

1 **Title page**

2 **Title: A systematic review and meta-analysis of transthoracic echocardiogram versus**
3 **cardiac magnetic resonance imaging for the detection of left ventricular thrombus**

4
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21 diagnosis; screening; sensitivity and specificity

22

1 Abstract

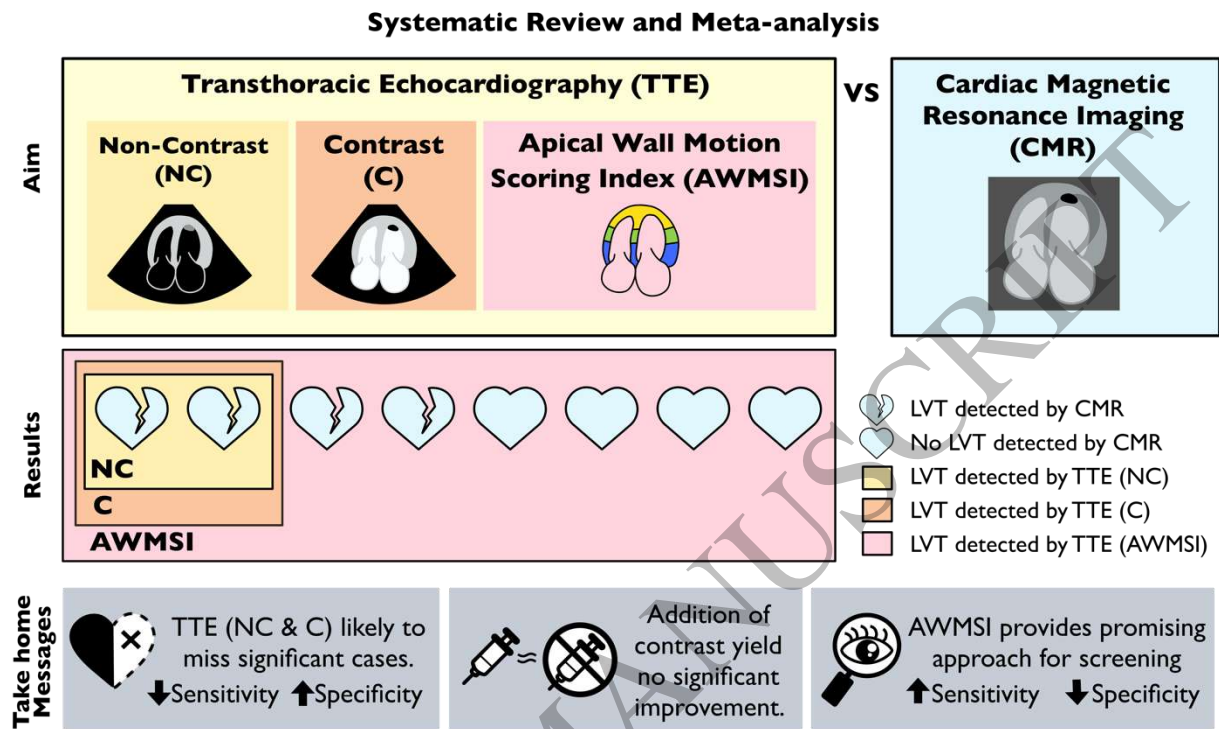
2 **Background:** Transthoracic echocardiography (TTE) is the most commonly used imaging
3 modality to diagnose left ventricular thrombus (LVT), however cardiac magnetic resonance
4 (CMR) remains the gold standard investigation. Comparison of the diagnostic performance
5 between two modalities is needed to inform guidelines on a diagnostic approach towards
6 LVT.

7
8 **Methods:** We performed a systematic review and meta-analysis to investigate the
9 diagnostic performance of three methods of TTE (non-contrast, contrast, and apical wall
10 motion scoring) for the detection of LVT compared to CMR as a reference test.

11
12 **Results:** Studies comprising 2113 patients investigated for LVT using both TTE and CMR
13 were included in the meta-analysis. For non-contrast TTE, pooled sensitivity and specificity
14 was 47% [95% confidence interval (CI): 32-62%], and 98% [95% CI: 96-99%] respectively. In
15 contrast TTE pooled sensitivity and specificity values were 58% [95% CI: 46-69%], and 98%
16 [95% CI: 96-99%] respectively. Apical wall motion scoring on non-contrast TTE yielded a
17 sensitivity of 100% [95% CI: 93-100%] and a specificity of 54% [95% CI: 42-65%]. The area
18 under the curve (AUC) values from our summary receiver operating characteristic curve
19 (SROC) for non-contrast and contrast TTE were 0.87 and 0.86 respectively, with apical wall
20 motion studies having the highest AUC of 0.93.

21
22 **Conclusions:** Despite high specificity, routine contrast and non-contrast TTE are likely to
23 miss a significant number of LVT, making it a suboptimal screening tool. The addition of
24 apical wall motion scoring provides a promising method to reliably identify patients requiring
25 further investigations for LVT, whilst excluding others from unnecessary testing.

1 Graphical abstract



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1 Highlights

- 2 1. Non-contrast and contrast TTE have high specificity compared to CMR (98% [95%
3 CI: 96-99%]) but is likely to miss a significant number of LVT due to low sensitivity
4 (47% [95% CI 32-62%] and 58% [95% CI: 46-69%] respectively).
- 5 2. This study did not find significant improvement in sensitivity and specificity of contrast
6 TTE compared to non-contrast TTE.
- 7 3. The addition of apical wall motion scoring to routine non-contrast TTE is a promising
8 approach to reliably screen for patients who require further investigations for LVT,
9 with a sensitivity and specificity value of 100% [95% CI: 93-100%], and 54% [95% CI:
10 42-65%] respectively.

ACCEPTED MANUSCRIPT

1 Lay summary

2 The formation of left ventricular thrombus (LVT), a blood clot in the left pumping
3 chamber of the heart, can lead to serious complications such as a stroke. Whilst cardiac
4 magnetic resonance (CMR) is the best imaging tool to detect these clots, the most used tool
5 is a transthoracic echocardiogram (TTE), which visualizes the heart by placing an ultrasound
6 on the chest. This is due to the affordability and widespread availability of TTE. Thus, it is
7 important to know how TTE compares to CMR when it comes to detecting LVT.

8
9 This study pools the results of previous research to compare the diagnostic
10 performance of three different methods of TTE compared to CMR for detecting LVT.

- 11 1. Non-contrast TTE.
- 12 2. Contrast TTE: The addition of an enhancing dye thought to improve imaging.
- 13 3. Apical wall motion scoring: Evaluating the movement of the heart's walls using TTE.

14
15 Our results show that current methods of TTE may miss half of the patients with LVT, and
16 that the use of contrast did not provide significant improvement. Interestingly, the use of
17 apical wall motion scoring was able to accurately detect all the patients with LVT. This shows
18 promise as a future tool to reliably exclude patients from unnecessary testing, whilst
19 identifying those who need further investigations.

20

1 Introduction

2 Left ventricular thrombus (LVT) is an important complication of cardiac disorders
3 such as severe ischaemic and non-ischaemic cardiomyopathy, and is associated with a
4 significant risk of embolic events such as stroke(1): 2.5% to 15% of patients with acute
5 myocardial infarction (AMI) develop LVT. There is a significantly increased risk of major
6 adverse cardiovascular events at one year in LVT vs non-LVT patients (36% vs 5.8%) driven
7 by systemic embolization and stroke (20% in LVT vs 2.1% in non-LVT patients)(2). The
8 detection of LVT is therefore critical for the management of patients with cardiac diseases,
9 as it can help guide management of antithrombotic treatment to improve patient outcomes.

10

11 Two imaging modalities commonly used for the detection of LVT are transthoracic
12 echocardiography (TTE) and cardiac magnetic resonance imaging (CMR). Key imaging
13 characteristics of LVT in both CMR and TTE are summarised in supplementary figure 1. TTE
14 is widely available, non-invasive, and has a relatively low cost, while CMR offers superior
15 spatial resolution and tissue characterization (3, 4). Non-contrast echocardiography is the
16 most used imaging modality to detect LVT, and its use is recommended in guidelines by the
17 European Society of Cardiology and the American Heart Association (5, 6). Additionally,
18 widespread use of CMR is impractical due to limited availability of the technique alongside
19 significant costs. However, TTE has a lower sensitivity than CMR (when surgical or
20 pathological validation of LVT is used as the index test) (7). This brings into question
21 whether TTE can serve as an alternative to CMR as a diagnostic tool, and how clinicians
22 should determine who to refer to CMR.

23

24 There have been several studies comparing the diagnostic accuracy of TTE versus
25 CMR for the detection of LVT (7, 8, 9). Notably, a previous meta-analysis of studies
26 published before May 2020 (8) reported TTE as a reasonable alternative to CMR. However,
27 this study was limited by the fact that results from both contrast and non-contrast TTE were

1 combined, making it difficult to interpret the findings. The use of echocardiography-
2 enhancing contrast agents has been recommended to increase the sensitivity of LVT
3 detection, but evidence on its diagnostic utility is mixed (6). Additionally, whilst calculation of
4 the wall motion score index is classically used to investigate left regional contractile
5 dysfunction (10), apical wall motion scoring applied to routine non-contrast TTE has been
6 proposed as a potential screening test for LVT(11) [infographic on Supplementary Figure 1].
7 Therefore, a comprehensive assessment of the diagnostic performance of these three
8 applications of TTE compared to CMR as a reference is needed.

9
10 This paper provides an updated meta-analysis comparing the diagnostic
11 performance of non-contrast and contrast TTE versus CMR separately for the detection of
12 LVT in patients with cardiac disease. We also further investigate the diagnostic performance
13 of apical wall motion scoring versus CMR for the detection of LVT. The results of this meta-
14 analysis will help inform future guidelines on the diagnostic algorithm for LVT, and hopefully
15 will bring attention to the need of more primary research on this important topic.

16 2 Methods

17 In this study, we aimed to evaluate the diagnostic yield of LVT using various forms of
18 TTE, including contrast, non-contrast, and apical wall motion scoring, compared to CMR as
19 a reference standard. We followed the Preferred Reporting Items for Systematic Reviews
20 and Meta-Analyses (PRISMA) guidelines to conduct a systematic review and meta-analysis
21 of original research studies (12).

22
23 The primary outcome of interest was the sensitivity and specificity of TTE compared to
24 CMR for the detection of LVT. Additionally, we examined secondary diagnostic accuracy
25 measures such as the area under curve (AUC) value of the summary receiver operating

1 characteristic (SROC) curve, diagnostic odds ratio (DOR), and positive and negative
2 likelihood ratios (LR+ and LR-).

3

4 **2.1 Eligibility Criteria**

5 The following are the inclusion criteria for the relevant studies:

6 1) Studies including adult patients who are at high risk of developing LVT, such as
7 those with left ventricular ejection fraction <50%, or patients post-MI.

8 2) The study must assess thrombosis in the left ventricle.

9 3) Studies evaluating the diagnostic yield of TTE compared to CMR.

10 4) The study must report the sensitivity and specificity of the diagnostic test.

11 5) Study is an original work written in English.

12 Any studies which do not meet the above criteria, such as case reports, commentaries,
13 review articles will be excluded.

14

15 **2.2 Information sources and Search strategy**

16 We conducted a comprehensive search of the Ovid Medline and EMBASE databases
17 from January 1, 1960, to May 1st, 2023. Details on our search strategy can be seen in
18 Supplementary Table 1. Additionally, we reviewed the reference lists of relevant meta-
19 analyses and review papers to identify potential articles.

20

21 **2.3 Study selection process**

22 Rayyan was utilized to manage and organize the selected abstract and article
23 information. To ensure a thorough selection process, five independent investigators (YP, YT,
24 JW, SS, SU) conducted a screening of study titles and their abstracts, with a minimum of two
25 investigators screening each study. Eligibility assessment was made by a minimum of two
26 investigators on the full texts from the studies that passed screening. In instances where
27 discrepancies arose, consensus was reached through a discussion with other co-authors
28 (YP, YT).

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2.4 Data collection process

Data collection involved extracting diagnostic test accuracy parameters for three different modalities of TTE in comparison to CMR. Specifically, contrast TTE, non-contrast TTE, and apical wall motion studies on non-contrast TTE were analysed. From each study, four key parameters were collected for TTE versus CMR in diagnosing LVT: 1) true positive, 2) false positive, 3) true negative, and 4) false negative values. These values were then reported along with sensitivity and specificity results. Additional data points, including the type of CMR imaging utilized as a reference, the time interval between TTE and CMR, and patient demographics such as age, male percent (%) were collected. Patient data on cardiovascular risk factors (hypertension, hypercholesterolemia, diabetes mellitus, tobacco use) and medications (aspirin, beta-blockers, angiotensin-converting enzyme inhibitors/angiotensin receptor blockers, statins, loop diuretics) was also collected. All data was collected using a standardized proforma, reviewed by at least two independent reviewers. In cases where certain data was not reported in a study, it was assumed to be missing at random.

2.5 Risk of bias and applicability

The Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2) was used to evaluate the risk of bias and applicability of included studies(13). Signalling questions were tailored to our study, and two independent reviewers assessed all included studies using the tool. In cases of discrepancies, a consensus was reached through discussion with other co-authors.

2.6 Synthesis of results

We conducted three separate meta-analyses for non-contrast TTE, contrast TTE, and apical wall motion scoring. Quantitative analysis was performed using R studio (Version 2022.12.0+353). For the meta-analysis, the metaprop function was used, whilst meta-

1 regression analysis was performed using the metareg function. A random effects model was
2 used to conduct our univariate analysis. A forest plot with corresponding 95% confidence
3 intervals (95% CI) was used to represent the sensitivities and specificities of each modality.
4 The I^2 statistic was used to determine between-study heterogeneity. We defined the
5 thresholds for low, moderate, and high levels of heterogeneity with an I^2 value of 25%, 50%,
6 and 75% respectively(14). The reitsma function was used for our bivariate analysis, which
7 implements the Reitsma model, demonstrated by Harbord et al 2007 to be equivalent to the
8 hierarchical SROC model of Rutter and Gatsonis 2001 (15, 16, 17). This was done to obtain
9 an SROC curve, which illustrates the DOR and accuracy of the tests. This model accounted
10 for both within- and between-study heterogeneity. A weighted average and standard
11 deviation were used to present pooled patient data.

12

13 **2.7 Heterogeneity analysis**

14 We conducted a sensitivity analysis on the non-contrast and contrast TTE group
15 using the leave-one-out study approach to explore the sources of heterogeneity in study
16 outcomes. Furthermore, we performed a subgroup analysis on non-contrast TTE studies
17 using meta-regression to identify potential contributors to heterogeneity. The subgroup
18 analysis was based on three factors: 1) CMR type, 2) indication for LVT imaging, and 3)
19 study population size.

20 **3 Results**

21 **3.1 Study selection**

22 Abstract screening was performed on 306 unique citations. Subsequently, 22 studies
23 were assessed via full text screening. A total of 11 studies were included in our quantitative
24 analysis (Supplementary Figure 2).

25

1 **3.2 Baseline characteristics**

2 In the pooled population of 2113 patients from included studies, mean age was 58.2
3 ± 12.8 years, with a 78.0 $\pm 9.3\%$ male predominance. Time between imaging modalities was
4 reported to be within seven days for all studies, with six studies performing both within 24
5 hours of each other. The pooled cohort included patients investigated for LVT using TTE and
6 CMR, indicated due to severe heart failure or following AMI. Study characteristics can be
7 found in Table 1, with results of individual studies in Supplementary Table 2. Patient data on
8 cardiovascular risk factors and medication history are presented in Table 2. Ten studies with
9 2019 patients were included for the analysis of non-contrast TTE vs CMR, whilst the contrast
10 TTE vs CMR group included four studies with 542 patients. Two studies comprising of 275
11 patients were included for apical wall motion scoring on non-contrast TTE.

13 **3.3 Risk of bias and Applicability**

14 Of the 11 studies included, nine were found to be of low risk of bias. Sürder 2015
15 (18) was classified as high risk because operators of TTE were not blinded to CMR results.
16 Garg 2012 and Chaosuwannakit 2021 were classified as unclear risk, as information
17 relevant to our risk of bias assessment was unavailable (19, 20). A tabular representation of
18 the results of our QUADAS2 assessment is on Supplementary Table 3.

19 **3.4 Results of synthesis**

20 ***3.4.1 Non-contrast TTE vs CMR***

21 In our meta-analysis of non-contrast TTE vs CMR (10 studies), pooled sensitivity and
22 specificity values were 47% [95% CI 32-62%, $I^2=56\%$, $p=0.02$; Figure 1a], and 98% [95% CI:
23 96-99%, $I^2=67\%$, $p<0.01$; Figure 1b] respectively. Pooled DOR was 24.8 [95% CI, 11.6-
24 46.9], with pooled LR+ and LR- being 14.0 [95% CI, 7.63-23.5] and 0.58 [95% CI, 0.47-0.69]
25 respectively. The shape of the bivariate SROC curve (Supplementary Figure 3a) and an
26 AUC of 0.87 suggests good discriminative capacity.

27

1 **3.4.2 Contrast TTE**

2 Pooled comparison of contrast TTE vs CMR (4 studies) showed pooled sensitivity
3 and specificity values of 58% [95% CI: 46-69%, $I^2=0\%$, $p=0.41$; Figure 2a], and 98% [95%
4 CI: 96-99%, $I^2=23\%$, $p=0.27$; Figure 2b] respectively. Pooled DOR was 60.9 [95% CI: 15.6-
5 165], with pooled LR+ and LR- being 24.5 [95% CI, 8.34-56.6] and 0.43 [95% CI, 0.30-0.58]
6 respectively. The shape of the bivariate SROC curve (Supplementary Figure 3b) and an
7 AUC of 0.86 suggests similar discriminative capacity compared to non-contrast TTE.
8

9 **3.4.3 Apical wall motion studies applied to non-contrast TTE**

10 Meta-analysis comparing the diagnostic yield of apical wall motion scoring applied to
11 non-contrast TTE versus CMR (2 studies) showed a sensitivity and specificity values of
12 100% [95% CI: 93-100%, $I^2=0\%$, $p=1.00$; Figure 3a], and 54% [95% CI: 42-65%, $I^2=82\%$,
13 $p=0.02$; Figure 3b] respectively. Pooled DOR was 60.3 [95% CI, 3.15-299], with pooled LR+
14 and LR- being 2.08 [95% CI, 1.39-3.12] and 0.11 [95% CI, 0.01-0.45] respectively. The
15 shape of the bivariate SROC curve (Supplementary Figure 3c) and an AUC of 0.93 suggests
16 better discriminative capacity than both contrast and non-contrast TTE despite its lower
17 specificity.
18

19 **3.5 Investigation of heterogeneity**

20 **3.5.1 Sensitivity analysis for non-contrast and contrast TTE**

21 A leave-one-out analysis for non-contrast TTE vs CMR (Supplementary Table 4)
22 resulted in pooled sensitivity ranging from 39% - 49%, whilst pooled specificity had a small
23 range of 97-98%. Exclusion of Sürder 2015 (18), which had a high risk of bias, resulted in a
24 pooled sensitivity and specificity of 43% [95% CI: 30-58%, $I^2=48\%$] and 98% [95% CI: 96-
25 99%, $I^2=71\%$], which was not significantly different to the original pooled effect sizes. Whilst
26 the exclusion of this study resulted in a lower I^2 value, heterogeneity was still considered to
27 be at moderate to borderline-high levels. Similarly, exclusion of studies of unclear risk of bias
28 (Garg 2012 and Chaosuwanakit 2021) did not significantly impact on the effect size or

1 heterogeneity of both sensitivity and specificity for non-contrast TTE (19, 20). Meurin et al
2 2015 was the greatest contributor of heterogeneity in sensitivity results, with its exclusion
3 leading to an I^2 of 21% along with the greatest decrease in pooled sensitivity at 39% [95%CI:
4 33%-46%] (21). Our sensitivity analysis on contrast TTE (Supplementary Table 5) resulted in
5 pooled sensitivity from 55% - 64%, and specificity from 97-99%. Interestingly, the exclusion
6 of Garg et al 2012, which had an unclear risk of bias, led to a sensitivity of 64% [95% CI:
7 50%-76%](19). Thus, whilst pooled sensitivity for contrast and non-contrast TTE was not
8 significantly different, the exclusion of outlier studies such as Meurin et al 2015 and Garg et
9 al 2012 led to a significant improvement in the pooled sensitivity of contrast TTE compared
10 to non-contrast TTE(19, 21).

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3.5.2 Subgroup analysis

The indication for LVT imaging was found to have a significantly impact on specificity for non-contrast TTE. Studies investigating non-contrast TTE vs CMR in post-AMI patients were more likely to yield higher specificity results (coefficient = 1.4, $p < 0.05$) compared to other indications. No significant results were found for the remaining subgroups. In all subgroups, the test for residual heterogeneity was significant ($p < 0.05$). Further subgroup analysis with patient cardiovascular risk factors and medication use was not done due to missing data.

4 Discussion

4.1 Summary of Evidence

To the best of our knowledge, this is the first meta-analysis evaluating the diagnostic yield of 3 different modalities of TTE for the diagnosis of LVT. Our assessment is important to inform future guidelines on the diagnostic approach for LVT, where TTE is used as a potential screening tool to stratify patients requiring further investigations. We aim to build upon a previous meta-analysis by performing the analysis of contrast and non-contrast TTE studies separately, as well as investigating apical wall motion scoring as a potential screening tool for LVT (8).

Whilst both non-contrast and contrast TTE studies showed very high pooled specificity of 98% (95% CI: 96-99%) for LVT compared to CMR, they suffer from low pooled sensitivity values (47% [95% CI: 32-62%] and 58% [95% CI: 46-69%] respectively). This suggests that both non-contrast and contrast TTE is likely to miss approximately half of LVT in patients. Interestingly, contrast TTE did not significantly improve sensitivities for LVT compared to non-contrast TTE. Similarly, there were no significant differences between the pooled DOR, LR+ and LR- values of contrast and non-contrast TTE studies. Additionally,

1 bivariate SROC curves and AUC values for contrast and non-contrast TTE (0.86 and 0.87
2 respectively) indicates similar discriminative capacity.

3

4 The use of contrast-echocardiography, especially post-AMI, is not without its risks.
5 Contrast-echocardiography with Sonovue is contraindicated in patients with recent acute
6 coronary syndrome, or in patients with clinically unstable ischaemic heart disease (22).
7 Current recommendations by the American Heart Association on the diagnosis of LVT
8 support the use of contrast TTE to improve diagnostic sensitivity for LVT(6). Our study
9 suggests that the use of contrast TTE provides limited utility for the diagnosis of LVT in
10 terms of sensitivity and specificity.

11

12 In studies applying apical wall motion scoring to non-contrast TTE, pooled sensitivity
13 compared to CMR was significantly higher than routine contrast and non-contrast studies at
14 100% [95% CI: 93-100%]. However, pooled specificity was significantly reduced at 54%
15 [95% CI: 42-65%]. This suggests that despite the risks of falsely diagnosing patients with
16 LVT, apical wall motion scoring on non-contrast TTE may reliably exclude those without
17 LVT. This was reflected in reduced LR+ and LR- values, whilst no significant difference was
18 seen in the DOR. Bivariate analysis of apical wall motion studies yielded the highest AUC
19 (0.93) of the three modalities investigated. Differences in specificity results for apical wall
20 motion studies seen between Weinsaft et al 2016 (cut-off score of ≥ 5) and Kim et al 2017
21 (cut-off score of ≥ 3) may be attributed to the different cut-off scores used for diagnosis of
22 LVT(11, 23). However, we were unable to do a subgroup analysis to further investigate this
23 due to the limited number of primary studies on apical wall motion scoring and LVT
24 detection.

25

26 LVT is typically identified on TTE through direct visualization of the echo-dense
27 mass, which most likely contributes to the high specificity seen in our analysis (24).
28 However, it suffers from poor sensitivity, possibly due to poor image quality or smaller LVT

1 size (25). The addition of apical wall motion scoring on routine non-contrast TTE removes
2 the need to directly visualize LVT and provides a promising approach to reliably stratify
3 patients at risk of LVT and exclude patients from unnecessary further testing. A diagnostic
4 approach using apical wall motion scoring for LVT following AMI was recently proposed by
5 Camaj et al 2022(25). A potential approach in LVT diagnosis could incorporate the
6 diagnostic criteria of routine TTE studies with the apical wall motion cut-off score for risk
7 stratification. This may provide high specificity when LVT can be diagnosed through direct
8 visualisation, whilst utilising the high sensitivity of apical wall motion scoring to identify
9 individuals who may require further investigations with CMR for LVT which are not directly
10 visible via TTE.

11
12 The prognostic utility of using apical wall motion scoring as a screening tool for LVT
13 has yet to be evaluated (26). A cohort study comparing embolic outcomes between patients
14 who had LVT detected on CMR but not echocardiography versus LVT detected by both
15 found no significant difference in the cumulative incidence of embolic events(26). Thus, more
16 studies are needed to investigate if the usage of apical wall motion scoring would
17 significantly improve clinical outcomes of patients whose LVT would have been missed on
18 routine TTE. Additionally, due to inconsistencies in the cut-off scores used, it is unclear as to
19 what degree of apical wall motion abnormality should be considered a significant risk factor
20 to the development of LVT. According to the wall motion scoring index (supplementary figure
21 1), a single segment akinesia or dyskinesia would have a score of 3 and 4 respectively,
22 which would have met the threshold for Kim et al 2017 but not Weinsaft et al 2011(7, 10, 11,
23 23, 27, 28). Thus, further studies are required to further understand how different degrees of
24 severity for apical wall motion abnormalities are associated with an increased risk of
25 developing LVT.

26
27 Whilst apical wall motion scoring displayed 100% sensitivity compared to CMR, it is
28 important to consider that TTE methods can be limited by suboptimal acoustic windows,

1 which is an inherent limitation compared to using CMR in LVT diagnosis. In the context of
2 this analysis, none of the two studies investigating apical wall motion scoring reported any
3 patient exclusions due to suboptimal acoustic windows(11, 23). However, given the relatively
4 small sample size of this analysis, further research ensuring to include patients despite
5 suboptimal acoustic windows may yield lower sensitivity values seen thus far. Nonetheless,
6 whilst apical wall motion scoring was never likely to match CMR as a gold standard imaging
7 test for LVT, the issue of acoustic windows should not detract from its potential as a
8 promising screening test compared to routine contrast and non-contrast TTE.

9
10 Our sensitivity analysis found that most of the heterogeneity in the sensitivity and
11 specificity of non-contrast TTE results could be attributed to one or two outlier studies. It also
12 suggests that the lack of significant difference in the pooled diagnostic performance between
13 contrast and non-contrast studies may be attributed to outlier studies. However, the reasons
14 for such different results are uncertain. Additionally, whilst our subgroup analysis suggests
15 that specificity in non-contrast TTE improved for post-AMI patients, the reasons for this are
16 unclear. Thus, further studies are needed to clarify sources of heterogeneity seen here, and
17 to verify if contrast TTE truly provides diagnostic benefit over non-contrast TTE.

18 19 **4.2 Limitations**

20 The main limitation of our study is the small number of primary studies included in the
21 analysis for contrast TTE and apical wall motion studies, thus reducing the power and
22 certainty of our results. Whilst there are other existing studies on the imaging of cardiac
23 thrombus, many did not meet the inclusion criteria detailed above. For example, some
24 studies did not perform a direct comparison between TTE and CMR on the same patient or
25 may have failed to report values such as the sensitivity and specificity for LVT diagnosis.
26 More primary studies would be needed to confidently identify how contrast TTE affects
27 diagnostic performance, as well as testing for apical wall motion studies to understand
28 whether such high sensitivity levels can be replicated. Additionally, due to inconsistency in

1 patient demographic data reported in each study, we were unable to perform a subgroup
2 analysis due to the missing data. Increased reporting of baseline characteristics within these
3 studies would have enabled a more comprehensive subgroup analysis.

4
5 Another limitation was the lack of anatomical reference standards from cardiac
6 surgery or forensic examination, as well as the pooling of studies using different forms of
7 CMR as a reference standard. However, our subgroup analysis based on the CMR modality
8 used as a reference in the studies included did not find a significant difference between
9 modalities. Despite this, a future analysis with more primary studies is required to verify this.

10

11 5 Conclusions

12 Both contrast and non-contrast TTE have good specificity compared to CMR but are
13 suboptimal as a screening test to reliably exclude patients without LVT. The addition of
14 contrast was not found to improve diagnostic performance compared to non-contrast TTE,
15 suggesting reduced utility in clinical practice. Apical wall motion scoring applied to non-
16 contrast TTE has lower specificity, yet it represents a promising screening tool to identify
17 patients requiring further investigations. Further studies are encouraged to validate the
18 findings of our analysis, which may involve investigating contrast and non-contrast TTE
19 alongside apical wall motion scoring for the diagnosis of LVT in a large patient population.

20 6 Funding

21 No funding to declare.

22 7 Conflict of interest

23 Nothing to disclose

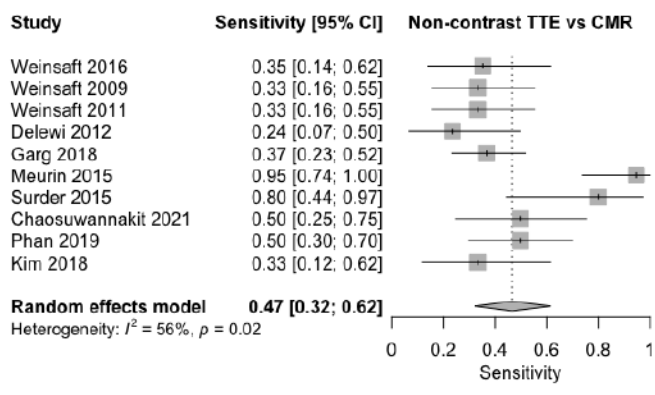
1 Figures and Tables

Study, year	Patients (n)	Age \pm std	Male %	Population*	Reference standard	Technique used**	Time between imaging modalities
Weinsaft 2016 (11)	201	56 \pm 12	84.1	A	DE-CMR	1 + 2	24 hours
Weinsaft 2009 (3)	121	61.2 \pm 13.3	76.9	B	DE-CMR	1 + 2	within 7 days
Weinsaft 2011 (27)	243	60 \pm 15	63.4	C	DE-CMR	1	within 7 days
Delewi 2012 (29)	194	56.1 \pm 9.4	84.9	A	cine-CMR	1	24 hours
Garg 2012 (19)	481	N/R	N/R	B	CE-CMR	1 + 2	within 7 days
Meurin 2015 (21)	78	59.1 \pm 12.1	72	A	DE-CMR	1	24 hours
Sürder 2015 (18)	113	56.8 \pm 10.2	88.3	A	LGE-CMR	1	24 hours
Chaosuwannakit 2021 (20)	206	60.2 \pm 14.2	68.4	C	LGE-CMR	1	
Kim 2017 (23)	74	54 \pm 11	91.2	A	DE-CMR	3	24 hours
Phan 2019 (30)	210	N/R	85	A	LGE-CMR	1	within 7 days
Kim 2014 (31)	192	N/R	N/R	A	DE-CMR	1+2	24 hours

2 Table 1: Study characteristics. *(A = post-MI, B = mixed [E.g., Post-MI, heart failure, stroke].
 3 C = left ventricular systolic dysfunction). **(1 = non-contrast TTE, 2 = contrast TTE, 3 =
 4 apical wall motion scoring). Data that was not reported (N/R) in the primary paper was
 5 assumed to be missing at random.

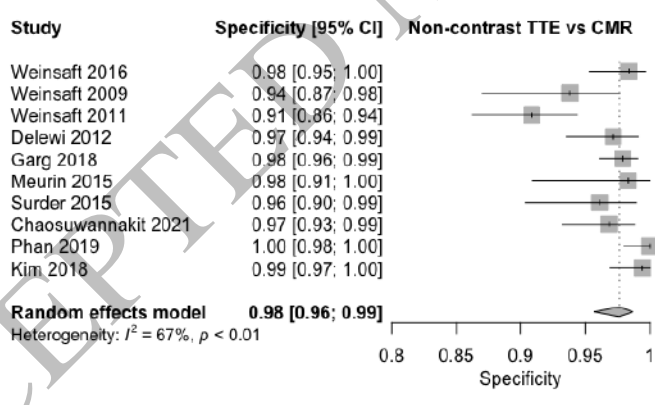
Study	Risk factors (%)					Medication history (%)				
	Hypertension	Hypercholesterolaemia	Diabetes Mellitus	Tobacco use	Aspirin	Beta-blockers	ACE/ARB*	Statins	Loop diuretic	
Weinsaft 2016 (11)	43.8	49.8	23.4	N/R	99.0	95.5	58.7	97.0	6.0	
Weinsaft 2009 (3)	66.9	88.4	33.1	33.1	85.1	77.7	66.9	79.3	16.5	
Kim 2017 (23)	47.3	45.9	24.3	27.0	97.3	98.6	73.0	94.6	N/R	
Weinsaft 2011 (27)	61.3	38.7	35.4	23.9	57.6	51.4	45.7	N/R	31.3	
Delewi 2012 (29)	27.8	19.6	6.2	46.9	96.4	N/R	N/R	N/R	N/R	
Garg 2012 (19)	N/R	N/R	N/R	N/R	N/R	N/R	N/R	N/R	N/R	
Meurin 2015 (21)	33.0	8.0	20.0	43.0	100.0	100.0	99.0	99.0	N/R	
Sürder 2015 (18)	41.8	41.2	10.7	58.2	97.3	91.1	85.7	99.1	33.9	
Chaosuwannakit 2021 (20)	N/R	N/R	N/R	N/R	76.2	N/R	N/R	N/R	N/R	
Phan 2019 (30)	47.1	45.7	19.5	57.6	N/R	94.3	82.9	97.6	7.1	
Kim 2014 (31)	N/R	N/R	N/R	N/R	N/R	N/R	N/R	N/R	N/R	

2 Table 2: Demographical characteristics. (N/R = data not reported in primary paper)



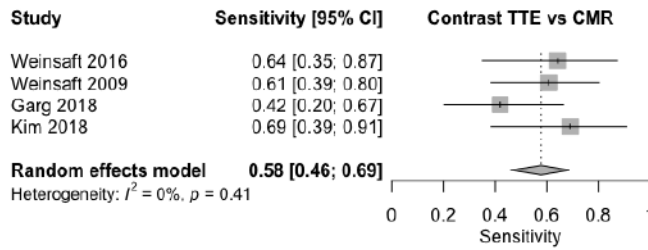
1

2 Figure 1a: Sensitivity of non-contrast TTE for the detection of LVT compared to CMR



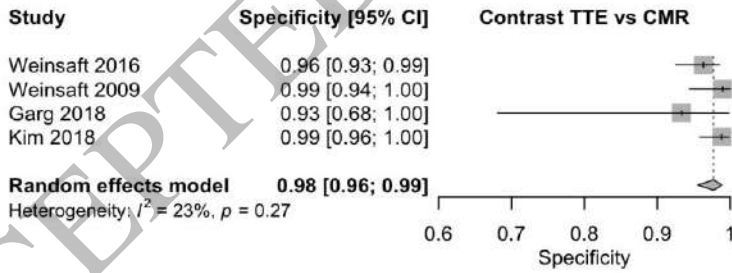
3

4 Figure 1b: Specificity of non-contrast TTE for the detection of LVT compared to CMR



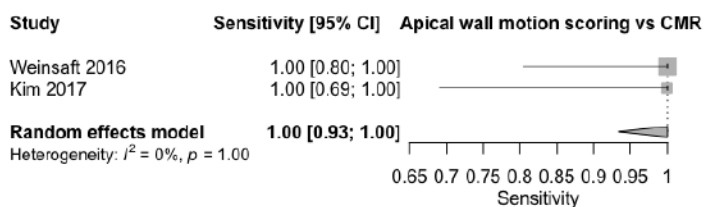
1

2 Figure 2a: Sensitivity of contrast TTE for the detection of LVT compared to CMR



3

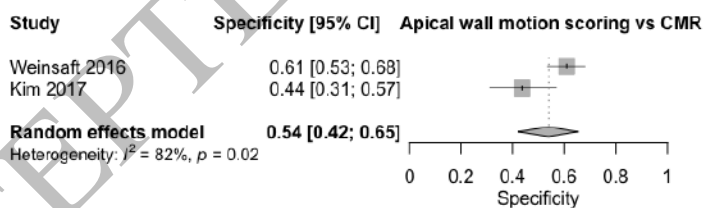
4 Figure 2b: Specificity of contrast TTE for the detection of LVT compared to CMR



1

2 Figure 3a: Sensitivity of apical wall motion scoring on non-contrast TTE for the detection of

3 LVT compared to CMR



4

5 Figure 3b: Specificity of apical wall motion scoring on non-contrast TTE for the detection of

6 LVT compared to CMR

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24 Data Availability Statement

25 The data underlying this article was derived from the following articles available in the public
26 domain –

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2 Contrast-Enhanced Anatomic Imaging as Compared to Contrast-Enhanced Tissue
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