Serial cardiac SPECT studies: Technical issues and clinical implications

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The significance of serial change of various imaging parameters has been previously reported. In patients with heart failure, changes (of more than 5 units) in left ventricular (LV) ejection fraction from baseline at 6 months and 1 year are the strongest predictors of mortality among the serial measurements, and are significant after adjustment for therapy and baseline LV ejection fraction. On the other hand, baseline clinical variables are not helpful in predicting the patients who would experience an improvement in LV ejection fraction.[1] The relation between subsequent development of cardiac events and progression of coronary artery calcium has also been documented.[2] Stress gated single-photon emission computed tomography (SPECT) myocardial perfusion imaging (MPI) provides valuable information on the extent and severity of myocardial perfusion abnormalities. MPI is a suitable imaging method for the evaluation of patients who have undergone percutaneous coronary intervention or coronary artery bypass grafting and subjects with diabetes mellitus, and it has been used in the follow-up of such patients.[3–5] The availability of softwares for automated quantitative assessment of myocardial perfusion has allowed MPI to be particularly effective in serial evaluation, and might be useful clinically and in research studies.[6] Although appropriateness use criteria have not yet been clearly defined, serial MPI is used in guiding patient care. Serial MPI testing is useful in patients with known or high pre-test likelihood of coronary artery disease when there is new or worsening symptoms, after incomplete coronary revascularization, after medical stabilization of acute coronary syndrome or myocardial infarction if treated medically, after coronary revascularization for ''silent ischemia,'' and in ischemic cardiomyopathy treated with medical therapy or coronary revascularization. Serial MPI has also been utilized in randomized controlled trials to evaluate the impact of medical and interventional therapies on myocardial perfusion. Research use of serial MPI has expanded over the years, and it has been applied for evaluating new radiotracers, new stress agents, new types of gamma cameras, and for assessing anti-ischemic effect of a given therapy or treatment strategy. However, serial testing has more stringent requirements and is subject to variability because of technical, procedural, interpretational, and biological factors. The intrinsic variability of MPI becomes important in interpreting serial tests in order to define a true change in a given patient and to guide clinical decision making.[7]

It should be also noted that in trials using MPI to assess the effects of therapy, serial imaging would be stronger if at least moderate ischemia is an inclusion criterion, exceeding the variability of MPI, and thus assuring that the enrolled patients actually have ischemia.[6] Farzaneh-Far et al[8] identified 1425 consecutive patients with angiographically documented coronary artery disease who underwent two serial MPI scans within a 36-month time frame. They found that ischemia worsening is an independent predictor of death or myocardial infarction, resulting in significantly improved risk reclassification when added to previously

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known predictors. Despite this finding, the authors concluded that their results could not be used as justification for performing serial MPI scans, and that randomized prospective trials are required before any such recommendations can be proposed. The ongoing International Study of Comparative Health Effectiveness With Medical and Invasive Approaches (ISCHEMIA) Trial attempts to demonstrate the extent to which an angiographic-driven strategy for higher risk stable ischemic heart disease patients with moderate-severe ischemia will or will not improve clinical outcomes.[9] This trial will be completed in three years. In the meantime, recent data of El-Hajj et al[10] further suggest that if a patient has had two consecutive MPI studies performed for appropriate clinical reasons, the information regarding perfusion change may be used to improve prognostication and can guide clinical practice.

In this issue of the *Journal*, Germano et al[11] described the application of a novel approach (same-patient processing, or SPP) aimed at improving LV segmentation accuracy in patients undergoing multiple SPECT studies, and evaluated its performance compared to conventional processing in a large population of 962 patients undergoing rest- and stress gated SPECT MPI, for a total of 5772 image datasets (i.e., 6 per patient). A companion paper by the same authors[12] in the same issue of the *Journal* investigated the ability of grouped quantification (an expression of the same-patient processing approach, or SPP) to improve repeatability of measurements in patients with multiple SPECT studies, and evaluated its performance compared to standard quantification in a population of 100 patients undergoing rest, stress, gated rest, and gated stress SPECT MPI. All acquisitions were performed twice, back-to-back, for a total of 800 image datasets (i.e., 8 per patient).

In the first study,[11] each dataset was independently processed using a standard algorithm, and a shape quality control score was produced for every segmentation. Datasets with a shape quality control score higher than a specific threshold, suggesting algorithmic failure, were automatically reprocessed with the SPP-modified algorithm, which incorporates knowledge of the segmentation mask location in the other datasets belonging to the same patient. Experienced operators were blinded as to whether datasets had been processed based on the standard, or SPP approach assessed segmentation success/failure for each dataset. The SPP approach reduced segmentation failures from 219/5772 (3.8 %) to 42/5772 (0.7 %) overall. Of note, there was a particular improvement in attenuation-corrected datasets with high extra-cardiac activity from 100/962 (10.4 %) to 12/962 (1.4 %) for rest and from 41/962 (4.3 %) to 9/962 (0.9 %) for stress attenuation-corrected datasets. The number of patients who had at least one of their 6 datasets affected by segmentation failure decreased from 141/962 (14.7 %) to 14/962 (1.7 %) using the SPP approach. Therefore, whenever multiple image datasets for the same patient exist and need to be processed, it is possible to deal with the images as a group rather than individually. The same-patient processing approach can be implemented automatically, and may substantially reduce the need for manual reprocessing due to cardiac segmentation failure.

In the second study,[12] each dataset was automatically processed independently (using standard quantitative software) and as a group (together with the other seven datasets belonging to the same patient), using an SPP-modified version of the software that registered the images to one another using a downhill simplex algorithm for the search of optimal translation, rotation, and scaling parameters. Overall, grouped quantification resulted in significantly lower differences between repeated measurements of stress ungated volumes (1.40 ± 2.76 mL vs 3.33 ± 5.06 mL, $P < .05$), end-diastolic volumes (1.78 ± 2.78 mL vs 3.49 ± 5.35 mL, $P < .05$), end-systolic volumes (1.17 ± 1.96 mL vs 2.44 ± 3.35 mL, $P < .05$), and LV ejection fraction (−0.45 ± 2.29 % vs −1.16 ± 3.30 %, $P < .05$). Additionally, grouped quantification produced better repeatability (lower repeatability coefficients) for stress- and rest ungated volumes (5.4 vs 9.9 and 5.2 vs 13.1, respectively), stress total perfusion deficit (2.6 vs 3.6), stress and rest end-diastolic volumes (5.5 vs 10.5 and 7.2 vs 14.7, respectively), stress and rest end-systolic volumes (3.8 vs 6.6 and 5.3 vs 10.3, respectively), stress and rest LV ejection fraction (4.5 vs 6.5 and 4.7 vs 8.2, respectively), and rest total motion deficit (5.6 vs 9.6). These results show that it is possible to improve the repeatability of quantitative measurements of parameters of myocardial perfusion and function derived from SPECT MPI studies of a same patient by group processing of image datasets belonging to that patient. This application of the same-patient processing approach is an extension of the ''paired processing'' technique already described by the same authors, and can be performed in automated fashion through incorporation in the quantitative algorithm.

In summary, the ''same-patient processing'' approach proposed by Germano et al[11,12] reduces segmentation failure from 3.8 % to 0.7 % overall, with particular improvements in attenuation-corrected images, and result in lower differences between, and better repeatability of, several quantitative measurements of global LV perfusion and function, particularly in stress images. Therefore, these two studies support the concept that processing and quantifying different image

datasets of a same patient as a group can result in improving both LV segmentation and repeatability of quantification. This new approach may potentially significantly improve the accuracy of quantitative parameters derived from SPECT MPI and increase the clinical usefulness of serial MPI studies in a given patient.

Disclosure

The authors have indicated that they have no financial conflict of interest.

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