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Diagnostic accuracy of transthoracic three-dimensional left ventricular function analysis compared with cardiac magnetic resonance imaging: a bivariate meta-analysis

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Summary

Studies evaluating the diagnostic concordance of three-dimensional echocardiography (3DE) and cardiac magnetic resonance imaging (CMR) for quantification of left ventricular ejection fraction (LVEF) have yielded inconsistent findings.

We searched PubMed, Embase and Cochrane Library databases for prospective studies that compared the diagnostic accuracy of 3DE for quantification of systolic left ventricular function in adults with that of CMR (the gold standard method). We constructed 2 × 2 tables at the study-level based on an LVEF threshold of 55%. We performed a bivariate random-effects meta-analysis to calculate summary estimates of diagnostic accuracy.

Twelve studies involving 581 patients were included. 3DE showed overall sensitivity and specificity of 76% (95% confidence interval [CI] 59–88%) and 91% (95% CI 84–95%), respectively. The diagnostic accuracy of 3DE was high with an area under the hierarchical summary receiver-operating characteristic curve (HSROC) of 0.92 (95% CI 0.90–0.94) for appropriate quantification of LVEF. The diagnostic performance was high irrespective of the applied method (semi-automated or automated algorithm) of 3D left ventricular quantification. Between-study heterogeneity was high (p <0.001 for Q statistic).

The high diagnostic accuracy of 3DE as compared with CMR allows safe use of the method, especially for follow-up of patients requiring serial quantification of left ventricular function.

Keywords: *transthoracic three-dimensional left ventricular function, cardiac magnetic resonance imaging, bivariate meta-analysis, left ventricular ejection fraction*

Author contributions
Raffaele Piccolo is the guarantor of the entire manuscript. Raffaele Piccolo analysed the data. All authors contributed to the study conception and design; data acquisition; interpretation of the findings; critical revision of the manuscript for important intellectual content; and final approval of the version to be published.

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Introduction

Owing to the high image quality, accuracy and ability to make three-dimensional measurements, cardiac magnetic resonance imaging (CMR) has become the gold standard method to assess left ventricular ejection fraction (LVEF) and left ventricular volumes [1–3]. However, three-dimensional echocardiography (3DE) has been increasingly recognised as an alternative method to estimate LVEF with increased diagnostic accuracy compared with two-dimensional assessment. So far, a relatively small number of studies have compared the diagnostic concordance of the two diagnostic methods (3DE and CMR) for quantification of systolic left ventricular function, with inconsistent findings in more recent studies. Against this background, we aimed to summarise the available evidence on the diagnostic accuracy of transthoracic 3DE for quantification of LVEF compared with CMR, through a bivariate meta-analysis.

Methods

We developed the protocol according to PRISMA-P [4] and registered it at PROSPERO (CRD42018094137). The manuscript was prepared according to PRISMA diagnostic test accuracy (PRISMA-DTA) guidelines [5]. We conducted a broad computerised literature search of the PubMed, Embase and Cochrane Library databases up to March 2018 to identify studies of prospective design that evaluated systolic left ventricular function in terms of LVEF in adults with 3DE (manual, semi-automated or automated algorithm) in comparison with CMR as the gold standard method. We used the following keywords: three-dimensional echocardiography, cardiac magnetic resonance, left ventricular ejection fraction, left ventricular systolic function. We then constructed 2 × 2 tables at the study level, based on an LVEF threshold of 55%, which contained the number of individuals with LVEF ≥55% based on both methods (true positives), with LVEF <55% based on both methods (true negatives), with LVEF≥55% based only on 3DE (false positives) and with LVEF <55% based only on 3DE (false negatives). Data were extracted at the individual patient level through plot digitisation (Engauge Digitizer 10.4, Mark Mitchell, Torrance, CA) showing the LVEF

according to the two methods. We used data acquired with a semi- or fully automated algorithm rather than manual 3DE.

We performed a bivariate random-effects meta-analysis by using a linear mixed model to calculate summary estimates of diagnostic accuracy [6–8]. The bivariate model is for meta-analysing diagnostic studies reporting pairs of sensitivity and specificity [6]. Although traditional diagnostic meta-analysis unifies sensitivity and specificity into one measure (the summary receiver operating characteristic), bivariate meta-analysis maintains their distinct characteristics and takes into account their potentially negative correlation. Preserving the bivariate structure of the data, pairs of sensitivity and specificity are jointly analysed. We calculated summary estimates of sensitivity, specificity, positive likelihood ratio and negative likelihood ratio, and fit a hierarchical summary receiver operating characteristic (HSROC) curve with 95% region of confidence [9]. All analyses were performed in Stata version 15.0.

Results

A total of 12 studies were deemed eligible and information on LVEF based on both diagnostic methods were extracted in individual-level for 581 patients (table 1). LVEF was measured with semi-automated 3DE (6 studies, 277 individuals) [10, 11, 13, 15, 18, 20] or fully automated 3DE (6 studies, 304 individuals) [12, 14, 16, 17, 19, 21]. As shown in the figure 1A, diagnostic agreement for LVEF quantification was high between 3DE and CMR (R = 0.88 and R = 0.86 for semi-automated and automated 3DE, respectively). The bivariate box plot in figure 1B describes the degree of interdependence, identifies four outliers at the study level, and demonstrates a skewedness of the 3DE performance measures toward a higher specificity with lower sensitivity. For LVEF quantification based on 3DE, the overall sensitivity and specificity from a bivariate random-effects model were 76% (95% confidence interval [CI] 59–88%) and 91% (95% CI 84–95%), respectively; the diagnostic odds ratio was also high: 32 (95% CI 14–70). The corresponding synthesis of negative likelihood ratio was estimated at 0.26 (95% C, 0.15–0.47), which translates into a fourfold increased chance of correct LVEF quantification based on 3DE in the presence of normal LVEF. Between-study heterogeneity was high (p <0.001 for Q statistic). Also, 3DE showed highly accurate diagnostic performance with an area under the HSROC curve of 0.92 (95% CI 0.90–0.94) (fig. 1C). A stratified analysis according to the LVEF 3DE quantification method yielded similar diagnostic operating characteristics compared with the main analysis for both methods. Finally, the area under the HSROC did not differ after excluding the four outliers studies, which resulted in an area under the HSROC curve of 0.92 (95% CI 0.89–0.94).

We found a cut-off value of 49% with 3DE to estimate a normal LVEF based on CMR. A Bland-Altman plot of agreement was finally designed to compare 3DE LVEF with LVEF from CMR (fig. 2).

Discussion

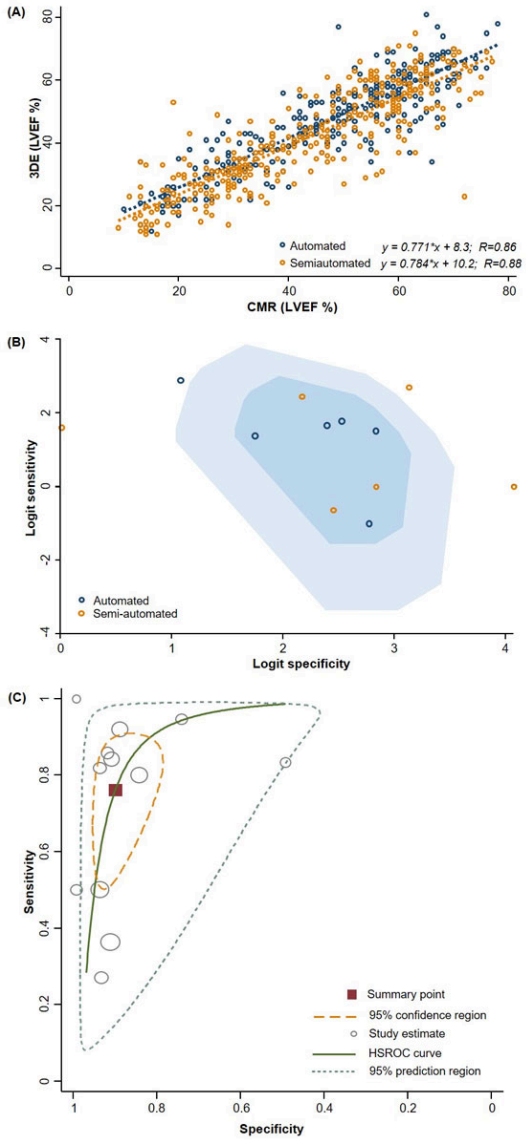
To our knowledge, this is the first bivariate meta-analysis comparing the diagnostic accuracy of 3DE and CMR in the quantification of left ventricular function solely by including patient-level information. Our findings suggest that transthoracic 3DE for LVEF quantification shows high agreement and diagnostic accuracy compared with CMR, with an area under the HSROC curve exceeding 0.90, irrespective of the algorithm applied (semi- or fully automated). Furthermore, on visual inspection of the correlation plot, we noted a greater agreement between the two diagnostic techniques. This is more pronounced in patients with lower LVEF than those with a higher LVEF. Although this may suggest a lower accuracy with 3DE in the high range of LVEF, this is expected to not have a relevant impact from a clinical standpoint. The latest publications comparing LVEF assessment by 3DE versus CMR often did not show a high diagnostic concordance towards these two modalities, the problem being that 3DE was often seen as underestimating left ventricular volume. Against this background, our meta-analysis showed high diagnostic accuracy of 3DE as compared with CMR.

This study has several limitations. First, we focused on the accuracy between 3DE and CMR in terms of LVEF. Hence the role of other promising indexes, such as the global longitudinal strain, remains to be addressed. Second, we did not formally assess the quality of the studies. Third, we noted high heterogeneity across studies and this could be a result of several factors: the 3D LVEF measurement uses different algorithms depending on the echo machines; semi-automated and automated modes were used to measure LVEF; and the study population was quite heterogeneous, ranging from healthy to severely ill patients from

Table 1: Characteristics of included studies.

Year	First author [ref.]	Number of patients	Male, n (%)	3D echo algorithm	3D echo device
2004	Kühl P, et al. [10]	24	n/a	Semiautomated	Sonos 7500, Philips
2008	Pouleur AC, et al. [11]	83	67 (80.7%)	Semiautomated	IE33 Philips
2008	Mor-Avi V, et al.	92	69 (75%)	Semiautomated	IE33 Philips
2012	Thavendiranathan P, et al. [12]	91	19 (20.8%); 23 (25.2%); 17 (18.6%)	Automated	Acuson SC2000, Siemens
2012	Moceri P, et al. [13]	24	17 (70.8%)	Semiautomated	IE33 Philips
2012	Shibayama K, et al. [14]	41	30 (73.1%)	Automated	Acuson SC2000, Siemens
2014	Aurich M, et al.	47	21 (44.6%)	Automated	Vivid E9 BT 11, GE
2014	Driessen M, et al. [15]	35	19 (54%)	Semiautomated	IE33 Philips; Artida-4D, Toshiba
2016	Tsang W, et al. [16]	159	44 (27.6%); 31 (19.4%)	Automated	EPIQ and IE33, Philips
2016	Levy F, et al. [17]	54	40 (74%)	Automated	EPIQ 7C, Philips
2017	Tamborini G, et al. [18]	189	130 (68.7%)	Semiautomated	EPIQ and IE33, Philips
2018	Muraru D, et al. [19]	92	63 (68.5%)	Automated	Acuson SC2000, Siemens; IE33 Philips; Vivid E9 BT 11, GE

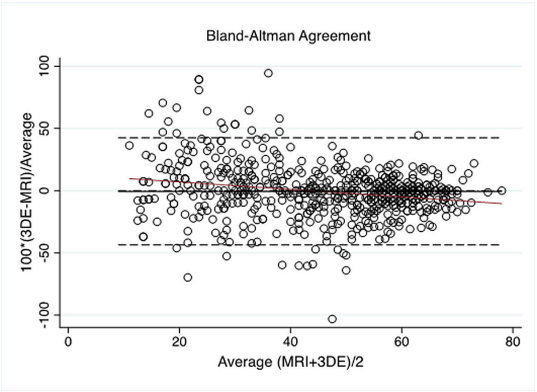
Figure 1: A. Correlation plot comparing LVEF quantification with semi-automated 3DE algorithms (six studies [9–11, 13, 15, 20] of 304 individuals) and fully-automated algorithms (six studies [12, 14, 16–18, 21] of 277 individuals) compared with CMR. **B.** Bivariate box plot with most studies clustering within the median distribution. The inner oval region represents the median distribution of the data points and the outer oval represents the 95% confidence bound. Overall, 4 observations outside the region of 95% confidence bound are flagged as outliers [9, 13, 17, 20]. **C.** Hierarchical summary receiver-operating characteristic (HSROC) curve for the diagnostic performance of 3DE to quantify LVEF, among all studies, compared with CMR as the gold standard method. The size of the circles indicates the weight of the individual studies in the meta-analysis. The summary sensitivity and specificity is shown with a red square and the respective 95% confidence region is plotted. For all studies, the area under the HSROC curve was 0.92 (95% CI 0.90–0.94).



the cardiac point of view. Locally available expertise and the patient's relevant contraindications for each test should be considered when deciding on the appropriate imaging modality. Lower cost, and broader availability of 3DE allow safe use of the method as an alternative to CMR, especially for follow-up of patients required serial quantification of left vemtricular function.

Data sharing: All data are available upon request.

Figure 2: Bland-Altman plot comparing LVEF (%) from 3DE with LVEF (%) from CMR.



Disclosure statement

No financial support and no potential conflict of interest relevant to this article was reported.

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