Stent-Based Approach for Ventricle–to–Coronary Artery Bypass

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Background—Ventricle-to–coronary artery bypass (VCAB) is an experimental revascularization procedure that provides predominantly systolic instead of diastolic blood flow to a coronary artery.

Methods and Results—In a pig model, a stent-based procedure (VSTENT) was developed to create a VCAB. After thoracotomy, a covered VSTENT was implanted between the left ventricle and the left anterior descending coronary artery (LAD). Distal LAD flow, regional myocardial function, and intracoronary pressures were determined at different degrees of LAD stenosis and during complete LAD occlusion. During 3 hours of LAD occlusion, VSTENT preserved net forward flow at 70±6% and regional myocardial function at 71±8% of baseline. Preservation of net flow was influenced by the positioning of the VSTENT, with higher preservation also under conditions of increased oxygen demand if a "valve-like mechanism" was present during diastole. At a hemodynamically relevant level of LAD stenosis (>70%), systolic inflow was predominant after VSTENT implantation. Changes in mean diastolic intracoronary pressure that resulted from different degrees of LAD stenosis were linearly correlated to net flow after VSTENT implantation ($r=0.88$; $P<0.001$).

Conclusions—VSTENT for ventricle-to–coronary artery bypass was feasible and preserved 70±6% of baseline flow during complete LAD occlusion. The degree of preservation was dependent on the position of the VSTENT creating a valve-like mechanism during diastole. Residual diastolic blood flow through a high-grade LAD stenosis influenced net flow favorably, because diastolic backflow decreased with increasing mean diastolic intracoronary pressure. **(*Circulation*. 2002;106:1000-1006.)**

Key Words: arteries ■ revascularization ■ shunts ■ stents

Ventricle–to–coronary artery bypass (VCAB) is an experimental revascularization procedure providing predominantly systolic instead of diastolic blood flow directly from the left ventricle to a coronary artery. Previous attempts at VCAB were based on artificial conduits such as tubes connecting the left ventricle to the coronary artery.[1–3]

More recently, a rigid transmyocardially inserted titanium tube was introduced and reported to provide 76% of baseline flow in a pig model with proximal occlusion of the coronary artery.[4] Systolic inflow, however, was counteracted by a significant diastolic backflow under these conditions.[4] Similar flow patterns have been observed in a dog model using early VCAB prototypes. Interestingly, regional blood flow and function increased substantially if a Starling resistor was interposed in the VCAB conduit for graded regulation of backward flow.[5] Of note, all of the early VCAB procedures provided blood flow only downstream into the coronary artery because of the complete occlusion at the site of VCAB connection. Apparently, blood supply to the coronary artery upstream and downstream of the connection would be favorable, as experienced from conventional bypass surgery.

Aiming at a VCAB procedure that combines upstream and downstream systolic blood supply with some restriction to diastolic backflow, we developed a stent-based approach for minimally invasive surgical insertion (VSTENT). Using this approach, we were able, for the first time, to also determine the influence of different degrees of proximal stenosis and thus residual diastolic blood flow of the native vessel on flow characteristics and functional consequences of VSTENT implantation.

Methods

The present investigation was carried out according to the *Guide for the Care and Use of Laboratory Animals* published by the US National Institutes of Health and was approved by the Bavarian Animal Care and Use Committee.

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Twenty German farm pigs (49±5 kg) were premedicated with clopidogrel 300 mg PO and aspirin 300 mg PO the day before the intervention. Anesthesia was induced by ketamine (500 mg IM) and azaperone (10 mg/kg IM) and maintained by intravenous midazolam and piritramide and inhaled Enflurane 0.5% to 2.0%.[6] Heparin 20,000 IU IV was injected before catheterization, followed by continuous 5000 IU/h IV infusion.

Access to the heart was through a sternotomy. Echocardiography (Vingmed) at the surface of the heart was used to locate the target site for device insertion through the left anterior descending coronary artery (LAD). The angle of insertion and the thickness of the myocardium as well as such anatomic structures as the mitral valve and papillary muscles were determined. The LAD was dissected (2 to 3 mm) from the epicardium distal to the first diagonal branch for later insertion of the VSTENT. An ultrasonic flow probe (Transonic) was placed 2 to 3 cm distal to the first diagonal branch. Regional myocardial function was determined by sonomicrometry (HSE) in the LAD region distal to the second diagonal branch.[7]

Regional myocardial blood flow was measured with fluorescent microspheres.[8] Microspheres ($n=1\times10^7$) were injected into the left atrium (Molecular Probes). Reference blood samples were withdrawn from the abdominal aorta (4.1 mL/min). Three transmural myocardial probes from the LAD region supplied by the VSTENT were obtained 1 cm (proximal), 2 cm (mid), and 3 cm (distal) distal to the implant and from the control region. Each transmural probe was divided into 3 layers (epicardial, midmyocardial, and subendocardial). Tissue sample digestion and fluorescence measurement were carried out in an automated sample-processing unit using single-tube filtration.[8] For assessment of global left ventricular function (left ventricular end-diastolic pressure, dP/dt_{max}), a pressure-tip catheter (SPG-572, Millar) was placed into the left ventricle. A pressure wire (RADI) was used for assessment of intracoronary pressure.

VCAB by VSTENT

A stent-based approach was used for creating a conduit between the left ventricle and the LAD. The left coronary artery was catheterized, and the distal LAD was wired (0.014 ACS). At the previously determined site of insertion for the VSTENT, a needle was punctured through the LAD into the left ventricle. The direction of the puncture was perpendicular to the LAD or up to 30° oblique toward the basis of the ventricle. Direct visualization of graduated markings on the hollow needle indicated the depth of insertion. After the left ventricle had been wired, the needle was replaced by a 4F arterial sheath. An expanded polytetrafluoroethylene–covered stent (VSTENT, Percardia) of a predetermined length (mean 22±3 mm) was mounted onto a 3.0-mm balloon and inserted through the 4F sheath into the myocardium. The VSTENT was retracted under fluoroscopic control until the proximal end of the VSTENT was in line with the posterior wall of the LAD. After VSTENT delivery, the deflated balloon was removed. A previously placed epicardial monofilament suture was used for closure after removal of the sheath. The integrity of the LAD and the patency of the VSTENT were confirmed by fluoroscopy (Figure 1).

In a prospective series of experiments (n=10), the positioning of the VSTENT was randomized to be within the LAD (group C, n=5) or to be ≈1.0 to 1.5 mm below the posterior wall of the LAD (group D, n=5). Distinct VSTENT positioning was possible by placing the VSTENT on a 3.0-mm balloon (30-mm length, 2 markers) with the VSTENT (20 to 26-mm length) starting at the site of the first marker of the balloon (group C) or 1.0 to 1.5 mm distal to the first marker of the balloon (group D). After the VSTENT had been placed through the sheath at the projected site of implantation, the balloon was first inflated at 2 to 3 atm, leading to some extension of the balloon at both ends, where the VSTENT was not mounted. The small inflation of the balloon proximal to the first marker was used to place it at the floor of the LAD. Thus, the first marker of the balloon was in line with the floor of the LAD. Depending on the distance from the VSTENT to the first marker, full inflation of the balloon (16 atm) resulted in a position of the VSTENT within the LAD (group C) or beyond the floor of the LAD (group D).

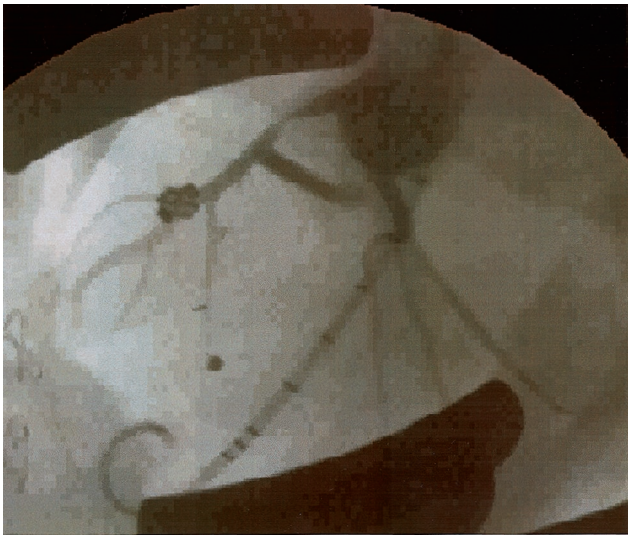

Figure 1. Angiogram of left coronary artery after VSTENT insertion and induction of a high-grade proximal LAD stenosis by an externally sutured stent. Contrast agent fills distal LAD as well as VSTENT, which drains into left ventricular cavity during diastole. Ultrasonic flow probe placed ≈1.5 cm distal to VSTENT. Pig-tailed Millar tip catheter placed in left ventricular cavity.

Study Protocol

Baseline measurements were performed after sternotomy and 15 minutes after placement of the left ventricular catheter, the flow probe, the ultrasonic crystals, and the intracoronary pressure wire. The proximal LAD was occluded completely for 60 seconds (control occlusion) with a PTCA balloon in all pigs. After placement of the VSTENT, measurements were repeated without balloon occlusion of the LAD. Subsequently, the LAD was completely occluded, which was confirmed by fluoroscopy. All measurements were repeated 10 minutes after complete LAD occlusion. In 5 pigs (group A), the LAD was kept occluded for 3 hours. After 3 hours of ischemia, regional myocardial blood flow was determined by microsphere injection.

In another 5 pigs (group B), the balloon in the proximal LAD was deflated, allowing reperfusion for 30 minutes. Thereafter, the proximal LAD was partially occluded with different sizes (2.5, 3.0, and 3.5 mm) of semicompliant balloons as well as different inflation pressures (6, 8, 10, 12, and 16 atm) in a randomized sequence. The degree of stenosis was calculated by dividing the cross-sectional area for the actual balloon diameter and inflation pressure (balloon diameters verified by a caliper after the experiment) by the cross-sectional area of the balloon size at total occlusion of the vessel. Each balloon size was held for 2 minutes, and intracoronary pressure recordings in the distal LAD were taken.

Thereafter, the LAD proximal to the VSTENT was stented with an intracoronary stent (9 mm length, AMG) at the site of the previous balloon inflations with the same balloon size and inflation pressure as during complete balloon occlusion of the LAD. An external suture was placed around the vessel at the site of the intracoronary stent to create a stable high-grade stenosis of the proximal LAD. The suture was tightened and fixed at a degree of stenosis that was similar to the 84% to 90% stenosis observed during the partial occlusions of the proximal LAD by balloon inflation. Flow measurements were repeated 3 hours after induction of this high-grade LAD stenosis.

At the conclusion of the experiment, all pigs were killed and the heart was excised. The position of the VSTENT in relation to the posterior wall of the LAD was documented by use of a longitudinal view and a perpendicular view.

In groups C and D, atrial pacing (90–110–130 bpm) was performed at baseline and after induction of a high-grade stenosis (87% to 92%) of the proximal LAD as described above. After the measurements, the stenosis was eliminated by inflation of an appropriate balloon. After implantation of the VSTENT, atrial

TABLE 1. Performance of VSTENT During Complete LAD Occlusion

	Baseline (n=10)	LAD− (60 s) (n=10)	LAD+/VSTENT+ (n=10)	LAD−/VSTENT+ (10 min) (n=10)	LAD−/VSTENT+ (180 min) (n=5)
LAD flow					
Net flow, mL/min	25.1±1.8	0	31.7±2.3*	17.6±2.3*	17.8±2.5*
Net flow, % baseline	100	0	127.5±5.5*	70.2±5.6*	70.9±6.6*
Flow diastolic, mL/min	21.3±1.4	0	20.1±1.5	−10.4±1.9*	−10.5±1.9*
Flow systolic, mL/min	3.8±0.7	0	11.6±2.6*	28.0±3.6*	28.3±2.9*
Regional myocardial function					
Segment shortening, %	32.0±2.3	3.6±2.1*	30.6±2.9	23.2±3.3*	23.9±3.5*
Segment shortening, % baseline	100	11.3±7.7*	95.0±3.3	70.5±8.0*	74.6±7.5*
Hemodynamics					
dP/dt_{max}, mm Hg/s	723.4±38.9	597±59.4*	838.4±190.8	599.4±89.7*	605.0±79.7*
LVEDP, mm Hg	8.7±1.2	13.8±3.0*	9.9±3.3	11.3±4.2	11.0±3.5
LV pressure systolic, mm Hg	87.3±3.6	76.5±2.6*	85.2±4.1	77.9±2.9*	79.4±3.9
Heart rate, bpm	70±4.2	70.3±4.7	77.4±4.8	77.3±4.7	76.3±4.8

LAD− indicates complete occlusion of the LAD; LAD+, LAD without obstruction; VSTENT+, VSTENT implanted; and LVEDP, left ventricular end-diastolic pressure.
*$P<0.05$ vs baseline.

pacing was repeated before and after induction of a similar degree of LAD stenosis as well as during complete occlusion of the proximal LAD.

In 3 pigs of group D, a second flow probe was placed distal to the intracoronary stent (later used for induction of the proximal LAD stenosis) but proximal to the VSTENT. Thus, LAD blood flow was measured simultaneously distal and proximal to the VSTENT. LAD blood flow at rest and adenosine ($0.15\ mg \cdot min^{-1} \cdot kg^{-1}$ IC)-induced LAD flow reserve were determined with unrestricted proximal LAD flow before and after implantation of the VSTENT.

Statistics

All data were analyzed with SPSS software. Data are presented as mean±SEM. Differences between time points were assessed with ANOVA. Data obtained during pacing (groups C and D) under different conditions within the same group were compared by ANOVA. Comparisons between groups C and D during high-grade stenosis with and without VSTENT were performed by *t* test. The relationship between mean diastolic intracoronary pressure, degree of LAD stenosis, and net distal LAD flow was analyzed by linear regression using the Pearson's correlation coefficient (*r*). A probability value of $P<0.05$ was considered statistically significant.

Results

Baseline measurements were similar in all groups (A through D). Complete occlusion of the proximal LAD for 60 seconds (Table 1) resulted in cessation of LAD flow and concomitant decrease of regional myocardial function. Intracoronary pressure decreased from 49.4±3.6 to 6.8±2.9 mm Hg (group B, Table 2).

Effects of VSTENT Implantation During Unimpaired LAD Flow

VSTENT insertion was finished within 11±5 minutes after puncture of the LAD. After VSTENT insertion, mean net flow in the distal LAD increased by 28±6% because of a small but consistent systolic inflow that occurred in addition to diastolic flow (Table 1). The conditions of an open VSTENT, unimpaired proximal LAD flow, and atrial pacing resulted in distal LAD flow and regional myocardial function similar to those observed before VSTENT implantation (Figure 2). Interestingly, LAD blood flow measured proximal to the VSTENT (unrestricted LAD flow, VSTENT open) was increased ≈3-fold at rest (72±8 versus 23±4 mL/min, n=3), whereas distal LAD flow was increased by ≈25% at rest (28±5 mL/min). Intracoronary delivery of adenosine resulted in a similar flow reserve measured by the distal LAD flow probe before (ratio 4.5±0.5 compared with baseline, n=3) and after (4.2±0.6) VSTENT implantation.

Effects of VSTENT During Complete LAD Occlusion

During complete occlusion of the proximal LAD, the coronary flow pattern in the distal LAD immediately changed to systolic inflow and diastolic backflow (Figure 3, A and B). Despite complete LAD occlusion (10 minutes), mean net flow was preserved at 70±6% of baseline flow (Table 1). Correspondingly, mean regional myocardial function (subendocardial segment shortening) was preserved at 71±8% (Table 1). Despite preservation of net flow and regional myocardial function, there was a significant decrease in dP/dt_{max} (Table 1).

Net LAD flow of individual pigs ranged between 57% and 85%. Higher net flow (range 72% to 85%, mean 76.6±2%, n=5) was associated with a decrease in diastolic backflow (Figure 3B). In these pigs, the position of the VSTENT was 1 to 2 mm below the coronary artery. Thus, the orifice of the VSTENT did not extend into the floor of the coronary artery (Figure 4B), providing a "valve-like mechanism" by the oval opening formed by the arterial wall. In contrast, the VSTENT was fully expanded into the floor of the coronary artery (Figure 4A) in pigs with lower net flow (range 57% to 62%, mean 60.3±0.8%, n=5, $P<0.05$). Mean diastolic intracoronary pressure in the distal LAD was higher in pigs with a valve-like mechanism of the VSTENT (18±11 mm Hg, n=2) than in pigs without a valve-like mechanism (4±6 mm Hg, n=3).

In a prospective randomized series of experiments, pigs without (group C) or with (group D) a valve-like mechanism

TABLE 2. Performance of VSTENT With High-Grade LAD Stenosis (n=5)

	Baseline	LAD− (60 s)	LAD+/ VSTENT+	Stenosis (70%–76%)	Stenosis (77%–83%)	Stenosis (84%–90%)	Stenosis (91%–97%)	LAD−/ VSTENT+
Distal LAD flow								
Net flow, mL/min	26.0±3.1	0	33.1±3.9*	24.8±2.5	24.1±1.8	20.3±2.8*	18.0±1.5*	17.7±2.7*
Net flow, % baseline	100	0	127.3±4.4*	95.4±6.0	92.7±5.1	78.1±5.5*	69.2±6.7*	68.1±4.4*
Flow diastolic, mL/min	24.2±2.1	0	22.5±2.7	2.2±3.5*	−5.0±1.8*	−9.0±2.2*	−14.4±1.2*	−14.4±1.9*
Flow systolic, mL/min	1.8±1.5	0	10.6±5.4*	22.7±3.1*	29.2±3.5*	29.4±4.3*	32.4±1.4*	32.1±3.7*
Regional myocardial function								
SS, %	31.3±3.1	2.9±3.2*	28.8±2.9	28.2±2.5	25.9±1.9*	26.0±2.4*	21.2±1.9*	20.3±3.9*
SS, % baseline	100	9.3±4.9*	92.0±2.3	90.1±2.0	82.7±2.1*	83.1±2.2*	67.8±2.0*	64.9±3.0*
Hemodynamics								
dP/dt_{max}, mm Hg/s	715.8±47.9	550±68.1*	728.8±116.1	699.2±133.9	671.8±112.0	658.7±69.0	645.4±48.2*	633.8±55.1*
LVEDP, mm Hg	8.6±1.6	14.9±3.7*	8.3±4.0	9.2±2.0	8.7±1.5	9.5±1.4	10.3±1.6	11.2±3.1
LV pressure systolic, mm Hg	84.6±3.3	77.3±3.2*	87.5±4.4	88.8±4.4	85.0±4.5	82.3±5.0	79.0±4.1	79.1±3.4
Heart rate, bpm	61.5±1.7	62.8±3.0	71.8±5.9	71.5±4.7	68.5±3.3	71.5±1.7	77.2±3.8	73.5±7.0
Intracoronary pressure								
Mean diastolic	49.4±3.6	6.8±2.9*	50.2±4.5	33.1±4.2*	22.9±2.3*	21.2±2.0*	15.6±2.5*	15.1±3.7*

LAD− indicates complete occlusion of the LAD; LAD+, LAD without obstruction; VSTENT+, VSTENT implanted; SS, subendocardial segment shortening; and LVEDP, left ventricular end-diastolic pressure.

*$P<0.05$ vs baseline.

of the VSTENT were studied. During high-grade stenosis of the LAD (without a VSTENT), distal LAD blood flow and regional myocardial function decreased during pacing to a similar extent in groups C and D (Figure 2). After VSTENT insertion, distal LAD blood flow increased during pacing under the condition of a high-grade LAD stenosis (Figure 2) and was significantly higher in both groups. In pigs with a valve-like mechanism of the VSTENT (group D), net distal LAD flow was significantly higher than in group C during complete LAD occlusion at rest (73.6±4.1% versus 56.4±3.4% of baseline) and under the condition of a high-grade LAD stenosis during pacing (Figure 2). Preservation of distal LAD flow by the VSTENT during pacing was paralleled by a significant preservation of regional myocardial function under all conditions of complete LAD occlusion or high-grade LAD stenosis.

After 3 hours of complete LAD occlusion, preservation of net LAD flow and regional myocardial function was similar to that observed after 10 minutes of ischemia (Table 1). Systemic hemodynamics, dP/dt_{max}, and left ventricular end-diastolic pressure were preserved at the same level as after 10 minutes of ischemia. Regional myocardial blood flow after 3 hours of ischemia was distributed nonhomogeneously, showing a gradient from the epicardial to the endocardial probes as well as a gradient from the proximal to the distal probes (Figure 5).

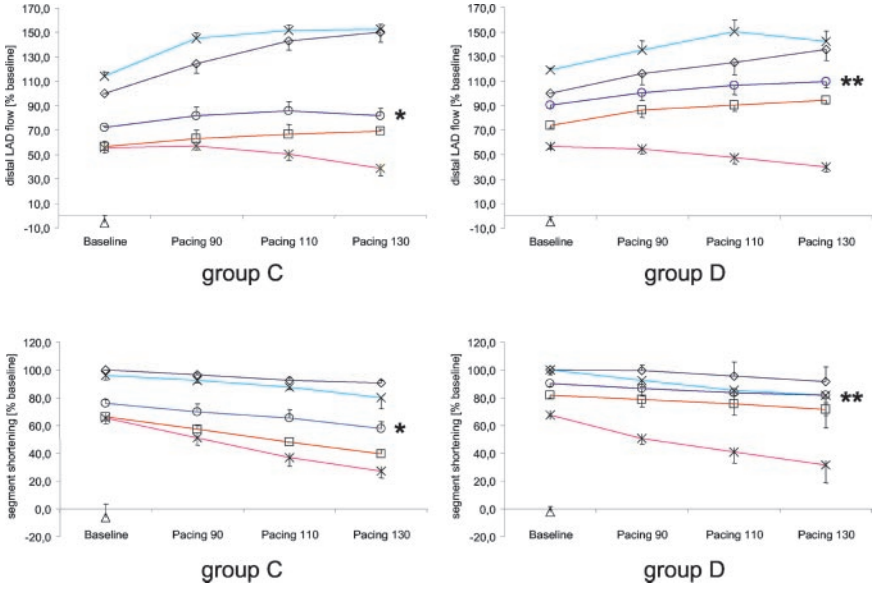

Figure 2. VSTENT performance under conditions of increased oxygen demand (atrial pacing) with (group D) or without (group C) a valve-like mechanism of VSTENT. Mean net distal LAD flow (distal LAD flow) and subendocardial segment shortening determined under different conditions: ◇ (black line), LAD open, no VSTENT; × (blue line), LAD open, VSTENT open; x (pink line), LAD 87% to 93% stenosis, no VSTENT; ○ (dark blue line), LAD 87% to 93% stenosis, VSTENT open; □ (red line), complete proximal LAD occlusion, VSTENT open; Δ, control occlusion of proximal LAD (60 seconds); *$P<0.05$ vs condition x (pink line), LAD 87% to 93% stenosis, no VSTENT; **$P<0.05$ vs condition x (pink line), LAD 87% to 93% stenosis, no VSTENT, and $P<0.05$ vs same condition of group C.

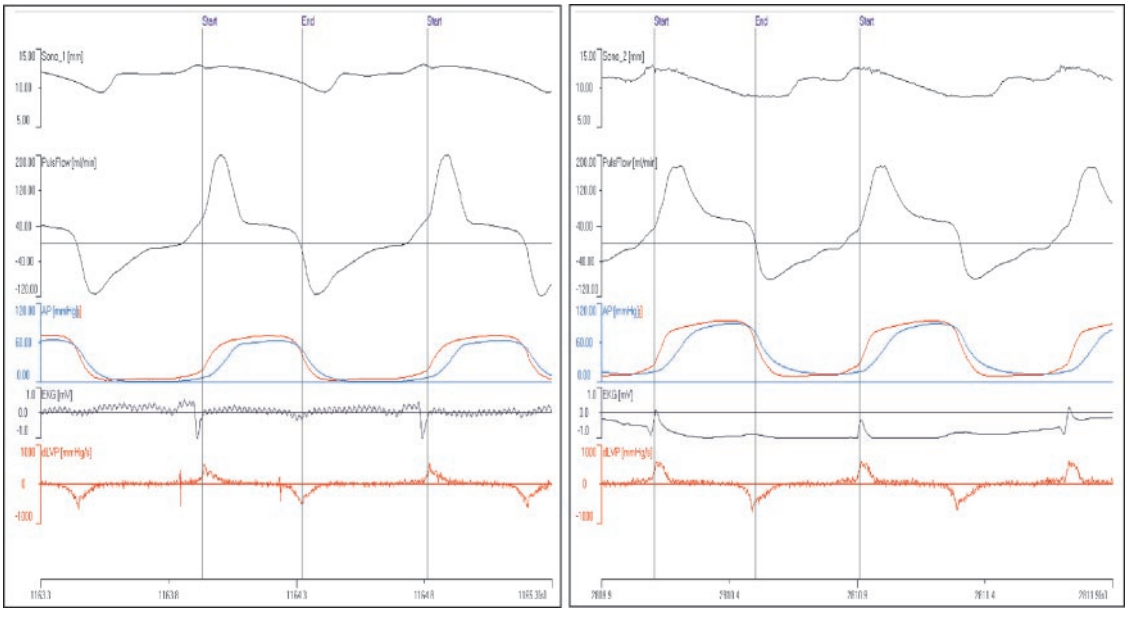

Figure 3. Original recordings of subendocardial segment shortening (Sono_1), LAD flow (PulsFlow), left ventricular (LVP, red line) and intracoronary (AP, blue line) pressures, ECG (EKG), and dP/dt (dLVP): A, during complete LAD occlusion in a pig without a valve-like mechanism; B, during complete LAD occlusion in a pig with a valve-like mechanism.

Effects of LAD Stenosis on Coronary Flow Pattern After VSTENT Insertion

To study the effects of residual diastolic blood flow, the proximal LAD was partially occluded by a short PTCA balloon in group B (n=5). Interestingly, systolic and diastolic coronary flow patterns changed stepwise with each degree of stenosis. In general, lowering the degree of stenosis led to a reduction of diastolic backflow and an increase of net LAD flow (Table 2). The degree of LAD stenosis was inversely related to mean diastolic intracoronary pressure ($r=0.82$). Net LAD flow increased with increasing mean diastolic intracoronary pressure ($r=0.88$; $P<0.001$) (Figure 6). This relationship was observed whether (n=2) or not (n=3) a valve-like mechanism was present. In case of a valve-like mechanism, pigs started at higher mean diastolic intracoronary pressures and net flows during complete occlusion of the LAD.

The degree of balloon-induced stenosis (86±2%, n=5) was similar to the degree of stenosis induced by an externally sutured stent (85±3%, n=5) that was narrowed to a net flow (20.1±3.1 mL/min) similar to that during balloon-induced stenosis (20.3±2.8 mL/min). The effects of a high-grade stenosis on net flow (20.5±3.0 mL/min, n=5) after VSTENT implantation were maintained over 3 hours.

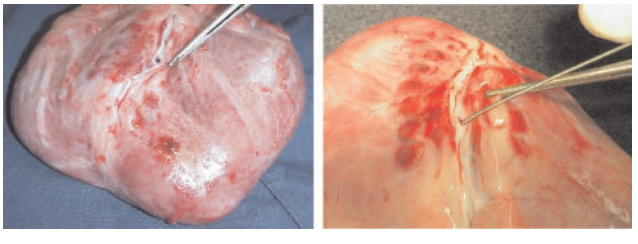

Figure 4. Longitudinal transsection of LAD. A, VSTENT without a valve-like mechanism: VSTENT fully expanded into floor of LAD artery; B, VSTENT with a valve-like mechanism: oval orifice of VSTENT, which was implanted 1 to 2 mm beyond floor of LAD.

Discussion

Technical Considerations of the VSTENT Approach

Previous attempts to perform a VCAB have not focused on a stent-based approach. There were several reasons for choosing this approach, which was well known from endoluminal treatment of coronary artery disease.

First, the device should be easy to implant with minimal trauma to the coronary artery and myocardium, which was realized by a puncture-sheath approach.

Second, VSTENT should provide upstream and downstream flow into the coronary artery in conjunction with a valving mechanism present during diastole.[5] By placing the

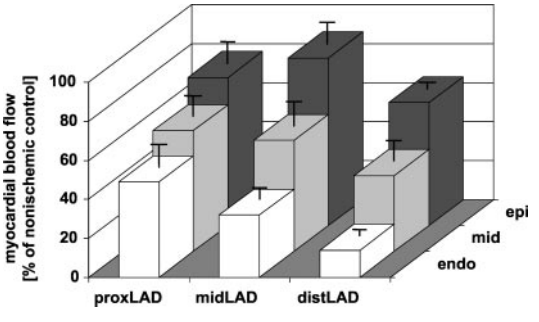

Figure 5. Distribution of regional myocardial blood flow in LAD territory after VSTENT insertion and 180 minutes of complete occlusion of LAD (n=5). ProxLAD indicates proximal LAD distal to VSTENT; midLAD, middle of LAD territory distal to VSTENT; distLAD, distal LAD territory; epi, epicardial; mid, midmyocardial; and endo, endocardial. [%], normalized to average regional myocardial blood flow of left circumflex territory.

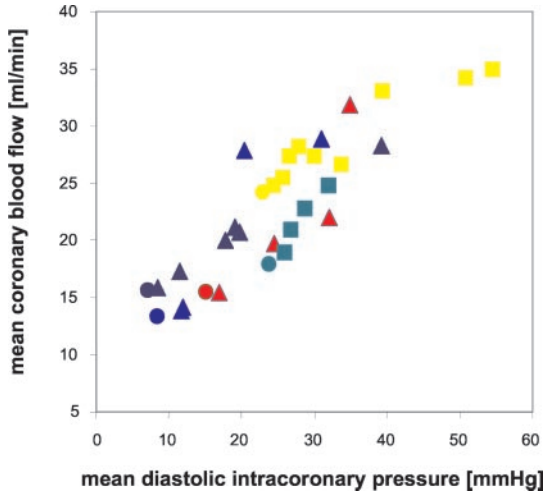

Figure 6. Relationship between net LAD flow and intracoronary pressure determined in distal LAD after VSTENT insertion with different degrees of stenosis of proximal LAD. Each color represents 1 of 5 pigs. Circles represent complete occlusion of LAD. Triangles represent 3 pigs without a valve-like mechanism. Squares represent 2 pigs with a valve-like mechanism. Yellow, $r=0.94$; red, $r=0.95$; blue, $r=0.92$; dark blue, $r=0.92$; green, $r=0.98$; all, $r=0.88$.

stent extraluminally or within the posterior wall of the coronary artery, unimpeded upstream and downstream flow was consistently achieved. In addition, distinct extraluminal placement of the stent orifice provided a valve-like mechanism (Figures 3 and 4).

Third, displacement and external compression of the device and bleeding into the myocardium should be prevented. As a consequence, a first series of balloon-expandable expanded polytetrafluoroethylene-covered stent grafts with a high radial resistance was developed (Percardia) and used in this study. All stents that were deployed successfully remained in place and were expanded completely after 3 hours of ischemia.

Coronary Flow Pattern After VSTENT Insertion Without LAD Obstruction

Because VSTENT insertion did not lead to any significant obstruction of the coronary artery at the site of insertion, it was possible for the first time to the study coronary flow pattern that resulted from diastolic flow through the native LAD and from the VCAB. After VSTENT insertion, there was a small but significant increase of net distal LAD flow. This increased net flow, however, did not change regional myocardial function (Table 1). In addition, the functional response to an increase in oxygen demand by atrial pacing was also not altered, which argues against a functionally relevant steal phenomenon after VSTENT insertion (Figure 2). However, LAD blood flow determined proximal to the VSTENT increased ≈3-fold under resting conditions, indicating that there was a considerable shunt from the proximal LAD through the VSTENT into the left ventricle during diastole. Because proximal LAD blood flow was increased ≈3-fold under resting conditions, intracoronary adenosine resulted in a limited further increase of proximal LAD blood flow. Distal LAD flow reserve, however, was similar to baseline conditions in the presence of the VSTENT. Apparently, an adenosine-induced decrease in vascular resistance of the LAD territory distal to the VSTENT resulted in an appropriate increase in distal LAD blood flow, which was also the case if the functional reserve was tested by atrial pacing (Figure 2).

Performance of VSTENT During Complete LAD Occlusion

During complete occlusion of the proximal LAD, VSTENT provided systolic flow, leading to a net distal LAD flow similar to 70% of baseline (Table 1). The corresponding preservation of regional myocardial function was at a level that would also have been expected under diastolic flow conditions.[9]

Extraluminal VSTENT implantation beyond the posterior wall of the coronary artery resulted in a partial valve-like mechanism, which increased net forward LAD flow by decreasing diastolic backflow. The presence of a valve-like mechanism was supported by the observation that diastolic intracoronary pressure determined in the distal LAD was higher than in pigs without a valve-like mechanism. In a prospective series of experiments, pigs with a valve-like mechanism of the VSTENT (group D) also had a significantly increased functional reserve during atrial pacing compared with pigs without a valve-like mechanism (Figure 2). However, this was still below the baseline conditions with unimpaired LAD flow.

Regardless of the presence of a valve-like mechanism, net flow and regional as well as global myocardial function did not deteriorate after 3 hours of ischemia. Assessment of regional myocardial blood flow by microspheres after 3 hours of ischemia revealed a nonhomogeneous distribution with a gradient from the epicardial to the endocardial and from the proximal to the distal probes (Figure 5). Microsphere techniques have not been validated for bidirectional flow conditions and may yield conflicting results, as demonstrated for the retrograde perfusion of coronary veins.[10] Although bidirectional flow conditions with systolic inflow and diastolic backflow also occurred after VSTENT implantation, the distribution of regional myocardial blood determined in this study might be representative of an ischemic territory completely dependent on the VSTENT, suggesting a moderate subendocardial ischemia, whereas epicardial regional myocardial blood flow was almost normal.

Effects of High-Grade LAD Stenosis on Coronary Flow Pattern After VSTENT Insertion

Another important observation of this study was that residual blood flow through a high-grade stenosis of the native vessel was associated with higher net flow and reduced diastolic backflow compared with the coronary flow pattern observed during complete occlusion of the native vessel after VSTENT implantation. Furthermore, the linear relationship between mean diastolic intracoronary pressure and net flow after VSTENT implantation (Figure 6) points toward a crucial importance of the level of diastolic pressure that is maintained after VSTENT implantation. Regardless of whether diastolic intracoronary pressure increased as a consequence

of residual blood flow through a high-grade stenosis or because of a valve-like mechanism, each of them resulted in an increase in net distal LAD flow. Accordingly, the combination of the two led to the highest preservation of net flow. Also under conditions of increased oxygen demand (atrial pacing) and in the case of a high-grade proximal LAD stenosis, preservation of distal LAD blood flow and regional myocardial function was substantially higher in the presence of a VSTENT with a valve-like mechanism (Figure 2).

Intracoronary pressure and flow measurements also provided evidence that systolic and diastolic flow supported each other with regard to preservation of regional myocardial function of the tissue supplied by the VSTENT. This might be an important distinction from conventional bypass surgery, in which competing diastolic flows through the native vessel and the conduit are known to promote occlusion of the proximal stenotic native vessel.[11–13]

Limitations and Clinical Implications of the Study

Although our data were consistent during short-term acute ischemia (3 hours), they still must be confirmed in a chronic model to study long-term patency of the VSTENT and possible restenotic processes at the site of insertion into the coronary artery and within the VSTENT, in particular with regard to the maintenance of a valve-like mechanism of the VSTENT. Preliminary data (not shown) indicate that a valve-like mechanism of the VSTENT can be maintained in the pig for at least several weeks, which might be supported further by the development of a specifically designed VSTENT.

A model of chronic ischemia might also allow the study of the effects of residual blood flow through a high-grade stenosis and the development of collateral blood flow on intracoronary pressure and the coronary flow pattern after VSTENT implantation.

Whether the implantation of the VSTENT is realized by a minimally invasive surgical (VCAB) and/or interventional approach (VPASS), its clinical usefulness will depend on the net flow provided under resting conditions and during exercise. If residual blood flow through a high-grade stenosis or by collaterals improves net flow after VSTENT implantation in a supportive instead of competitive manner during long-term application as well, it might broaden the potential indications for the device.

Thus, in a long-term perspective, implantation of a VSTENT might be an alternative revascularization procedure for patients with degenerated saphenous vein grafts or a lack of suitable conduits and patients at high risk for conventional bypass surgery or who have had reoperations. A catheter-based percutaneous insertion of the VSTENT (VPASS) after recanalization of an occluded artery or after predilatation of a high-grade stenosis might enable the cardiologist for the first time to treat patients with long lesions or reopened total occlusions with a device implantation into the nondiseased or less diseased part of the distal vessel, similar to bypass surgery.

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