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EDITORIAL

Sealing old plaques, seeding new plaques

Matteo Ghione, Kadriye Kilickesmez*, and Carlo Di Mario

National Institute of Health Research Cardiovascular Biomedical Research Unit, Royal Brompton and Harefield NHS Foundation Trust, Royal Brompton Hospital, Sydney Street, London SW3 6NP, UK

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In stent restenosis (ISR) is a heterogeneous phenomenon. The classical paradigm is neointimal proliferation in response to vessel wall injury often in combination with incomplete stent expansion. Drug-eluting stents (DES) have been designed to reduce or eliminate hyperplasia and in fact dramatically reduced restenosis and target lesion revascularization (TLR). The drawback of DES has been an increase in late and very late stent thrombosis, a potentially life-threatening complication considered a consequence of delayed and incomplete strut endothelialization.

The article of Habara *et al.*[1] challenges this concept by analysing in-stent restenosis with optical coherence tomography (OCT) in the first generation DES at different time intervals from the implantation. In this study of 86 sirolimus-eluting Cypher and paclitaxel-eluting Taxus stents ISR they described different neointimal patterns and assessed their prevalence at various time intervals from DES implantation. They demonstrated that restenotic tissue changes its characteristics over time. In the first months after implantation a speckled pattern is frequent and they hypothesized this was caused by proteoglycan deposition and delayed arterial healing. Later after implantation neoatherosclerosis develops with a pattern of thin-cap fibroatheroma (TCFA) observed in >10% of 1–3 years old ISR and >30% IRS older than 3 years, some with plaque rupture and thrombus formation. The majority of these patients was identified with elective angiography and since restenosis is rare also in first generation DES they had to perform control angiography in 2666 patients to identify 91eligible ISR patients.

Stent neoatherosclerosis has been described more than a decade ago but the reports were dismissed as non-clinically relevant anectodical findings till a growing series of OCT and pathology studies suggested that this was a frequent mode of failure of bare metal stent (BMS) and first generation DES. A histopathological study on autoptic specimens by Nakazawa *et al.* [2] found that the incidence of neoatherosclerosis was higher and occurred earlier in DES compared with BMS. In particular, foamy macrophage clusters and TCFAs were found more frequently in DES (14 and 13% within 2 years) than in BMS.

The question that arises is why DESs accelerate the neoatherosclerotic process? Angioplasty and more specifically stent implantation with its predictable neointimal coverage has been advocated as a technique to achieve plaque sealing and passivate active atherosclerotic plaques.[3] Specific designs of very thin self-expanding stents with low radial force were tested as prophylactic treatment of thin-capped fibroatheromas at risk of rupture.[4] Interventionalists may accept that neotherosclerosis develops several years after stent implantation but are puzzled and in denial of a radical acceleration of the same phenomenon stents are expected to cure and prevent. Delayed healing with an incomplete dysfunctional endothelium has been blamed as the cause of the increment in late and very late stent thrombosis observed with first generation DES. Possibly the same process of prolonged neointimal disruption may facilitate macrophage infiltration and lipid accumulation, developing vulnerable plaques prone to rupture as early as 1–3 years after stenting. We concentrated our prevention measures on strengthening and prolonging the antiplatelet treatment. If the mechanism is more complex than persistence of bare struts in contact with blood we may need to rethink our approach. How frequent is the phenomenon? Ten to thirty per cent of the very few DES that failed and develop restenosis in Habara's study may look trivial but still represents a significant percentage which may grow for IRS occurring 5–10 years post-implantation. We always consider ISR a stable process and the first reaction when we find a borderline significant narrowing is to assess functional severity with FFR. Maybe we should change our attitude, image them with OCT[5] and, if we find high-risk patterns, have a more liberal approach to treatment, as the Authors actually did in this study and as we normally do for lesions in saphenous vein grafts, prone to rapid progression and occlusion. Is the phenomenon specific of the first generation DES? The characteristics of the polymers and platforms radically differentiate stent performance and the lower incidence of restenosis, stent thrombosis, and mortality with the second generation vs. the first generation DES is reassuring.[6] Still we may need to wait few years from the introduction of second generation DES in Japan and another careful OCT Japanese follow-up serial study to have this important answer.

References

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* Corresponding author. Tel: +44 905327881360; fax: +44 902124592069. Email: kadriye11@yahoo.com

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IMAGE FOCUS

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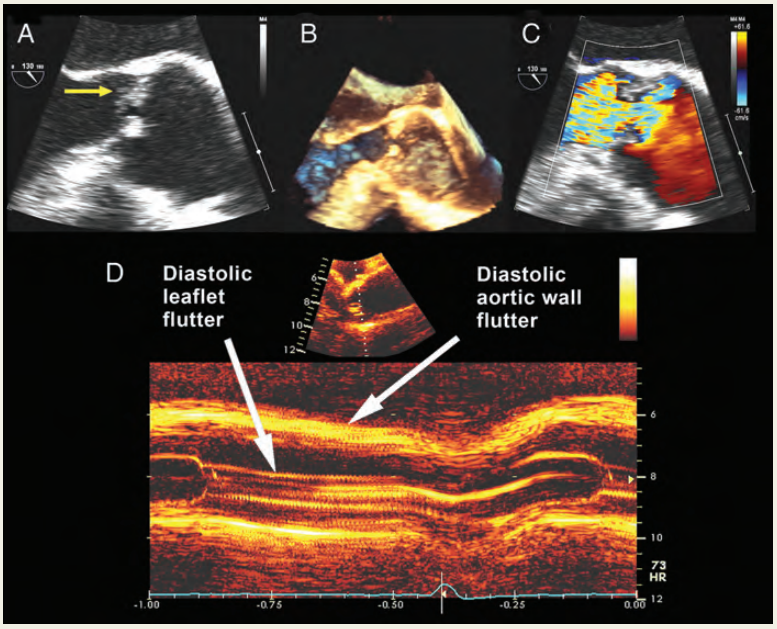
Diastolic fluttering of the aortic valve: pathognomonic M-mode features of flail cusp

Shahid Qamar, Khawaja Afzal Ammar*, Timothy E. Paterick, and A. Jamil Tajik

Aurora Cardiovascular Services, Aurora Sinai/Aurora St Luke's Medical Centers, University of Wisconsin School of Medicine and Public Health, 2801 W. Kinnickinnic River Parkway, #845, Milwaukee, WI 53215, USA

* Corresponding author. Tel: +1 414 649 3909; fax: +1 414 649 3551, Email: publishing28@aurora.org



An 85-year-old woman presented with recent-onset dyspnoea and fatigue, blood pressure of 120/45 mm Hg, diastolic thrill on the left sternal border, and grade V/VI, high-frequency harsh (buzzing) holodiastolic murmur radiating to shoulder, spine, and vertex of the head. Two-dimensional (2D) (*Panel A*, see Supplementary data online, *Video S1*), three-dimensional (3D) (*Panel B*, see Supplementary data online, *Video S2*), colour-flow Doppler (*Panel C*, see Supplementary data online, *Video S3*), and M-mode transthoracic and transoesophageal echocardiographic images revealed severe aortic regurgitation due to an unsupported non-coronary flail cusp with high-frequency diastolic flutter, and diastolic aortic wall flutter responsible for the murmur's transmission to the upper torso (*Panel D*). Surgery confirmed the flail cusp. Pathology showed myxoid degeneration with no endocarditis. Flail aortic valve leaflet results in pathognomonic high-frequency diastolic flutter of the torn aortic cusp and occasionally of the aortic walls. This condition is best demonstrated by M-mode echocardiography because of its higher temporal resolution than other imaging modalities including 2D/3D echocardiography, computed tomography, and magnetic resonance imaging.

Supplementary data are available at *European Heart Journal – Cardiovascular Imaging* online.

Conflict of interest: none declared.