Percutaneous In Situ Coronary Venous Arterialization
Report of the First Human Catheter-Based Coronary Artery Bypass

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Abstract—Diffuse coronary artery disease is frequently untreatable by coronary artery bypass or angioplasty. Many such “no-option” patients have been subjects for trials of angiogenesis using growth factor manipulation or laser injury. We think these novel revascularization strategies are limited by insufficient inflow to putative areas of new microvasculature and thus seek a more mechanical solution. We report the use of a catheter-based system for arterializing the adjacent anterior cardiac vein in a patient with chronic total occlusion of the left anterior descending coronary artery. A composite catheter system (phased-array ultrasound imaging system mounted on a catheter with extendable nitinol needle) was used to deliver an exchange-length intracoronary guidewire from the proximal left anterior descending coronary artery into the parallel anterior interventricular vein. Using standard angioplasty techniques, a fistula was then constructed from the proximal artery to the coronary vein using a self-expanding connector. The proximal vein was blocked with a novel self-expanding “blocker,” thus precluding “steal” through the coronary sinus and forcing retroperfusion of the anterior wall. The procedure was completed without complication, and a follow-up angiogram at 3 months confirmed continued patency of the arteriovenous connection. This patient, who had severe angina before the procedure, has been asymptomatic for 12 months. Percutaneous in situ venous arterialization may be an effective therapy for diffuse, “untreatable” coronary disease by supplying a robust inflow of arterialized blood via retroperfusion to severely ischemic myocardium. (Circulation. 2001;103:2539-2543.)

With the combination of coronary artery bypass surgery and percutaneous coronary interventions, many patients with symptomatic coronary insufficiency can be effectively revascularized. Each year in the United States alone, nearly 1 million individuals undergo a percutaneous catheter-based intervention, with intracoronary stents used in most. An additional half million Americans have their coronary disease treated by aortocoronary surgical bypass.

Despite the successful and widespread application of these revascularization procedures, a large number of patients are not good candidates for either angioplasty or surgery. These “no-option” patients frequently have diffuse coronary disease without a discrete target for angioplasty, stenting, or surgical bypass. It has been estimated that >100,000 patients each year may fall beneath the no-option rubric. Many of these patients have recently been investigational subjects in trials focused on angiogenesis by vascular growth factor infusions or laser injury.

We suspect that gene therapy and laser revascularization strategies may have a fundamental flaw: the creation of new blood vessels in ischemic myocardial tissue requires significant arterial inflow, which is not obviously enhanced by these techniques. Therefore, we sought a novel percutaneous revascularization approach with the potential to provide robust arterial inflow to a severely ischemic region. Recalling the possibility of venous retroperfusion, we developed catheter techniques for arterializing the in situ coronary vein from an adjacent proximal coronary artery, blocking the proximal vein, and thus forcing retrograde venous perfusion.

Percutaneous in situ coronary venous arterialization (PICVA) is one of a series of catheter-based techniques we are developing for bypassing severe coronary disease without surgery. We now report the first successful catheter-based coronary bypass procedure in a human.

Methods

The PICVA Procedure

A series of specialized catheters and implantable devices (TransVascular, Inc) are required to perform the PICVA procedure. These catheter-based devices can be divided into the following 4 categories:

1. Coronary sinus and subslective guiding catheters, which were developed to access the coronary sinus and then maintain a stabilization platform for devices to be intro-
1. Coronary sinus catheterization is performed using a Sones catheter with an integrated phased-array IVUS imaging element. The catheter is introduced into the coronary sinus and the branching coronary venous system.

2. TransAccess catheters, which are unique devices designed to introduce a guidewire from one vessel to another (from artery to adjacent vein and vice versa) with precision and control. The TransAccess catheters are guided through vascular segments using fluoroscopy, and vessel-to-vessel targeting is performed using an integrated intravascular ultrasound (IVUS) guidance system (Figure 1).

3. Flow-directing/blocking devices and delivery systems for deliberate total occlusion of targeted venous segments; they prevent shunting of arterial inflow back to the coronary sinus and into the right atrium.

4. Channel creation and maintenance devices, which are designed to be delivered over a 0.014-inch arteriovenous guidewire and are used to create a permanent conduit between the vessels.

In addition to the above devices, standard angioplasty guides are used to support the devices entering the coronaries from the aorta, and standard PTCA balloon catheters are used at several stages to predilate and postdilate the connection between the arterial and venous vessels.

Each procedure begins with a standard coronary artery injection, with sufficient filming time to observe the delayed venous phase. While providing an important visual landmark indicating the location of the coronary sinus outlet into the right atrium, this initial step also provides a venous phase road map and a baseline visual correlation between the adjacent venous and arterial anatomy. Virtually all of the major left-sided epicardial coronary arteries have an adjacent companion vein (Figure 2).

From the femoral approach, a diagnostic catheter is introduced into the right ventricle and withdrawn across the tricuspid valve while being rotated in a clockwise direction. This directs the tip posterior, and the catheter will usually fall into the coronary sinus. After the coronary sinus is selectively catheterized, a guidewire is introduced and a special coronary sinus guide catheter is delivered over the wire and positioned in the proximal coronary sinus. This catheter serves to maintain access throughout the procedure and provides sufficient back support to advance blocking devices into the venous vasculature.

After wiring the proximal portion of the diseased coronary artery to be bypassed, a 6F TransAccess catheter is advanced over the wire through an arterial guiding catheter to the desired channel spot. An integrated phased-array IVUS system facilitates the targeting of the adjacent companion vein. With the vein located by the TransAccess IVUS array, a 24-gauge nitinol needle is obliquely delivered from the shaft of the catheter, exiting the artery and entering the targeted venous segment. A 0.014-inch exchange-length guidewire is then threaded from the artery to the vein. The needle is withdrawn, and the TransAccess catheter is removed over the exchange wire. Using a small PTCA balloon, the intervessel channel is first predilated and then a novel connector device is placed between the 2 vessels. This stent-like connector is then postdilated with a semicompliant balloon to approximate the intended diameter. The channel is created in the subadventitia, and hemorrhage into the pericardial space does not occur.

In the final step, an implantable blocking device is deployed in the venous system to isolate the arterialized conduit from the rest of the venous anatomy and prevent steal through the coronary sinus to the right atrium. Arterialized blood will thus be forced to retroperfuse the myocardial tissue in the distribution of the bypassed vessel. The completed procedure is schematized in Figure 3.

**Case Report**

A 53-year-old diabetic German man presented with class IV angina. The patient had difficulty completing an exercise test, developing chest pain at 50 to 80 W on the exercise bicycle. The ECG changes were nondiagnostic. A stress-sestamibi perfusion scan revealed an old apical infarct with a bordering region of apical ischemia. Coronary angiography was performed, and the patient was found to have a chronic total occlusion in the region of the mid-left anterior descending artery (Figure 4). Attempts to cross the total occlusion with a series of angioplasty guidewires were unsuccessful, and the patient was referred for surgical consultation. Because the distal left anterior descending coronary artery was diffusely diseased and a poor target for aortocoronary bypass, it was determined that the patient would not be an appropriate candidate for surgery. The patient was subsequently enrolled as a subject in the phase I safety trial of PICVA, which is currently being conducted at the Krankenhaus der Barmherzigen Brüder in Trier, Germany. The protocol for this phase
I study was reviewed by the German Ethics Committee in Freiburg and commenced with their approval. The patient gave informed consent for the PICVA procedure.

**Interventional Procedure**

The patient received minimal sedation and was given boluses of heparin to achieve an activated clotting time between 280 and 300 seconds. A 9F sheath and a 16F introducer sheath were placed in the right femoral artery and vein, respectively. An initial angiogram and limited coronary IVUS examination revealed a suitable parallel vein within 3 mm of the proximal portion of the coronary artery. Using a 5F AL1 angiographic catheter, the coronary sinus was engaged and a 0.035-inch hydrophilic guidewire was introduced into the coronary sinus. Once the wire was positioned in the anterior interventricular vein, a 16F CS2 coronary sinus guide catheter and introducer (TransVascular, Inc) were advanced over the 0.035-inch guidewire and positioned in the coronary sinus. Through the coronary sinus guide, a subselective delivery catheter and introducer (TransVascular, Inc.) were delivered deeper into the venous system, providing direct access to the region between the great cardiac vein and the anterior interventricular vein. Through a 9F VL3.5 Voda guide catheter (Boston Scientific/SciMed) positioned at the ostium of the left main coronary artery, a 6F TransAccess catheter (TransVascular, Inc) was advanced into the proximal coronary vessel.

The vein was then identified using the ultrasound imaging array on the TransAccess catheter, and a targeting pointer was positioned toward the adjacent vein. The nitinol needle was advanced through the arterial wall into the vein, and a 0.014-inch-high torque floppy exchange guidewire (Guidant Vascular Intervention) was passed through the needle and positioned in the distal anterior interventricular vein. The needle was retracted, and the TransAccess catheter was removed, leaving the exchange wire between the proximal coronary vessel and the anterior interventricular vein. A 3.5-mm Ninja PTCA balloon (Cordis) was used to predilate the channel between the vessels. After channel dilatation, a 3.5/4.0×23 mm self-expanding TransVascular Connector (arterial diameter, 3.5 mm; venous diameter, 4.0 mm) was introduced into the channel and positioned between the vessels. The connector was deployed by a retractable sheath delivery system. The channel was postdilated with a high-pressure 4.0-mm angioplasty balloon and then inspected for proper dimension and apposition with IVUS.

To prevent the shunting of blood to the coronary sinus, a 5-mm TransVascular Venous Blocker was delivered through the subselective venous catheter and released around the junction of the anterior interventricular vein and great cardiac vein.

At the end of the case, flow through the channel and graft appeared normal (TIMI 3; Figure 5). There were no periprocedural complications. Fluoroscopy time was 66 minutes, and ~500 cc of contrast was used.

A postoperative transthoracic echogram confirmed the absence of effusion or blood within the pericardial space. The patient had an uncomplicated postprocedural course and was free of angina in the hospital. Postoperative medications included aspirin 325 mg and clopidogrel 75 mg daily. To ensure that there were no unexpected postprocedural adverse events, the patients was kept in the hospital for 5 days of observation. Before discharge, the patient could perform at a level of 150 W on the treadmill without angina.

At 3-month follow-up, the patient was well and remained free of angina. On stress testing, the patient performed at 125 W without exercise-induced chest pain. Stress-sestamibi scanning revealed improved perfusion in the region bordering the infarct. A 3-month follow-up angiogram confirmed a
patent connector and normal flow through the venous graft (Figure 6).

At the time of this report, 12 months after the procedure, the patient is free of angina and has not developed an infarction. His medications include ramipril 2.5 mg, bisopridal 5 mg, aspirin 100 mg, spironolactone 100 mg, and furosemide 20 mg alternating with 40 mg daily. He had been on a similar diuretic regimen before the procedure.

Discussion

Diffuse coronary artery disease is commonly associated with severe angina. Chronic total occlusions, small vessels, and nondiscrete atheromatous disease present formidable challenges for both surgical bypass and angioplasty. Physicians have recently explored novel revascularization strategies in attempts to palliate ischemic symptoms in these patients.

Clinical trials of transmyocardial laser revascularization have yielded variable and incomplete angina relief for most patients.2–7 Although the mechanism for their putative benefit is controversial, these surgical and percutaneous laser procedures are widely believed to create clinical benefit through angiogenesis at the treatment sites.8 A more direct approach for angiogenesis has relied on the delivery of genes encoded for angiogenic and vasculogenic growth factors into ischemic myocardium. Limited data from small trials again suggest variable and incomplete clinical responses.9–13

We hypothesize that the inconsistent clinical responses from these procedures stem from inadequate inflow of arterial blood into the newly developed microvasculature. In the absence of adequate inflow, angiogenic strategies may only create small, nonperfusion capillary tufts in the ischemic zones, without significant improvement in perfusion.

We pursued PICVA with the belief that the coronary veins would be good alternatives for carrying oxygenated blood to ischemic regions. Despite the extremes of arterial atherosclerosis, the adjacent veins are rarely diseased. A redundant drainage system (epicardial collaterals and the Thebesian system) allows for the blockage of drainage through the coronary sinus and retroperfusion of the heart muscle.24 Retroperfusion via the coronary sinus has been a standard method of myocardial preservation during cardiopulmonary bypass for decades.15

Before the advent of coronary bypass, surgeons experimented with arterializing the coronary veins to relieve angina. In the 1940s, Beck et al16,17 suggested that the coronary veins could be grafted and used to deliver oxygenated blood in a retrograde fashion. The Beck II procedure was a staged procedure in which an arterial segment or venous graft was placed directly between the aorta and the coronary sinus, resulting in global retroperfusion of the heart. To avoid a significant arteriovenous fistula, the proximal portion of the coronary sinus was partially tied off. Beck and colleagues perfected this technique in animals and eventually performed it on nearly 200 patients suffering from severe ischemic heart disease. The researchers reported promising results; however, the high operative mortality of the procedure and other complications limited its acceptance.

In the 1970s, several surgeons reported on the application of a technique where either internal mammary artery grafts or aortosaphenous vein grafts were used to arterialize selected vein segments associated with ischemic regions of myocardium.18–21 They demonstrated the basic safety and feasibility of the technique after other authors had established the physiological mechanism of retroperfusion in animals.22–24 Although these anecdotal reports offered promising results, with many patients experiencing partial or complete relief of anginal symptoms, the surgical approach was inexplicably abandoned.

We recognized the potential for percutaneous venous arterialization using catheter-based technology and developed the concept in a series of animal studies.25 The initial human feasibility trial focuses on no-option patients, because they represent the most appealing patient group from an ethical standpoint.

This first successful case does not validate the concept. We do not yet know the durability of the arteriovenous channels or the long-term capability of the venous system to serve as a conduit for pulsatile arterial blood. Anecdotal experience with a limited surgical population is encouraging. A European and US multicenter trial of PICVA is contemplated after completion of the phase I safety and feasibility trial.

Limitations

This patient represents the first successful case of PICVA, although the procedure was attempted on one patient before this index patient. The procedure in that patient was not successful because of our inability to cross into the venous system due to a tortuous venous system. Several more patients have been attempted with mixed success. A more complete evaluation of PICVA technology will be appropriate when a larger clinical experience is collected. This report attempts to outline the result of the first successful PICVA patient.
As we learn more about these enabling devices, we foresee the potential for complete in situ bypass in patients with good distal coronary vessels. Percutaneous in situ coronary artery bypass is illustrated in Figure 7. Proximal and distal connections can be made using the TransAccess catheter from the venous side, creating a true bypass and potentially opening this technology to a much larger group of patients with chronic total occlusions, repetitive restenosis, and degenerative vein graft disease. Percutaneous in situ coronary artery bypass trials await unambiguous demonstration of catheter safety and durable clinical benefit in the PICVA subset.

Acknowledgment

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References

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