Three-dimensional stress echocardiography

Andreas Franke

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Over the last 25 years, stress echocardiography has become a widely used technique for diagnosis and risk stratification of patients with suspected or known coronary artery disease. However, relevant methodological limitations of conventional two-dimensional (2D) stress echocardiography still exist. It remains difficult to acquire high-quality data and to analyze the images with reproducible results which may lead to reduced test accuracy and a lack of ability to detect regional myocardial ischemia.

Image acquisition in 2D echocardiography may be impaired by (1) probe positioning errors resulting in inadequate image planes, e.g., LV foreshortening, (2) reduced image quality with poor visualization of especially anterior and lateral left ventricular (LV) walls, and (3) the time-consuming serial acquisition of different image planes (parasternal short and long axis, apical 4- and 2-chamber views as well as the apical long axis) in a narrow time window, during peak stress, while wall motion abnormalities are present. Even after successful image acquisition, subjectivity of image interpretation remains a major problem, causing limited interobserver agreement and relevant examiner-dependency [1].

Knowing all these limitations, several attempts have been undertaken to make stress echocardiography easier and more accurate. The use of pharmacological protocols (dobutamine plus atropine) instead of physical exercise protocols improves image quality and increases the time available for image acquisition at peak level. Harmonic imaging without use of contrast (tissue harmonics) has been demonstrated to improve endocardial visibility and test accuracy, which can be further increased by the additional application of left heart contrast for LV opacification.

Other advanced echocardiographic modalities such as tissue Doppler imaging or strain analysis may help obtain independence from subjective image interpretation, because they provide more objective and quantifiable information on wall motion abnormalities. Although promising, most of these techniques have not made their way into clinical routine mainly due to complexity. Not only technical factors may improve the accuracy of stress echocardiography, but training and increased experience of the individual examiner lowers interobserver variability and increases test sensitivity [2].

With the availability of matrix array transducers, the simultaneous acquisition of two or three image planes (bi- or triplanar imaging) or even the acquisition of a complete pyramidal volume dataset became possible (► Chapter 2). This new modality dramatically decreases the necessary number of serially acquired heart beats. Several of the above mentioned limitations of conventional 2D stress echocardiography can be potentially solved using this technique.

Matrix array transducer technology dramatically decreases the necessary number of serially acquired heart beats.

4.1 Method

Matrix array transducers allow different approaches to perform stress echocardiography: Rotating »monoplanar«, biplanar, triplanar or full volume mode.

Most vendors developed stress echo acquisition software that takes advantage of matrix array's potential to electronically rotate an image plane. As a consequence, the image plane can be changed – as a rotation around a stable central axis – without moving the transducer (iRotate mode). Once the echo window is found, the ultrasound probe can be held still which makes acquisition easier and more robust for beginners but also for experienced examiners. Nevertheless, serial acquisition of all image planes still remains time consuming. However, in newer three-dimensional (3D) echocardiography systems, stress echocardiography software has been included, allowing to program the iRotate angles for each 2-, 3-, and 4-chamber view. During the stress protocol, then, the software automatically rotates the scan plane with each push-button for acquisition to the next view in each stress level. This stress protocol can even programmed to include 3D full volume datasets at each stress level, however, without the ability to dem-

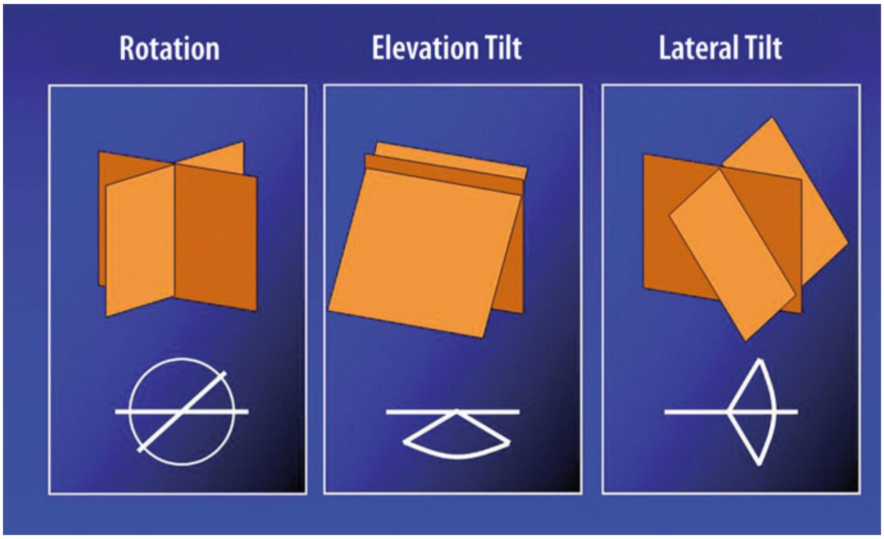
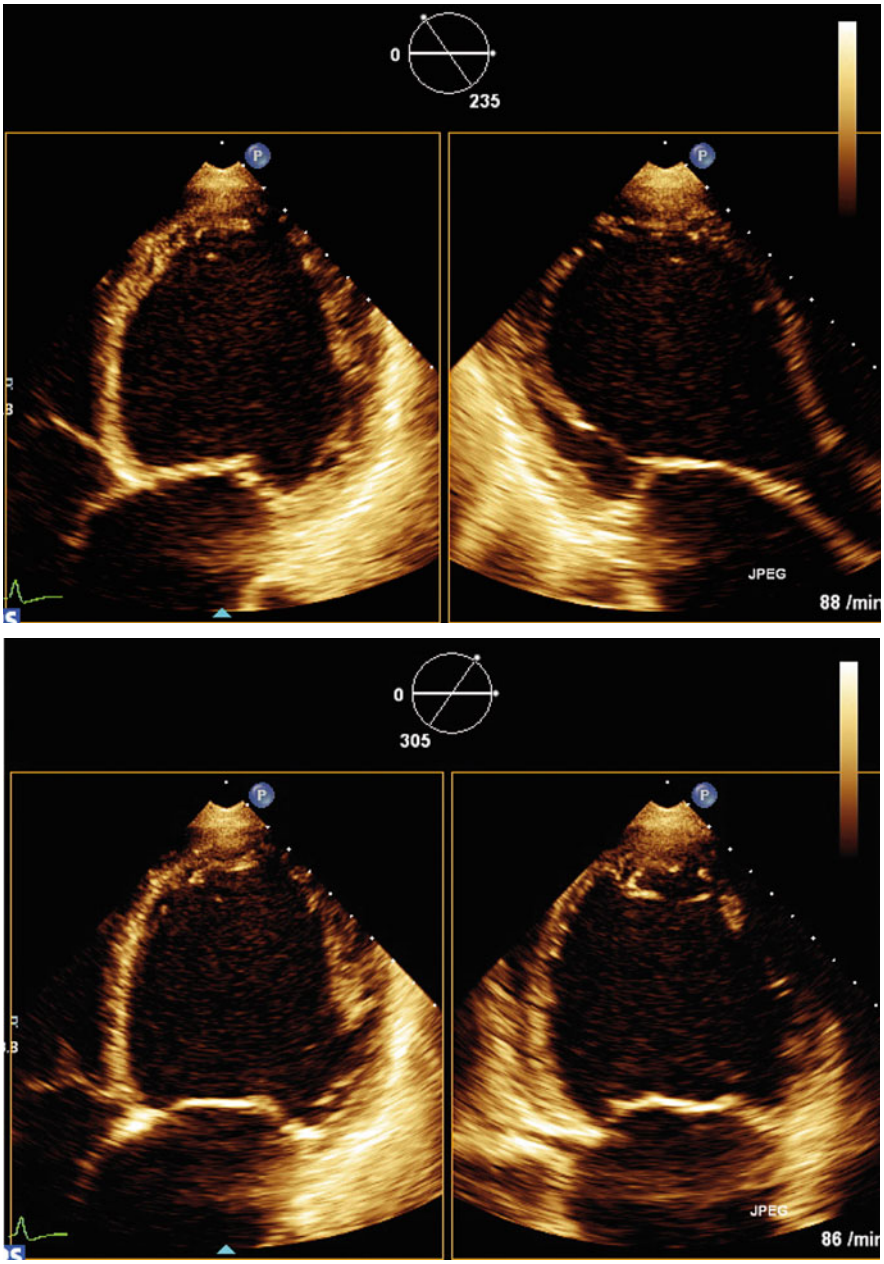


Fig. 4.1 Schematic drawing of the different spatial orientations of biplanar imaging



◘ **Fig. 4.2** Electronic rotation of 2D image planes during the stress echocardiographic protocol using the xPlane mode. *Top* The image shows simultaneously a 4-chamber view (*top left*) and at 235° rotation a long-axis view (*top right*). The electronic rotation of the right image relative to the left is indicated by the rotation symbol on top. *Bottom* Without rotating the matrix array transducer, the image plane on the right can be electronically rotated. Here a standard 2-chamber view is shown at 305° rotation. During a stress echocardiographic protocol, identical image plane rotations can be easily reproduced at any protocol step. [→Videos 4.2A,B]

onstrate 3D data of different stress level in a quad screen for side-by-side comparison (▶ Section 4.3).

Biplanar imaging (xPlane mode) allows the simultaneous visualization and acquisition of two image planes: the first oriented in a conventional way, the second in any desired angle of rotation or tilt (lateral and elevation tilt) which can be electronically steered by command panel buttons without changing the position of the transducer during the stress protocol (◘ Fig. 4.1 and ◘ Fig. 4.2). Typically, the biplanar mode from the parasternal echo window allows the simultaneous acquisition of a long axis and of an adapted short axis, and from the apical echo window a simultaneous apical 4-chamber and 2-chamber view [3][4]. Finally – using the rotation of one of the image planes – in a third heartbeat the apical long axis can be acquired (◘ Fig. 4.2). Image plane orientation can be stored in the echocardiographic system as an individual setting so that after acquisition of all planes, side-by-side visualization and synchronization is possible.

Other vendors allow the simultaneous scanning of three image planes (»triplanar«; mostly in 60° increments). Acquisition of triplanar data is typically only performed from a single apical echo window. Furthermore – when omitting parasternal recording – triplanar scanning facilitates a single transducer position

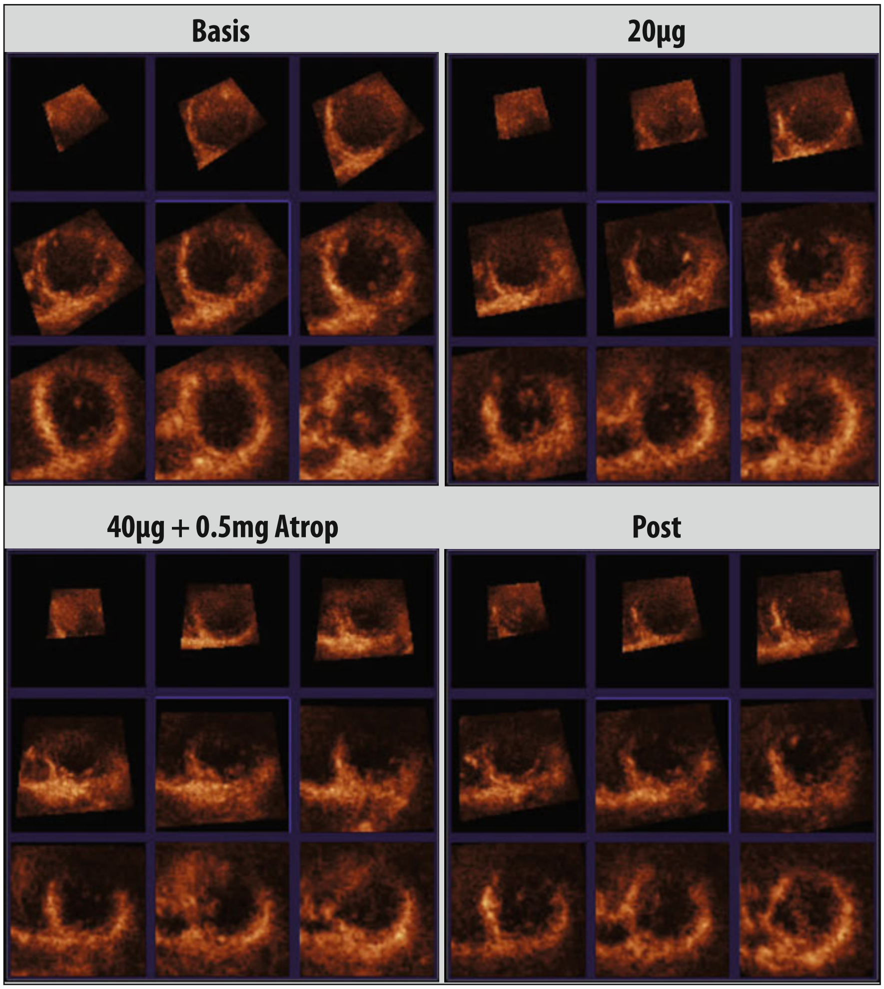


Fig. 4.3 Side-by-side analysis of a nine-slice view from baseline conditions (*upper left* set of short-axis slices), low dose dobutamine (*20 µg*, *upper right*), peak dose dobutamine (*40 µg +0.5 mg Atropine*; *lower left*), and during recovery (*5 min Post*; *lower right*). [→Videos 4.3A–D; see also →Videos 4.3E,F demonstrating a second dobutamine 3D stress study]

for acquisition of only one heartbeat at each stress stage [5]. Loops from all three image planes are stored separately and can be presented and analyzed side-by-side comparable to conventional 2D stress echocardiography. Bi- and triplanar techniques may serve as a first step toward »complete« 3D stress echocardiography.

The acquisition of wide-angle 3D datasets (so-called »full volume mode«) is based on the serial recording of four to seven narrow subvolumes in consecutive heartbeats (▶ Chapter 2, ▶ Fig. 2.15, and ▶ Fig. 2.20). Immediately after acquisition the subsegments are combined to a pyramidal 3D dataset with an overall angle of maximally 104°×104°, which can comprise a complete cavity even in patients with dilated left ventricles. There are also new approaches to acquire wide-angle 3D datasets with only a single heartbeat (one-beat acquisition; see ▶ Chapter 2). Of course, this accepts a trade-off in spatial and temporal resolution because line density is decreased, which results in poorer lateral image resolution, and time for sweeping the complete sector is increased, which also results in a somewhat decreased time resolution. Therefore, one-beat acquisition of full volume data still remains unsatisfactory and its image quality may not yet be optimal for 3D stress echocardiography.

As in conventional 2D stress echocardiography, the acquisition of 3D datasets in the stress echocardiographic workflow is performed at rest, at low and peak stress, and during recovery. Both physical stress (either bicycle or treadmill exercise) and pharmacological stress (mainly dobutamine plus atropine, rarely dipyridamole) have been used in combination with 3D techniques. Several studies described the additional use of left heart contrast agents for better endocardial delineation [6][7].

Besides the extraction of long-axis views from stress 3D datasets, multiple parallel short-axis slices allow systematic regional wall motion analysis.

Once the 3D dataset is acquired, image planes can be created in every desired orientation independent of the transducer position and beam direction during dataset acquisition. Besides the extraction of conventional 2-, 3-, and 4-chamber views (▶ Fig. 2.35 in Chapter 2), multiple parallel short-axis slices can be used for systematic regional wall motion analysis. These slices can be extracted semiautomatically as a set of three to nine parallel apical to basal slices of the LV (▶ Fig. 2.37 in Chapter 2 and ▶ Fig. 3.11 in Chapter 3). However, analysis of stress echocardiographic data – also in 3D – still remains a subjective interpretation of wall

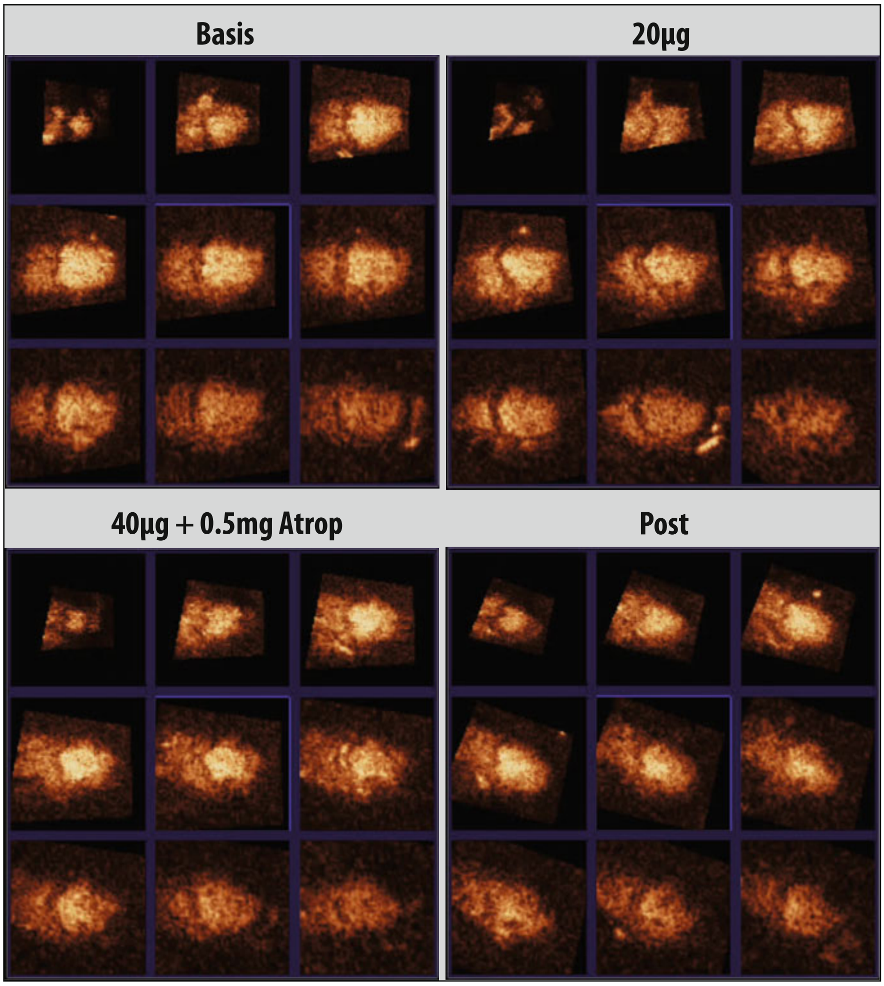


Fig. 4.4 Side-by-side analysis of a contrast-enhanced nine-slice view. Same orientation as in Fig. 4.3. [→Videos 4.4A–D]

motion analysis, optimally using a side-by-side display of the extracted image planes at different exercise levels (Fig. 4.3 and Fig. 4.4). For better visualization, the endocardial border can be highlighted by a yellow contour line which represents the 3D LV chamber surface after semiautomated 3D volume analysis (▶ Fig. 3.11 in Chapter 3).

New quantitative tools, e.g., parametric imaging of endocardial displacement, regional timing of endocardial motion, or parameters of left ventricular dyssynchrony such as the systolic dyssynchrony index (SDI), may serve as objective measures of regional ischemia (Fig. 4.5 and Fig. 4.6).

4.2 Clinical studies on 3D stress echocardiography

In the late 1990s, early studies using first-generation 3D equipment demonstrated that 3D volumetric imaging can be used to analyze regional left ventricular wall motion [8]. Other studies even claimed a high sensitivity and superiority over conventional 2D stress echocardiography [9][10]. However, the overall poor image quality of the purely 3D-dedicated echocardiographic system at that time prevented this first approach from widespread clinical use.

A major advantage of 3D stress echocardiography is that it requires significantly shorter scan times.

Since the advent of today's matrix array transducers, several studies have used bi- and triplanar techniques as a first step towards »complete« full volumetric 3D stress echocardiography. Most of them performed comparative studies versus conventional 2D echocardiographic or nuclear imaging [3][5] and found similar accuracy of 3D stress echocardiography compared with 2D and nuclear imaging. The major difference between 3D and 2D stress echocardiography was a significantly shorter scanning time to acquire a triplanar dataset covering the complete LV (=one loop in 4-chamber view, 2-chamber view and apical long-axis from a single apical window) compared to the serial scanning of three different 2D image planes. Importantly, a shorter scanning time did not reduce test accuracy.

Several studies on the use of full volume 3D echocardiography [4][11][12][13][14][15][16] described good correlation between conventional 2D and 3D stress echocardiography with nearly identical sensitivity, specificity, and accuracy. Again, the

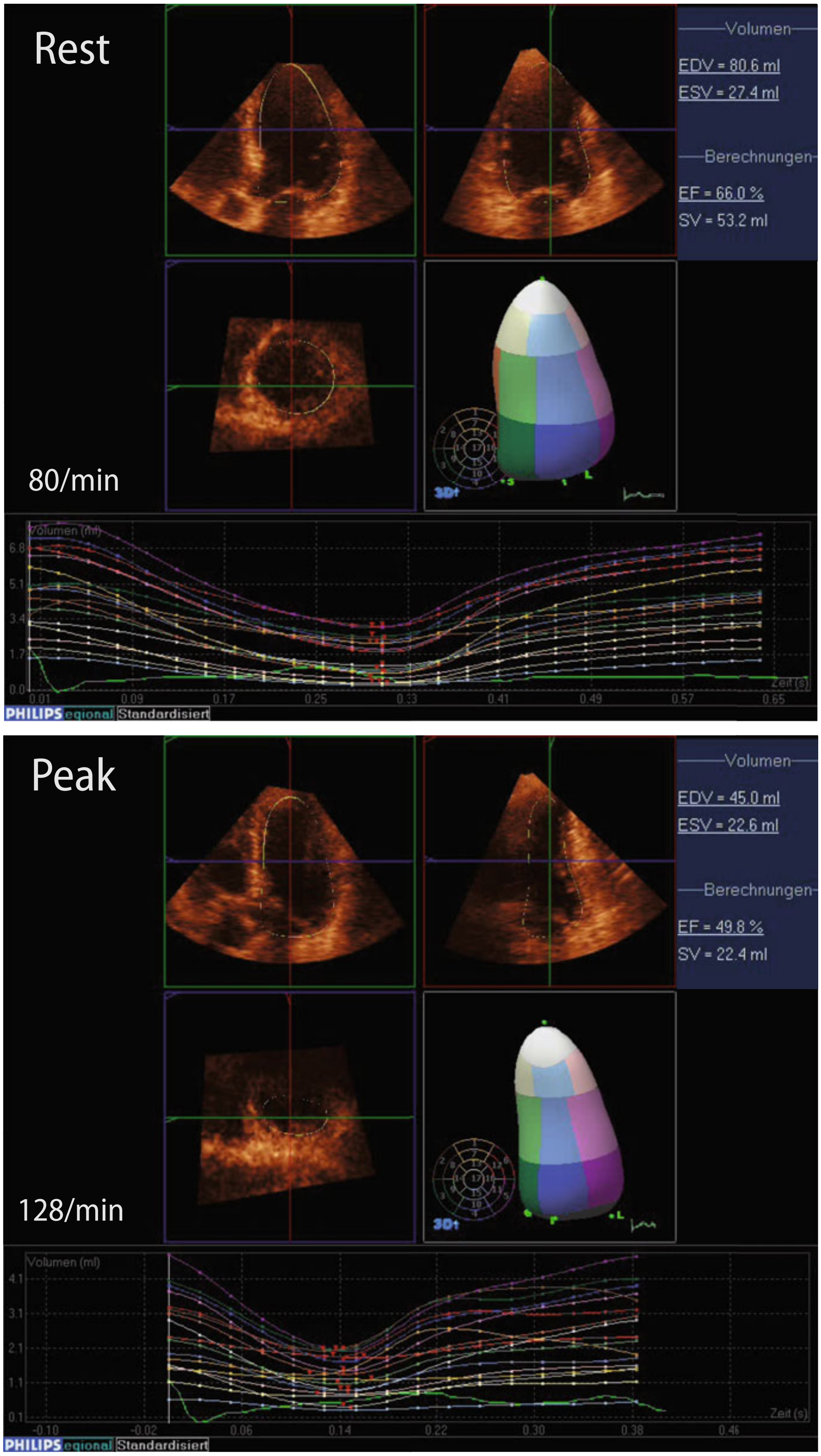
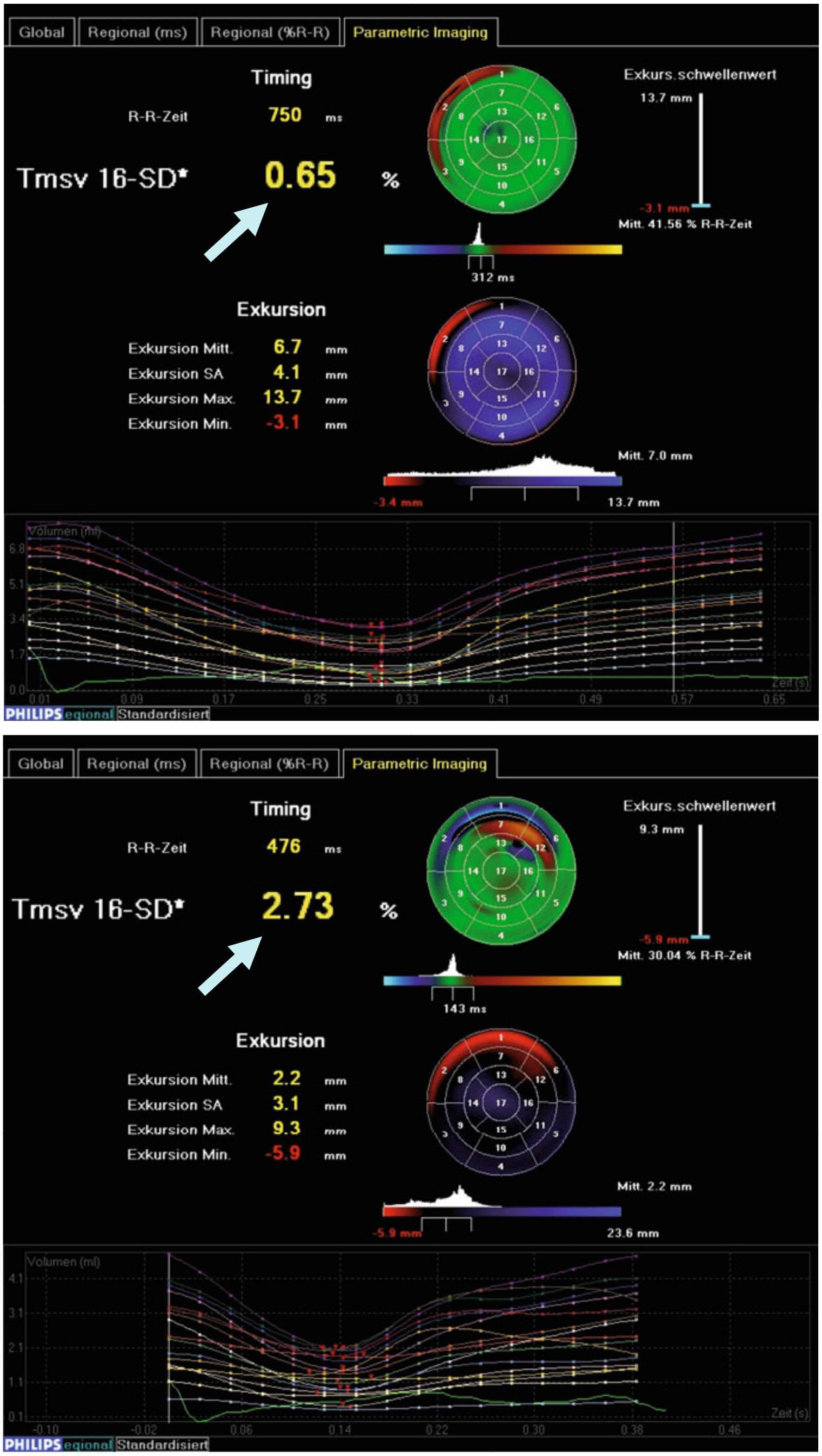


Fig. 4.5 Regional volume–time curves at rest (*top*) and during peak dobutamine stress (*bottom*). Precise analysis of wall motion excursion and temporal contraction patterns become possible



Timing

R-R-Zeit 750 ms

Tmsv 16-SD* 0.65 %

Exkursion

Exkursion Mitt. 6.7 mm
Exkursion SA 4.1 mm
Exkursion Max. 13.7 mm
Exkursion Min. -3.1 mm

Timing

R-R-Zeit 476 ms

Tmsv 16-SD* 2.73 %

Exkursion

Exkursion Mitt. 2.2 mm
Exkursion SA 3.1 mm
Exkursion Max. 9.3 mm
Exkursion Min. -5.9 mm

Fig. 4.6 Dyssynchrony and parametric imaging of regional contraction timing and excursion (same patient as in Fig. 4.5). Volume–time curves at rest (*top*) and during peak stress (*bottom*). During peak stress the systolic dyssynchrony index (*SDI*) increases from 0.65 to 2.73%, while a new anterior/anteroseptal wall motion abnormality occurs. The parametric color-coded image of contraction timing demonstrates regions of delayed contraction as *red* areas (both upper bull's eye views), whereas analysis of wall motion excursion (second row of bull's eyes in *blue*) shows no significant change major difference between the 2D and 3D techniques was a dramatically shorter scanning time to cover the complete LV compared to the serial scanning of three or more 2D image planes.

Analysis of 3D data in the majority of the published studies was performed using manually extracted cut planes from the LV (i.e., normally three long-axis planes and at least three short-axis planes). The examiner then looked for regional wall motion abnormalities in all stress levels separately. Some authors of recent studies used the multislice view integrated into most 3D machines today and performed a side-by-side comparison of loops at rest and at different stress levels (◘ Fig. 4.3 and ◘ Fig. 4.4). Independent of how the analysis was performed, duration tended to be longer than just looking at the conventional 2D stress echocardiography quad screen. This is, however, not due to difficulties of the image quality, the 3D data, or the observer but is caused by the lack of software solutions to automatically extract comparable image cut planes, to arrange them in a side-by-side manner, and to synchronize them.

❯ Dedicated 3D stress analysis software is urgently required to automatically extract image planes at different stress levels and to arrange them synchronized side-by-side.

As a consequence of these early studies, a skeptical question may evolve: is the benefit of 3D stress echocardiography worth all the trouble? Although sensitivity and specificity are similar to conventional 2D echocardiography, there are specific advantages of a 3D stress echocardiographic workflow:

- There is no need to change the transducer position during apical scanning once the echo window is found. This leads to easier acquisition for both beginners and expert echocardiographers. Moreover, image plane positioning errors including LV foreshortening, which might lead to false positive or negative 2D stress echocardiographic results, can be avoided.
- The narrow time window at peak stress can be used much more effectively when acquiring a complete 3D dataset. An earlier publication on biplanar stress echocardiography [3] demonstrated that this results in a higher heart rate during exercise stress acquisition, which is a prerequisite for the detection of ischemia.
- Three-dimensional stress echocardiography will result in a shorter scanning time at peak stress and perhaps also in a more sensitive monitoring, because more segments can be observed online using the multiple image plane (multislice mode) approach. This may reduce the potential risk of prolonged myocardial ischemia for the individual patient. Beyond this, reduction of stress echocardiography examination time may reduce costs and increase throughput in the stress echocardiography lab.
- Finally, there seem to be advantages not only during acquisition but also in the analysis of regional LV wall motion abnormalities. As in other imaging techniques (e.g., magnetic resonance imaging), interpretation of wall motion abnormalities is easier in short-axis slices instead of long-axis planes. In addition, quantitative parameters such as systolic dyssynchrony index (SDI) or parametric images of LV contraction patterns may reduce inter- and intraobserver variability compared to conventional 2D stress echocardiography.

4.3 Limitations

Despite all potential advantages of 3D echocardiography in combination with stress testing, there are also relevant limitations. Some recently developed matrix array transducers already provide a 2D image quality comparable to high-end 2D transducers. Nevertheless, overall image quality in full volume data sets is still inferior compared to 2D equipment. This is especially true for short-axis slices extracted from apically acquired 3D data caused by a limited line density and lateral resolution. The matrix array probes of several other vendors even today are relatively large and interfere with narrow intercostal spaces – thus, resulting in artifacts or dropouts.

Some authors, therefore, claim that 3D stress echocardiography cannot be performed without using left heart contrast for adequate endocardial delineation [7][16]. However, most recently published studies have used no contrast.

Time resolution of 3D full volume acquisition at present is limited to about 40–50 s (20–25 volumes/s) which is unsatisfactory especially during peak stress with high heart rates and will influence test sensitivity. Increasing time resolution without losing angle width of the acquired pyramidal 3D data set always means accepting a certain trade-off in line density (▶ Chapter 2). This is equivalent to reduced image quality. In a standard setting most 3D devices today allow the above mentioned temporal resolution – even in single beat acquisition. Using triggered mode (4–7 beats) or reduced acquisition angle (e.g., 80° instead of 108°) and reduced depth will allow significantly higher time resolution up to 100 volumes/s (=10 ms). However, the quality of triggered data always depends on the stability of heart rate, patients' breath hold, and probe position. Thus, the potential advantage of short acquisition time in 3D stress echocardiography may be reduced by the difficulties in obtaining an artifact-free data set.

The limited sector width in earlier versions of 3D echocardiographic equipment was sometimes not wide enough to encompass the complete LV in the ultrasound sector. This was especially true in patients where follow-up of LV function is crucial – those with an apical aneurysm or dilated ventricles. Nowadays, large sector angles up to 104° allow this problem to be circumvented in most cases.

Although acquisition of 3D data is faster than that of 2D images, the analysis requires more time [14]. This is due to the need for manual selection of the analyzed image planes, the larger number of myocardial regions analyzed, and the lack of a commercially available solution for synchronous display of rest, low, and peak dose as well as recovery loops. To date, nearly all vendors of the present 3D echocardiographic systems have not yet achieved internal software solutions that allow an easy-to-use method for the alignment of data at rest and during stress levels. In conventional 2D stress echocardiography, it is a standard technique to have side-by-side visualization of the corresponding image planes at rest and stress levels. With the completeness of 3D data, it becomes a new task to find the same image plane during different stress levels. An improper selection of image planes may add a new and unexpected source of error in the interpretation of 3D stress echocardiography.

Finally, the interpretation of image planes generated from the complete 3D data set remains subjective. The addition of more reliable quantitative tools such as speckle tracking or »3D strain« – at least at the present – is still scientific and challenging, and is still not clinical routine [17].

4.4 New approaches and future perspectives

In principle, a combination of 3D echocardiography with other new modalities such as contrast for myocardial perfusion imaging or strain imaging will open a variety of interesting and promising approaches. The combination of three modalities – 3D, contrast, and stress echocardiography – is challenging and remains difficult. Inherent problems like shadowing due to contrast application itself, rib and lung artifacts causing reduced image quality may interfere significantly with the ability to perform 3D myocardial contrast echocardiography. Nevertheless, there are early studies on the feasibility of such a combined approach which demonstrated not only the feasibility in principle [18] but also that pathological findings can be identified with good agreement to 2D echocardiography.

Tools for automated and quantifiable analysis of wall motion patterns will be helpful to overcome the inherent subjectivity of stress echocardiographic interpretation. This holds true not only for 2D but also for 3D echocardiography. Several approaches for quantitative global and regional wall motion analysis already exist in 3D echocardiography (segmental volume–time curves, systolic dyssychrony index, parametric imaging; ▶ Chapter 3 and ▶ Chapter 5).

Several studies evaluating the diagnostic value of stress echocardiography demonstrated that not only the severity of stress-induced regional wall motion abnormalities is predictive of outcome, but changes in ejection fraction and ventricular volume are at least equally important [19][20]. As many other studies have shown over the last two decades, 3D echocardiography permits a much more accurate assessment of left ventricular volume and ejection fraction especially in patients with resting wall motion abnormalities. Thus, 3D echocardiography has another potential to further improve the accuracy of 2D stress echocardiography, particularly if LV volume quantification becomes automated as presented for the Heart Model analysis (▶ Chapter 3).

Intraventricular dyssynchrony may also be a marker for stress-induced ischemia. Three-dimensional echocardiography is one of several techniques that have been demonstrated to be capable of detecting dyssynchrony and 3D stress studies are currently underway to evaluate the potential of this technique. Moreover, studies using dynamic maps of contraction, which are derived from full volume datasets, during stress appear promising to more accurately localize and estimate severity of stress-induced ischemia by identifying areas of delayed contraction (▶ Chapter 5) [21].

Another perspective for future use of 3D echocardiography in stress testing is the combination with perfusion imaging which has already been described in a few preliminary studies [22] but still remains difficult. Furthermore, several approaches have been used to quantify dysfunctional myocardial segments [23] to visualize dysfunctional myocardium based on parametric imaging [22], to improve temporal resolution using high volume–rate techniques [25] to analyze regional diastolic properties as an early marker of ischemia [26], or to use speckle tracking for 3D deformation imaging [17].

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