Iatrogenic coronary ostial stenosis (ICOS) following aortic valve replacement (AVR) is a rare but potentially lethal complication of aortic valve replacement (AVR). This complication is usually diagnosed by angiography and treated with aortocoronary bypass surgery.

Case Reports

In the present 3 cases pre-operative coronary angiography confirmed normal coronary arteries and they underwent uncomplicated AVR. Coronary lesions were clinically manifest within 4 months after surgery, and repeat coronary angiography demonstrated bilateral ostial stenosis in 1 patient and left main trunk stenosis in the other 2. Two cases were detected by multidetector computed tomography (MDCT) before angiography. MDCT and Virtual Histology suggested fibrous tissue formation in the lesions. All 3 patients were successfully underwent percutaneous coronary intervention (PCI) and stenting. The post-procedure clinical course has been uneventful, except for elective stenting of a recurrent lesion in 1 asymptomatic patient.

Conclusions

The incidence of ICOS after AVR is low. Noninvasive MDCT is useful for early diagnosis and PCI is a possible alternative treatment. ICOS may be caused by fibrous tissue formation, and therefore be distinct from conventional atherosclerosis. (Circ J 2006; 70: 1312–1317)

Key Words: Aortic valve replacement; Iatrogenic coronary ostial stenosis; Multidetector computed tomography; Percutaneous coronary intervention

Case 1

A 61-year-old woman with a history of hypertension was referred because of fatigue and dyspnea on exertion. On admission the ECG showed sinus rhythm and left ventricular (LV) hypertrophy. Preoperative coronary angiography demonstrated normal coronary arteries and severe calcific aortic valve stenosis. The echo-Doppler revealed a peak aortic gradient of 90 mmHg, mild aortic regurgitation, and an aortic valve area of 0.7 cm² with normal LV function. We performed a modified Bentall procedure with the button technique. The patient’s tricuspid valve was thickened, and extremely calcified. Coronary arteries were reconstructed with a full root technique. There was no displacement or flexion of the coronary artery graft during the surgical procedure. Myocardial protection with intermittent direct coronary cold blood cardioplegia was used. The first dose was administered by retrograde infusion from the coronary sinus (retro-cannula, RC014I, 14Fr, 4.7 mm, Edwards), and subsequently by antegrade direct cannulation of both coronary ostia using flexible, balloon-tipped cannulae (coronary perfusion cannula, Polystan). A Freestyle Prima PLUS 19-mm stentless valve (Edwards Lifesciences) was used to replace the native valve and aortic root using the full root technique. The patient made a complete recovery and was discharged on oral warfarin. Two months later she experienced severe chest pain and had a syncopal attack, and was taken to the center by ambulance. On admission the ECG showed transient ST-segment depression of 2 mm in the precordial leads, II, III, and aVF (Fig 1). Physical examination revealed normal prostatic valve sounds, a grade 4/6 systolic ejection murmur at the right second intercostal space, and absence of rales at the base of the lungs. There was no pedal edema. Echocardiography showed normal function of the left ventricle. Repeat coronary angiography showed severe (75%) LMT stenosis and 90% stenosis of the ostium of the RCA (Fig 2). Coronary bypass surgery was recommended as the first therapeutic option, but was rejected by the patient. For this reason she was scheduled for urgent PCI. On the same day PCI of the RCA was performed using a Runway FR3.5 6F guiding catheter (Boston
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Scientific) and a Neo’s Rinato guidewire (Getz Bros. Co, Ltd). Predilatation was carried out with a 3.5×14 mm balloon (Vento, Getz Bros.), and intra-aortic balloon pumping support was provided via the left femoral artery. Full balloon expansion was achieved at 8 atm with good immediate results and no apparent dissection. A 4.0×16 mm bare-metal stent (BMS) (Express 2, Boston Scientific) was deployed at 16 atm and was postdilated with a 4.5×8 mm low-compliance balloon (QUANTUM Maverick, Boston Scientific) up to 18 atm. During the procedure intravascular ultrasonography demonstrated localized severe RCA ostial stenosis. Virtual Histology tissue/plaque characterization (IVG3 ver.1.4J, Volcano Corp, Rancho Cordova, CA, USA) revealed massive fibrous plaque (Fig 3). On the following day PCI of the LMT lesion was carried out using a Mach 1 FR 3.5 6F guiding catheter (Boston Scientific) and a Neo’s Rinato guide wire (Getz Bros.). After pre-dilatation using a 3.5×15 mm balloon-catheter (Avita, Neich Medical), a 3.5×18 mm sirolimus-eluting-stent (SES) (Cypher, Johnson & Johnson-Cordis) was successfully implanted at 20 atm. Further dilatation was performed using a 4.5×15 mm balloon (Quanum Maverick, Boston Scientific) up to 18 atm. At completion of this procedure, the patient had undergone successful PCI with stenting of both lesions (Fig 4). The postoperative course was uneventful and 1 month later a follow-up coronary angiogram showed no apparent resteno-
sis, and the patient was discharged. Seven months after PCI she remained asymptomatic, but follow-up coronary angiography now showed >50% restenosis at the proximal edge of the stent implanted in the RCA ostium, but no restenosis in the LMT. In retrospect, strenuous movement of the RCA proximal site was thought to have caused stent edge injury, with resulting in-stent restenosis. The restenosed RCA ostial lesion was successfully treated by deploying a 3.5×13 mm SES (Cypher, Johnson & Johnson-Cordis), with post-dilatation using a 4.5×13 mm balloon-catheter (Fortis, Kaneka Corp).

### Case 2

A 75-year-old man with normal preoperative coronary angiography underwent AVR with a 25-mm Carpentier-Edwards Perimount bioprosthetic valve (Edwards Lifesciences). Myocardial protection was achieved by antegrade intermittent cold blood cardioplegia. Both main coronary vessels were perfused using cannulae with a soft silicon tip (CPCS 4 mm and 5 mm, Edwards). Three months later the patient presented with angina. Urgent multidetector computed tomography (MDCT) (Brilliance 16, Philips, Cleveland, OH, USA) imaging showed significant stenosis of the LMT (Fig 5). In the stenotic lesion the minimum CT density of the plaque was 59.5 Hounsfield units (HU). Coronary angio-

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<td>Fibrous</td>
<td>74%</td>
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<td>Fibro-Fatty</td>
<td>18%</td>
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Fig 3. Case 1: Virtual Histological findings of massive fibrous plaque in the right coronary artery ostial stenosis.

Fig 4. Case 1: Postprocedural angiogram.

Fig 5. Case 2: (A) Volume-rendering computed tomography image providing an overview of the anatomy of the left main trunk and showing severe ostial stenosis. (B) Curved multiplanar reconstruction.
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Angiography revealed ostial stenosis of the LMT. The patient rejected re-operation, but was amenable to treatment by PCI. A stent (BMS, Driver 4.0×9mm, Medtronic) was implanted (Fig 6) and 1 year later the patient was asymptomatic and follow-up coronary angiography showed no restenosis.

**Case 3**

A 63-year-old-woman underwent uncomplicated AVR with a 21-mm Carpentier-Edwards Perimount biological valve (Edwards Lifesciences) for calcific aortic stenosis with a gradient of 89 mmHg. She had normal LV function, and no coronary artery stenoses. Myocardial protection with intermittent direct coronary cold blood cardioplegia was used. The first dose was delivered at the aortic root (Standard Aortic Root Cannulae 12G, 9F. Medtronic), and subsequently via the coronary ostia (coronary perfusion cannula, Polystan). The patient presented 4 months later with unstable angina. Urgent MDCT imaging revealed significant stenosis of the LMT (Fig 7), with a minimum CT density of the plaque of 71.7 HU. Follow-up coronary angiography confirmed the presence of critical LMT ostial stenosis, which was successfully treated with PCI and stent (BMS, Driver 4.0×9mm, Medtronic) implantation because the patient rejected re-operation (Fig 8). At her recent examination 6 months after PCI the patient was asymptomatic and a follow-up coronary angiogram showed no restenosis.

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**Fig 6.** Case 2: Pre- and postprocedural angiograms.

**Fig 7.** Case 3: (A) Volume-rendering computed tomography, (B) multiplanar reconstruction. The images show severe ostial stenosis of the left main trunk.

**Fig 8.** Case 3: Pre- and postprocedural angiograms.
Discussion

An infrequent but potentially quite serious complication after AVR surgery is the occurrence of ICOS. Several pathophysiologic mechanisms for this complication have been proposed. The insertion of perfusion cannulae and direct coronary perfusion for myocardial protection during AVR may produce immediate traumatic lesions and late stenosis of the coronary arteries. Micro-injuries and local pressure necrosis might be related to the infusion pressure of the cardioplegic fluid and overdistention of the vessel by the catheter tip. In addition, there may also be intimal thickening and fibrous proliferation in proximity to the aortic root as a reaction to turbulent flow around the prosthetic valve.1 Histological examination of a ported intimal fibrous thickening in the aortic root and bioprosthetic valves may be the cause of ICOS.

Symptoms of ICOS, which usually develop within 6 months of surgery, can be rapidly progressive and may include angina pectoris and LV failure or acute pulmonary edema. This complication requires prompt clinical recognition and early treatment because of the possibility of sudden death. Coronary angiography is warranted in the event of typical exertional angina, even after angiographic exclusion of coronary artery stenosis prior to AVR.

As an alternative, MDCT is a promising noninvasive coronary imaging technique. Several studies have reported its high negative predictive value (≥95%) and moderate positive predictive value, and recent results indicate high diagnosis accuracy. Mollet et al.19 and Kuettner et al.20 who studied the diagnostic performance of MDCT for detection of significant lesions (≥50%) compared with that of quantitative coronary angiography, reported that all patients with significant left main disease were correctly identified. Moreover, they also demonstrated high diagnostic accuracy for proximal lesions of the RCA. MDCT imaging is becoming increasingly accurate, and may be useful in early diagnosis of ICOS. Accordingly we recommend its use within the first 6 months after AVR for early detection of ICOS.

The incidence of ICOS has been estimated as between 1% and 5%2-7 but may be even higher, considering that some unexplained sudden deaths after AVR may have been the result of ICOS. From 2000 to 2005, there have been 3 cases of ICOS at our center among 125 cases of AVR (mechanical valve in 44 cases, biological valve in 81 cases), representing 2.4% of all cases, which is a comparable frequency to that in past reports. It is perhaps noteworthy that immunological reaction to the heterograft was a potential mechanism causing ostial coronary artery stenosis.

Roberts and Morrow examined the postoperative pathological findings at necropsy in patients with AVR, and reported intimal fibrous thickening in the aortic root and proximal coronary artery.1 Histological examination of a specimen taken by directional coronary atherectomy (DCA) showed intimal hypertrophy, mucinous degeneration, and hyaline degeneration but no evidence of atherosclerosis. Schroeder et al reported that MDCT can determine coronary lesion configuration, and that an intermediate CT density (50–119 HU) corresponded to the presence of fibrous plaque. The CT density of ICOS in the present case 2 and case 3 was 59.5 HU and 71.7 HU, respectively, which is characteristic of fibrous tissue. Virtual Histological findings in case 1 revealed massive fibrous tissue with surrounding slightly arteriosclerotic tissue (Fig 3). We presume that the calcified layer represented the boundary of the preoperative vessel lumen, and that the fibrous and fibrofatty tissue within the calcified layer represented a secondary proliferative fibrotic reaction that increased within the next 2 months. Our findings are in accord with previous necropsy and DCA specimen findings, and this type of stenosis is thought to be distinct from conventional atherosclerosis.

ICOS may occur proximally in both the right and left coronary arteries, but occurs more often in the left coronary system.2-4 There have been several case reports of bilateral coronary ostial stenosis after AVR.1,2,10-12,25-27 and also some cases treated with PCI.28-30 We treated the present 3 cases of ICOS with PCI because the patients rejected re-operation and were willing to undergo PCI. We used 3 BMS and 1 SES (case 1 LMT) to treat 4 ICOS lesions (3 LMT and 1 RCA ostial lesion).

Chavanon et al demonstrated that ICOS is associated with high operative mortality and morbidity rates and poor long-term outcome.26 On the other hand, Marti et al in 1995 reported 3 cases of LMT stenosis after AVR treated with balloon angioplasty that all had a good outcome;11 at long-term follow-up (4, 6, and 11 years, respectively) no clinical or angiographic signs of restenosis were seen. Despite those good results the authors recommended that PCI only be considered in patients who would otherwise be deemed inoperable, or who refused re-operation but were willing to undergo PCI.

In recent years PCI has been used more frequently as revascularization therapy for unprotected LMT stenosis. Although long-term follow-up may sometimes reveal angiographic restenosis, the need for repeat revascularization, or even cardiac death, in selected patients with normal LV function and large reference vessel diameter the long-term prognosis has been reported to be favorable.29,30 In such carefully selected cases coronary stenting of unprotected LMT stenoses is a safe and effective alternative to bypass surgery. In addition, SES implantation for unprotected LMT stenosis may be even more effective in preventing restenosis because of the stent’s immunosuppressive effects.

Aortocoronary ostial lesions have higher restenosis rates than other lesions and SES implantation appears to be safer and more effective than BMS, and to reduce significantly the incidence of restenosis.22 In-stent restenosis is mainly due to neoimimal hyperplasia, and SES implantation has been shown to reduce this and hence risk of restenosis. It is for this reason that we used SES implantation at the second PCI for the recurrent RCA ostial stenosis in case 1.

Among the case reports describing use of PCI for ICOS,11-13 several have reported good mid- and long-term outcomes. The histopathological differences between stenosis in atherosclerotic and iatrogenic coronary lesions may result in different outcomes. However PCI is currently not routinely recommended for treating unprotected LMT that occurs following ICOS, although it can be used in carefully selected patients in the absence of other options. Further clinical studies of the long-term outcomes in more patients will be required to evaluate the role of PCI for ICOS in the future.

Conclusions

The incidence of ICOS after AVR is very rare, but it
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References