

Influence of Intracoronary Shunt Size on Coronary Endothelial Function during Off-Pump Coronary Artery Bypass

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ABSTRACT

Objective: The insertion of intracoronary shunts during off-pump coronary artery bypass surgery may induce severe endothelial dysfunction in the target arteries. The purpose of this study was to determine the role of the ratio of the shunt diameter to the target artery diameter in the development of endothelial dysfunction and to develop guidelines for selecting the most appropriate shunt size.

Methods: Nine swine (25 ± 4 kg) were used for this study. Three ClearView shunts 3 mm, 2 mm, and 1.25 mm in diameter were inserted proximally to distally via 3 arteriotomies into the right coronary artery to obtain oversizing with the 3-mm shunt, undersizing with the 1.25-mm shunt, and a satisfying congruence with the 2-mm shunt. The shunts were left in place for 15 minutes, and the levels of bleeding were quantified. Coronary rings upstream and downstream from the arteriotomies were then harvested and placed in organ chambers to study endothelium-dependent relaxations to serotonin and bradykinin. Noninstrumented coronary arteries served as controls.

Results: A decrease of endothelium-dependent relaxation occurred with the 3-mm shunts ($P < .005$), which were associated with an adequate hemostasis. A decrease of endothelium-dependent relaxation occurred with the 2-mm shunts ($P < .05$), which were associated with intermittent bleeding, and no significant decrease of endothelium-dependent relaxation occurred with 1.25-mm shunts ($P > .05$), which were associated with continuous bleeding.

Conclusions: Intracoronary shunts are associated with different disadvantages, depending on the mismatch to the target coronary artery, and whatever their size, shunts are not the ideal device for safely obtaining a satisfactory hemostasis. These results support our clinical attitude of the selective use of intracoronary shunts.

INTRODUCTION

Off-pump coronary artery bypass (OPCAB) surgery has regained popularity in recent years [Pfister 1997] with a reduction of morbidity for selected patients and significant decreases in cost compared with conventional on-pump surgery in some series [Ascione 1999]. However, specific technical difficulties are associated with this approach, such as heart stabilization, coronary bleeding at the anastomotic site, or the maintenance of distal perfusion during coronary occlusion. The insertion of intracoronary shunts has been used in coronary surgery since 1975 [Trapp 1975] with satisfactory clinical results [Franzone 1977]. This hemostatic system has the double theoretical advantage of drying the anastomotic site (hemostatic effect) while allowing an effective distal coronary perfusion (myocardial protection), which may sometimes be necessary in OPCAB surgery, particularly during occlusion of the right coronary artery [Levinson 1995].

Concomitant with these technical advances in surgery, the better understanding of the role of the endothelium in the regulation of vascular tone and coagulation control has led to the knowledge that the structural and functional integrity of the endothelial layer are fundamental to optimize the patency of the surgical coronary reconstruction [Vanhoutte 1989]. Studies of the effects of intracoronary shunts on the endothelium in porcine coronary arteries have demonstrated the deleterious consequences on endothelial reactivity [Chavanon 1999]. Perioperatively, the selection of the appropriate shunt diameter by the surgeon usually relies on matching the shunt to the internal diameter of the target coronary artery as closely as possible, but the relationship between the shunting efficacy (hemostasis, myocardial protection) to the adapted shunt size and the effects on the endothelial layer remain unknown. This purpose of this study was to assess the role of the ratio of the shunt diameter to the target artery diameter in the development of endothelial dysfunction to determine the best strategy for shunt selection in OPCAB surgery, and this study accomplishes this goal by taking into account the shunt's efficacy as a hemostatic device and the alterations of the arterial wall biology.

MATERIALS AND METHODS

Experimental Surgery

Nine white Landrace swine of either sex, aged 8 ± 1 weeks and weighing 25 ± 4 kg, were included in this study. Animals

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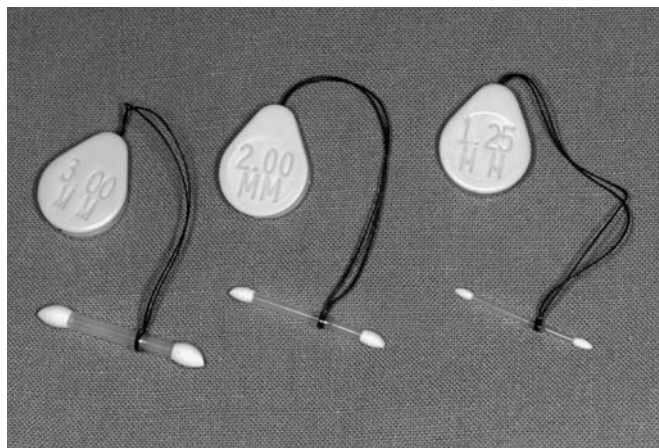


Figure 1. The 3-mm, 2-mm, and 1.25-mm shunts (ClearView; Medtronic) used in these experiments. Shunt lengths were 19 mm for the 1.25-mm shunt, 20 mm for the 2-mm shunt, and 22 mm for the 3-mm shunt.

were maintained and tested in accordance with the recommendations of the Guidelines on the Care and Use of Laboratory Animals issued by the Canadian Council on Animals and the Guidelines of Animal Care, and these practices were approved by a local ethics committee.

The animals were sedated by an intramuscular injection of 25 mg/kg ketamine hydrochloride (Ayerst Veterinary Laboratories, Guelph, Ontario, Canada) associated with 10 mg/kg xylazine (Boehringer Ingelheim, Burlington, Ontario, Canada), intubated, and mechanically ventilated with a 3:2 oxygen-air mixture. Anesthesia was maintained with 1% to 2.5% halothane inhalation (Halocarbon Laboratories, River Edge, NJ, USA). The electrocardiogram was recorded with 3 subcutaneous limb electrodes. After the skin was prepared, the heart was exposed via a median sternotomy approach. To improve visualization of the heart, we tied 2 pericardial stitches on the right side of the pericardium. After intravenous administration of 300 U/kg heparin (Leo Pharma, Ajax, Ontario, Canada) and after the external and internal coronary artery diameters had been evaluated to a precision of 0.001 mm with an electronic digital caliper, 3 intracoronary shunts (ClearView; Medtronic, Grand Rapids, MI, USA) with bulb sizes of different external diameters (Figure 1) were inserted via 3 longitudinal arteriotomies 5 mm in length on the right coronary artery (RCA) with the help of manual stabilization and the aid of $2.5\times$ surgical magnification.

The shunts were inserted first downstream to the arteriotomy and then proximally to position the shunt's 2 stoppers on either side of the arteriotomy. Three bulb intracoronary shunts 3 mm, 2 mm, and 1.25 mm in external diameters were inserted proximally to distally to obtain oversizing with the 3-mm shunt (mean internal coronary artery diameter, 2.7 ± 0.2 mm), undersizing with the 1.25-mm shunt (mean internal coronary artery diameter, 2.0 ± 0.2 mm), and congruence with the 2-mm shunt (mean internal coronary artery diameter, 2.2 ± 0.2 mm) (Figure 2). Shunts were left in place

for 15 minutes (to mimic a longer-than-average time for performing an anastomosis), and bleeding at the anastomotic site was quantified (+++, impossible anastomosis; ++, possibility of anastomosis despite bleeding; +, very little bleeding; and 0, no bleeding). The shunts were then removed, and the heart was rapidly excised and placed in a modified Krebs-bicarbonate solution (118.3 mmol/L NaCl, 4.7 mmol/L KCl, 1.2 mmol/L $MgSO_4$, 1.2 mmol/L KH_2PO_4 , 11.1 mmol/L glucose, 2.5 mmol/L $CaCl_2$, 25 mmol/L $NaHCO_3$, and 0.026 mmol/L ethylenediaminetetraacetic acid).

Functional Coronary Testing

Less than 10 minutes after heart excision (heart weight relative to body weight, 4.68 ± 0.22 g/kg), coronary arteries were carefully dissected free of the myocardium and fatty epicardial tissue in a Petri dish filled with oxygenated modified Krebs-bicarbonate solution and were divided into rings 4 mm in length. Six instrumented rings were obtained from the RCA upstream (proximal) and downstream (distal) from each arteriotomy at the sites of shunt positioning (Figure 2). Eighteen instrumented rings were obtained for each of the 3 shunt sizes. Control rings were obtained from the left anterior descending artery (LAD) (4 rings) and from the circumflex artery (CX) (4 rings) for a total of 72 control rings. All rings were placed in organ chambers (Emka Technologies, Paris, France), filled with 20 mL modified Krebs-bicarbonate solution continuously heated at $37^\circ C$, and oxygenated with a carbogen mixture (95% oxygen and 5% carbon dioxide). The rings were suspended between two metal stirrups with the upper one connected to an isometric force transducer connected to a signal amplifier and then were allowed to stabilize

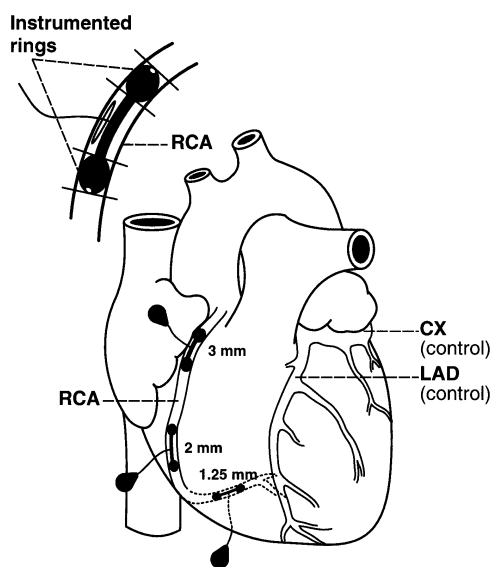


Figure 2. Schematic depicting the experimental set up on the swine heart with the 3 shunts in position in the right coronary artery and showing the sites of instrumented and control rings selected for vascular reactivity studies. RCA indicates right coronary artery; LAD, left anterior descending artery; CX, circumflex coronary artery.

for 30 minutes. Data were collected with biological signal data acquisition software (IOX 1.203; Emka Technologies).

Each arterial ring was stretched to the optimal point of its active length-tension curve, determined in previous experiments by measuring the contraction to 30 mmol/L KCl at different levels of stretch (the stretch for an optimal response is approximately 3.5 g). The maximal contraction of rings was then obtained with the addition of 60 mmol/L KCl. After a plateau was obtained, all baths were washed twice with a modified Krebs-bicarbonate solution containing 10^{-5} mol/L indomethacin to exclude production of endogenous prostanooids, 10^{-7} mol/L propranolol (Biomol Research Laboratories, Plymouth Meeting, PA, USA) to prevent the activation of β -adrenergic receptors, and 10^{-6} mol/L ketanserin to block serotonin 5-HT₂ receptors.

After 45 minutes of stabilization, 2×10^{-6} mol/L to 3×10^{-5} mol/L prostaglandin F_{2 α} (Cayman Chemical Company, Ann Arbor, MI, USA) was added to obtain a contraction averaging 50% of the maximal contraction to KCl. Endothelium-dependent relaxation to 10^{-10} to 10^{-5} mol/L serotonin (5-hydroxytryptamine creatinine sulfate), an agonist that binds to receptor coupled to G_i proteins, and to 10^{-12} to 10^{-6} mol/L bradykinin, an agonist that binds to receptor coupled to G_q proteins, were quantified. At the completion of serotonin testing, the rings were left to recontract until a plateau was reached, and then bradykinin testing was initiated for each ring. At the end of the experiment, endothelium-independent relaxations were studied with the addition of a bolus of 10^{-5} mol/L sodium nitroprusside.

All drugs were prepared daily. Serotonin, bradykinin, indomethacin, ketanserin, and sodium nitroprusside were obtained from Sigma Chemical Company (Oakville, Ontario, Canada).

Morphologic Coronary Examination

Segments of fresh instrumented and control coronary arteries were stained with silver nitrate to visualize the remaining intact endothelium. Rings from each group (3-mm, 2-mm, and 1.25-mm shunts and controls) were opened longitudinally to obtain strips 4×8 mm in size and were pinned to the bottom of a Petri dish filled with saline solution. The strips first were fixed for 10 minutes with 0.1 mol/L phosphate buffer containing paraformaldehyde and glutaraldehyde. After a 1-minute wash with sucrose solution, 0.25% silver nitrate (Sigma Chemical Company) was added, followed 1 minute later with a second 1-minute wash. This wash was followed with a second fixation period of 2 minutes, and incubation was carried out for 3 hours in a sodium cacodylate solution under a spotlight. The stained specimen was

mounted whole on glass slides and labeled. The percent surface area covered by intact endothelium was then estimated by 2 examiners with the aid of a microscope (magnification $\times 250$).

Statistical Analysis

All values are expressed as the mean \pm SEM. Contractions to prostaglandin F_{2 α} are expressed as a percentage of the maximal contraction to 60 mmol/L KCl. Relaxations are expressed as the percentage of the maximal contraction to prostaglandin F_{2 α} for each ring. Two-way repeated analyses of variance were performed to compare the control rings and instrumented rings for each shunt at each point of the concentration-response curves. Statistical analysis was realized with SAS computer software (SAS Institute, Cary, NC, USA). A *P* value less than .05 was considered statistically significant.

RESULTS

Experimental Surgery

All shunts were positioned in the coronary artery after a single attempt and remained patent during the experiment. Insertion of the 3 shunts into the RCA was well tolerated hemodynamically during the whole experiment.

An optimal hemostasis (0) was always obtained at the arteriotomy site with the 3-mm shunt. Intermittent bleeding (+ or ++) at the arteriotomy site that varied with time and heart position was observed with the 2-mm shunt. Continuous bleeding (+++) at the arteriotomy site occurred with the 1.25-mm shunt.

Coronary Reactivity Study

Contractions. All rings contracted when KCl was added to the baths. The amplitudes of the contraction to 60 mmol/L KCl and to prostaglandin F_{2 α} (2×10^{-6} mol/L to 3×10^{-5} mol/L) quantified for all groups (3-mm, 2-mm, and 1.25-mm shunts and controls) are presented in the Table. There were no significant differences in contractions between instrumented groups.

Endothelium-Dependent Relaxations. There were statistically significant decreases (*P* < .005) in the endothelium-dependent relaxations to serotonin and bradykinin in rings instrumented with the 3-mm shunts, compared with the controls (Figure 3). There were statistically significant decreases (*P* < .05) in endothelium-dependent relaxations to serotonin in rings instrumented with the 2-mm shunts and no significant decreases in endothelium-dependent relaxations to bradykinin (Figure 4). No statistically significant decreases in endothelium-dependent relaxations to serotonin and bradykinin occurred with the 1.25-mm shunts (*P* > .05) (Figure 5).

Amplitudes of Contraction to 60 mmol/L KCl and Prostaglandin F_{2 α} *

	3-mm Shunt	2-mm Shunt	1.25-mm Shunt	Controls
KCl (60 mmol/L) contraction, g	11.4 \pm 1.1	13.2 \pm 1	13.9 \pm 1.5	12.5 \pm 0.7
PG F _{2α} contraction, g	5.6 \pm 0.7	5.4 \pm 0.6	6 \pm 1	9.2 \pm 0.6
PG F _{2α} contraction, % KCl contraction	56.6 \pm 7.7	43 \pm 4.4	48.5 \pm 5.9	76 \pm 3.2
PG F _{2α} concentration, 10^{-6} mol/L	13.3 \pm 2.9	18.2 \pm 2.9	9.4 \pm 3.1	3.6 \pm 0.3

*Values are expressed as the mean \pm SEM. PG F_{2 α} indicates prostaglandin F_{2 α} .

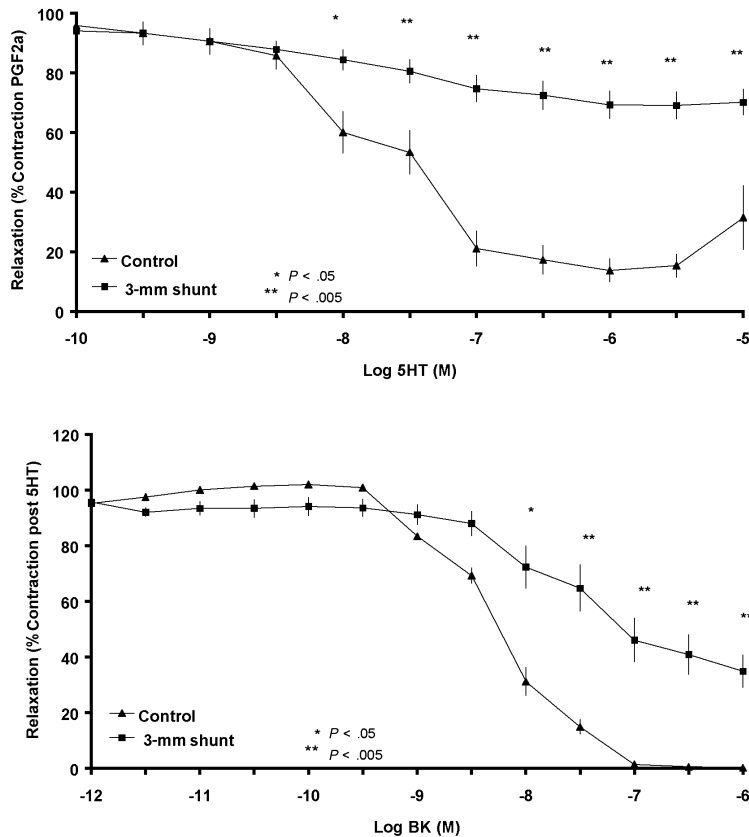


Figure 3. Cumulative concentration-relaxation response curves to serotonin (5-HT) and bradykinin (BK) in porcine coronary artery rings submitted to the 3-mm shunt and in control rings. A P value less than .05 was considered statistically significant.

Endothelium-Independent Relaxations. No statistically significant differences in relaxations to sodium nitroprusside were observed between groups (data not shown), and all rings achieved 100% relaxation.

Coronary Morphologic Study

All instrumented strips were compared with control strips. Histologic study of endothelial cell coverage demonstrated the preservation of the endothelial layer with the 1.25-mm shunts (90%-100% of controls), a reduction in the intact endothelium (40%-60% of controls) with the 2-mm shunts with the presence of several grooves from the rubbing of the shunts against the endothelium, and a total disappearance of the endothelium (0% of controls) from strips instrumented with the 3-mm shunts (Figure 6).

DISCUSSION

The major findings of this study are the severe decreases in endothelium-dependent relaxation involving both biochemical pathways of endothelium-dependent relaxation (G_i protein-mediated release of nitric oxide evoked by serotonin and G_q protein-mediated release of nitric oxide evoked by bradykinin [Boulangier 1997]) with the 3-mm shunts and the associated adequate hemostasis observed with these

shunts. The 2-mm shunts exhibited a lesser and selective endothelial dysfunction involving only G_i protein-mediated relaxations and were associated with intermittent bleeding. No significant endothelial dysfunction occurred with the 1.25-mm shunts, but continuous and cumbersome bleeding occurred when anastomoses were performed with shunts of this size.

These functional results are confirmed and better understood with the morphologic studies showing a total disappearance of the endothelium (0% of controls) on strips instrumented with the oversized 3-mm shunts, a reduction in the percentage of intact endothelium (40%-60% of controls) with the 2-mm shunts, and preservation of the endothelial layer with the undersized 1.25-mm shunts (90%-100% of controls).

It is obvious that the concept of oversizing, undersizing, or adequate congruence is based not only on perioperative measurement of the coronary artery, the size of which should vary during the experiment, but also on the reproductive anatomy of swine coronary arteries. That consideration was also the reason for our shunt diameter choices for this experiment. Furthermore, the lack of bleeding at the anastomotic site is indirect proof of oversizing with pressure on the arterial wall, and continuous bleeding is indirect proof of undersizing with low or absent pressure on the arterial wall. The study of the relationships between shunt size, efficacy, and

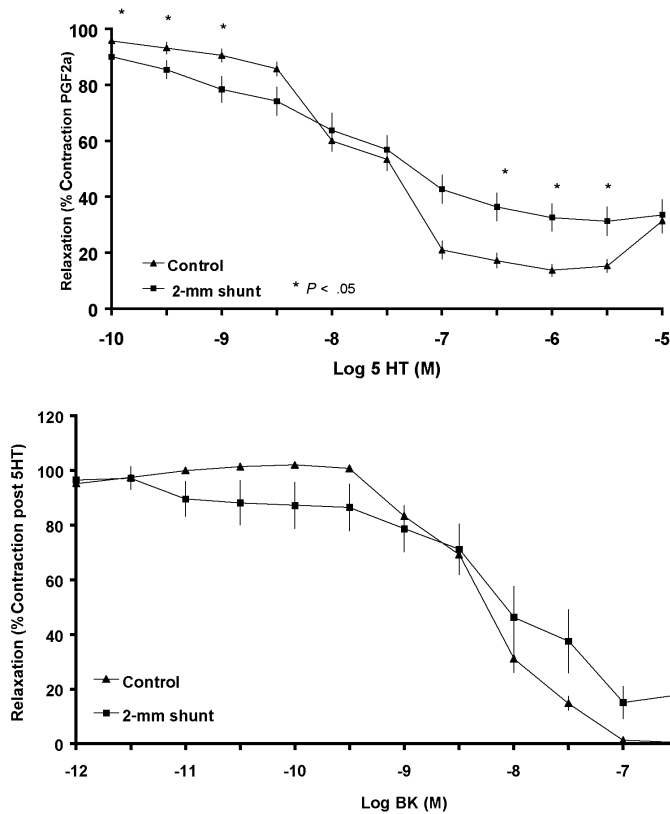


Figure 4. Cumulative concentration-relaxation response curves to serotonin (5-HT) and bradykinin (BK) in porcine coronary artery rings submitted to the 2-mm shunt and in control rings. A *P* value less than .05 was considered statistically significant.

side effects on the endothelium in this experimental setting appears to be valuable, and it has clinical implications.

The necessity of a bloodless field for optimal visibility during an anastomosis is an issue of concern in OPCAB. Direct vascular clamping upstream and downstream from the anastomotic site was probably the first technique used to occlude an artery to obtain hemostasis. Different studies done on the internal mammary artery (IMA) have shown that endothelial dysfunction due to extravascular clamping of the IMA is related to the type of clamp jaw and is due to a loss of endothelial coverage at the clamp site [Fonger 1992], which can induce postoperative spasm and the development of focal intimal hyperplasia. In addition, this technique may cause major damage, especially on atherosclerotic arteries, with the risks of parietal plaque rupture, dissection, and early thrombosis.

For this reason, the most widely used variant of OPCAB involves the use of sutures or tapes to snare the coronary artery extravascularly upstream and downstream from the anastomotic site on the target artery. An experimental study showed that snaring with 4/0 Gore-Tex thread (W. L. Gore & Associates, Flagstaff, AZ, USA) on silicone tubing to achieve hemostasis at the anastomotic site does not cause endothelial dysfunction in normal porcine coronary arteries [Perrault 1997]. However, a recent morphologic experimental study showed that coronary artery snaring in dogs resulted in ultrastructural injury to the coronary artery endothelium, which was ameliorated

by the use of elastic sutures instead of nonelastic sutures [Okazaki 2001]. Hangler and colleagues described coronary artery lesions secondary to snare application in patients prior to the removal of the recipient heart during transplantation procedures. Examination with scanning electron microscopy showed that the snares caused focal endothelial denudation, microthrombosis, and atherosclerotic plaque rupture [Hangler 2001], all of which may have severe clinical consequences [Demaria 2001]. Furthermore, these occlusive systems do not allow distal coronary artery perfusion.

Intracoronary shunts are also used as hemostatic devices in OPCAB. In addition to their function in obtaining hemostasis, shunts are designed to provide flow [Robison 1986] to optimize myocardial protection during OPCAB. Some shunts are specifically designed for this goal and have no hemostatic function; such external shunt catheters maintain only a distal coronary perfusion from the femoral artery [Arai 2000]. Experimental studies [Dapunt 1999] and clinical studies [Lucchetti 1999] have demonstrated that shunting can prevent acute left ventricular dysfunction during beating heart coronary revascularization and be a useful surgical tool in patients with left ventricular dysfunction or unstable angina or when a longer time is anticipated for performing the anastomosis, such as in the training of residents [Ricci 2000].

However, a comparative study of 2 different intracoronary shunts (the Anastaflo shunt [Edwards Lifesciences, Irvine,

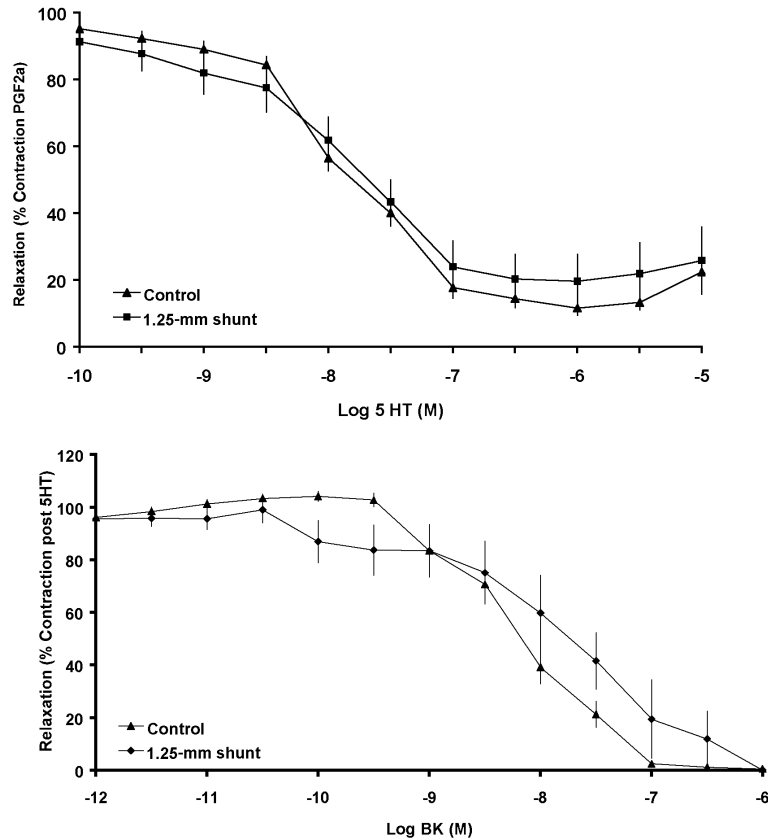


Figure 5. Cumulative concentration-relaxation response curves to serotonin (5-HT) and bradykinin (BK) in porcine coronary artery rings submitted to the 1.25-mm shunt and in control rings. A *P* value less than .05 was considered statistically significant.

CA, USA] and a silicone perfusion catheter) has been performed with healthy porcine coronary arteries. The shunt diameter size was 2.5 mm for Anastaflo and 2 mm for the silicone perfusion catheter. The external shunt diameter and the internal artery diameter were matched as closely as possible. There was no difference between the 2 devices; both caused severe endothelial dysfunction [Chavanon 1999] due to the rubbing of the endothelial layer during the positioning and removal of the devices. This mechanism of injury is well known, because rubbing of the inner surface of isolated vessels is used in pharmacology experiments to remove the endothelial layer [Vanhoutte 1989]. However, the precise relationships between shunt size, the hemostasis obtained, and endothelial injury have not yet been studied.

Ip and colleagues classified vascular injury into 3 types: type I, functional alteration of endothelial cells without significant morphologic changes; type II, endothelial denudation and intimal damage with intact internal elastic lamina and media; and type III, endothelial denudation with damage to both intima and media [Ip 1990]. Such damage was demonstrated in the morphologic part of the present study, and if the shunt diameter is matched or oversized relative to the internal coronary diameter to obtain effective hemostasis, the contact and rubbing will necessarily denude the endothelial layer with a significant decrease in endothelium-dependent

relaxation, as has been demonstrated in the present functional study. However, the endothelium-independent relaxations were unaffected by the use of such shunts, demonstrating the integrity of the underlying smooth muscle cells and the avoidance of severe arterial wall lesions (Ip type III injury). Thus, arterial exposure to shunts with a satisfying hemostatic result produces a type II vascular injury. A type II or III injury with intense platelet aggregation appears to be the prerequisite for the subsequent accelerated fibroproliferative responses and thrombosis [Ip 1990].

Intracoronary shunts have a second function besides hemostasis, which is to maintain adequate flow during the completion of the anastomosis for optimal myocardial protection during surgery. The use of an undersized intracoronary shunt associated with adapted hemostatic systems to avoid any rubbing of the endothelium may not allow a sufficient flow into the coronary artery run-off. Indeed, Jaggy and colleagues have demonstrated that at adequate perfusion pressure only shunts 3 mm and 4 mm in diameter provided enough flow to ensure satisfactory myocardial protection (40-60 mL/min) [Jaggy 1999]. Rubbing on the intima and the endothelial layer cannot be avoided with a tube 3 or 4 mm in diameter except in large arteries and may carry a risk of medial injury (Ip type III), which is more prone to inducing a smooth muscle cell proliferative response [Ip 1990].

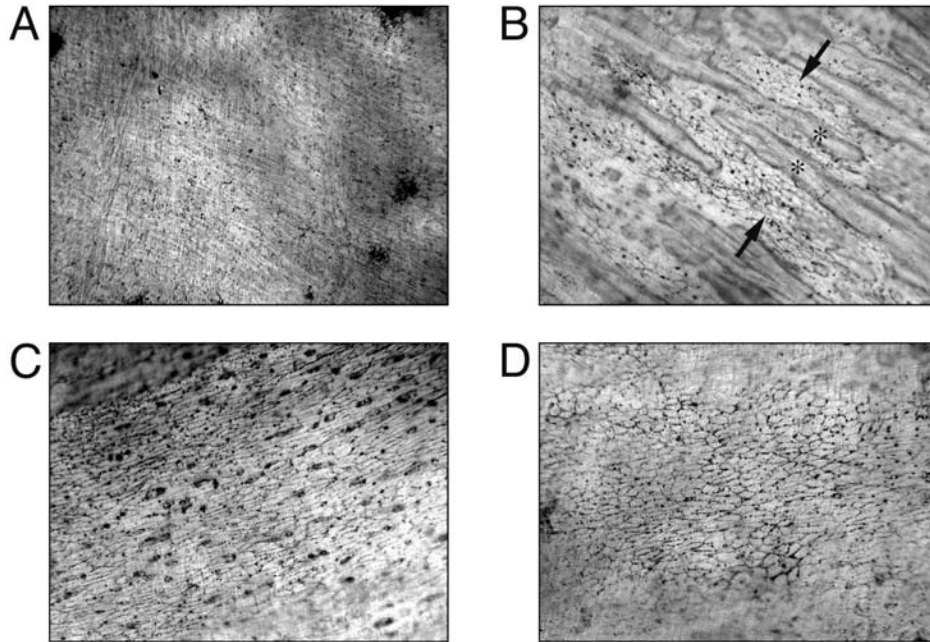


Figure 6. Representative photomicrographs of silver nitrate staining of coronary strips. Strip previously instrumented with the 3-mm shunt (A), the 2-mm shunt (B), the 1.25-mm shunt (C), and control (D) (original magnification $\times 250$). The photomicrograph of the strip with the 2-mm shunt (B), which matched the internal diameter of the artery, also shows the creation of several denuded grooves (stars) between zones where the endothelial cells remain in place (arrows).

The main limitation of the present study is the use of healthy coronary arteries in a swine model. Experiments performed on atherosclerotic arteries reproduce more closely the clinical reality. In studies with a swine model [Shimokawa 1987, Perrault 2000], coronary arteries were submitted percutaneously to balloon denudation 1 month prior to surgical experimentation with shunts, and this denudation caused an intimal hyperplasia resembling atherosclerosis. In this model, denuded arteries showed a generalized dysfunction affecting both G_i protein- and G_q protein-mediated relaxations, and the application of all the hemostatic devices studied, including intracoronary Anastaffo shunts, did not induce a significantly greater dysfunction in these arteries, which were already very dysfunctional [Perrault 2000] with both G_i protein- and G_q protein-mediated pathways of endothelium-dependent relaxation already affected. Furthermore, the depressed release of endothelium-derived relaxing factor(s), especially that mediated by serotonin, may coexist with the augmented liberation of endothelium-derived constricting factor(s) in the chronic regenerated endothelium [Shimokawa 1987]. Indeed, because the endothelium of atherosclerotic arteries is already severely dysfunctional, the endothelial trauma induced by shunts in these arteries may not have any functional drawbacks, but this hypothesis remains to be proven by further experimental studies specifically focused on the vascular reactivity of atheromatous vessels.

However, this possibility does not exempt surgeons from using elementary caution in their application of shunts, because all shunts can generate serious macroscopic complications, such as extensive intimal denudation and atheroma

plaque rupture inducing spasm or acute thrombosis, arterial dissection, or distal embolism. The occlusion of very calcified coronary arteries during OPCAB surgery, especially in diabetic patients, may be difficult and traumatic with snares and carries a high risk of plaque rupture with late graft failure and recurrent angina. Shunting or jet-gas insufflation may be valuable alternatives for patients with these difficult conditions [Demaria 2001].

Another limitation of this study is our use of an acute animal model. It should be interesting to allow some animals to recover to evaluate, in a chronic study, how well these denuded areas regenerate endothelium and to determine the time course for such regeneration. However, the properties of posttraumatic regenerated endothelium are well known and are mentioned above [Shimokawa 1987, Boulanger 1997, Perrault 2000]. Notably, the impairment of G_i proteins in regenerated endothelial cells predisposes the vessel to vasospasm and to the initiation of the atherosclerotic process [Boulanger 1997]. The use of LAD and CX as controls rather than as parts of the RCA not exposed to the shunt is to compare instrumented rings with normal arteries without any surgical manipulation or ischemia. Furthermore, the RCA was chosen because of its homogeneous diameter all the way to the origin of the posterior descending artery and is in contrast to the LAD, which rapidly becomes intramyocardial and smaller, and to the underdeveloped CX. In the swine model, previous experiments have shown no significant differences in endothelium-dependent relaxations between the LAD, the CX, and the RCA (data not shown). The differences between the instrumented parts of the RCA and the control part

appear to be due to shunt size mismatch alone and cannot be due to differences in endothelial function between the RCA and the LAD or the CX. Furthermore, although ischemia and reperfusion can potentially cause endothelial dysfunction, the ischemia duration during shunt insertion is very short and comparable for the instrumented rings on the RCA and should not influence comparative results with control rings [Perrault 1997]. In addition, the obligatory complete ischemia due to the need to excise the heart and make the rings was the same for all the arteries, providing for a reliable comparative study.

Adequate anticoagulation therapy appears to be very important for optimizing clinical results and avoiding acute thrombosis. Indeed, patients undergoing off-pump coronary operations show an increased level of procoagulant activity on the first postoperative day. Therefore, these patients should be considered at increased risk of thrombotic graft occlusion, and this risk may be higher in cases of endothelial or arterial wall injury. A recommendation is to keep the intraoperative activated clotting time longer than 300 seconds, not to neutralize the heparin with protamine unless uncontrollable bleeding occurs [Mariani 1999], and to introduce antiplatelet drugs as soon as possible.

The ideal shunt to avoid endothelial damage is an undersized shunt that exhibits a minimum of endothelial rubbing associated with the obligatory movement of the shunt during installation and removal, which are probably the most deleterious maneuvers for the endothelium. However, an undersized shunt is associated with a greater amount of bleeding at the anastomotic site, which may considerably impair the ease of performance and quality of the anastomosis, and can translate into suboptimal long-term patency as well as suboptimal quality of heart stabilization [Gundry 1998].

CONCLUSIONS

Shunting to obtain total hemostasis at the anastomotic site and a satisfactory intracoronary flow to perform anastomosis under optimal conditions requires a slightly oversized shunt, but an oversized shunt is associated with severe endothelial dysfunction and intimal lesions. In contrast, congruent shunts induce a lesser and selective endothelial dysfunction with intermittent bleeding at the anastomotic site. Undersized shunts do not induce endothelial dysfunction or morphologic lesions of the endothelium but do not allow the safe completion of the anastomosis because of the significant bleeding that occurs at the anastomosis site. Furthermore, the flow provided with such undersized shunts is unlikely to be sufficient to ensure effective myocardial protection. Despite their routine use by some surgeons, different shunts sizes are associated with various drawbacks in OPCAB. Whatever the size, shunts are not the ideal device to safely obtain satisfactory hemostasis. These results support our clinical attitude of the selective use of intracoronary shunts.

In the Montreal Heart Institute experience, shunts are necessary to maintain distal perfusion during coronary occlusion for minimizing ischemia in less than 5% of cases of beating heart coronary artery bypass surgery (unpublished obser-

vation). However, if endothelial damage remains inevitable, the use of such intracoronary shunts must always be guided by the concern of inducing as little trauma as possible to avoid the dissection or atheromatous plaque rupture that can occur by slight undersizing. Optimal anticoagulation and antiplatelet drug therapy should be given to prevent acute thrombosis due to the obligatory endothelium damage.

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REVIEW AND COMMENTARY

1. Editorial Board Member YT31 writes:

Actually, the authors themselves mention a weakness; that is, what are the long-term effects that would have a bearing on their conclusions for selective shunting.

Authors' Response by Dr. Roland G. Demaria:

Beating heart coronary artery bypass grafting surgery necessitates the use of technical devices for the control of the target coronary artery to obtain a bloodless field and eventual distal myocardial perfusion. Endothelium-dependent relaxations of normal porcine epicardial coronary arteries to serotonin and bradykinin were studied in standard organ chamber experiments immediately after the application of different sizes of intracoronary shunts.

We have not studied the long-term effects of intracoronary shunt application on the arterial wall. However, in the same swine model, coronary arteries were submitted percutaneously in our laboratory to balloon denudation 1 month prior to another surgical experiment, causing intimal hyperplasia resembling atherosclerosis with a very dysfunctional regenerated endothelium. The long-term effect of shunts 3 mm in diameter should create the same lesions. This conclusion remains to be proven by further experimental studies specifically focused on the vascular reactivity of vessels a long time after shunt application.

In conclusion, the greater preservation of endothelial coverage may translate acutely into a lesser propensity for endothelial dysfunction at the site of application and probably into a lower risk of intimal hyperplasia at long-term follow-up. This consideration should guide selection of the optimal technique for obtaining a bloodless field during beating heart coronary artery bypass grafting surgery.