Intraluminal Coronary Shunting Preserves Regional Myocardial Perfusion and Function

(#2003-41143 . . . July 8, 2003)

Jerome Sepic, MD,[1] Jon O. Wee, MD,[1] Edward G. Soltesz, MD,[1]
Rita G. Laurence, BS,[1] Lishan Aklog, MD[2]

[1]Division of Cardiac Surgery, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts; [2]Department of Cardiothoracic Surgery, Mount Sinai Hospital, Mount Sinai School of Medicine, New York, New York, USA

Dr. Sepic

ABSTRACT

Background: Coronary artery hemostasis during off-pump coronary artery bypass (OPCAB) may be achieved with extraluminal coronary occlusion or intraluminal coronary shunting. We sought to determine with a normal porcine beating-heart model whether coronary shunting preserves regional myocardial perfusion and function compared with coronary occlusion.

Methods: Six pigs (50-60 kg) underwent sternotomy and instrumentation. Two pairs of ultrasonic crystals were placed in the distribution of the left anterior descending (LAD) and left circumflex (LCx) arteries for measurement of fractional change in area (FCA), an index of regional contractility. Regional myocardial blood flow (RMBF) was determined with radiolabeled microspheres. Data were recorded for each animal at baseline and after LAD arteriotomy and vascular control with (1) a 1.5-mm intraluminal shunt, (2) proximal occlusion, and (3) proximal and distal occlusion.

Results: One pig experienced ventricular fibrillation during LAD manipulation and was excluded from the study. Data were summarized for the remaining 5 animals. Coronary shunting maintained RMBF and function (FCA) compared with baseline. Proximal occlusion led to 50% (P = .05) and 47% (P = .04) decreases in RMBF and FCA, respectively, in the LAD region. Proximal and distal occlusion led to 55% (P = .03) and 51% (P = .02) decreases in RMBF and FCA, respectively, in the LAD region. There were no significant changes in RMBF or FCA in the LCx (control) region.

Conclusion: Intraluminal coronary shunting is capable of preserving distal myocardial perfusion and function in a normal porcine heart. Coronary occlusion, in contrast, significantly reduces regional perfusion and function. More frequent use of intracoronary shunting may facilitate OPCAB by minimizing ischemia and hemodynamic compromise.

Received July 1, 2003; accepted July 8, 2003.

Address correspondence and reprint requests to: Jerome Sepic, MD, Division of Cardiac Surgery, Brigham and Women's Hospital, 75 Francis St, Boston, MA 02115, USA; 1-617-432-2005; fax: 1-617-432-0606 (e-mail: jsepic@partners.org).

INTRODUCTION

Recent technical advances have allowed multivessel coronary artery bypass grafting (CABG) to be performed more frequently without the use of cardiopulmonary bypass (CPB). Potential benefits of off-pump CABG (OPCAB) compared with conventional CABG with CPB may include reduced neurocognitive dysfunction [Diegeler 2000], myocardial injury [Penttila 2001], postoperative length of stay, hospital costs, and transfusion rate [Puskas 1999].

Coronary artery hemostasis during OPCAB has been achieved most frequently with extraluminal coronary occlusion using silicon vascular loops or sutures. Low-profile, pliable intraluminal coronary shunts are now available and provide the surgeon with a bloodless anastomotic field while, in theory, maintaining some degree of coronary perfusion to the myocardium distal to the anastomotic site.

Some surgeons have argued against routine use of intraluminal shunts in OPCAB [van Aarnhem 1999]. In most patients, brief periods of extraluminal coronary occlusion are generally well tolerated. Some authors have questioned whether shunts are capable of generating enough nutritive flow to prevent ischemia. Others have raised concern about possible endothelial injury and difficulty suturing around the shunt.

Surgeons in favor of routine intracoronary shunting point to several potential benefits of this approach. Insertion of a shunt has, at least anecdotally, successfully reversed clear-cut ischemia that occasionally develops during occlusion of the right coronary artery or any large collateralizing vessel. This finding suggests that shunts *are* capable of providing adequate nutritive flow. Patients undergoing coronary occlusion without obvious electrocardiographic or hemodynamic changes may have low-grade ischemia, particularly to the subendocardium, and the ischemia may make it more difficult to manipulate the heart and maintain hemodynamic stability. This issue may be particularly important in patients with poor left ventricular function and those with subcritical stenosis with poor collateral formation. The detrimental effects of the cumulative ischemic burden may make off-pump grafting progressively more difficult in these patients. These surgeons also argue that, with appropriate attention to sizing, modern intracoronary shunts can be inserted atraumatically and can actually protect the endothelium from the effects of the mister-blower, which can be used sparingly. Finally, with surgeons' experience, intracoronary shunting can actually facilitate precise suturing by "presenting" the vessel, protecting against "back-walling" the vessel, and providing a handle (the string) for countertraction and exposure of the edge of the vessel.

Only a few studies to date have examined the effects of intracoronary shunting, and they focused on the use of echocardiography for assessment of regional myocardial function [Dapunt 1999, Lucchetti 1999]. In this study we sought to compare the effects of coronary occlusion and shunting on regional myocardial perfusion *and* on function. Our hypothesis was that shunting would preserve regional blood flow and, as a direct result, regional function, whereas coronary occlusion would compromise both.

MATERIALS AND METHODS

Animals received humane care in compliance with the *Principles of Laboratory Animal Care* published by the National Institutes of Health (NIH publication no. 86-23, revised 1985). Six Yorkshire pigs of either sex weighing 45 to 50 kg were used in this study.

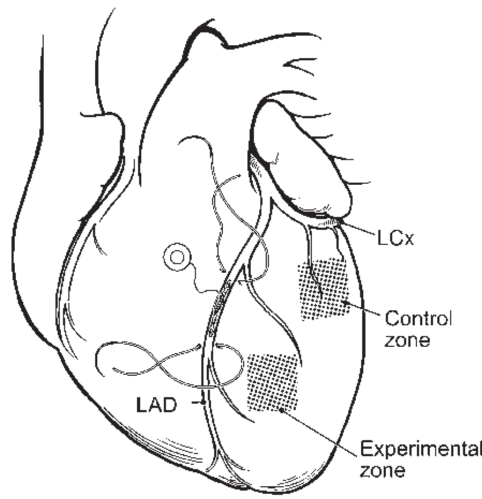

Figure 1. Illustration of the intraluminal coronary shunt in the left anterior descending artery (LAD) with relaxed proximal and distal extraluminal vascular loops. The LAD (experimental) and the left circumflex artery (LCx) (control) regions are shaded.

Surgical Preparation and Instrumentation

After premedication with intramuscular tiletamine-zolazepam (Telazol) (5 mg/kg), the animals were intubated and mechanically ventilated (Drager, Telford, PA, USA). Anesthesia was maintained with 2% isoflurane and 100% O_2. Electrocardiogram was continuously recorded. Central venous access was established via the left internal jugular vein. A 16-gauge catheter was inserted in the left femoral artery for subsequent reference blood sampling. Intravenous $MgSO_4$ (2 g) and lidocaine (50 mg) were given to prevent ventricular arrhythmias. Four thousand units of heparin were administered to each animal. After median sternotomy, the pericardium was incised, and the heart was suspended in the pericardial cradle with retention sutures.

A 5F pressure transducing catheter (Micro-Tip; Millar, Houston, TX, USA) was inserted directly into the left ventricle through a small apical stab incision and held in place with a pursestring suture. An electromagnetic flow probe (Carolina Medical Electronics, King, NC, USA) was positioned around the aortic root, and flow was measured with a square-wave electromagnetic flowmeter (Carolina). A 16-gauge catheter was inserted in the left atrium for subsequent microsphere injections.

Experimental Protocol

Data were collected in each animal during 4 different experimental phases:

1. Baseline control;
2. LAD arteriotomy with coronary shunt placement;
3. Removal of the coronary shunt, extraluminal occlusion proximal to the LAD arteriotomy; and
4. Extraluminal occlusion proximal and distal to the LAD arteriotomy.

For each of the phases, hemodynamic data were collected at least 5 minutes after the specified intervention. The arteriotomy (approximately 5-8 mm) was made distal to the first diagonal branch of the LAD. For phase 2, a 1.5-mm–diameter intraluminal coronary shunt (FloCoil; Guidant, Menlo Park, CA, USA) was inserted directly through the arteriotomy. The FloCoil shunt consists of an internal coil with tapered tips and an offset tab for positioning and removal. For phase 3, after coronary shunt removal, a Vas-Ties (Sil-Med, Taunton, MA, USA) Silastic vascular loop was placed around the LAD between the first diagonal branch and the arteriotomy site on the LAD. For phase 4, an additional occluding vascular loop was placed approximately 1 cm distal to the LAD arteriotomy (Figure 1).

Regional Myocardial Function

The ischemic zone was defined as the area between the LAD and the first diagonal branch of the LAD. The nonischemic zone was defined as the area between the first and second obtuse marginal branches of the left circumflex (LCx) coronary artery (Figure 1). Two pairs of 2-mm 1.5-MHz piezoelectric ultrasonic crystals (Sonometrics, London, ON, Canada) were placed in the subendocardium in a rectangle configuration, approximately 1 cm apart, in both the ischemic and nonischemic zones. Each pair of crystals was perpendicular to the other pair. A sonomicrometer (Sonometrics) was used to transduce the crystal signals. Fractional change in area (FCA), an index of regional contractility, was determined in both the ischemic and the nonischemic zones during each experimental phase: FCA = (End-diastolic area – End-systolic area)/End-diastolic area.

Regional Myocardial Perfusion

Regional myocardial blood flow (RMBF) was determined in the ischemic and nonischemic zones of all 6 animals with stable-labeled microspheres by an established technique [Bartrum 1974].

Table 1. Comparison of Regional Myocardial Perfusion*

	LAD (Experimental Region)				LCx (Control Region)			
	Baseline	Shunt	Proximal Occlusion	Proximal + Distal Occlusion	Baseline	Shunt	Proximal Occlusion	Proximal + Distal Occlusion
Mean ± SD, mL/min per gram	0.44 ± 0.18	0.46 ± 0.17	0.22 ± 0.22	0.20 ± 0.16	0.43 ± 0.20	0.43 ± 0.13	0.40 ± 0.17	0.35 ± 0.09
P†		.82	.05	.03		.95	.59	.35

*LAD indicates left anterior descending artery; LCx, left circumflex artery.
†Relative to baseline values.

A 16-gauge catheter in the left atrium was used for injection of 15-µm microspheres (BioPal, Worcester, MA, USA). The 16-gauge catheter in the left femoral artery was used for reference blood sample collection. A different isotope of microspheres was used in each of the 4 different experimental phases. The microsphere suspensions were sonicated for 15 minutes and shaken for 2 minutes prior to injections. Each injection was performed over 10 seconds, approximately 10 million microspheres being injected in a volume of 10 mL. Reference blood sample collection was performed at a rate of 9.8 mL/min with a withdrawal pump (Harvard, South Natick, MA, USA). Blood sample collection was started 10 seconds prior to each injection and carried out 2 minutes after its completion. After explantation of the heart, transverse sections of the ischemic and nonischemic zones were obtained. Each of the heart samples was weighed, and microsphere count was determined (BioPhysics Assay Laboratory, Worcester, MA, USA) along with the reference blood samples. RMBF (mL/min per gram) for each section was determined by multiplying the heart sample microsphere count by the known reference withdrawal rate and dividing by the reference blood sample microsphere count.

Data Collection and Analysis

For each experimental phase, data were acquired over multiple cardiac cycles during steady-state conditions. At least 5 cardiac cycles were used to calculate each parameter, and data runs containing ectopic beats were excluded. Analog data from the electrocardiogram (ECG), left ventricular pressure transducer, and aortic flow probe were digitized. These digital hemodynamic data and the digital piezoelectric crystals data were stored on a personal computer via a TRx series transceiver unit (Sonometrics) using SonoLAB software (Sonometrics).

Statistical Analysis

All data are presented as mean ± SD and as percentage of baseline control. One-way analysis of variance with adjustment for replicate measures in each animal was used to compare values under each condition. Statistical analysis was performed with Stata version 7 software (Stata, College Station, TX, USA). Significant differences compared with baseline values were established at $P < .05$.

RESULTS

Of the 6 animals, 5 survived the entire experiment without arrhythmia or need for inotropic support. One animal experienced unstable ventricular arrhythmia during the proximal coronary occlusion portion of the experiment, needed electrical cardioversion, and was not used in the final data analysis. Data from the remaining 5 animals were used to compare regional myocardial function and perfusion. Experimental data and control data were obtained from the LAD and the LCx artery regions, respectively. In all animals, both coronary shunting and extraluminal coronary occlusions provided adequate and comparable coronary hemostasis.

Regional Myocardial Perfusion

The effects of coronary and extraluminal coronary occlusion on RMBF are summarized in Table 1. In the LAD (experimental) region, coronary shunting preserved RMBF. In this same region, RMBF decreased 50% ($P < .05$) relative to baseline with proximal occlusion and 55% ($P = .03$) with proximal and distal occlusions (Figure 2A). There were no significant changes in RMBF in the LCx (control) region (Figure 2B).

Regional Myocardial Function

The effects of coronary shunting and extraluminal coronary occlusions on FCA, an index of regional contractility, are summarized in Table 2. In the LAD (experimental) region, coronary shunting resulted in no significant change in FCA compared with baseline. In the same region, proximal occlusion resulted in a 47% ($P = .04$) decrease, and proximal and distal occlusion resulted in a 51% ($P = .02$) decrease in FCA compared with baseline (Figure 3A). There were no significant changes in FCA in the LCx (control) region (Figure 3B).

DISCUSSION

Although OPCAB has become increasingly popular, the best technique for obtaining coronary hemostasis during the performance of the anastomosis remains a point of debate. A bloodless field is essential for anastomotic precision during OPCAB and may be achieved by either extraluminal coronary occlusion or intraluminal coronary shunting. The purpose of this study was to compare intraluminal coronary shunting and extraluminal coronary occlusion with regard to regional myocardial perfusion and function in a normal porcine beating-heart model. Our hypothesis was that coronary shunting would maintain perfusion and function in myocardium distal to the coronary arteriotomy and that extraluminal occlusion would compromise both myocardial perfusion and function

The key results of this study are that, in a normal porcine beating-heart model, (1) proximal occlusion of the LAD, with

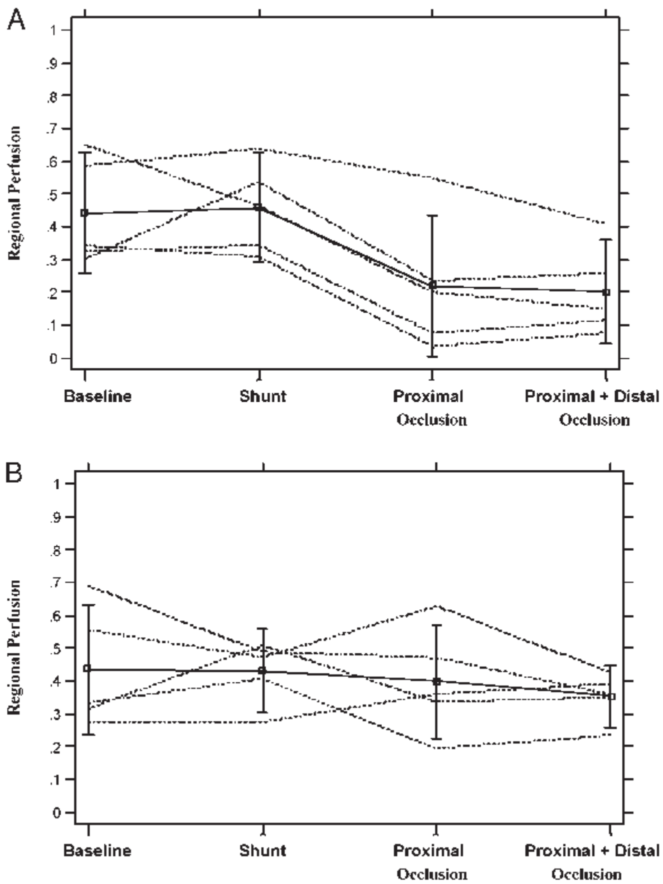

Figure 2. Regional myocardial blood flow at baseline, with left anterior artery (LAD) shunting, and with LAD occlusion(s). A, Experimental (LAD) region. B, Control (left circumflex artery) region. Regional perfusion (milliliters per minute per gram). Solid line indicates mean ± 95% confidence interval; dashed line, individual animals.

or without distal occlusion, resulted in approximately 50% reduction in distal myocardial perfusion and a similar decrease in regional contractility, and (2) intraluminal shunting maintained regional contractility in the LAD distribution. We used sonomicrometry to determine differences between shunting and coronary occlusion in terms of effect on FCA, an index of regional contractility. The regional contractility in the control LCx coronary artery distribution did not significantly vary during these LAD interventions. This finding confirmed the fact that these data were reflective of regional LAD rather than global ventricular function. Our results support those of other studies that had similar findings with echocardiography [Dapunt 1999].

The degree of mechanical trauma to the coronary artery and the significance of any endothelial disruption with these techniques, however, are not completely defined. In comparison with nonelastic sutures, elastic occlusion sutures have been shown to reduce coronary endothelial injury [Okazaki 2001]. Regardless of the type of device used, extraluminal occlusion in human coronary arteries may cause endothelial disruption, microthrombosis, and plaque rupture [Hangler 2001]. Perrault et al demonstrated that, in healthy porcine coronary arteries, extraluminal occlusion produces no endothelial dysfunction but that intracoronary shunts cause significantly greater endothelial dysfunction [Perrault 1997, Perrault 2000a]. In a porcine model mimicking atherosclerotic coronary arteries, Perrault et al showed *no* difference in endothelium-dependent coronary relaxation with shunting compared with extraluminal occlusion [Perrault 2000b].

The effects of transient ischemia associated with extraluminal coronary artery occlusion depend on several factors, including (1) the artery being occluded, (2) location of occlusion, (3) duration of occlusion, (4) amount of preexisting blood flow in the artery, and (5) degree of collateral blood flow.

Critics of shunting claim that OPCAB procedures can be performed safely with coronary occlusions and that shunting adds little, if any, benefit. However, both clinical and research studies have shown evidence that coronary occlusion may result in ischemia and associated hemodynamic compromise. Dapunt et al, who used a healthy porcine model, reported echocardiographic and metabolic myocardial marker data that suggested significant myocardial stunning with transient coronary occlusions. In contrast, intraluminal shunting under similar conditions minimized ischemia/reperfusion injury and preserved ventricular function [Dapunt 1999]. In an echocardiographic study of patients undergoing OPCAB, Lucchetti et al found significant left ventricular dysfunction with transient occlusion of the LAD and a return to baseline function on reperfusion. Intracoronary shunting was found to preserve left ventricular function during graft anastomosis [Lucchetti 1999]. Recently, Gandra and Rivetti compared coronary occlusion and intraluminal shunting in a healthy porcine beating-heart model to assess regional myocardial ischemia. The shunted group, compared with the temporary occlusion group, showed less ischemia as demonstrated by preservation of monophasic action potential and reduction in both the incidence of ventricular arrhythmias and serum levels of ischemic

Table 2. Comparison of Regional Myocardial Function: Fractional Change in Area*

	LAD (Experimental Region)				LCx (Control Region)			
	Baseline	Shunt	Proximal Occlusion	Proximal + Distal Occlusion	Baseline	Shunt	Proximal Occlusion	Proximal + Distal Occlusion
Mean ± SD, %	32.9 ± 7.4	38.6 ± 11.8	17.6 ± 5.8	16.3 ± 3.0	18.4 ± 6.3	20.4 ± 9.2	17.3 ± 7.4	16.7 ± 7.4
P†		.18	.04	.02		.46	.75	.59

*LAD indicates left anterior descending artery; LCx, left circumflex artery.
†Relative to baseline values.

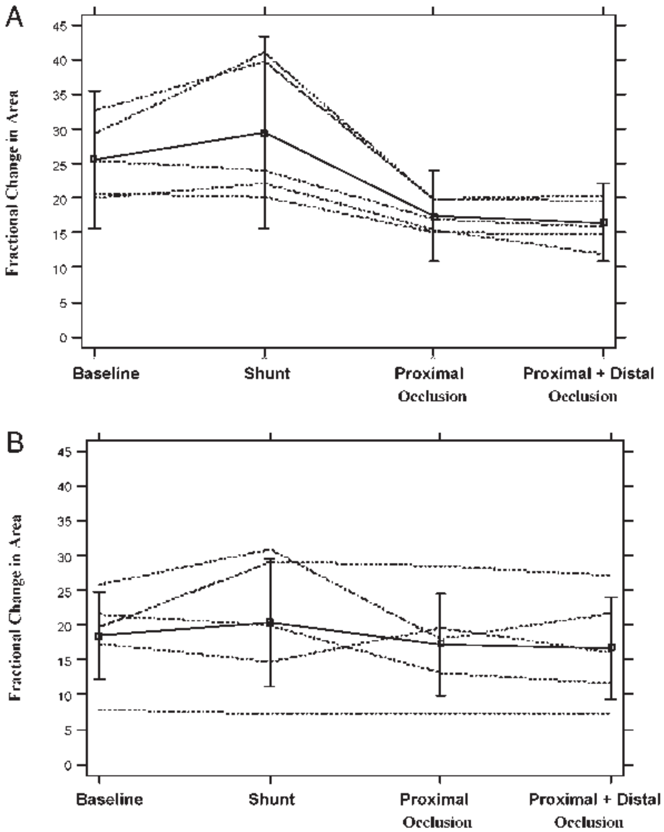

Figure 3. Fractional change in area (FCA [%]) at baseline, with left anterior artery (LAD) shunting, and with LAD occlusion(s). A, Experimental (LAD) region. B, Control (left circumflex artery) region. Solid line indicates mean ± 95% confidence interval; dashed line, individual animals.

by-products [Gandra 2002]. This finding is consistent with the results of our study, but we were able to go one step farther and show concomitant preservation of regional contractility with coronary shunting compared with occlusion(s).

In selected cases, OPCAB can be performed successfully without ischemia by use of coronary shunts [Rivetti 1998]. Critics of shunting would argue that in most cases any transient ischemia associated with coronary occlusion could be tolerated with little risk of significant hemodynamic compromise. However, clinical evidence, including ECG and echocardiographic data, has demonstrated that coronary occlusions may result in local ischemia and hemodynamic compromise [Franzone 1977, Lucchetti 1999]. Under such uncertain conditions, OPCAB safety may be compromised, the result being poor anastomosis quality, incomplete revascularization, or conversion to CPB.

Limited information is available regarding the quantitative blood flow achieved through intraluminal coronary shunts. Theoretically, flow through the intraluminal shunt depends on certain factors, such as preload, afterload, and luminal diameter. By using radiolabeled microspheres, a proven method of determining tissue perfusion, our study quantified the blood flow to myocardial tissue distal to the arteriotomy during the different experimental phases [Domenech 1969, Heymann 1977, Prinzen 1994]. We used a small-diameter (1.5 mm) intraluminal shunt with the assumption that larger-diameter shunts would result in equal or greater distal perfusion. Shunting maintained distal myocardial perfusion, whereas extraluminal occlusion(s) resulted in significant ($P < .05$) approximately 50% reduction in distal perfusion. These data confirm that intraluminal shunts may maintain distal blood flow sufficient to support regional cardiac function.

A limitation of this study was that data were obtained on healthy porcine hearts without coronary artery stenosis or collateral vessel development. Patients undergoing coronary revascularization have at least some degree of proximal coronary stenosis and often have collateral perfusion, possibly allowing tolerance of temporary extraluminal occlusion without significant myocardial ischemia or dysfunction. However, patients with severe, multivessel coronary disease and poor cardiac function or patients with more moderate disease and poor collateral perfusion may not tolerate temporary extraluminal occlusion and may benefit from perfusion provided by shunting.

A second limitation was that the experimental phases were not randomized. Intraluminal shunting always was performed prior to the extraluminal occlusion phases, because we found that extraluminal occlusions resulted in significant myocardial ischemia and depressed cardiac function. One animal experienced ventricular arrhythmia and cardiac arrest due to ischemia during the proximal extraluminal phase. In other words, the intraluminal shunt phase was always conducted prior to the extraluminal occlusion phases, because the shunting caused no significant change in myocardial function or perfusion compared with baseline, therefore allowing accurate assessment of the subsequent extraluminal occlusion phases.

In conclusion, these results support the hypothesis that intraluminal coronary shunting, compared with extraluminal coronary occlusion(s), maintains distal regional myocardial perfusion and contractile function in a healthy porcine beating-heart model. Although both shunting and occlusion techniques provided similar hemostasis and an adequate bloodless field at the arteriotomy site, coronary occlusion was found to significantly compromise regional myocardial blood flow and function. Further human clinical studies will help to characterize any potential benefits of coronary shunting in a wide spectrum of patients with varying degrees of coronary artery disease. Intraluminal coronary shunts should facilitate safer off-pump coronary revascularization in a larger group of patient candidates by providing improved distal myocardial perfusion and function.

REFERENCES

Bartrum RJ, Berkowitz DM, Hollenberg NK. 1974. A simple radioactive microsphere method for measuring regional flow and cardiac output. Invest Radiol 9:126-32.

Dapunt OE, Raji MR, Jeschkeit S, et al. 1999. Intracoronary shunt insertion prevents myocardial stunning in a juvenile porcine MIDCAB model absent of coronary artery disease. Eur J Cardiothoracic Surg 15:173-9.

Diegeler A, Hirsch R, Schneider F, et al. 2000. Neuromonitoring and neurocognitive outcome in off-pump versus conventional coronary bypass operation. Ann Thorac Surg 69:1162-6.

Domenech RJ, Hoffman JIE, Noble MIM, Saunders KB, Henson JR, Subijanto S. 1969. Total and regional coronary blood flow measured by radioactive microspheres in conscious and anesthetized dogs. Circ Res 25:581-96.

Franzone AJ, Wallsh E, Stertzer SH, DePasquale NP, Bruno MS. 1977. Reduced incidence of intraoperative myocardial infarction during coronary bypass surgery with use of intracoronary shunt technique. Am J Cardiol 39:1017-20.

Gandra SMA, Rivetti LA. 2002. Experimental evidence of regional myocardial ischemia during beating heart coronary bypass: prevention with temporary intraluminal shunts. Heart Surg Forum 6:10-8.

Hangler HB, Pfaller K, Antretter H, Dapunt OE, Bonatti JO. 2001. Coronary endothelial injury after local occlusion on the human beating heart. Ann Thorac Surg 71:122-7.

Heymann MA, Payne BD, Hoffman JIE, Rudolph AM. 1977. Blood flow measurements with radionuclide-labeled microspheres. Prog Cardiovasc Dis 20:55-79.

Lucchetti V, Capasso F, Caputo M, et al. 1999. Intracoronary shunt prevents left ventricular function impairment during beating heart coronary revascularization. Eur J Cardiothoracic Surg 15:255-9.

Okazaki Y, Takarabe K, Murayama J, et al. 2001. Coronary endothelial damage during off-pump CABG related to coronary-clamping and gas insufflation. Eur J Cardiothoracic Surg 19:834-9.

Penttila HJ, Lepojarvi MVK, Kiviluoma KT, Kaukoranta PK, Hassinen IE, Peuhkurinen KJ. 2001. Myocardial preservation during coronary surgery with and without cardiopulmonary bypass. Ann Thorac Surg 71:565-71.

Perrault LP, Desjardins N, Nickner C, Geoffroy P, Tanguay J, Carrier M. 2000. Effects of occlusion devices for minimally invasive coronary artery bypass surgery on coronary endothelial function of atherosclerotic arteries. Heart Surg Forum 3:287-92.

Perrault LP, Menasche P, Bidouard J, et al. 1997. Snaring of the target vessel in less invasive bypass operations does not cause endothelial dysfunction. Ann Thorac Surg 63:751-5.

Perrault LP, Nickner C, Desjardins N, Carrier M. 2000. Effects on coronary endothelial function of the Cohn stabilizer for beating heart bypass operations. Ann Thorac Surg 70:1111-4.

Prinzen FW, Glenny RW. 1994. Developments in non-radioactive microsphere techniques for blood flow measurement. Circ Res 28:1467-75.

Puskas JD, Wright CE, Ronson RS, Brown WM 3rd, Gott JP, Guyton RA. 1999. Clinical outcomes and angiographic patency in 125 consecutive off-pump coronary bypass patients. Heart Surg Forum 2:216-21.

Rivetti LA, Gandra SMA. 1998. An intraluminal shunt for off-pump coronary artery bypass grafting: report of 501 consecutive cases and review of the technique. Heart Surg Forum 1:30-6.

van Aarnhem EEHL, Nierich AP, Jansen EWL. 1999. When and how to shunt the coronary circulation in off-pump coronary artery bypass grafting. Eur J Cardiothoracic Surg 16(suppl 2):S2-6.