

STUDY PROTOCOL

**The Use of Single-Beat TE-e' in the Evaluation of Left Atrial
Pressure in Critically Ill Patients**

(TELAP-ICU Trial)

Study Site: Adult Intensive Care Unit (AICU), Queen Mary Hospital (QMH)

Version 1.0

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1. Background and Rationale

Left atrial pressure (LAP) is a key haemodynamic variable in the assessment and management of critically ill patients, informing decisions on fluid therapy, diuresis, and the diagnosis of cardiogenic pulmonary oedema. Direct measurement of LAP requires invasive catheterisation and is not routinely feasible at the bedside; echocardiography therefore remains the principal non-invasive means of estimating LAP in the intensive care unit (ICU).

Time to onset of the mitral annular early diastolic velocity (e') relative to time to onset of mitral inflow early velocity (E), referred to as TE- e' , has recently been incorporated into the 2025 American Society of Echocardiography (ASE) guidelines for the evaluation of left ventricular (LV) diastolic function, particularly in patients with mitral valve disease (mitral regurgitation and mitral stenosis).

Physiologically, LV relaxation (reflected by onset of e' on tissue Doppler imaging) normally precedes transmitral blood flow (reflected by onset of E on pulsed-wave mitral inflow Doppler). When LAP is elevated, the elevated atrial pressure drives blood flow into the LV earlier, such that onset of E precedes onset of e' . This time relationship is expressed as TE- e' (TE minus Te'): a value ≥ 0 reflects the normal sequence, while a value < 0 suggests elevated LAP.

The conventional method of deriving TE- e' requires separate measurement of Te' (QRS to onset of septal e' , from tissue Doppler imaging) and TE (QRS to onset of mitral inflow E wave, from pulsed-wave Doppler) across two different cardiac cycles. Because these intervals are obtained in separate beats, the derived TE- e' is subject to variation introduced by beat-to-beat differences in heart rate – a particularly relevant limitation in critically ill patients, who frequently have variable heart rates.

A novel single-beat method has been developed in which both the mitral inflow E wave and septal e' wave are visualised on the same Doppler display within a single cardiac cycle (apical 4-chamber, RV-focused view; pulsed-wave Doppler, 10 mm sample volume placed at the septal mitral annulus; low velocity rejection set to minimum; scale and gain adjusted to optimise visualisation of e' onset and E wave onset). This approach removes the need to compare two separate cardiac cycles and, in principle, eliminates the confounding effect of heart-rate variability between measurements. It may also be applicable in atrial fibrillation, although this population is not included in the present study.

The use of TE- e' – by either the conventional or the novel method – has not been well studied in critically ill patients, and whether TE- e' can meaningfully aid the determination of LAP in this population remains uncertain. Preliminary (pilot) data have been collected in 44 patients, and this protocol describes the planned prospective study to formally address these questions.

2. Study Objectives

2.1 Primary Objectives

- To determine whether the novel single-beat method of measuring TE- e' is equivalent to the conventional (two-beat) method of measuring TE- e' .

- To determine whether a TE-e' value < 0 (by either method) is associated with elevated left atrial pressure in critically ill patients.

3. Hypotheses

- H1: The single-beat (novel) method of TE-e' measurement produces values that correlate closely with, and are clinically equivalent to, the conventional two-beat method.
- H2: A TE-e' value < 0 (i.e. onset of mitral inflow E wave preceding onset of septal e') identifies patients with elevated left atrial pressure.

4. Study Design

Design: Single-centre, prospective, observational study

Setting: Adult Intensive Care Unit (AICU), Queen Mary Hospital (QMH)

Population: Critically ill adult patients requiring transthoracic echocardiography (TTE) for clinical indications

Comparator: Each patient serves as their own control – conventional versus novel TE-e' measurement is performed within the same TTE study

5. Study Population

5.1 Inclusion Criteria

- Adult patients ≥ 18 years of age admitted to the QMH Adult Intensive Care Unit (AICU)
- Patients requiring a transthoracic echocardiogram (TTE) examination as part of routine clinical care
- Patients in whom TE-e' is obtainable by both the conventional and the novel method

5.2 Exclusion Criteria

- Patients < 18 years of age
- Patients in atrial fibrillation
- Patients with a poor TTE acoustic window
- Patients in whom TE-e' is technically difficult to obtain, or difficult to interpret, by either the novel or the conventional method

6. Sample Size

The total planned sample size for this study is 50 patients. This builds on pilot data already obtained in 44 patients, which are being used to inform the formal sample size calculation and study design; recruitment will continue prospectively to reach a total analysable cohort of 50 patients.

Enrolment will be consecutive, subject to the inclusion and exclusion criteria above, among patients undergoing clinically indicated TTE in the AICU during the recruitment period.

7. Study Procedures / Measurements

7.1 Conventional Method (Two-Beat)

- Time to E wave (TE): time interval from the QRS complex to the onset of the mitral inflow E wave, measured by pulsed-wave (PW) Doppler.
- Time to septal e' wave (Te'): time interval from the QRS complex to the onset of the septal e' wave, measured by tissue Doppler imaging (TDI).
- TE-e' is derived as TE minus Te', using measurements obtained across two separate cardiac cycles (one for TE, one for Te').

7.2 Novel Method (Single-Beat)

The novel method captures both the mitral inflow E wave and septal e' wave within a single cardiac cycle, using the following technique:

- Apical 4-chamber (A4C), right-ventricle (RV)-focused view
- Pulsed-wave Doppler with a sample volume of 10 mm
- Cursor placed at the septal mitral annulus
- Low velocity rejection set to minimum
- Doppler scale reduced to optimise the e' wave signal
- Gain decreased to optimise identification of e' origin and start-time measurement
- Gain then increased to identify the origin of the E wave and place the end-time measurement

TE-e' by the novel method is derived directly from onset times observed on the same single-beat display, without the need to combine measurements from separate cardiac cycles.

7.3 Additional Echocardiographic Parameters of Left Atrial Pressure

The following supplementary echocardiographic parameters relevant to LAP assessment will also be recorded for each patient:

- Mitral E wave velocity
- Mitral E wave deceleration time (DT)
- Mitral E/A ratio
- Septal and lateral E/e'
- Isovolumic relaxation time (IVRT)
- Pulmonary vein (PV) Doppler, if obtainable
- Left atrial volume index (LAVi)

- Tricuspid regurgitation peak velocity (TR Vmax)
- Lung ultrasound (LUS), 6-point protocol

7.4 Clinical Correlation

Clinical assessment of volume status / LAP (as determined by the treating clinical team and/or available invasive haemodynamic data where present) will be recorded for correlation with echocardiographic TE-e' and related parameters.

8. Study Outcomes

8.1 Primary Outcome

Correlation between the novel (single-beat) and conventional (two-beat) methods of measuring TE-e'.

8.2 Secondary Outcomes

- Correlation between the novel and conventional methods in obtaining septal e' and s' velocities
- Correlation between clinical evaluation of LAP and TE-e' value
- Correlation between other echocardiographic parameters of LAP (as listed in Section 7.3) and TE-e' value

9. Statistical Analysis

Agreement and correlation between the novel and conventional TE-e' measurements will be assessed using appropriate correlation (e.g. Pearson or Spearman, as distribution dictates) and agreement statistics (e.g. Bland-Altman analysis), together with intraclass correlation coefficients where appropriate. The association between TE-e' (< 0 vs ≥ 0) and clinical/echocardiographic indices of elevated LAP will be examined using appropriate univariate methods. Sample size and power calculations, informed by the pilot dataset of 44 patients, are being finalised to support the planned total cohort of 50 patients. Detailed statistical methodology will be specified in a statistical analysis plan prior to database lock.

10. Data Collection and Management

- Data will be collected prospectively on a standardised case report form (CRF) at the time of clinically indicated TTE.
- Data will include patient demographics, relevant clinical variables, and all echocardiographic parameters listed in Section 7.
- All patient data will be de-identified and stored securely in accordance with institutional data governance policies.

11. Ethical Considerations

- Institutional Review Board / Research Ethics Committee approval obtained prior to commencement of enrolment (Reference no: UW 26-246, approval granted June 24, 2026).
- Patient confidentiality will be maintained throughout data collection, analysis, and reporting.