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'Pharmacological distal protection' with intragraft administration of diltiazem as pre-treatment during saphenous vein graft intervention

„Dystalna ochrona farmakologiczna" przez podanie diltiazemu do pomostu naczyniowego w ramach leczenia wstępnego podczas interwencji w obrębie pomostu naczyniowego z żyły odpiszczelowej

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Abstract

Percutaneous coronary intervention (PCI) of vein graft lesions is associated with a high risk of peri-procedural myocardial infarction and greater mortality than routine native coronary intervention. Embolic protection devices have been advocated to reduce the risk of distal embolisation during vein graft PCI.

Here, we report the case of a 72 year-old diabetic male smoker who had coronary artery bypass surgery three years previously who presented with acute coronary syndrome. Repeat coronary angiography revealed patent grafts except for a discrete eccentric critical lesion in ostium of saphenous vein graft to obtuse marginal. The lesion was crossed using a 0.014" runthrough wire (Terumo, Japan). Intragraft diltiazem (5 mg) was administered through the guiding catheter each time before predilatation and stenting (total dose = 30 mg). It was finally stented by deploying a 3.5 × 23 mm Xience Prime everolimus-eluting stent (Abbott, USA) at 13 atm pressure achieving TIMI III flow. He was discharged the next day with acetylsalicylic acid — 75 mg/day, ticagrelor — 90 mg twice daily, atorvastatin — 40 mg/day, metoprolol — 100 mg/day, and ramipril — 5 mg/day. The patient has been doing extremely well since then, with regular follow-ups at our institute.

Key words: embolic protection devices, intragraft diltiazem, percutaneous coronary intervention, coronary artery bypass graft

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Introduction

The saphenous vein is commonly used as a graft (SVGs) along with the left internal mammary artery during coronary artery bypass graft surgery (CABG). However, they have poor long-term patency compared to arterial grafts because they suffer both from degeneration and a failure rate of as high as 25% in the first 12 months [1]. Percutaneous coronary intervention (PCI) of vein graft lesions is associated with a high risk of peri-procedural myocardial infarction (MI) and greater mortality than routine native coronary PCI as a result of distal embolisation manifesting as the slow flow and no-reflow phenomenon (SFNR) which is encountered in 10–15% of cases [1]. Furthermore, deteriorating SVG lesions also possess thinner, more friable fibrous caps compared to native lesions, which further aggravates the incidence of plaque embolisation and platelet aggregation [2]. Although what causes no-reflow remains

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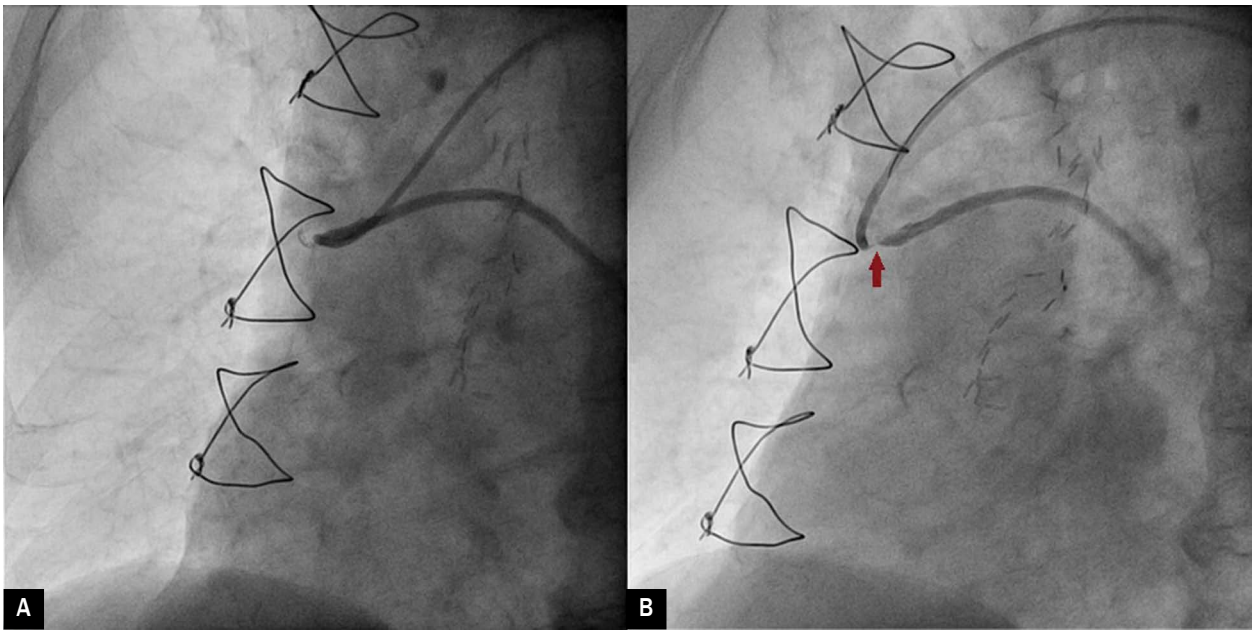

Figure 1A, B. Aorto-ostial lesion of saphenous vein graft to obtuse marginal showing discrete eccentric critical lesion (**A** — antero-posterior view; **B** — straight lateral view)

unclear, endothelial swelling, neutrophil infiltration, and platelet aggregation inducing microvasculature spasm and obstruction are a few of the plausible mechanisms. Combined together, these are associated with a higher rate of in-stent restenosis and target vessel revascularisation (TVR). The severity of these potential consequences makes finding the optimal technique essential during invasive SVG revascularisation.

Case report

A 72 year-old diabetic male smoker presented with sudden onset chest pain radiating to the right arm of 10 minutes' duration with diaphoresis. Past medical history included CABG three years earlier in lieu of triple vessel disease involving distal left main bifurcation. He was receiving acetylsalicylic acid (ASA) — 75 mg, metoprolol — 100 mg, atorvastatin — 20 mg, and ramipril — 5 mg, and gilbenclaimide daily. His vitals, physical examination, and biochemistry were all unremarkable. Electrocardiogram revealed mild ST-T changes in precordial leads. Echocardiography revealed mild concentric hypertrophy of left ventricle, and grade-II diastolic dysfunction with normal ejection fraction (EF = 55%). His troponin T level was raised (0.4 ng/L) when measured six hours after presentation. His coronary angiography three years before had revealed a left main bifurcation lesion (medina class: 1, 1, 1) involving the left anterior descending artery (LAD) and the left circumflex artery (LCx) with left dominant circulation. Right coronary artery showed mid tubular 90% lesion.

CABG was done using a left internal mammary artery (LIMA) graft as conduit to LAD, and SVG was anastomosed to obtuse marginal (OM), and posterior descending artery (PDA). Repeat coronary angiography revealed patent LIMA and SVG to PDA while there was a discrete eccentric critical lesion in ostium of SVG to OM with 99% stenosis (Figure 1). Intervention of critical SVG was planned after proper consent. SVG was cannulated using a 6 F Judkins right (JR) guiding catheter after failing to cannulate with a multipurpose catheter (Figure 2). The lesion was crossed and parked distally using a 0.014" runthrough wire (Terumo, Japan). Intragraft diltiazem (5 mg) was administered through the guiding catheter. The lesion was sequentially and gradually predilated using a 2 × 10 mm and a 2.4 × 10 mm Traveller semicompliant balloon (Abbott, USA). Diltiazem (5 mg) was injected each time before upsizing the balloon. As the lesion was not properly opening up because of its fibrotic nature, it was further dilated using a 3 × 10 mm cutting balloon (Flextome, Boston Scientific, USA) at 16 atm pressure by further administering 5 mg diltiazem (Figure 3). It was finally stented by deploying a 3.5 × 23 mm Xience Prime everolimus-eluting stent (Abbott, USA) at 13 atm pressure achieving TIMI III flow (Figures 4, 5). He was discharged the next day with ASA — 75 mg/day, ticagrelor — 90 mg twice daily, atorvastatin — 40 mg/day, metoprolol — 100 mg/day, and ramipril — 5 mg/day. The patient has

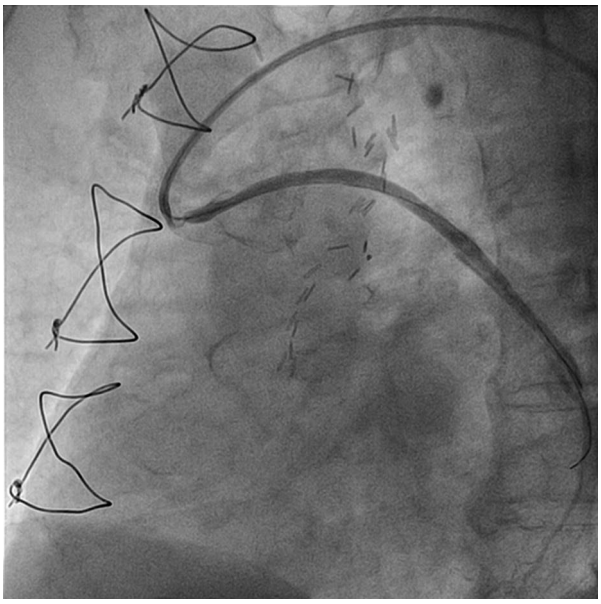

Figure 2. Saphenous vein graft was cannulated using 6 F Judkins right guiding catheter in straight lateral view

been doing excellently since then with regular follow-ups at our institute.

Discussion

Embolic protection devices (EPD) have been advocated in the American Heart Association/American College of Cardiology/Society For Cardiac Angiography And Interventions (AHA/ACC/SCAI) percutaneous coronary intervention (PCI) guidelines, when technically feasible, to reduce the risk of distal embolisation during SVG PCI. These guidelines were influenced by the SAFER (Saphenous vein graft Angioplasty Free of Emboli Randomized) study, a single randomised controlled trial which showed a significant reduction in major adverse cardiac events (MACE) with the use of a distal balloon occlusion device [3, 4].

There are several different types of commercially available embolic protection device with well-established efficacy, including the Filter wire/Spider/TRAP distal embolic filter, the Guardwire distal occlusion/aspiration device, and the Proxis proximal occlusion/aspiration device. Embolised debris includes necrotic atheromatous core, lipid-rich foam cells, cholesterol clefts, and fibrin, and most (80%) of them are < 100 μm in diameter. Larger particulate debris causes more plugging and compromise to myocardial perfusion than do smaller particles. These devices have pore sizes of between 100 and 110 μm and therefore capture particles > 110 μm and thereby protect against macroembolisation. However, their efficacy is not uniform because of the large crossing profile which further disrupts plaque and device-related trauma. Incomplete conduit occlusion or filter apposition, filter movement, incomplete aspiration, filter embolic overload, and side branch backwash are a few of the causes of incomplete embolic protection, even when used correctly.

The coronary bed, being an intermediately-sensitive vascular bed, can withstand ischaemia from distal embolisation unless it is very intense in proportion, affects an extensive segment of the viable myocardium, or it is

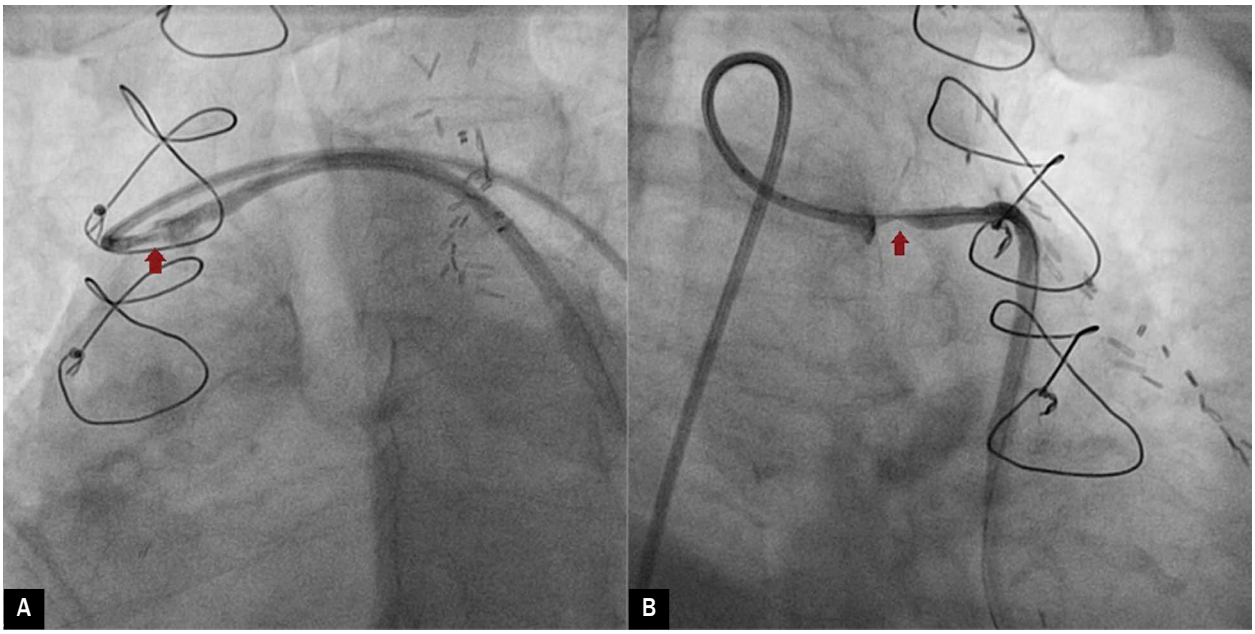

Figure 3A, B. Residual lesion despite repeated pre-dilatation with different balloons (A — straight lateral view; B — antero-posterior projection)

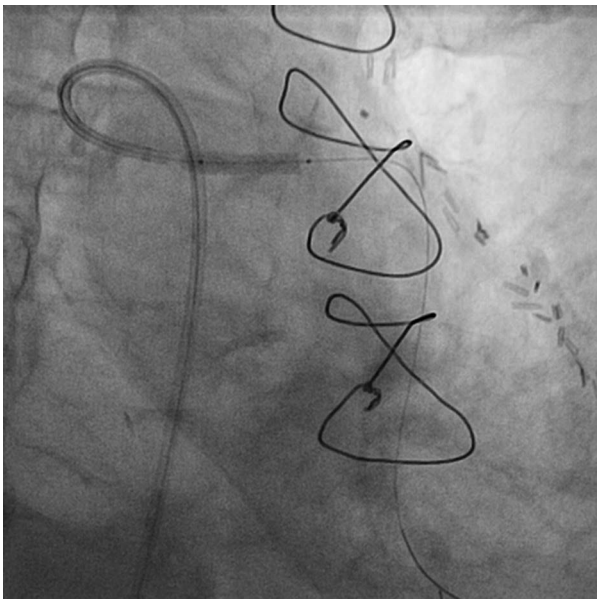

Figure 4. Lesion was stented by deploying 3.5 × 23 mm Xience Prime everolimus-eluting stent at 13 atm pressure

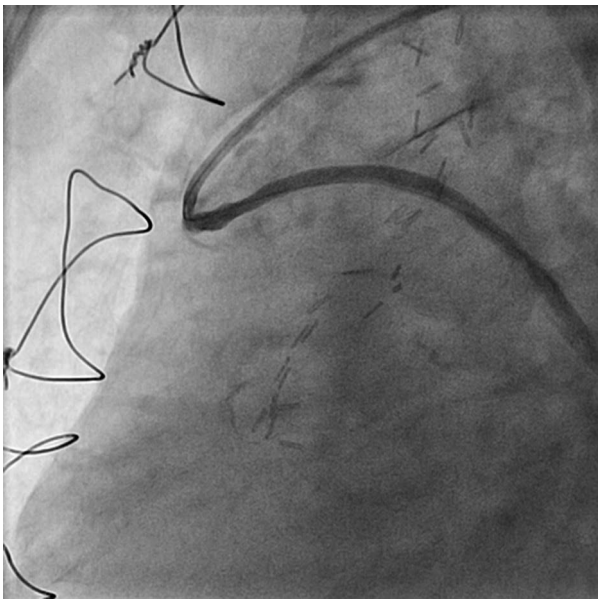

Figure 5. Saphenous vein graft to obtuse marginal showing TIMI III flow after successful stenting

already a jeopardised myocardium with left ventricular dysfunction. Therefore, a normally functioning left ventricular myocardium can withstand small-to-moderate intensity transient ischaemic insult without any consequences, whereas even smaller territory transient ischaemia may be clinically significant in the setting of left ventricular dysfunction. Focal fibrotic lesions, aorto--ostial lesions, distal anastomotic lesions, and in-stent restenosis lesions have a low embolisation risk and can be treated without EPD.

A sole surviving graft, large area of viable myocardium supplied by the SVG, left ventricular dysfunction, or atrioventricular nodal artery supply through the SVG in the absence of an artificial pacemaker all increase the clinical risk after an episode of slow flow. They should therefore be treated with EPD if feasible. This includes direct stenting, stent undersizing, the use of covered stent grafts, aspiration thrombectomy, adjunctive administration of intragraft anti-thrombotic agents (abciximab and thrombolytics in setting of thrombus), and prophylactic use of vasodilators (verapamil, nicardipine, adenosine, and nitroprusside). These have yielded positive outcomes in anecdotal reports and small studies but their efficacy has not been confirmed in large randomised trials.

Intragraft administration of vasodilators targets microvasculature to combat slow and no-reflow phenomena. Pre-treatment with intracoronary adenosine, a potent dilator of arteries and arterioles, decreases peri-procedural myocardial infarction after elective PCI because it improves myocardial flow and lowers the incidence of no-reflow in the setting of acute MI [5–8]. High doses of intragraft adenosine (at least five boluses of 24 μg each) may help to reverse slow and no-reflow phenomena in patients undergoing SVG intervention [9, 10]. Similar results have been observed with prophylactic administration of intragraft verapamil [11–14], and nicardipine [15] in reducing no-reflow in SVG PCI.

Based on these findings, we decided to try intragraft diltiazem to reduce slow flow in SVG PCI. This is also another calcium channel blocker like verapamil and nicardipine. The reason for success in our case was that the lesion was discrete, aorto-ostial, and fibrotic, as a cutting balloon was used to open up the lesion.

Therefore, if the morpho-anatomy is carefully assessed before attempting an SVG, one can achieve success without using an EPD.

Conflict(s) of interest

The authors declare no conflict of interest.

Streszczenie

Przezskórna interwencja wieńcowa (PCI) w obrębie wszczepionego pomostu żylnego wiąże się z wysokim ryzykiem okołozabiegowego zawału serca i większą śmiertelnością niż rutynowe zabiegi tego typu w naczyniach natywnych. Zaleca się stosowanie urządzeń zabezpieczających przed zatorami w celu obniżenia ryzyka odległych zatorów w trakcie PCI w pomoście żylnym.

Autorzy przedstawili przypadek 72-letniego pacjenta, aktywnego palacza, z ostrym zespołem wieńcowym, u którego 3 lata wcześniej wykonano chirurgiczne pomostowanie aortalno-wieńcowe. Powtórna koronarografia wykazała drożność stentu poza nieciągłą ekscentryczną krytyczną zmianą w miejscu połączenia pomostu z żyły odpiszczelowej z gałęzią brzeżną. Przez zwężenie przeprowadzono prowadnik angioplastyczny 0,014" typu *runthrough* (Terumo, Japonia). Przed każdą predylacją balonową i implantacją stentu do pomostu podawano diltiazem (5 mg) przez cewnik prowadzący (łączna dawka = 30 mg). Ostatecznie w miejscu zwężenia umieszczono i rozprężono stent uwalniający ewerolimus Xience Prime 3,5 × 23 mm (Abbott, USA), stosując ciśnienie 13 atm. Uzyskano przepływ TIMI III. Pacjenta wypisano następnego dnia z zaleceniem przyjmowania następujących leków: kwasu acetylosalicylowego — 75 mg/dobę, tikagreloru — 90 mg 2 razy/dobę, atorwastatyny — 40 mg/dobę, metoprololu — 100 mg/dobę i ramiprilu — 5 mg/dobę. Od czasu zabiegu chory czuł się bardzo dobrze i regularnie zgłaszał się na wizyty kontrolne do placówki autorów.

Słowa kluczowe: urządzenia do ochrony przeciwzakrzepowej, podanie diltiazemu do pomostu naczyniowego, przezskórna interwencja wieńcowa, pomostowanie aortalno-wieńcowe

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