EDITORIAL

Virtual histology: does it add anything?

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Heart 2007;**93**:897–898. doi: 10.1136/hrt.2006.109371

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Cardiovascular disease is the principal cause of death in developed countries.[1] Rupture of the atherosclerotic plaque is the pathological substrate underlying up to 75% of episodes of acute coronary syndromes and the most common cause of sudden death. Although pathological findings at autopsy have helped our understanding of the various types of coronary plaques underlying thrombosis, clinically we have been unable to detect lesions prior to rupture. Therefore, intervention strategies have focused on the management of acute coronary syndrome following thrombosis or at sites of severe narrowing.[2 3]

As most rupture-prone or vulnerable plaques have <75% cross-sectional area luminal narrowing (ie, <50% diameter stenosis), angiography is not useful in early detection. What distinguish these lesions from others in the coronary arteries are their morphological features, which consist of a thin fibrous cap infiltrated by macrophages and a large necrotic core. The development of new modalities to identify vulnerable plaques on the basis of morphological features is beginning to offer the possibility of identifying these lesions in vivo.[4] One of those modalities, virtual histology (VH) intravascular ultrasound (IVUS), is based on spectral analysis of radiofrequency data and has begun to provide detailed assessment of plaque composition in vivo.[5]

In this issue of *Heart* (***see article on page 928***), Surmely *et al*[6] investigated the relationship between arterial remodelling and VH-IVUS-based plaque composition.[6] The concept that human coronary arteries dilate as plaque size increases in order to preserve luminal diameter was initially reported by Glagov *et al*[7]. Two studies on the pathological features of patients dying due to coronary artery disease demonstrated a relationship between positive remodelling and morphological features of plaque vulnerability such as high lipid content, increased macrophage infiltration and less fibrous tissue.[8 9] Previous in vivo studies using IVUS supported the concept that positive coronary arterial remodelling predominantly occurs in plaques of patients with acute coronary syndromes.[10 11] Surmely *et al*[6] confirm this observation in a larger series of patients by using VH-IVUS. In a series of 85 patients, 25% of patients with negative remodelling by IVUS presented with acute coronary syndrome compared with 52% of patients whose plaque had evidence of positive remodelling ($p = 0.02$).

As the advantage of VH-IVUS over grey-scale IVUS is the possibility of more accurate characterisation of plaque components, the authors also report on the differences in plaque morphology in negatively remodelled lesions compared with positively remodelled lesions. By VH-IVUS, there was a striking disparity between the authors' findings regarding plaque morphology stratified by remodelling index and previous pathological findings. They report that lesions with positive remodelling had less percentage of necrotic core and more fibrous tissue at the minimal lumen diameter compared with intermediate/negative remodelling lesions. These data agreed with one previous IVUS study but were conflicted with another.[12 13] Although differences in patient selection, definition of positive/negative remodelling and resolution of VH-IVUS compared with histological features might help explain these differences, studies such as this one are obviously limited by the fact that verification of the findings is not possible because of lack of histopathological evidence. Moreover, previous validation of VH-IVUS in ex vivo specimens may be biased by lesion selection and by tightly controlled experimental conditions, which may not be reliably translated in vivo.[5] In addition, VH-IVUS has trouble distinguishing necrotic core from calcification and, indeed, in the initial study by Nair *et al*[5] these were combined into a single colour and were called calcified necrosis, a terminology that does not distinguish between necrotic core and calcification. Pathological studies have clearly shown that there are definite areas of necrotic core that lack calcifications.

Despite these limitations, studies such as this one demonstrate the potential of in vivo plaque characterisation to begin to identify high-risk plaques. In previous times, we were limited to autopsy findings to study the relationship between arterial remodelling and coronary atherosclerosis, but this type of technology allows us to understand how such data compare with what is possible in the clinical setting. Moreover, autopsy data may not be applicable to living patients, especially those with acute coronary syndrome. However, there is little doubt that the larger necrotic core is more likely to be positively remodelled. This was also confirmed by greyscale IVUS data analysis in the current study by Surmely *et al*[6] in this issue of *Heart*.

However, this acknowledgement should not be taken as an endorsement of the reliability of VH-IVUS to define plaque characteristics with high accuracy. Newer modalities and improvement in the existing technology for evaluating coronary plaques that can better distinguish plaque morphology are needed. As the pathological definition

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Abbreviations: IVUS, intravascular ultrasound; VH, virtual histology

of vulnerable plaque is characterised by a necrotic core with an overlying fibrous cap of <65 μm, better imaging capability using higher-resolution devices is the only way to identify these plaques more accurately. Probably, the virtual histological definition of vulnerable plaque is not accurate as it has not been validated against histopathological features, and the spatial resolution of VH-IVUS (ie, 100–200 μm) is far below that needed to detect these plaques using the histological definition. Currently, optical coherence tomography yields a higher spatial resolution (10–20 μm), and offers the potential to provide more accurate information on coronary plaques.[14] However, optical coherence tomography is limited by its inability to image through blood, which makes this technology cumbersome and often not reproducible except in the most skilled hands.

Nonetheless, what we should note from studies such as this one is that we are entering a new age in cardiology where precise identification of plaque composition may, one day, allow us to identify high-risk plaques before they rupture, and thereby save lives.

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Competing interests: CVPath Institute, Inc. receives company sponsored research support from Volcano Therapeutics Inc., and Renu Virmani is a consultant for Volcano Therapeutics, Inc.

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IMAGES IN CARDIOLOGY

doi: 10.1136/hrt.2006.098475

Spontaneous intraoperative ventricular haematoma in a neonate

A 1-day-old boy was referred to our institution with cyanosis and respiratory distress. The chest radiograph demonstrated cardiomegaly and increased pulmonary vascularity. A cross-sectional echocardiogram disclosed obstructed mixed total anomalous pulmonary venous connections with a large secundum atrial septal defect and enlarged right cardiac chambers. The patient underwent surgical correction at 2 weeks of age. The intraoperative transoesophageal echocardiogram showed poor biventricular function along with a large hypoechogenic mass in the basal inferior septum (panel). A diagnosis of spontaneous intraventricular haematoma was made. The child left the operating room on extracorporeal membrane oxygenation (ECMO) support. Serial transthoracic echocardiograms showed progressive improvement of the ventricular function, and complete spontaneous resolution of the haematoma was noted 11 days after surgery. ECMO was discontinued on postoperative day 4 and the child was discharged home 1 month after surgery. Intraoperative spontaneous haematoma is an uncommon finding. In our experience, expectant management is warranted.

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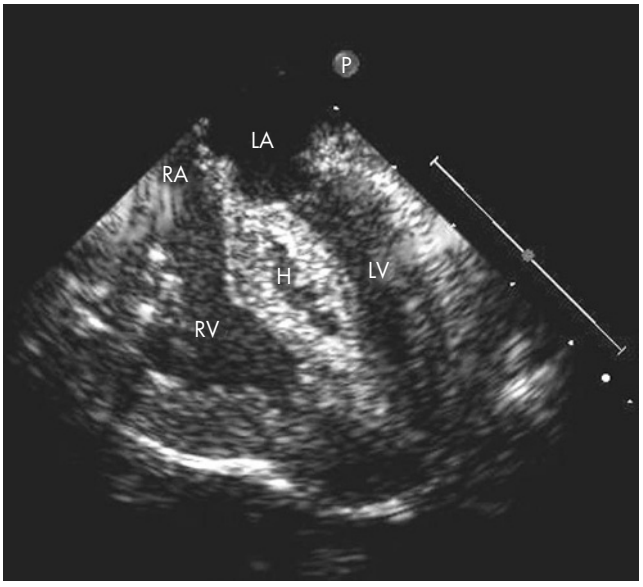

Transoesophageal echocardiogram from a four-chamber view showing a haematoma (H) in the basal inferior septum. LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle.