SCIENTIFIC LETTER

Adventitia measurement in coronary artery: an in vivo intravascular ultrasound study

G Rioufol, M Elbaz, O Dubreuil, A Tabib, G Finet

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Recent studies have highlighted the dynamic role of the adventitia in the genesis of atherosclerosis,¹ atherothrombotic events² and restenosis after balloon angioplasty.³

Intravascular ultrasound (IVUS) provides a unique means of studying atherosclerosis in vivo, but the lack of any acoustic interface behind the adventitia notoriously prevents analysis of the adventitia. Careful analysis of IVUS images, however, often finds slight pericardial detachments just to the rear of the artery being explored. This situation creates a new anechogenic acoustic medium at the external edge of the adventitia, setting up a new acoustic interface, thus clearly identifying the adventitial tunica (fig 1).

We first conducted an ex vivo study to test this hypothesis and validate the precision of the adventitia measurements. The relevance of such data in humans in vivo was then assessed by IVUS studies of the left anterior descending (LAD) artery.

METHODS

The first 5 cm of 30 LAD arteries and the facing myocardium were placed on a dedicated bench. Adventitial thickness was measured by 30 MHz IVUS from the inner (external elastic membrane) to the outer border (pericardial detachment). Histological analysis was carried out precisely at the IVUS measurement location independently and blindly with respect to IVUS.

We took advantage of IVUS (30 MHz) procedures indicated for invasive exploration of the LAD in 38 patients with chronic angina without evidence of destabilisation during the

last three months. We reviewed the images a posteriori for analysis of the adventitia. In case of atheroma, qualitative plaque data and the usual quantitative stenosis and remodelling data were obtained. Adventitia thickness was measured as in the ex vivo study.

RESULTS

In all 30 LAD arteries sampled, the adventitia was clearly visible in agreement with histological results. Mean adventitial thickness was 183 (SD 99) μ m on histological analysis versus 258 (57) μ m on IVUS ($p < 0.0001$). Adventitia of varying thickness was found in histological studies (range 60–400 μ m), closely correlated to IVUS findings ($y = 158 + 0.62x$, $r = 0.54$, $p = 0.01$). The Bland–Altman plot shows limited difference of measurements without any systematic bias ($p = 0.46$).

A segment of adventitia was clearly identifiable in all patients, with a mean analysable segment length of 28 (12) mm in each artery. The artery was normal on IVUS in nine patients. Atherosclerosis was present in 29 without difference in adventitia assessment between these situations. Adventitia in atheromatous arteries was significantly thicker than in IVUS normal ones (353 (75) μ m v 233 (42) μ m, $p < 0.0001$), but thickening did not differ according to the type of remodelling with respect to risk factors or distance from the ostium.

DISCUSSION

To the best of our knowledge, this is the first observation that the LAD adventitial wall can be identified and correctly

Figure 1 (A) Typical example of visualisation of adventitia during in vivo intravascular ultrasound (IVUS) examination in the left anterior descending artery. (B) Bland–Altman plot comparing adventitial thickness with histological results and IVUS. *IVUS probe.

measured by IVUS in vivo in humans. Adventitia is classically non-analysable during routine IVUS examination but is on the other hand properly detectable under the conditions of observation here described and, at least in some segments, can be looked out for. Given the particular anatomical pattern being studied here measurement was from inner border (external elastic membrane) to outer border; this is a limitation that reduces the accuracy of our measurements, as outer border data are well known to depend on the radiofrequency envelope thickness and to be affected by the gain. This explains why the minimum distinguishable distance between two finite points should at best correspond to the system's axial resolution (190 μm at 30 MHz). These acoustic limitations account for the 158 μm offset from the regression slope in our findings. Adventitia has recently been reported visualised by high frequency epicardial echocardiography during heart surgery.⁴ The periarterial halo that the authors identify as being the adventitia was significantly thicker in case of atherosclerosis detected on angiography than in an angiographically normal artery (0.92 (0.2) mm v 0.54 (0.2) mm; $p < 0.001$), but unfortunately this was not correlated with histological studies. These values are twice as high as our own, probably because of the poorer resolution of their measurement system: 6–15 MHz. Some pathological studies, however, do confirm our finding of significant adventitial thickening in case of atherosclerosis.^{2–5} We observed no significant difference in adventitial thickness according to the type of arterial remodelling. The adventitia is widely recognised as being implicated in the constrictive remodelling subsequent to balloon angioplasty,³ but the findings are much less well established in the case of native atherosclerosis. In a recent autopsy series, Burke *et al*⁵ found that negative remodelling appeared to be associated with thicker adventitia. On multivariate analysis, however, the involvement of the adventitia in the type of remodelling proved insignificant. Very recently, Moreno *et al*² reported

adventitial inflammation in aorta sections associated with the largest intraplaque lipid zones, especially in association with the largest atheromatous plaques.

The coronary adventitia is often detected in the LAD artery and is shown to be easily and reliably analysable on IVUS with an increased thickness in the case of coronary atherosclerosis.

Authors' affiliations

G Rioufol*, **M Elbaz**, **O Dubreuil**, **G Finet***, Department of Hemodynamics and Interventional Cardiology, Cardiovascular Hospital, Hospices Civils de Lyon and Claude Bernard University, Lyons, France
A Tabib, Department of Pathology, Cardiovascular Hospital, Hospices Civils de Lyon and Claude Bernard University, Lyons, France

*Also INSERM E 0226, Lyons, France

Correspondence to: Dr Gilles Rioufol, Department of Hemodynamics, Cardiovascular Hospital, B P Lyon-Monchat, 69394 Lyons Cedex 03, France; gilles.rioufol@univ-lyon1.fr

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IMAGES IN CARDIOLOGY

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An unusual post mortem illustration of twiddler's syndrome

This photograph shows a postmortem heart. The right atrium and right ventricle have been opened, showing the tricuspid valve. A permanent pacemaker lead descends from the superior vena cava to the right atrium and thence the right ventricle. A loop of twisted pacemaker lead of at least 10 coils is shown orientated left and superiorly. There was loss of electrical insulation proximal to the twisted segment. At fresh postmortem examination, manual torsion of the wire at the left infraclavicular pulse generator site resulted in transmission of the twist right down to the right ventricle despite the presence of numerous endocardial adhesions around the wire.

The patient, a woman aged 85, had received a unipolar VVI pacemaker six years previously for third degree atrioventricular heart block. Six months later re-programming for pocket twitch was required. Eighteen months after that, further pocket twitch prompted reoperation, finding the pulse generator turned over, exposing pectoral muscle to its non-insulated aspect. The pulse generator was replaced with another firmly stitched down. Four years later she presented with heart failure, atrial flutter and intermittent failure to capture the ventricle. A major cerebral infarction caused death.

Usually, twiddler's syndrome results in loops of wire at the pulse generator site. This unusual case shows how, despite

multiple adhesions, torsion can be transmitted to within the heart. As usual, the patient stoutly denied twiddling.

B Thwaites
N Gehdu

barnaby.thwaites@weht.swest.nhs.uk