INTRODUCTION

Need of Standardisation in Echocardiography:

Echocardiography is a non-invasive method to study the morphology and function of the heart and its structures. It is a technique, which can enable diagnosis in experienced hands or complement other non-invasive and invasive procedures. The main cornerstone of this technique is image quality, therefore, there is a need for standardisation. It is important to reduce inter-observer variability evoked by the use of specific postprocessing softwares enabling objective and reproducible image analysis. In particular, deformation imaging requires interpretation of software-independent values in 2D and 3D echocardiography.

Deformation imaging:

Deformation imaging is one of the fastest growing branches of echocardiography. Strain is used to describe the morphological changes of the myocardium. Strain is a dimensionless physical term expressing the deformation of an object relative to its initial shape by a percentage of its base value. Three types of strain values can be measured during the 3D movement of the heart: Longitudinal, radial and circumferential strain. It should be distinguished from the global and regional (segmental) strains. The first one is the mean of the segmental strain values. Considering the techniques of strain measurements, tissue Doppler imaging (TDI) uses one dimension, while speckle tracking applies two or three dimensions. TDI is based on the Doppler effect and enables the quantification of velocity in all heart segments during cardiac cycle. Speckle tracking uses the so-called speckles. The term "speckle" is used to describe the gray scale ultrasound pattern of the heart muscle. This unique pattern is created by the interference of the ultrasound beams due to their spreading across the fine structures of the myocardium.

Foreshortening:

Foreshortening means the scanning of oblique longitudinal views representing shortened left ventricular (LV) segments. A main problem in clinical practice is foreshortening of the apical views. It occurs when the operator places the transducer in a suboptimal – mostly too cranial and too medial – position to get a presumably better view of the heart, which does not correspond to the apical standardised view. It has an effect on the measurements of both conventional and deformation imaging echocardiography.

Cardiotoxicity:

Over the past decade, the early detection of malignancies and the rapid development of oncological therapies have led to a significant improvement in cancer survival, but at the same time, a marked increase in mortality has been observed in cancer survivors due to cardiovascular diseases, which may develop from the beginning of chemotherapeutic treatment through the whole course of the malignant disease and is a potential complication of oncotherapy.

Detection of cardiac impairment:

Biomarkers are an essential component of the diagnosis of acute and chronic heart disease and they are also important in monitoring cardioprotective treatment responses. Nevertheless, the significance of cardiac imaging has changed in recent years. Echocardiography is a widely used technique with the advantage of easy access, repetitive follow-ups, and multimodality, and it is safe for people with concomitant kidney disease without the hazard of x-ray exposure. The commonly used imaging parameter to detect cardiotoxicity was LV ejection fraction (LVEF) in former years. Cancer therapy-associated cardiac dysfunction is defined as a decrease in LVEF below 50% or by >10% from baseline to a value below the lower limit of normal (53%); it is also considered when the global longitudinal strain (GLS) falls below -18% or shows a >15% relative reduction to a value below the normal range (0% to -17.9%)

AIMS

1. To investigate strain patterns and cardiotoxicity using standardised new echocardiographic methods.

   The first study was designed to underline the importance of standardisation in echocardiography.
2. To evaluate the effect of foreshortening on the quantitative parameters of tissue Doppler and 2D speckle tracking.

   Considering that chemotherapy-associated cardiac dysfunction may result in an increased mortality, early detection of specific echocardiographic parameters, and thus, the modification of chemotherapy and/or the initiation of cardioprotective treatment may improve survival. Therefore, the aim of the second study was:
3. To determine whether early cardiac manifestations in patients receiving chemotherapy can be detected by standardised 2D and 3D echocardiography using conventional and deformation parameters.

PATIENTS AND METHODS

Study subjects:

In the study evaluating the impact of foreshortening, 54 patients with normal wall motion pattern and normal ejection fraction (EF 65.5±6.8%) were enrolled in the Department of Cardiology and Angiology, University of Leipzig, Leipzig, Germany. All patients had sinus rhythm and optimal acoustic window using the apical transthoracic approach during the echocardiographic examination. Patients whose heart segments were not clearly visible throughout the whole cardiac cycle were excluded from the study. The study group consisted of 32 men and 22 women with a mean age of 49±17 years (range 23 to 83 years). Forty-six percent of them had hypertensive heart disease, while the rest of them had no signs of any kind of heart disease.

In the study evaluating the early detection of cardiotoxicity, two groups, each involving 25 study subjects (N=50), were enrolled in the aforementioned cardiology department. It should be underlined, that only subjects with excellent image quality were included in the study, because only this enables reliable tracking of the myocardial speckles and thus good tracking curves. In group 1 twenty-five healthy subjects (controls) without any cardiovascular diseases or cardiovascular risk factors were analysed. In group 2 twenty-five patients with various malignancies undergoing several types of cardiotoxic chemotherapies were investigated before and during chemotherapy for a mean follow-up of 3 months (±2 weeks). All procedures were approved by the local ethics committee.

Methods:

Standard 2D and Doppler echocardiography were performed with a 1.5-4.6 MHz matrix array transducer at a frame rate between 40-80 frames/sec. A defined five chamber view (5ChV) was acquired in addition to the standard four chamber view (4ChV) to demonstrate the foreshortening. The angle of foreshortening was measured by the diastolic diameter of the mitral annulus and the diastolic and systolic length of the left ventricle applying the monoplane Simpson´s rule and the auto EF method View acquisition was repeated three times, and then stored in a cine loop format for offline analysis with EchoPAC software.

In the study of early detection of cardiotoxicity all controls and patients underwent 2D and 3D transthoracic echocardiography 1 MHz to 4 MHz phased-array matrix probe for 3D image acquisition. LVEF, left ventricular end-diastolic volume (LVEDV), left ventricular end-systolic volume (LVESV), left ventricular muscle mass, global longitudinal strain (GLS), global radial strain (GRS), and global circumferential strain (GCS) were measured offline using the 16-segment model of 2D and 3D echocardiography. Two-dimensional parasternal short axis views were acquired at the level of the left ventricular apex, the papillary muscles, and the mitral valve for the measurement of global radial and circumferential strains by 2D speckle tracking (ST). Two-dimensional apical long axis, two- and four-chamber views were acquired for the assessment of GLS by 2D ST. Two-dimensional apical views were acquired at fixed sectional planes with differences of ~60° between each other. All 2D views were compared to the views of the triplane approach. Longitudinal, radial and circumferential time-to-peak intervals were measured in all 3D data sets of all controls and patients. LVEF was measured with semiautomatic 3D wall motion tracking. The frame rate was between 30 and 60 fps, with mean values of 57±6 and 25±2 in 2D and 3D ST, respectively. The width of the tracking area was manually selected. The end-systole was determined automatically by the software at the time of aortic valve closure.

STATISTICS

All data are presented as mean ±standard deviation and standard error of the mean.

1. Study investigating the impact of foreshortening:

Comparisons between the 4ChV and the defined foreshortened 5ChV were performed using a paired sample t-test in both subgroups. A p-value<0.05 was considered statistically significant. Agreement between the TVI and speckle tracking based strain imaging methods was assessed by Bland-Altman analysis.

2. Study investigating the impact of foreshortening:

Comparisons between groups 1 and 2 were performed by independent sample t-test. In group 2 data obtained before and during chemotherapy were compared with the help of paired sample t-test. P-values <0.05 were considered statistically significant.

RESULTS

1. Study investigating the impact of foreshortening:

The defined foreshortened view was characterised by a diastolic LV length of 75±8 mm. In comparison, the LV length, determined by a standardized 4ChV, was 81±8 mm ($p<0.001$). The systolic LV length was 58±7 mm in the defined foreshortened view and 63±7 mm in the standardised 4ChV ($p<0.001$). The diastolic diameter of the mitral valve annulus changed significantly as well (29±4 mm vs. 16±4 mm; $p<0.001$). The EF was 66±7% and 69±8% ($p=0.001$), measured in the standardised 4ChV and foreshortened view, respectively. Cardiac output, stroke volume as well as systolic and diastolic volumes were underestimated by the foreshortened views.

No statistical differences were obtained in the PSS parameters between the standard 4ChV and the defined foreshortened view, analysed by the tissue Doppler-derived method. However, the basal septal PSS, determined by 2D speckle tracking, was significantly lower in the defined foreshortened view than the standardised 4ChV.

2. Study evaluating the early detection of cardiotoxicity:

Compared to group 1, LVEF was reduced in group 2 at both time points (before and during chemotherapy). However, LVEF was not different in group 2 at the 3-month follow-up. For left ventricular volumes and left ventricular muscle mass, no significant differences were observed in the two study groups. In comparison to group 1, 2D GCS and 2D GLS were significantly higher at the 3-month follow-up, although there was no significant difference between group 1 and baseline group 2 data (before chemotherapy). However, for 2D radial strain, significant differences were observed between group 1 and baseline group 2 data (before chemotherapy), and between baseline and 3-month follow-up group 2 data. Values of 3D global circumferential strain were significantly higher in group 2 (both before and during chemotherapy) in comparison to group 1.

CONCLUSION

Compared to TVI, it may be easier to detect differences between regional LV deformation by 2D speckle tracking. However, an adequate image quality is a prerequisite. In contrast, TVI can be rated as the more robust technique in patients with inadequate acoustic windows. It is essential to avoid foreshortening and to ensure standardisation. If these prerequisites are not fulfilled, even normal regional PSS values significantly differ.

Preclinical myocardial dysfunction, induced by cardiotoxic chemotherapy, can be detected by the deformation parameters of ST.

We suggest that 2D global radial strain as a potential parameter can help to detect early myocardial damage during chemotherapy just after 3 months.