Acute coronary syndrome as a result of left main coronary artery stenosis after aortic valve replacement. A report of three cases

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Abstract
Acute coronary syndrome (ACS) as a result of iatrogenic coronary ostial stenosis (ICOS) is a rare but potentially life-threatening complication of aortic valve replacement (AVR). We present three cases of patients with ACS shortly after AVR, in whom ICOS were revealed. They refused an operation and thus they were treated with percutaneous coronary intervention. The potential pathomechanisms of ICOS and treatment options are discussed.

Key words: left main coronary artery stenosis, aortic valve replacement, acute coronary syndrome.

Introduction
Acute coronary syndrome as a result of iatrogenic ostial coronary artery stenosis (ICOS) is a rare but potentially life-threatening complication of aortic valve replacement (AVR). Iatrogenic ostial coronary artery stenosis was first described by Roberts and Morrow in 1967 and the incidence of this complication has been estimated as between 0.3% to 5% of all AVR procedures [1-6]. Ostial stenosis can occur both in the left main coronary artery (LMCA) and in the right coronary artery (RCA) and may have serious clinical sequelae [1-6]. The symptoms are often severe and may appear within 6 months after an operation. The underlying cause of ICOS still remains undetermined.

We present 3 cases of left main coronary artery stenosis after AVR, describe their clinical presentation and discuss the treatment strategy.

Case reports
Case 1
A 70-year-old man was referred with a history of syncope, chest pain, and exertional dyspnoea. Echocardiography revealed aortic stenosis with peak gradient 110 mm Hg and aortic valve area (AVA) 0.6 cm² and severe mitral insufficiency and calcifications. Preoperative coronary angiography (CA) demonstrated normal coronary arteries. In September 2005 the patient underwent aortic and mitral valve replacement. Mechanical prostheses ON-X-19A and ON-X-25M (Medical Carbon Research Institute, Austin, TX, USA) were implanted respectively. Cold (4°C) cardioplegic solution was administered antegrade by means of selective ostial perfusion and use of coronary artery perfusion cannulae in RCA and in LMCA. The patient made a complete recovery and was discharged on oral warfarin. In December 2005 he experienced anginal pain at rest. Admission ECG revealed ST segment elevation in the aVR lead and ST depression and negative T waves in leads V5-V6. Troponin I level was 1.48 ng/ml. Coronary angiography showed isolated severe LMCA stenosis. Echocardiography revealed correct function of both prostheses and left ventricle ejection fraction of 58%. The patient refused reoperation. Percutaneous coronary intervention (PCI) of LMCA with bare metal stent implantation (Multi-Link Vision 3.5 mm × 15 mm) was thus performed (Figure 1). The stent was post-dilated with a non-compliant balloon to 20 atm. The patient was discharged on aspirin, clopidogrel and warfarin and simvastatin, bisoprolol and ramipril. Four months later the patient was admitted because of increasing effort angina. Coronary angiography showed in-stent restenosis in the LMCA. Percutaneous coronary intervention was performed...
using an everolimus-eluting stent (3.5 mm × 23 mm). In intra-vessel ultrasound examination minimal lumen diameter after the procedure was 10.1 mm². The patient was discharged home on dual antiplatelet therapy and warfarin and he was recommended to maintain INR 2.0-3.0 for 12 months. In 2-year follow-up the patient was asymptomatic.

Case 2
A 61-year-old male patient with history of arterial hypertension, chronic atrial fibrillation and with normal preoperative CA underwent AVR for calcific aortic stenosis with mean gradient of 52 mm Hg (AVA 0.6 cm²). An ON-X 21 mechanical prosthesis was successfully implanted in July 2010. Both main coronary vessels were perfused antegrade using soft silicon tip cannulae (4 mm and 5 mm, Edwards). Four months later the patient presented with resting angina and heart failure symptoms. His troponin I level was 1.2 ng/ml. Coronary angiography revealed critical LMCA stenosis. The patient rejected re-operation but was amenable to treatment by PCI. The stenosis was crossed with a Balance Middleweight guidewire (Abbot Vascular, Abbot Park, Illinois). A complex PCI using double

![Fig. 1](image)

**Fig. 1.** A – Left main stenosis (white arrow). B – Right coronary artery – no significant changes. C – Percutaneous coronary intervention. Guidewires in left anterior descending and circumflex artery. Bare metal stent was implanted to LM/LAD and final kissing was performed. D – Final view after PCI
stent technique (T-stenting – zotarolimus-eluting stent – Endeavor Resolute, Medtronic, Minneapolis, Minnesota to LMCA-LAD and Endeavour Resolute 3.0 mm × 15 mm to circumflex) (Figure 2) was successfully performed and 6 months later he was asymptomatic and follow-up CA showed no signs of restenosis.

Case 3

In August 2010 a 72-year-old man with a history of aortic stenosis underwent AVR and tricuspid valve annuloplasty. A preoperative echocardiogram showed aortic stenosis with peak gradient 80 mm Hg (AVA 0.4-0.5 cm²) and significant tricuspid valve insufficiency with dilated annulus (46 mm). The CA revealed no stenosis in coronary arteries. A 21 mm mechanical aortic prosthesis (ON-X 21) was implanted and tricuspid annuloplasty was performed. Cold cardioplegic solution was administered antegrade by means of selective ostial perfusion and the use of soft tip cannulae. Six months later the patient presented with unstable angina. Urgent CA revealed ostial LMCA stenosis. Coronary artery bypass graft (CABG) was declined by the patient; therefore urgent PCI with Biolimus-eluting stent implantation (BioMatrix 3.5 mm × 24 mm, Biosensors Interventional Technologies Ltd., Singapore) was performed with good hemodynamic and clinical results (Figure 3).

![Fig. 2. A – Critical stenosis of LMCA (white arrow). B – Stent implantation in circumflex artery. C – Stent implantation in LMCA/left anterior descending artery with final kissing. D – Final effect after the procedure](image-url)

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Discussion

Several pathophysiological mechanisms of ICOS have been proposed. The insertion of perfusion cannulae during AVR may produce microinjuries and local hyperplastic reaction due to perfusion pressure of cardioplegic fluid and over-dilation of the vessel by the tip of the catheter [7-9]. There may also be intimal thickening and fibrosis in proximity of the aortic root as a reaction to turbulent flow around the prosthetic valves, leading to obstruction of the coronary ostia. Tukiji et al. reported that immunological reaction to the heterograft in patients with implanted bioprostheses was a potential mechanism of ICOS [7]. Roberts and Morrow showed in autopsy material in patients with AVR fibrous thickening in the aortic root and proximal coronary artery [1]. Histological examination of a specimen taken by directional atherectomy showed intimal hypertrophy, mucinous degeneration and hyaline degeneration, but no evidence of atherosclerosis [8]. An et al. revealed in multislice computed tomography (MSCT) examination that CT density of ICOS (79.5 Hounsfield units) indicated fibrous tissue [8]. Funanda et al. showed in virtual histology in a patient with ICOS of the left main artery massive fibrous tissue with surrounding slightly arteriosclerotic tissue [9]. They suggested that the slightly 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

Fig. 3. A – Severe stenosis of LMCA (white arrow). B – Stent implantation in LMCA/left anterior descending artery. C – Kissing balloon postdilatation. D – The effect of the procedure
increased after AVR. These findings showed that ICOS is an in-stent restenosis-like process rather than an atherosclerotic lesion. There may also be a genetic predisposition for developing this complication, since 70% of affected patients as compared to 10-15% in a control group had an epsilon 4 allele apolipoprotein E genotype [10].

Avoiding cannulation of the coronary ostia for antegrade cardioplegia but instead using retrograde delivery (through the coronary sinus) as an alternative method for myocardial perfusion may reduce the postoperative risk of ICOS. However, retrograde cardioplegia alone might not be effective in the entire myocardial protection including the right ventricle. Therefore, the best method of cardioplegia still remains unclear [8, 11, 12].

Chavanon et al. showed that ICOS is associated with high operative mortality and morbidity rates and poor long-term outcome [13]. On the other hand, there are several reports of PCI with stent implantation treatment in ICOS with good early and late results [5-9]. Despite those good results, some authors recommended that PCI should only be considered in patients who would otherwise be deemed inoperable or who refused re-operation but were willing to undergo PCI [12]. However, since most patients with ICOS have acute coronary syndrome and the risk of re-operation is increased, in our opinion, PCI with drug-eluting stent implantation (due to a lower in-stent restenosis rate) is the best treatment option [14, 15].

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