Assessment of RV function using gated blood pool SPECT

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Dysfunction of the right ventricle (RV) can occur in several aspects of cardiovascular disease (CVD) such as pulmonary hypertension (PH), congenital heart disease, left-sided heart failure (HF), coronary artery disease, and RV myocardial infarction, or valvular heart disease. The independent prognostic value of RV function is most strongly established for HF and PH,[1] but the role of the RV in CVD has thus far remained relatively neglected.[2]

Cardiac magnetic resonance (CMR) imaging is often considered the gold standard in RV function assessment[3] because it provides high-resolution images of the RV cavity and myocardium. This allows for RV measurements without the need for geometric assumptions required with 2D echo-based techniques or planar radionuclide ventriculography (PRNV). An important advantage of CMR is the high spatial and temporal resolution of the images, while the lack of fully automated processing introduces operator dependence and therefore increases inter- and intra-observer variability.

In this issue of the Journal of Nuclear Cardiology®, Dercle et al report on the use of three algorithms for the assessment of RV function using gated blood pool SPECT (GBPS) and compare the results of these methods with CMR-derived values. GBPS offers several potential advantages over other imaging modalities for RV analysis; notably, the acquisition is fast and technically simple, the resulting images are fully three-dimensional (3D, or rather 4D if one includes gating), and processing is comparatively operator-independent due to the availability of automatic or semi-automated analysis algorithms. The ability to automatically and reproducibly analyze 3D images of the RV is important given its complex geometry, characterized by a triangular shape in horizontal long-axis view and a crescent shape in short-axis view. While the left ventricle (LV) can adequately be modeled by an ellipsoid clipped by a singular plane that represents both the mitral and aortic valves, RV segmentation is further complicated by the fact that the tricuspid and pulmonary valves are not coplanar and are separated by the ventriculoinfundibular fold, as opposed to the fibrous continuity of the LV valves.

Given the anatomy of the RV, the main drawbacks of GBPS are the absence of tissue differentiation and the low resolution of the images (typically in the order of 6 mm/voxel, isotropically). This low resolution in turn leads to several challenges: partial volume effect renders segmentation error-prone when the apical portion of the RV cavity contracts, count spillover complicates visualization and segmentation of the interventricular septum, and the lack of fine anatomical detail virtually eliminates the ability to accurately locate the pulmonary valve. These effects are often exacerbated by the use of a low cutoff (smooth) reconstruction filter, a common occurrence in laboratories that primarily perform myocardial perfusion studies where such filter settings may be advisable and are generally the default for cardiac SPECT.

The results described by Dercle et al confirm the impact of such challenges: while RV end-diastolic volumes (EDV) correlate moderately to well with CMR

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($r = .53$-$.77$), ejection fraction (EF) measurements do not. The authors did note excellent inter-observer agreement (low inter-observer variability) with each of the GBPS measurements. As mentioned in the manuscript's discussion, there are multiple factors that can lead to discrepancies between the two techniques. One such factor is the inclusion or exclusion of trabeculations and papillary muscles during CMR analysis, especially at end-systole. This may explain the increased variability of CMR-measured RV end-systolic volume (ESV) compared to LV ESV.[4] Another is the relatively large slice spacing of CMR images (approx. 10 mm), which can affect volume estimates by magnifying ventricular cavity delineation imprecision or by introducing an error at the base due to incorrect basal slice selection.[5] The effect of slice spacing on CMR could be mitigated by employing an algorithm other than Simpson's rule to generate volumes[6] or by acquiring additional views (such as a two-chamber RV view or an outflow tract view), but this is not routine clinical practice, and commercially available CMR analysis software is commonly designed to process short-axis slices only, not to integrate measurements from multiple RV views.

For clinical purposes, one could use contrast-enhanced CT images to derive RV volume and EF measurements. CT provides a high-resolution, isotropic volumetric dataset of the heart that obviates the need to acquire images in specific orientations. High correlations between CMR and CT measurements of RV volumes and EF have been reported, with lower inter-observer variability with CT.[7] For CT RV assessment, specific acquisitions would be required so as to achieve adequate contrast in the right ventricle.

Is there an alternative to CMR and CT to calibrate GBPS processing algorithms? Previously, attempts have been made to use a mechanical, gated phantom to validate GBPS volume measurements.[8] Such a device, however, is only an approximation of cardiac anatomy and physiology and is limited in its assessment of the performance of processing algorithms as they may rely on characteristics that are not duplicated by the phantom. In particular, QBS depends on an analysis of count variations between the atria and ventricles to perform part of the segmentation process, and on expected geometric (anatomical) relationships between chambers and great vessels. For validation purposes, an interesting approach may be to model various pathologies using a mathematical phantom such as XCAT,[9] although even there the complexity of cardiac anatomy and physiology is only approximated, not faithfully reproduced. In particular, the RV outflow tract and pulmonary arteries are not included in the model.

The fact remains, however, that even for an experienced observer, it is extremely difficult to locate the pulmonary valve plane in a GBPS image, and this difficulty is likely the major source of error of the measurement. The pulmonary conus tends to be relatively hypokinetic compared to other parts of RV anatomy, limiting visual motion cues and decreasing the usefulness of analyzing count variations to automate locating the pulmonary valve. Some clinical populations do lead to GBPS images that are more readily analyzed by automated algorithms. RV enlargement is less likely to lead to partial volume effect-related issues, and LV hypertrophy leads to better ventricular separation. For patients in whom such conditions are known or suspected, GBPS may provide more useful measurements than in patients with a smaller RV or thinner LV myocardium, though neither of these conditions ease the task of locating the pulmonary valve.

What can we do to improve our chances of success in assessing RV function from GBPS? Current processing methods have historically mostly focused on LV analysis. Obtaining better RV measurements may require a number of steps. First, the image acquisition and reconstruction should be performed with optimal settings for the task at hand. This includes adequate count statistics, and optimal reconstruction and reorientation. There are several ways to improve count statistics: increase the injected dose, which is undesirable; increase the duration of the acquisition, which can be uncomfortable for the patient and decreases departmental throughput; or limit the number of time bins (or sum adjacent time bins in a 16-frame acquisition, as Dercle et al did for the TOMPOOL analysis), which has been shown to decrease LVEF measurements for myocardial perfusion SPECT,[10] though GBPS RVEF measurements may not be affected in the same manner.[11] Certain types of dedicated cardiac cameras may also provide more counts without increasing the dose or the acquisition duration.[12] Post acquisition, an appropriate reconstruction filter for the type of SPECT camera used should be selected, along with reconstruction limits that do not truncate the pulmonary outflow tract, and proper reorientation into a short-axis volume should be performed as algorithms can be sensitive to severe deviation from canonical orientation. Next, the processing algorithm may have parameters that can be calibrated against a chosen gold standard for a specific combination of equipment, orbit range and shape, and reconstruction settings. In particular, threshold settings for count operations directly impact volume measurements: lowering a region of interest (ROI) threshold increases the size of the ROI that represents the cavity volume, while increasing the threshold lowers the size of the ROI. Finally, careful and critical review of the results of automatic segmentation (ROI contours) is perhaps even more necessary than it is for the LV, but is more difficult

due to the challenging anatomy of the RV. Manual correction of the segmentation can be used when unsatisfactory contours have been computed.

Two final points should be made. The first, as indicated by Dercle's data, is that highly accurate measurements may not be needed to identify specific conditions: it is possible to detect RV EF impairment or RV enlargement with satisfactory sensitivity and specificity (see Table 2 in the manuscript) as long as the appropriate, algorithm-dependent thresholds are used. The second is that GBPS may provide additional information that is not commonly obtained using other modalities. One such example would be to analyze aspects of interventricular dyssynchrony using quantitative techniques[13,14] or the 3D equivalent of the phase and amplitude images routinely generated for PRNV studies, without the drawback of structure overlap.

The work of Dercle et al points out that there are major limitations in the quantitative measurements of the right ventricle from GBPS. Nonetheless, the acceptable correlations of the RV EDV by GPBS with CMR and the low inter-observer variability suggest that this measurement might be of clinical value in the serial assessment of patients in whom right ventricular size is of clinical importance. Should we assess RV function using gated blood pool SPECT? Yes, in selected patients, but we must be aware of GBPS' shortcomings and pitfalls. Further investigation may allow us to improve the algorithms as well, perhaps, as finding new uses for a well-established imaging technique.

Disclosures

Cedars-Sinai Medical Center receives royalties for the QBS software, a portion of which is distributed to the authors.

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