Real-Time Quantitative Automatic Assessment of Left Ventricular Ejection Fraction and Regional Wall Motion by Speckle Imaging

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Abstract

Background: Echocardiographic assessment of left ventricular function includes calculation of ejection fraction and regional wall motion analysis. Recently, speckle imaging was introduced for quantification of left ventricular function.

Objectives: To assess LVEF by speckle imaging and compare it with Simpson's method, and to assess the regional LV strain obtained by speckle imaging in relation to conventional echocardiographic scores.

Methods: Thirty consecutive patients, 28 with regional LV dysfunction, underwent standard echocardiographic evaluation. LV end-diastolic volume, LV end-systolic volume and EF were calculated independently by speckle imaging and Simpson's rule. The regional peak systolic strain presented by speckle imaging as a bull's-eye map was compared with the conventional visual estimate of echo score.

Results: Average EDV obtained by speckle imaging and by Simpson's method was 85.1 vs. 92.7 ml (P = 0.38), average ESV was 49.4 vs. 48.8 ml (P = 0.94), calculated EF was 43.9 vs. 50.5% (P = 0.08). The correlation rate with Simpson's rule was high: 0.92 for EDV, 0.96 for ESV, and 0.89 for EF. The peak systolic strain in two patients without wall motion abnormality was 17.3 ± 4.7; in normal segments of patients with regional dysfunction, peak systolic strain (13.4 ± 4.9) was significantly higher than in hypokinetic segments (10.5 ± 4.5) (P < 0.000001). The strain in hypokinetic segments was significantly higher than in akinetic segments (6.2 ± 3.6) (P < 0.000001).

Conclusions: Speckle imaging can be successfully used for the assessment of LV volumes and EF. Bull's-eye strain map, created by speckle imaging, can achieve an accurate real-time segmental wall motion analysis.

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Accurate assessment of left ventricular ejection fraction is part of a comprehensive echocardiographic examination and is a routine daily clinical problem. Traditionally, LVEF has been calculated based on the biplane Simpson's rule algorithm. This method requires high image quality and is entirely operator-dependent. Since second harmonic imaging has been introduced, several different echocardiographic techniques have been suggested for calculating EF: automatic border detection, contrast echocardiography, and three-dimensional echocardiography. These methods are either time consuming, or require an experienced operator, good image quality and special and often expensive equipment.

Recently, we and others investigated the accuracy of speckle imaging, a novel non-tissue Doppler-based software (termed also 2-D strain) for quantitative assessment of LV function [1-3]. Most recently, this new algorithm was extended and is now ready for the assessment of LV volumes, ejection fraction and regional LV strain.

In this study we compare end-diastolic volume, end-systolic volume, and LVEF calculated by speckle imaging with Simpson's method, and regional myocardial strain obtained by speckle imaging with conventional echocardiographic wall motion score.

Patients and Methods

Thirty patients, 28 with regional LV dysfunction, underwent standard echocardiographic assessment (General Electric, Vivid 7 software). Apical four, two and three-chamber views were obtained in digital format for subsequent offline analysis. Apical views were tracked by speckle imaging, and biplane end-diastolic and end-systolic volumes and EF were calculated by speckle imaging based on the previously published algorithm [2,3]. The same four-chamber and two-chamber loops were analyzed independently by two different observers using the standard Simpson's method; biplane Simpson's volumes and EF were calculated and compared with volumes and EF was obtained with speckle imaging.

Regional peak systolic strain was calculated by speckle imaging and compared with conventional echo score (1 = normal, 2 = hypokinetic, 3 = akinetic, 4 = dyskinetic). Strain results were displayed as a bull's-eye map according to 18 cardiac segments [3,4]. Wall motion score was assigned by an independent observer (Z.V.) and the results were compared with regional strain calculated by a different observer (M.L.).

Statistical analysis

EDV, ESV and EF obtained by speckle imaging and Simpson's rule were compared in the first part of the study. In the second part, results of the regional peak systolic strain obtained by speckle imaging were analyzed in relation to conventional echo score. Correlations were measured by the linear correlation coefficient. Significance of measurements was tested by Student's

LV = left ventricular ejection fraction
EDV = end-diastolic volume
ESV = end-systolic volume

t-test. $P < 0.05$ was considered significant. Bland and Altman calculations were also performed.

Results

Of 540 cardiac segments 532 were adequately tracked by speckle imaging. Average EDV obtained by speckle imaging and by Simpson's method was 85.1 vs. 92.7 ml (P = 0.38), average ESV was 49.4 vs. 48.8 ml (P = 0.94), calculated EF was 43.9 vs. 50.5% (P = 0.08). The correlation rate with Simpson's rule was high: 0.92 for EDV, 0.96 for ESV, and 0.89 for EF 0.89 [Figure 1A-C]. EF obtained by Simpson's method tended to be higher due to a tendency toward higher EDV obtained by Simpson's method than by speckle imaging. The results were confirmed by Bland and Altman analysis [Figures 2A-C]. The differences between the two methods within mean difference ± 1.96 SD for EDV, ESV and EF are not clinically important. There are consistent biases for: EDV (7.5 ml), ESV (-0.6 ml) and EF (6.6%). EDV and EF biases can be adjusted for by subtracting the mean difference from the speckle imaging score. ESV bias is not significant. The 95% difference confidence intervals were 2.5–12.5 ml for EDV, -3.8–2.6 ml for ESV and 3.9–9.2% for EF.

Peak systolic strain is presented as a bull's-eye map [Figures 3A-D and 4A-D]. Inadequately tracked segments are gray in the map [Figure 4A]. The peak systolic strain in the two patients without wall motion abnormality was 17.3 ± 4.7. In the 28 patients with LV regional dysfunction, peak systolic strain in the "normally" contracting segments (13.4 ± 4.9) was significantly higher than in hypokinetic segments (10.5 ± 4.5) (P < 0.000001). Strain in hypokinetic segments was significantly higher than in akinetic segments (6.2 ± 3.6) (P < 0.000001). There was no significant difference between strain in akinetic and dyskinetic segments (4.8 ± 3.1) (P = 0.22), but only 18 dyskinetic segments were present.

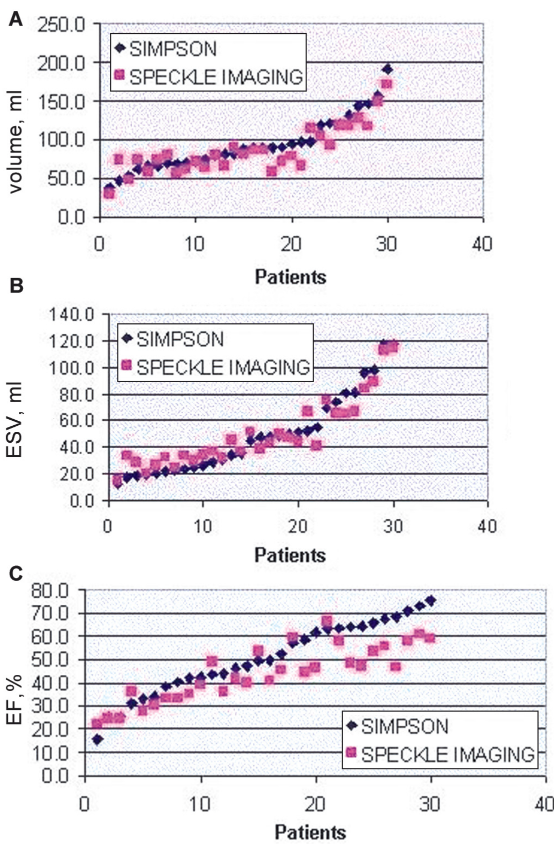

Figure 1. Volumes and ejection fraction obtained by speckle imaging (violet) and by Simpson's method (blue). **[A]** End-diastolic volume. **[B]** End-systolic volume. **[C]** Ejection fraction obtained by speckle imaging (violet) and by Simpson's rule (blue). EF, obtained with Simpson's method, tended to be higher.

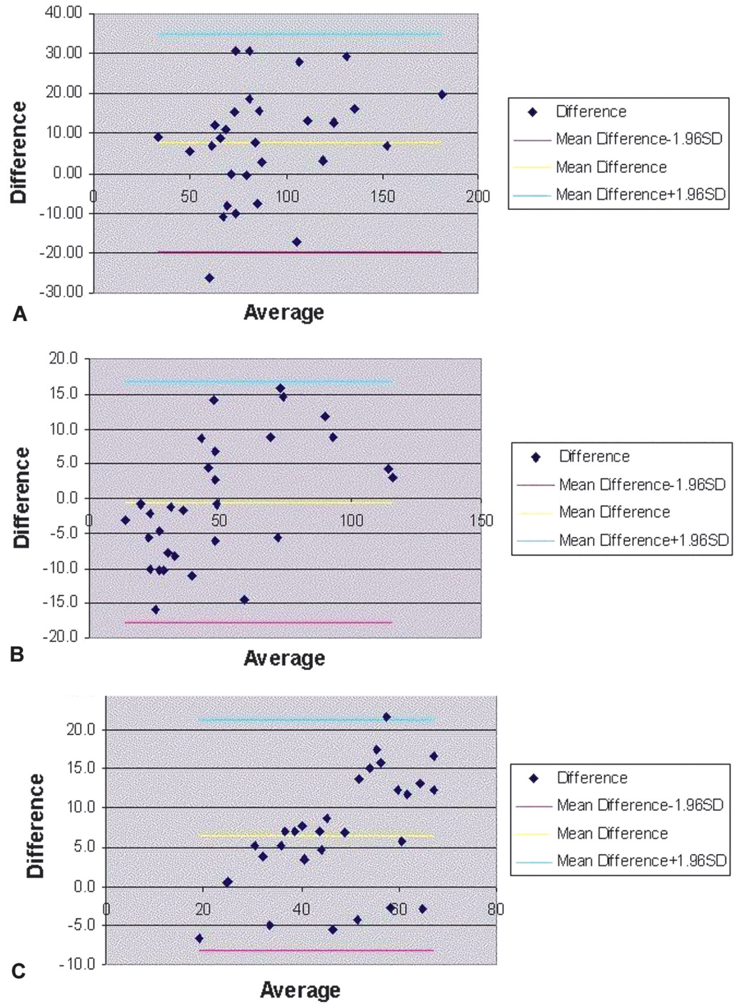

Figure 2. Bland and Altman analysis of the results obtained with two methods: speckle imaging and Simpson's rule. **[A]** EDV, **[B]** ESV, **[C]** EF. The graphs show a scatter diagram of the differences plotted against the mean of the results obtained by the two methods. Horizontal lines represent the mean difference and mean difference plus and minus 1.96 times the standard deviation (SD) of the differences.

Discussion

The first experience in quantitative assessment of left ventricular function comes from linear M-mode measurements: LV internal dimensions in diastole and systole and fractional shortening and cubed LV volumes [5]. For two-dimensional quantitative

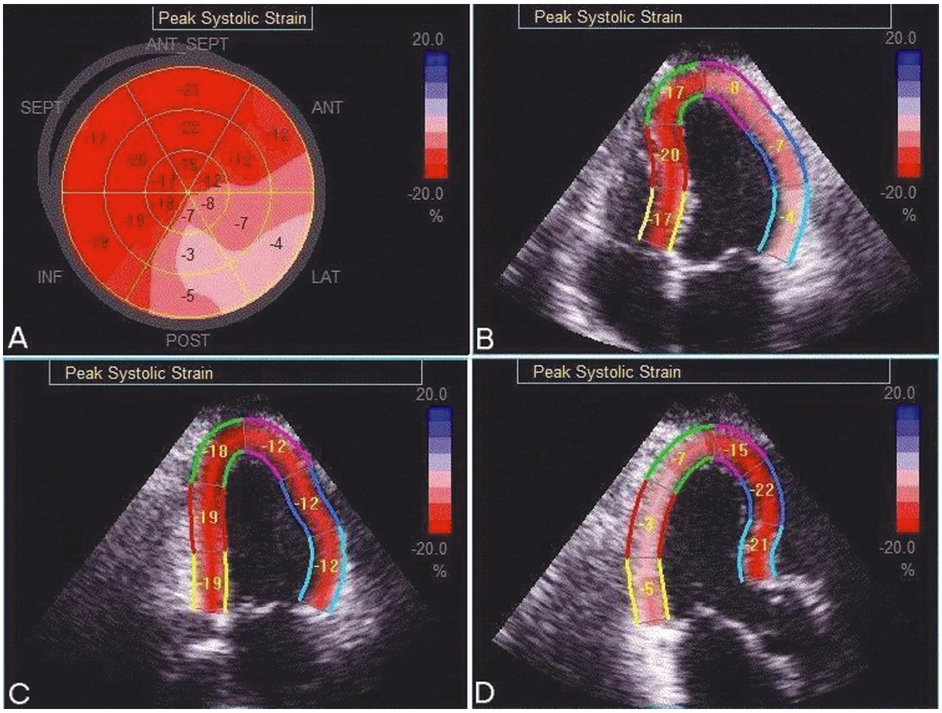

Figure 3. Peak systolic strain of a patient with posterolateral myocardial infarction (MI). **[A]** Bull's-eye map based on 18 cardiac segments. The color scale is represented in the right upper corner. Low intensity pink color in the posterolater segments with lower numbers of the peak systolic strain are indicative of posterolateral wall motion abnormalities. **[B]** Four-chamber view, **[C]** Two-chamber view, **[D]** apical three-chamber (long axis) view.

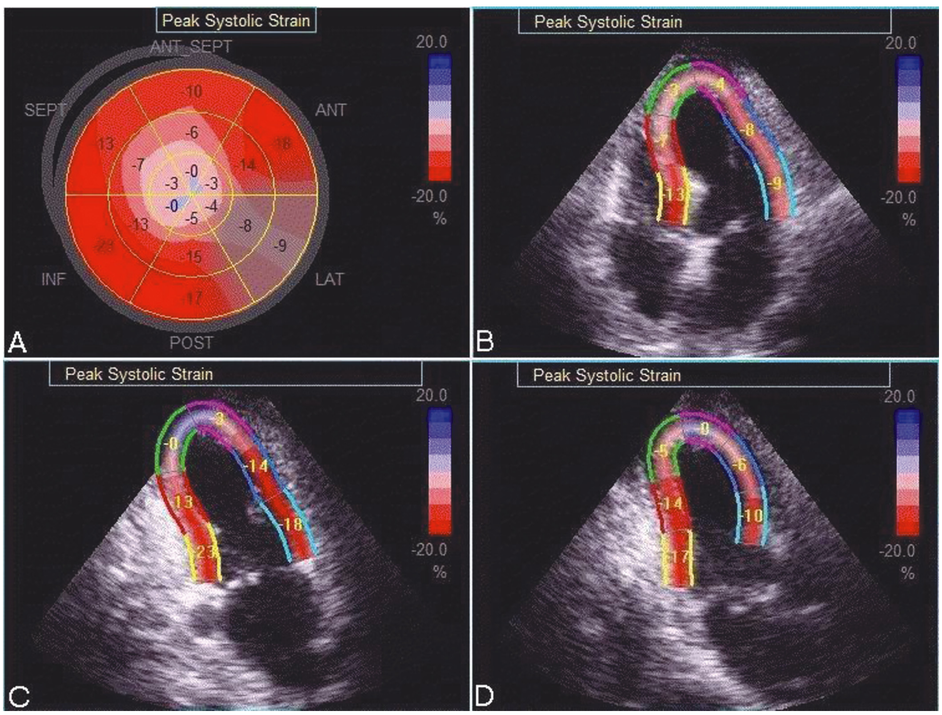

Figure 4. Peak systolic strain of a patient with anterosepto-apical MI. **[A]** Bull's-eye map, **[B]** Four-chamber view, **[C]** Two-chamber view, **[D]** Apical three-chamber view. Low intensity pink color in the septo-apical-anterior segments is characteristic for septo-apical MI. Gray color in the mid-lateral and lateral basal segments suggests inappropriate tracking of the lateral wall.

assessment of global LV function, Simpson's ("rule of disks") is considered to be the best method [6]. The main problem is accurate delineation of the endocardial border and dropouts [5], but Simpson's rule algorithm for calculation of left ventricular volume and ejection fraction was found to be reliable and highly reproducible [7]. Determination of stroke volume and cardiac output with pulsed-wave Doppler adjacent to the aortic valve is a part of the routine echocardiographic report in many laboratories [8,9]. Automatic border detection and color kinesis have been suggested for online quantitative estimation of LV function. Fractional area change with automatic border detection correlated well with ejection fraction obtained with radionuclide ventriculography [10]. 3-D echocardiography showed excellent correlation with radionuclide angiography for calculation of left ventricular ejection fraction at a slice thickness of up to 15 mm. The standard deviation of the mean difference showed a stepwise increase, particularly at thickness < 15 mm [11]. 3-D echo has been applied *in vitro* to regular and irregular ventricular phantoms, and for normal subjects and patients with cardiac diseases, providing good results compared with other independent imaging techniques [12]. 3-D echocardiography by multiplane transesophageal transducer showed a very high accuracy for volume measurements and ejection fraction calculation *in vitro*, but with increasing heart rate there was progressive underestimation of ejection fraction calculation. I*n vivo* there was good agreement for patients with normal left ventricular shape, but significantly more variability in patients with left ventricular aneurysms [13].

In patients with suboptimal image quality, intravenous contrast improved endocardial border detection

3-D = three-dimensional

and accuracy of Simpson's method as compared with radionuclide angiography [14]. Assessment of mitral annulus motion has been reported to be less dependent on image quality compared with Simpson's method and has been proposed as a surrogate to the biplane disk summation method [15]. Ejection fraction was calculated by an algorithm derived from the indicator-dilution theory after analysis of time-intensity curves, obtained from contrast echocardiography of the LV in dogs [16]. Endocardial border-enhancing effects of contrast echocardiography were successfully combined with an automatic border detection technique [17]. Many of these techniques have gained popularity, but none has yet become the standard for a real-time, automatic quantitative method for assessing global LV function, and in many laboratories visual estimation of LV function is the common practice.

Speckle imaging, a novel non-tissue Doppler-based software, enables calculation of global LV function almost independently of an operator: the operator chooses three marginal points and the software completes the analysis of the LV function automatically. The operator can then determine whether LV tracking is optimal. If not, the operator can correct the edocardial border curve manually. In our study 532 of 540 cardiac segments were tracked adequately by the software. This is a huge improvement over the previous implementation [2]. The correlation rate between EDV, ESV and EF calculated by speckle imaging and Simpson's method was high. In better-contracting left ventricles (EF > 45%), EF calculated with Simpson's method tended to be higher than EF calculated with speckle imaging.

Regional myocardial function has traditionally been evaluated by visual "semi-quantitative" conventional wall motion analysis and by quantitative methods: integrated backscatter [18], tissue Doppler imaging [19] and, recently, speckle imaging [1-3]. Most of these studies examined longitudinal strains, while during the last years more and more data on radial and circumferential strain are available. In our recent report [2] the longitudinal myocardial strain was uniform over the LV and correlated well with tissue Doppler imaging. Based on this and a more recent publication [3], we chose longitudinal myocardial strain as the preferred parameter of regional LV function. Strain is displayed as a bull's-eye map, which is easy to comprehend, and in the current study correlated well with visual conventional regional wall motion analysis. In a few segments there was discrepancy between visual assessment and strain that did not significantly affect the overall assessment of regional LV function in those patients. Some overlap between strain in normal, hypo- and akinetic segments in these patients can be explained by tethering and perhaps by different anatomic determination of the segments' borders by the different methods.

It is also noteworthy that strain in "normally contracting segments" in patients with regional dysfunction was lower than regional strain in patients without wall motion abnormalities (17.3 ± 4.7 vs. 13.4 ± 4.9). These discrepancies can also probably be attributed to tethering. Tissue tracking for the assessment of LV volumes by the new software is simple and much easier and user-friendly than by Simpson's rule. The new software permits avoiding cavity artifacts that can occur with the standard Simpson's rule. The results obtained by the new software are highly reproducible [2].

Limitations

In the current study no correlation was made between speckle imaging and a different technique, such as nuclear ventriculography or magnetic resonance imaging. We believe that a correlation with the conventional widely used echocardiographic method is of clinical importance and the current technique offers a far better and nearly operator-independent solution for the assessment of LV function. The new software requires a high frame rate and relatively good image quality free of artifacts. As the new software operates with 2-D images, some foreshortening of the apex may occur that can be overcome in the future with 3-D images.

Conclusions

Speckle imaging can be successfully used for real-time automatic assessment of LV volumes and ejection fraction. It is relatively operator-independent (though correctable when tracking is inadequate), and is user-friendly. Bull's-eye presentation of the strain map, created by speckle imaging, can successfully accomplish regional LV segmental assessment, similar to visual assessment of wall motion. Speckle imaging in its current version has the potential to become the standard for a real-time, accurate and reliable method for quantitative assessment of global and regional LV function by rapid assessment of LV volumes, LVEF, quantitative regional function as well as myocardial velocities, strain and strain rate, as shown previously.

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Capsule

Limits on viral transmission

Transmission between hosts is a crucial choke point in viral evolution – viral fitness is measured by transmission. Tumpey and group show that one or two amino acid substitutions in influenza hemagglutinin that modify its sialic acid linkage specificity from mammalian to avian greatly reduce transmissibility of a recombinant 1918 influenza A virus in ferrets. This implies that hemagglutinin receptor specificity in this pandemic strain plays an essential role in influenza virus transmission.

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Capsule

Remodeling the joint in RA

Rheumatoid arthritis (RA) is a debilitating autoimmune disorder that is characterized by a profound remodeling of tissue architecture at the joint, which results, most notably, in a permanent loss of bone. Therapies that reduce joint inflammation have been somewhat successful in delaying the onset and progression of the disease, but they have not been able to reverse joint damage once it has occurred. Because the recovery of joint function in RA will probably require therapeutic approaches that trigger the formation of new bone, there is growing interest in understanding the molecular mechanisms that regulate bone remodeling within the joint. Following up on previous evidence that identified the Wnt signaling pathway as a determinant of bone mass, Diarra et al. investigated whether manipulation of this pathway would affect joint pathology in mice overexpressing the pro-inflammatory molecule tumor necrosis factor-alpha (TNFα), a widely used animal model of human rheumatoid arthritis. They found that the antibody-mediated blockade of Dickkopf-1 (DKK-1), which is an endogenous inhibitor of Wnt signaling, induced the formation of osteophytes (bone spurs) at the inflamed joints and also prevented the resorption of bone by specialized cells called osteoclasts. As was consistent with the mouse data, they observed that DKK-1 was expressed at aberrantly high levels in joint specimens from humans with RA and that in both species DKK-1 expression was induced by TN-α. These results identify the Wnt pathway as an important regulator of joint remodeling in RA. Because Wnt signals influence both the formation and the destruction of bone, future therapies targeting this pathway could in principle be applied not only to rheumatoid arthritis, which is characterized by bone loss, but also to osteoarthritis and other joint diseases.

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