Heart failure and cardiomyopathies

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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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. 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.

The miniaturisation of ultrasound technology has led to the introduction of handheld cardiac ultrasound devices (HUD). 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. 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.

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 9 recruiting 562 patients. 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.

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 >7 days. 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 operators could determine reduced LVEF, LV dilatation, WMA and LVH with pooled specificities of 83%, 88%, 85% and 85%, respectively (figures 2–4). In inexperienced hands, pooled specificities measured were 83%, 88%, 85% and 85%, respectively.
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, 43 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

| Study                  | Country | Design       | Study period   | Size | Male (%) | Age, years | Level of experience | HUD      |
|------------------------|---------|--------------|----------------|------|----------|------------|---------------------|----------|
| Aldaas et al           | USA     | Consecutive  | NR             | 70   | 50       | 61±18      | Both                | Vscan    |
| Alexander et al        | USA     | NR           | April–November 2000 | 537  | 53       | 59         | Inexperienced       | Optigo   |
| Andersen et al         | Norway  | Random       | March–September 2010 | 108  | 64       | 69.1±14    | Experienced        | Vscan    |
| Blais et al            | France  | Consecutive  | February–May 2011 | 151  | 35       | 55±20      | Experienced        | Vscan    |
| Bruce et al            | USA     | NR           | NR             | 374  | 62       | 66         | Both                | SonoHeart|
| Coletta et al          | Italy   | Consecutive  | April–June 2003 | 112  | 57       | 61±11      | Experienced        | Optigo   |
| Cullen et al           | USA     | Consecutive  | 2012–2013      | 190  | 49       | 62±17      | Experienced        | Vscan    |
| DeCara et al           | USA     | NR           | NR             | 300  | NR       | NR         | Experienced        | Optigo   |
| Fedson et al           | USA     | Consecutive  | NR             | 103  | NR       | NR         | Inexperienced      | Optigo   |
| Galasko                | UK      | Consecutive  | 2000–2001      | 562  | 56       | 62±11      | Experienced        | Optigo   |
| Ghanii et al           | USA     | Consecutive  | NR             | 80   | 51       | 75±13      | Inexperienced      | Optigo   |
| Giusca et al           | Romania | Consecutive  | NR             | 56   | 54       | 60±12      | Inexperienced      | Acuson P10|
| Gulici et al           | Slovenia| Consecutive  | NR             | 200  | 43       | 70         | Both                | Vscan    |
| Khan                   | USA     | Consecutive  | 2012–2013      | 240  | 53       | 71±17      | Experienced        | Vscan    |
| Kirkpatrick            | USA     | NR           | NR             | 63   | 46       | 65±16      | Inexperienced      | Optigo   |
| Kobal et al            | USA     | Consecutive  | NR             | 61   | 62       | 70±19      | Inexperienced      | Optigo   |
| Liebo                  | USA     | Consecutive  | February–March 2010 | 97   | 45       | 68±17      | Both                | Vscan    |
| López-Palmero et al    | Spain   | Consecutive  | July–December 2013 | 223  | 42       | 76         | Inexperienced      | Vscan    |
| Lucas et al            | USA     | Consecutive  | March–May 2007  | 322  | 53       | 56±13      | Inexperienced      | Micromaxx|
| Lucas et al            | USA     | Consecutive  | 2008–2009      | 210  | 55       | 55         | Inexperienced      | NR       |
| Martin et al           | USA     | Consecutive  | 2004–2005      | 354  | 47       | 63±19      | Inexperienced      | Sonosite Elite|
| Mehta et al            | USA     | NR           | NR             | 250  | 66       | 61±15      | Experienced        | Vscan    |
| Mjialized et al         | Norway  | Consecutive  | April–June 2011 | 199  | 54       | 66±18      | Inexperienced      | Vscan    |
| Nilsson et al          | Sweden  | NR           | 2016–2017      | 100  | 55       | 70±12      | Inexperienced      | Vscan    |
| Olesen                 | Denmark | NR           | NR             | 260  | 49       | 80         | Experienced        | Vscan    |
| Perez-Avraham et al    | Israel  | Consecutive  | July–December 2004 | 85   | 37       | 59±14      | Inexperienced      | Optigo   |
| Razi et al             | USA     | Consecutive  | NR             | 50   | 58       | 57±17      | Inexperienced      | Vscan    |
| Ruddox et al           | Norway  | NR           | 2011–2012      | 303  | 61       | 73         | Inexperienced      | Vscan    |
| Stokke et al           | Norway  | Random       | February–May 2012 | 72   | 72       | 65±16      | Both                | Vscan    |
| Vignon et al           | France  | Consecutive  | NR             | 55   | 69       | 61±16      | Experienced        | SonoHeart|
| Vourvouri et al         | The Netherlands | Consecutive | NR             | 88   | 64       | 59±12      | Experienced        | SonoHeart or Optigo|
| Wejner-Mik et al       | Poland  | Consecutive  | NR             | 87   | 67       | 61±16      | Experienced        | Lumify   |
| Xie et al              | USA     | Consecutive  | NR             | 100  | 55       | 59±17      | Experienced        | SonoHeart|
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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 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 2  Meta-analyses of left ventricular ejection fraction (LVEF) and left ventricular (LV) dilatation. Sensitivity and specificity (95% CI) values are reported.
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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 can be more accurately measured by clinicians with minimal training.

Figure 3  Meta-analyses of wall motion abnormality (WMA) and left ventricular hypertrophy (LVH). Sensitivity and specificity (95% CI) values are reported.
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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. 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. 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 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. 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 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 ≥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. The current technological capabilities of most HUDs do not include PWD and therefore filling pressures cannot be measured using these devices. 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. 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 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. Further developments in HUD therefore

| Table 2 | Results of meta-analyses comparing the diagnostic accuracy of HUD with first-line TTE |
|-----------------------------------------------|-----------------------------------------------|
| HUD compared with TTE | Total | Experienced | Inexperienced |
| Sensitivity % | 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 | 87 (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) | 6 (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 (1171) | 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.

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.
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. 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.

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.

REFERENCES
1. Mitchell C, Rahko PS, Blauwet LA, et al. Guidelines for performing a comprehensive transthoracic echocardiographic examination in adults: recommendations from the American Society of echocardiography. J Am Soc Echocardiogr 2019;32:1–64.
2. Sirci R, Galderisi M, Voigt J-U, et al. The use of pocket-size imaging devices: a position statement of the European association of echocardiography. Eur J Echocardiogr 2011;12:85–7.
3. Wharton G, Steeds R, Allen J, et al. A minimum dataset for a standard adult transthoracic echocardiogram: a guideline protocol from the British Society of echocardiography. Echo Res Pract 2015;2:G9–24.
4. Bhavnani SP, Narula J, Sengupta PP. Mobile technology and the digitization of healthcare. Eur Heart J 2016;37:1428–38.
5. Pathan F, Fonseca R, Marwick TH. Usefulness of Hand-Held Ultrasound as a Gatekeeper to Standard Echocardiography for “Rarely Appropriate” Echocardiography Requests. Am J Cardiol 2016;118:1588–92.
6. Diagnostic test accuracy (DTA) reviews. Available: https://training.cochrane.org/ diagnostic-test-accuracy-dta-reviews [Accessed 6 Jul 2021].
7. Galasko GW, Lahrin A, Senior R. Portable echocardiography: an innovative tool in screening for cardiac abnormalities in the community. Eur J Echocardiogr 2003;4:119–27.
8. Bruce CJ, Montgomery SC, Bailey KR, et al. Utility of handheld-carried ultrasound devices used by cardiologists with and without significant echocardiographic experience in the cardiology inpatient and outpatient settings. Am J Cardiol 2002;90:1273–5.
9. Greaves K, Jetley P, Hickman M, et al. The use of hand-carried ultrasound in the hospital setting—a cost-effective analysis. J Am Soc Echocardiogr 2005;18:620–5.
10. Spencer KT, Kimura BJ, Korczak CE, et al. Focused cardiac ultrasound: recommendations from the American Society of echocardiography. J Am Soc Echocardiogr 2013;26:567–81.

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

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Heart failure and cardiomyopathies

12 Wilkinson JS, Barake W, Smith C, et al. Limitations of condensed teaching strategies to develop hand-held cardiac ultrasonography skills in internal medicine residents. *Can J Cardiol* 2016;32:1034–7.

13 Stokke TM, Ruddox V, Sarvari SI, et al. Brief group training of medical students in focused cardiac ultrasound may improve diagnostic accuracy of physical examination. *J Am Soc Echocardiogr* 2014;27:1238–46.

14 Hammoudi N, Arangalage D, Boubrit L, et al. Ultrasound-based teaching of cardiac anatomy and physiology to undergraduate medical students. *Arch Cardiovasc Dis* 2013;106:487–91.

15 Mjølstad OC, Dalen H, Graven T, et al. Routinely adding ultrasound examinations by pocket-sized ultrasound devices improves interpretative diagnostics in a medical department. *Eur J Intern Med* 2012;23:185–91.

16 C3 Overview – Hand-held Curvilinear Ultrasound Scanner – Clarius. Available: https://clarius.com/gb/scanners/c3/ [Accessed 24 May 2021].

17 Rykkje A, Carlsen JF, Nielsen MB. Hand-Held ultrasound devices compared with High-End ultrasound systems: a systematic review. *Diagnostics* 2019;9: doi:10.3390/diagnostics9020061. [Epub ahead of print: 15 06 2019].

18 Narula S, Shameer K, Salem Omar AM, et al. Machine-Learning algorithms to Automate morphological and functional assessments in 2D echocardiography. *J Am Coll Cardiol* 2016;68:2287–95.

19 Sengupta PT, Narula N, Modesto K, et al. Feasibility of intercity and trans-Atlantic telediagnostic remote ultrasound: assessment facilitated by a nondedicated bandwidth connection. *JACC Cardiovascular Imaging* 2014;7:804–9.

20 Boman K, Olufsson M, Berggren P, et al. Robot-assisted remote echocardiographic examination and teleconsultation: a randomized comparison of time to diagnosis with standard of care referral approach. *JACC Cardiovascular Imaging* 2014;7:799–803.

21 Aldaas OM, Igata S, Raisinghani A, et al. Accuracy of left ventricular ejection fraction determined by automated analysis of handheld echocardiograms: a comparison of experienced and novice examiners. *Echocardiography* 2019;36:2145–51.

22 Alexander JH, Peterson ED, Chen AX, et al. Feasibility of point-of-care echocardiography by internal medicine house staff. *Am Heart J* 2004;147:476–81.

23 Andersen GN, Haugen BO, Graven T, et al. Feasibility and reliability of point-of-care pocket-sized echocardiography. *Eur J Echocardiogr* 2011;12:665–70.

24 Biais M, Carrié C, Delaunay F, et al. Evaluation of a new pocket echocardiographic device for focused cardiac ultrasonography in an emergency setting. *Crit Care* 2012;16:R82.

25 Coletta C, De Marchis E, Lenoli M, et al. Reliability of cardiac dimensions and valvular regurgitation assessment by sonographers using hand-carried ultrasound devices. *Eur J Echocardiogr* 2006;7:275–83.

26 Cullen MW, Blauwet LA, Vatury OM, et al. Diagnostic capability of comprehensive hand-held vs transthoracic echocardiography. *Mayo Clin Proc* 2014;89:790–8.

27 DeCana JM, Lang RM, Koch R, et al. The use of small personal ultrasound devices by internists with formal training in echocardiography. *Eur J Echocardiogr* 2003;4:141–7.

28 Fedson S, Neihardt G, Thomas P, et al. Unexpected clinically important findings detected with a small portable ultrasound device in patients admitted to a general medicine service. *J Am Soc Echocardiogr* 2003;16:901–5.

29 Ghan SN, Kirkpatrick JN, Spencer KT, et al. Rapid assessment of left ventricular systolic function in a pacemaker clinic using a hand-carried ultrasound device. *J Interv Card Electrophysiol* 2006;16:39–43.

30 Giussa S, Jurch T, Ticulencu R, et al. Accuracy of handheld echocardiography for bedside diagnostic evaluation in a tertiary cardiac center: comparison with standard echocardiography. *Echocardiography* 2011;28:136–41.

31 Guliz TG, Makuc J, Prosen G, et al. Pocket-size imaging device as a screening tool for aortic stenosis. *Wien Klin Wochenschr* 2016;128:348–53.

32 Khan HA, Wineinger NE, Uddin PQ. Can Hospital rounds with pocket echocardiography by cardiologists reduce standard transthoracic echocardiography? *Am J Med* 2014;127:669.e1–669.e7. doi:10.1016/j.amjmed.2014.03.015

33 Kirkpatrick JN, Ghani SN, Spencer KT. Hand carried echocardiography screening for LV systolic dysfunction in a pulmonary function laboratory. *Eur J Echocardiogr* 2008;9:381–3. doi:10.1016/j.euje.2007.06.013

34 Kobal SL, Trento L, Bahrami S, et al. Comparison of effectiveness of hand-carried ultrasound to bedside cardiovascular physical examination. *Am J Cardiol* 2005;96:1002–6.

35 Liebe M, Israel RL, Lillie EO. Pocket mobile echocardiography: the next-generation stethoscope? A comparison of rapidly acquired PME images to standard TTE. *Ann Intern Med* 2011;155:33–8. doi:10.7326/0003-4819-151-1-201107050-00005

36 López-Palmero S, Bolivar-Herrera N, López-Lloret G, et al. Diagnostic utility of handheld ultrasonography as an extension of the physical examination of patients with heart failure. *Rev Clin Esp* 2015;215:204–10.

37 Lucas BP, Candotti C, Magenta B, et al. Diagnostic accuracy of hospitalist-performed hand-carried ultrasound echocardiography after a brief training program. *J Hosp Med* 2009;4:340–9. doi:10.1002/jhm.438

38 Lucas BP, Candotti C, Magenta B, et al. Hand-Carried echocardiography by hospitalists: a randomized trial. *Am J Med* 2011;124:766–74.

39 Martin LD, Howell EE, Ziegelstein RC, et al. Hand-carried ultrasound performed by hospitalists: does it improve the cardiac physical examination? *Am J Med* 2009;122:35–41.

40 Mehra M, Jacobson T, Peters D, et al. Handheld ultrasound versus physical examination in patients referred for transthoracic echocardiography for a suspected cardiac condition. *JACC Cardiovascular Imaging* 2014;7:983–90.

41 Mjølstad OC, Andersen GN, Dalen H, et al. Feasibility and reliability of point-of-care pocket-size echocardiography performed by medical residents. *Eur J Heart Cardiovascular Imaging* 2013;14:1195–202.

42 Nilsson G, Söderström L, Alferink L, et al. Hand-Held cardiac ultrasound examinations performed in primary care patients by nonexperts to identify reduced ejection fraction. *BMC Med Educ* 2019;19:282.

43 Olesen LL, Andersen A, Thaulow S. Hand-Held echocardiography is useful for diagnosis of left systolic dysfunction in an elderly population. *Dan Med J* 2015;62:A5100.

44 Perez-Arumah G, Kobal SL, Etzioni Q, et al. Left ventricular geometric abnormality screening in hypertensive patients using a hand-held ultrasound device. *J Clin Hypertens* 2010;12:181–6.

45 Razi R, Estrada JR, Doll J, et al. bedside hand-held ultrasound by internal medicine residents versus traditional clinical assessment for the identification of systolic dysfunction in patients admitted with decompensated heart failure. *J Am Soc Echocardiography* 2011;24:1319–24.

46 Ruddox V, Stokke TM, Edvardsen T, et al. The diagnostic accuracy of pocket-size cardiac ultrasound performed by unselected residents with minimal training. *Int J Cardiovascular Imaging* 2013;29:1749–57.

47 Vignon P, Frank MB, Lesage J, et al. Hand-held echocardiography with Doppler capability for the assessment of critically-ill patients: is it reliable? *Intensive Care Med* 2004;30:718–23.

48 Vousouci EC, Schinkel AF, Roelandt JRTC, et al. Screening for left ventricular dysfunction using a hand-carried cardiac ultrasound device. *Eur J Heart Fail* 2003;5:767–74.

49 Weijer-Milk P, Kasprzak JD, Filipiak-Strecca D, et al. Personal mobile device-based pocket echocardiography-The diagnostic value and clinical utility. *Adv Med Sci* 2019;64:157–61.

50 Xie T, Chamoun A J, McCulloch M, et al. Rapid screening of cardiac patients with a miniaturized hand-held ultrasound imager—comparisons with physical examination and conventional two-dimensional echocardiography. *Clin Cardiol* 2004;27:241–5. doi:10.1022/clic.4962070414
HUD MA Supplementary Material

Search terms used in MA

Medline

|   | Search Term                                                                 | Results  |
|---|-----------------------------------------------------------------------------|----------|
| 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

|   | Search Term                                                                 | Results  |
|---|-----------------------------------------------------------------------------|----------|
| 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      |
| Biag 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      |
| Study                | Methodology                        | LVEF Criteria | LVEF | P | A | C | F |
|---------------------|-----------------------------------|---------------|------|---|---|---|---|
| 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  |
| Mjolstad 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  |
| Study            | Methodology                          | Method Details                                                                 | LVEF % | 72 | 101 | 59 | 92 | 67 | 79 | 85 |
|------------------|--------------------------------------|--------------------------------------------------------------------------------|--------|----|-----|----|----|----|----|----|
| Stokke (exp) 2014| Visual estimation of LV systolic function | LVEF <45%                                                                     |        |    |     |    |    |    |    |    |
| 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**

| Study            | Methodology                          | Method Details                                                                 | Presence | 374| 124 | 97 | 88 | 82 | 94 | 65 |
|------------------|--------------------------------------|--------------------------------------------------------------------------------|----------|----|-----|----|----|----|----|----|
| Bruce 2002       | Qualitative assessment               | Present                                                                        |          |    |     |    |    |    |    |    |
| 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 |
| Study          | Description                                                                 | Present | 97 | 80 | 10 | 60 | 94 | 60 | 94 |
|---------------|------------------------------------------------------------------------------|---------|----|----|----|----|----|----|----|
| 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**

| Study | Description | Yes/No | SE = LV dilation >55mm | 151 | 151 | 8 | 94 | 96 | 57 | 100 |
|-------|-------------|--------|------------------------|-----|-----|---|----|----|----|-----|
| 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 |
| Study                      | Methodology                  | Criteria                          | Values   |
|---------------------------|------------------------------|-----------------------------------|----------|
| 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 >=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 >=13mm             | 562 540 31 94 93 45 99.6         |
| Galasko 2003              | IVS or PW >=12mm             | 562 540 55 82 96 69 98           |
| Giusca 2010               | End-diastolic thickness of interventricular septum >=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>=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 >=12mm | 322 314 33 70 73 23 95           |
| Lucas 2011                | Posterior/septal wall thickness >=1.4 (M), >=1.3 (F) | 210 209 34 50 68 23 88           |
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:**

| Study            | Parameter                  | Value     | Value     | Value | Value | Value | Value | Value | Value |
|------------------|----------------------------|-----------|-----------|-------|-------|-------|-------|-------|-------|
| Perez-Avraham    | IVS or PW                  | IVS>=11.7, | PW>=9.8   | 85    | 85    | 18    | 100   | 99    | 95    | 100   |
| (2010)           |                            |           |           |       |       |       |       |       |       |
| Senior 2004      | LVMI                       | >134gm2/m2 | (M), 110 (F) | 189   | 179   | 46    | 72    | 91    | 73    | 90    |
| Vourvouri 2002   | LVMI                       | >134gm2/m2 | (M), 110 (F) | 100   | 100   | 18    | 83    | 96    | 79    | 96    |
| Xie 2006         | Septal wall thickness      | >=12mm    |           | 100   | 100   | 41    | 80    | 93    | 89    | 87    |
- 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.
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.

**Figure 1.** Tabulated and graphical displays for QUADAS-2 results.
| Study               | Patient Sampling | Index Test | Reference Test | Flow and Timing |
|--------------------|------------------|------------|----------------|-----------------|
| Aldaas 2019        | +                | (1)        | (+)            | (+)             |
| Alexander 2004     | (1)              | (+)        | (+)            | (+)             |
| Biais 2012         | +                | (1)        | (+)            | (+)             |
| Bruce 2002         | +                | (1)        | (+)            | (+)             |
| Coletta 2006       | +                | (1)        | (+)            | (+)             |
| Cullen 2013        | +                | (1)        | (+)            | (+)             |
| DeCara 2003        | +                | (1)        | (+)            | (+)             |
| Fedson 2003        | +                | (1)        | (+)            | (+)             |
| Galasko 2003       | +                | (1)        | (+)            | (+)             |
| Giusca 2010        | +                | (1)        | (+)            | (+)             |
| Gulic 2016         | +                | (1)        | (+)            | (+)             |
| Khan 2014          | +                | (1)        | (+)            | (+)             |
| Kobal 2005         | +                | (1)        | (+)            | (+)             |
| Liebo 2011         | +                | (1)        | (+)            | (+)             |
| Lopez-Palmero 2015 | +                | (1)        | (+)            | (+)             |
| Lucas 2009         | +                | (1)        | (+)            | (+)             |
| Lucas 2011         | +                | (1)        | (+)            | (+)             |
| Martin 2009        | +                | (1)        | (+)            | (+)             |
| Nilsson 2019       | +                | (1)        | (+)            | (+)             |
| Olsen 2015         | +                | (1)        | (+)            | (+)             |
| Perez-Avraham 2010 | +                | (1)        | (+)            | (+)             |
| Ruddox 2013        | +                | (1)        | (+)            | (+)             |
| Weijer-Mik 2019    | +                | (1)        | (+)            | (+)             |
| Xie 2006           | +                | (1)        | (+)            | (+)             |
| Vignon 2004        | +                | (1)        | (+)            | (+)             |

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

1. Macaskill P, Gatsonis C, Deeks J, Harbord R, Takwoingi Y. Cochrane Handbook for Systematic Reviews of Diagnostic Test Accuracy. :61.

2. Shim SR, Kim S-J, Lee J. Diagnostic test accuracy: application and practice using R software. Epidemiol Health [Internet]. 2019 Mar 28 [cited 2021 Mar 26];41. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6545496/

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.