LEFT VENTRICULAR EJECTION FRACTION: A RETROSPECTIVE STUDY COMPARING 2D ECHOCARDIOGRAPHY AND GATED SINGLE PHOTON EMISSION COMPUTED TOMOGRAPHY (SPECT) IN CLINICAL USE.

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ABSTRACT

Objectives

The aim of this study was to compare left ventricular ejection fraction (LVEF) results derived from gated single photon emission computed tomography (SPECT) using Cedars-Sinai quantitative gated SPECT (QGS) processing software with results from 2D echocardiography, both obtained in routine clinical diagnostic use.

Methods

Data from previously performed tests were obtained from 73 patients who had undergone both 2D echocardiography and gated SPECT within a time span of 6 months and had not had significant events that could influence LVEF. LVEF from 2D echocardiography was reassessed to obtain discrete values and then the data was compared using Bland-Altman analysis.

Results

The correlation between the tests was shown to be good, but precision lacked. Bland-Altman analysis showed a bias of -0.8 percentage points when gated SPECT compared to mean values and 2 standard deviations (SD) ranged from -20.2 to 18.6.

Conclusions

LVEF values from the two methods can differ quite a bit and comparisons between them should be done with great caution.

Keywords: Cedar-Sinai quantitative gated SPECT, QGS, comparison, re-evaluation, subjective assessment
INTRODUCTION

A common measurement of heart function is the left ventricular ejection fraction (LVEF). LVEF has been shown to be an important factor for the survival of patients with coronary artery disease (CAD) and heart failure [9]. Many tests can be used to derive values of LVEF. Two commonly used tests that give values on LVEF are transthoracic 2D echocardiography and gated single photon emission computed tomography (gated SPECT) with evaluation software from Cedars-Sinai called QGS which stands for quantitative gated SPECT. Comparisons between these tests have been done before [3, 6, 7], but with mixed results and never with information about regional abnormalities in the movement pattern of the heart.

Transthoracic 2D echocardiography is one of the most generally accepted methods for measuring LVEF. It offers many ways of calculating LVEF but a subjective visual assessment is considered one of the best and shows good correlation with Simpson measurements. Gated SPECT with Cedars-Sinai QGS is widely used because of its ability of simultaneously assessing cardiac perfusion and function [5, 9]. It offers an objective assessment, but with regionally lowered perfusion of the myocardium or isotope uptake in close proximity to the heart, the results can be less reliable [1]. Sometimes the software can miscalculate LVEF even when the isotope uptake is satisfying. One example of this is if the heart has a small left ventricle [4].

The aim of this study was to get a picture of how well the results, regarding LVEF, from 2D echocardiography and gated SPECT with Cedars-Sinai QGS match up in our own routine examinations and through analysing of raw data find possible explanations to differing results. These possible explanations can be important to consider when interpreting results derived from these tests. They can also be interesting objects of further study.

METHODS

Patient group

73 patients (38 men, 35 women) with a mean age of 61 years (range: 30-84 years) where included in the study. All patients who had undergone both transthoracic 2D echocardiography and gated SPECT inside a time window of 6 months were selected. The period of selection started 04/01-2007, which was the time when the hospitals single photon emission computed tomography/computed tomography (SPECT/CT) camera (brand: Siemens Symbia T2) was in full use, and ended 3/11-2009, which was the date of the last search for patients in the database. All medical records of patients available to the hospital where searched, in order to exclude any patients who had had potentially LVEF changing events between the two exams. Sepsis without significant generalized symptoms, myocardial infarct with troponin release < 1.0 μg/L and anaemia, stable between tests, were not considered to be relevant LVEF changing events. Sepsis with significant generalized symptoms and myocardial infarct with troponin I release ≥ 1.0 μg/L between the tests or shortly before the first test and also atrial fibrillation/atrial flutter, if present at only one of the tests, were considered to be relevant LVEF changing events and these patients were excluded. Percutaneous
coronary intervention (PCI) was considered able to cause stunning in the myocardium, hence PCI a few hours before any of the tests caused exclusion. In some of the tests LVEF measurements were not possible, and in those cases the patients were excluded from the study. When more than one echocardiography or gated SPECT had been performed on a patient the echocardiography and gated SPECT closest to each other in time were selected. When possible, gated SPECT performed at rest was chosen before gated SPECT performed after stress, but rest exam is done only when needed for diagnostic reasons. The sex of the patients were determined from their Swedish social security number.

**Echocardiographies (performed in the routine diagnostics)**

The unit for clinical physiology (where all the echocardiographies in this study was performed) has several different routine protocols for echocardiography. If needed the test is tailored to suit the specific questions asked. Common to all tests are measurements of the left ventricle at end systole and end diastole in parasternal long axis. When difficulties in assessing LVEF occurs, M-mode measurements of the left ventricle in parasternal long axis, atrioventricular (AV) plane measurements and Simpson measurements can also be performed. LVEF is most frequently reported as ranges as <30 %, 30-40 %, 40-50 % to >50 %. LVEF 50 % is considered the lower limit for normality.

**Gated SPECT (performed in the routine diagnostics)**

Before stress testing the patients are prohibited from consuming caffeine and using nitrates. The stress test is done using an exercise bike with stepwise increasing load while monitoring electrocardiogram (ECG), heart rate, blood pressure, effort level and pain level. 600 MBq $^{99m}$technetium-sestamibi (Cardiolite) is administered intravenously when the patients have reached a certain level of pain or effort. After injection the patients are required to continue cycling for at least one min, preferably two. If stress by physical activity is not possible, maximum heart rate is too low, the patient has a pacemaker or if left bundle branch block is present on ECG, stressing of the heart is performed by continuous infusion of adenosine if no contraindications are present. Adenosine is infused 4-6 min. Infusion speed is normally (0.14 mg × kg bodyweight) / min. After 3 min the isotope is injected. Image acquisition is performed with the Symbia T2 at least 1 h after isotope injection, preferably longer. The patients are asked to drink 1 L of water and to eat at least 50 g milk chocolate (which they are given) and preferably more foods rich on fat. They are also asked to take a walk. This all is to minimize abdominal isotope uptake.

Gated SPECT acquisition and processing

At the image acquisition the patients are in supine position with arms over their heads monitored by a 3-lead ECG. Two low energy high resolution (LEHR) collimators in
90° configuration are gated to 8 frames per cardiac cycle. The R wave identifies the beginning of the cardiac cycle and one cardiac cycle is represented by one R-R interval. Image acquisitions are performed in 32 views in a contour based step and shoot rotation of 180° with 30 s acquisition per view. No attenuation correction is made in the acquisition and the pictures are saved in a 128 × 128 resolution matrix. If overlapping bowel isotope uptake is present when starting the acquisition the acquisition is aborted and restarted about 1 h later. The last acquisition is a spiral CT with breath holding for attenuation correction of perfusion images. The images are processed with the Cedars-Sinai QGS computer software. If the perfusion images are not completely without remark the patients do a revisit about one week later for another image acquisition, after injection at rest.

Processing of retrospective data

The reported results from the tests were checked and information about LVEF and factors related to LVEF was noted. Raw data from the tests were acquired. The echocardiographies were scrutinized and LVEF and measurements concerning LVEF was noted. All echocardiographies were reassessed and LVEF values were noted as discrete numbers, due to the wide intervals used in the routine reporting. In cases where reassessment of LVEF was impossible the patients were excluded from the study. All reassessments were made by one experienced physiologist blinded to previous reported values on LVEF. The gated SPECT images were checked for those particular tests where LVEF differed from echocardiography by 20 percentage points to make sure the image quality was satisfactory.

Statistical analysis

Comparison was made between LVEF values from the two tests using Bland-Altman analysis [2], and scatter plots for visualization. Analysis was performed on the material as a whole, the material without patients with regional abnormalities on their echocardiography and on material from only the patients with regional abnormalities in their echocardiographies. Only akinesis, hypokinesis and dyskinesis are deemed abnormalities. When presenting data from only patients with regional abnormalities location of the abnormalities are presented as to where they are most prominent. For statistical calculation Microsoft Excel 2007 were used.

RESULTS

Bland-Altman analysis of the whole study material (Fig. 1) showed a mean difference (bias) of -0.8 percentage points and a mean difference ±2 standard deviations (SD) of 18.6 and -20.2 percentage points when gated SPECT LVEF values compared to mean gated SPECT and echocardiography LVEF values. Scatter plotting (Fig. 2) showed a linearity with a slope of 0.827 and an intersect point (gated SPECT LVEF when echocardiography LVEF is 0) at 9.545 when gated SPECT LVEF compared to
echocardiography LVEF. The same analysis for the study material without patients with regional abnormalities in their echocardiogram (n = 63) showed a mean difference of -1.5 percentage points and a mean difference ±2 SD of 17.7 and -20.7 percentage points at Bland-Altman analysis (Fig. 3) and a linearity with a slope of 0.845 and an intersect point at 8.101 when scatter plotting (Fig. 4). Bland-Altman analysis of the test data from the patients with regional abnormalities (n = 10) show no apparent trends for any of the present abnormalities, mostly apical, mostly basal and mostly septal (Fig. 5).

**Figure 1** Bland-Altman plot of all data with gated SPECT LVEF compared to mean LVEF from gated SPECT and echocardiography. Mean difference ± 2SD ranges from -20.2 to +18.6.
Figure 2 Scatter plot of all data. \( R = 0.704 \).

Figure 3 Bland-Altman plot of study material without regional abnormalities. Gated SPECT LVEF compared to mean LVEF from gated SPECT and echocardiography. Mean difference ± 2SD ranges from -20.7 to +17.7.
Figure 4 Scatter plot of study material without regional abnormalities. R = 0.5856.
DISCUSSION

Our results show good correlation and very little bias between the 2 tests, as also shown by others [3, 6]. However, precision on individual basis is far from perfect (with 2 SD from +18.6 to -20.2 in Bland-Altman analysis). These results are similar to studies performed by others [3] but our interpretations of them differ. Cwajg et al, [3] considered results like ours to show good correlation but did not comment on the lack of precision.

Some issues with gated SPECT are known. Repeatability of gated SPECT LVEF is significantly reduced when background corrected counts are low compared to when they are high [10]. Regionally lowered perfusion of the myocardium or isotope uptake in close proximity to the heart can cause less reliable results [1]. Cedars-Sinai QGS has been shown to overestimate LVEF in hearts where end diastolic volume (EDV) is <70 mL [4].

One major factor for differing results can of course be the need for subjective assessment in echocardiography. At the same time subjective assessment can also be something good. Of course not all of the lack in precision in our results is due to flaws in the two tests. Spontaneous variation of LVEF and ventricular reserve are higher for patients with normal LVEF than for patients with reduced LVEF [11]. The largest portion of our patient group lies in this category. Stunning as a result from cardiac stressing causing >5% decrease in LVEF has been shown in 36% of ischemic patients. This has however not been observed in non ischemic patients [9]. Stunning should have minimal influence on our results since reduced LVEF from cardiac stressing is most prominent < 1 h after stress testing [8]. One of our goals was to identify if regional abnormalities could cause differing results. The results do however not support that theory. When removing the results from patients with regional abnormalities, neither

Figure 5 Bland-Altman plot of study from patients with regional abnormalities. Gated SPECT LVEF compared to mean LVEF from gated SPECT and echocardiography.
the precision nor the correlation was improved. There was no distinct pattern in the results from patients with regional abnormalities either. It is important to keep in mind that the number of patients with regional abnormalities was small (n=10), thus no conclusions can be drawn, but regional abnormalities did not seem to be one of the dominating reasons for differing results.

CONCLUSION

Both 2D echocardiography and gated SPECT are both very useful tools for diagnosing cardiac diseases. LVEF values from the two tests can differ quite a lot and comparisons between them should be done with great caution.

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REFERENCES


