Work in progress report - Coronary

The Monoshunt: a new intracoronary shunt design to avoid distal endothelial dysfunction during off-pump coronary artery bypass (OPCAB)*

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Abstract

Insertion of intracoronary shunts during off-pump coronary artery bypass surgery can induce a severe endothelial dysfunction. The purpose of this study was to propose a new intracoronary shunt design called Monoshunt, to avoid distal endothelial damage of the target artery in a porcine model. The use of the Monoshunt avoids distal endothelial denudation and allows distal coronary perfusion.

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1. Introduction

Insertion of intracoronary shunts has been used in coronary artery bypass grafting surgery since 1975 [1]. This hemostatic system has the double advantage of drying the anastomotic site (hemostatic effect) while allowing an effective distal coronary perfusion (myocardial protection), which may sometimes be necessary in off-pump coronary artery bypass (OPCAB) surgery. Studies of the effects of intracoronary shunts on the endothelium of porcine coronary arteries have demonstrated deleterious consequences on endothelium-dependent reactivity [2], due to the rubbing of the shunt on the endothelial layer. Distal endothelial lesions and dysfunction are particularly worrisome because they may involve the distal run-off of the bypass. The purpose of this study was to propose a new intracoronary shunt design called Monoshunt, to avoid distal endothelial damage of the target coronary artery in a porcine model.

2. Materials and methods

2.1. Monoshunt design

A standard commercially available intracoronary shunt 2.5 mm diameter (Clearview®, Medtronic, Grand Rapids, MI, USA) was cut off to obtain an isolated occluder. The distal part of an intravenous catheter (Cathlon Johnson® and Johnson, Arlington, TX, USA) was cut to obtain a tube 2 cm in length and 1.8 mm in external diameter, which was imbricated into the occluder to obtain the Monoshunt (Fig. 1).

2.2. Experimental surgery

Six white Landrace swine of either gender, aged 8 ± 1 weeks and weighing 24.9 ± 4.0 kg were included in this study. Animals 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. The animals were sedated with an intramuscular injection of 25 mg/kg of ketamine hydrochloride (Ayerst Veterinary Laboratories, Guelph, ON, Canada) and 10 mg/kg of xylazine (Boehringer Ingelheim, Burlington, ON, Canada), intubated and...
mechanically ventilated with an oxygen/air mixture (3:2). Anesthesia was maintained with 1–2.5% halothane inhalation (Halocarbon Laboratories, River Edge, NJ, USA). The electrocardiogram was recorded from three subcutaneous limb electrodes. The heart was then exposed via a median sternotomy approach and 300 U/kg heparin (Leo pharma, Inc., Ajax, ON, Canada) were given intravenously. The Monoshunt was then inserted via a 5-mm longitudinal arteriotomy on the proximal part of the right coronary artery (RCA). It was inserted first downstream to the arteriotomy and then proximally to position the shunt’s occluder. The Monoshunt was then removed and the heart was excised despite bleeding, + ++: possibility of anastomosis, ++: very little bleeding and 0: no bleeding) [3]. The flow through the Monoshunt was measured by quantification of the quantity of blood per min. The Monoshunt was then removed and the heart was excised and placed in a modified Krebs-bicarbonate solution (composition in mmol/l: NaCl 118.3, KCl 4.7, MgSO4 1.2, KH2PO4 1.2, glucose 11.1, CaCl2 2.5, NaHCO3 25, and ethylenediaminotetraacetic acid 0.026).

2.3. Functional coronary testing

Coronary arteries were dissected free of the fatty epicardial tissue in a Petri dish filled with oxygenated modified Krebs-bicarbonate and were divided into rings 5 mm in length. Two instrumented rings were obtained from the RCA, upstream (proximal) and downstream (distal) from each arteriotomy at the site of the Monoshunt positioning. Control rings were obtained from non-instrumented coronary arteries. All rings were placed in organ chambers (Emka Technologies Inc., Paris, France) which were covered by intact endothelium was then estimated under a UV spotlight exposure for 3 h. The stained specimen were mounted whole on glass slides and labeled. The percent surface area covered by intact endothelium was then estimated under microscope magnification (× 250).

2.4. Morphologic coronary examination

Segments of fresh instrumented and control coronary arteries were used for silver nitrate staining to visualize the remaining intact endothelium. Rings from each group (3, 2, 1.25 mm, controls) were opened longitudinally to obtain 4 × 8 mm strips and pinned to the bottom of a Petri dish filled with saline solution. The strips were first fixed for 10 min with a phosphate buffer (0.1 mol/l) added with paraformaldehyde and glutaraldehyde. After a 1-min wash with sucrose solution, 0.25% silver nitrate (Sigma Chemical Co., ON, Canada) was added, followed 1 min later by a second washing during 1 min. This was followed by a second fixation period during 2 min and incubation was done in a sodium cacodylate solution under a UV spotlight exposure for 3 h. The stained specimen were mounted whole on glass slides and labeled. The percent surface area covered by intact endothelium was then estimated under microscope magnification (× 250).

2.5. Statistical analysis

All values are expressed as the mean ± standard error of the mean. Contractions to prostaglandin F2α (PGF2α) were expressed as a percentage of the maximal contraction to KCl (60 mmol/l). Relaxations are expressed as the percentage of the maximal contraction to prostaglandin F2α for each ring. Two-way repeated analysis of variance were performed to compare each point of the concentration-response
curves between control rings and instrumented rings upstream and downstream from the anastomotic site. Statistical analysis was realized with the computer software S.A.S. (Insert Inc., Cary, NC, USA). A \( P \)-value of less than 0.05 was considered statistically significant.

3. Results

3.1. Experimental surgery

All Monoshunts were positioned into the right coronary artery after a single attempt and remained patent throughout the duration of the experiment. Insertion of the Monoshunts into the RCA and the left anterior descending (LAD) was well tolerated hemodynamically during the whole experiment (data not shown). Hemostasis (0 or +) was always obtained at the arteriotomy site with the Monoshunt. The flow was 30 ml/min under 55 ± 10 mmHg of mean blood pressure (40 ml/min for the standard shunt).

3.2. Coronary reactivity study

3.2.1. Contractions

The amplitude of the contraction to KCl (60 mmol/l) and to prostaglandin \( F_2\alpha \) (2 \( \times \) 10\(^{-6} \)–3 \( \times \) 10\(^{-5} \) mol/l) (Fig. 2) was quantified for all groups (upstream, downstream, controls) and there was no significant differences in contractions between the different groups.

3.3. Relaxations

3.3.1. Endothelium-dependent relaxations

There was a statistically significant decrease \( (P < 0.05) \) in endothelium-dependent relaxation to 5-HT in rings located upstream (occluder side) from the arteriotomies, compared with the control group. There was no statistically significant decrease of relaxations to 5-HT in rings located downstream (no occluder side) from the arteriotomies, compared with the control group (Fig. 3A).

There was a statistically significant decrease \( (P < 0.05) \) in endothelium-dependent relaxation to BK in rings located upstream (occluder side) from the arteriotomies, compared with the control group. There was no statistically significant decrease of relaxations to BK in rings located downstream (no occluder side) from the arteriotomies, compared with the control group (Fig. 3B).

3.4. Endothelium-independent relaxations

No differences in endothelium-independent relaxations to the NO donor SNP were observed in coronary rings between groups (Fig. 3C).

3.5. Coronary morphologic study

All instrumented strips were compared with control strips (Fig. 4A). Histological study of the endothelial cell coverage demonstrated preservation of the endothelial layer with the distal part of the Monoshunts (90–100% of controls) (Fig. 4B), and a total disappearance of the endothelium (0% of controls) on strips instrumented with the proximal part of the Monoshunts (Fig. 4C).

4. Discussion

The major findings of this study: (1) there is marked decrease of endothelium-dependent relaxation due to the Monoshunt upstream from the arteriotomy, and no
significant endothelial dysfunction downstream associated with no or minor bleeding allowing the performance of anastomosis. The upstream endothelial dysfunction involves Gi protein and Gq mediated endothelium-dependent relaxations suggestive of a severe endothelial dysfunction. Endothelium-independent relaxations were unaffected both upstream and downstream by the use of such shunts, demonstrating the integrity of the underlying smooth muscle cells.

Fig. 3. (A) Cumulative concentration-relaxation response curves to serotonin (5-HT) in porcine right coronary arteries rings submitted to the Monoshunt and in controls rings. (B) Cumulative concentration-relaxation response curves to bradykinin (BK) in porcine right coronary arteries rings submitted to the Monoshunt and in control rings. (C) Cumulative concentration-relaxation response curves to sodium nitroprussiate (SNP in porcine right coronary rings submitted to the Monoshunt and in control rings. A P-value less than 0.05 was considered statistically significant.
The necessity of a bloodless field to obtain optimal visibility during performance of the anastomosis is an issue of concern in OPCAB. The most widely used variant of OPCAB involves use of sutures or silastic tapes to snare the coronary artery extravascularly, upstream and downstream from the anastomotic site on the target artery. However, examination with scanning electron microscopy showed that snares cause focal endothelial denudation, microthrombosis, and atherosclerotic plaque rupture [4] which may have severe clinical consequences, especially in diabetic patients [5].

Intracoronary shunts used as hemostatic devices in OPCAB also have the advantage of allowing myocardial protection by maintaining distal coronary perfusion. Experimental [6] and clinical studies [7] have demonstrated that shunting can prevent acute left ventricular dysfunction during beating heart coronary revascularization and is a useful tool in patients with left ventricular dysfunction or unstable angina, as well as for teaching OPCAB to residents [8]. However, shunts cause a severe endothelial dysfunction [2] due to rubbing of the endothelial layer [9] during the positioning and the removal of the devices. This can acutely compromise the patency of the bypasses and contribute to late graft failure and recurrent angina by favoring the development of intimal hyperplasia. The use of the Monoshunt with a distal undersized and flexible part avoids rubbing of the device on endothelial layer and, as a result, the occurrence of the endothelial dysfunction in the distal run-off. Furthermore, hemostasis was satisfactory and allows completion of an anastomosis.

The main limitation of this study is the use of healthy coronaries arteries, with a large and unimpaired run-off, and experiments should be repeated on atherosclerotic arteries [10], but the lack of rubbing by the distal part would also protect the endothelium in these arteries. Furthermore, as the endothelium of atheromatous arteries endothelium is already dysfunctional [11], the differences of effect of the Monoshunt between both sides of the anastomotic site would not appear as clearly in these experiments.

Finally, in chronically occluded vessels with a large collateral bloodflow and generous retrograde perfusion, back bleeding at the anastomotic site may be controlled imperfectly by the Monoshunt’s distal area. However, these occluded vessels will seldom need shunting for myocardial protection.

Surgeons should use caution in application of the device because all shunts can generate serious macroscopic complications such as extensive intimal denudation and atheromatous plaque rupture inducing acute thrombosis, arterial dissection or distal embolism. The ideal shunt to avoid endothelial damage is an undersized shunt with minimal endothelial rubbing associated with the obligatory shunt’s movement for positioning and removal, which is the most deleterious maneuver for the endothelium. However, if endothelial damage remains inevitable upstream, use of the Monoshunt should avoid distal endothelial denudation, protect the run-off of the bypass and allows distal coronary perfusion. Further experiments are warranted before definitely establishing on the harmlessness and effectiveness of this new device.

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References


Fig. 4. Coronary artery Silver Nitrate staining: (A) showing a preserved endothelial layer. (B) Showing preservation of the endothelial layer with the distal part of the Monoshunt (50–100% of controls). (C) Showing disappearance of the endothelial layer due to the rubbing with the proximal part of the Monoshunt (0% of controls).


