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iREVIEWS

STATE-OF-THE-ART PAPER

Assessment of Subendocardial Structure and Function

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The combination of high energy expenditure and the borderline adequacy of perfusion make the subendocardium uniquely vulnerable to injury. Selective subendocardial involvement is usually a marker of subclinical disease. Technical advances in new noninvasive imaging modalities, especially in spatial resolution, now permit qualitative and quantitative assessment of subendocardial structure, function, and perfusion. Many newer techniques have the potential to provide superior prognostic information to current standard assessment methods. This review describes the contemporary capabilities of multiple imaging modalities for assessment of the subendocardium, and seeks to guide the clinician regarding the information and technical deficiencies of each modality. (J Am Coll Cardiol Img 2010;3:867–75) © 2010 by the American College of Cardiology Foundation

Differences in function, loading, coronary perfusion, and pathology of the subendocardium make this a unique component of the myocardium. The importance of subendocardial function to overall cardiac mechanics has long been recognized (1). At a cellular level, myocytes are bound together in sheets, or laminae, typically 4 cells thick, which allow the heart to contract in longitudinal, radial, and circumferential planes (2). These vectors are different in the subendocardium and subepicardium, as the laminae are almost perpendicular to each other. Subendocardial contraction is greatest in the longitudinal plane, with both electrical and mechanical activation at this level propagating from apex to base. Conversely, subepicardial contraction generates circumferential shortening and left ventricular (LV) twist. The impairment of contraction in either layer is typically compensated by augmentation of the other (3). This compensatory mechanism allows preservation of overall LV ejection fraction in the face of abnormal diastolic function, but may be the harbinger of future systolic dysfunction if disease evolves to transmural involvement.

The subendocardium is vulnerable to change early in the course of disease due to several factors; it is the furthest layer from epicardial coronary flow, it undergoes extreme fluctuations in pressure and compression in both systole and diastole, and also appears prone to early structural microvascular architectural change such as fibrosis (4). Thus, the subendocardium is often the earliest myocardial layer affected in many disease processes. Advances in noninvasive imaging, and in particular improvements in spatial and temporal resolution, have allowed the investigation of disease processes within the subendocardium, identifying both perfusion and functional abnormalities. This has led to greater understanding of both

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disease mechanisms and possible treatment strategies. This understanding may allow us to better understand the progression of disease from diastolic dysfunction to overt systolic heart failure. In nonischemic heart failure with normal ejection fraction (HFNEF), arterial stiffness and fibrosis cause subendocardial function to be reduced both at rest and on exercise (5), resulting in diastolic dysfunction. Coronary ischemia also initially brings about diastolic dysfunction due to impairment of subendocardial perfusion prior to the development of overt systolic dysfunction (6).

This review will mainly focus on the contribution of recent imaging advances to evaluation of the subendocardium. For most clinicians, echocardiography remains the initial and most easily accessible cardiac imaging modality. Although this technique provides good spatial and excellent temporal resolution, other techniques offer higher contrast resolution. The optimal method to investigate subendocardial function will vary according to the question posed (Table 1).

ABBREVIATIONS AND ACRONYMS

2DS = 2-dimensional speckle

CMR = cardiac magnetic resonance

CT = computed tomography

CTA = computed tomography angiography

CVIB = cyclic variation of backscatter

LGE = late Gadolinium-DTPA enhancement

LV = left ventricular

MCE = myocardial contrast echocardiography

MDCT = multidetector computed tomography

PET = positron emission tomography

SPECT = single-photon emission computed tomography

Tissue Characterization of the Subendocardium

Integrated backscatter. Myocardial integrated backscatter is a modality used to assess the reflection of ultrasound waves from cardiac tissue. It can be measured as calibrated backscatter, whereby the reflection is normalized to adjacent high (e.g., pericardial) or low density (e.g., LV cavity) myocardium. Subendocardial scar has increased calibrated backscatter. Additionally, integrated backscatter varies throughout the cardiac cycle and is normally increased in systole (cyclic variation integrated backscatter [CVIB]) due to changes in acoustic properties related to tissue compression and alignment of reflectors (Fig. 1). Transmural CVIB is decreased in ischemic myocardial segments (7).

Normal contraction is heterogeneous, with subendocardial contraction being markedly greater than subepicardial contraction (1). By placing a manual region of interest in either the subendocardial or subepicardial half of the LV wall offline, Colonna et al. (8) localized the influence of stress-induced (atrial pacing) ischemia on subendocardial and subepicardial layers in 25 patients with known coronary artery disease and 12 controls. During stress in myocardial segments supplied by nonstenosed coronary vessels, the investigators were able to show a transmural gradient of CVIB from subendocardium to subepicardium. However, there was blunting of the CVIB signal exclusively in the subendocardial region in segments supplied by stenosed vessels (≥50% angiographically evaluated by 2 observers), elegantly illustrating the ability of this technique to reliably quantify differences in function between the subendocardial and subepicardial layers. Although this approach is technically challenging (including requiring the availability of raw data) and is limited to the anteroseptal and inferolateral walls because of anisotropy, the measurement of CVIB is closely linked to strain.

Computed tomography. Multidetector computed tomography (MDCT) has undergone rapid advances in recent years, with improvements in spatial and temporal resolution. Although attention has been on the delineation of coronary anatomy, recent advances have allowed direct imaging of the subendocardium.

Iodinated contrast agents (iomeperol and gadodiamide) used in MDCT (contrast enhanced [CE]-MDCT) have similar kinetics to gadolinium-DTPA as used in CE cardiac magnetic resonance (CMR). Gerber et al. (9) demonstrated that gated 16-slice CE-MDCT was able to distinguish between infarcted and normal myocardium with similar efficacy as CE-CMR in patients with acute and chronic myocardial infarcts. Two patterns were typically seen, an early hypoenhancement pattern was seen shortly after contrast administration (demonstrating subendocardial microvascular obstruction), and late hyperenhancement (reflecting increased distribution volume of contrast within the myocardium with reduced flow). Other investigators have shown similar findings (10–12) in both animal and patient studies.

Although these data are encouraging, the radiation required for MDCT remains a disadvantage compared with other imaging techniques. Table 2 documents the average effective radiation doses incurred as background and by various imaging modalities (13). An imaging procedure imparting 10 mSV is estimated to increase the lifetime risk of dying of a malignancy by 0.05% although factors such as patient age, race, and sex will also modify risk considerably (14).

The use of potentially nephrotoxic contrast agents is also of concern. Given these reservations, it may be reasonable to suggest that myocardial characterization using MDCT should only be un-