Looking inside AND outside the heart

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Cardiac amyloidosis (CA) refers to the involvement of the heart by amyloid fibril deposition in the extracellular space. Clinical features include restrictive infiltrative cardiomyopathy and heart failure.[1] Based on the amyloid protein involved, it can be subtyped as transthyretin cardiac amyloidosis (ATTR-CA) and the immunoglobulin light chain cardiac amyloidosis. Clinical management depends on earlier diagnosis and accurate characterization of the type of cardiac amyloid, as treatments differ for the specific type.

Gold standard for diagnosis of cardiac amyloid is endomyocardial biopsy.[2] However, due to the high risk associated including myocardial perforation and tamponade, various imaging modalities are used to diagnose and assess disease burden. Echocardiography (ECHO) is a valuable and widely accessible tool for investigating heart failure, but ECHO is neither sensitive nor specific for CA. Cardiac magnetic resonance (CMR) imaging can offer a much greater diagnostic value in CA. Cardiac MR is costly, not widely available, contraindicated in a substantial proportion of patients with devices, along with false positive and negative results. Both echocardiography and Cardiac MR do not distinguish types of cardiac amyloid.

Nuclear molecular imaging with bone seeking radiopharmaceuticals can provide relatively specific diagnosis of ATTR-CA. Bone scans have been widely studied for imaging ATTR-CA, with proposed mechanism of Tc-99m phosphate derivatives binding to transthyretin amyloid fibrils, which have high calcium content. Tc-99m pyrophosphate (PYP), Tc-99m methylene diphosphonate (MDP), Tc-99m hydroxymethylene diphosphonate (HMDP), and Tc-99m 3,3-diphosphono-1,2-propanodicarboxylic acid (DPD) are bone seeking imaging agents, with lower sensitivity of Tc-99m MDP relative to Tc-99m DPD or PYP in evaluating CA. Thus, 99mTc-methylene diphosphonate (99mTc-MDP), is not recommended for ATTR-CA imaging.

There are two accepted methods for nuclear image interpretation: the first introduced by Perugini et al, based on visual assessment, comparing myocardial to bone uptake, and the second described by Bokhari et al, which consists of a quantitative relationship between the counts in the heart and the contralateral hemithorax (H/CL ratio). The diagnosis of ATTR cardiac amyloidosis cannot be made solely based on PYP H/CL ratio alone. H/CL ratio is not recommended if there is absence of myocardial uptake on SPECT. Additionally, if the visual grade is 2 or 3, diagnosis is confirmed and H/CL ratio assessment is not necessary. H/CL ratio is typically concordant with visual grade. If discordant or the visual grade is equivocal, H/CL ratio may be helpful to classify equivocal visual grade 1 vs 2 as positive or negative.[3] ATTR-CA can be diagnosed when there is a myocardial radiotracer uptake in the scintigraphy study (99mTc-PYP, DPD, HMDP), and absence of a clonal peak in plasma and urine.

In this issue of the Journal, DePuey, highlights incidental findings that may interfere with image interpretation and/or have clinical significance in patients undergoing PYP cardiac amyloid imaging or bone scintigraphy.[4] He has numerous illustrative examples of physiologic calcifications including costochondral calcifications, soft tissue calcifications, and myocardial

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infarct and diffuse pericardial calcifications, that can be problematic on planar images and can obscure the evaluation of myocardial radiotracer uptake. SPECT and SPECT/CT can differentiate myocardial uptake vs blood pool activity. Myocardial 99mTc-PYP uptake patterns are categorized as absent, focal, diffuse, or focal on diffuse. Scans with focal 99mTc-PYP uptake could represent rib fracture or previous myocardial infarction. Following a myocardial infarction, myocardial 99mTc-PYP uptake may be positive for up to 7 days and rarely may remain persistently positive. In elderly patients with osteopenia, and in patients with prior radiation, comparing with rib activity may be confounded and SPECT imaging can be helpful in semi quantitative estimation of myocardial uptake by comparison to background activity.

It is essential to carefully evaluate extracardiac regions on these cardiac nuclear scans, which can identify neoplasms in the lungs and breast that may demonstrate microcalcification and may be visualized with cardiac amyloid scintigraphy. Osseous metastasis, visceral metastasis, nonmalignant conditions including osteoid osteoma, extensive degenerative changes, metabolic changes in bones, viscera, reactive marrow changes and increased uptake in cases with anemia are other important incidental findings on these scans with clinical implications. Thus thorough image analysis of cardiac and extracardiac findings is imperative.

If SPECT/CT is performed, an unenhanced, non-gated, free tidal breathing CT scan (5-mm slice thickness) for attenuation correction is obtained. Collaborative guideline by the Society of Nuclear Medicine and Molecular Imaging, American Society of Nuclear Cardiology and Society of Cardiovascular Computed Tomography recommends CT scanning for attenuation correction with shallow tidal breathing, tube current and voltage of approximately 10-20 mA and 80-140 kVp, gantry rotation speed of 1 seconds or slower, relatively high pitch (e.g., 1:1), and reconstructed slice thickness of 4-7 mm approximating SPECT.[5] Given parameters of Computed tomography for attenuation correction (CTAC), CT is usually able to identify the more obvious, larger and advanced extra cardiac tumors/disease findings and potentially miss the smaller, earlier stage and possibly innocuous findings resulting in the lower prevalence and higher cancer specific mortality as observed by Qureshi et al[6]

Our overriding responsibility is always to do right by our patients. This includes keeping up to date with existing and evolving scientific information, proficiency with current technologies, comparison with prior imaging to establish stability, and hence probable benignity, reporting 'all' findings (incidental and nonincidental) seen in the image, and using evidence based recommendations where available in our reporting to assist the referring physician, and ultimately help the patient.

Disclosures

Authors have no conflict of interest.

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