RESEARCH

Analysis of chronic aortic regurgitation by 2D and 3D echocardiography and cardiac MRI

Stephan Stoebe[1], Michael Metze MD[1], Daniel Jurisch MD[1], Bhupendar Tayal MD[2], Kilian Solty BoA[3,4], Ulrich Laufs PhD[1], Dietrich Pfeiffer PhD[1] and **Andreas Hagendorff PhD[1]**

[1]Department of Cardiology, Leipzig University Hospital, Leipzig, Germany
[2]Department of Cardiology, Aalborg University Hospital, Aalborg, Denmark
[3]Department of Diagnostic and Interventional Radiology, Leipzig University Hospital, Leipzig, Germany
[4]Integrated Research and Treatment Center (IFB) Adiposity Diseases, University of Leipzig, Leipzig, Germany

Correspondence should be addressed to S Stoebe: stephan.stoebe@gmx.de

Abstract

Purpose: The study compares the feasibility of the quantitative volumetric and semi-quantitative approach for quantification of chronic aortic regurgitation (AR) using different imaging modalities.
Methods: Left ventricular (LV) volumes, regurgitant volumes (RVol) and regurgitant fractions (RF) were assessed retrospectively by 2D, 3D echocardiography and cMRI in 55 chronic AR patients. Semi-quantitative parameters were assessed by 2D echocardiography.
Results: 22 (40%) patients had mild, 25 (46%) moderate and 8 (14%) severe AR. The quantitative volumetric approach was feasible using 2D, 3D echocardiography and cMRI, whereas the feasibility of semi-quantitative parameters varied considerably. LV volume (LVEDV, LVESV, SV_{tot}) analyses showed good correlations between the different imaging modalities, although significantly increased LV volumes were assessed by cMRI. RVol was significantly different between 2D/3D echocardiography and 2D echocardiography/cMRI but was not significantly different between 3D echocardiography/cMRI. RF was not statistically different between 2D echocardiography/cMRI and 3D echocardiography/cMRI showing poor correlations ($r < 0.5$) between the different imaging modalities. For AR grading by RF, moderate agreement was observed between 2D/3D echocardiography and 2D echocardiography/cMRI and good agreement was observed between 3D echocardiography/cMRI.
Conclusion: Semi-quantitative parameters are difficult to determine by 2D echocardiography in clinical routine. The quantitative volumetric RF assessment seems to be feasible and can be discussed as an alternative approach in chronic AR. However, RVol and RF did not correlate well between the different imaging modalities. The best agreement for grading of AR severity by RF was observed between 3D echocardiography and cMRI. LV volumes can be verified by different approaches and different imaging modalities.

Introduction

According to current EACVI/ESC and ASE recommendations a multi-parametric approach is proposed for grading of aortic regurgitation (AR) severity (1, 2, 3). Semi-quantitative parameters, e.g. vena contracta (VC) or pressure-half-time (PHT), are remarkably influenced by loading conditions and left ventricular (LV) compliance (4). Further, the principle of VC is based on the assumption that the regurgitant orifice is almost circular, which is often not fulfilled (1, 2). The determination of the regurgitant volume (RVol) and effective regurgitant orifice area (EROA) by proximal isovelocity surface area (PISA) is less affected by loading conditions. However, flow convergence zones can often not be correctly identified due to interposition of valve tissue and AR severity can be overestimated or underestimated by invalidation of the hemispheric assumption (1, 2). In addition, PISA does not correspond to a conclusive quantitative approach because both RVol and EROA are not correlated to the total stroke volume (SV_{tot}). For this reason, AR quantification should focus on a conclusive quantitative parameter, e.g. regurgitant fraction (RF), to characterise the hemodynamic situation in relation to the SV_{tot} (1, 4, 5). The assessment of LV volumes, SV_{tot}, SV_{eff} to calculate RVol and RF by the volumetric approach is currently proposed as an alternative approach for AR quantification and can be performed by 2D, 3D echocardiography and cardiac magnet resonance imaging (cMRI) (1, 2, 3, 4). In patients with chronic AR studies comparing LV volume analysis and the assessment of RVol and RF using 2D, 3D echocardiography or cMRI are lacking. Thus, no methodological gold standard is currently accepted for AR assessment. However, multi-modality imaging including quantitative flow measurements by phased-contrast cMRI seems to be preferred because of practical aspects (3, 4).

Accordingly, in the present study, we (1) investigated the feasibility of AR quantification by different quantitative volumetric approaches using 2D/3D echocardiography and cMRI and by semi-quantitative approaches using 2D echocardiography; (2) compared RVol, RF calculations by various quantitative volumetric approaches using 2D/3D echocardiography and cMRI.

Methods

In the present retrospective study, 55 chronic AR patients were analysed using 2D echocardiography. All investigations were performed in the period from March 2013 to June 2015. Data sets of 3D echocardiography were available in 42 patients and cMRI in 35 patients. In 32 of 55 patients, data sets of all three imaging modalities were available and the time interval between echocardiography and cMRI was ±10 days. All patients provided informed consent after full explanation of the purpose and order of all procedures. The study design was approved by the Local Ethical Committee. In the present study, adult patients with sufficient image quality, complete TTE documentation and at least chronic mild AR were included. Patients with acute AR or cardiac decompensation due to AR, concomitant moderate or severe valvular defects, atrial fibrillation, frequent ventricular extrasystoles, previous myocardial infarction or insufficient image quality (*n*=2) were excluded.

Echocardiography

Transthoracic (TTE) and transesophageal (TEE) echocardiography were performed according to national and international recommendations using a GE Vivid E9 system with a M5S phased array and a 6VT probe (GE Healthcare Vingmed Ultrasound AS, Horten, Norway) (5, 6, 7, 8). All investigations and measurements were performed by experienced investigators (first and last author) who have worked in the field of echocardiography for many years, have the highest national level of accreditation and are national and international teachers in echocardiography. Further, the senior author is an accredited teacher of international 3D echo courses. Echocardiographic analyses were performed using the EchoPac software (version 12.0.1, GE Healthcare Vingmed Ultrasound AS).

Assessment of quantitative parameters by volumetric approach using 2D echocardiography

SV_{tot} was calculated by: (A) Left ventricular outflow tract diameter (D_{LVOT}) approximately 5 mm proximal to the aortic valve (AV) annulus in the parasternal long axis view and velocity time integral of the LVOT PW Doppler signal (VTI_{LVOT}) determined in the apical long axis view at the D_{LVOT} measurement position according to the following equation: $SV_{LVOT} = 0.785 \times D_{LVOT}^2 \times VTI_{LVOT}$; (B) LV volumes – LV end-diastolic volume (LVEDV), LV end-systolic volume (LVESV) – and LVEF were determined by LV biplane planimetry using the modified Simpson's rule in the apical 2- and 4-chamber view (Fig. 1) (9).

SV_{eff} was assessed by D_{PV} and the VTI of the PW Doppler signal of the PV (VTI_{PV}) according to the following equation: $SV_{PV} = 0.785 \times D_{PV}^2 \times VTI_{PV}$. D_{PV} and VTI_{PV} were assessed in the short-axis view at the level of the AV
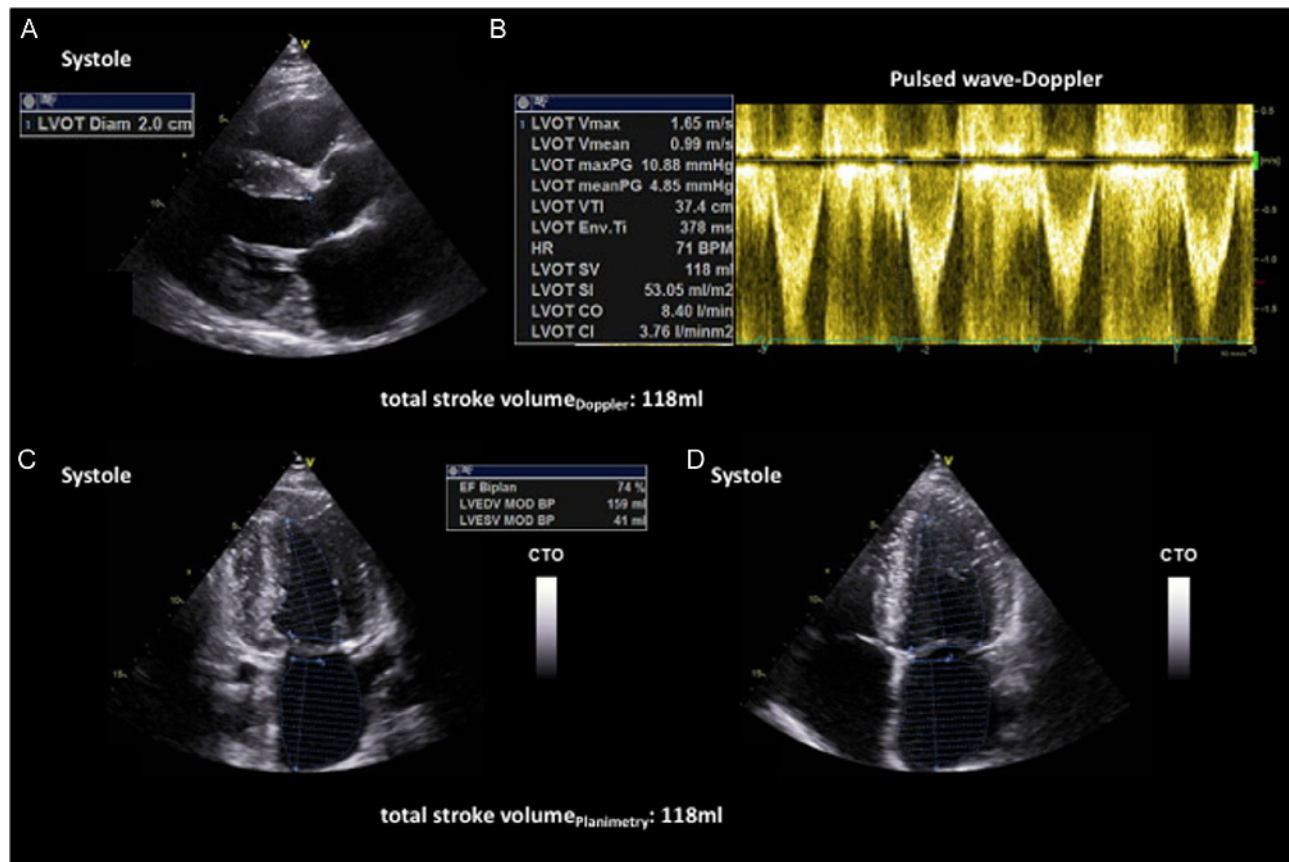
Figure 1

Assessment of total stroke volume (SV_{tot}) by 2D Doppler echocardiography (A – measurement of the left ventricular outflow tract diameter (D_{LVOT}) in the parasternal long axis view; B – Doppler spectrum of the velocity time integral of the LVOT (VTI_{LVOT}) obtained by pulsed-wave Doppler in the apical long axis view) and by 2D left ventricular biplane planimetry in the apical 2 (C) – and 4 (D)-chamber view using the modified Simpson's rule.

at the pulmonary ring level (Fig. 2). TEE was generally performed in all patients with at least moderate valvular defect to find the correct diagnosis and to possibly be able to more correctly determine SV_{eff} (D_{PV}/VTI_{PV}). D_{PV} by TEE was only used in four patients. The RF was assessed by the following calculation: RF=($SV_{tot\ (planimetry)}$ − $SV_{eff\ (PV)}$)/ $SV_{tot\ (planimetry)}$) × 100) and was used for grading of AR severity (mild: <30%, moderate: 30–50%, severe: >50%) (4). RVol was calculated by subtracting SV_{eff} from SV_{tot} (1, 10).

Assessment of semi-quantitative parameters using 2D echocardiography

PHT, VC, RVol/EROA by PISA and the ratio of AR jet width/LVOT width were assessed in optimised views to maximise Doppler signals, reduce angular errors and optimise the visualisation of the regurgitant jet and the proximal convergence zones (1). VC was assessed by the smallest diameter of the main regurgitant jet formation below the AV ring. The VTI and the proximal convergence zones were documented and visualised after adjusting

image settings (colour maps, pulse repetition frequency, zoom settings) to determine RVol/EROA by PISA. In 30 chronic AR patients, the PW Doppler spectrum of the left subclavian artery was documented with a pencil probe to assess the ratio of the diastolic/systolic VTI (VTI_{dia}/VTI_{sys}) and the ratio of the maximum diastolic/systolic velocity ($Vmax_{dia}/Vmax_{sys}$). The diastolic flow reversal in the left subclavian artery has been proposed as a non-inferior approach in comparison to the assessment of the diastolic flow reversal in the descending aorta and as an adjunctive technique for grading of AR severity (11, 12).

Quantitative assessment of cardiac volumes and LVEF using 3D echocardiography

3D left (LVEDV, LVESV, SV_{tot}) and right ventricular (RV) volume analyses (SV_{eff}) were performed by automatic endocardial contour detection (TomTec, Unterschleissheim, Germany, 2014, version 3.1.0). Endocardial contour was manually adjusted and optimised. 6-beat full volume acquisition has been performed.
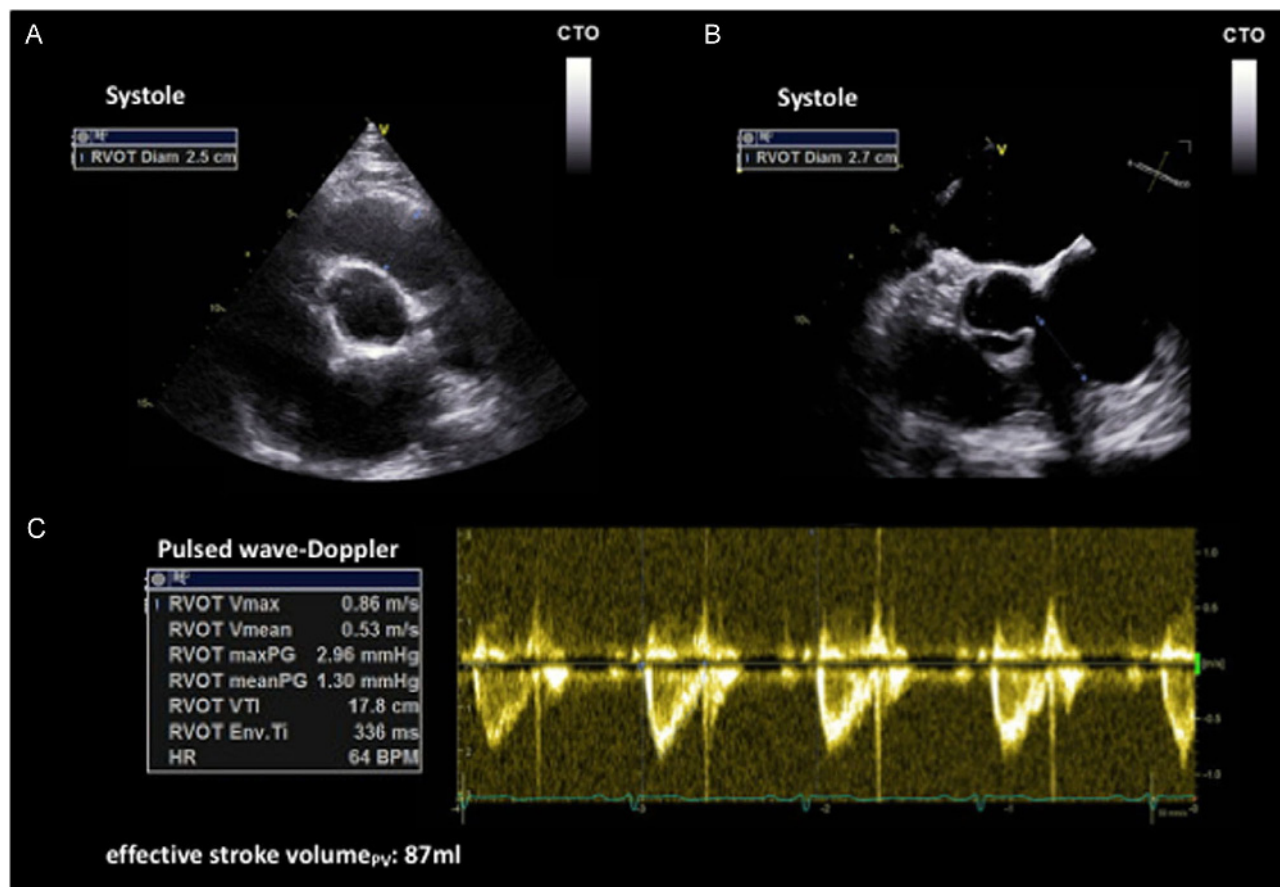
Figure 2
Assessment of the effective stroke volume (SV$_{eff}$) by 2D Doppler echocardiography using the diameter of the pulmonary valve (D$_{PV}$) at the level of the pulmonary ring in the parasternal short-axis view at the level of the aortic valve (A – transthoracic; B – transesophageal). The Doppler spectrum of the VTI of the pulmonary valve obtained by pulsed-wave Doppler in the parasternal short-axis view is shown in (C).

cMRI

cMRI was carried out on a 3T magnet resonance scanner (Philips Achieva, Best, the Netherlands) equipped with a standard five-element cardiac phased array coil. Post-processing analyses were performed using commercially available software (Philips extended MR Workspace 2.6.3.5, 2013, Philips Medical Systems, The Netherlands). LV volume analyses (LVEDV, LVESV) were analysed by endocardial contour detection in the apical 2- and 4-chamber view as well as by summation of the volume (area thickness) of the short-axis slices during diastole and systole using steady state free precession (SSFP) pulse sequences. RVol and RF assessment were based on the abovementioned calculations. Cine image sequences were SSFP (Philips Cinematic – BTFE – balanced fast field echo): temporal resolution: TFE shot interval and TFE shot/acquisition interval 57–65 ms, echo time: 1.3–1.6 ms, repetition time: 2.7–3.1 ms, field of view: 320 mm × 349 mm × 8 mm. Flow analyses were performed by measuring forward and regurgitant aortic flow by through-plane phase-contrast velocity mapping. Quantitative flow measurements by phased-contrast cMRI were performed to determine SV$_{tot}$ and SV$_{eff}$ (Fig. 3) (13, 14). Flow image sequences were acquired within a single breath hold (10–16 heart beats). Image parameters were the following: temporal resolution: TFE shot interval and TFE shot/acquisition interval 58–64 ms, echo time: 2.7–3.1 ms, repetition time 4.3–6.4 ms, field of view: 336 mm × 295 mm × 8 mm, PC velocity: 250–450 cm/s. Velocity settings were adjusted to avoid aliasing. In order to determine RF correctly, the plane position for phase-contrast velocity imaging was at the maximum diameter of the sinus of Valsalva (13).

Statistical analysis

Data are expressed as mean ± standard deviation (s.d.) and compared by Student's *t*-test. Normality of distribution was tested by Kolmogorov–Smirnov test. Pearson correlation was performed to compare coherences between the different
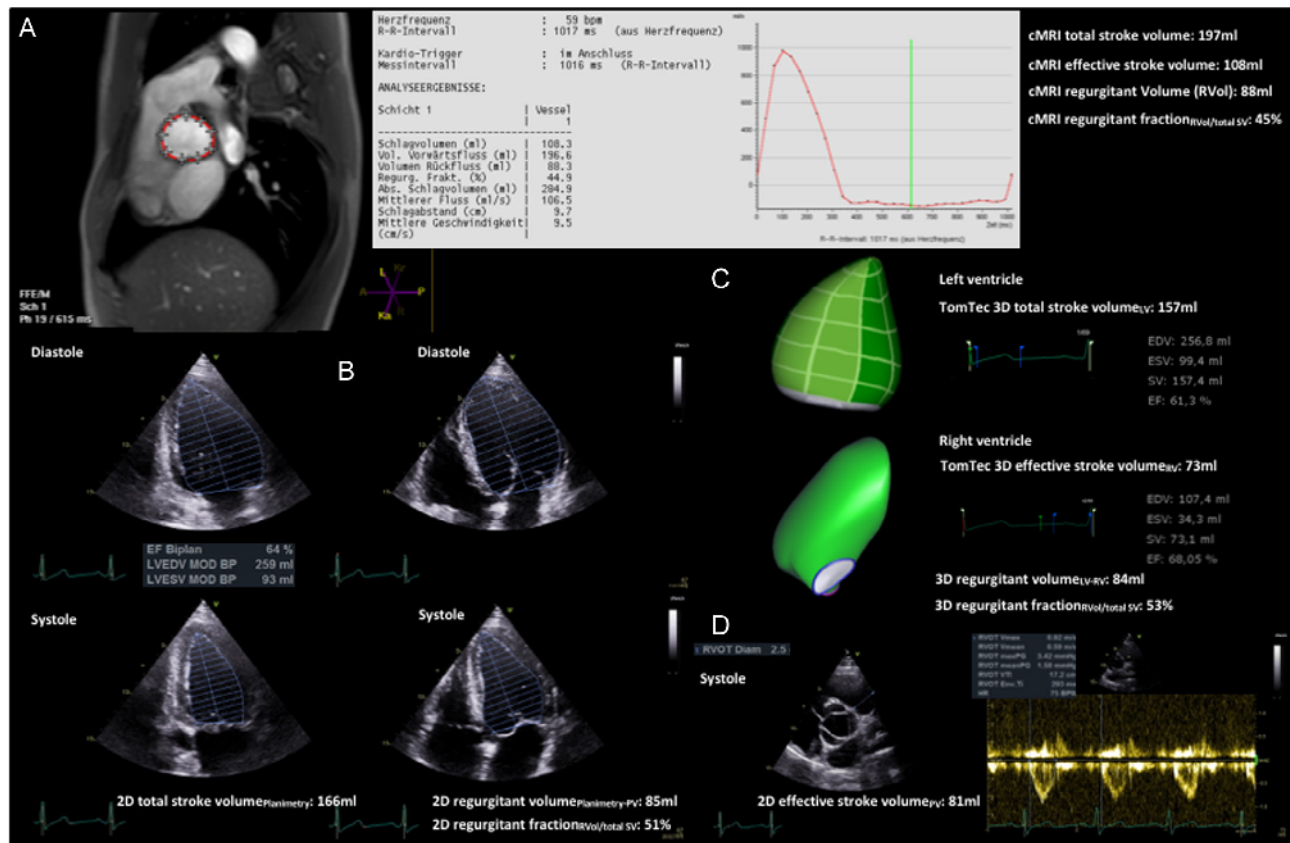
Figure 3
Assessment of SV_{tot}, SV_{eff}, the regurgitant volume (RVol) and the regurgitant fraction (RF) by cardiac magnet resonance imaging (cMRI) (A), by 2D biplane planimetry in the apical 2-and 4-chamber view (B) and 2D Doppler echocardiography (D) and by left and right ventricular volume analyses by 3D echocardiography (TomTec) (C).

parameters assessed by the different approaches and imaging modalities. Poor correlation was defined as $r \leq 0.5$, intermediate as $r = 0.5–0.7$ and good correlation as $r \geq 0.7$ (15). Bland–Altman plots were carried out for the comparison of SV_{tot}, RVol and RF between the different approaches and imaging modalities. Statistical significance was defined by two-tailed P value $P < 0.05$ (confidence interval 95%). For grading of AR severity, strength of agreement was tested by Cohen kappa (k) analysis and was defined by the following: <0.2 (poor), 0.21–0.4 (fair), 0.41–0.6 (moderate), 0.61–0.80 (good) and 0.81–1.0 (very good) (16). Statistical analyses were performed using SPSS software, version 17.0 (IBM Deutschland GmbH, Ehningen, Germany).

Results

Quantitative assessment of AR severity by 2D echocardiography

Clinical data are summarised in Table 1. According to quantitative assessment of RF using 2D echocardiography:

22 (40%) patients had mild, 25 (46%) moderate and 8 (14%) severe AR. Determinations of LVEDV, LVESV, SV_{tot}, SV_{eff}, RVol and RF were feasible in all patients ($n = 55$). The assessment of SV_{tot} by 2D Doppler echocardiography and 2D biplane planimetry resulted in good correlations ($r = 0.93$, $P = 0.001$); (Table 2). Further, RVol and RF did show good correlations regardless whether SV_{tot} has been measured by 2D Doppler echocardiography or 2D biplane planimetry (Table 2).

Assessment of semi-quantitative parameters using 2D echocardiography

The feasibility of the assessment of semi-quantitative parameters varied considerably. In total, a reliable determination of all semi-quantitative parameters was only possible in a minority of patients (Table 3). $V\text{max}_{dia}/V\text{max}_{sys}$, VTI_{dia}/VTI_{sys} obtained by analysis of left subclavian artery flow ($n = 29/30$) and PHT ($n = 44/55$) could be assessed in most of the patients. $V\text{max}_{dia}/V\text{max}_{sys}$, VTI_{dia}/VTI_{sys} and PHT were significantly lower in patients

Table 1 Clinical characteristics of patients with chronic AR.

Characteristics	Chronic AR patients (*n* = 55)
Age (years)	51 ± 15
Male	42 (76%)
Female	13 (24%)
BMI (kg/m²)	25.9 ± 3.6
BSA (m²)	1.98 ± 0.2
NYHA	2 ± 0.5
Blood pressure sys/dia (mmHg)	131 ± 11/77 ± 9
Bicuspid valve	22 (40%)
Diameter of sinus of valsalvae (mm)	38 ± 5
Hypertension	40 (73%)
Coronary heart disease	3 (5%)
Diabetes mellitus	3 (5%)

AR, aortic regurgitation; BMI, body mass index; BSA, body surface area; NYHA, New York Heart Association.

with mild than in patients with moderate/severe AR (Table 3).

Comparison of LV volumes/function and RVol, RF by 2D/3D echocardiography and cMRI

According to Lang *et al*. (males: LVEDV >74 mL/m²; females: LVEDV >61 mL/m²) half of the patients with chronic AR (*n* = 28/55, 51%) had increased LVEDV assessed by 2D echocardiography (9). In chronic AR patients, in whom 2D, 3D echocardiography and cMRI were available (*n* = 32): 4 (13%) patients had mild, 21 (65%) moderate and 7 (22%) severe AR evaluated by quantitative assessment of RF using 2D echocardiography. In these patients LVEDV, LVESV

and SV_{tot} showed good correlations between the different imaging modalities, although significantly increased LV volumes were assessed by cMRI (Table 4, Bland–Altman plots Fig. 4). Intermediate statistical agreement was found for SV_{eff} between all imaging modalities. The assessment of RVol resulted in significant differences between 2D/3D echocardiography, 2D echocardiography/cMRI, showing intermediate correlations. RVol was not significantly different between 3D echocardiography/cMRI, showing only poor correlation (Table 4, Bland–Altman plots Fig. 5). RF was not statistically different between 2D echocardiography/cMRI and 3D echocardiography/cMRI. Correlation coefficients for RF were poor ($r < 0.5$) between the different imaging modalities (Table 4, Bland–Altman plots Fig. 6). Strength of agreement for AR grading has been tested for RF showing moderate agreement between 2D/3D echocardiography ($k = 0.42$) and 2D echocardiography/cMRI ($k = 0.44$) and good agreement between 3D echocardiography/cMRI ($k = 0.62$).

Discussion

In the present study, the quantitative volumetric approach using 2D echocardiography was applicable in all patients. The feasibility of the assessment of semi-quantitative parameters varied considerably. Further, the present data confirmed that LV volume analyses (LVEDV, LVESV and SV_{tot}) were comparable between 2D, 3D echocardiography and cMRI showing good correlations. Otherwise, SV_{eff},

Table 2 Quantitative assessment of LVEDV, LVESV, SV_{tot}, SV_{eff}, RVol, RF, LVEF and GLPSS using 2D echocardiography in all patients with chronic AR (*n* = 55).

Parameters	Chronic AR (*n* = 55)	Pearson correlation coefficient *r* (*P*); *t*-test *P*
LVEDV (mL) (2D planimetry)	147 ± 39.79	
LVESV (mL) (2D planimetry)	52 ± 17.84	
SV_{tot} (mL) (2D Doppler)	100 ± 25.84	*r* = 0.93 (*P* = 0.001); *P* = 0.331
Indexed SV_{tot} (mL/m²) (2D Doppler)	51 ± 13.05	
SV_{tot} (mL) (2D planimetry)	95 ± 25.13	
Indexed SV_{tot} (mL/m²) (2D planimetry)	48 ± 12.69	
SV_{eff} (PV) (mL)	68 ± 18.32	
RVol (SV_{tot} 2D Doppler − SV_{eff} PV) (mL)	32 ± 15.37	*r* = 0.84 (*P* = 0.001); *P* = 0.130 *Compared to* RVol (SV_{tot} 2D planimetry − SV_{eff} PV)
RVol (SV_{tot} 2D planimetry − SV_{eff} PV) (mL)	28 ± 17.02	
RF (SV_{tot} 2D Doppler − SV_{eff} PV) (%)	27 ± 13.79	*r* = 0.98 (*P* = 0.001); *P* = 0.814 *Compared to* RF (SV_{tot} 2D planimetry − SV_{eff} PV)
RF (SV_{tot} 2D planimetry − SV_{eff} PV) (%)	28 ± 12.37	
LVEF (mL)	66 ± 5.45	
GLPSS (%)	−20 ± 3.14	

Statistical significance was accepted for *P* < 0.05.
AR, aortic regurgitation; GLPSS, global longitudinal peak systolic strain; LVEDV, left ventricular end-diastolic volume; LVEF, left ventricular ejection fraction; LVESV, left ventricular end-systolic volume; PV, pulmonary valve; PW, pulsed wave; RF, regurgitant fraction; RVol, regurgitant volume; SV_{eff}, effective stroke volume; SV_{tot}, total stroke volume; VTI, velocity time integral.

Table 3 Semi-quantitative parameters obtained by 2D echocardiography in patients with chronic AR.

Parameters	Chronic AR patients (*n* = 55)
EROA (cm²)	0.2 ± 0.08
RVol (mL)	47 ± 18.54
(*PISA method*)	12 of 55 patients (21%)
$V\text{max}_{dia}/V\text{max}_{sys}$	29 of 30 patients (97%)
(*Doppler subclavian artery*)	*Mild AR: 0.26 m/s ± 0.10 (n = 11/29)*
	Moderate/severe AR: 0.38 m/s ± 0.11 (n = 18/29)
	P = 0.041
VTI_{dia}/VTI_{sys} (*Doppler subclavian artery*)	29 of 30 patients (97%)
	Mild AR: 29% ± 22.06 (n = 11/29)
	Moderate/severe AR: 47% ± 13.36 (n = 18/29)
	P = 0.038
Vena contracta (mm)	3 ± 1.04
	31 of 55 patients (56%)
PHT (ms)	543 ± 181.38
	44 of 55 patients (80%)
Ratio AR jet width/LVOT width (%)	34 ± 11.81
	24 of 55 patients (44%)

Statistical significance was accepted for $P < 0.05$.
AR, aortic regurgitation; dia, diastolic; EROA, effective regurgitant orifice area; LVOT, left ventricular outflow tract; PHT, pressure-half-time; RVol, regurgitant volume; V_{max}, maximum velocity; sys, systolic; VTI, velocity time integral.

RVol and RF did not correlate well between 2D, 3D echocardiography and cMRI. The best agreement for chronic AR quantification by RF was observed between 3D echocardiography/cMRI.

Quantitative approach for grading of AR severity

Although the quantitative volumetric approach was more feasible in comparison to semi-quantitative parameters, especially the assessment of RF is sensitive to measurement errors due to its challenging assessment, which requires the acquisition of data sets with sufficient image quality and the consideration of basic methodological aspects in echocardiography (1, 2, 4, 10, 17). According to the present data, the assessment of SV_{tot} by 2D Doppler echocardiography and 2D biplane planimetry can be compared to each other to verify the reliability of the determined SV_{tot} by congruence of both approaches. This might be helpful to minimise the sources of errors for the assessment of SV_{tot} and RF. Further, 3D data sets can help to avoid oblique views and enable a more precise assessment of the anatomical shape of the LVOT (10, 17, 18, 19). Generally, the determination of D_{PV} is challenging because of the inhomogeneous shape of the RV outflow tract, probably leading to higher variations in clinical routine.

In general, the levels of feasibility for the quantitative assessment of RVol and RF are obviously different in chronic AR patients. Thus, the consideration of patients with sufficient image quality can be discussed as a limiting aspect in the present study as well as in clinical routine. Further, the challenging assessment of RVol and RF requires a certain degree of expertise or at least a certain time of training. In the present study, quantitative measurements were only performed by very experienced investigators, which can be discussed as another limiting aspect and might be another reason why quantitative measurements have come out very well in the present study (4).

Semi-quantitative parameters for grading of AR severity

PISA, VC, PHT, $V\text{max}_{dia}/V\text{max}_{sys}$ and VTI_{dia}/VTI_{sys} (left subclavian artery) are often limited by measurement errors and are inconsistent in grading of AR severity. Especially AR grading by the visual assessment of the regurgitant jet area is misleading and not recommended (2, 4, 5). According to the current recommendations the PISA method seems to be one of the most favoured methods in patients with AR (1, 4). However, PISA was only applicable in a minority of patients in the present study. The present study has shown that semi-quantitative parameters are less feasible and the failure to completely assess all available semi-quantitative parameters reflects the reality in clinical routine and represents a limitation for grading of AR severity. Generally, the limited feasibility of semi-quantitative parameters might be due to methodological limitations and physiological alterations (1, 17). Eccentric jet formations due to anomalies of the cusps, cusps restriction and ectasia of the ascending aorta have a relevant influence on VC, PHT and ratio of AR jet width/left ventricular outflow tract (LVOT) width in chronic AR. The analysis of the left subclavian artery flow was more feasible in the present study and has already shown to be an alternative semi-quantitative approach for chronic AR quantification in clinical routine (12).

Volume analyses by 2D, 3D echocardiography and cMRI in chronic AR

In the present study, the majority of patients could be classified as moderate or severe AR (*n* = 33/55, 60%) and LV dilatation could be observed in half of the patients. According to the pathophysiology of chronic

Table 4 Analysis of LV volumes, LVEF and quantitative parameters (SV$_{eff}$, RVol, RF) using 2D, 3D echocardiography and cMRI in patients with chronic AR ($n=32$).

Parameters (chronic AR, **$n=32$**)	2D echo-cardiography	3D echo-cardiography	cMRI	Pearson correlation coefficient r (P); t-test P
LVEDV (mL) (planimetry)	172±29.22	169±34.29	189±44.05	2D vs 3D: $r=0.94$ ($P<0.001$); $P=0.851$ 2D vs cMRI: $r=0.86$ ($P<0.001$); $P=0.012$ 3D vs cMRI: $r=0.84$ ($P<0.001$); $P=0.012$
LVESV (mL) (planimetry)	57±15.98	56±15.77	67±27.59	2D vs 3D: $r=0.88$ ($P<0.001$); $P=0.948$ 2D vs cMRI: $r=0.80$ ($P<0.001$); $P=0.021$ 3D vs cMRI: $r=0.79$ ($P<0.001$); $P=0.017$
SV$_{tot}$ (mL) (planimetry)	107±21.41	103±21.71	119±37.64	2D vs 3D: $r=0.95$ ($P<0.001$); $P=0.431$ 2D vs cMRI: $r=0.80$ ($P<0.001$); $P=0.012$ 3D vs cMRI: $r=0.74$ ($P<0.001$); $P=0.002$
LVEF (mL)	65±5.67	66±7.69	67±7.20	2D vs 3D: $r=0.79$ ($P<0.01$); $P=0.753$ 2D vs cMRI: $r=0.57$ ($P<0.01$); $P=0.188$ 3D vs cMRI: $r=0.56$ ($P<0.01$); $P=0.387$
SV$_{eff}$ (mL)	75±17.79 (PV)	63±14.32 (TomTec analysis)	84±19.52	2D vs 3D: $r=0.51$ ($P=0.003$); $P=0.004$ 2D vs cMRI: $r=0.63$ ($P<0.001$); $P=0.004$ 3D vs cMRI: $r=0.54$ ($P=0.002$); $P<0.001$
RVol (mL)	35±13.11 (SV$_{tot}$ planimetry − SV$_{eff}$ PV)	41±12.27 (TomTec SV$_{tot}$ − TomTec SV$_{eff}$)	44±10.42	2D vs 3D: $r=0.55$ ($P=0.001$); $P=0.001$ 2D vs cMRI: $r=0.61$ ($P<0.001$); $P=0.001$ 3D vs cMRI: $r=0.43$ ($P=0.014$); $P=0.784$
RF (%)	34±10.76 (SV$_{tot}$ planimetry − SV$_{eff}$ PV)	40±12.64 (TomTec SV$_{tot}$ − TomTec SV$_{eff}$)	36±11.43	2D vs 3D: $r=0.40$ ($P=0.020$); $P=0.009$ 2D vs cMRI: $r=0.46$ ($P=0.007$); $P=0.173$ 3D vs cMRI: $r=0.33$ ($P=0.047$); $P=0.174$

Statistical significance was accepted for $P<0.05$.
AR, aortic regurgitation; cMRI, cardiac magnet resonance imaging; LVEDV, left ventricular end-diastolic volume; LVEF, left ventricular ejection fraction; LVESV, left ventricular end-systolic volume; PV, pulmonary valve; RF, regurgitant fraction; RVol, regurgitant volume; SV$_{eff}$, effective stroke volume; SV$_{tot}$, total stroke volume.

AR, LV dilatation and increased SV$_{tot}$ due to LV volume overload is not uncommonly be seen in these patients. In the literature, no specific LVEDV-cut-off values do exist for chronic AR patients. Both cut-off values (males >74 mL/m², females >61 mL/m²) were based on reference values of normal subjects (9). These cut-off values will probably be frequently exceeded in patients with valvular regurgitations. However, none of the patients in the present study matches the cut-off values for that surgery is recommended (LV end-systolic diameter >50 mm (>25 mm/m²), LVESV >45 mL/m²) (1, 4).

The present data confirm that LV volume analyses are comparable between 2D, 3D echocardiography and cMRI showing good correlations for the assessment of LVEDV, LVESV and SV$_{tot}$ (20, 21, 22, 23, 24, 25, 26). In former studies, LV volumes obtained by 2D/3D echocardiography and cMRI were not different and correlation coefficients were remarkably better between
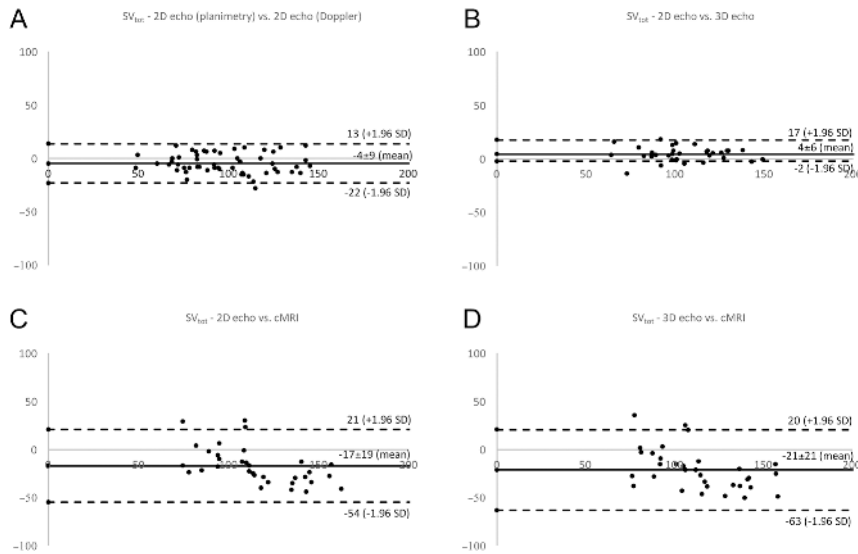
Figure 4
Comparison of total stroke volume (SV_{tot}) assessed by 2D left ventricular (LV) planimetry and 2D Doppler echocardiography (A), 2D (planimetry) and 3D echocardiography (B), 2D echocardiography and cMRI (C) and 3D echocardiography and cMRI (D).

these imaging modalities which has been described in healthy subjects and in patients with reduced LVEF and LV dilatation (21, 22). In contrast, recent studies have shown that significantly larger LV volumes will be assessed by cMRI in comparison to 2D/3D echocardiography which is in line with the results of the present study (23, 24). Further, slightly lower correlation coefficients have been described in comparison to Jenkins *et al.* and Nikitin *et al.* (24). The discrepancies between the different studies cannot sufficiently be explained. However, the spatial and temporal resolution of 3D echocardiography was not that good ten years ago and echocardiography as well as cMRI will always be slightly influenced by errors due to inter-/intraobserver variability, oblique sectional planes, etc. Although contrast agents are not routinely used in clinical routine, they can be used to improve accuracy and reduce inter- and intraobserver variability in 2D/3D echocardiography (23, 25).

In the present study, RVol and RF did not correlate well between the different imaging modalities. Only 3D echocardiography and cMRI provided values that were not

significantly different for both RVol and RF. As mentioned above, the poor correlations and partly significant differences might be owing to the challenging assessment of RVol and RF which are sensitive to measurement errors and require the consideration of several methodological aspects in echocardiography (1, 2, 4, 10, 17). Further, spatial and temporal resolution are still limited in 3D echocardiography. Another reason for the poor correlation can be assumed due to the challenging echocardiographic evaluation of the RV. Several studies have analysed the assessment of RV volumes/-ejection fraction by 2D, 3D echocardiography and cMRI. The majority of these studies have been performed in animal models or healthy subjects (27, 28, 29). Ewe *et al.* has evaluated the accuracy of 2D/3D echocardiography and cMRI for AR quantification demonstrating intermediate correlation between 2D echocardiography/cMRI and good correlation between 3D echocardiography/cMRI. In the study by Ewe *et al.*, primarily semi-quantitative approaches estimating EROA by PISA (2D) or by planimetry of VC (3D) were used. RVol was further estimated by multiplying the 2D or 3D EROA with the VTI of the AR jet (30). In contrast,
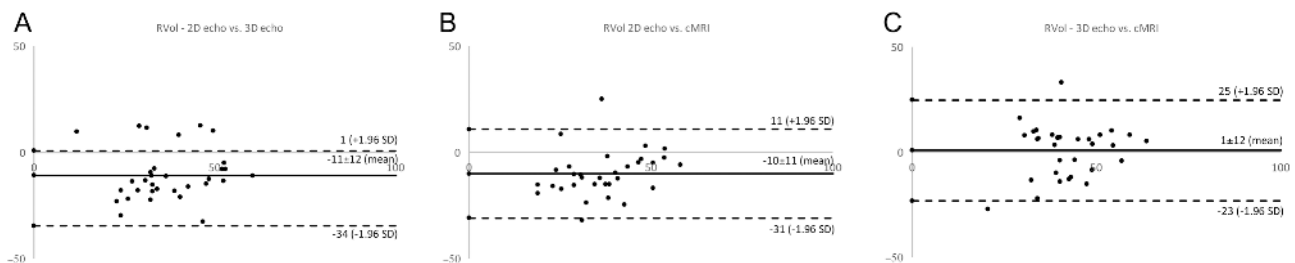

Figure 5
Comparison of regurgitant volume (RVol) assessed by 2D and 3D echocardiography (A), 2D echocardiography and cMRI (B) and 3D echocardiography and cMRI (C).
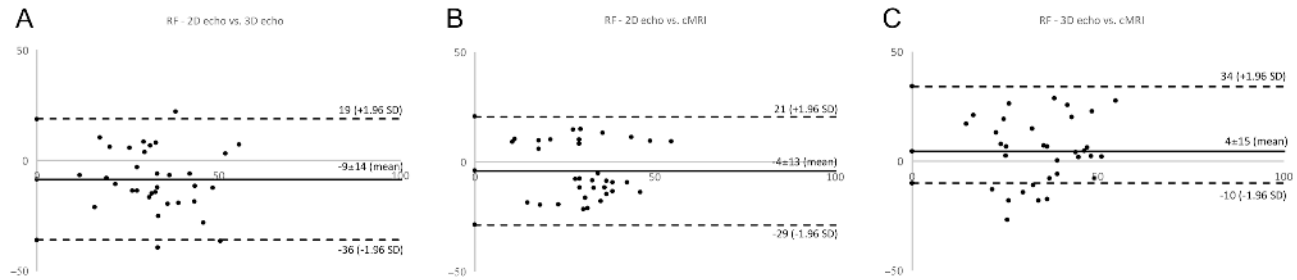
Figure 6

Comparison of regurgitant fraction (RF) assessed by 2D and 3D echocardiography (A), 2D echocardiography and cMRI (B) and 3D echocardiography and cMRI (C).

in the present study, RVol was estimated by the volumetric approach showing intermediate correlation between 2D echocardiography/cMRI, and seemingly poor correlation between 3D echocardiography/cMRI. These discrepancies could be explained by the different methodological approaches, which were used in the respective studies. Further, SV_{eff} seems to be underestimated by volumetric analysis using 3D echocardiography. This might be mostly due to the complex RV anatomy, which might have a greater influence on RV SV_{eff}.

According to the results of the present study, grading of chronic AR severity by RF might differ depending on the image modality that was used for AR quantification. However, better strength of agreement for grading of chronic AR by RF was observed between 3D echocardiography and cMRI in comparison to 2D/3D echocardiography and 2D echocardiography/cMRI showing only moderate strength of agreement.

Conclusions

Semi-quantitative parameters of AR quantification are difficult to determine by 2D echocardiography in clinical routine. The quantitative volumetric assessment of RF seems to be feasible and can be discussed as an alternative approach in chronic AR. However, RVol and RF did not correlate well between the different imaging modalities. The best agreement for grading of AR severity by RF was observed between 3D echocardiography and cMRI. Parameters of LV volume analysis (LVEDV, LVESV, SV_{tot}) can be verified by different approaches and different imaging modalities.

Limitations

Due to the retrospective study design, the analysis of the data sets was limited concerning the following aspects:

D_{LVOT} was determined by 2D echocardiography. 3D LVOT planimetry could not be analysed with sufficient image quality. In four patients D_{PV} was determined by TEE because the transthoracic documentation was insufficient. Generally, patients with non-sufficient imaging quality were not considered for the analysis. It has been proposed that the analysis of the diastolic flow reversal in the left subclavian artery is not inferior to the analysis of the diastolic flow reversal in the descending aorta and the authors have much experience with the assessment of this parameter so it is preferred at the author's department and the diastolic flow reversal in the descending aorta could not be considered in the present retrospective study. Statistical significance between mild and moderate/severe AR was only tested for $Vmax_{dia}/Vmax_{sys}$, VTI_{dia}/VTI_{sys} (subclavian artery) and PHT, because only these semi-quantitative parameters were feasible in the majority of patients. Thus, AR quantification by 2D PISA could not have been correlated to the volumetric approach. The small number of patients – especially of severe AR – and the availability of all three imaging modalities (2D, 3D echocardiography and cMRI) in 32 of 55 chronic AR patients are limiting the power of the study.

References

1 Lancellotti P, Tribouilloy C, Hagendorff A, Moura L, Popescu BA, Agricola E, Monin JL, Pierard LA, Badano L & Zamorano JL. European Association of Echocardiography – recommendations for the assessment of valvular regurgitation. Part 1: aortic and

pulmonary regurgitation (native valve disease). *European Journal of Echocardiography* 2010 **11** 223–244. (https://doi.org/10.1093/ejechocard/jeq030)

2 Lancellotti P, Tribouilloy C, Hagendorff A, Popescu BA, Edvardsen T, Pierard LA, Badano L & Zamorano JL. Recommendations for the echocardiographic assessment of native valvular regurgitation: an executive summary from the European Association of Cardiovascular Imaging. *European Heart Journal: Cardiovascular Imaging* 2013 **14** 611–644. (https://doi.org/10.1093/ehjci/jet105)

3 Zhogbi WA, Adams D, Bonow RO, Enriquez-Sarano M, Foster E, Grayburn PA, Hahn RT, Han Y, Hung J, Lang RM, *et al*. Recommendations for noninvasive evaluation of native valvular regurgitation – a report from the American Society of Echocardiography Developed in Collaboration with the Society for Cardiovascular Magnetic Resonance. *Journal of the American Society of Echocardiography* 2017 **30** 303–371. (https://doi.org/10.1016/j.echo.2017.01.007)

4 Vahanian A, Alfieri O, Andreotti F, Antunes MJ, Baron-Esquivias G, Baumgartner H, Borger MA, Carrel TP, De Bonis M, Evangelista A, *et al*. Guidelines on the management of valvular heart disease. *European Heart Journal* 2012 **33** 2451–2496. (https://doi.org/10.1093/eurheartj/ehs109)

5 Hagendorff A. Transthoracic echocardiography in adult patients – a proposal for documenting a standardized investigation. *Ultraschall in der Medizin* 2008 **29** 2–31. (https://doi.org/10.1055/s-2008-102749)

6 Flachskampf FA, Wouters PF, Edvardsen T, Evangelista A, Habib G, Hoffman P, Hoffmann R, Lancellotti P & Pepi M. Recommendations for transoesophageal echocardiography: EACVI update 2014. *European Heart Journal: Cardiovascular Imaging* 2014 **15** 353–365. (https://doi.org/10.1093/ehjci/jeu015)

7 Strasser RH, Andresen D, de Haan F, Ertl G, Mudra H, Osterspey A, Trappe HJ, Werdan K, Arnold G, Hoffmeister HM, *et al*. Positionspapier zu qualitätsstandards in der echokardiographie. *Zeitschrift für Kardiologie* 2004 **93** 975–986. (https://doi.org/10.1007/s00392-004-0181-2)

8 Buck T, Breithardt OA, Faber L, Fehske W, Flachskampf FA, Franke A, Hagendorff A, Hoffmann R, Kruck I, Kücherer H, *et al*. Manual zur indikation und durchführung der echokardiographie. *Clinical Research in Cardiology Supplements* 2009 **4** 3–51. (https://doi.org/10.1007/s11789-009-0051-6)

9 Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, Flachskampf FA, Foster E, Goldstein SA, Kuznetsova T, *et al*. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *European Heart Journal: Cardiovascular Imaging* 2015 **16** 233–270. (https://doi.org/10.1093/ehjci/jev014)

10 Enriquez-Sarano M, Bailey KR, Seward JB, Tajik AJ, Krohn MJ & Mays JM. Quantitative Doppler assessment of valvular regurgitation. *Circulation* 1993 **87** 841–848. (https://doi.org/10.1161/01.CIR.87.3.841)

11 Omran H, Fehske W, Hagendorff A, Pizzulli L & Luderitz B. Paraprosthetic regurgitation in aortic prostheses: determination of the hemodynamic significance by pulsed Doppler examination of the subclavian artery flow. *Journal of Heart Valve Disease* 1995 **4** 166–170.

12 Spampinato RA, Jahnke C, Paetsch I, Hilbert S, Busch F, Schloma V, Dmitrieva Y, Bonamigo Thome F, Löbe S, Strotdrees E, *et al*. Quantification of aortic valve regurgitation by pulsed Doppler examination of the left subclavian artery velocity contour: a validation study with cardiovascular magnetic resonance imaging. *Journal of the American Society of Echocardiography* 2018 **31** 42–51. (https://doi.org/10.1016/j.echo.2017.10.004)

13 Chaturvedi A, Hamilton-Craig C, Cawley PJ, Mitsumori LM, Otto CM & Maki JH. Quantitating aortic regurgitation by cardiovascular magnet resonance: significant variations due to slice location and breath holding. *European Radiology* 2016 **26** 3180–3189. (https://doi.org/10.1007/s00330-015-4120-6)

14 Gelfand EV, Hughes S, Hauser TH, Yeon SB, Goepfert L, Kissinger KV, Rofsky NM & Manning WJ. Severity of mitral and aortic regurgitation as assessed by cardiovascular magnetic resonance: optimizing correlation with Doppler echocardiography. *Journal of Cardiovascular Magnetic Resonance* 2009 **8** 503–507. (https://doi.org/10.1080/10976640600604856)

15 Bühl A. *SPSS 16 – Einführung in Die Moderne Datenanalyse*. Munich, Germany: Pearson Studium 2008

16 Altman DG. *Practical Statistics for Medical Research*. London, UK: Chapman and Hall, 1991.

17 Hagendorff A, Stoebe S, Tarr A & Pfeiffer D. Standard transthoracic echocardiography examination in patients with degenerative stenosis of the aortic valve. *Ultraschall in der Medizin* 2012 **33** 2–25. (https://doi.org/10.1055/s-0032-1325584)

18 Agricola E, Badano L, Mele D, Galderisi M, Slavich M, Sciomer S, Nistri S, Ballo P, D'Andrea A & Mondillo S. Real-time three dimensional transesophageal echocardiography: technical aspects and clinical applications. *Heart International* 2010 **5** 22–26. (https://doi.org/10.4081/hi.2010.e6)

19 Arribas-Jimenez A, Rama-Merchan JC, Barreiro-Pérez M, Merchan-Gómez S, Iscar-Galán A, Martín-García A, Nieto-Ballestero F, Sánchez-Corral E, Rodriguez-Collado J, Cruz-González I, *et al*. Utility of real-time 3-dimensional transesophageal echocardiography in the assessment of mitral paravalvular leak. *Circulation Journal* 2016 **80** 738–744. (https://doi.org/10.1253/circj.CJ-15-0802)

20 Lang RM, Badano LP, Tsang W, Adams DH, Agricola E, Buck T, Faletra FF, Franke A, Hung J, Perez de Isla L, *et al*. EAE/ASE recommendations for image acquisition and display using three-dimensional echocardiography. *European Heart Journal: Cardiovascular Imaging* 2012 **13** 1–46. (https://doi.org/10.1093/ehjci/jer316)

21 Jenkins C, Bricknell K, Hanekom L & Marwick TH. Reproducibility and accuracy of echocardiographic measurements of left ventricular parameters using real-time three-dimensional echocardiography. *Journal of the American College of Cardiology* 2004 **44** 878–886. (https://doi.org/10.1016/j.jacc.2004.05.050)

22 Nikitin NP, Constantin C, Loh PH, Ghosh J, Lukaschuk EI, Bennett A, Hurren S, Alamgir F, Clark AL & Cleland JGF. New generation 3-dimensional echocardiography for left ventricular volumetric and functional measurements: comparison with cardiac magnetic resonance. *European Journal of Echocardiography* 2006 **7** 365–372. (https://doi.org/10.1016/j.euje.2005.09.005)

23 Hoffmann R, Barletta G, von Bardeleben S, Vanoverschelde JL, Kasprzak J, Greis C & Becher H. Analysis of left ventricular volumes and function: a multicenter comparison of cardiac magnetic resonance imaging, cine ventriculography, and unenhanced and contrast-enhanced two-dimensional and three-dimensional echocardiography. *Journal of the American Society of Echocardiography* 2014 **27** 292–301. (https://doi.org/10.1016/j.echo.2013.12.005)

24 Gardner BI, Bingham SE, Allen MR, Blatter DD & Anderson JL. Cardiac magnetic resonance versus transthoracic echocardiography for the assessment of cardiac volumes and regional function after myocardial infarction: an intrasubject comparison using simultaneous intrasubject recordings. *Cardiovascular Ultrasound* 2009 **7** 38–44. (https://doi.org/10.1186/1476-7120-7-38)

25 Wood PW, Choy JB, Nanda NC & Becher H. Left ventricular ejection fraction and volumes: it depends on the imaging method. *Echocardiography* 2014 **31** 87–100. (https://doi.org/10.1111/echo.12331)

26 Gutiérrez-Chico JL, Zamorano JL, Perez de Isla L, Orejas M, Almeria C, Rodrigo JL, Ferreiros J, Serra V & Macaya C. Comparison of left ventricular volumes and ejection fractions measured by three-dimensional echocardiography versus by two-dimensional echocardiography and cardiac magnetic resonance in patients with

various cardiomyopathies. *American Journal of Cardiology* 2005 **95** 809–813. (https://doi.org/10.1016/j.amjcard.2004.11.046)

27 Vogel M, Gutberlet M, Dittrich S, Hosten, N & Lange PE. Comparison of transthoracic three dimensional echocardiography with magnetic resonance imaging in the assessment of right ventricular volume and mass. *Heart* 1997 **78** 127–130. (https://doi.org/10.1136/hrt.78.2.127)

28 Gopal AS, Chukwu EO, Iwuchukwu CJ, Katz AS, Toole RS, Schapiro W & Reichek N. Normal values of right ventricular size and function by real-time 3-dimensional echocardiography: comparison with cardiac magnetic resonance imaging. *Journal of the American Society of Echocardiography* 2007 **20** 445–455. (https://doi.org/10.1016/j.echo.2006.10.027)

29 Fujimoto S, Mizuno R, Nakagawa Y, Dohi K & Nakano H. Estimation of the right ventricular volume and ejection fraction by transthoracic three-dimensional echocardiography. A validation study using magnetic resonance imaging. *International Journal of Cardiac Imaging* 1998 **14** 385–390. (https://doi.org/10.1023/A:1006117321095)

30 Ewe SH, Delgado V, van der Geest R, Westenberg JJM, Haeck MLA, Witkowski TG, Aufer D, Marsan NA, Holman ER, de Roos A, *et al*. Accuracy of three-dimensional echocardiography for quantification of aortic regurgitation and validation by three-dimensional three-directional velocity-encoded magnetic resonance imaging. *American Journal of Cardiology* 2013 **112** 560–566. (https://doi.org/10.1016/j.amjcard.2013.04.025)