CLINICAL RESEARCH

Performance of new automated transthoracic three-dimensional echocardiographic software for left ventricular volumes and function assessment in routine clinical practice: Comparison with 3 Tesla cardiac magnetic resonance

Performance d’un nouveau logiciel automatisé d’évaluation des volumes et de la fonction ventriculaire gauches en échocardiographie tridimensionnelle transthoracique en routine clinique. Comparaison avec l’IRM cardiaque 3 Tesla

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Abbreviations: 2D, Two-dimensional; 3D, Three-dimensional; CMR, Cardiovascular magnetic resonance; EDV, End-diastolic volume; ESV, End-systolic volume; COV, Coefficients of variation; HM 90–50, 3D default border detection set to 90–50; HM 80–40, 3D default border detection set to 80–40; HM 70–30, 3D default border detection set to 70–30; LV, Left ventricular; LVEF, Left ventricular ejection fraction; TTE, Transthoracic echocardiography.
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KEYWORDS
3D echocardiography; HeartModel\textsuperscript{A.I.}; 3 tesla cardiac magnetic resonance

Summary
Background. — Three-dimensional (3D) transthoracic echocardiography (TTE) is superior to two-dimensional Simpson’s method for assessment of left ventricular (LV) volumes and LV ejection fraction (LVEF). Nevertheless, 3D TTE is not incorporated into everyday practice, as current LV chamber quantification software products are time-consuming.

Aims. — To evaluate the feasibility, accuracy and reproducibility of new fully automated fast 3D TTE software (HeartModel\textsuperscript{A.I.}; Philips Healthcare, Andover, MA, USA) for quantification of LV volumes and LVEF in routine practice; to compare the 3D LV volumes and LVEF obtained with a cardiac magnetic resonance (CMR) reference; and to optimize automated default border settings with CMR as reference.

Methods. — Sixty-three consecutive patients, who had comprehensive 3D TTE and CMR examinations within 24 hours, were eligible for inclusion. Nine patients (14%) were excluded because of insufficient echogenicity in the 3D TTE. Thus, 54 patients (40 men; mean age 63 ± 13 years) were prospectively included into the study.

Results. — The inter- and intraobserver reproducibilities of 3D TTE were excellent (coefficient of variation < 10%) for end-diastolic volume (EDV), end-systolic volume (ESV) and LVEF. Despite a slight underestimation of EDV using 3D TTE compared with CMR (bias = −22 ± 34 mL; \( P < 0.0001 \)), a significant correlation was found between the two measurements (\( r = 0.93; P = 0.0001 \)). Enlarging default border detection settings leads to frequent volume overestimation in the general population, but improved agreement with CMR in patients with LVEF ≤ 50%. Correlations between 3D TTE and CMR for ESV and LVEF were excellent (\( r = 0.93 \) and \( r = 0.91 \), respectively; \( P < 0.0001 \)).

Conclusion. — 3D TTE using new-generation fully automated software is a feasible, fast, reproducible and accurate imaging modality for LV volumetric quantification in routine practice. Optimization of border detection settings may increase agreement with CMR for EDV assessment in dilated ventricles.

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Background

Global left ventricular (LV) quantification is essential during any cardiomyopathy. Assessment of LV volumes and LV ejection fraction (LVEF) is critical in various settings, such as myocardial infarction, valve diseases and heart failure. Measurement of LVEF is the most common reason for referring a patient for an echocardiogram [1]. Two-dimensional (2D) transthoracic echocardiography (TTE) using the volumetric Simpson’s biplane method is the first-line strategy for the assessment of LVEF [2], but has some classic limitations, such as foreshortening of the apex and restriction to only two planes [3]. Three-dimensional (3D) echocardiography does not rely on geometric assumptions for volume calculations, and is not subject to plane positioning errors, which can lead to chamber foreshortening [1]. Compared with cardiac magnetic resonance (CMR), which is the gold standard for cardiac chamber quantification, LV volumes calculated from 3D TTE showed significantly smaller bias and lower intra- and interobserver variability than 2D echocardiography [1]. Nevertheless, time-consuming workflow and the need for 3D expertise have limited the implementation of 3D quantification into clinical practice [4]. Recently, initial validation of new fully automated 3D TTE prototype software, which does not require any input once the dataset has loaded, has shown good accuracy and reproducibility, with promising time saving potential [4].

Thus, the aims of this prospective real-life clinical study were: to evaluate the feasibility, accuracy and reproducibility of this new commercially-available automated 3D TTE software (HeartModelA.I.; Philips Healthcare, Andover, MA, USA) for the quantification of LV volumes and LVEF in routine clinical practice; to compare the 3D LV volumes and LVEF obtained with a CMR reference; and to optimize automated default border settings and obtain the most accurate LV volume measurements compared with CMR.

Methods

Between February and June 2016, 63 consecutive patients who had comprehensive 3D TTE and CMR examinations within 24 hours were eligible for inclusion into the study. Patients with atrial fibrillation and controlled heart rate <100 beats/minute (n=3; 5.5%) were not excluded. Exclusion criteria were standard contraindications to CMR and poor TTE imaging quality. Institutional review board approval was obtained before conducting the study. The study was conducted in accordance with institutional policies, national legislation and the revised Helsinki declaration.

Echocardiography

All patients underwent comprehensive 2D and 3D transthoracic echocardiographic examinations, using a commercially-available ultrasound system (EPIQ 7C; Philips Healthcare, Andover, MA, USA). The 2D LVEF was calculated using Simpson’s biplane method. 3D LV volumes were acquired with an X5-1 matrix array transducer (5–1 MHz), from the standard apical four-chamber window, with the patient in the left lateral decubitus position. The left ventricle and left atrium were centred along the volume axis by adjusting depth and sector. Sector width was adjusted and narrowed to increase the frame rates of the volume. Special care was taken to ensure optimal gain and compression, to minimize dropout of the LV myocardial borders. A novel acquisition mode (HM ACQ) allowed fast acquisition of one-beat full-volume data sets, with a high-volume rate. Multiple consecutive cardiac beats could be acquired during a single breath hold. All 3D volumes were obtained in digital format, and were stored for analysis using dedicated fully automated quantification software (HeartModelA.I.). This new commercially-available software is a unique model-based segmentation algorithm using knowledge-based identification followed by patient-specific adaptation [4]. After initiating the programme, the software automatically identifies the heart chambers, and determines the end-diastolic and end-systolic frames using motion analysis. The software then automatically builds end-diastolic and end-systolic 3D volumes. The position of the border of the volume can be close to the blood-endocardial interface or more inside the compacted myocardium, according to user preference. The algorithm detects both inner and outer myocardial borders in end diastole and end systole. The final border position can be set by choosing a value between 0 (fully inside the myocardium, at the blood-endocardium interface) and 100 (near the compacted myocardium). Each volume was analysed with different automated default end-diastolic and end-systolic border setting values, named HM 80–40, HM 70–30 and HM 90–50, successively. As recommended by the vendor, HM 80–40 was chosen as the “standard” default setting for 3D TTE. HM 70–30 is a narrower border detection setting and HM 90–50 is a larger border detection setting. The software then reveals a display of 2D views (apical two-, three- and four-chamber views) from a 3D volume, and allows global and regional editing of the end-diastolic volume (EDV) and end-systolic volume (ESV) border. Volume borders can be edited either regionally or globally, by moving the entire border, if the user is not fully satisfied with the automated LV contour [5].

CMR technique

All patients underwent comprehensive TTE and CMR examinations within 24 hours, in comparable haemodynamic states. Patients were imaged with a 3 Tesla Skyra scanner (Siemens, Erlangen, Germany), 18-channel body flex coils and 45 mT/m gradients. Assessment of cardiac function was performed with a cine steady-state free-precession pulse sequence (True-Fisp sequence), with retrospective gating (or prospective gating in case of atrial fibrillation), in end-expiration breath hold. The following projections were acquired: two-chamber, four-chamber and parallel contiguous short axis (to cover the entire left ventricle from the mitral plane to the apex). Typical variables were: repetition time/time to echo (RT/TE), 2.8–1.23 ms; field of view (FOV), 341*430; matrix, 216*272; flip angle, 47–38° depending on the specific absorption rate (SAR) limit; slice thickness, 6 mm; parallel acquisition with iPAT GRAPPA (factor ×3); number of phases, 25; and temporal resolution, 48 ms. CMR data were processed offline by an independent
observer (L. I.), who was blinded to the results of the TTE. Data were analysed using dedicated software (circle CVI 42, version 5.1; circle cardiovascular imaging, Calgary, Canada). On the cine images, LVEF, EDV and ESV were calculated using the standard formula.

**Statistical analysis**

Data for the study population and TTE and CMR measurements are presented as numbers (percentages) or means±standard deviations after testing for normal distribution (Kolmogorov-Smirnov test). CMR and TTE measurements were compared using Wilcoxon rank test or the Bland-Altman test, as appropriate. Correlation and agreement between CMR and TTE measurements were assessed by Pearson’s correlation, intraclass correlation coefficients and Bland-Altman comparisons. Test-retest and inter- and intraobserver variability were examined for 3D TTE measurements. For interobserver variability, measurements were performed in all patients by one observer, then repeated offline on two separate days by two independent observers (F.L. and E.D.S.), who were blinded to each other’s measurements and to the study time point. For intraobserver variability, one observer (F.L.) analysed the data 1 week apart, and was blinded to the data from the first read. For test-retest reproducibility, a first 3D volume was obtained, then, after repositioning of the patient and the transducer, a second 3D volume was acquired by a different observer (E.D.S.). Test-retest was assessed in 41 patients. Variability data are presented as concordance correlation coefficients and as coefficients of variation (COV). For the comparison between the different border settings, folded empirical cumulative distribution plots (mountain plots) were plotted. Mountain plots make it easier to find the central 95% of the data, and it is easier to estimate percentiles for large differences [6]. If the two methods are unbiased with respect to each other, the mountain will be centred over zero. Long tails in the plot reflect large differences between the methods. All statistical analyses were performed using commercially-available software (MedCalc, version 16.8; MedCalc Software, Mariakerke, Belgium). All P-values are the results of two-tailed tests. A value of P < 0.05 was considered significant.

**Results**

**Study population and feasibility**

Nine patients (14%) were excluded because of insufficient echogenicity in 3D TTE. Thus, the final study group consisted of 54 patients (40 men; mean age: 63 ± 13 years). Baseline demographic and clinical characteristics of the 54 patients are displayed in Table 1. Using CMR as a reference, 16 patients (30%) had an LVEF ≤ 50%. Despite using one-beat full-volume acquisition, the average 3D volume rate was high (19.6 ± 2.1 Hz; range: 14–23 Hz), even in patients with 3D TTE LV volumes > 200 mL (n = 20; 18.9 ± 2.4 Hz; range: 14–23 Hz).

**Comparison with CMR**

EDV obtained by the different methods was: 215 ± 104 mL by CMR; 150 ± 69 mL by 2D TTE; and 193 ± 64 mL by 3D TTE with the default border set to HM 80–40 (Table 2). Despite a systematic underestimation of EDV using 3D TTE compared with CMR (bias = −22 ± 34 mL, median absolute percentage error = 8%), a significant correlation was found between the two measurements (r = 0.93; P < 0.0001) (Fig. 1A; Table 3). When considering the patients with LVEF ≤ 50% and larger volumes, this underestimation tended to increase (bias = −49 ± 41 mL, median absolute percentage error = 14%) with a significant but weaker correlation (r = 0.87, P < 0.0001) (Table 4).

ESV obtained by the different methods was: 104 ± 74 mL by CMR; 72 ± 54 mL by 2D TTE; and 92 ± 50 mL by 3D TTE with HM 80–40 (Table 2). Despite a significant underestimation of ESV using 3D TTE compared with CMR (bias = −13 ± 33 mL, median absolute percentage error = 14%), a significant correlation was found between the two measurements (r = 0.93; P < 0.0001) (Fig. 1B; Table 3). When considering the patients with LVEF ≤ 50%, this underestimation tended to increase (bias = −43 ± 45 mL, median absolute percentage error = 19%) (Table 4).

LVEF obtained by the different methods was: 55 ± 16% by CMR; 55 ± 15% by 2D TTE; and 54 ± 13% by 3D TTE with HM 80–40 (Table 2). A significant correlation was found between 3D TTE with HM 80–40 and CMR (r = 0.91; P < 0.0001), with a good agreement (bias = −0.7 ± 7.0%, median absolute percentage error = 7%) (Fig. 1C; Table 3). When considering the patients with LVEF ≤ 50%, LVEF tended to be overestimated by 3D TTE with HM 80–40 compared with CMR (37% ± 8% vs 33% ± 11%; bias = +3.2 ± 5.8%, median absolute percentage error = 6%) (Table 4).

**Reproducibility of 3D TTE measurements**

Using standard HM 80–40 settings, intraobserver variability for EDV, ESV and LVEF was excellent: r = 0.99, COV = 8% for EDV; r = 0.98, COV = 9% for ESV; r = 0.96, COV = 8% for LVEF (all P < 0.0001) (Fig. 2). Interobserver variability was: r = 0.93, COV = 3% for EDV; r = 0.97, COV = 6% for ESV; and r = 0.90, COV = 5% for LVEF (all P < 0.0001). Test-retest variability was: r = 0.96, COV = 6% for EDV; r = 0.96, COV = 10% for ESV; and r = 0.91, COV = 6% for LVEF (all P < 0.0001).

**Accuracy of the different default border settings**

Using larger default settings (HM 90–50) for the automated border detection, both EDV and ESV were larger compared with ‘standard’ HM 80–40 settings (bias = 17 ± 17 mL and 8 ± 19 mL, respectively) (Supplementary Fig. 2).

Using larger default settings (HM 90–50) resulted in better EDV and ESV agreement with CMR (bias = −5 ± 32 mL and −11 ± 29 mL, respectively) (Table 3, Supplementary Fig. 3), particularly in larger volumes (Table 4). Nevertheless, EDV with HM 90–50 was overestimated by more than 10 mL compared with CMR in 17 patients (31.5%), as represented by a larger negative tail on the mountain plot (Fig. 3). Larger default settings (HM 90–50) also overestimated LVEF...
significantly compared with CMR, in patients with LVEF ≤ 50% (bias = 3.7 ± 7.9%, median absolute percentage error = 24%) (Table 4, Fig. 4).

Narrowing down default settings (HM 70–30) for the automated border detection, both EDV and ESV were underestimated compared with both “standard” HM 80–40 settings (bias = −5 ± 13 mL and −8 ± 19 mL, respectively) (Supplementary Fig. 1) and CMR (bias = −27 ± 31 mL and −14 ± 30 mL, respectively) (Table 3). The HM 70–30 setting underestimated EDV by more than 20% compared with CMR in 13 patients (24%). Using HM 70–30, LVEF was significantly overestimated compared with CMR in patients with LVEF ≤ 50% (41 ± 9% vs 33 ± 11%; P = 0.002; bias 7.1 ± 8.1%, median absolute percentage error = 26%) (Table 4, Fig. 4).

Discussion

Our results, based on a prospective analysis of a cohort of consecutive patients, show that 3D TTE using new-generation fully automated software is a feasible, fast, reproducible and accurate imaging modality for LV volumetric quantification in routine practice, compared with CMR. Optimization of border detection settings may increase agreement with CMR for EDV assessment in dilated ventricles.

We found a feasibility of only 86% for 3D TTE, similar to previous studies [7, 8] and to other imaging techniques, such as speckle-tracking echocardiography [9]. Such studies in real-life echocardiographic practice, particularly in routine in-hospital practice, often involve suboptimal acoustic...
windows and/or imaging [9]. Moreover, echocardiographers are often reluctant to adopt 3D TTE in routine clinical practice because of time-consuming multiple subvolume acquisitions requiring breath holds. Recently, single-beat full-volume capture was reported to be superior [7,10] to previous multiple-beat captures. Indeed, using single-beat acquisition avoids the stitching artefacts commonly seen in case of arrhythmias or inadequate breath holds [7,10]. A previous study [4] reported that four-beat full-volume acquisition mode required a larger sector in patients with dilated ventricles, leading to reduced 3D volume rate and increased variability. In our study, a novel single-beat acquisition mode allowed fast acquisition of sufficient temporal resolution in all patients, including those with dilated cardiomyopathy.

We found excellent reproducibility of 3D TTE using HeartModelA.I., with low interobserver and intraobserver variability, with a coefficient of variation <10% for all variables, which is consistent with previous data [4,5,10]. This new automated application uses knowledge-based identification of LV chambers followed by patient-specific adaptation [4]. This reliable automated detection of heart chambers does not need the user’s input, which improves the consistency of measurements, and reduces the time required for analysis [4]. Our results confirm the robustness of this new automated software, especially when used without contour correction, with an interobserver variability of zero in the study by Tsang et al. [4]. However, in routine settings, subtle manual regional contour adjustment is necessary in a number of patients, particularly when endocardial visualization is suboptimal or in ischaemic cardiomyopathy with apical scar. Another vendor’s automated algorithm produced similar results, as less than half were analysed successfully without minimal additional manipulation [7]. Reliability of LV volume measurements compared with CMR was also demonstrated, as in numerous previous studies with both multiple and single-beat full-volume capture [11–14]. A recent meta-analysis [11] confirmed that 3D TTE, in experienced hands, systematically underestimates volumes compared with CMR, but is more accurate and more reproducible than 2D TTE. Recently, Mor-Avi et al. [15] nicely ruled out potential sources of error inherent to the technique, such as calibration errors or differences between analysis techniques used for CMR and 3D TTE. The authors also showed that the major source of error is the spatial resolution of 3D TTE being insufficient to provide clear definition of endocardial trabeculae, which are, as a result, lumped together with the myocardium rather than being included in the LV cavity, as during analysis of CMR images [15]. This source of error could be minimized by learning how to identify true endocardial limits and manually enlarging volume border beyond the blood-trabeculae interface. The software used in our study may overcome

Figure 1. Linear regression (left) and Bland-Altman (right) diagrams of comparison between three-dimensional transthoracic echocardiography using the HeartModelA.I. (HM) with 80–40 border settings and cardiac magnetic resonance (CMR) for the assessment of: (A) left ventricular end-diastolic volume (EDV); (B) left ventricular end-systolic volume (ESV); and (C) left ventricular ejection fraction (EF). SD: standard deviation.
such drawbacks, as it offers the possibility to define larger default border detection settings, within the myocardium. We have shown that, despite a slight underestimation of EDV, automated border detection set to HM 80–40 correlates best with CMR in the total population. Nevertheless, the volume underestimation is known to be higher in severely dilated ventricles with reduced LVEF, in which the distinction between the trabecular endocardium and the compacted myocardium is exaggerated [8, 15]. In our study, enlarging border detection settings to HM 90–50 in patients with LVEF ≤ 50%, improved agreement with CMR. This is concordant with previous data from Thavendiranathan et al. [8], who proposed automatically adding a fixed volume value to the tracked border to reduce underestimation of 3D TTE.

<table>
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<th>Table 3</th>
<th>Correlation coefficients and difference between cardiac magnetic resonance and transthoracic echocardiography in the study patients (n = 54).</th>
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2D: two-dimensional; 3D: three-dimensional; CI: confidence interval; CMR: cardiovascular magnetic resonance; EDV: end-diastolic volume; ESV: end-systolic volume; HM 90–50: 3D default border detection set to 90–50; HM 80–40: 3D default border detection set to 80–40; HM 70–30: 3D default border detection set to 70–30; ICC: intraclass correlation coefficient; LVEF: left ventricular ejection fraction; TTE: transthoracic echocardiography.

<sup>a</sup> Data are expressed as mean ± standard deviation.

<table>
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<th>Table 4</th>
<th>Correlation coefficients and difference between cardiac magnetic resonance and transthoracic echocardiography in patients with left ventricular ejection fraction ≤ 50% with cardiac magnetic resonance (n = 16).</th>
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2D: two-dimensional; 3D: three-dimensional; CI: confidence interval; CMR: cardiovascular magnetic resonance; EDV: end-diastolic volume; ESV: end-systolic volume; HM 90–50: 3D default border detection set to 90–50; HM 80–40: 3D default border detection set to 80–40; HM 70–30: 3D default border detection set to 70–30; ICC: intraclass correlation coefficient; LVEF: left ventricular ejection fraction; TTE: transthoracic echocardiography.

<sup>a</sup> Data are expressed as mean ± standard deviation.
These authors reported that a higher correction value is required for patients with LVEF < 50% versus normal LVEF. Indeed, more accurate assessment of LV volumes seems to require larger 3D border settings in patients with a dilated LV and altered LVEF.

Ideally, longitudinal follow-up of patients, especially in heart failure or valvular disease, involves multiple imaging modalities. Nevertheless, in clinical practice, CMR suffers from several limitations [2], such as restricted availability, local expertise or the presence of cardiac pacemakers and implantable cardioverter-defibrillators, which remain an absolute contraindication for 3 Tesla CMR, as magnetic resonance-conditional devices are limited to 1.5 Tesla scanners. More accurate and reproducible LVEF determination is mandatory, as recent heart failure European society of cardiology guidelines [2] defined a new category of heart failure, with a mid-range LVEF ranging from 40% to 49%. A more reproducible assessment of LVEF is also important for patients with heart failure undergoing serial examinations to determine improvement or worsening under treatment [11]. The benefit of 3D TTE in the assessment of LVEF has been demonstrated in several research studies [11]. This new-generation time-saving software may facilitate integration of 3D TTE assessment of LVEF into real-life everyday practice. Adequate configuration of the software is, however, mandatory, as we have shown that narrowing border detection settings may induce a significant overestimation of LVEF.

Figure 2. Interobserver, intraobserver and test-retest variability for: (A) left ventricular end-diastolic volume (EDV); (B) left ventricular end-systolic volume (ESV); and (C) left ventricular ejection fraction (EF), using linear regressions. HM: HeartModelA.I.

Figure 3. Mountain plot analyses between different default settings of the automated border detection of the HeartModelA.I. (HM 90–50, HM 80–40 and HM 70–30) for the measurement of left ventricular end-diastolic volume (EDV) compared with cardiac magnetic resonance (CMR). A. For HM 80–40 and HM 90–50 settings. B. For HM 80–40 and HM 70–30 settings. C. For HM 80–40 and HM 90–50 settings in the 16 patients with LVEF ≤ 50%. For HM 80–40, HM 90–50 and HM 70–30 settings, median values were 16, –1 and 21, respectively. For HM 90–50, the mountain was almost centered over zero (unbiased) with, however, a larger negative tail, caused by the frequent overestimation of EDV over CMR in the total population. In the 16 patients with LVEF ≤ 50%, the mountain was centered over zero without major overestimation.
Study limitations

Our results have some limitations as they are derived from a single-centre experience. We did not use ultrasound contrast agent in any patient in this study, which could have improved the feasibility of 3D TTE. Nevertheless, our study provides insight into real-life echocardiographic practice, and performance of the 3D software with echocardiographic contrast agents is unknown [4]. Another limitation is cardiac arrhythmia. Nevertheless, recent data suggest that 3D TTE remains reliable in atrial fibrillation, provided that average values of LV volumes are measured during multiple consecutive beats [10]. As this study was set in routine practice, we did not record the time required for all 3D analyses in all patients. Previous studies have specifically shown a reduction in the duration of examination using this software [4].

Conclusions

3D TTE using new-generation, fully automated software is a feasible, fast, reproducible and accurate imaging modality for LV volumetric quantification in routine practice. Adequate configuration of the software is mandatory, as enlarging border detection settings may improve agreement with CMR in dilated ventricles, but may lead to volume overestimation in the general population.

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Disclosure of interest

The authors declare that they have no competing interest.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.acvd.2016.12.015.

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