CARDIOVASCULAR

Intramyocardial Left Ventricle-to-Coronary Artery Stent: A Novel Approach for the Treatment of Coronary Artery Disease

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Background. **The direct intramyocardial left ventricle-to-coronary artery stent may provide an optional minimally invasive technique for coronary artery bypass graft surgery. We seek to test whether blood flow and regional myocardial function improve with this stent in totally ischemic myocardium.**

Methods. **The stent device was implanted in 8 anesthetized dogs using an open chest approach, arteriotomy of the proximal left anterior descending coronary artery, and connection of the vessel to the left ventricular chamber. Regional coronary blood flow and myocardial function were monitored under three conditions: normal coronary flow (baseline), coronary ligation, and stent flow.**

Results. **Left anterior descending coronary ligation markedly reduced coronary artery blood flow and regional myocardial function. With flow solely from the stent, the blood flow pattern changed to one with high peak forward flow during systole compared with baseline (94.8 ± 48.9 versus 56.8 ± 21.1 mL/min; $p < 0.05$) and one with significant negative backflow during diastole compared with baseline (−37.4 ± 23.1 versus 11.3 ± 17.2 mL/min; $p < 0.05$). However, the resultant mean forward flow increased to approximately 50% of baseline compared with less than 5% of baseline after coronary ligation. Regional myocardial function diminished entirely after coronary ligation, but recovered to approximately 60% of baseline with the stent. Normal systemic hemodynamics and global ventricular contractile function were maintained with the stent.**

Conclusions. **The left ventricle-to-coronary artery stent is a simple and readily deployable device that allows the perfusion of epicardial vessels directly from the left ventricle and can provide significant blood flow to improve the performance of ischemic myocardium. It may provide an effective, alternative means of treating coronary artery disease when standard coronary artery bypass graft surgery is not suitable.**

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More than 800,000 coronary artery bypass graft (CABG) procedures are performed each year to relieve symptoms and increase survival among patients with coronary artery disease [1]. Currently, CABG is still the most common surgical operation performed in the United States with half a million procedures performed annually [2]. Most of these cases are done with an open chest approach, use multiple native, biologic grafts, and include the use of cardiopulmonary bypass. Recent developments in total myocardial revascularization have enabled surgeons to perform this procedure without the use of the heart-lung machine in select patients through an operation termed off-pump CABG [3]. The benefits of off-pump CABG in select patient groups are clear and have paved the way toward novel approaches of revascularizing the myocardium. A more recent investigational strategy has been developed to facilitate total myocardial revascularization through the use of a device that establishes blood circulation between the left ventricle (LV) and a highly stenotic coronary artery—VSTENT (Percardia, Inc, Merrimack, NH) [4, 5]. This unique device is able to be deployed during off-pump CABG or traditional CABG using cardiopulmonary bypass.

To supply oxygenated blood to the coronary vasculature, the VSTENT establishes a direct channel from an epicardial coronary artery to the LV chamber. With the VSTENT in place, the normal blood flow relationship between the LV and the newly shunted epicardial coronary artery is altered because forward flow occurs primarily during systole, and, in the absence of any native or

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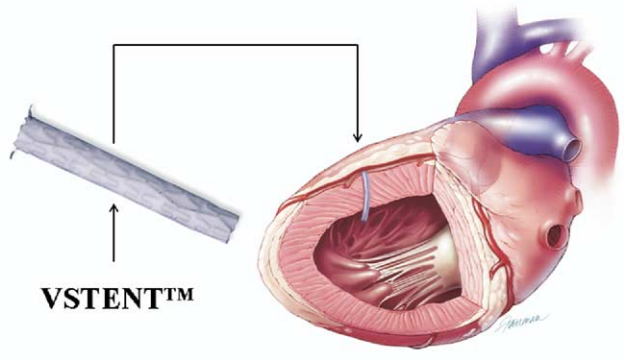

Fig 1. The VSTENT myocardial implant is placed through the myocardium to establish a connection between the coronary artery and the left ventricle.

stent valves, there is substantial backflow from the coronary artery to the LV.

The concept of using the LV as a source of oxygenated blood has been previously reported, although results suggested flow was insufficient to prevent ischemia [6–8]. In one particular study, high flow rates were reported, but these values were not correlated with improvements in regional function [9]. In a previous study by our group, we examined the concept of ventricular–coronary artery flow by the use of an extracorporeal off-artery device [4]. These results showed feasibility in such a way that enough net forward flow could be provided to prevent further myocardial ischemia and support regional myocardial function. In the present study, a VSTENT device amenable to minimally invasive delivery and deployment was assessed for its ability to preserve coronary blood flow and regional myocardial function in the face of varying levels of coronary occlusion.

Material and Methods

Studies were performed in compliance with the "Guide for the Care and Use of Laboratory Animals" by the Institute of Laboratory Animal Resources, National Research Council (Washington, DC), 1996. This study was approved by the Institutional Animal Care and Use Committee of Columbia University. The study was supported by the manufacturer of the VSTENT device, Percardia, Inc, which otherwise took no role in the design or control of the study, or the collection or interpretation of these data.

Device and Implantation Approach

The VSTENT device is a balloon-deployable, stainless steel, expanded polytetrafluoroethylene–covered stent, similar to traditional coronary stents (Fig 1). Its diameter is 2.5 mm, and it comes in five different lengths (14, 18, 21, 25, and 28 mm). For all animals in this study, the 25-mm length was sufficient to extend beyond the thickness of the myocardial wall. The device is implanted by means of a coronary arteriotomy between the first and second diagonal branches of the left anterior descending (LAD) coronary artery by using off-pump CABG surgery stabilization techniques. When implantation is complete, the VSTENT forms a 2.5-mm diameter direct channel between the LAD and the LV chamber through the intervening myocardium.

Surgical Procedure

Eight adult mongrel dogs of either sex weighing 26 to 32 kg were used in this study. Aspirin (325 mg oral) was administered daily for 3 days before surgery. Anesthesia induction was carried out with thiopental (5 to 7 mg/kg intravenously) and maintained with 1.5% to 2.0% inhaled isoflurane. Catheter-tip transducers (Millar Instruments, Inc, Houston, TX) were inserted into the LV and descending aorta through the right and left carotid arteries to measure LV pressure and aortic pressure, respectively. A 10- to 15-cm left thoracotomy was performed through the fifth intercostal space, and the pericardium was opened. A transit-time ultrasonic flow probe (Transonic Systems Inc, Ithaca, NY) was placed on a distal segment of the LAD to measure coronary artery blood flow. A pair of sonomicrometry crystals was placed mid-myocardium into the region supplied by the VSTENT (Sonometrics Corp, London, Ontario, Canada) to monitor segment shortening. All data were recorded by a digital sonomicrometry system (frequency approximately 200 Hz).

Before implantation of the VSTENT device, the dog was anticoagulated with 10,000 U of heparin intravenously. A 6-mm coronary arteriotomy was made and an intravascular shunt was placed for distal coronary artery protection. The VSTENT was then inserted into the underlying myocardium. This was accomplished with a delivery system by placing a needle through the arteriotomy and posterior wall of the artery, through the myocardium, and into the ventricle. A guide wire was inserted through the needle and into the LV, and the needle was removed. The VSTENT was premounted onto a balloon catheter and delivered until its upper edge was flush with the floor of the artery. This precise placement was achieved using a seating tool. The VSTENT was then

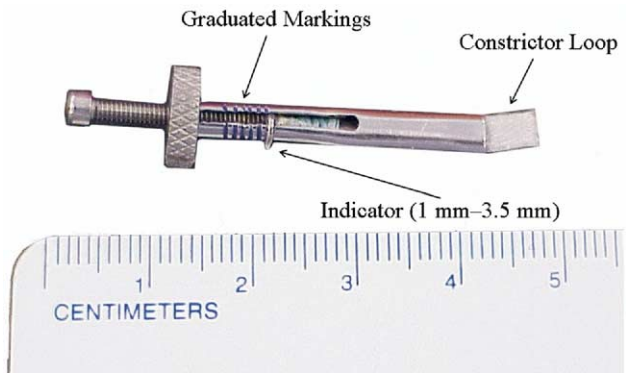

Fig 2. A microconstrictor device occludes the left anterior descending coronary artery proximal to the VSTENT in stepwise fashion to induce upstream coronary artery stenosis.

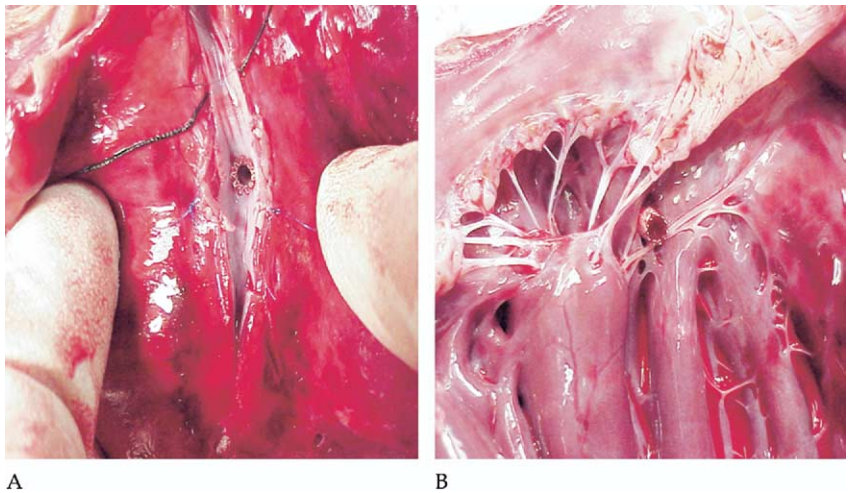

Fig 3. Deployment of the VSTENT. (A, epicardial view) Proper seating of the VSTENT with its flared head at the bottom of the coronary artery. (B, left ventricular chamber view) VSTENT expanded by a balloon to form a channel between the left ventricle and the left anterior descending coronary artery.

expanded with an inflation tool, resulting in a strong compression fit within the myocardium. The entire implantation procedure took approximately 2 minutes. A piece of pericardium was used for patch repair of the arteriotomy. Once the shunt and VSTENT balloon were removed from the artery, complete arteriotomy closure was achieved by quickly tightening the sutures and securing the knot.

Experimental Protocol

Left ventricular pressure, electrocardiographic data, aortic pressure, LAD flow distal to the VSTENT, and regional segment length were measured at three time points—baseline, immediately after LAD ligation, and after VSTENT implantation. In all 8 dogs, a post-LAD ligation baseline was measured by transiently ligating the LAD before VSTENT implantation. Once hemodynamic values were obtained, the LAD was released to allow time for the arteriotomy, VSTENT insertion, and patch closure procedures. With the VSTENT in place, LAD ligation was again carried out—completely in the first 4 dogs and to varying degrees in the remaining 4 dogs. The gradual occlusion of the LAD in the latter 4 dogs was achieved with a mechanical microconstrictor device (Fig 2) to simulate a chronic proximal LAD stenosis. This permitted observation of blood flow through the VSTENT and characterization of flow pattern changes according to serial degrees of stenosis. Hemodynamic measurements were then repeated after both VSTENT implantation and LAD ligation.

Data Analysis

All data were digitized at 200 Hz and analyzed offline. Recorded signals were analyzed to determine regional pressure–segment length relations. As an index of regional LV systolic function, regional preload recruitable stroke work was computed. This was calculated by re-

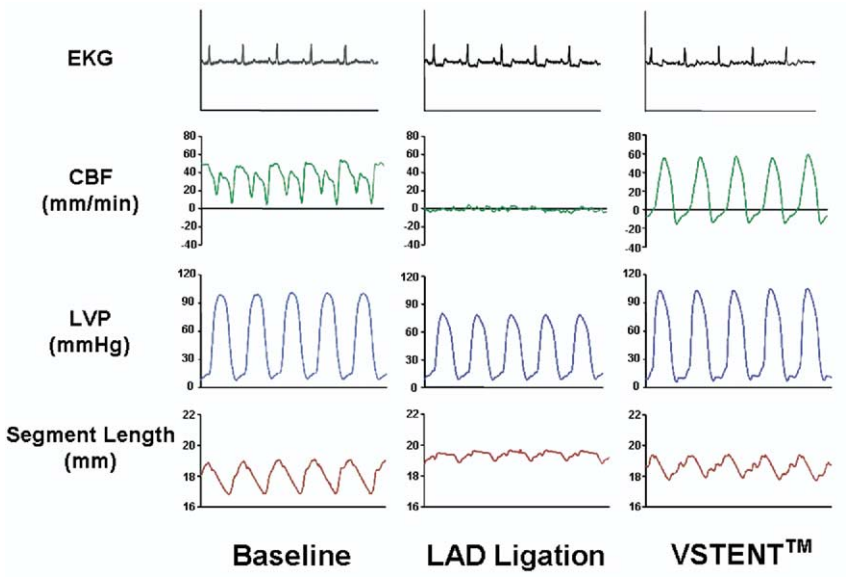

*Fig 4. Hemodynamic variables at baseline, after left anterior descending (*LAD*) coronary artery ligation, and after VSTENT implantation. On deployment of the VSTENT, coronary blood flow (*CBF*), left ventricular pressure (*LVP*), and regional contractile function improved significantly. (*EKG *= electrocardiogram.)*

Table 1. Hemodynamic Measurements (n = 8)

Variable	Baseline	LAD Ligation	VSTENT
LVP (mm Hg)	93.6 ± 8.2	82.7 ± 12.2[a]	94.4 ± 10.5[b]
LV dP/dt (mm Hg)	1575.4 ± 806.3	1195.0 ± 352.5	1650.0 ± 751.0
Systolic AoP (mm Hg)	89.6 ± 9.3	76.0 ± 8.2[a]	84.5 ± 8.3[b]
Diastolic AoP (mm Hg)	58.7 ± 9.3	44.7 ± 5.5[a]	49.4 ± 6.4
Mean AoP (mm Hg)	70.6 ± 9.0	56.5 ± 4.8[a]	62.7 ± 5.2[b]

[a] $p < 0.05$ versus baseline. [b] $p < 0.05$ versus LAD ligation.

All values expressed as mean ± standard deviation.

AoP = aortic pressure; LAD = left anterior descending coronary artery; LV dP/dt = left ventricular pressure/time differential; LVP = left ventricular pressure.

gional stroke work (pressure–segment length loop area) divided by end-diastolic segment length.

Statistics

All data are presented as mean and standard deviation. Statistical comparisons were performed by variance analysis for randomized block design with post hoc tests.

Results

Deployment of the VSTENT

Figure 3 shows a representative deployment of the VSTENT. The VSTENT was secured by a flare at the device end, which helped seat it properly with the posterior wall of the coronary artery (Fig 3A). The other side of the VSTENT terminates inside the LV chamber (Fig 3B), allowing blood communication through the 2.5-mm-diameter stent channel.

Impact of the Device on Systemic Hemodynamics

Electrocardiographic data, LAD blood flow, LV systolic pressure, and myocardial regional segment length were assessed at baseline, immediately after LAD ligation, and after VSTENT implantation (Fig 4, Table 1). Left anterior descending ligation completely attenuated LAD blood flow, causing decreased LV systolic pressure and impaired regional contractile function as evidenced by LV bulging and paradoxical motion during systole. Once the VSTENT was deployed, coronary blood flow, LV systolic pressure, and myocardial regional contractile function improved significantly.

Impact of the Device on Coronary Blood Flow

Under normal baseline conditions, peak coronary blood flow occurred during diastole and there was continued positive flow during systole without backflow. After VSTENT placement, coronary blood flow was characterized by a peak forward flow during systole and negative backflow during diastole (Fig 4). This large backflow resulted in a reduced net mean forward flow.

Ligation of the LAD completely eliminated blood flow in the distal coronary artery. Flow through the VSTENT was higher during systole compared with baseline, but there was also significant negative backflow during the diastolic phase. Although the net mean coronary blood flow was lower than that of baseline, the VSTENT restored approximately 52% of baseline blood flow after LAD ligation. Coronary blood flow characteristics at baseline, after LAD occlusion, and after VSTENT placement are summarized in Table 2.

Regional Myocardial Contractility

Regional myocardial function was assessed by the relationship between LV pressure and segment length. The pressure–segment length loop area to end-diastolic segment length was used as an index of regional myocardial contractile function. Figure 5 shows representative LV pressure–segment length loops. The dark gray loops represent regional function at baseline. After LAD ligation (black loops), the pressure–segment length loops were shifted to the right and the normal rectangular shape of these loops disappeared, indicating regional myocardial bulging and paradoxical motion caused by

Table 2. VSTENT Coronary Blood Flow Patterns (n = 8)

Variable	Baseline	LAD Ligation	VSTENT
Peak LADF (mL/min)	56.8 ± 21.1	3.6 ± 4.1[a]	94.8 ± 48.9[ab]
Minimum LADF (mL/min)	11.3 ± 17.2	−2.6 ± 3.0[a]	−37.4 ± 23.1[ab]
Mean LADF (mL/min)	37.9 ± 16.6	1.6 ± 2.4[a]	18.4 ± 8.6[ab]
Forward LADF (μL/beat)	312.3 ± 140.6	12.5 ± 21.2[a]	416.1 ± 573.9[b]
Backward LADF (μL/beat)	−0.6 ± 1.8	−3.7 ± 2.5[a]	−135.5 ± 212.9[ab]

[a] $p < 0.05$ versus baseline. [b] $p < 0.05$ versus LAD ligation.

All values expressed as mean ± standard deviation.

LAD = left anterior descending coronary artery; LADF = left anterior descending coronary artery flow.

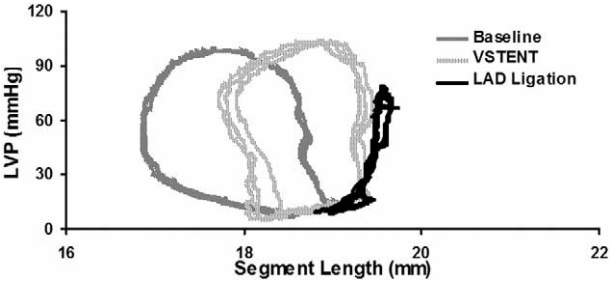

*Fig 5. Left ventricular pressure (*LVP*)–segment length loops at baseline, after left anterior descending (*LAD*) coronary artery ligation, and after VSTENT placement. After VSTENT placement, the loops and end-systolic point underwent a marked leftward shift and there was an increase in regional stroke work performed.*

myocardial ischemia. With partial restoration of coronary blood flow by the VSTENT, regional myocardial function was also partially restored, as indicated by the enlarged pressure–segment length loops and leftward shift of these loops (light gray) toward the baseline position.

After LAD ligation, both regional coronary blood flow and regional myocardial function were significantly blunted. VSTENT restored blood flow to 46% of normal, and regional myocardial function recovered to approximately 66% of baseline.

Impact of Proximal Left Anterior Descending Stenosis on VSTENT Flow

A coronary artery microconstrictor device (Fig 2) was used in 4 dogs to serially occlude the LAD (five graded steps, equivalent to 30%, 55%, 75%, 90%, and 98% stenosis) proximal to the VSTENT and to induce varying degrees of upstream coronary artery stenosis. Baseline measurements were made before and after implantation of the VSTENT. Left anterior descending blood flow remained unchanged by the device in the absence of proximal LAD constriction. There was no backward flow measured by the flowmeter so long as the proximal LAD remained open. After gradual proximal LAD occlusion, the difference between peak and trough (backward) coronary blood flow was increased. The characteristic VSTENT flow pattern was triggered even with minimal coronary stenosis (Fig 6).

Comment

Blood flow through the VSTENT placed distal to an acutely occluded LAD was characterized by peak forward flow during systole and significant backflow during diastole. Under such conditions, VSTENT restored approximately 50% of normal coronary blood flow and approximately 60% of normal regional myocardial function. Systemic hemodynamic variables were restored by the VSTENT in the face of acute ischemia. Overall, the VSTENT proved to be a practical device and was easy to deploy.

In our previous study, regional myocardial function and coronary blood flow were shown to increase through

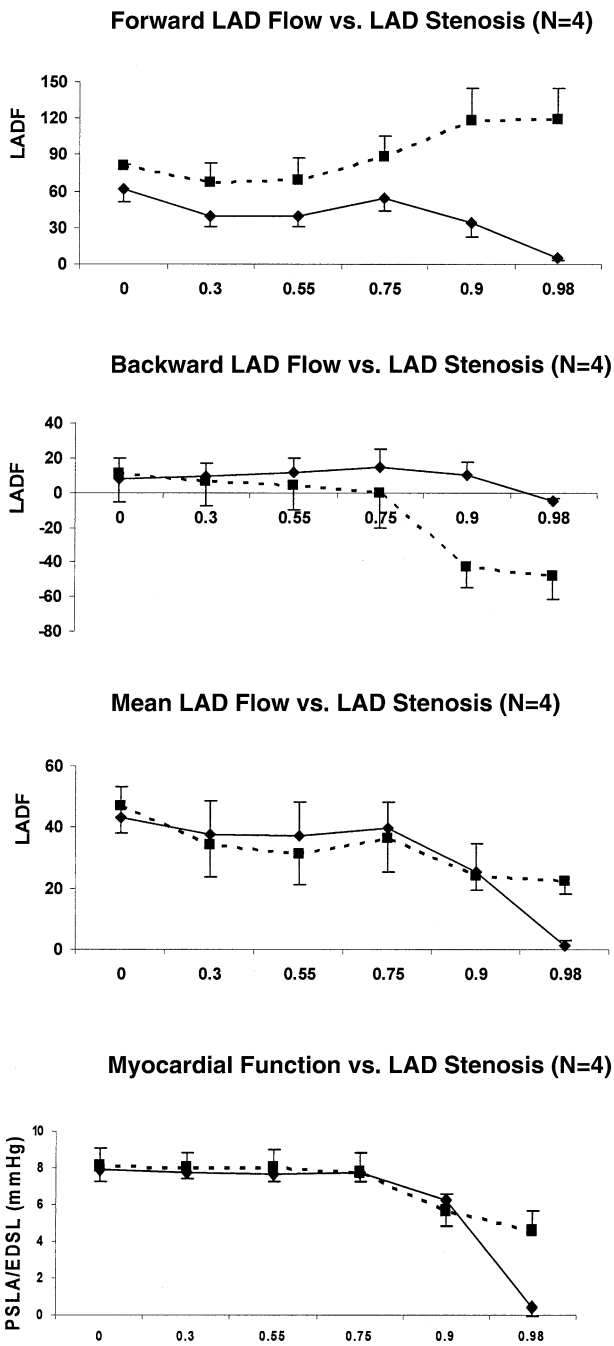

*Fig 6. Changes in VSTENT flow patterns and regional myocardial function according to graded left anterior descending (*LAD*) coronary artery stenosis. After stepwise occlusion of the left anterior descending coronary artery (30%, 55%, 75%, 90%, 98%) by the microconstrictor device, the gradient of peak and minimal (backward) coronary blood flow was increased. The characteristic VSTENT flow pattern was triggered once the critical stenosis point was reached. Regional myocardial function was partially restored with VSTENT. ◆ = control; ■ = VSTENT. (*EDSL = *end-diastolic segment length;* LADF = *left anterior descending coronary artery flow;* PSLA = *pressure–segment length loop area.)*

the use of an extracorporeal ventricle-to-coronary artery bypass device. Both flow and function were increased further when a Starling flow resistor was implemented to reduce backward diastolic flow [4]. Although this approach offered significant advantages, from a practical standpoint, the device was not readily translatable to clinical application. In contrast, a readily deployable covered stent has been developed, tested, and shown to provide hemodynamic benefits to an extent that could prove to be clinically meaningful. This novel device design features much less blood-contacting surfaces as well as a shorter circuit, resulting in lower flow resistance properties within the circuit itself.

The rationale behind the development of the VSTENT device was to provide an alternative revascularization strategy that addresses the limitations CABG may impose on certain patients. Examples in which the traditional CABG approach is limited include instances in which there is a lack of acceptable native tissue available for grafting, unacceptable anastomotic targets such as heavily calcified aortas and coronary vessels, patients with an increased risk of morbidity because of vessel harvesting, and extended operating times when performing multiple anastomotic procedures. In principle, the VSTENT could be deployed by minimally invasive techniques and offers several unique advantages—an anastomosis does not need to be created with either the aorta or the target vessel, native tissue conduits do not need to be harvested, and the surgical procedure can be shortened significantly. It is possible that with select coronary lesions, the VSTENT can be deployed through a mini–left thoracotomy. As technology and minimally invasive instruments improve further, the VSTENT may even bear application through robotic surgery approaches. Current minimally invasive techniques achieve the goals of smaller incisions and decreased postoperative pain, but are still restrained by the need to identify and harvest suitable conduits. The VSTENT eliminates this often time-consuming step, and, consequently, may offer a surgical alternative to patients who are otherwise deemed inoperable. The VSTENT may therefore provide the cardiac surgeon with a novel approach to treat increasingly complex patients who present late in the course of their disease.

A recent article describing the first clinical experience with the VSTENT in 12 patients suggests the left ventricle-to-coronary artery bypass procedure is feasible and potentially safe with a short-term follow-up interval of 9 $\pm$ 5 days [10]. A mean time of 23 minutes was required for VSTENT implantation in these patients, but these intervals were shortened with increased experience with the device. Patch closure was also performed (11 saphenous vein, 1 radial artery), and none of the patches showed intraoperative bleeding, required revision, or exhibited narrowing in the postoperative angiograms.

A particular concern that was raised before this study was whether the absence of a total occlusion proximal to the VSTENT might result in significant backward flow from the coronary artery to the LV. In theory, this would occur during diastole because, with no impediment to backward flow, a "steal" phenomenon from coronary blood flow might ensue that would potentially adversely affect net perfusion. The present study addressed these concerns, however, as the VSTENT was able to maintain at least 50% of net forward mean blood flow under conditions ranging from partial (approximately 75%) stenosis to complete stenosis.

Backward coronary flow through the VSTENT occurred at LAD stenoses greater than 75%, yet forward flow was sufficiently high at these levels of stenoses to result in a net positive mean flow. At LAD stenosis greater than 90%, the mean flow curves of the control and VSTENT groups diverge, such that the VSTENT continues to achieve net positive mean flow whereas the control group declines to a no-flow state. Perhaps more clinically relevant is the fact that this net forward flow was able to maintain regional contractile function of greater than 60% of normal. With 60% of regional function sustained, the global function of the LV and systemic hemodynamic variables fell within normal range. These findings are in concurrence with other ventricular sourcing studies in which systolic inflow is predominant and negative backward flow is initiated at 70% to 77% LAD stenosis after ventricle-to-coronary artery bypass [5]. Our study shows how proximal subtotal stenosis regulates VSTENT perfusion from the LV and upstream coronary blood flow. With partial proximal LAD stenosis, regional myocardial function and blood supply were more preserved than with total LAD occlusion. In essence, this correlation undermines the concept that a coronary artery steal from proximal LAD occlusion can result in a net decrease in myocardial perfusion. Ultimately, the combination of forward and backward coronary flows through the VSTENT with varying levels of LAD stenoses was adequate to sustain meaningful regional myocardial function. Whether that regional function can be maintained for longer periods will be the focus of future related studies.

Study Limitations

The current feasibility study was carried out solely in the acute setting, and, as such, the long-term impact of the VSTENT device on coronary artery flow patterns as well as on the anatomic and physiologic properties of the subtended vascular bed are yet unknown.

In this study, although we used a mechanical microconstrictor device for the establishment of chronic proximal LAD stenosis, a technique that achieved accurate, consistent results, we acknowledge that at least 19% of the entire blood flow to the subserved region of myocardium is derived from preformed collateral blood vessels. This is particularly true with canine species as opposed to the porcine or ovine species. As such, it is possible the targeted area of myocardium was not as ischemic as intended, and any restoration of regional myocardial function may be imprecisely attributed to the VSTENT device.

The proper function of the VSTENT device requires a patent distal coronary vessel to shunt ventricular blood flow downstream. In this regard, it simulates the mech-

anism of CABG surgery, only using a different blood source. However, it does not contend with the purported mechanism of transmyocardial laser revascularization, which creates direct channels within the myocardium itself irrespective of patency of distal coronary vessels. In fact, transmyocardial laser revascularization is often used as an alternate revascularization procedure when traditional bypass procedures are either contraindicated or unfeasible.

Future studies are warranted to explore the chronic effects of the VSTENT, particularly in regard to regional and global cardiac function when the device is implanted in the chronically ischemic myocardium. Chronic device patency will also need to be demonstrated. There may, in fact, be heightened potential for thrombosis at either end of the VSTENT, which may stem from a combination of atypical blood flow patterns (forward and backward flow), foreign material construct, small internal diameter, and a relatively long channel length. Recent experience with antiproliferative agents in improving small diameter stent patency may provide important insights to this issue.

It is known that the myocardium changes its thickness by as much as 20% to 30% throughout the cardiac cycle in conjunction with systole and diastole. Although the VSTENT is positioned so that its coronary end is seated securely against the base of the vessel, it remains unclear whether, and to what extent, the stent moves during myocardial contraction, either by projecting into the artery or further into the ventricular chamber. Again, a chronic, survival study using the VSTENT in a similar setting would be able to determine the answer to this question.

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