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EDITORIAL COMMENT

Gated SPECT: What's the ideal method to measure LVEF?

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Among the variables that characterize mechanical cardiac performance, left ventricular ejection fraction (LVEF) has attracted broad clinical interest, as various studies have provided ample evidence that LVEF is a major prognostic parameter [1–4]. Also, LVEF is among the selection criteria for device-based anti-arrhythmic or resynchronization therapy [5, 6]. Several imaging techniques allow for the assessment of LVEF, e.g., 2D and 3D echocardiography, gated SPECT, contrast angiography, cardiovascular magnetic resonance imaging (CMR) and computed tomography [7]). In patients with suspected ischemia, a common strategic sequence in which imaging techniques are being utilized is echocardiography, gated SPECT and coronary angiography, the latter frequently combined with or followed by intervention. As these three imaging techniques may all yield LVEF values it is not uncommon in clinical practice to have access to multiple LVEF measurements of the same patient.

If, in one patient, these three LVEF values are available, what would be the measure of preference? The answer to this question depends upon the reliability of the measurement technique and on its proven prognostic value. Whether or not the echocardiogram, gated SPECT and the ventriculogram determined during angiography faithfully assess LVEF depends on a large variety of factors: the build of the patient, the technical quality of the equipment, amount of views (monoplane/biplane), quality of the analyzing software/algorithms, the potential for quantitative analysis, and of the operator/analyst being the most important ones [8–13].

Comparison with CMR, an important reference technique often being considered as a gold standard [14–19], can help in getting an impression of the relative accuracy of LVEF as measured by echocardiography, gated SPECT and contrast ventriculography [20–22].

- Jenkins et al. [23] compared serial LVEF values from 2D biplane and 3D echocardiography with serial MRI measurements in patients with prior myocardial infarction. They found that LVEF values measured with 2D and 3D echocardiography correlated significantly with MRI; $r = 61\%$ and 86% for baseline, and 70% and 82% for follow-up, respectively. However, when a comparison is made of the serial changes in LVEF, only 3D echocardiography correlated significantly with MRI ($r = 58\%$).
- In a review article, Sciagrà [24] cites 21 studies in which SPECT- and CMR-determined LVEF values were compared. Correlations measured in these studies ranged between 70 and 94%; 5 studies report correlations between 70 and 79%, 11 between 80 and 89% and 5 above 90%.

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– Several studies compared contrast monoplane or biplane ventriculography with CMR [25–28]. Correlation coefficients in these studies ranged from 72% to 98%.

When realizing that correlations of, e.g., 80 and 86%, roughly stand for 2/3 and 3/4 explained variance, respectively, echocardiography, gated SPECT and contrast ventriculography may yield LVEF values that differ considerably from CMR despite the statistical significance of the linear relationship. However, CMR is not suitable for large scale application in the context of the regular clinical diagnostic procedures for the evaluation of patients with suspected or known ischemic heart disease. Hence, in clinical practice, a certain (considerable?) amount of LVEF imprecision or uncertainty is inevitable.

Mutual comparison of LVEF determined by echocardiography, gated SPECT and contrast ventriculography demonstrates that these measurements contain to a certain extent different information and/or noise: correlations of 72–75% in 2D biplane echocardiography versus gated SPECT [29, 30], 93% in 3D echocardiography versus gated SPECT [31], 49–93% in 2D biplane echocardiography versus ventriculography [12, 32, 33], 80% between 3D echocardiography and ventriculography [34] and 69–87% for gated SPECT versus contrast left ventriculography [32, 35–37] were reported. Hence, potentially, one measurement could bear other diagnostic and prognostic information than the other.

It is the merit of Gimelli et al. [38] to have compared the prognostic value of LVEF determined by echocardiography (single plane), gated SPECT and contrast ventriculography (single plane). The authors found, in a large population of patients with known or suspected ischemic heart disease, a superior predictive value of gated SPECT (resting, not post-exercise) LVEF. What can explain this finding? It is well known that systematic differences exist because SPECT may exclude part of the outflow tract [36]. Also, it may well be that the single plane LVEF measurements in the echocardiograms and in the contrast ventriculograms could not compete with the tomographic gated SPECT technique. Finally, the SPECT LVEF calculation is more objective and reproducible due to automated analysis [39].

Gimelli et al. studied a large group of 422 patients with for the larger part an adequate cardiac function. Ejection fractions below, but also above 50%, the lower limit of normal in male subjects, are represented in the study group. Possibly (this was not made explicit in their publication), part of the patients had symptoms of overt, stage C, heart failure, but most of the other patients in the study group can be characterized as stage B heart failure (patients with structural heart disease, at risk for heart failure but still without symptoms of this disease [40]), several of them with asymptomatic LV systolic dysfunction and angina pectoris/myocardial infarction.

In a review article [41], Goldberg and Jessup state that the number of stage B heart failure patients with LV systolic dysfunction is four times greater than the number of patients who are in stages C (structural heart disease with prior or current symptoms of heart failure) and D (refractory heart failure requiring specialized interventions) combined. Coronary artery disease is the prevailing etiology of asymptomatic LV systolic dysfunction. In the Framingham study, half of the subjects with asymptomatic LV systolic dysfunction at entry had a previous myocardial infarction versus 2% of the subjects with a normal LV function at entry [42]. The prognosis of asymptomatic LV systolic dysfunction was unfavorable: 26% developed overt heart failure after 5 years of follow-up, and 40% died (compared to 12% of the subjects with a normal baseline left-ventricular function). The median survival for subjects with asymptomatic LV systolic dysfunction was only 7.1 years. Similarly alarming numbers were provided by the ECHOES (Echocardiographic Heart of England Screening) study [43], reporting a 69% five-year survival for asymptomatic LV systolic dysfunction (compared to 93% for the general population, 62% for subjects with heart failure but without LV systolic dysfunction, and 53% for subjects with heart failure and LV systolic dysfunction).

No specific treatment is currently available for patients with asymptomatic LV systolic dysfunction. However, a recent AHA Scientific Statement [44] mentions this group of patients as a main target for further study, because LV systolic dysfunction is the first step in the remodeling process that finally leads to overt heart failure. Research recommendation 4 reads: “Develop appropriate studies to identify and eventually treat asymptomatic individuals with LV dysfunction (stage B) and to prevent its development.”

Most likely, the findings of Gimelli et al. reflect partly the prognosis of stage B heart failure patients. Therefore, it could be worthwhile to carefully monitor patients for cardiac remodeling, possibly by repeated 3D echocardiography [23, 45], after they have been identified as asymptomatic LV systolic dysfunction patients by gated SPECT (of which Gimelli et al. demonstrated prognostic value additional to clinical variables) or, possibly, by a reliable biplane echocardiogram or ventriculogram or by a 3D echocardiogram. A similar study as that by Gimelli et al., in which, in this setting, the prognostic power additional to clinical variables of LVEF determined by gated SPECT is compared with LVEF determined by biplane echocardiography or contrast ventriculography or by 3D echocardiography would be a logical next step.

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