

# Utility of Modern-era Transthoracic Echocardiography in Diagnostic Decision-Making for Complex Left-Sided Infective Endocarditis

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**Introduction:** Current infective endocarditis(IE) imaging pathways focus heavily on TOE, based on evidence from research ≥20 years ago. Despite a substantial improvement in TTE image resolution and transducer technology, there's a void of information to guide physician decision-making based on TTE. In Australian context this is particularly important in regional centres, reliant on TTE to triage urgency of transfer.

**Aim:** To evaluate modern era TTE diagnostic accuracy of Left Sided Endocarditis (LSE) pathology, utilising a novel disease classification

**Methods:** Retrospective analysis of 242 patients undergoing TTE, TOE ≤14 days from surgery, for native(Nv) or prosthetic(Pv) endocarditis pathology from May 2005-Dec 2017. Valve-level LSE pathology was classified i) on an 8-point pathology orientated ordinal scale and ii) into 3 categories: 0=no IE, 1=mimickers (nil or mimicker), 2=vegetation, 3=leaflet disruption (perforation, destruction, flail) +/- vegetation, (leaflet pathology) 4=periannular (abscess/pseudoaneurysm/dehiscence), 5=periannular + vegetation, 6= periannular+leaflet disruption, 7=fistula +/- other (periannular or fistula). Imaging data was collected from pre-reported studies by an echocardiologist. The method was validated in a smaller substudy where images were blindly reviewed by 2 of the study investigators. Agreement between TTE/TOE and pathology observed at surgery was assessed using Bland-Altman 95% limits of agreement (LOA) and weighted kappa statistics. Effects of covariates on within-patient severity assessment were assessed using linear mixed effects modelling.

**Results:** Agreement (TOE vs TTE, ≤5days) at lesion level ranged from good to poor, AV site: Nv/Pv vegetation (n=77, k=0.64, CI=0.46-0.81), abscess/pseudoaneurysm (n=76, k=0.70.53-0.88, CI=0.62-0.95), Nv perforation (n=53, k=0.24, CI=-0.07- 0.56); MV site: Nv/Pv vegetation (n=78, k=0.78, CI=0.56-0.87, abscess/pseudoaneurysm (n=77, k=0.22, CI=-0.18-0.62), and Nv perforation (n=55, k=0.52, CI=0.23-0.8). On average, TTE underestimated severity compared to surgery or TOE. Mean difference in overall disease severity between surgery and echo was <1 grade: surgery vs. TTE =0.62( [LOA], -2.70 to 3.95) and 0.22(LOA, -2.43 to 2.87); surgery vs. TOE=0.01(LOA, -2.17 to 2.14) and 0.11(LOA, -2.30 to 2.08), at AV/MV sites, respectively. Mean difference in severity for TTE vs TOE within 3 days of surgery: AV: -1.45(CI -2.09 to -0.81, p<0.001). MV:-0.62(CI -1.18 to -0.06, p<0.001). Significant interaction terms indicated disparity between surgery and TTE worsened with moderate-severe valve regurgitation. Agreement (TTE and surgery: 3 categories – nil/mimicker, vegetation/disruption, periannular) at AV:k=0.66,(k=0.24[Pv]vs 0.69[Nv]), ≥moderately-severe AR (k=0.46 vs 0.58[<moderate-severe]), moderate-severe AS(k=0.2 vs 0.69) and LVEF≥30%(k 0.23 vs 0.68). Time:day=0(from surgery) AUC=0.95(CI 0.91 to 0.99) vs. day=14 AUC=0.81(CI 0.61 to 1.0). For TTE vs TOE, image quality ≥good no difference (k=0.83, both). TTE vs surgery at MV: agreement=79% (k=0.61); 77% (k=0.56) vs TOE. Moderating variables: Pv k=0.3 vs 0.63 (native). MV surgery vs TTE: overall k=0.61, time interval 0-3d k=0.7, ≥moderate-severe MR 0.55, MS 0.6, image quality <good 0.67, BMI ≥30kg/m2 no 0.59 vs 0.53 yes.

**Conclusion:** Integrating findings of TTE accuracy with disease severity, an imaging algorithm is proposed. For an inconclusive TTE study, TOE is recommended if: i)poor (<fair) image quality, ii)Pv, iii)EITHER ≥moderately-severe AR /AS, iv)periannular involvement OR suspected, OR poorly visualised, and v)IE mimickers present. Favourable features for a true negative TTE study without a clear indication for TOE, include: i)≥fair image quality, ii)Nv, iii)no mimickers and iv)≤moderate valve dysfunction.

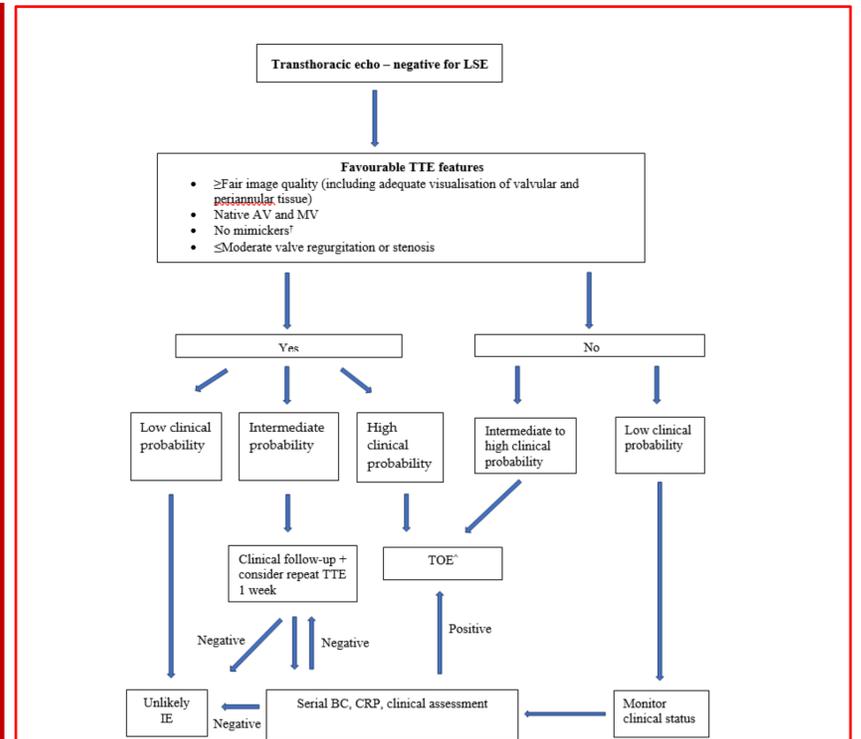


Figure 1. Transthoracic echo imaging pathway for a negative infective endocarditis imaging study

^ Unless clinical contraindication; † mimicker is a finding on echo which appears similar or identical to a pathological IE finding but occurs due to artefact or other non- infective structure or process.

AV denotes aortic valve, MV mitral valve, BC blood culture, CRP C-reactive protein, IE infective endocarditis, and LSE left-sided infective endocarditis

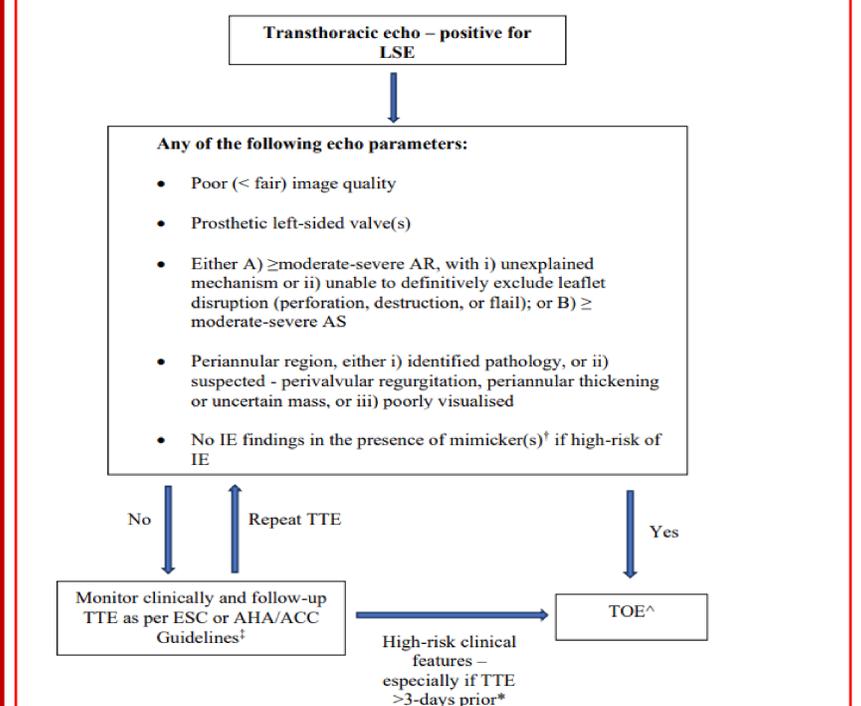


Figure 2. Transthoracic echo imaging pathway for a positive infective endocarditis imaging study

\*AV site, time interval 0-3 days: TTE vs TOE kappa 0.76, versus 4-14 days: kappa 0.57, though p-value did not reach statistical significance; ^ Unless clinical contraindication; † mimicker is a finding on echo which appears similar or identical to a pathological IE finding but is due to another cause such as artefact or other non-infective structure or process; ‡ European Society of Cardiology (ESC) and American Heart Association/American College of Cardiology (AHA/ACC) guidelines

IE denotes infective endocarditis, LSE left-sided infective endocarditis, LVEF left ventricular ejection fraction, AR aortic regurgitation, and AS aortic stenosis