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Jenkins, S., Alabed, S. orcid.org/0000-0002-9960-7587, Swift, A. et al. (10 more authors) (2021) Diagnostic accuracy of handheld cardiac ultrasound device for assessment of left ventricular structure and function: systematic review and meta-analysis. *Heart*, 107 (22). pp. 1826-1834. ISSN 1355-6037

<https://doi.org/10.1136/heartjnl-2021-319561>

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Original research

Diagnostic accuracy of handheld cardiac ultrasound device for assessment of left ventricular structure and function: systematic review and meta-analysis

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► Additional supplemental material is published online only. To view, please visit the journal online (<http://dx.doi.org/10.1136/heartjnl-2021-319561>).

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Received 20 April 2021
Accepted 12 July 2021



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To cite: Jenkins S, Alabed S, Swift A, *et al.* Heart Epub ahead of print: [please include Day Month Year]. doi:10.1136/heartjnl-2021-319561

ABSTRACT

Objective Handheld ultrasound devices (HUD) has diagnostic value in the assessment of patients with suspected left ventricular (LV) dysfunction. This meta-analysis evaluates the diagnostic ability of HUD compared with transthoracic echocardiography (TTE) and assesses the importance of operator experience.

Methods MEDLINE and EMBASE databases were searched in October 2020. Diagnostic studies using HUD and TTE imaging to determine LV dysfunction were included. Pooled sensitivities and specificities, and summary receiver operating characteristic curves were used to determine the diagnostic ability of HUD and evaluate the impact of operator experience on test accuracy.

Results Thirty-three studies with 6062 participants were included in the meta-analysis. Experienced operators could predict reduced LV ejection fraction (LVEF), wall motion abnormality (WMA), LV dilatation and LV hypertrophy with pooled sensitivities of 88%, 85%, 89% and 85%, respectively, and pooled specificities of 96%, 95%, 98% and 91%, respectively. Non-experienced operators are able to detect cardiac abnormalities with reasonable sensitivity and specificity. There was a significant difference in the diagnostic accuracy between experienced and inexperienced users in LV dilatation, LVEF (moderate/severe) and WMA. The diagnostic OR for LVEF (moderate/severe), LV dilatation and WMA in an experienced hand was 276 (95% CI 58 to 1320), 225 (95% CI 87 to 578) and 90 (95% CI 31 to 265), respectively, compared with 41 (95% CI 18 to 94), 45 (95% CI 16 to 123) and 28 (95% CI 20 to 41), respectively, for inexperienced users.

Conclusion This meta-analysis is the first to establish HUD as a powerful modality for predicting LV size and function. Experienced operators are able to accurately diagnose cardiac disease using HUD. A cautious, supervised approach should be implemented when imaging is performed by inexperienced users. This study provides a strong rationale for considering HUD as an auxiliary tool to physical examination in secondary care, to aid clinical decision making when considering referral for TTE.

Trial registration number CRD42020182429.

INTRODUCTION

Echocardiography is the first-line imaging modality for assessing cardiac size and function. Indications

for transthoracic echocardiography (TTE) as recommended by the British Society of Echocardiography and other international societies include but not limited to: murmur in the presence of cardiac or respiratory symptoms, valvular stenosis or regurgitation, ischaemic heart disease, any suspicion of heart failure (HF) and arrhythmias.^{1–3} TTE allows determination of left ventricular (LV) dysfunction by assessing LV cavity size, wall thickness, valvular appearances and function as well as for the presence of abnormal blood flow within the heart.⁴

The miniaturisation of ultrasound technology has led to the introduction of handheld cardiac ultrasound devices (HUD).⁵ The portability and accessibility of HUD allow for the augmentation of the bedside physical examination. While physical examination remains the primary method for screening cardiovascular disease, the quality and subsequent referral to echocardiography depend on the examiner's experience and skill, or lack thereof.⁶ HUD therefore can bridge the gap between the physical examination and the more costly and time-consuming departmental TTE.

Several recent studies have assessed the performance of HUD in diagnosing cardiac disease. The aim of this systematic review and meta-analysis is to assess the diagnostic accuracy of HUD to detect LV abnormalities when compared with TTE in both experienced and non-experienced users.

METHODS

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines and the Cochrane Handbook of Diagnostic Test Accuracy were followed in the study selection, review process and evidence synthesis.^{7 8}

Patient and public involvement

Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

Eligibility criteria

Any study comparing the diagnostic performance of HUD and TTE was eligible. The index test was any type or size of a HUD performed by operators of any level of experience. The reference standard was

TTE performed by experienced imagers. Studies were included if subjects were aged >18 years, sensitivity, specificity, true positive and negative and false positive and negative findings were reported or if diagnostic data could be extrapolated from the results. Studies with a sample size of <20 participants were excluded.

Search strategy and study selection

MEDLINE (ProQuest, 1946 to 13 October 2020), EMBASE (Ovid, 1974–2020 week 42) were searched on 13 October 2020. No search filters were applied. The full search strategy is available in the online supplemental document. The references of the included studies were also screened for relevant studies.

Two authors (SJ and PG) screened the titles and abstracts and reviewed full texts for inclusion criteria. Any disagreements were discussed with a third author (SA). Data extraction and risk of bias analysis was performed by two authors (SJ and PG) and disagreements discussed with a third author (SA). Methods for the quality assessment of individual studies are detailed in online supplemental figure 1.

Statistical analysis

A bivariate random-effects model was used to obtain the summary point for the sensitivity and specificity and estimate the corresponding 95% CI and prediction regions for all meta-analyses including four or more studies. The *metandi* command in Stata V.16 (StataCorp, College Station, Texas, USA) was used to perform the analyses and create summary receiver operating characteristics (SROC). The mada package in R was used to calculate the diagnostic ORs (DORs) for each study and the summary DOR for the pooled results with their respective 95% CIs (R Core Team, R: A Language and Environment for Statistical Computing, Vienna, Austria; R Foundation for Statistical Computing, 2020). The Wilson method was used to calculate the CIs for sensitivities, specificities and false positive rates. The Yates correction was used for testing the equality of sensitivities and specificities. The input for the mada command was the number of true positives (TP), false negatives (FN), true negatives (TN) and false positives (FP) for each study.

The effect of operator experience on the effect size of the diagnostic accuracy was assessed in a subgroup analysis and graphically represented in SROC curves comparing the diagnostic accuracy of experienced and inexperienced operators. A meta-regression was also performed to assess the effect of operator experience.

RESULTS

Search results

Our comprehensive search identified 33 studies which were incorporated into the meta-analysis. The results of the literature search are outlined in the study flow diagram (figure 1).

Description of included studies

All studies had a prospective design, with consecutive or random patient selection reported in 21 studies. The studies were published between 2002 and 2019. The majority of studies (22 studies) had a large sample size ≥ 100 participants, with the largest study by Galasko *et al*⁸ recruiting 562 patients.⁹ Individual study data incorporated into the meta-analysis can be found in online supplemental table 1 and a summary graph of the overall risk of bias is shown in online supplemental figure 1.

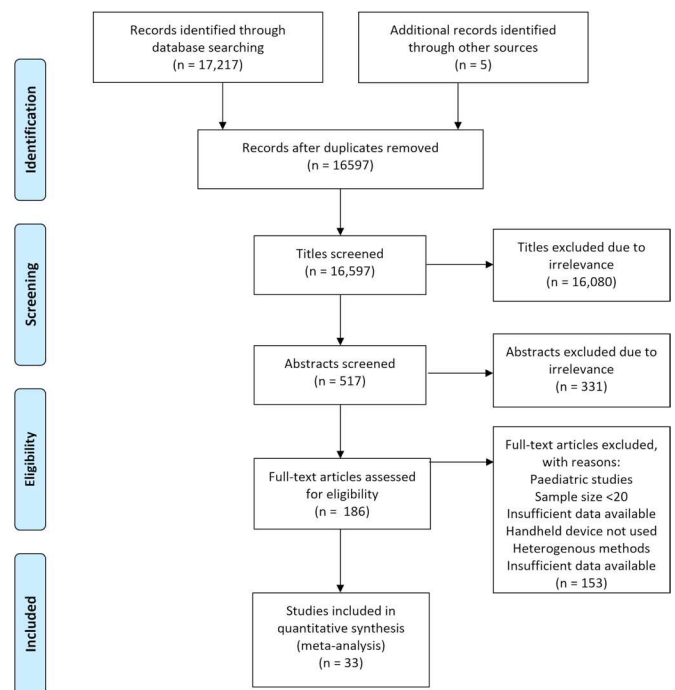


Figure 1 The Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow chart of literature search.

Study characteristics

A total of 6062 patients conducted in 13 different countries were included in the meta-analysis. The mean age of patients was 65 ± 5 years with a slight male predominance (54%). Study characteristics are presented in table 1. Study-level HUD data including sensitivity and specificity to predict reduced LV ejection fraction (LVEF), wall motion abnormality (WMA), LV dilatation and hypertrophy (LVH) are reported in the online supplemental materials.

Assessment of methodological quality

The majority of studies (19/25) reported a prospective and consecutive or random design. Only one study reported that HUD assessors were unblinded to TTE results while three studies were judged to incorporate a high risk of bias with TTE assessors unblinded to HUD results. There was some concern for bias when time between HUD and TTE was >48 hours. One study was judged to have a high risk of bias as time between HUD and TTE was >7 days.¹⁰ The detailed results of the quality assessment are outlined in online supplemental figure 2.

Meta-analysis of HUD indices

Each characteristic was separated into subgroups based on the investigator's level of experience. Inexperienced operators were those that learnt HUD as part of the study with limited or no prior echocardiography experience. This subgroup included nurses, medical students, residents, general practitioners and inexperienced cardiology trainees. Experienced operators were those who had undergone level II/III echocardiography training or who were stated to be experienced, expert, or trained in echocardiography.

Experienced operators could determine reduced LVEF, LV dilatation, WMA and LVH with pooled sensitivities of 88%, 89%, 85% and 85%, respectively (figures 2–4). In inexperienced hands, pooled sensitivities measured were 83%, 68%, 78% and 80%, respectively. Pooled specificities of HUD by experienced

Table 1 Characteristics of included studies

Study	Country	Design	Study period	Size	Male (%)	Age, years	Level of experience	HUD
Aldaas <i>et al</i> ²¹	USA	Consecutive	NR	70	50	61±18	Both	Vscan
Alexander <i>et al</i> ²²	USA	NR	April–November 2000	537	53	59	Inexperienced	Optigo
Andersen <i>et al</i> ²³	Norway	Random	March–September 2010	108	64	69.1±14	Experienced	Vscan
Biais <i>et al</i> ²⁴	France	Consecutive	February–May 2011	151	35	55±20	Experienced	Vscan
Bruce <i>et al</i> ⁹	USA	NR	NR	374	62	66	Both	SonoHeart
Coletta <i>et al</i> ²⁵	Italy	Consecutive	April–June 2003	112	57	61±11	Experienced	Optigo
Cullen <i>et al</i> ²⁶	USA	Consecutive	2012–2013	190	49	62±17	Experienced	Vscan
DeCara <i>et al</i> ²⁷	USA	NR	NR	300	NR	NR	Experienced	Optigo
Fedson <i>et al</i> ²⁸	USA	Consecutive	NR	103	NR	NR	Inexperienced	Optigo
Galasko ⁸	UK	Consecutive	2000–2001	562	56	62±11	Experienced	Optigo
Ghani <i>et al</i> ²⁹	USA	Consecutive	NR	80	51	75±13	Inexperienced	Optigo
Giusca <i>et al</i> ³⁰	Romania	Consecutive	NR	56	54	60±12	Inexperienced	Acuson P10
Gulič <i>et al</i> ³¹	Slovenia	Consecutive	NR	200	43	70	Both	Vscan
Khan ³²	USA	Consecutive	2012–2013	240	53	71±17	Experienced	Vscan
Kirkpatrick ³³	USA	NR	NR	63	46	65±16	Inexperienced	Optigo
Kobal <i>et al</i> ³⁴	USA	Consecutive	NR	61	62	70±19	Inexperienced	Optigo
Liebo ³⁵	USA	Consecutive	February–March 2010	97	45	68±17	Both	Vscan
López-Palmero <i>et al</i> ³⁶	Spain	NR	July–December 2013	223	42	76	Inexperienced	Vscan
Lucas <i>et al</i> ³⁷	USA	Consecutive	March–May 2007	322	53	56±13	Inexperienced	Micromaxx
Lucas <i>et al</i> ³⁸	USA	Consecutive	2008–2009	210	55	55	Inexperienced	NR
Martin <i>et al</i> ³⁹	USA	Consecutive	2004–2005	354	47	63±19	Inexperienced	Sonosite Elite
Mehta <i>et al</i> ⁴⁰	USA	NR	NR	250	66	61±15	Experienced	Vscan
Mjølstad <i>et al</i> ⁴¹	Norway	Consecutive	April–June 2011	199	54	66±18	Inexperienced	Vscan
Nilsson <i>et al</i> ⁴²	Sweden	NR	2016–2017	100	55	70±12	Inexperienced	Vscan
Olesen ⁴³	Denmark	NR	NR	260	49	80	Experienced	Vscan
Perez-Avraham <i>et al</i> ⁴⁴	Israel	Consecutive	July–December 2004	85	37	59±14	Inexperienced	Optigo
Razi <i>et al</i> ⁴⁵	USA	Consecutive	NR	50	58	57±17	Inexperienced	Vscan
Ruddox <i>et al</i> ⁴⁶	Norway	NR	2011–2012	303	61	73	Inexperienced	Vscan
Stokke <i>et al</i> ¹³	Norway	Random	February–May 2012	72	72	65±16	Both	Vscan
Vignon <i>et al</i> ⁴⁷	France	Consecutive	NR	55	69	61±16	Experienced	SonoHeart
Vourvouri <i>et al</i> ⁴⁸	The Netherlands	Consecutive	NR	88	64	59±12	Experienced	SonoHeart or Optigo
Wejner-Mik <i>et al</i> ⁴⁹	Poland	Consecutive	NR	87	67	61±16	Experienced	Lumify
Xie <i>et al</i> ⁵⁰	USA	Consecutive	NR	100	55	59±17	Experienced	SonoHeart

HUD, handheld ultrasound devices; NR, not reported.

users compared with inexperienced users for reduced LVEF, LV dilatation, WMA and LVH measured 96% vs 89%, 98% vs 95%, 95% vs 88% and 91% vs 87%. Online supplemental figure 3 displays a box plot assessing the pooled accuracy of HUD to diagnose moderate/severe LVEF (<45%). SROC curves show an improvement in diagnostic accuracy of reduced LVEF, WMA and LV dilatation when performed by experienced users (figure 5). A summary of the meta-analysis data is provided in table 2.

The highest diagnostic ORs were in assessing LV dilatation (DOR 96, 95% CI 40 to 229). This result indicates that the odds of a positive result in a patient with LV dilatation is approximately 96 times higher than the odds for a positive result in a person with no LV dilatation. There was a significant difference in the diagnostic accuracy between experienced and inexperienced users in LV dilatation, LVEF (moderate/severe) and WMA. The DOR for LVEF (moderate/severe), LV dilatation and WMA in an

experienced hand was 276, 225 and 90, respectively, compared with 41, 45 and 28, respectively, for inexperienced users. The total effect sizes and subgroup differences test comparing the HUD parameters in experienced and inexperienced users are shown in online supplemental table 2. A sensitivity analysis excluding studies that visually assessed LVH and LV dilatation showed that quantitative analysis improves the diagnostic accuracy of HUD. Meta-regression analysis confirmed experience to be a significant factor in the detection of any degree of LVEF dysfunction (p=0.04) and WMA (p=0.01) (online supplemental table 3).

Heterogeneity

Heterogeneity can be visualised in all the forest plots depicting sensitivity and in the LVEF and LVH plot depicting specificity. Despite there being some overlap of CIs, sampling variation

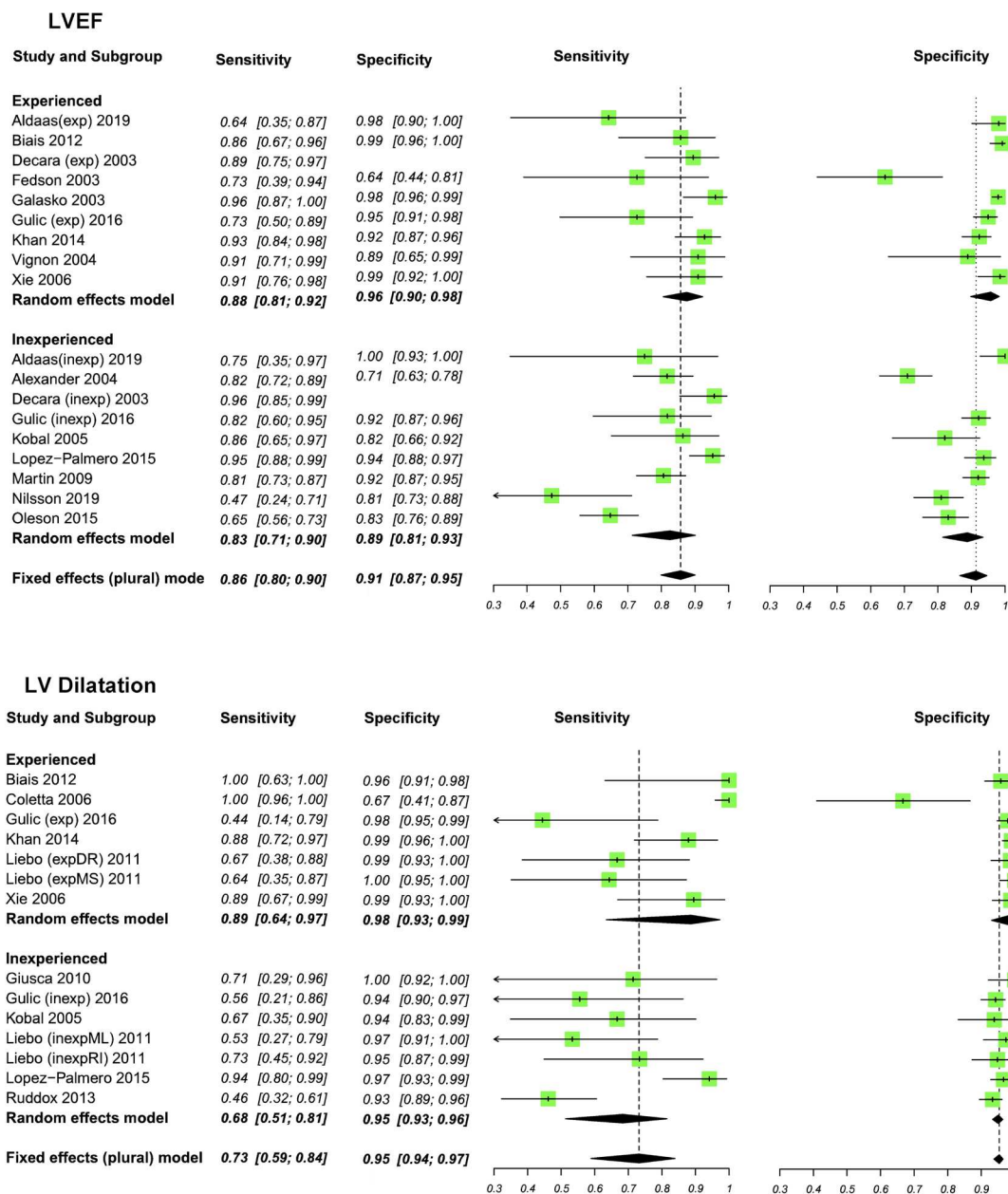


Figure 2 Meta-analyses of left ventricular ejection fraction (LVEF) and left ventricular (LV) dilatation. Sensitivity and specificity (95% CI) values are reported.

does not completely explain the differences between studies. This apparent heterogeneity can also be observed in the SROC curves for LVEF, WMA and LV dilatation. The increased heterogeneity in the sensitivity plots may be partly explained by fewer patients with the target condition than without. This provides less certainty and results in wider CIs.

A negative correlation between sensitivity and specificity was shown in the meta-analysis of LVEF < 45%, WMA and LV dilatation indicating no significant heterogeneity. The correlation coefficients for LVEF (any abnormality) and LVH was positive indicating the presence of possible heterogeneity in the results. We planned to assess the effect of operator experience, pre-existing comorbidities and baseline LV function on the results in a meta-regression covariate analysis. However, only operator experience was sufficiently reported and showed that

experience was a significant factor in detecting LVEF, WMA and LV dilatation.

Variation in thresholds likely accounts for some heterogeneity when measuring LVEF (any abnormality), LV dilatation and LVH. Studies with both qualitative and quantitative methodologies were incorporated into the meta-analysis. Quantitative thresholds of LV dilatation ranged from >53 mm to >59 mm, with some studies classifying LV dilatation subject to gender. Similarly, studies measuring LVH were both qualitative and quantitative, with thresholds ranging from >10 mm to >12 mm. A sensitivity analysis excluding qualitative assessment of LVH and LV dilatation showed an improvement in the diagnostic accuracy (online supplemental table 3).

Other sources of heterogeneity may also exist that cannot be assessed including functionality and technological advancement

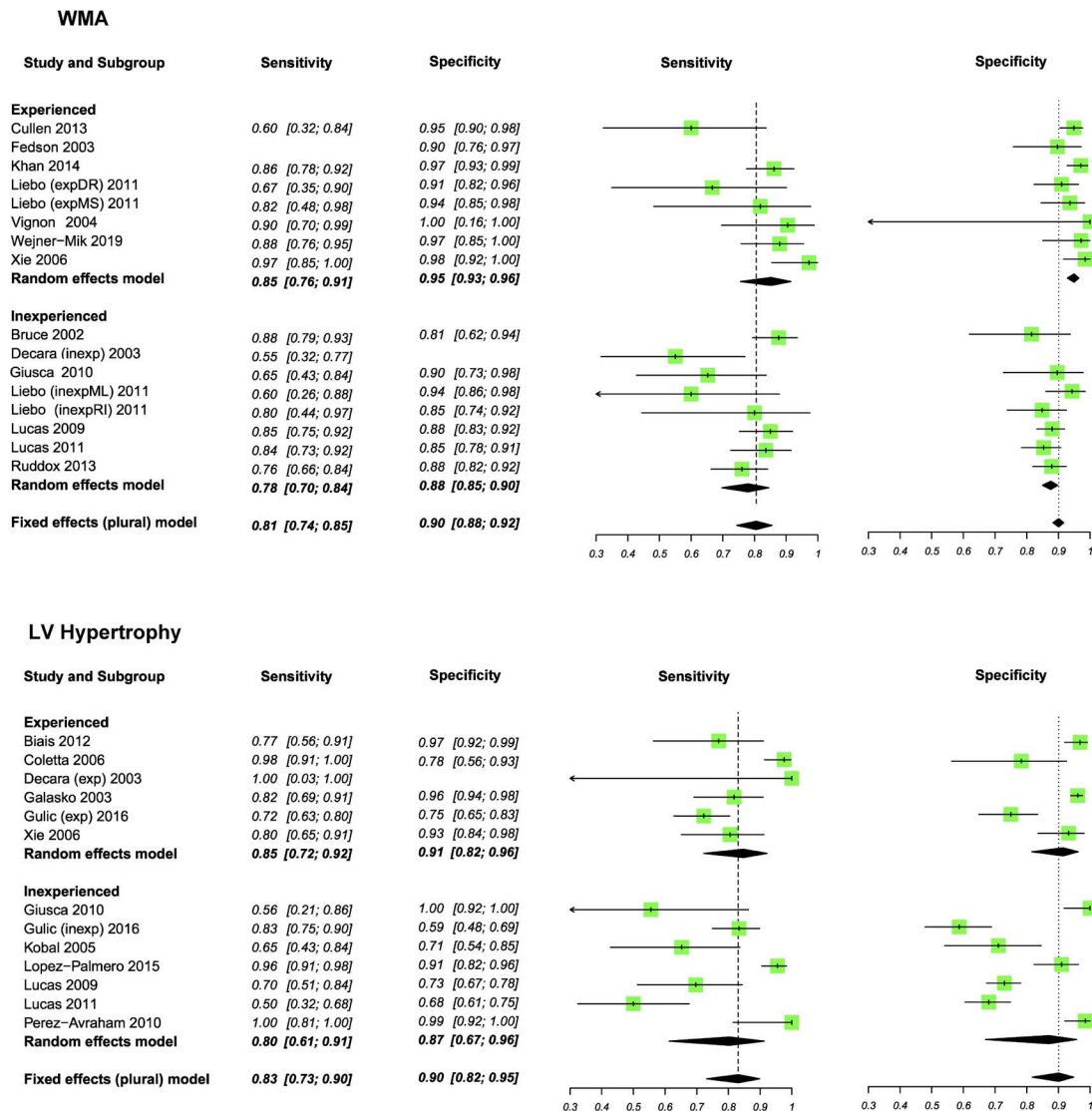


Figure 3 Meta-analyses of wall motion abnormality (WMA) and left ventricular hypertrophy (LVH). Sensitivity and specificity (95% CI) values are reported.

of handheld devices that may allow for more accurate results to be obtained. Some studies reported any abnormality in LVEF as a positive finding without quantifying the results into mild, moderate or severe, which may have led to heterogeneity between studies. However, to limit the effect of the possible heterogeneity we analysed studies reporting LVEF <45% (moderate and severe degrees of LV dysfunction) separately. This analysis allowed for a detailed assessment of HUD in significant disease.

Varying levels of experience using HUD by experienced echocardiographers may account for some heterogeneity. The level and volume of training received by non-experienced users prior to each study was also variable adding to heterogeneity within the non-experienced subgroup.

DISCUSSION

To the best of our knowledge, this is the first meta-analysis of the diagnostic accuracy of HUD for imaging LV cardiac structural and functional abnormalities and the first to report the impact of user experience. The meta-analysis shows that HUD is both a sensitive and specific method for assessing LV function and morphology when performed by experienced operators. While a basic competence in HUD can be achieved in a

relatively short period of time, in clinical practice, a cautious, supervised approach should be applied when inexperienced users are acquiring and interpreting images. This mostly applies to secondary care where the prevalence of disease and the availability of experienced echocardiographers is greatest. Our findings demonstrate that HUD is a valuable bedside tool that can be used to identify those who require further investigation and as a result may lead to a reduction in the number of unnecessary echo referrals (table 3).

Training is required to be able to use HUD competently and therefore the results of our study should be interpreted based on the level of operator experience. The amount of training offered and ability to practise using HUD will also impact the diagnostic outcome that can be expected. Operators with limited training however were less able to detect LV dilatation and WMA, recording pooled sensitivities of 68% and 78%, respectively compared with 89% and 85% achieved by experienced echocardiographers. A positive scan in an experienced hand had a 3–6 times higher odds of showing true LV impairment, LV dilatation or WMA compared with inexperienced operators. Operator experience was not a significant discriminating factor when measuring LVH suggesting that it

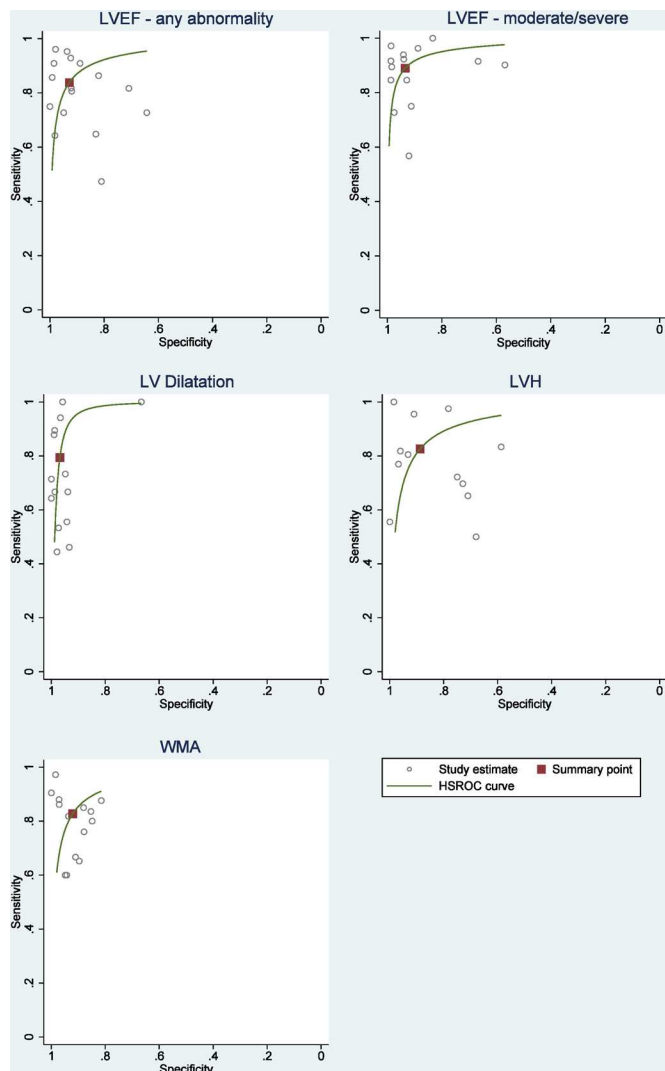


Figure 4 Summary receiver operating characteristic curve (SROC) for the pooled sensitivity and specificity with the summary point for the different handheld ultrasound devices assessments. HSROC, hierarchical summary receiver operator curves; LVEF, left ventricular ejection fraction; LVH, left ventricular hypertrophy; LV, left ventricular; WMA, wall motion abnormality.

can be more accurately measured by clinicians with minimal training.

Important logistical points need to be considered including cost-effectiveness, training and accessibility by clinicians. HUD has been shown to be more cost-effective in comparison to TTE and reduces overall costs when compared with physical examination.^{6 11} Despite these potential savings, implementation requires training and frequent revalidation to maintain the clinician’s skill. Didactic and practical sessions are required before clinicians can achieve basic competence in HUD. A minimum of 30 scans has been recommended, however brief training is associated with an increased false-positive rate.^{12 13} This first highlights that HUD performed by inexperienced users should be supervised by experienced echocardiographers as previously mentioned and second, the importance of frequent training and consolidation in echocardiography before allowing users to image patients without supervision. Accessibility of recorded

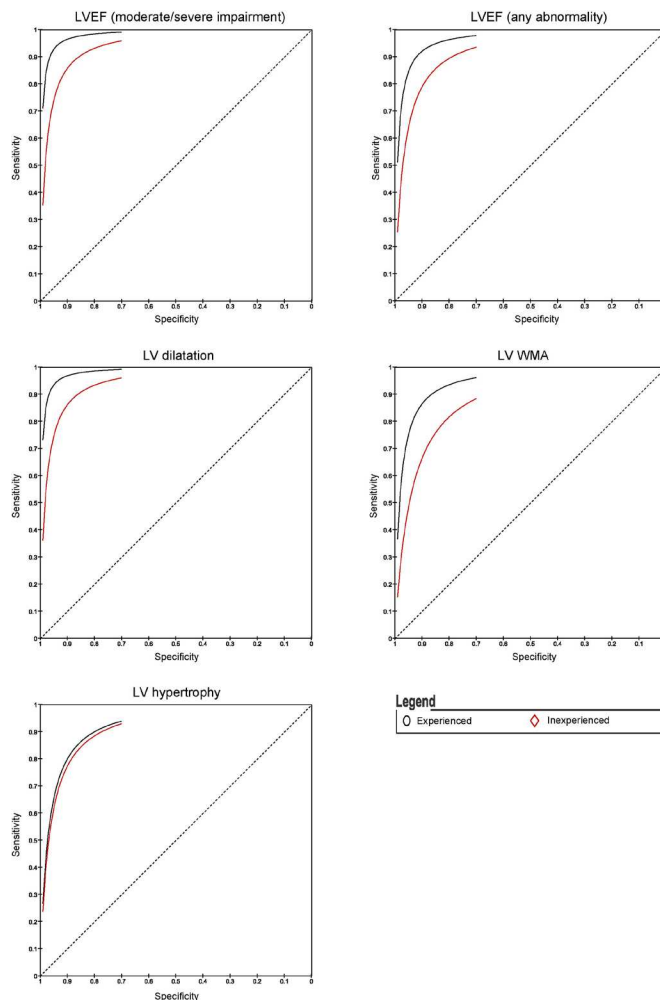


Figure 5 Summary receiver operating characteristic curves for LV parameters comparing effect user experience on handheld ultrasound devices diagnostic accuracy. LVEF, left ventricular ejection fraction; LV, left ventricular; WMA, wall motion abnormality.

images is therefore a fundamental property of a HUD if sufficient supervision is to be achieved.

Our data suggest that HUD is best positioned at the beginning of the clinical pathway when suspicious of cardiac pathology, thus augmenting the cardiovascular examination. Detecting cardiac disease earlier, when the prevalence of any abnormality is at its lowest, is likely to incur higher rates of false positives. However, HUD should be considered as a method of triaging patients who may require further investigation. HUD should not be considered as a replacement to TTE. HUD can be conducted at the bedside and take <6 min.¹⁴ It can be argued that this is preferable compared with the potential of unnecessarily having to wait for a more complex scan, which may require the patient to return on a separate day or result in a longer stay in hospital. However, a negative finding on HUD and not proceeding to full TTE risks cardiac abnormalities being missed, a factor which should be considered on an individual patient basis.

Negative results (ie, specificity) can be used with reasonable confidence used to determine normal cardiac physiology. However, positive results need to be interpreted with caution, especially when performed by inexperienced HUD users. Clinical decision making should not be solely guided by the interpretation of HUD images, even by experienced echocardiographers. Instead, these results suggest that HUD should act as an initial

Table 2 Results of meta-analyses comparing the diagnostic accuracy of HUD with first-line TTE

HUD compared with TTE									
Sensitivity %	Total			Experienced			Inexperienced		
	Studies (n)	Prevalence	Sensitivity (95% CI)	Studies (n)	Prevalence	Sensitivity (95% CI)	Studies (n)	Prevalence	Sensitivity (95% CI)
LVEF (any abnormality)	15 (2936)	0.23	86 (80 to 90)	9 (1406)	0.18	88 (81 to 92)	9 (1530)	0.28	83 (71 to 90)
LVEF (moderate/severe)	10 (1611)	0.27	91 (86 to 94)	5 (722)	0.27	93 (89 to 96)	7 (889)	0.27	84 (72 to 92)
WMA	13 (1931)	0.27	81 (74 to 85)	6 (794)	0.26	85 (76 to 91)	7 (1137)	0.28	78 (70 to 84)
LV dilatation	10 (1966)	0.13	73 (59 to 84)	6 (966)	0.17	89 (64 to 97)	6 (1000)	0.09	68 (51 to 81)
LVH	12 (2229)	0.24	83 (73 to 90)	6 (1096)	0.23	85 (72 to 92)	7 (1133)	0.26	80 (61 to 91)
LVEF (any abnormality)	14 (2851)	0.21	91 (87 to 95)	8 (1368)	0.16	96 (90 to 98)	8 (1483)	0.26	89 (81 to 93)
LVEF (moderate/severe)	10 (1611)	0.27	92 (87 to 96)	5 (722)	0.27	96 (87 to 99)	7 (889)	0.27	91 (83 to 95)
WMA	12 (1876)	0.28	90 (88 to 92)	6 (759)	0.27	95 (93 to 96)	6 (1117)	0.28	88 (85 to 90)
LV dilatation	10 (1966)	0.13	95 (94 to 97)	6 (966)	0.17	98 (93 to 99)	6 (1000)	0.09	95 (93 to 96)
LVH	11 (2228)	0.25	90 (82 to 95)	5 (1095)	0.23	91 (82 to 96)	7 (1133)	0.26	87 (67 to 96)

HUD, handheld ultrasound devices; LV, left ventricular; LVEF, LV ejection fraction; LVH, LV dilatation and hypertrophy; TTE, transthoracic echocardiography; WMA, wall motion abnormalities.

diagnostic test to aid decision making on whether further investigation, including TTE, and treatment is required.

Given the excellent sensitivity and specificity particularly seen with more experienced operators, it is likely that the role of HUD will become even more prominent in future clinical practice. We would support earlier teaching and training of HUD and its incorporation into the medical school curriculum, thus providing an important way of ensuring adequate training for all future doctors.

Strengths and limitations

An extensive literature search was performed. No search filters were used revealing results from an unpublished source, thus minimising the risk of publication bias. To limit the effect of any reporting bias, data were carefully extracted from the results of some studies that did not explicitly state sensitivity and specificity values. The search and data extraction were performed by two authors independently to minimise the bias in the review process.

Half of the included studies are >10 years old and improvement in screen technology, image processing and other advancements might play a pivotal role in improving the diagnostic accuracy of HUD.

The lack of a common threshold for WMA, LV dilatation and LVH means the diagnostic performance may vary between centres. Our results do however show that despite variation in

thresholds, the specificity of HUD remains $\geq 87\%$ for all characteristics. Even if sensitivity is reduced, the use of HUD as an initial diagnostic tool means diagnosing a condition and determining disease severity is not the aim of this test. Any uncertainty when interpreting the image should result in referral for further investigation. Clinical suspicion of HF and measurement of LV filling pressures is an important indication for echocardiography assessment and would be a valuable bedside tool. Clarius is one of the only scanners on the market capable of pulse-wave Doppler (PWD), permitted by the installation of a liquid heating device which prevents overheating.¹⁵ The current technological capabilities of most HUDs do not include PWD and therefore filling pressures cannot be measured using these devices.¹⁶ We were therefore unable to analyse sufficient data regarding this variable.

Future applications

With advancement of technology, LV border tracking and other methods of automatic, device-generated, quantitative measures of ejection fraction may become routinely available.¹⁷ Incorporation of PWD and continuous-wave Doppler technology into a greater number of available HUDs will also allow for a more extensive range of quantitative cardiovascular assessments to be undertaken at the bedside. Qualitative assessment of valvular heart disease using colour-flow Doppler is available on most HUDs, however is outside the scope of this review. Images may

Table 3 Summary of findings

Review question	Is handheld echocardiography able to accurately diagnose LV dysfunction compared with TTE?			
Population	6062 participants aged 65±5 years with a male predominance of 54% requiring routine referral for TTE			
Setting	Single centres with access to TTE			
Studies	Studies of diagnostic tests			
Quality of evidence	Majority of studies reported consecutive or random sampling, blinding of assessors and short time between HUD and TTE imaging (24–28 hours)			
Pooled results	Sensitivity (95% CI)		Specificity (95% CI)	
	Experienced	Inexperienced	Experienced	Inexperienced
LVEF (any abnormality)	88 (81 to 92)	83 (71 to 90)	96 (90 to 98)	89 (81 to 93)
LVEF (moderate/severe)	93 (89 to 96)	84 (72 to 92)	96 (87 to 99)	91 (83 to 95)
WMA	85 (76 to 91)	78 (70 to 84)	95 (93 to 96)	88 (85 to 90)
LV dilatation	89 (64 to 97)	68 (51 to 81)	98 (93 to 99)	95 (93 to 96)
LVH	85 (72 to 92)	80 (61 to 91)	91 (82 to 96)	87 (67 to 96)

HUD, handheld ultrasound devices; LV, left ventricular; LVEF, LV ejection fraction; LVH, LV dilatation and hypertrophy; TTE, transthoracic echocardiography; WMA, wall motion abnormalities.

ultimately be sent remotely following acquisition directly to an experienced echocardiographer who can review and interpret images immediately, fast-tracking patients who require further investigation.^{18 19} Further developments in HUD therefore have the potential to revolutionise the bedside cardiovascular examination.

This study highlights the need to further develop methods to bridge the gap between experienced and inexperienced users. Education and introduction of an ultrasound curriculum for medical students and junior doctors can improve understanding of clinical anatomy, develop basic ultrasound skills and later their diagnostic ability.^{20 21} Formulation of a designated HUD training pathway would allow for standardisation of HUD competencies and provide structure to those wishing to advance their experience using HUDs. These suggestions are limited by the financial burden this would incur as well as a shortfall of clinicians adequately trained using HUDs.

CONCLUSION

This meta-analysis supports the use of HUD as a powerful modality for predicting LV size and systolic function. HUD diagnostic yield is superior when performed by experienced echocardiographers. Images acquired by an inexperienced operator should be done under direct supervision or validated by a more experienced user. This study provides a strong rationale for considering HUD as an auxiliary tool to the physical examination in secondary care, to aid the clinical decision making when considering referral for TTE.

Key messages

What is already known on this subject?

- ▶ Handheld cardiac ultrasound device (HUD) offers rapid bedside assessment of cardiac morphology and function.
- ▶ The diagnostic accuracy of HUD previously reported has shown heterogeneity between studies and its clinical value has yet to be determined.

What might this study add?

- ▶ To the best of our knowledge, this is the first study to perform a meta-analysis evaluating the diagnostic accuracy of HUD devices to detect cardiac dysfunction and the impact of operator experience on test accuracy.
- ▶ This study reports that HUD test accuracy is significantly improved when performed by experienced operators.

How might this impact on clinical practice?

- ▶ The clinical utility of HUD is rapidly expanding.
- ▶ Augmentation of the physical cardiovascular examination using HUD may improve detection of cardiac size and function at the bedside and lead to a reduction in the number of unnecessary departmental transthoracic echocardiography referrals.
- ▶ Image interpretation by inexperienced operators should be confirmed by more experienced echocardiographers before clinical decisions and referral for further imaging are made.

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Contributors SJ, SA and PG contributed to the study conception and design. Material preparation, data collection and analysis were performed by SJ, SA and PG. SA performed the meta-analysis of the diagnostic accuracy parameters. All authors contributed to the interpretation of data. The first draft of the manuscript was written by SJ and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Funding This work was funded in part by the Wellcome Trust (215799/Z/19/Z, 214567/Z/18/Z and 205188/Z/16/Z). For the purpose of Open Access, the authors have applied a CC BY public copyright licence to any Author Accepted Manuscript version arising from this submission.

Competing interests PG is an advisor for Pie Medical Imaging and Medis Medical Imaging. JW lists commercial relationships with AstraZeneca, Bayer and Novartis.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement All data relevant to the study are included in the article or uploaded as supplementary information.

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HUD MA Supplementary Material

Search terms used in MA

Medline

5	(handheld OR hand?held OR pocket?siz* OR hand?carried OR mobile OR bed?side OR bedside).ti,ab	141,288
6	(echocardiogram OR echocardiography OR ultrasound).ti,ab	359,331
7	(5 AND 6)	6,198

EMBASE

1	(handheld OR hand?held OR pocket?siz* OR hand?carried OR mobile OR bed?side OR bedside).ti,ab	183,391
2	(echocardiogram OR echocardiography OR ultrasound).ti,ab	580,544
3	(1 AND 2)	11,019

Table 1. Individual study data incorporated into the meta-analysis.

Study	Parameter	Threshold	Whole Sample Size	Total Number Measured	Total Number Positive	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
LVEF									
Aldaas (exp) 2019	LV border detection and tracking	LVEF <50% - At least adequate image quality	70	56	8	75	98	N/A	N/A
Aldaas (inexp) 2019	LV border detection and tracking	LVEF <50% - At least adequate image quality	70	56	8	75	100	100	96
Alexander 2004	Visual estimation of LV systolic function	LVEF <55%	537	533	223	82	71	67	85
Andersen 2011	Qualitative assessment	SE>=moderate pathology	108	108	35	97	99	97	99
Biais 2012	Visual estimation of LV systolic function	LVEF <50%	151	151	28	86	99	96	97
Decara (exp) 2003	Qualitative assessment	LV dysfunction	300	149	38	89	N/A	N/A	N/A
Decara (inexp) 2003	Qualitative assessment	LV dysfunction	300	151	47	97	N/A	N/A	N/A
Fedson 2003	Qualitative assessment	>=mild	103	39	11	73	64	44	86
Galasko 2003	Visual estimation of LV systolic function	LVEF <50%	562	531	51	96	98	83	99.6
Ghani 2006	Visual estimation of LV systolic function	LVEF <40%	80	73	16	75	91	71	93
Gulic (exp) 2016	Qualitative assessment	Any reduction in LVEF	200	200	22	72	94	64	97
Gulic (inexp) 2016	Qualitative assessment	Any reduction in LVEF	200	200	22	84	92	58	98
Khan 2014	Visual estimation of LV systolic function	Normal >=55%, moderate 35%-<55%, severely reduced <35%	240	239	70	93	92	84	97

Kirkpatrick 2005	Visual estimation of LV systolic function	LVEF <40%	63	63	3	100	83	23	100
Kobal 2005	Visual estimation of LV systolic function	LVEF <50%	61	61	22	86	82	73	91
Liebo (expDR) 2011	Visual estimation of LV systolic function	LVEF <45%	97	91	13	85	99	92	97
Liebo (expMS) 2011	Visual estimation of LV systolic function	LVEF <45%	97	90	12	92	99	92	99
Liebo (inexpRI) 2011	Visual estimation of LV systolic function	LVEF <45%	97	97	13	85	93	65	98
Liebo (inexpML) 2011	Visual estimation of LV systolic function	LVEF <45%	97	92	11	73	98	80	96
Lopez- Palmero 2015	Qualitative assessment	Normal or depressed	223	212	85	95.2	93.7	91	96.7
Martin 2009	Qualitative assessment	Normal or abnormal	354	336	124	81	92	85	89
Mehta 2014	Qualitative assessment	LVEF<40%	250	250	54	96	89	70	99
Mjølstad 2013	Systolic excursion of AV plane and visual estimation of LV systolic function	LVEF <45% = moderate+	199	129	30	92	94	80	98
Nilsson 2019	Visual estimation of LV systolic function	LVEF<50%	100	140	19	47	81	28	91
Oleson 2015	Qualitative assessment	LVEF<50%	260	255	125	65	83	79	71
Razi 2011	Visual estimation of LV systolic function	LVEF <40%	50	50	33	94	94	97	88
Ruddox 2013	Visual estimation of LV systolic function	LVEF<40%	303	283	81	57	92	74	84
Stokke (inexp) 2014	Visual estimation of LV systolic function	LVEF <45%	72	105	61	90	57	74	81

Stokke (exp) 2014	Visual estimation of LV systolic function	LVEF <45%	72	101	59	92	67	79	85
Vignon 2004	Not specified	Not specified	55	42	22	91	89	91	89
Vourvouri 2003	Visual estimation of LV systolic function	LVEF <40%	88	82	19	89	98	94	97
Xie 2006	Not Specified	LVEF<50%	100	100	33	91	99	97	96
WMA									
Bruce 2002	Qualitative assessment	Present	374	124	97	88	82	94	65
Cullen 2013	Based on 16-segment model	Present	190	190	15	60	95	50	97
Decara (exp) 2003	Qualitative assessment	Present	300	149	14	79	N/A	N/A	N/A
Decara (inexp) 2003	Qualitative assessment	Present	300	151	20	55	N/A	N/A	N/A
Fedson 2003	Qualitative assessment	Present	103	39	0	N/A	90	N/A	N/A
Giusca 2010	Not Specified	Present	56	52	23	65.2	89.5	76.5	83.3
Khan 2014	Lack of normal systolic thickening or translational motion towards centreline	Present	240	232	94	86	97	95	91
Liebo (expDR) 2011	Lack of normal systolic thickening or translational motion towards centreline	Present	97	90	15	67	91	53	95
Liebo (expMS) 2011	Lack of normal systolic thickening or translational motion towards centreline	Present	97	74	11	82	94	69	97
Liebo (inexpRI) 2011	Lack of normal systolic thickening or translational motion towards centreline	Present	97	76	10	80	85	44	97

Liebo (inexpML) 2011	Lack of normal systolic thickening or translational motion towards centreline	Present	97	80	10	60	94	60	94
Lucas 2009	Abnormal wall movement/thickening during systole	Present	322	314	80	85	88	71	95
Lucas 2011	Abnormal wall movement/thickening during systole	Present	210	210	67	84	85	73	92
Ruddox 2013	Visual estimation	Present	303	261	96	76	88	79	86
Vignon 2004	Not specified	Not specified	55	23	21	90	100	100	50
Wejner-Mik 2019	Visual estimation	Present	87	85	50	88	97	98	86
Xie 2006	Not Specified	Present	100	100	36	97	98	97	98
LV Dilation									
Biais 2012	Qualitative assessment	Yes/No SE=LV dilation >55mm	151	151	8	94	96	57	100
Coletta 2006	LVEDD	Normal 30mm/m2	112	105	87	100	65	93	100
Giusca 2010	LV diameter	>59mm	56	52	7	71	100	100	95.7
Gulic (exp) 2016	Qualitative assessment	Yes/No	200	200	9	44	97	50	97
Gulic (inexp) 2016	Qualitative assessment	Yes/No	200	200	9	55	94	31	98
Khan 2014	LVEDD	>53mm women, >59mm men	240	225	33	87	98	91	98
Kobal 2005	Qualitative assessment	Yes/No SE>56mm	61	61	12	67	94	73	92
Liebo (expDR) 2011	LVEDD	>53mm women, >59mm men	97	92	15	67	99	91	94
Liebo (expMS) 2011	LVEDD	>53mm women, >59mm men	97	93	14	64	100	100	94

Liebo (inexpRI) 2011	LVEDD	>53mm women, >59mm men	97	92	15	73	95	73	95
Liebo (inexpML) 2011	LVEDD	>53mm women, >59mm men	97	90	15	53	97	80	91
Lopez-Palmero 2015	LVEDD	>53mm women, >59mm men	223	212	34	94	97	84.2	98.8
Ruddox 2013	LVEDD	Not specified	303	293	52	46	93	60	89
Xie 2006	LVEDD	LVEDD \geq 55mm	100	100	19	89	99	94	98
LVH									
Biais 2012	Qualitative assessment	Yes/No SE=IVS>13mm	151	151	26	77	97	83	95
Coletta 2006	IVS	Normal 12mm	112	105	82	97	79	94	88
Coletta 2006	PW	Normal 12mm	112	105	93	97	70	96	74
Decara (exp) 2003	Qualitative assessment	Severe	300	149	1	100	N/A	N/A	N/A
Galasko 2003	IVS or PW	\geq 13mm	562	540	31	94	93	45	99.6
Galasko 2003	IVS or PW	\geq 12mm	562	540	55	82	96	69	98
Giusca 2010	End-diastolic thickness of interventricular septum	\geq 11mm	56	52	9	56	100	100	91.5
Gulic (exp) 2016	Qualitative assessment	Yes/No SE=IVS>14mm	200	200	108	72	75	77	70
Gulic (inexp) 2016	Qualitative assessment	Yes/No SE=IVS>14mm	200	200	108	83	58	70	75
Kobal 2005	Qualitative assessment	Yes/No SE=IVS/PW \geq 12mm	61	61	23	65	71	58	77
Lopez-Palmero 2015	IVS or PW	>10mm	223	212	134	96	91	94.8	92.2
Lucas 2009	Posterior/septal wall thickness	\geq 12mm	322	314	33	70	73	23	95
Lucas 2011	Posterior/septal wall thickness	\geq 1.4 (M), \geq 1.3 (F)	210	209	34	50	68	23	88

Perez-Avraham 2010	IVS or PW	IVS \geq 11.7, PW \geq 9.8	85	85	18	100	99	95	100
Senior 2004	LVMi	>134gm ² /m ² (M), 110 (F)	189	179	46	72	91	73	90
Vourvouri 2002	LVMi	>134gm ² /m ² (M), 110 (F)	100	100	18	83	96	79	96
Xie 2006	Septal wall thickness	\geq 12mm	100	100	41	80	93	89	87

We extracted and collated data using a standardised, agreed upon, data extraction form. Data collected included:

1. Methods:
 - Study design
 - Total duration of study
 - Study setting
 - Date of study
 - Country of study
2. Participants:
 - Number included and analysed for the index and reference test
 - Mean age
 - Gender
 - Inclusion criteria
 - Exclusion criteria.
3. Index test:
 - Type of HUD
 - Experience of operators
 - Number of operators
 - Time between index and reference test
4. Reference Standard:
 - Type of standard echocardiography
 - Experience of operators
 - Number of operators
5. Outcomes: LV parameters including function, dilatation, wall motion abnormality and hypertrophy.
6. Thresholds:
 - LVEF
 - Mild = LVEF 45-55%
 - Moderate/severe = LVEF <45%
 - LV dilatation
 - LVEDD >53mm
 - WMA
 - Present/absent
 - LVH
 - Interventricular septum/posterior wall >10mm
7. Diagnostic data:

- Sensitivity/specificity/PPV/NPV
- TP/TN/FP/FN
- Prevalence
- Total number measured

Table 2. Diagnostic odds ratios for HUD cardiac assessment.

Characteristic	DOR Overall (CI)	DOR Experienced (CI)	DOR Inexperienced (CI)	p-value
LVEF (any abnormality)	58.63 (26.11-131.63)	131.24 (37.75-456.22)	28.11 (11.19-70.56)	0.051
LVEF (moderate/severe)	88.55 (38.88-201.68)	276.02 (57.70-1320.41)	41.45 (18.34-93.72)	0.035
WMA	40.81 (25.19-66.10)	89.97 (30.56-264.86)	28.34 (19.76-40.63)	0.047
LVH	26.69 (11.27-78.25)	54.92 (13.96-216.08)	18.17 (5.05-65.41)	0.248
LVH (quantitative only)	54.69 (11.99-249.45)	96.59 (50.81-183.59)	39.48 (4.81-323.90)	0.436
LV Dilatation	95.81 (40.12-228.85)	224.63 (87.38-577.51)	44.84 (16.38-122.77)	0.022
LV Dilatation (quantitative only)	142.29 (42.94-471.48)	405.51 (143.18-1148.50)	62.41 (14.30-272.40)	0.042

Table 3. Heterogeneity assessment and evaluation of operator experience on the diagnostic performance of HUD.

HUD Parameter	Heterogeneity Assessment	Operator Experience	
	Correlation coefficient between log Sp and log SN	Meta-regression covariate coefficient	P value
LVEF	0.3	-1.64	0.04
LVEF <40	-0.14	-1.65	0.04
LV dilatation	-0.39	-0.09	0.88
LVH	0.39	-1.08	0.31
WMA	-0.06	-1.055	0.01

Contrary to intervention meta-analyses, the I^2 statistic is not a reliable indicator for heterogeneity in diagnostic test accuracy reviews and therefore was not assessed(1). Instead, heterogeneity can be analysed by estimating the correlation between sensitivity and specificity(2). In a normal ROC curve, an increase in sensitivity is offset by a decrease in specificity and therefore they have a negative correlation. A correlation coefficient larger than zero indicates possible heterogeneity. The correlation coefficient of the logit-transformed sensitivity and specificity was calculated for all variables.

The sensitivity and specificity are proportion data and limited between the lower and upper limits of 0 and 1. To apply the correlation statistics and meet its distribution assumption, the proportion data are logit-transformed to release the upper and lower limits of the sensitivity and specificity data(2).

We planned to assess the effect of operator experience, pre-existing comorbidities and baseline LV function on the results in a meta-regression covariate analysis. However, only operator experience was sufficiently reported and showed that experience was a significant factor in detecting LVEF, WMA and LV dilatation.

Domain	Risk of bias (%)		
	High	Unclear	Low
Flow and Timing	3	27	70
Reference Standard	9	15	76
Index Test	3	15	82
Patient Selection	0	21	79

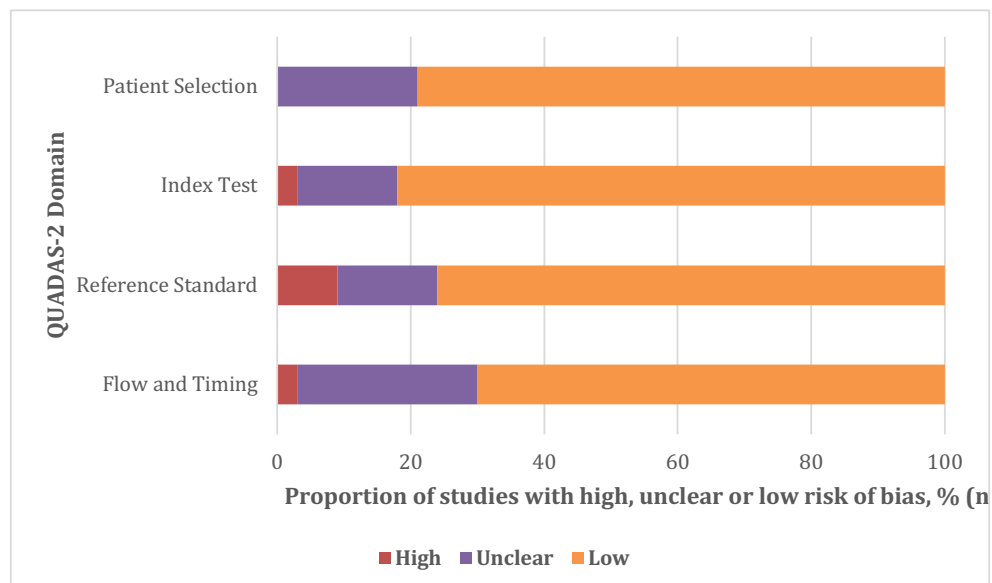


Figure 1. Tabulated and graphical displays for QUADAS-2 results.

The risk of bias was qualitatively assessed based on the domains of the Quality Assessment of Diagnostic Accuracy Studies (QUADAS)-2 tool. Parameters evaluated included random or consecutive recruitment of patients (patient sampling), blinding of assessors to index and reference test, and the time between HUD and TTE (flow and timing). Two reviewers (SJ and PG) independently assessed the risk of bias for each study with disagreements discussed with a third author (SA). Studies categorised as low for all domains were regarded as having a low risk of bias. Studies stated as being high or unclear in ≥ 1 domain were judged to be at risk of bias.

Study	Patient Sampling	Index Test	Reference Test	Flow and Timing
	Random or consecutive recruitment	HHE Blinded to TTE	TTE Blinded to HHE	Time between HHE and TTE
Aldaas 2019				
Alexander 2004				
Biais 2012				
Bruce 2002				
Coletta 2006				
Cullen 2013				
DeCara 2003				
Fedson 2003				
Galasko 2003				
Giusca 2010				
Gulic 2016				
Khan 2014				
Kobal 2005				
Liebo 2011				
Lopez-Palmero 2015				
Lucas 2009				
Lucas 2011				
Martin 2009				
Nilsson 2019				
Oleson 2015				
Perez-Avraham 2010				
Ruddox 2013				
Wejner-Mik 2019				
Xie 2006				
Vignon 2004				

Risk of bias	
High	
Some concerns / unclear	
Low	

Figure 2. Risk of bias summary for each included study

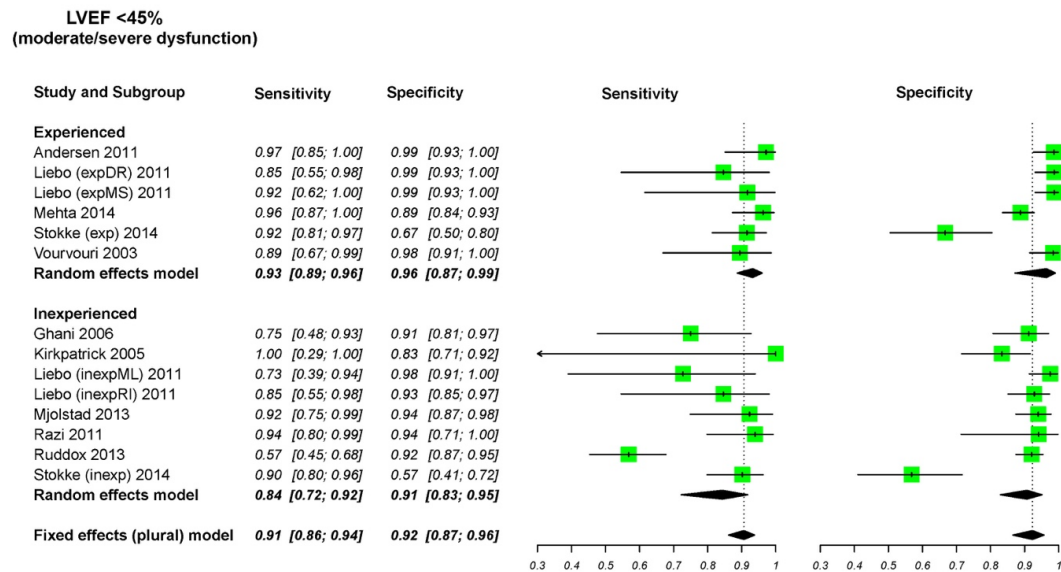


Figure 3. Meta-analyses of LVEF <45%. Sensitivity and specificity [CI] values are reported.

The bivariate method was used to calculate overall sensitivity and specificity and their 95% confidence intervals. The summary estimates of sensitivity and specificity using this method represent the average operating point across studies. The bivariate nature of the input data is maintained throughout the analysis using the bivariate model which allows the calculation of reliable summary estimates. Other advantages of the bivariate method include accounting for the study size, between-study heterogeneity and adjusting for the threshold effect seen when there is a negative correlation between the sensitivity and the specificity of the index test(3).

References

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3. Reitsma JB, Glas AS, Rutjes AWS, Scholten RJPM, Bossuyt PM, Zwinderman AH. Bivariate analysis of sensitivity and specificity produces informative summary measures in diagnostic reviews. *J Clin Epidemiol*. 2005 Oct;58(10):982–90.