Video Article

Transthoracic Speckle Tracking Echocardiography for the Quantitative Assessment of Left Ventricular Myocardial Deformation

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Abstract

The value of conventional echocardiography is limited by differences in inter-individual image interpretation and therefore largely dependent on the examiners' expertise. Speckle tracking Echocardiography (STE) is a promising but technically challenging method that can be used to quantitatively assess regional and global systolic and diastolic myocardial performance. Myocardial strain and strain rate can be measured in all three dimensions — radial, circumferential, longitudinal — of myocardial deformation. Standard cross-sectional two-dimensional B-mode images are recorded and subsequently postprocessed by automated continuous frame-by-frame tracking and motion analysis of speckles within the myocardium. Images are recorded as digital loops and synchronized to a 3-lead EKG for timing purposes. Longitudinal deformation is assessed in the apical 4-, 3-, and 2-chamber views. Circumferential and radial deformation are measured in the parasternal short axis plane.

Optimal image quality and accurate tissue tracking are paramount for the correct determination of myocardial performance parameters. Utilizing transthoracic STE in a healthy volunteer, the present article is a detailed outline of the essential steps and potential pitfalls of quantitative echocardiographic myocardial deformation analysis.

Video Link

The video component of this article can be found at https://www.jove.com/video/54736/

Introduction

Scientific and clinical scenarios in cardiovascular medicine are more and more addressed by continuous variables and cutoff values rather than simplistic "yes or no" algorithms. Imaging techniques have evolved to be able to assess cardiac function in ever increasing detail. Speckle tracking echocardiography (STE) is an emerging diagnostic tool for the quantitative evaluation of myocardial performance. While conventional echocardiography is limited by subjective image interpretation and a strong dependence on the individual examiner's expertise, STE has been introduced as a reproducible and more objective method to quantify global and regional systolic and diastolic function[1,2].

Left ventricular (LV) myocardial deformation — longitudinal and circumferential shortening as well as radial thickening in systole and vice versa in diastole — can be described measuring the parameters strain (ε) and strain rate (SR). ε is a dimensionless percent change in myocardial length. SR is a time derivate of ε[3]. These important indices of myocardial function have been shown to be able to identify myocardial ischemia[4], predict response to cardiac resynchronization therapy[5] and to detect subclinical myocardial dysfunction while conventional echocardiographic parameters still remain normal[6]. In a systematic meta-analysis, global longitudinal ε, the most frequently used quantitative LV systolic function parameter, has been shown to have superior prognostic value for the prediction of major adverse cardiac events then LV ejection fraction (EF), the current gold standard for the assessment of LV systolic function[7]. Even very subtle alterations such as the effect of short term metabolic changes on myocardial mechanics in asymptomatic patients can be detected utilizing STE[8].

Technically, STE uses greyscale 2D or 3D B-mode motion images recorded in standard echocardiography views. Several consecutive cardiac cycles are recorded in apical 4-, 3- and 2-chamber views to measure longitudinal deformation and in the parasternal short axis view for circumferential and radial deformation[9]. Moreover, by capturing the short axis view at the level of the mitral valve, the papillary muscles and the apex, LV torsion can be assessed[3]. Subsequently to image acquisition and storage as digital loops, myocardial deformation is measured on an off-line work station or on the ultrasound device itself. The software detects unique myocardial pixel patterns in the recorded greyscale images, so-called "speckles" and traces them throughout the analyzed cardiac cycle. Vectors are measured and deformation parameters are subsequently calculated. This way regional and global myocardial deformation can be assessed in systole and diastole for both the left and right ventricle and atrium[10].

Protocol

The protocol content has been ethically approved by the Witten/Herdecke University Ethics Committee.

1. Technical Requirements

1. Utilize an echocardiography device featuring speckle tracking technology equipped with an adequate sector array tissue harmonic imaging transducer.
2. During image acquisition, record and connect a standard 3-lead EKG directly to the echocardiography device in order to synchronize echocardiographic motion images to electromechanical activity. This is mandatory for timing purposes during subsequent postprocessing analyses. Connect the study subject to the EKG and unfreeze the ultrasound image to start detecting the EKG signal.
3. Record digital loops as explained in detail below (steps 2.1-2.5) and store the data as moving images in DICOM format on an external disk. Subsequently, transfer the files to an off-line workstation.
4. Perform post-processing analyses using appropriate software as outlined in detail below (steps 3.1-3.13).

2. Recording of Echocardiographic Digital Loops

1. Examine the patient in the left lateral decubitus position (patient lying on the left side with the left arm stretched above the head).
   NOTE: This part of the protocol requires the patient/study subject to be present.
2. Alternatively, when combining STE with stress echocardiography modalities such as a bicycle ergometer, ensure that the patient is in a 45-degree upright position. In this case, utilize a standard bicycle ergometry device and perform standard stress echocardiography testing as previously described[11]. During the recording of echocardiographic images, tilt the ergometer to achieve a left lateral body position in order to minimize artifacts by interfering lung tissue.
3. Take special care to optimize image quality to guarantee accurate assessment of myocardial deformation. To do so, adjust the frame rate between 60 and 80 frames per second using the "adjust frame rate" option. Furthermore, pay attention to include all aspects of the myocardial structures that shall be analyzed throughout the entirety of the cardiac cycle.
4. Obtain cross-sectional two-dimensional greyscale B-mode images in standard apical long axis and parasternal short axis planes as described by the European Association of Cardiovascular Imaging and the American Society of Echocardiography[12]. Record several consecutive cardiac cycles (actually only one is necessary, recording of at least three cardiac cycles is advised in order to be able to choose the one with the best image quality during subsequent post processing) in each of the following planes:
   1. For the assessment of longitudinal ε and SR, capture standard apical 4-, 3-, and 2-chamber views as previously described[12]. To do so, position the transducer at the apex of the heart near the apical impulse (usually between the 3rd and 5th intercostal space and between the mid-clavicular and anterior axillary line). Aim towards the right shoulder and angulate the transducer until all anatomical structures of interest become visible.
   2. Record images in the parasternal short axis view at the level of the mitral valve, the papillary muscles and the apex to detect circumferential ε and SR as well as radial ε and SR as described elsewhere in detail[12]. To do so, place the probe at the left parasternal border at the 2nd or 3rd intercostal space and angulate until you obtain a cross-sectional perpendicular view of the LV.
5. When combining STE with cardiac stress testing such as bicycle ergometry or any other functional testing modality requiring serial measurements (see step 2.2), repeat step 2.4 at each desired time point.

3. Postprocessing Analysis

NOTE: This part of the protocol includes the evaluation and interpretation of the recorded echocardiographic images. It does not require the patient to be present and can be performed at any time following the previous part of the procedure.

1. Utilizing the quantitative echocardiography analysis software, click 'File' and 'Open' and chose the desired echocardiographic study data. Select a patient/study and pick an echocardiographic plane that shall be analyzed.
2. Click the 'Q'-icon in the right lower corner of the selected image. Next, press the 'aCMQ' button on the left.
3. Chose the cardiac cycle of the highest image quality by using the green 'QRS' skip keys at the bottom of the screen. Use the keyboard space bar to play and pause the loop.
4. Select a region of interest (ROI) to be analyzed by confirming the echocardiographic view on the left side of the screen. Next, have the software automatically detect the timing of end-diastole and suggest a ROI.
   NOTE: A first speckle tracking analysis is subsequently being computed by the software. Segmental and global ε curves are displayed on the bottom of the screen.
5. Click 'Strain rate' below the graphs to visualize segmental and global SR.
6. Visually verify the tracking quality suggested by the software.
   NOTE: To do so, critically control whether all aspects of the myocardium to be analyzed are completely covered by the ROI during the entirety of the cardiac cycle. Avoid including surrounding non-myocardial tissues into the ROI.
7. If necessary, manually reposition the entire ROI or single aspects of it, or even re-draw the ROI completely (see 3.8-3.9) in order to guarantee exact measurements.
   NOTE: Optionally, set the ROI to be transparent to adjust the ROI coverage to the appropriate position and width of the myocardium.
8. In the apical 4-, 3-, and 2-chamber view, have the software automatically determine a possible ROI dividing the myocardium into seven segments.
   1. In case ROI re-definition is necessary, click 'Draw' on the left and start out tagging the endocardial border at three reference points: the two opposing insertion points of the AV valve and the LV wall starting with the basal infero-septal/ basal infero-lateral/basal inferior

part of the valve finishing with the center of the apex. Ensure that both endpoints of the tracked-endocardium are on the same level completely excluding the valvular tissue.

2. If repositioning is necessary in order to optimize position and width of the ROI, click 'Edit' on the left side of the screen. Move each segment margin as well as the endocardial and epicardial borders individually with the cursor. Utilize an orthogonal line pointing towards the apex for navigation/orientation when moving the ROI in its entirety.
3. Finally, start the speckle tracking re-analysis by pressing the 'Compute' button on the left side of the screen.
   NOTE: The software now automatically detects "acoustic markers", which deflect myocardial ultrastructures corresponding to myocardial fiber organization in their movement throughout the contraction and relaxation of the myocardium. These acoustic markers are traced through the entire duration of a complete cardiac cycle. The necessary calculation may take seconds to minutes. ε and SR are calculated by the software and presented in a numeric and graphic manner.

9. In the parasternal view, have the software automatically suggest a predefined ROI. Adjust this ROI manually, dividing the myocardium into six segments.
   NOTE: The width of the ROI, should exactly match the thickness of the myocardium. Where necessary, optimize position and width of the ROI as described in 3.8.2. A dot in the center of the ROI may be utilized for navigation/orientation when moving the ROI in its entirety.
   1. Next, start the speckle tracking re-analysis by pressing the 'Compute' button on the left side of the screen.
10. Chose segmental and global ε and SR to be displayed in curves or the comprehensive bull's eye format. To do so, click the 'Preferences' button at the bottom left corner of the screen. Different types of waveforms and displaying options can be selected in this menu.
11. If manual repositioning of the ROI is not sufficient to achieve appropriate overall speckle tracking quality, start over from 3.1 and redefine the ROI or consider selecting a different cardiac cycle prior to continuing to the next step.
12. Save and export the data for subsequent statistical analyses. If desired, cine loops or still frames can be exported as illustrations. To do so, click 'Export' at the bottom left corner of the screen and select the desired format and file directory.

Representative Results

The principle parameters for the quantitative assessment of myocardial performance are ε and SR. Technically, all cardiac chambers can be analyzed using STE. However, since speckle tracking methodology has been mostly used to study the LV, the focus of this article is on LV myocardial mechanics. Generally, longitudinal ε and SR are the most commonly assessed LV deformation parameters. Longitudinal ε and SR describe systolic shortening (and diastolic lengthening) of the myocardium. Hence, systolic values are annotated as negative numbers. **Figures 1** and **2** represent good examples of STE-derived segmental and global ε and SR analyses. Optimal image quality and adequate tissue coverage of the ROI are paramount for reliable assessment of myocardial deformation. Suboptimal tissue tracking frequently results in misinterpretation of true ε and SR values. An example of poor tissue tracking quality in the apical (purple) and mid-lateral (blue) segments is displayed in **Figure 3**. Apical and mid-lateral ε is largely underestimated in this example of a healthy patient, who — when correctly assessed — exhibits normal LV deformation with unremarkable heterogeneous ε and SR values in all LV segments.

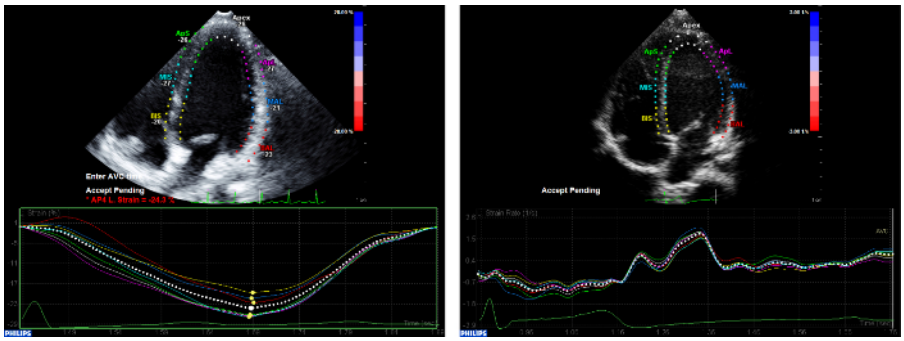

Figure 1: Apical 4-chamber view-derived longitudinal strain and strain rate. Apical 4-chamber view (AP4) derived ε and SR are presented in the left and right panels, respectively. Each colored time-strain curve (left and right, bottom) corresponds to one of the seven color-coded myocardial segments (left and right, top) and visualizes segmental (= regional) ε or SR, respectively. The white dotted line represents global longitudinal LV ε or SR, respectively. Note the smooth parallel shape of the segmental time-strain and SR curves. Please click here to view a larger version of this figure.

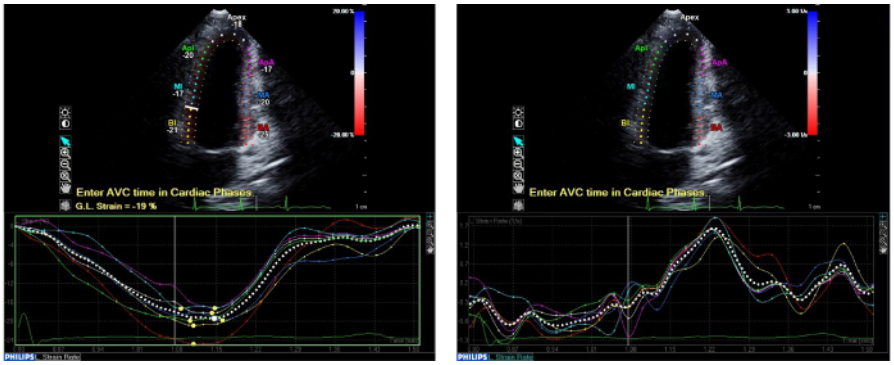

Figure 2: Apical 2-chamber view-derived longitudinal strain and strain rate. Left and right panels show Apical 2-chamber (AP2) derived LV myocardial ε and SR, respectively. Time-strain curves correspond to the color-coded segments as described above for **Figure 1**. Please click here to view a larger version of this figure.

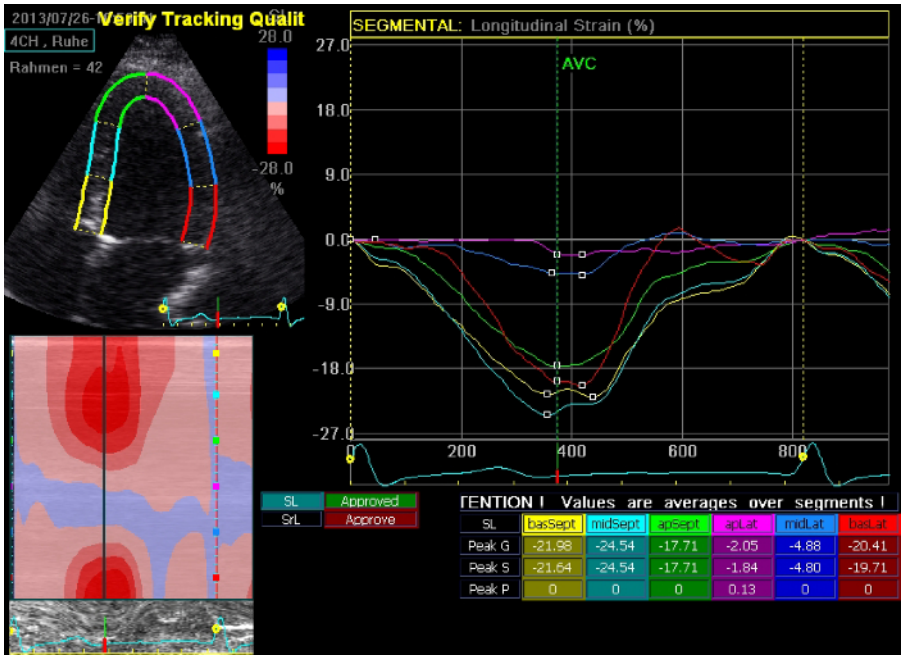

Figure 3: Inadequate apical tissue tracking: AP2-derived longitudinal strain. This healthy patient actually has normal LV myocardial ε values, when properly assessed. As an artifact, in this figure apical (purple) and mid-lateral (blue) segments exhibit poor tissue tracking quality and thus the real segmental ε is greatly underestimated. Peak LV global myocardial ε values are displayed (**Figure 2**, bottom right). Note the absence of dark red color-coding, representing myocardial contraction in the color-coded curved M-mode (**Figure 2**, bottom left). Please click here to view a larger version of this figure.

Circumferential ε and SR describe the circular systolic shortening of the LV myocardium (and its lengthening in diastole) and are therefore denoted as negative numbers in systole. Circumferential LV deformation is assessed in the parasternal short axis view in three different planes: at the level of the mitral annulus, the papillary muscles (**Figure 4**) and at the apex. Inclusion of all three levels yields LV myocardial torsion – basal clockwise and apical counterclockwise rotation in systole – expressed as LV systolic twist and diastolic untwist.

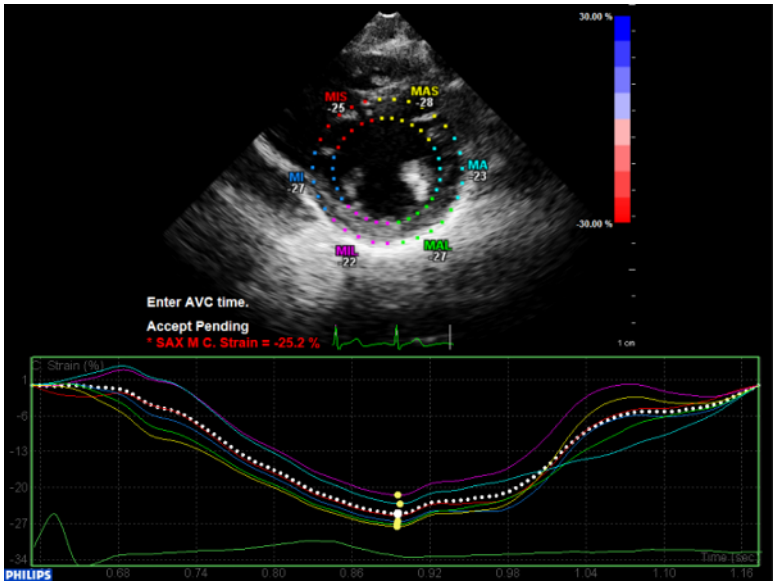

Figure 4: LV circumferential strain. Parasternal short axis view at the level of the papillary muscles yields circumferential ε. The myocardium is subdivided into six segments. Regional peak LV circumferential ε values are displayed at the top. Segmental colors correspond to the time-strain curves displayed at the bottom. The white dotted line represents global circumferential ε. Note the smooth and parallel shape of the segmental and global time-strain curves. Please click here to view a larger version of this figure.

While longitudinal and circumferential ε is negative in systole, radial ε reflects systolic myocardial thickening and is thus positive in systole. An example of a well-performed LV radial ε assessment is demonstrated in **Figure 5**. In contrast, **Figure 6** shows incorrect tissue tracking of the anteroseptal myocar — when adequately measured — unremarkable deformation parameters.

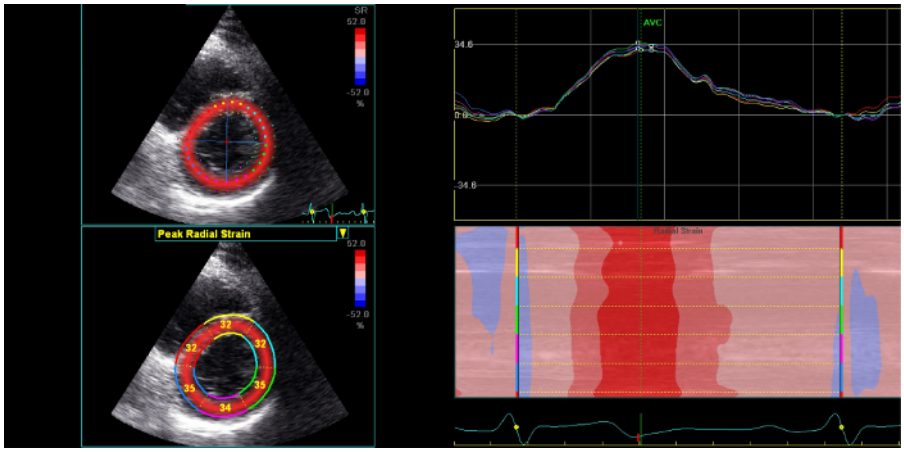

Figure 5: LV radial strain. Parasternal short axis view at the level of the papillary muscles also yields radial ε. Myocardial ROI coverage is displayed at the top left side. Segmental peak systolic radial ε values are presented (in %) in the bottom on the left. Radial time-strain curves are displayed at the top right aspect of the figure. Radial strain is displayed in % on the y-axis and time corresponding to the ECG (at the bottom) is presented on the x-axis. Colored curved M-mode with dark red representing positive radial ε is shown on the right side of the bottom. Note the homogeneous shape of the segmental radial ε curves corresponding well to the uniform curved M-mode color-coding. Please click here to view a larger version of this figure.

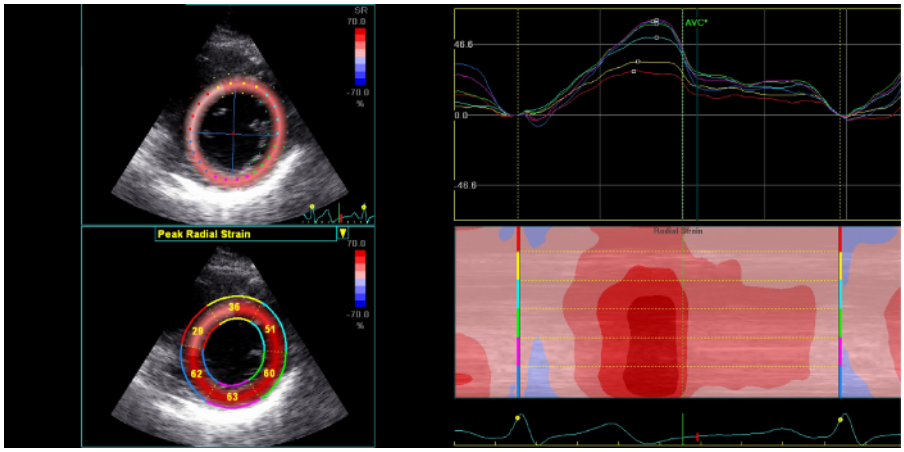

Figure 6: Inadequate tissue tracking: LV radial strain. The conceptual content and scaling of this figure correspond to **Figure 5**. In this example poor anteroseptal tissue tracking resulted in inaccurate radial ε values and heterogeneous radial time-strain curves in an asymptomatic healthy patient. Note the deviation of the septal (red) and anteroseptal (yellow) segmental radial ε curves. Please click here to view a larger version of this figure.

For a comprehensive illustration, LV myocardial longitudinal ε can be displayed in a so-called bull's eye view (**Figure 7**). This way, peak systolic longitudinal ε values of 17 segments altogether representing the entirety of the LV myocardium can be visualized in a single view. Time-strain curves for AP4-, AP2-, and AP3-derived segmental longitudinal ε are also depicted, corresponding to the color-coding as outlined for **Figures 1** and **2**. This illustration can be of benefit to visualize regionally varying deformation deficits such as in cardiac amyloidosis which is characterized by apical sparring in the bull's eye view**.**

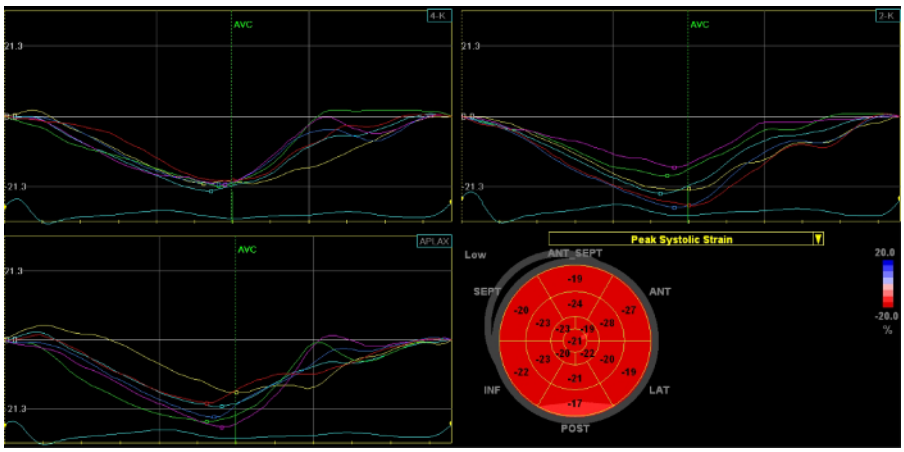

Figure 7: LV global strain: bull's eye view. Longitudinal time-strain curves are displayed for LV segmental myocardial ε derived from the AP4 (top left), AP2 (top right) and the AP3 (bottom left) planes. The differently colored curves correspond to the segmental division as indicated in **Figures 1** and **2**. Longitudinal ε is displayed in % on the y-axes and relative time corresponding to the ECG (at the bottom) is represented on the x-axis. Peak segmental longitudinal ε values are depicted in the bull's eye illustration (bottom right) for 17 segments analyzed in the AP4, AP2 and AP3 views. Red shaded color-coding corresponds to the legend indicated on the right. Note the higher homogeneity in the AP4-derived segmental time-strain curves when compared to AP2 and AP3. This correlates well with the challenging image acquisition of the anterior LV wall aspects oftentimes leading to artifacts and heterogeneous deformation parameters. Please click here to view a larger version of this figure.

Discussion

Significance of the technique with respect to alternative methods

The current gold standard for the echocardiographic assessment of LV systolic function is the LV ejection fraction (EF)[13]. However, determination of EF is based on a simplistic approach that is closely correlated to the radial component of myocardial contraction but does not take into consideration the important longitudinal and circumferential planes. Hence, EF oversimplifies the three-dimensional complexity of myocardial deformation. As a consequence, EF measurements do not unmask subtle cardiac dysfunctions but only detect LV deterioration at a relatively advanced state[14]. On the other hand, STE-derived ε and SR have been shown to detect subclinical cardiac alterations while EF still remained normal[15]. STE has emerged to be a robust tool for research and bare important clinical implications providing a significant advance in the management of cardiovascular patients[16]. Global LV longitudinal ε has the highest clinical value among the STE-derived LV deformation parameters and better reflects global myocardial function when compared to circumferential and radial ε[7].

Longitudinal ε and SR are assessed in the apical long axis views and reproducibly assess global and regional LV deformation (**Figures 1** and **2**). Caution must be paid to maintain highest requirements for image quality and myocardial tracing, since inadequate tissue-tracking yields incorrect

deformation parameters that often are not as obvious as demonstrated in **Figure 3**. Circumferential and radial wall motion can be quantitatively measured in the parasternal short axis (**Figures 4** and **5**). Even though global LV longitudinal ε has been pointed out as the most significant single STE-derived deformation parameter, circumferential and radial wall motion yield important additional information for a variety of clinical scenarios[17,18].

Fortunately, novel echocardiography devices provide the possibility to assess global longitudinal ε measurements at the patient's bedside within a few min. This gives the physician the possibility to perform a robust detection of LV myocardial deformation parameters without the time-consuming comprehensive STE-measurements that require the recording and off-line postprocessing of various cross-sectional echocardiographic images. Utilizing the bull's eye visualization, the physician can review global LV function at a glance (**Figure 7**).

Furthermore, besides the assessment of global LV function, segmental (regional) myocardial function can be analyzed using STE. This enables physicians to measure myocardial dyssynchrony and the response to cardiac resynchronization therapy[19,20].

Limitations, critical steps and troubleshooting

Despite the promising advantages of STE, the technology has important limitations. First and foremost, the dependence of reproducible STE-derived measurements on echocardiographic image quality cannot be overstated. It is therefore crucial to take special care improving image quality as far as possible[21]. Even subtle artifacts can lead to significant misinterpretations of ε or SR, as demonstrated in **Figures 3** and **6**. Furthermore, the tissue tracking software automatically includes all segments regardless of their image quality. At times it may even suggest unrealistic deformation parameters for ROIs that include non-cardiac tissue. Thus, dedicated verification of accurate ROI size and position and incremental fine-tuning using thorough visual assessment is absolutely essential.

Another approach aimed to avoid artifacts during echocardiographic image acquisition is to advise the patient to hold his/her breath for a few seconds. While this is usually feasible for regular echocardiographic studies in competent adult patients, it is certainly challenging and oftentimes plainly unrealistic to try so in pediatric patients or during cardiac stress testing such as bicycle ergometry.

Moreover, optimal adjustment of frame rate prior to image acquisition is mandatory. Frame rates of less than 30 frames per sec result in overly smooth time-strain curves and lack sufficient temporal resolution. High frame rates over 100 frames per sec oftentimes yield noisy ε curves that are only reliable with exceptionally high image quality. A range of 60 to 80 frames per sec has been established to best match the software requirements for optimal tissue tracking in average adult patient populations[16]. In pediatric cardiology and especially in neonatology, patients naturally have higher heart rates than adult individuals. Based on a recent STE study in premature neonates, the authors suggested to adjust frame rate settings according to the patients' heart rate. A frame rate/heart rate ratio of 0.7 to 0.9 frames per sec per bpm was proposed to achieve optimal myocardial speckle tracking results[22]. In conclusion, standardization of views, frame or volume rate and image quality should be prerequisites for STE-derived assessment of myocardial performance in order to achieve reliable, well-reproducible results.

In addition, it is noteworthy to mention that STE-derived assessment of myocardial performance currently is a reasonably time-consuming method. Despite the promising value for clinical decision making, the multiple step nature of the procedure including the many necessary quality control and software calculation steps are probably the most relevant limitation hindering STE from being used in day-to-day clinical routine care. Companies should be encouraged to optimize tissue tracking software development with a special focus on feasibility in order to expedite and improve the work-flow, rendering it more user friendly.

Finally, an important limitation of STE is the variance of STE-derived ε and SR values between different software packages. Various commercial companies supplying STE analysis software utilize different underlying mathematic algorithms that at times yield non-consistent deformation parameters. Thus, a given myocardial ε or SR measured with a device from company A has to be interpreted with caution when reference values are derived from an STE software package of company B.

Future applications

Currently, STE is increasingly used to detect subtle changes of myocardial performance that remain undetected by conventional echocardiography[23]. While the LV has been assessed in various STE studies, little is still known regarding left atrial, right ventricular and right atrial mechanics for a variety of clinical and scientific scenarios. Novel modifications to the technique even allow the assessment of vessel stiffness for large arteries utilizing speckle tracking technology. Furthermore, STE can be used in experimental animal models to gather valuable information regarding myocardial performance without the need for invasive procedures. 3D-STE is another promising development allowing comprehensive and time-efficient myocardial deformation analyses. Moreover, STE can be combined with pharmacological or ergometer stress testing to better detect wall motion abnormalities when compared to conventional stress echocardiography. In addition, myocardial twist and torsion can be assessed utilizing STE, which could add incremental clinical value to global ε and SR imaging. Further studies are needed in order to illuminate both the clinical significance and limitations of these potential implications of STE.

Disclosures

The authors have nothing to disclose.

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