Disclosures
None.

References
19. Celsmager DS, Sorensen KE, Gooch VM, Spiegelhalter DJ, Miller OM, Sullivan ID, Lloyd JK, Deanfield JE. Non-invasive detection of endothe-

**CLINICAL PERSPECTIVE**

Since its introduction in 1989, transluminal catheterization has gained popularity as an alternate approach for coronary diagnostic and interventional procedures. Recent advances in catheter sheaths include hydrophilic coatings, the aim of which is to reduce friction during sheath insertion and removal. The integrity of this artery is important because it might be harvested as a graft during coronary artery bypass surgery. Although there is evidence of reduced spasm with hydrophilic coating, there is no evidence regarding its impact on vascular function. Our study shows that vascular endothelial and smooth muscle function are reduced after radial artery sheath insertion. This effect is not mitigated by a hydrophilic-coated sheath. The potential benefits of hydrophilic-sheath coating need to be compared with increased cost, risk of inflammation, and reduction in endothelial function.
Impact of Introducer Sheath Coating on Endothelial Function in Humans After Transradial Coronary Procedures
Ellen A. Dawson, Sudhir Rathore, N. Timothy Cable, D. Jay Wright, John L. Morris and Daniel J. Green

doi: 10.1161/CIRCINTERVENTIONS.109.912022

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circinterventions.ahajournals.org/content/3/2/148

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation: Cardiovascular Interventions can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at: http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation: Cardiovascular Interventions is online at: http://circinterventions.ahajournals.org//subscriptions/